Vulnerable plaque update

Pathophysiology of ACS assessed by OCT

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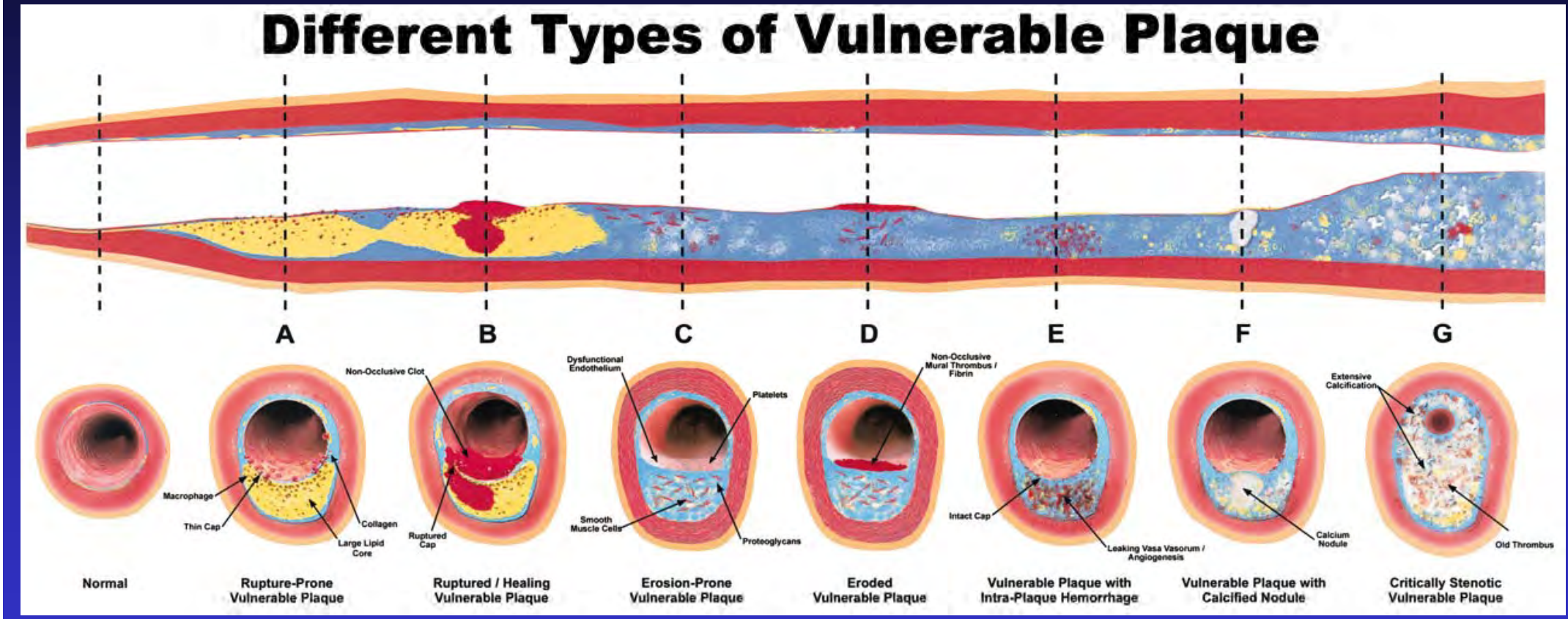
Progression of atherosclerotic plaque



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

Criteria for defining vulnerable plaque

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

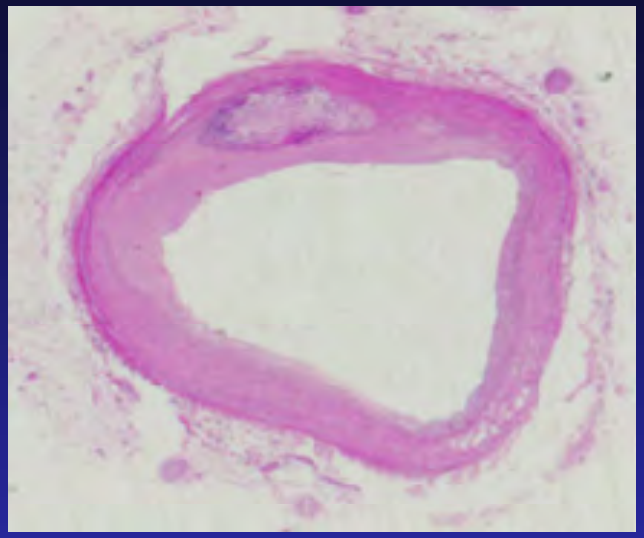
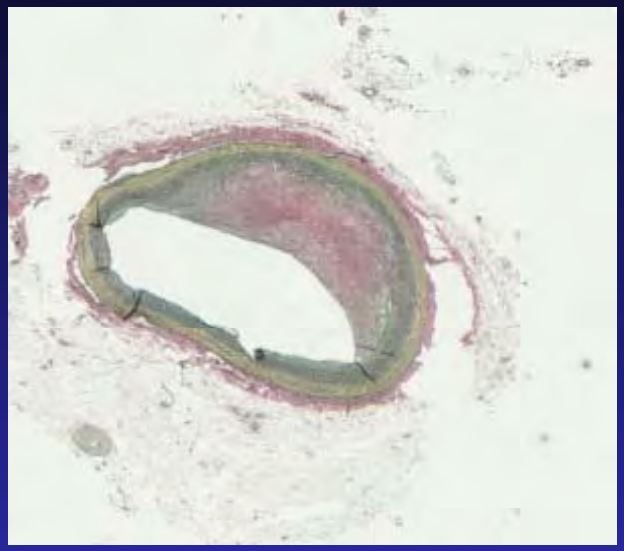
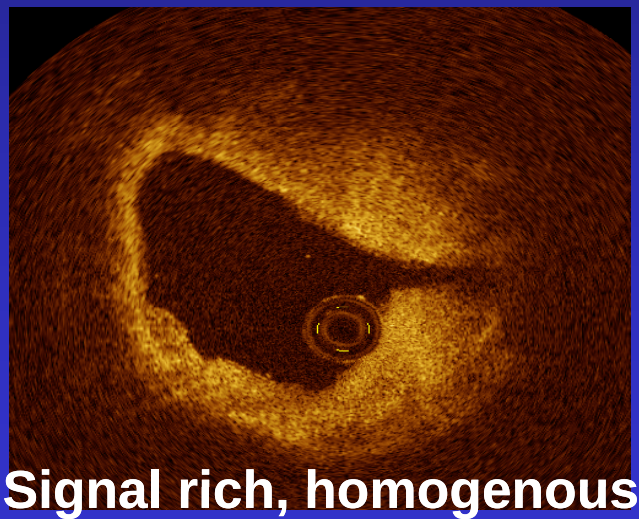
Major criteria

- **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

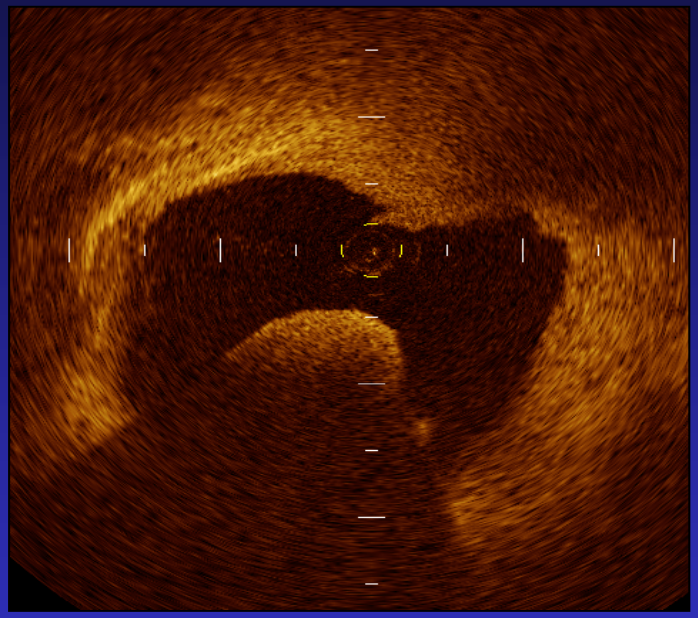
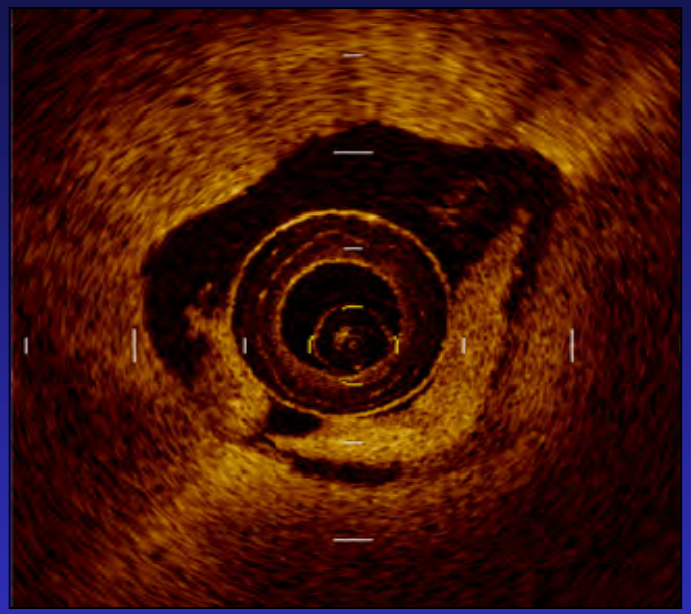
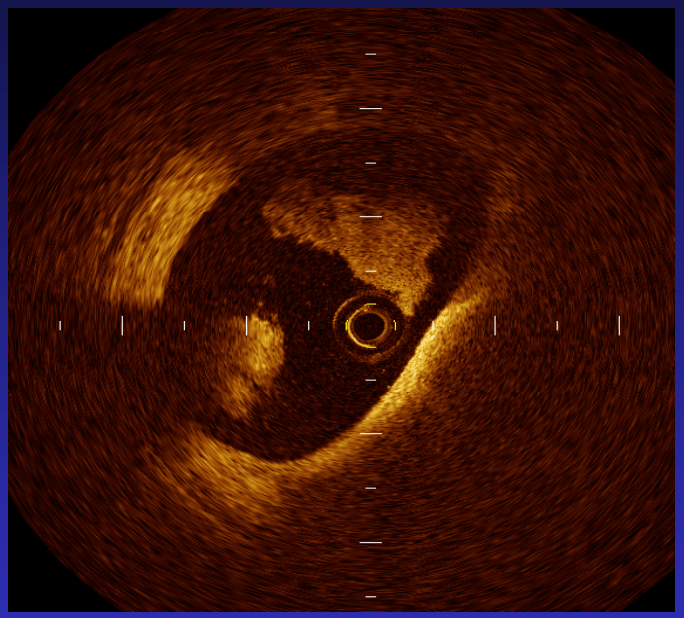
- **Superficial calcified nodule**
- **Glistening yellow**
- **Intraplaque hemorrhage**
- **Endotherial dysfunction**
- **Outward (positive) remodering**

OCT vs histology

Fibrous plaque	Fibro-calcific plaque	Fibro-lipidic plaque
		
		
Signal rich, homogenous	Signal poor, clear border	Signal poor, diffuse border

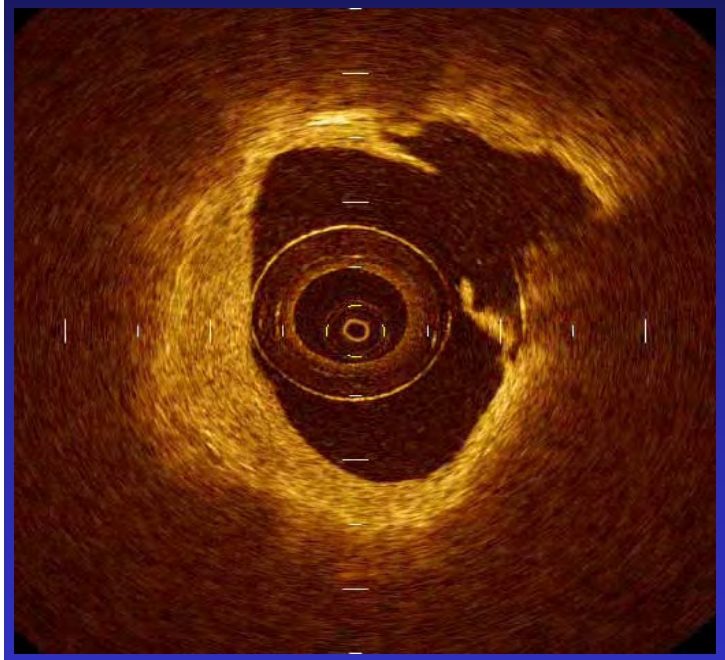
Yabushita H, et al. Circulation, 106:1640-1645, 2002
Kume T, et al. Am J Cardiol 97: 1172 - 75, 2006

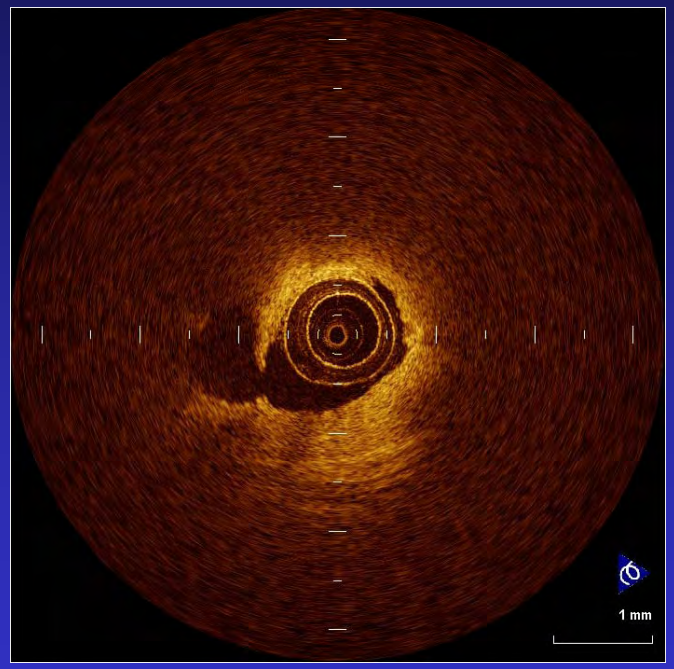
Red & white thrombus

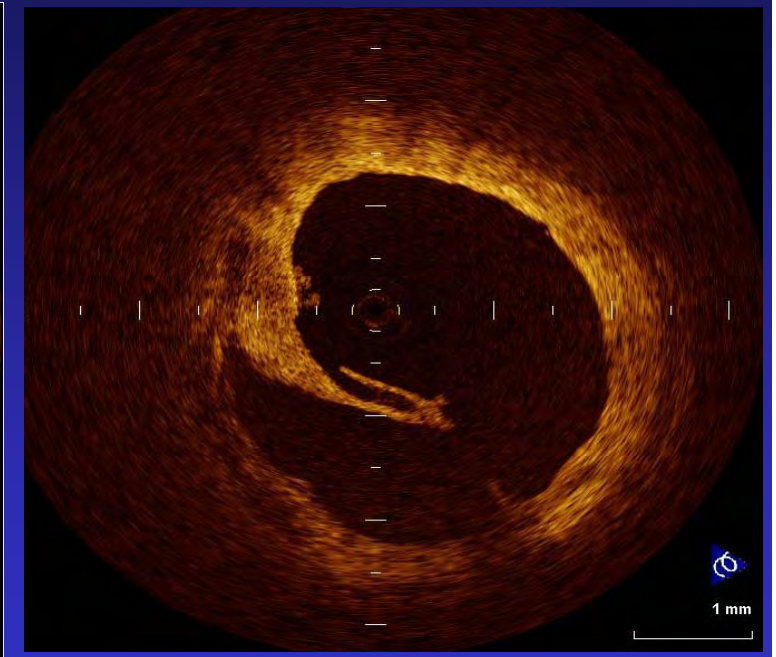
Red thrombus	White thrombus	Mixed thrombus
		
Protrusion mass with shadow	Protrusion mass without shadow	Protrusion mass with & without shadow

Kume T, Akasaka T, et al (Am J Cardiol 97:1713-1717, 2006)
Kubo T, Akasaka T, et al. (J Am Coll Cardiol 50:933-939,2007)

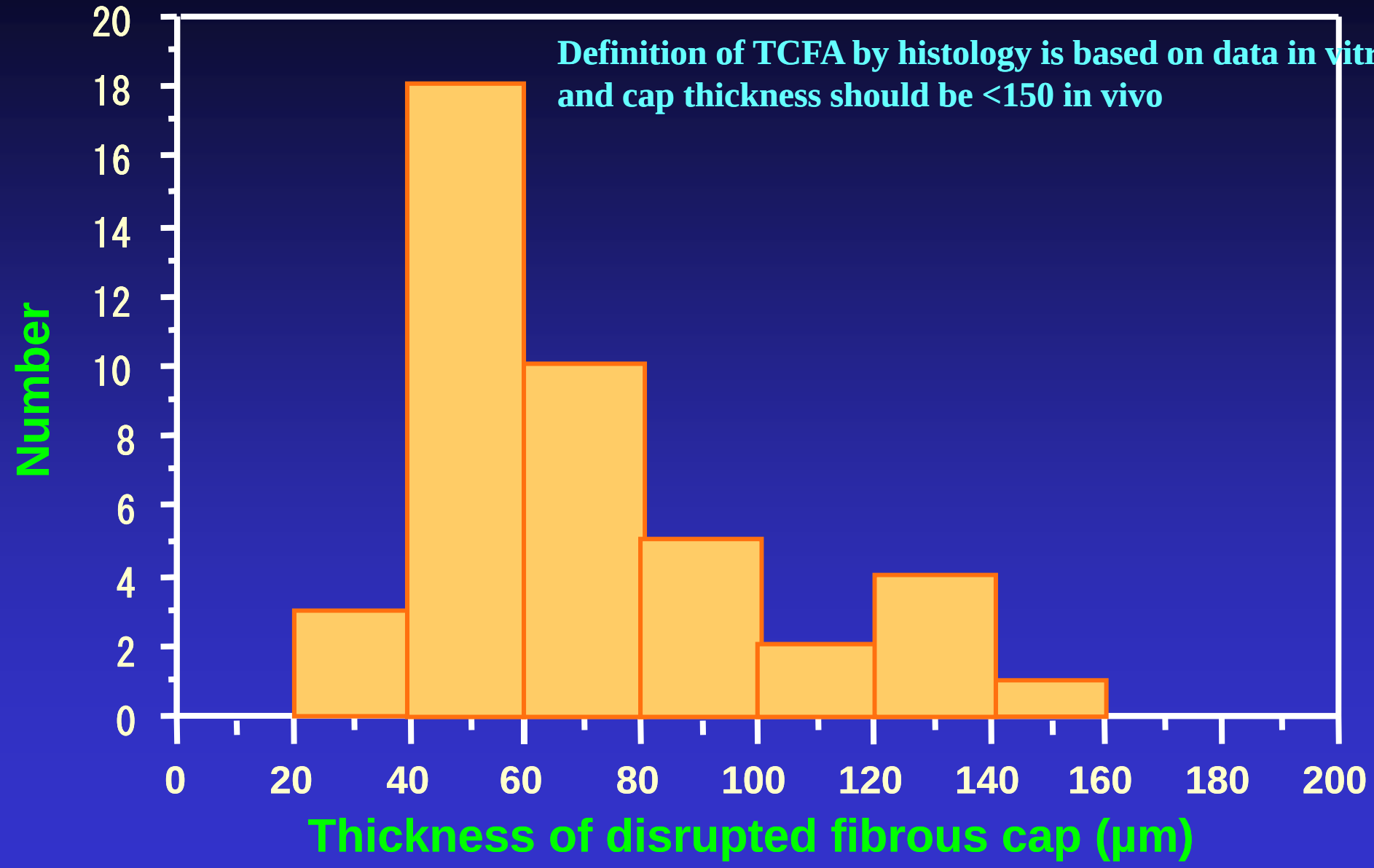
Plaque rupture (Plaque disruption)







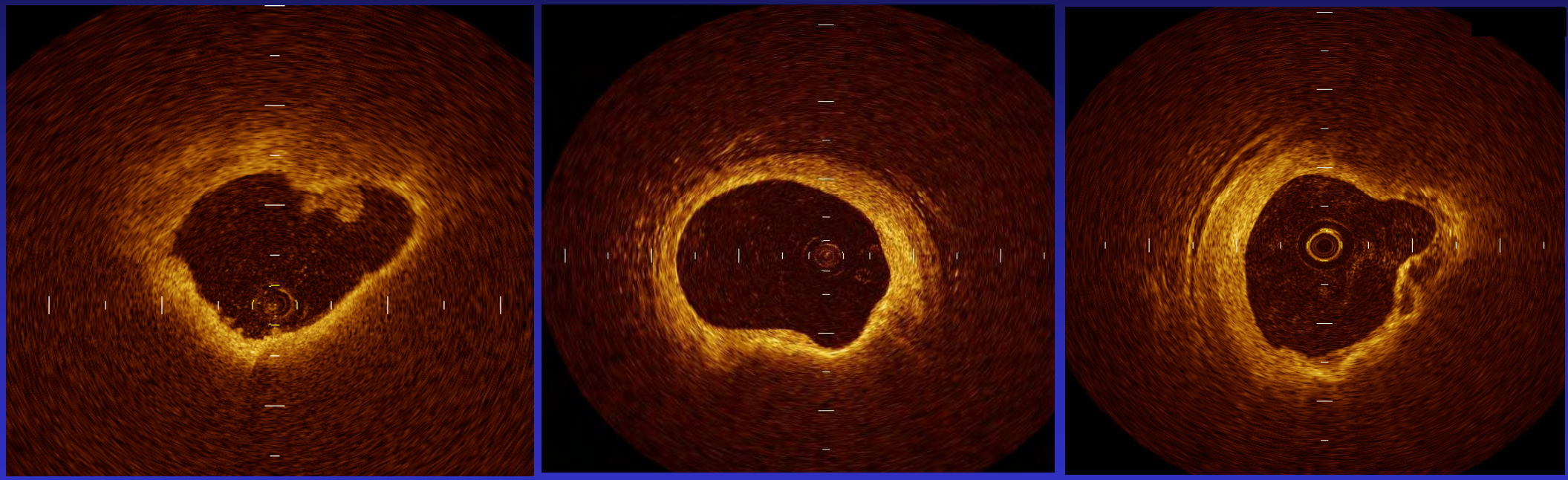
Distribution of disrupted fibrous-cap thickness



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

Plaque ulceration

Erosion



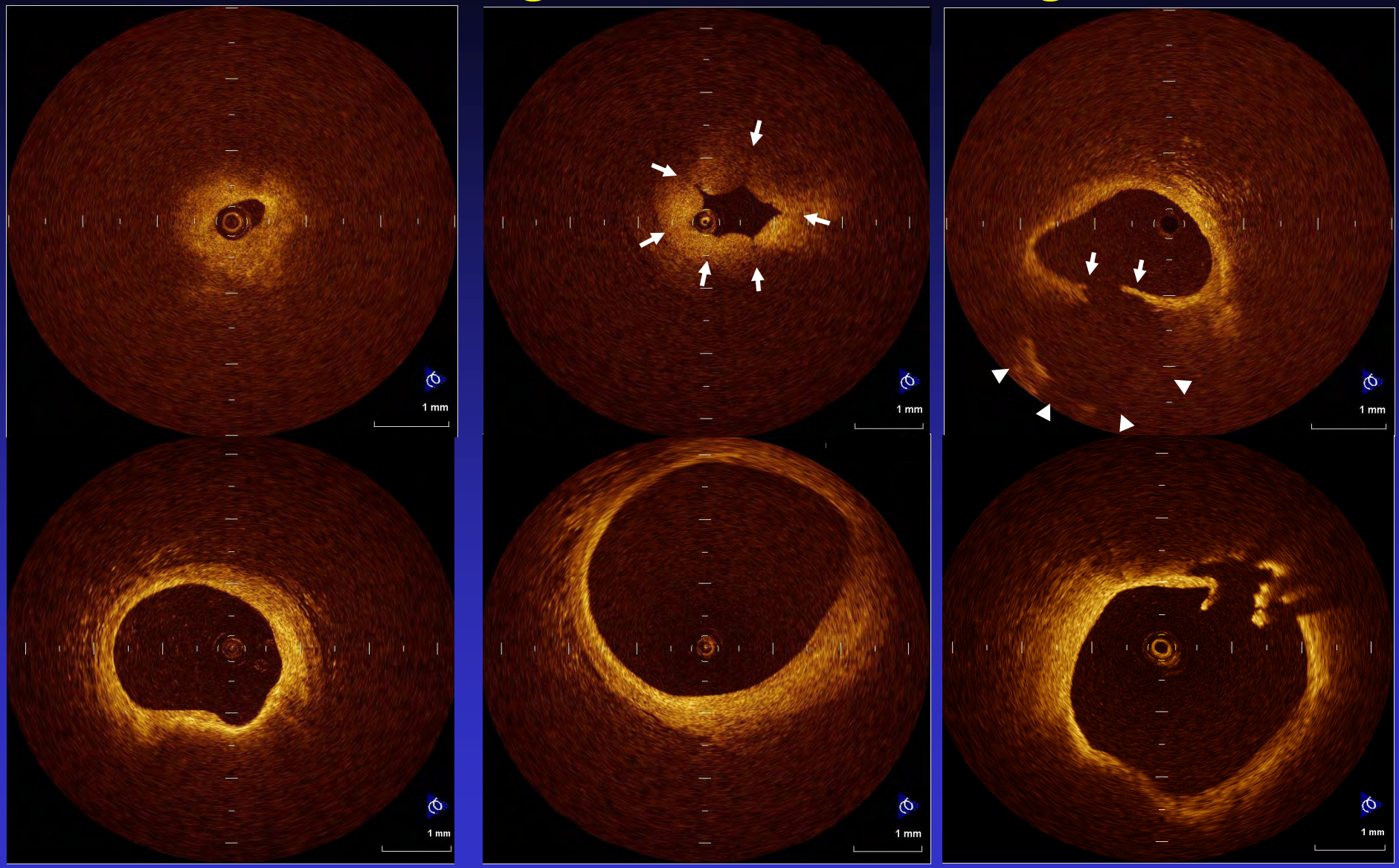
Comparison of plaque Images in AMI (OCT vs. CAS vs. IVUS) n=30

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

	OCT	*CAS	**IVUS	*p	**p
Plaque Rupture (%)	73	47	40	0.035	0.009
Ulceration (erosion) (%)	23	3	0	0.022	0.005
Thrombus (%)	100	100	33	1.000	<0.001
Red thrombus (%)	100	90	-	0.076	-
White thrombus (%)	100	93	-	0.150	-
TCFA（≦65μm）(%)	83	-	-	-	-
Fibrous cap thickness (μm)	49±21	-	-	-	-
LRP (Lipid Arch＞180°) (%)	83	-	67	-	NS

TCFA; Thin Cap Fibro-Atheroma, LRP; Lipid Rich Plaque

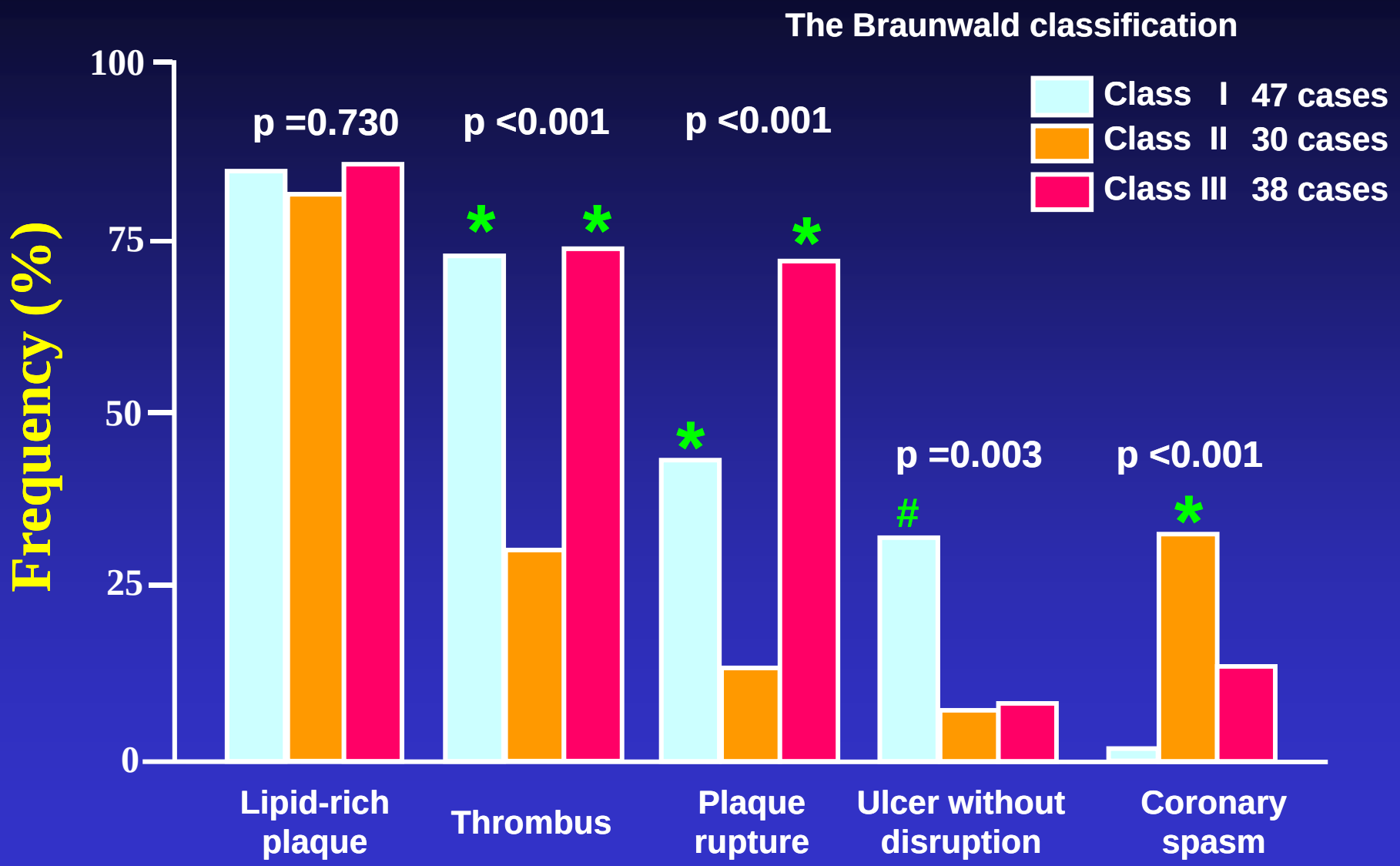
OCT findings in unstable angina



Class I　　Class II　　Class III

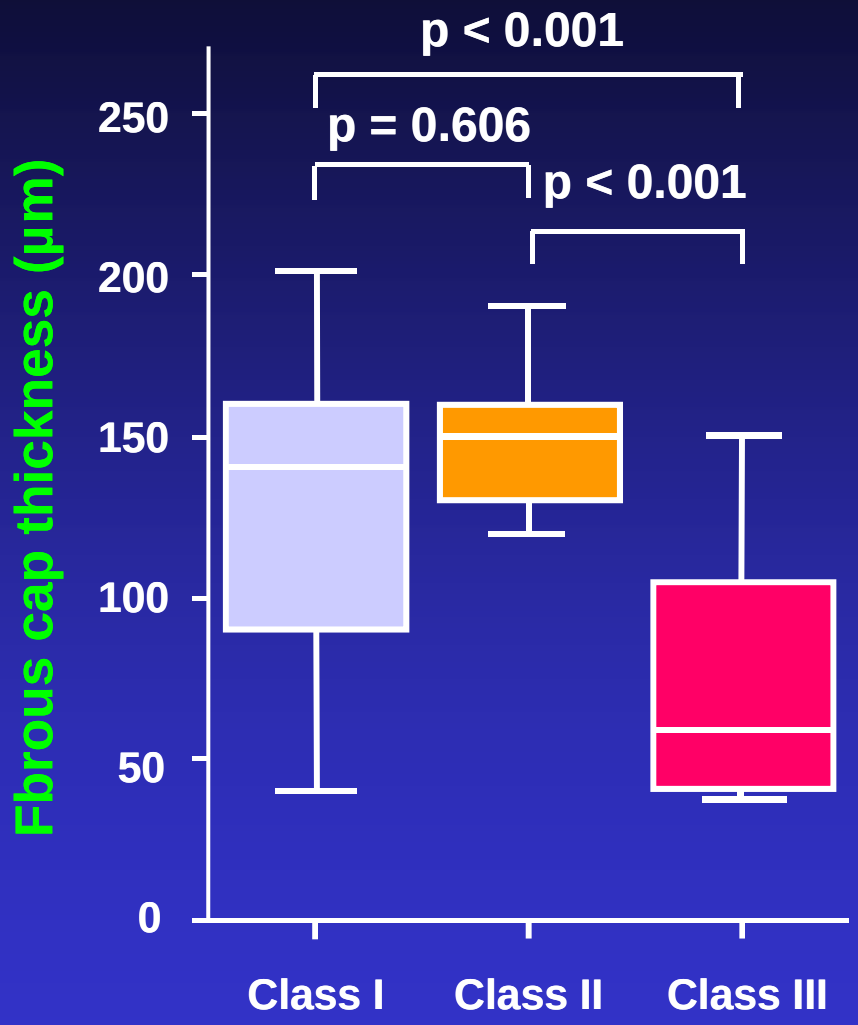
（Mizukoshi M, et al. Am J Cardiol 2010, 106: 323-328）

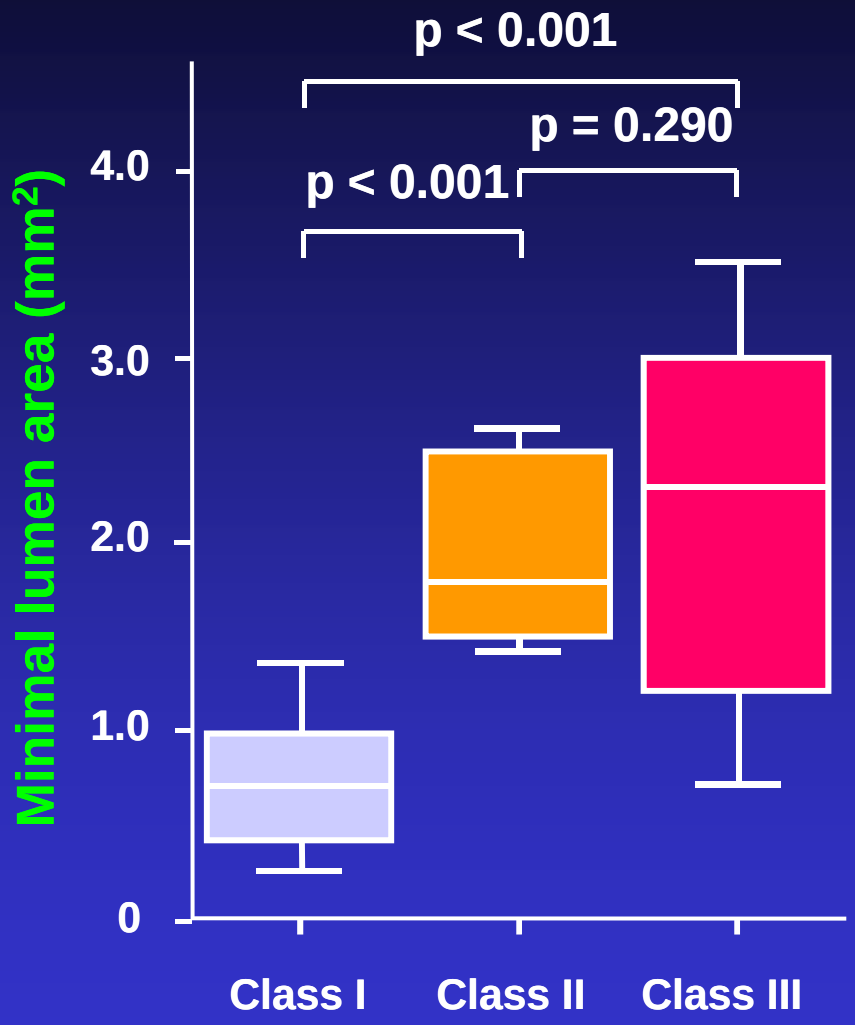
OCT findings in 115 cases with unstable AP



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

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

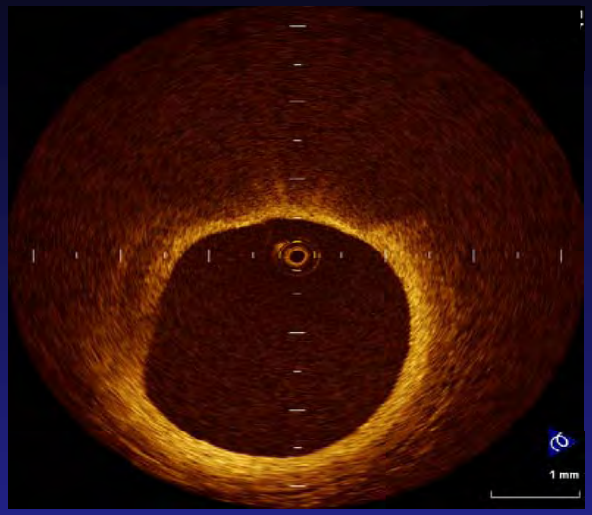


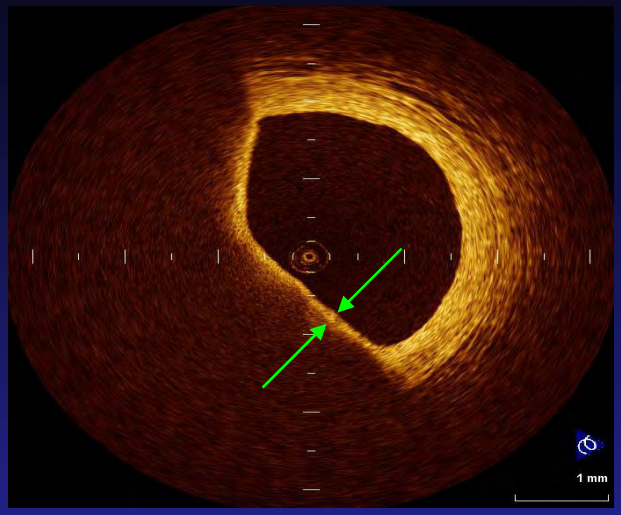


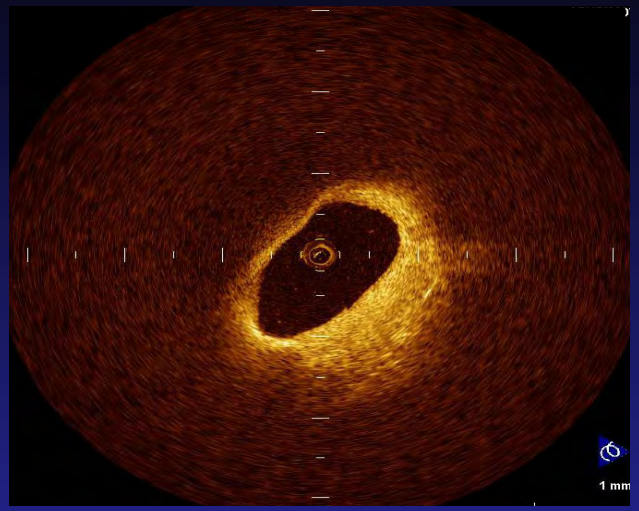
Braunwald classification

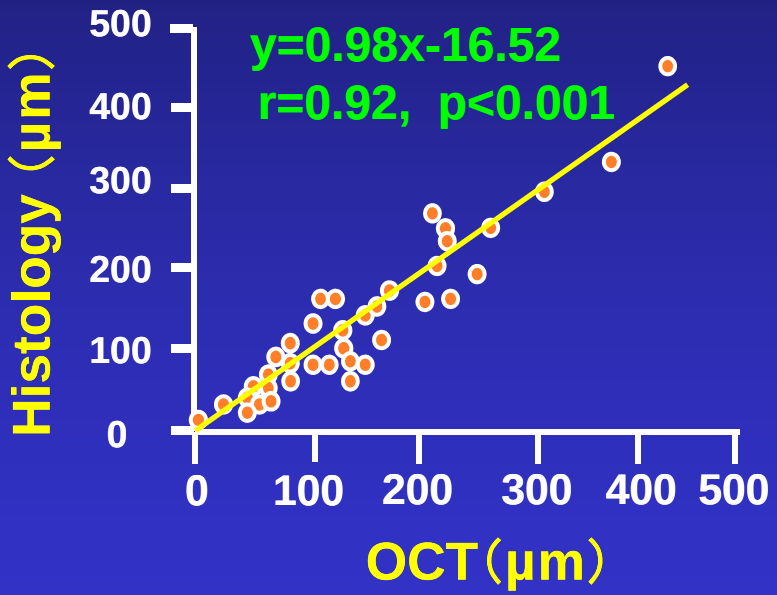
（Mizukoshi M, et al. Am J Cardiol 2010, 106: 323-328）

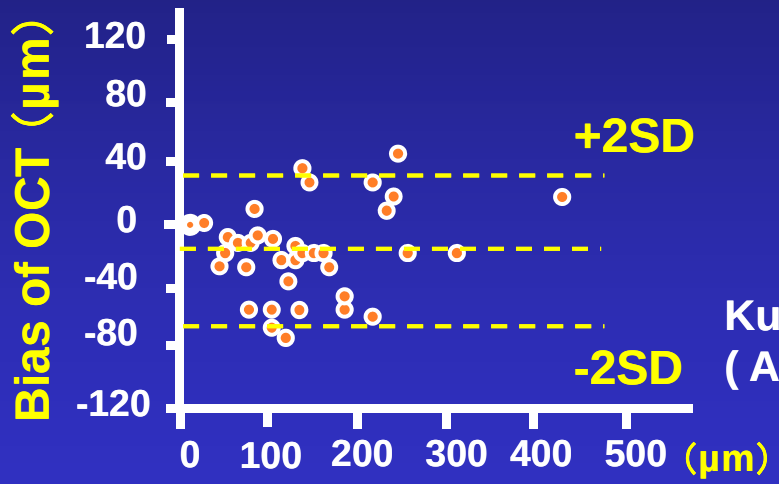
Thin-cap fibroatheroma (TCFA)







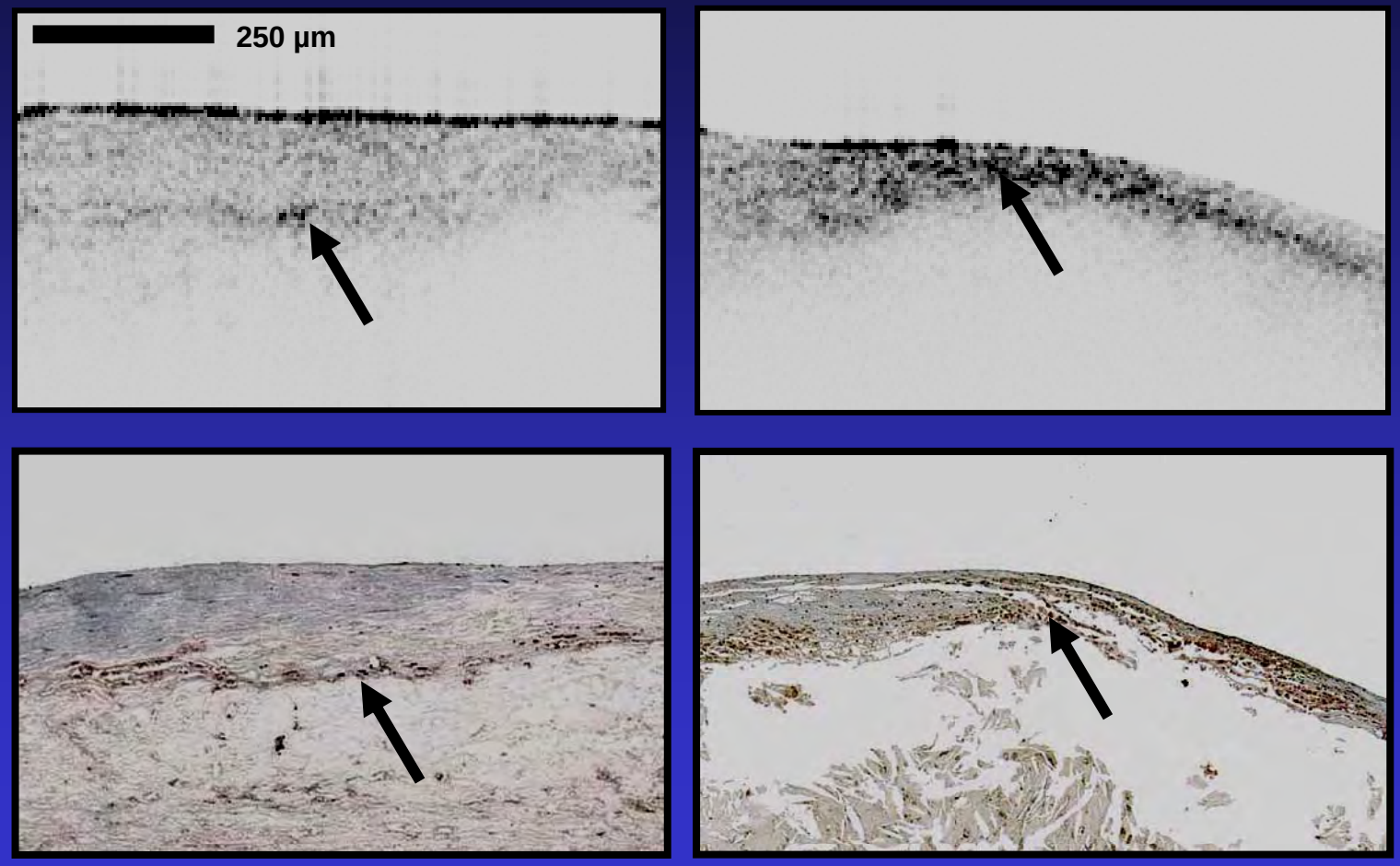




Kume T, Akasaka T, et al.
(Am Heart J.152:755, 2006)

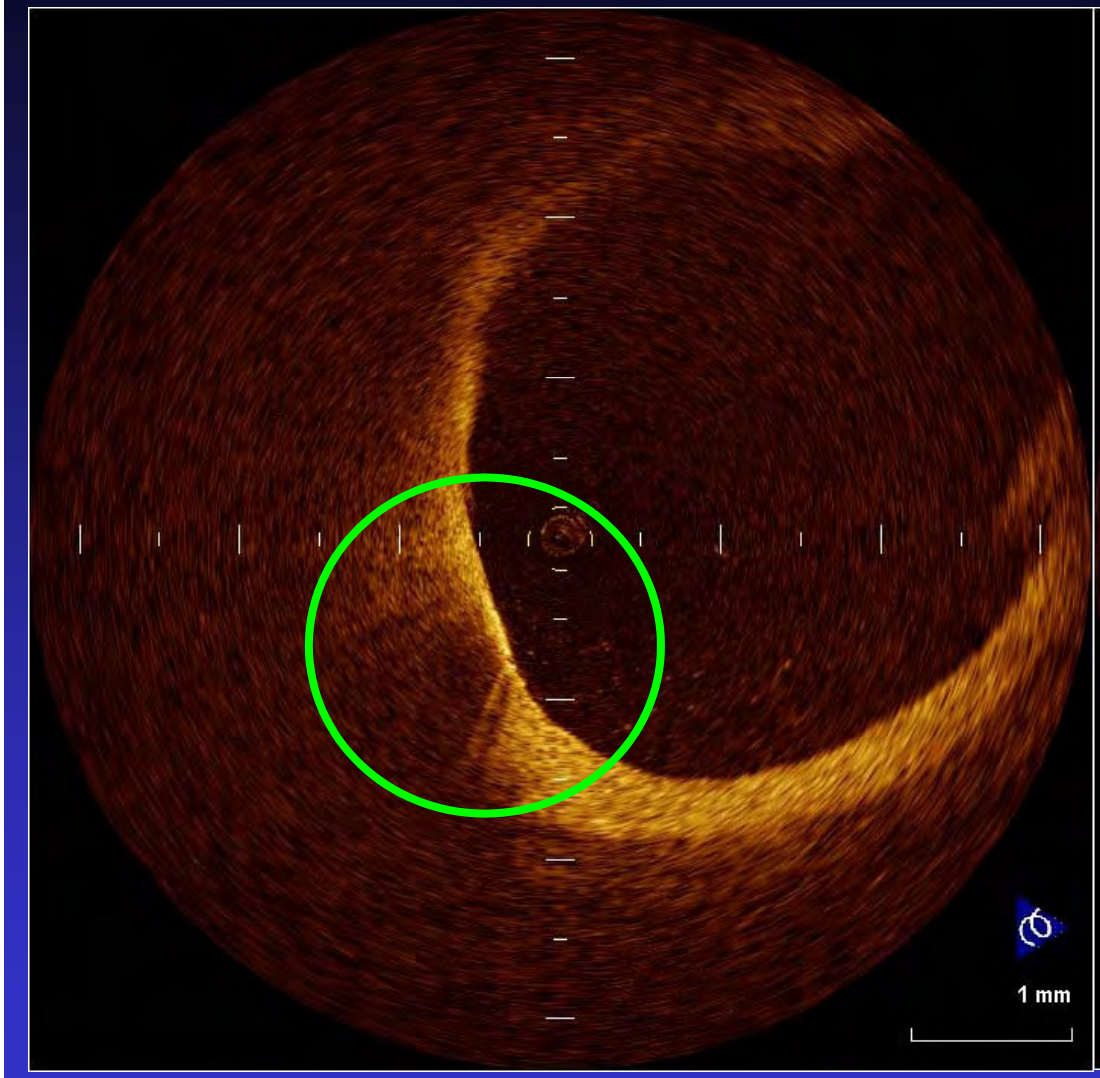
TCFA is thought to be vulnerable based on histological studies, and possibility to identify TCFA has been demonstrated by several pilot OCT studies.

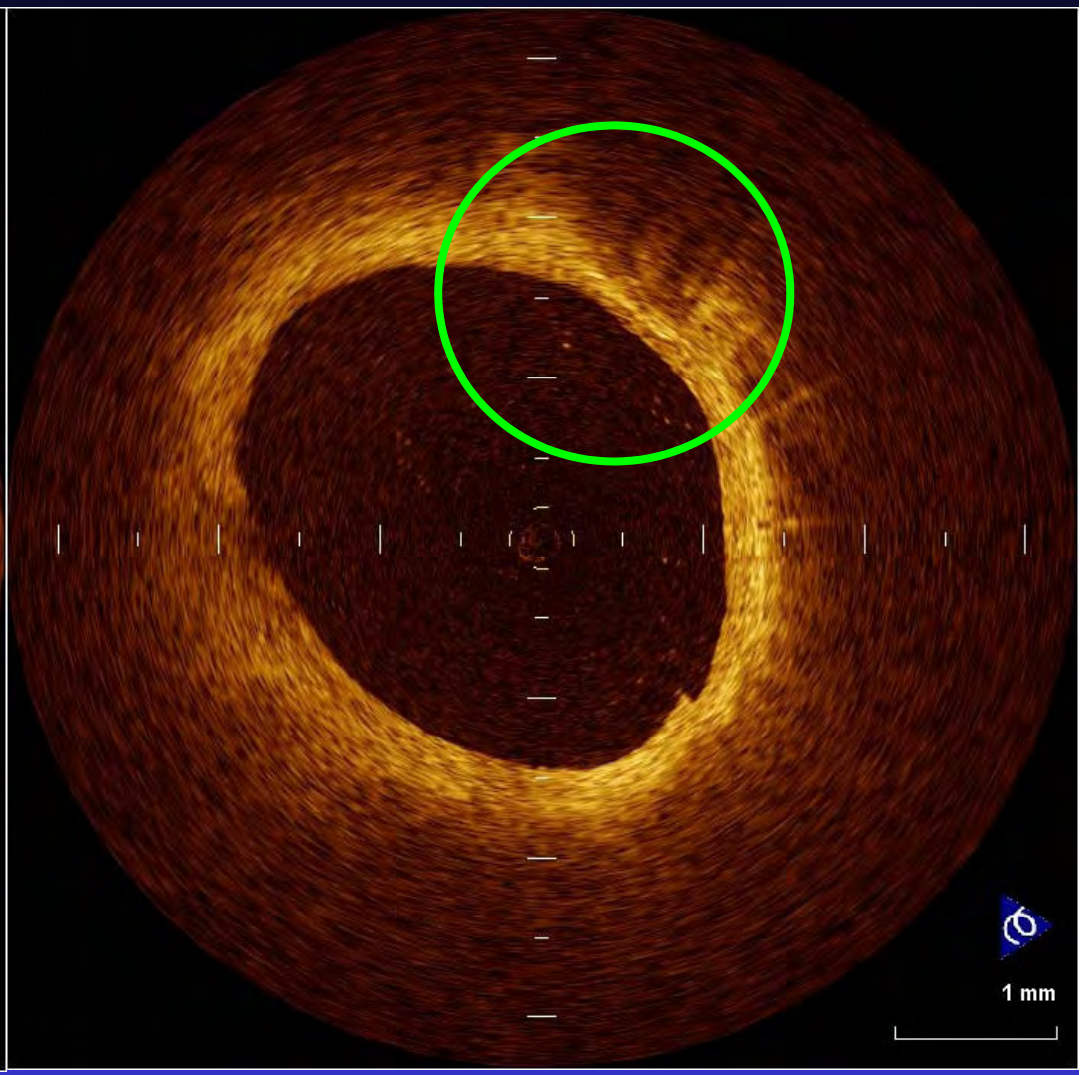
OCT findings of macrophages



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

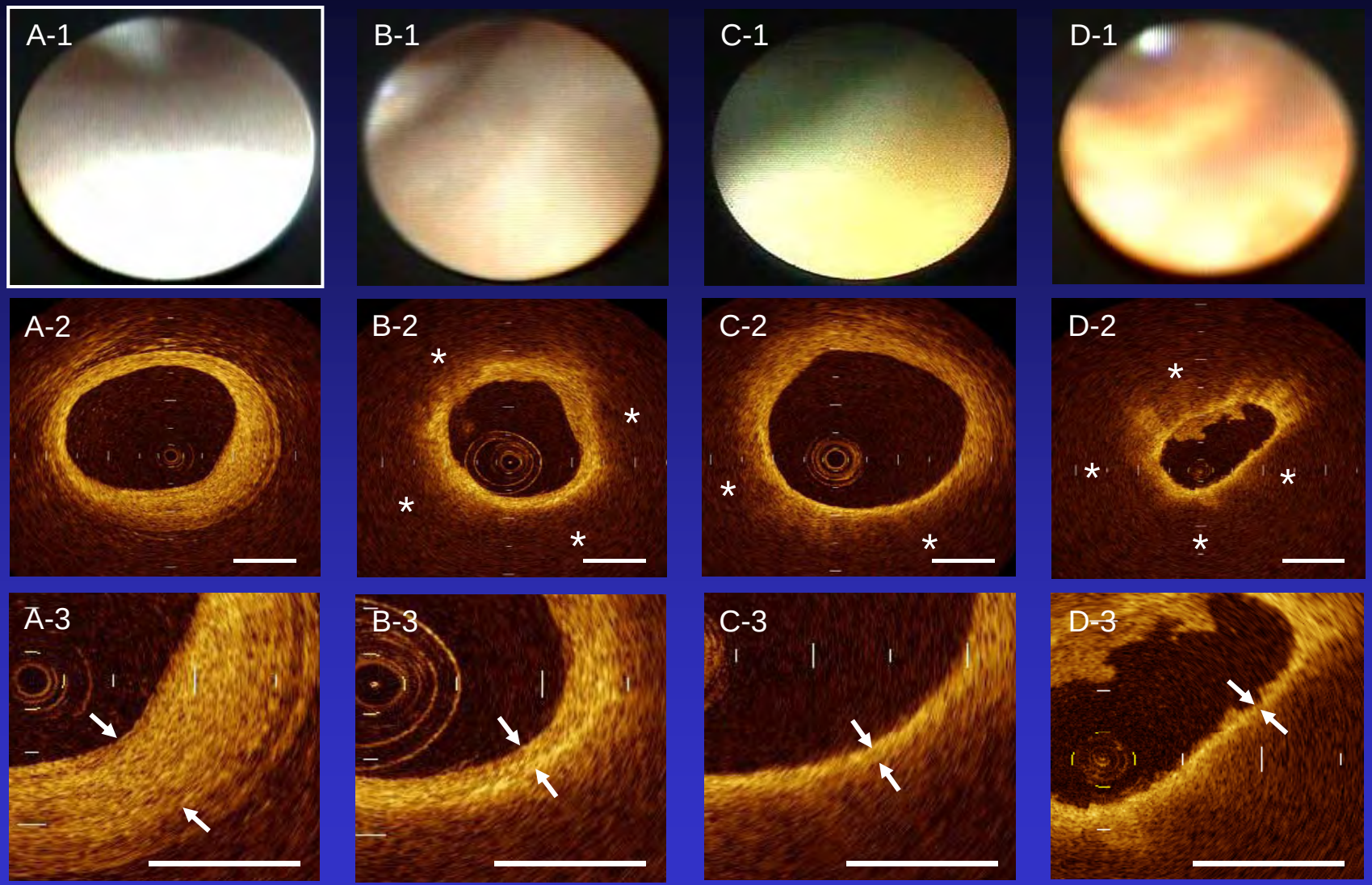
Identification of macrophage





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

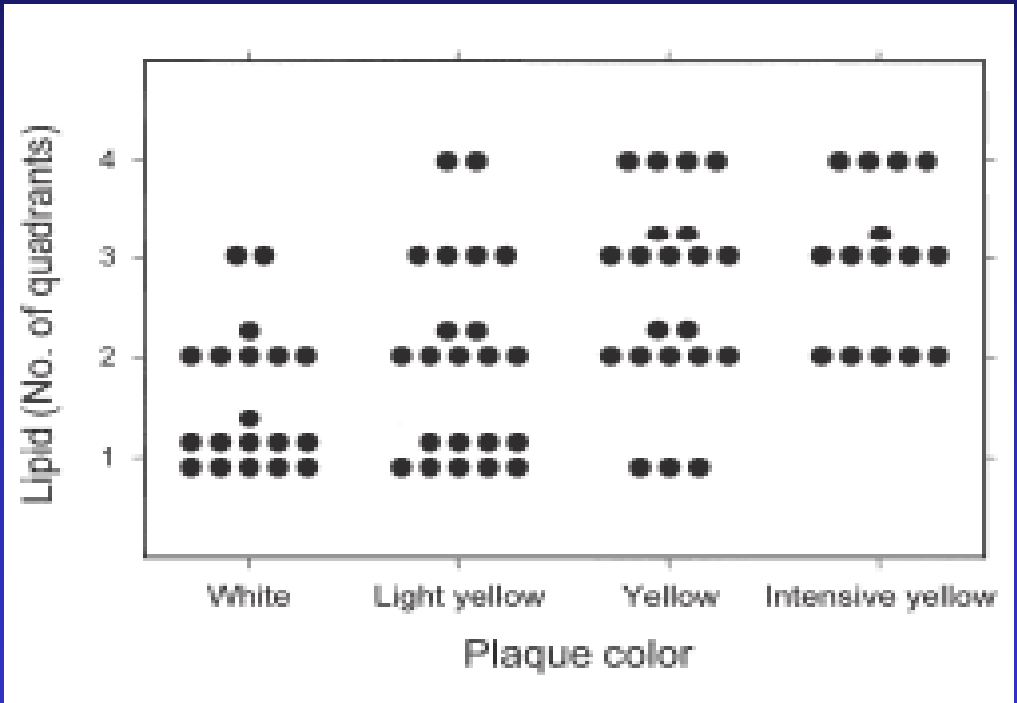
Corresponding Images of OCT and Angioscopy



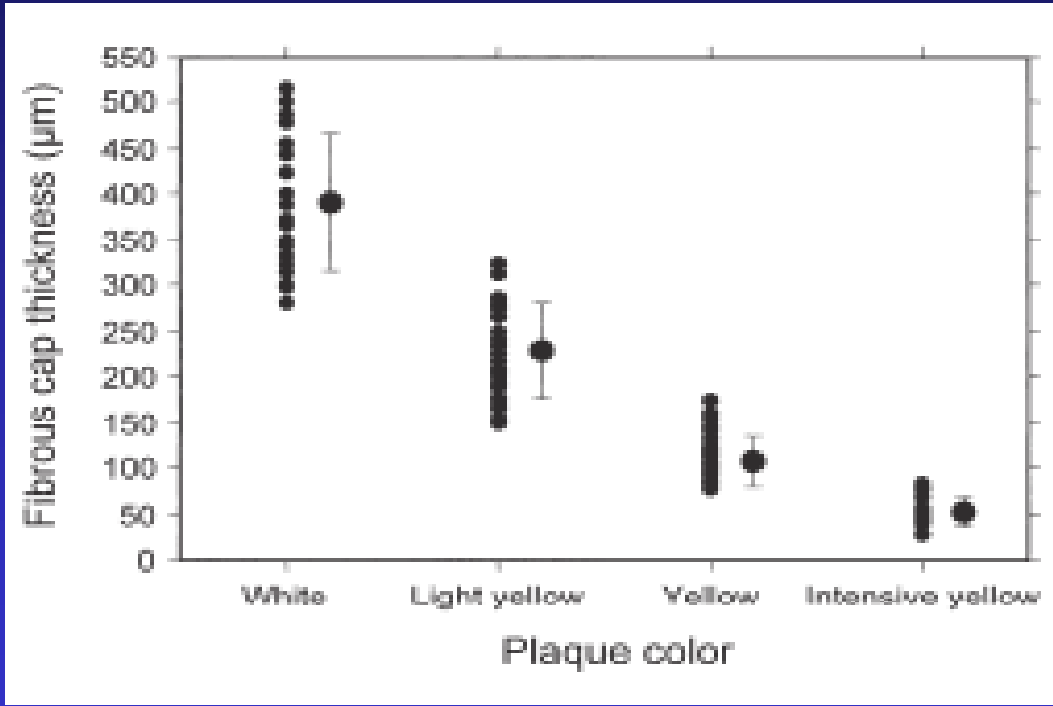
（Kubo T, et al. J Am Coll Cardiol Intv 1:74-80,2008）

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**
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- **Endotherial dysfunction**
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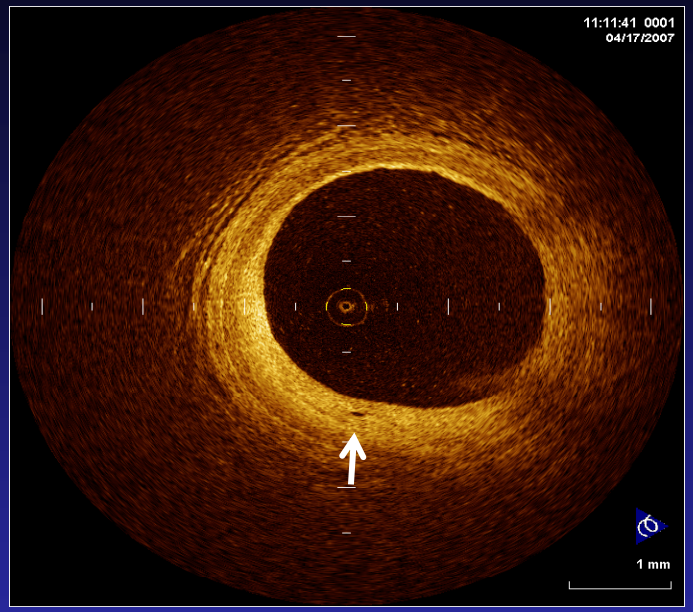
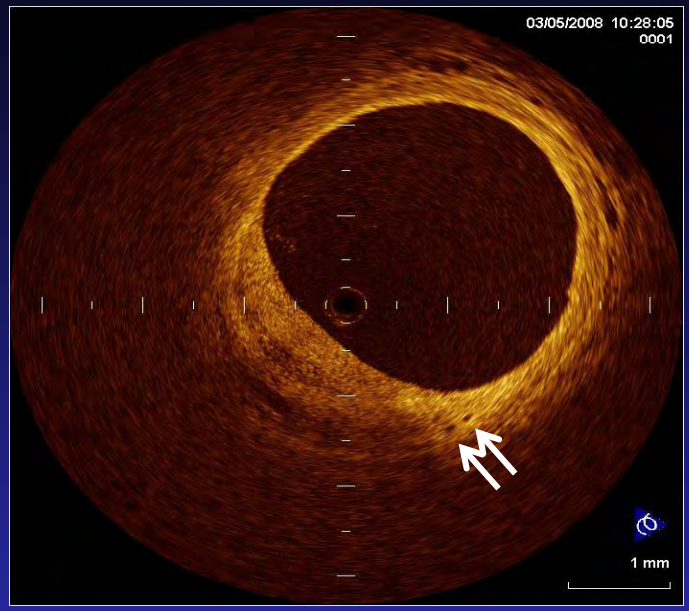
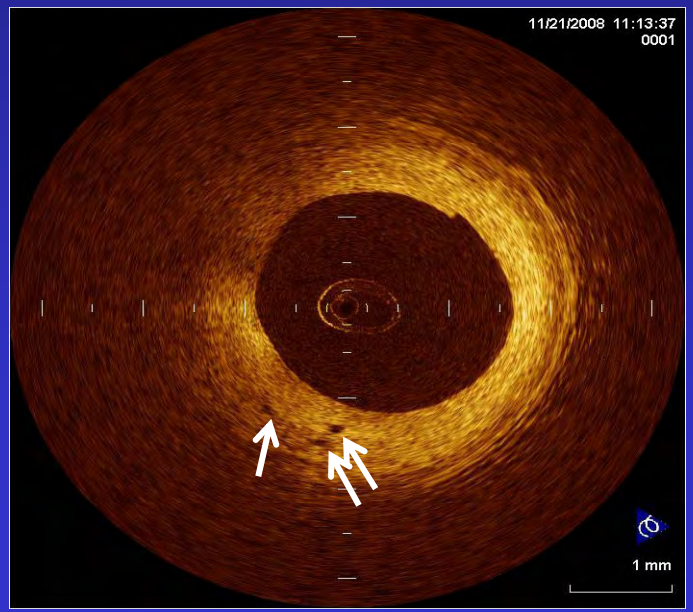
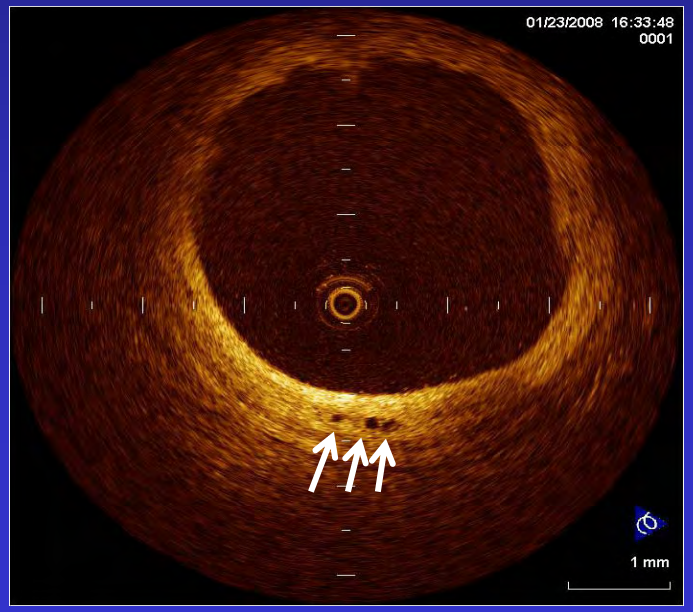
Micro-channels in non-culprit plaques



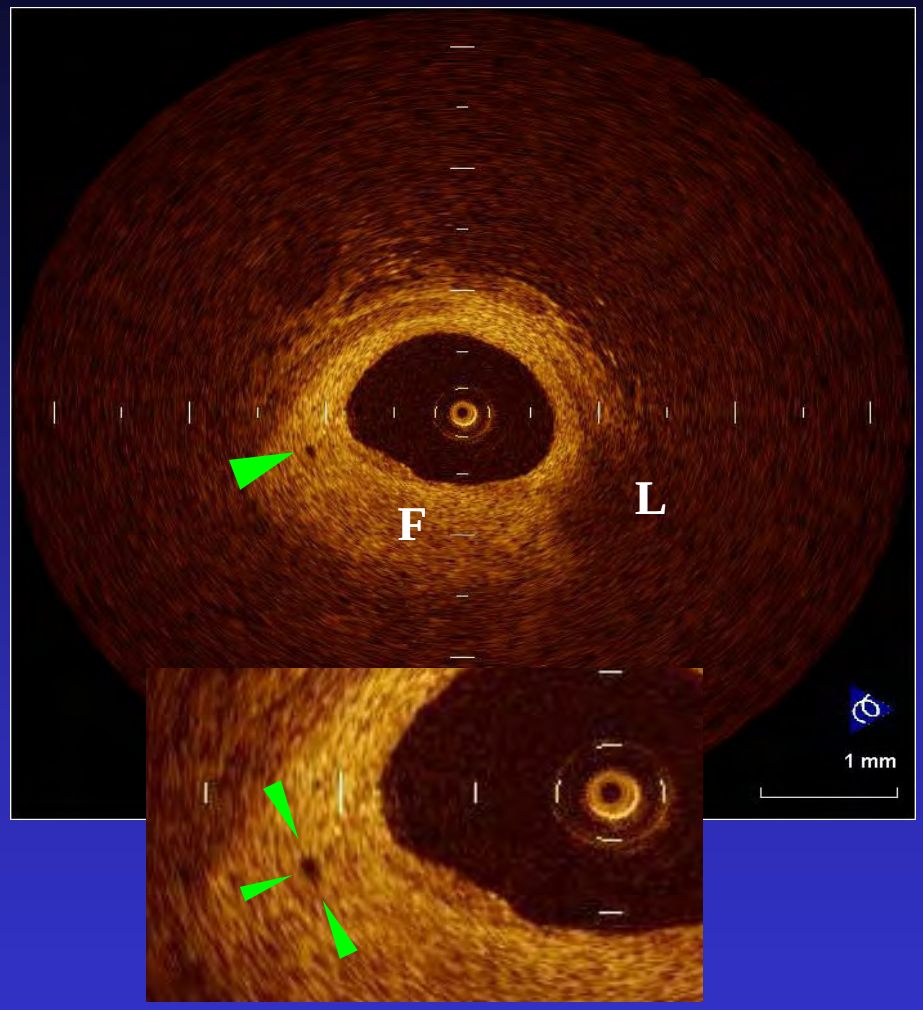


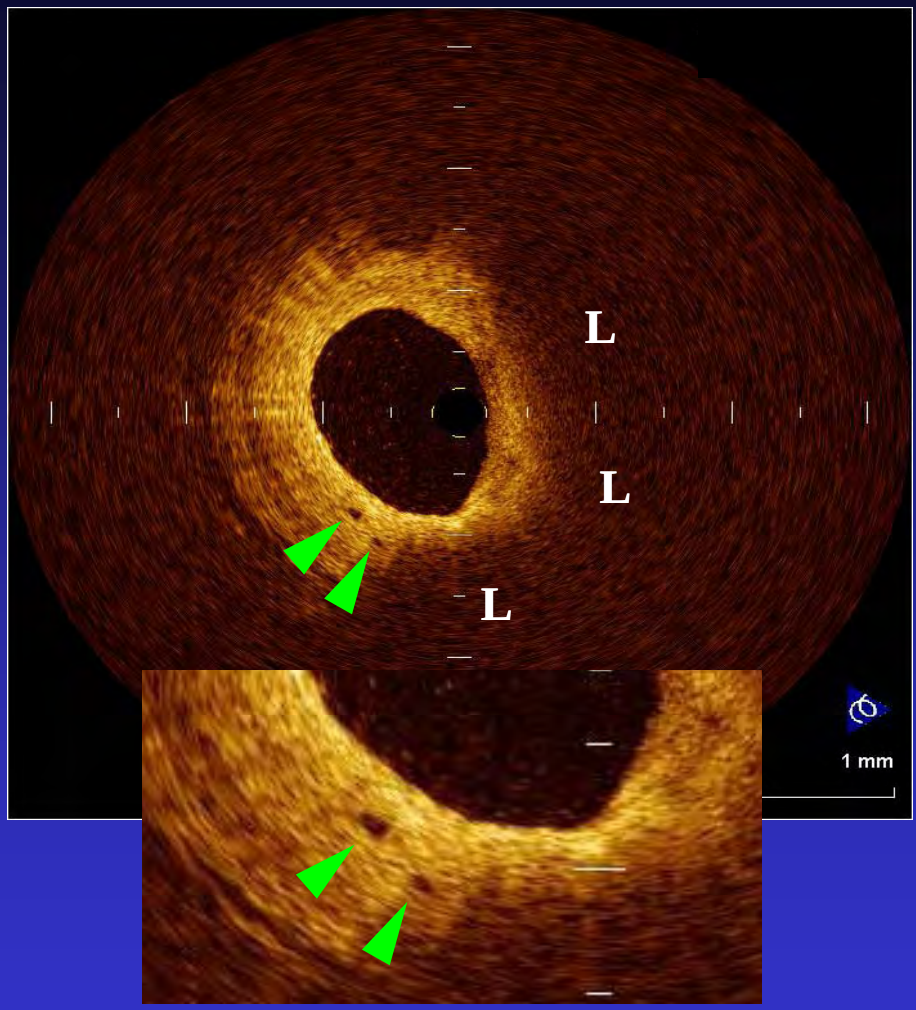




Kitabata H, et al. Am J Cardiol. 2010;105:1673-1678

Microchannel within plaque (Vasavasorum)





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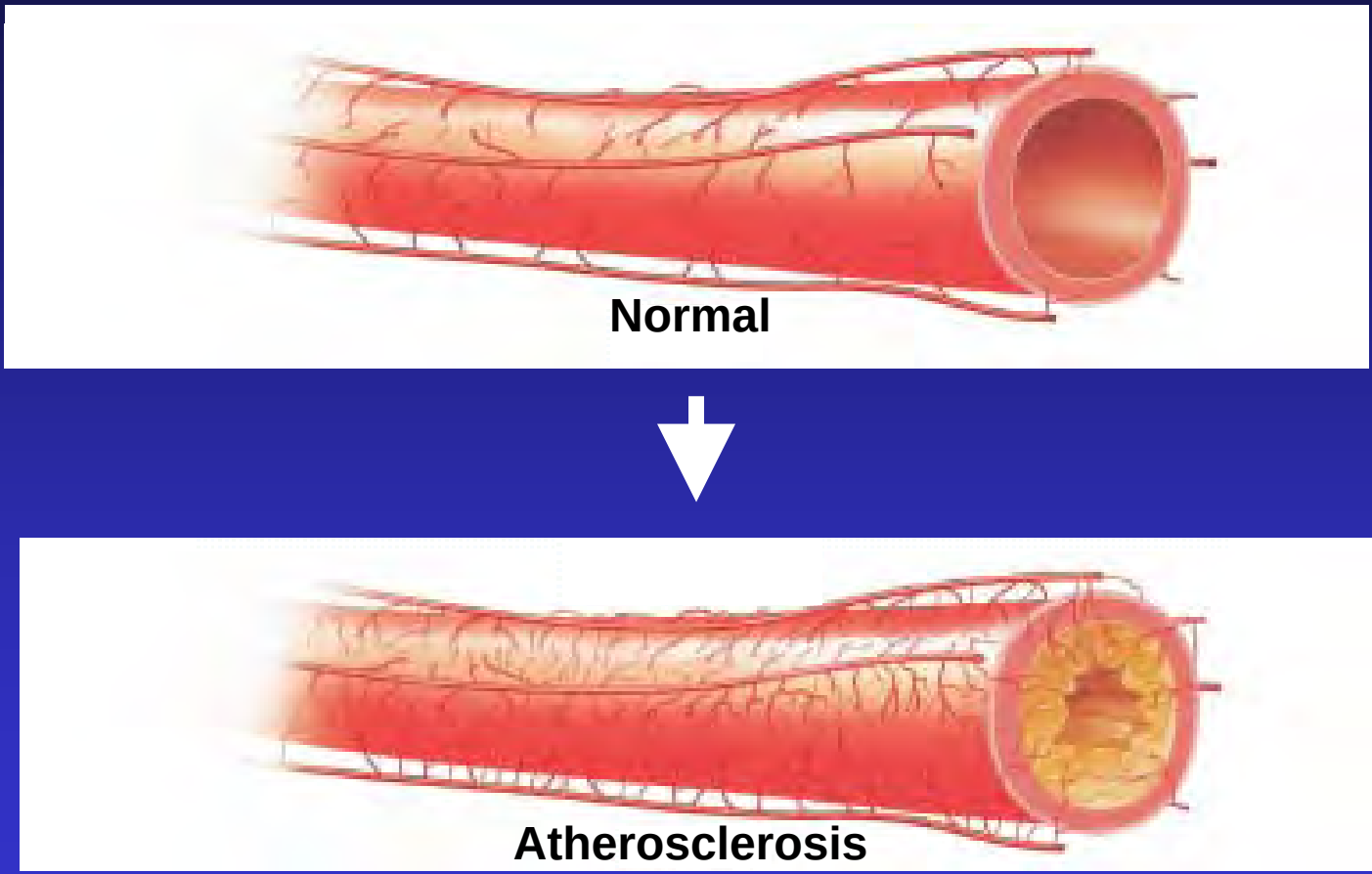
Vessel Wall Neovascularization in Atherosclerosis



(J Am Coll Cardiol 2007;49:2073–80)

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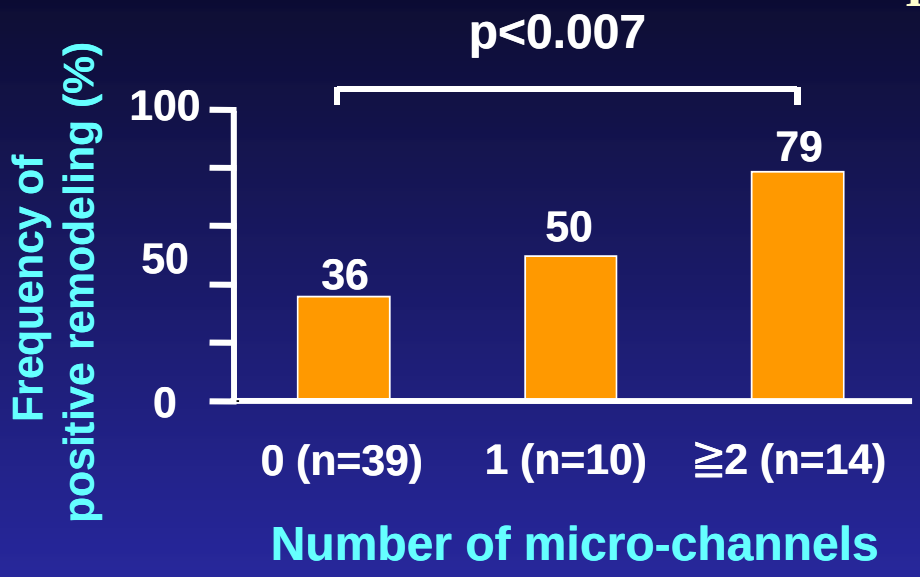
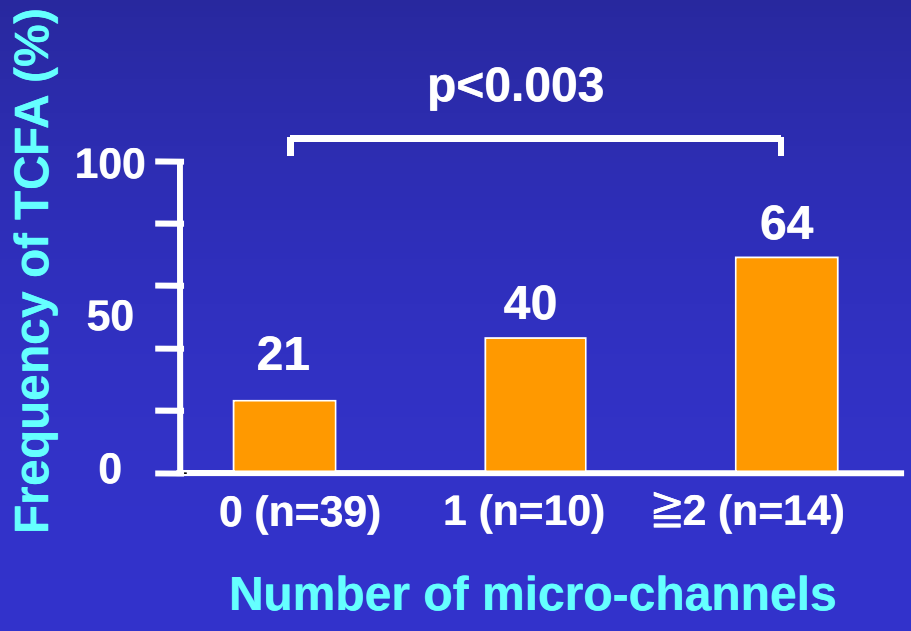
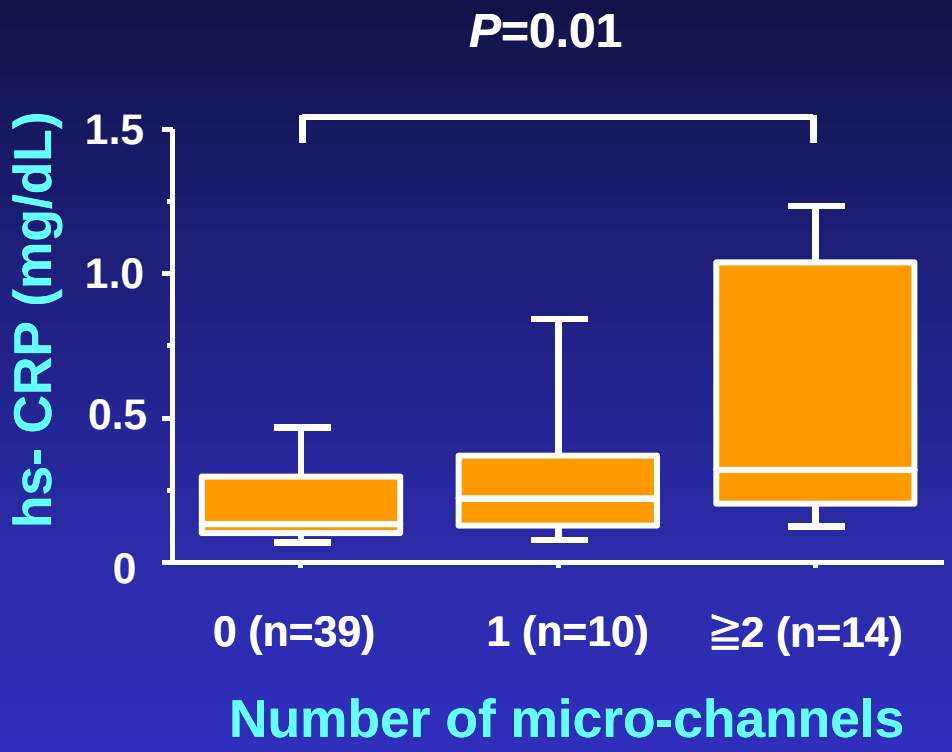
Kitabata H, et al. Am J Cardiol. 2010;105:1673-1678



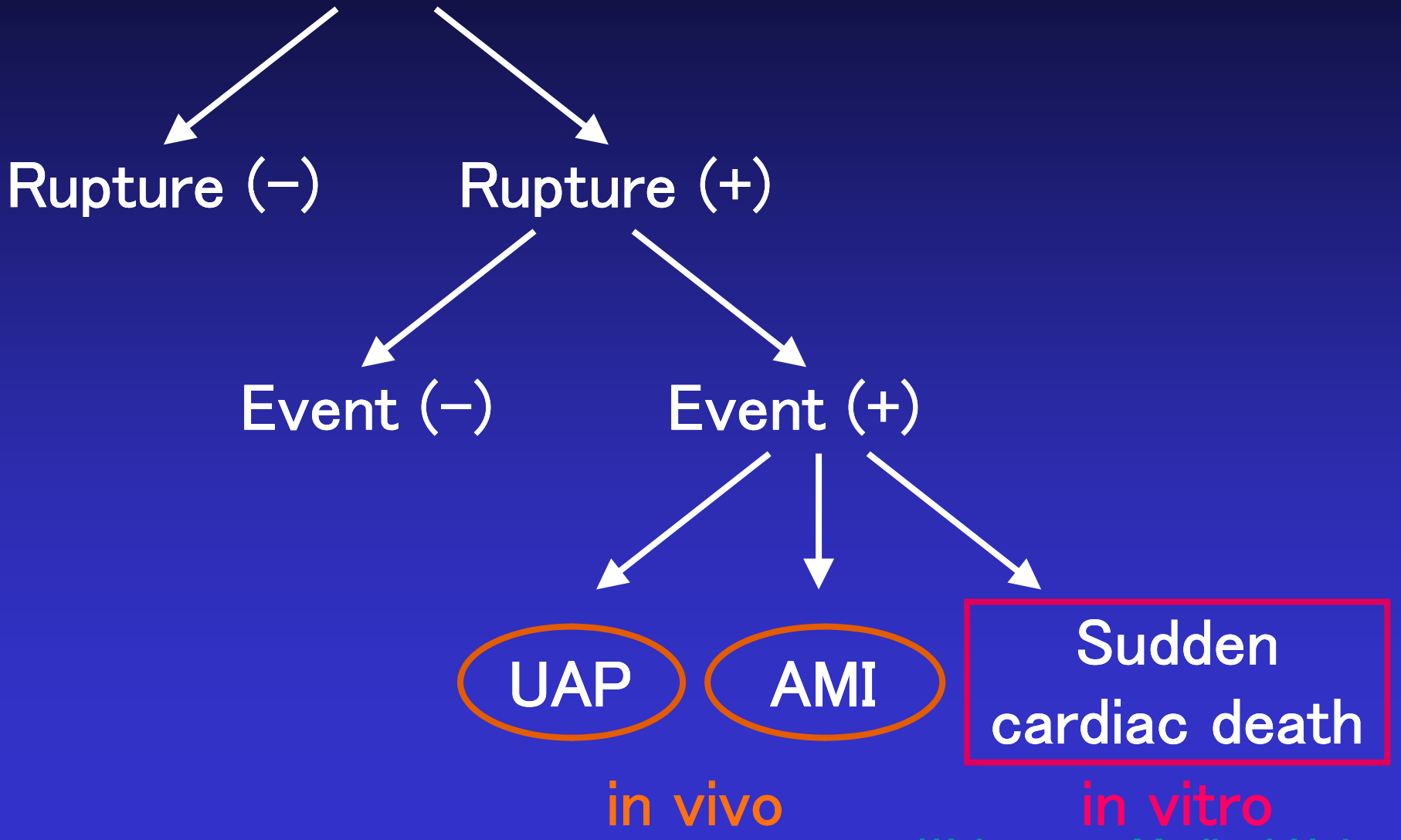




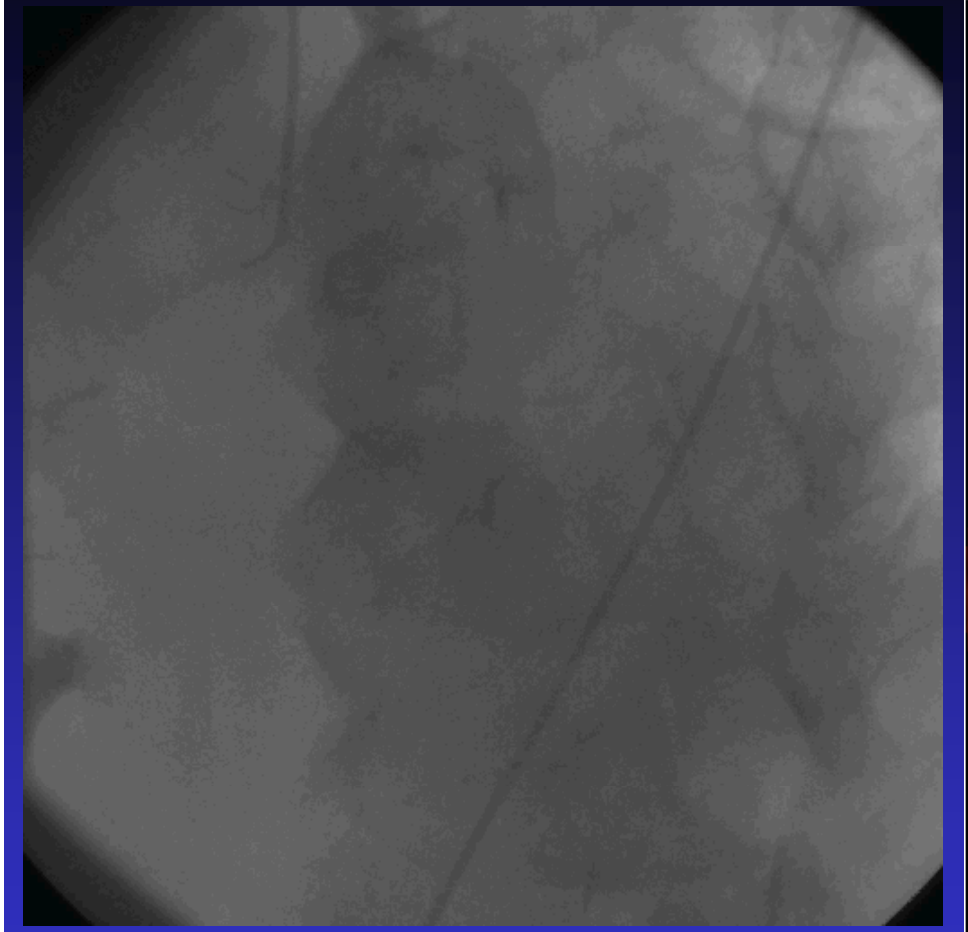
The presence of microvasculature (vasavasorum) may demonstrate the plaque vulnerability.

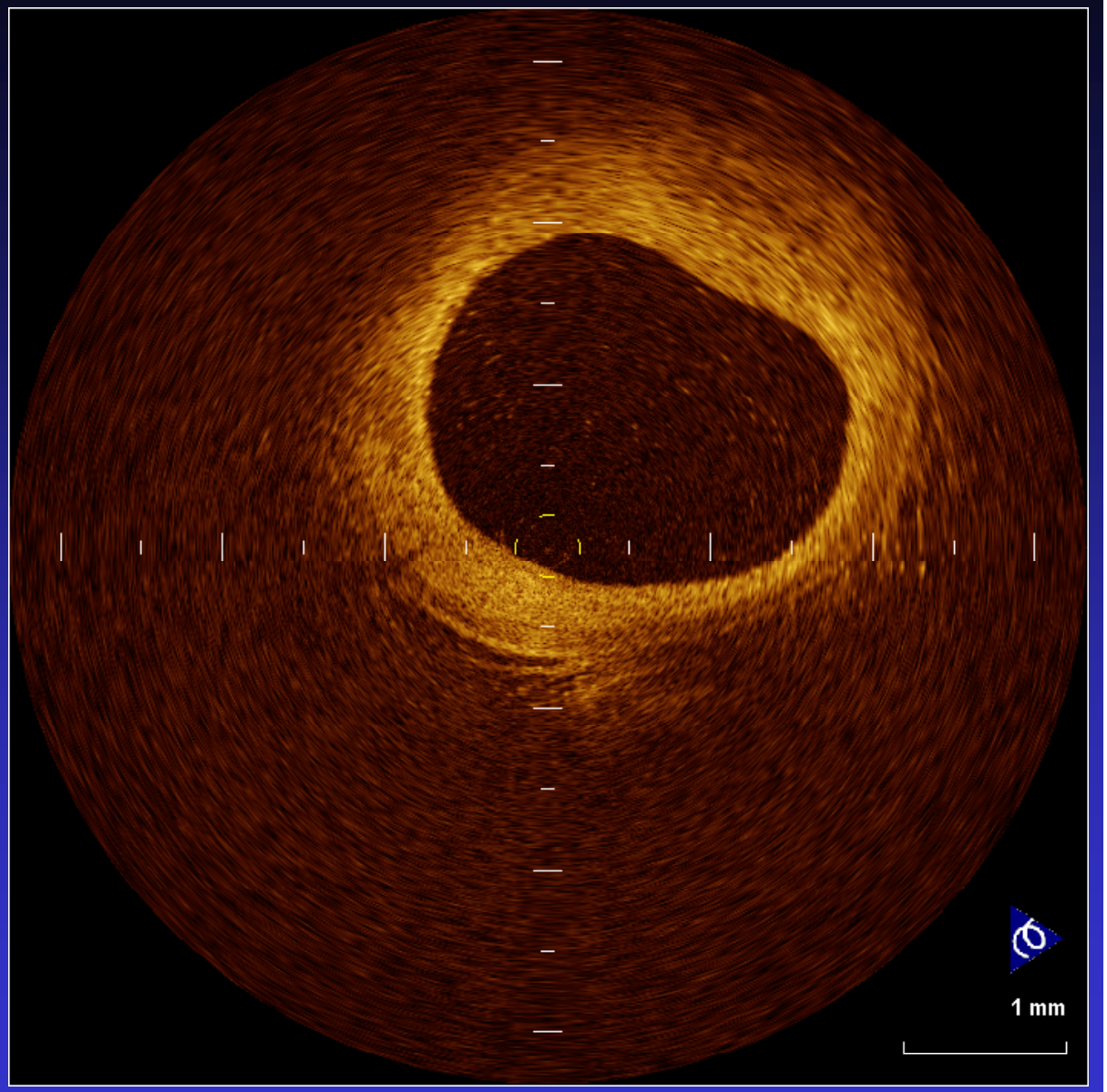
Identification of vulnerable plaque

- Plaque prone to rupture



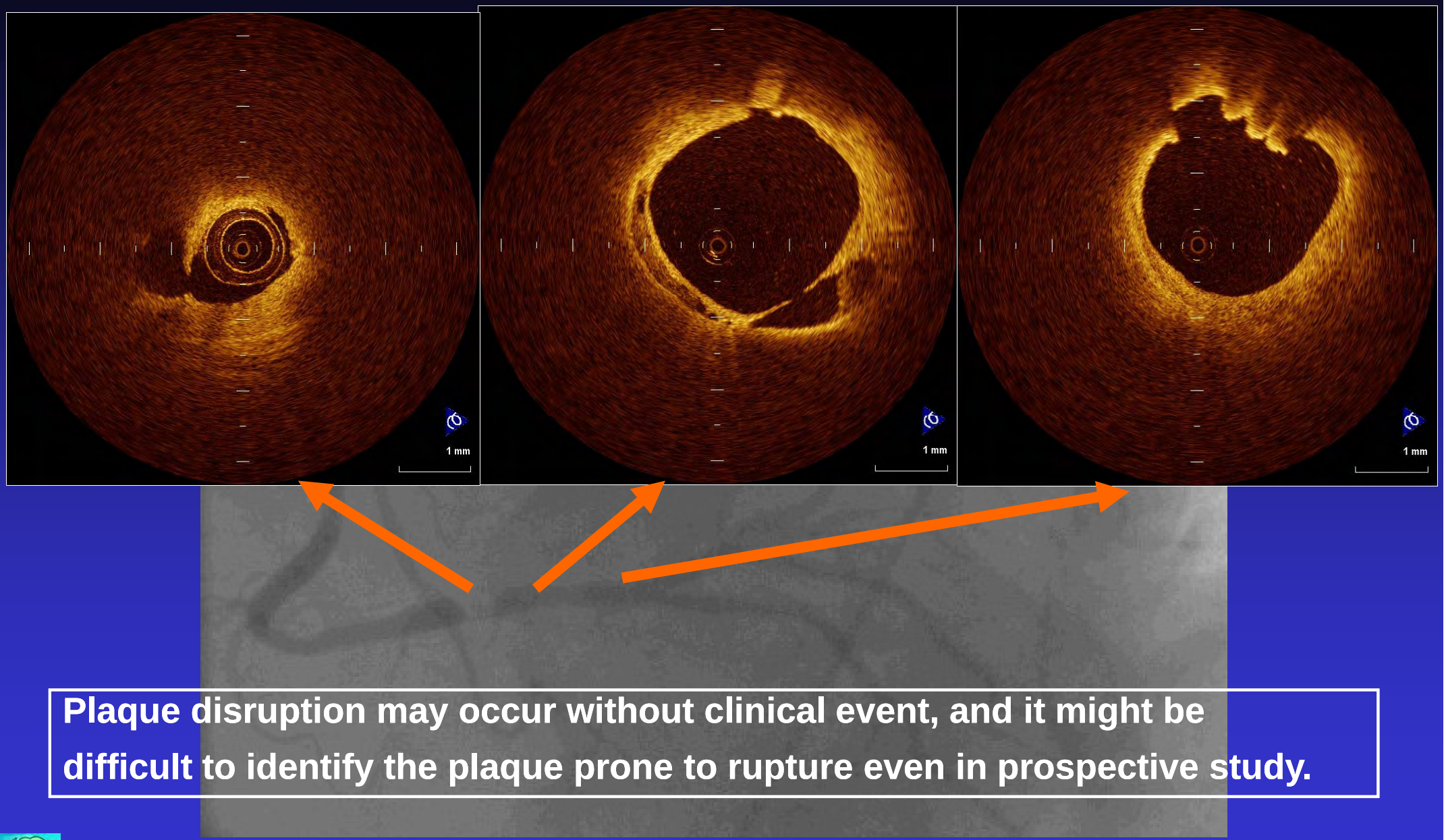
Unstable AP





（Tanimoto T, et al. Circ J 2009 ; 73:187-189 ）

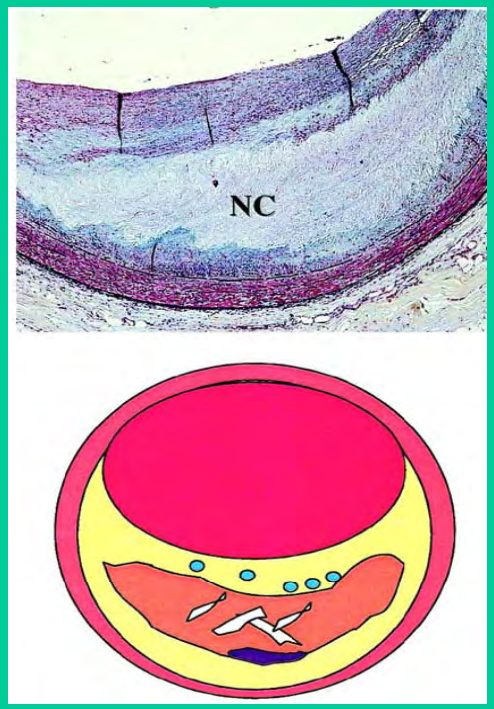
Unstable AP



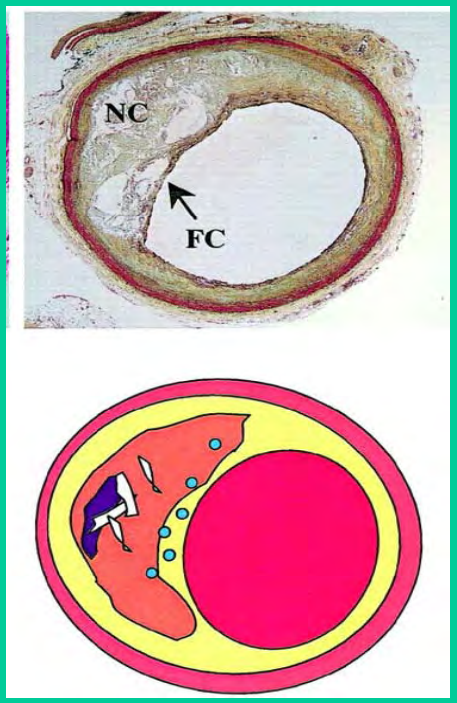
Plaque disruption may occur without clinical event, and it might be difficult to identify the plaque prone to rupture even in prospective study.

（Tanimoto T, et al. Circ J 2009 ; 73:187-189 ）

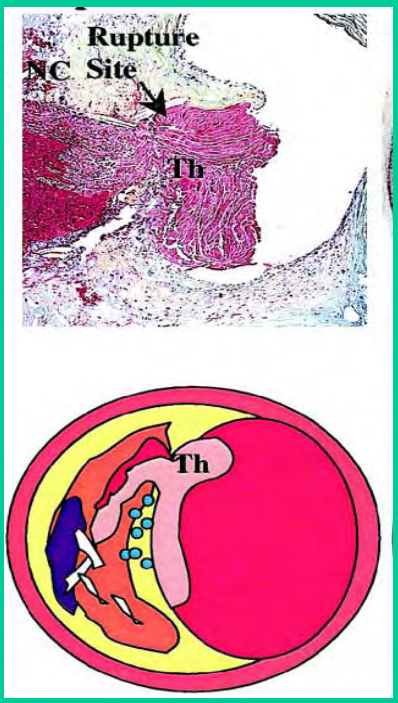
OCT findings in each atheromatous stage



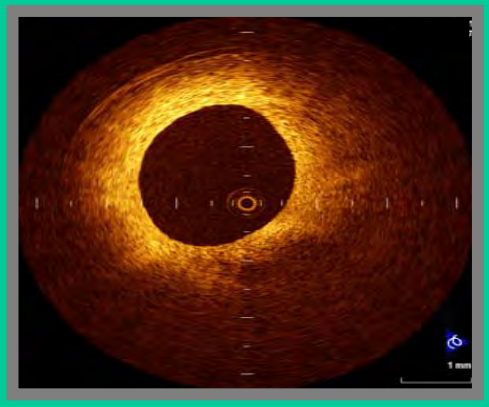
Thick fibrous-cap atheroma

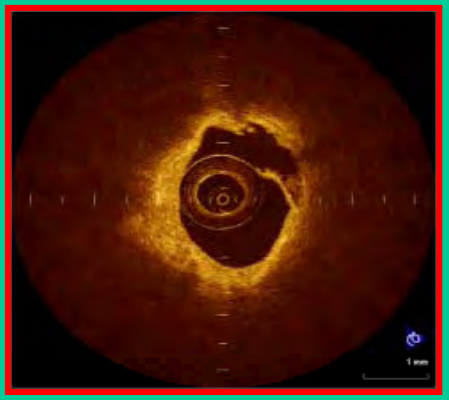


Thin fibrous-cap atheroma



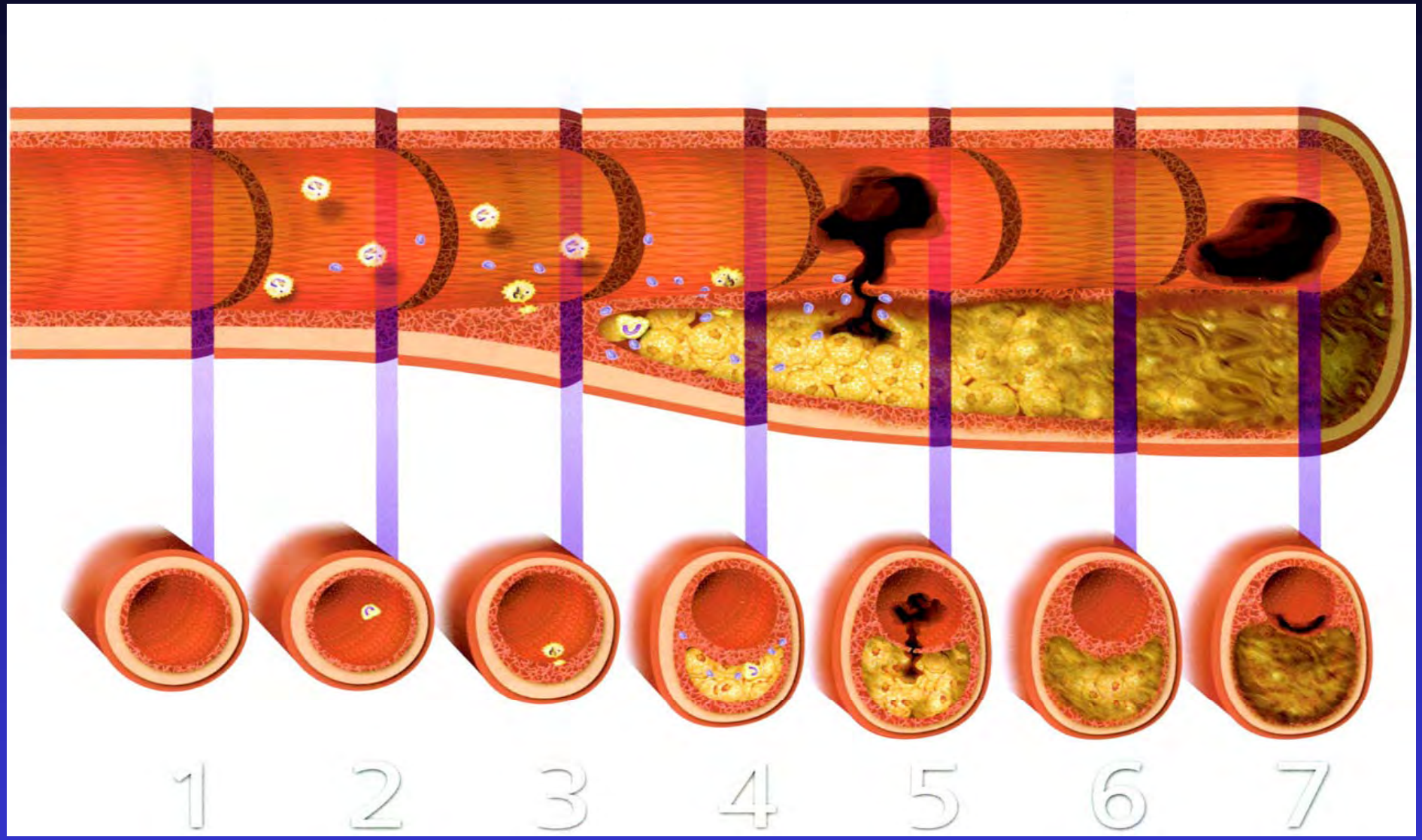
Ruptured plaque





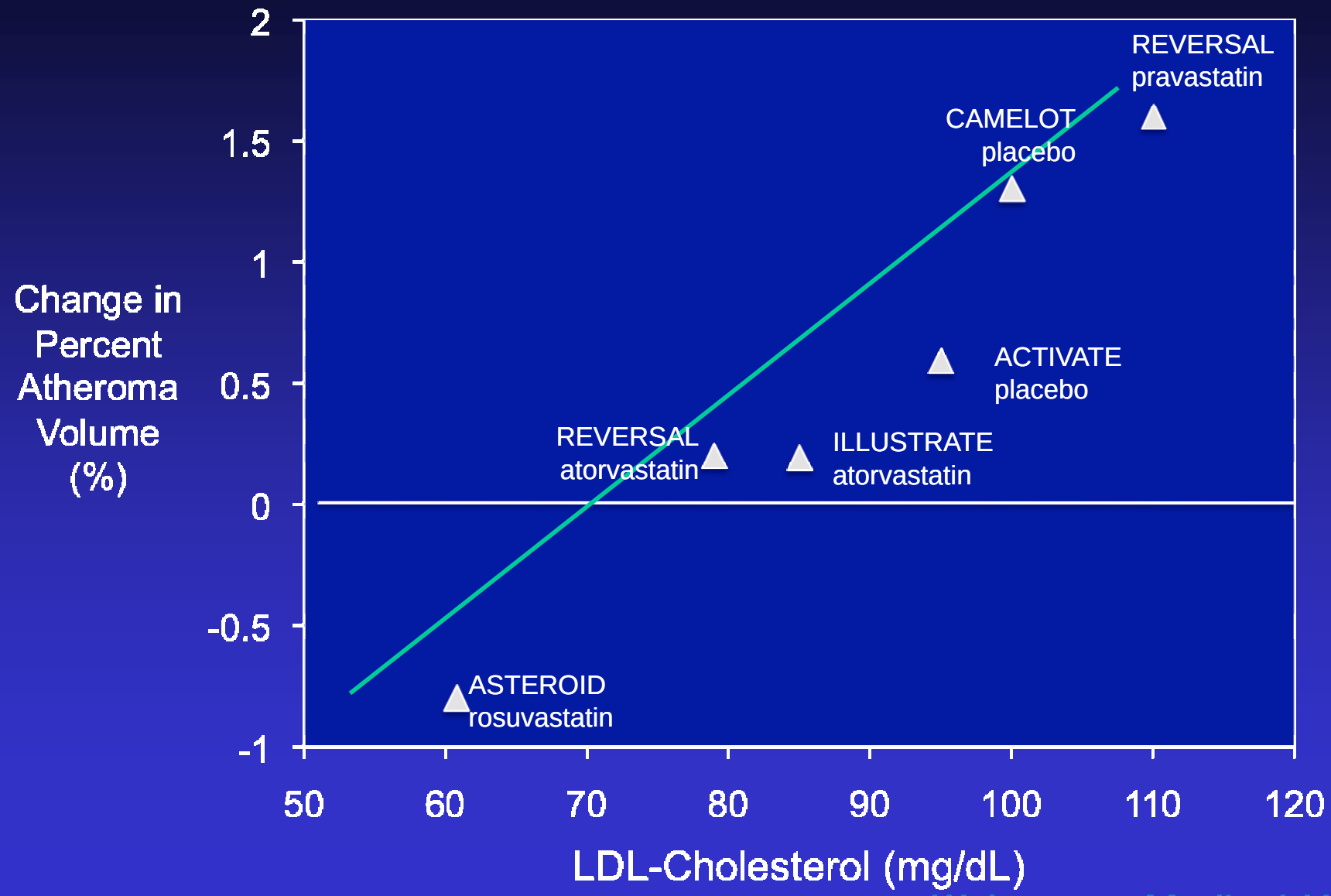
OCT is a high-resolution imaging modality for plaque characterization.

Progression of atherosclerotic plaque



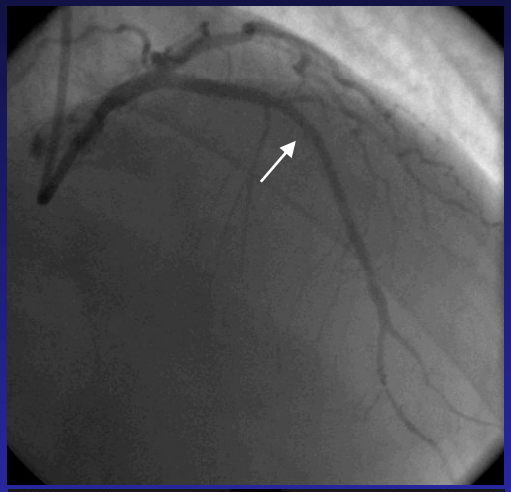
Libby, P. Circulation 2001;104:365-372

LDL vs Atheroma volume

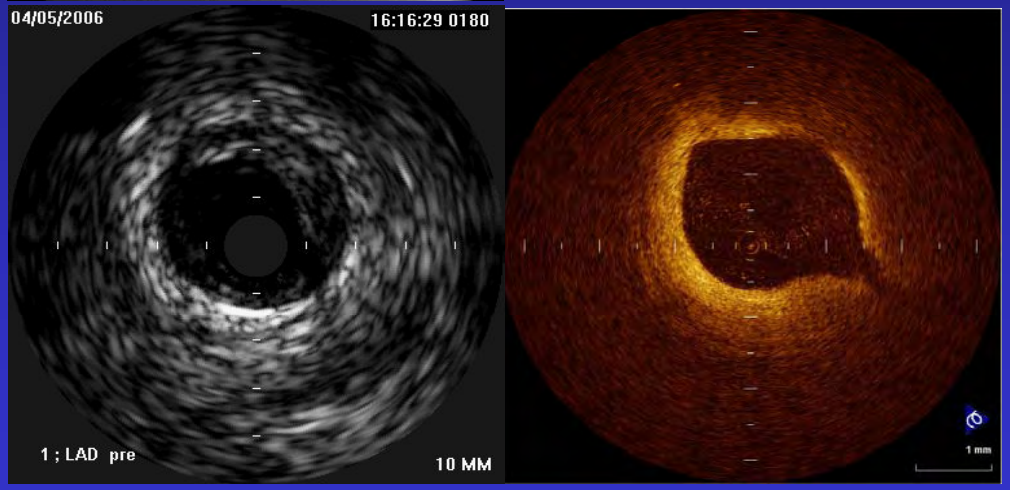


OCT assessment of non-culprit lesion (47y.o. male)

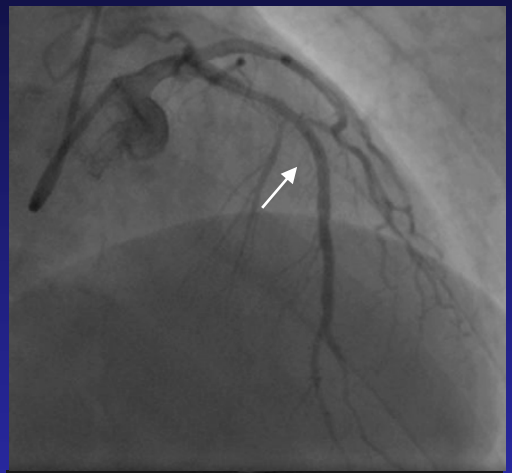
Baseline



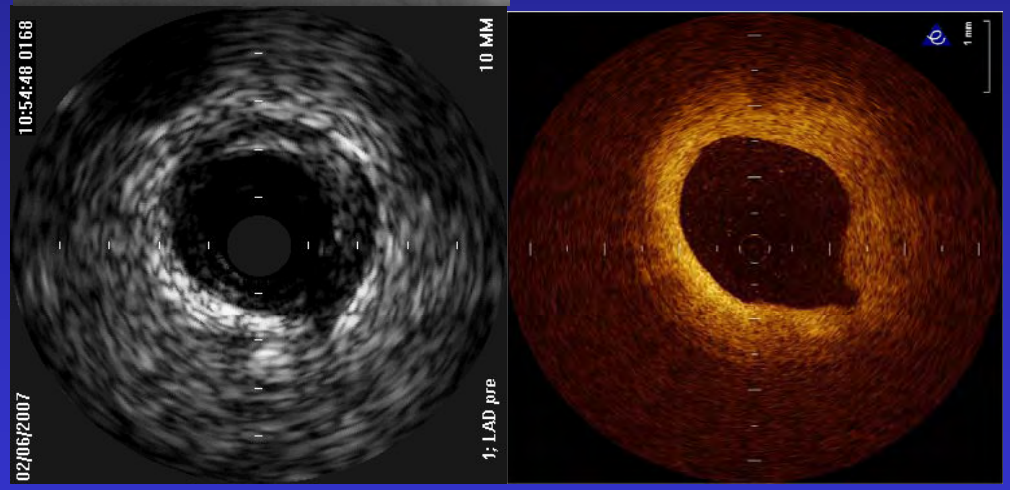
T.Chol.	200	mg/dl
TG	79	mg/dl
HDL-C	47	mg/dl
LDL-C	128	mg/dl



9 month later



T.Chol.	187	mg/dl
TG	133	mg/dl
HDL-C	49	mg/dl
LDL-C	98	mg/dl



（Takarada S, et al. Atherosclerosis 202: 491- 497, 2009）

Changes of plaque characteristics by statin

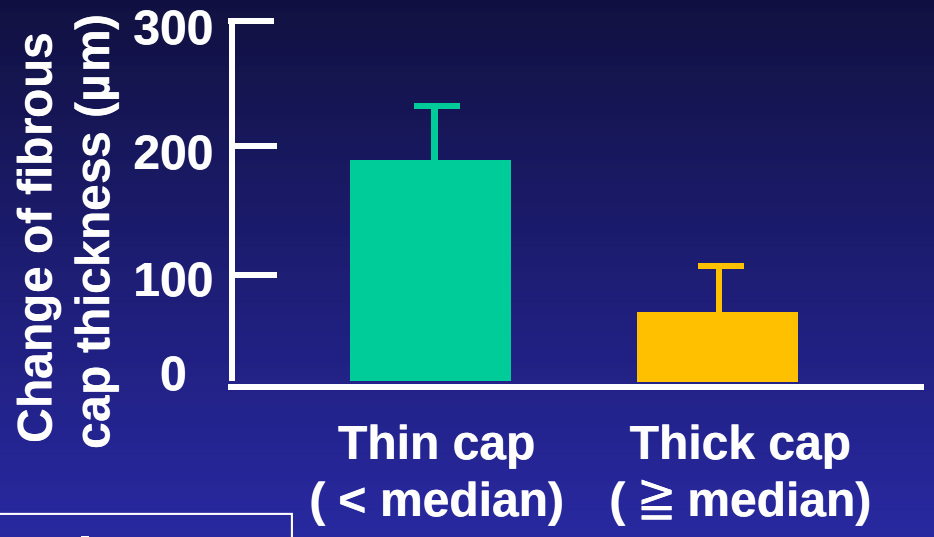
（Takarada S, et al. Atherosclerosis 202: 491-497, 2009）

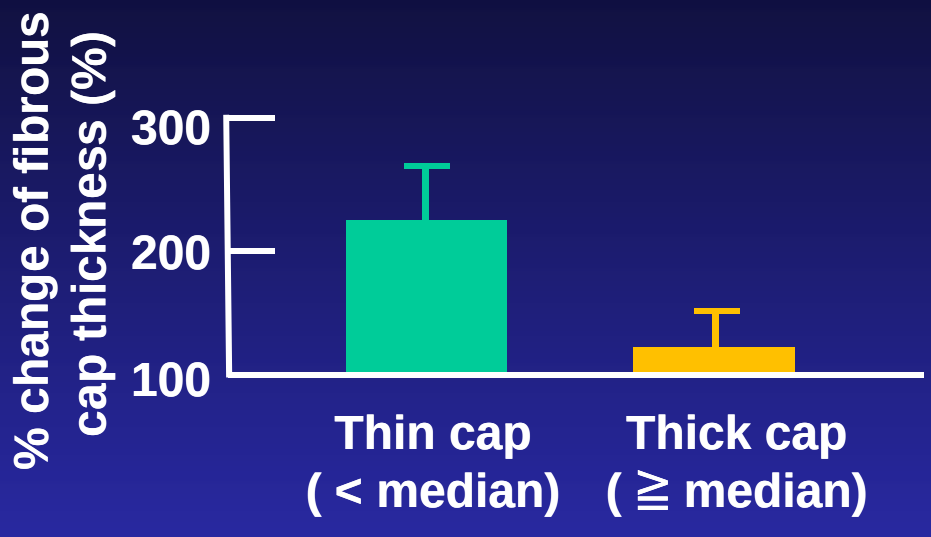
	Baseline	Follow-up	p
Statin group			
Fibrous cap thickness (μm)	114±83	162±75	<0.01
Lipid arc (degrees)	132±37	116±23	<0.01
Non-statin group (Control group)			
Fibrous cap thickness (μm)	117±78	129±54	ns
Lipid arc (degrees)	129±37	128±28	ns

Change in fibrous cap thickness

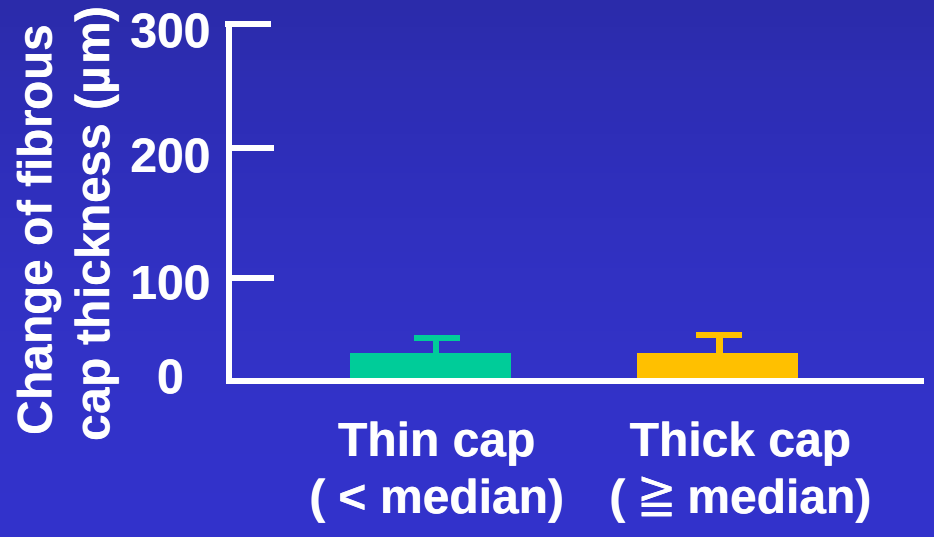
（Takarada S, et al. Atherosclerosis 202: 491- 497, 2009 ）

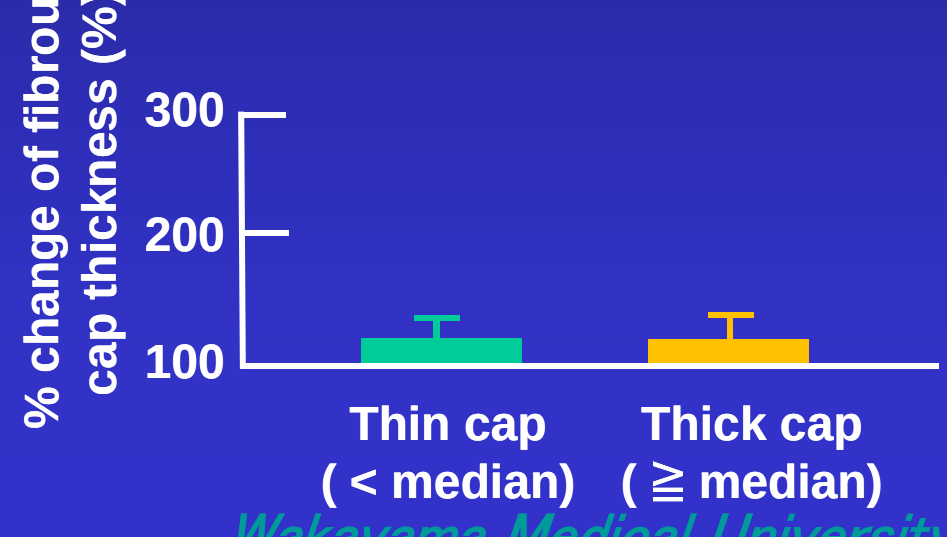
Statin Group





Control Group





Wakayama Medical University

Methods

Consecutive 160 NSTEACS patients who underwent emergency PCI

Exclusion:
3 left main, 6 CHF, 8 CKD (Cr>1.5 mg/dl)
12 lipid-lowering therapy

110 patients could be evaluated by IVUS & OCT

9-month follow-up period

28 patients withdraw

82 patients were enrolled in this study

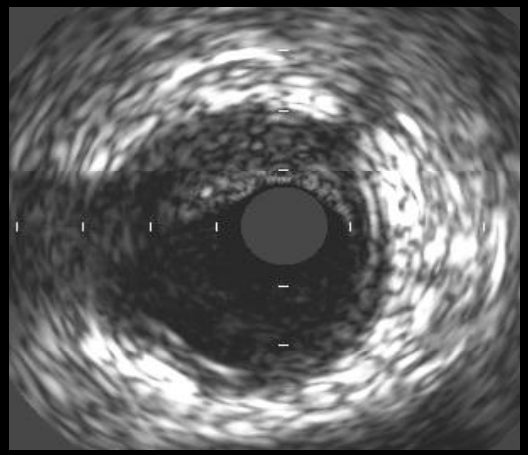
58 patients (71%) received statin during follow up

OCT and IVUS study :
Measured plaque :
Non-culprit site atheroma (>10mm proximal or distal to the PCI site)
Analysis
Fibrous-cap thickness (OCT)
Total atheroma volume (IVUS)

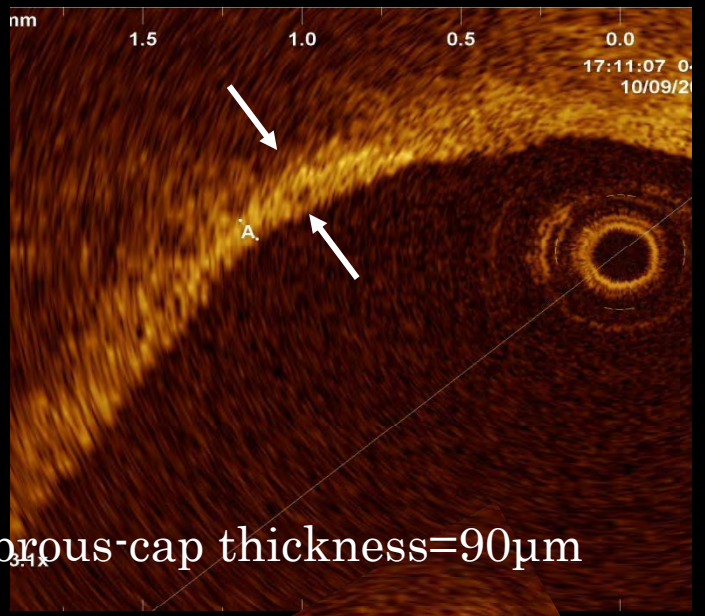
Laboratory examination :
LDL-C,HDL-C,hs-CRP
(The days of discharge, & the time of follow-up)

Representative case of plaque stabilization : 66yo, male

primary PCI

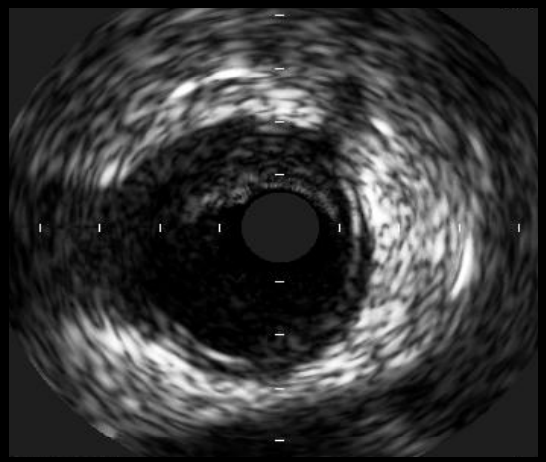


Total atheroma volume=63mm

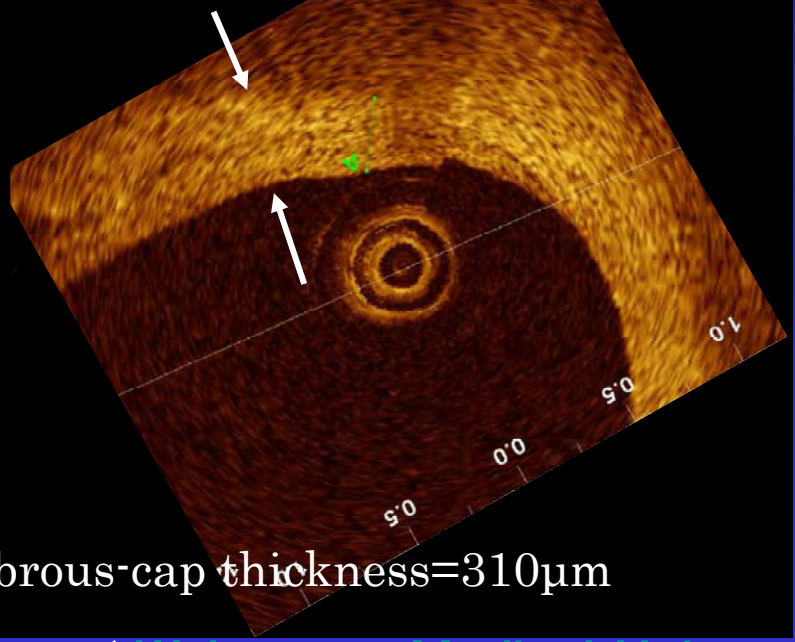


Fibrous-cap thickness=90μm

9-months follow-up

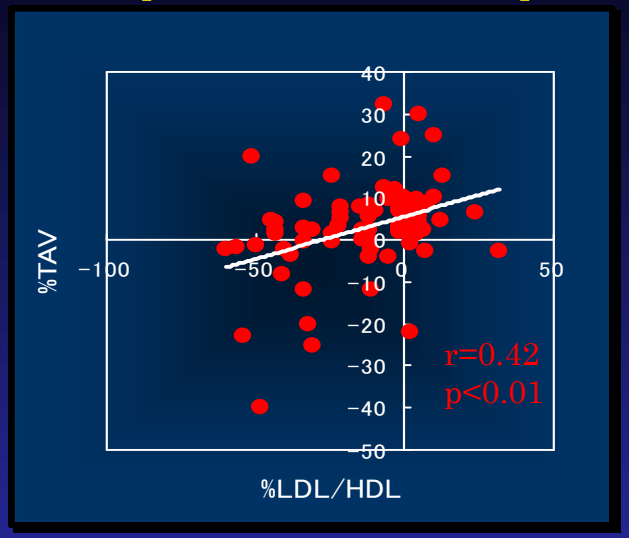


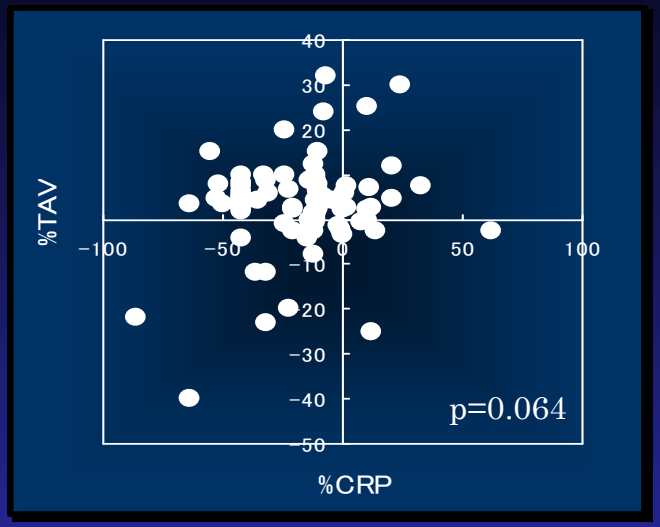
Total atheroma volume=61mm

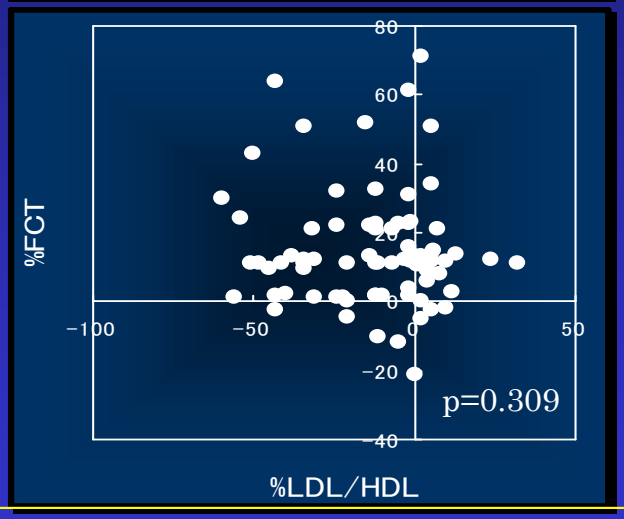


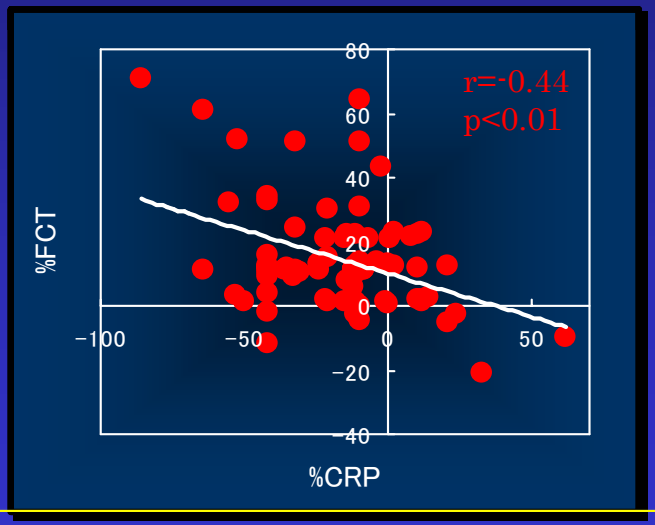
Fibrous-cap thickness=310μm

The correlation between the lipid profile and the % change of fibrous-cap thickness (FCT) and total atheroma volume (TAV).









%TAV and %LDL/HDL were positively correlated (p<0.01, r = 0.42).
%FCT and %CRP were inversely correlated (p<0.01, r = -0.44).

（Takarada S, et al. JACC Interv. 2010;3: 766-772）

Univariable and multivariable logistic regression analyses as predictors of plaque stabilization

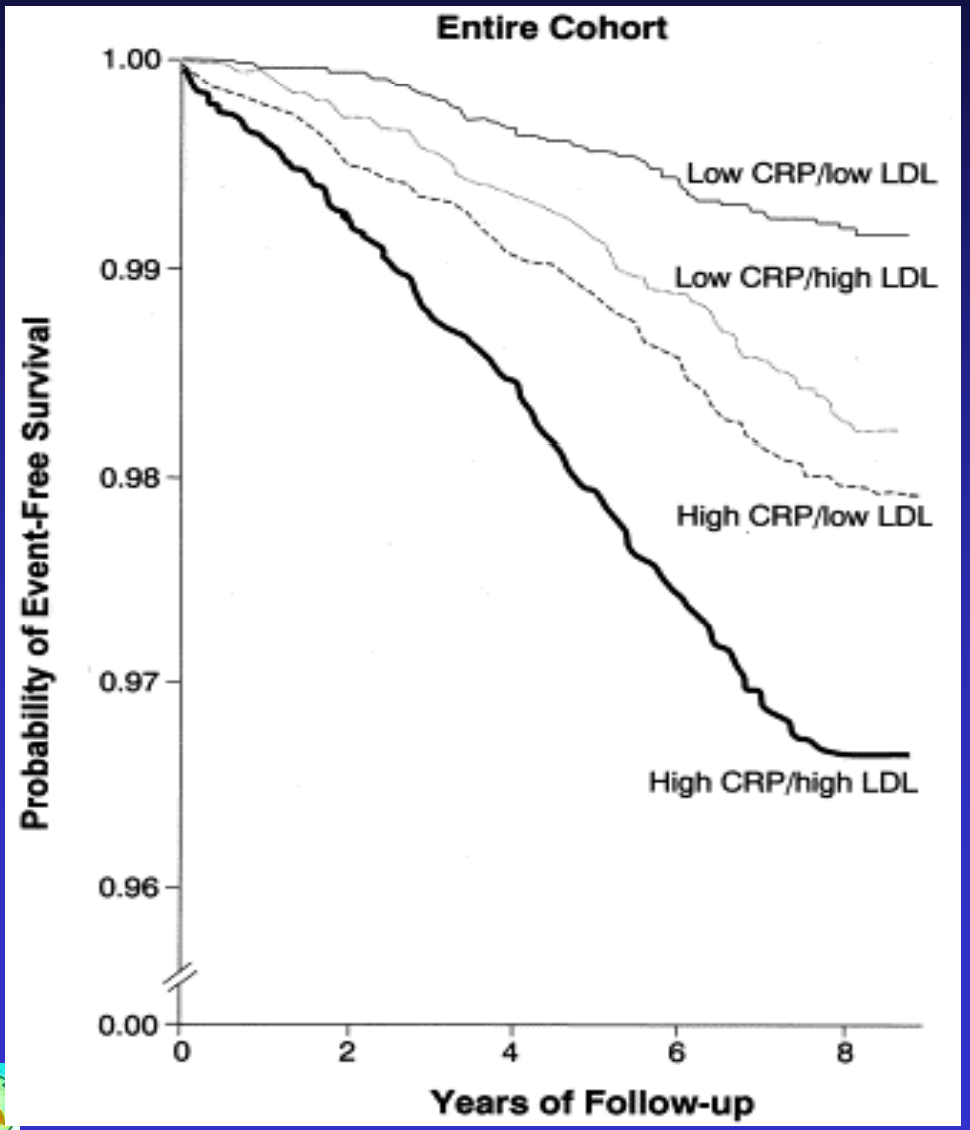
	univariable analysis : OR(95% CI)	p-value		multivariable analysis :OR(95%CI)	p-value
age,y	0.52 (0.93-1.04)	p=0.60			
gender	1.38 (0.46-5.4)	p=0.86			
HLP	0.91(0.33-2.51)	p=0.86			
HT	0.53 (0.17-1.09)	p=0.08		0.72 (0.22-1.7)	p=0.73
DM	0.56 (0.14-0.97)	p=0.04		0.74 (0.23-2.4)	p=0.84
statin	3.57 (1.66-12.6)	p=0.002		1.45 (1.15-15.9)	p=0.02

"Plaques stabilization" was defined by decreasing TAV and increasing FCT.
In the present study, 31 plaques (39%) stabilized.

（Takarada S, et al. JACC Interv. 2010;3:766-772 ）

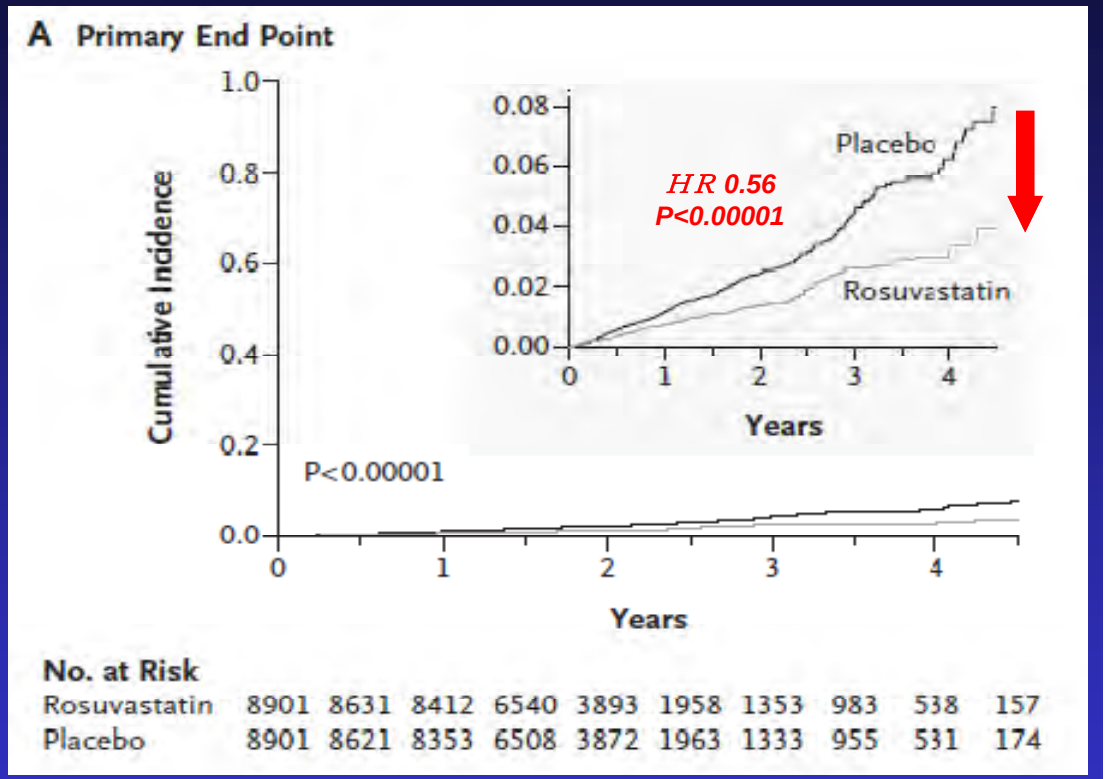
Cardiovascular event-free survival probability according to high or low hs-CRP and LDL cholesterol levels

Ridker PM et al. N Engl J Med 2002;347:1557-65

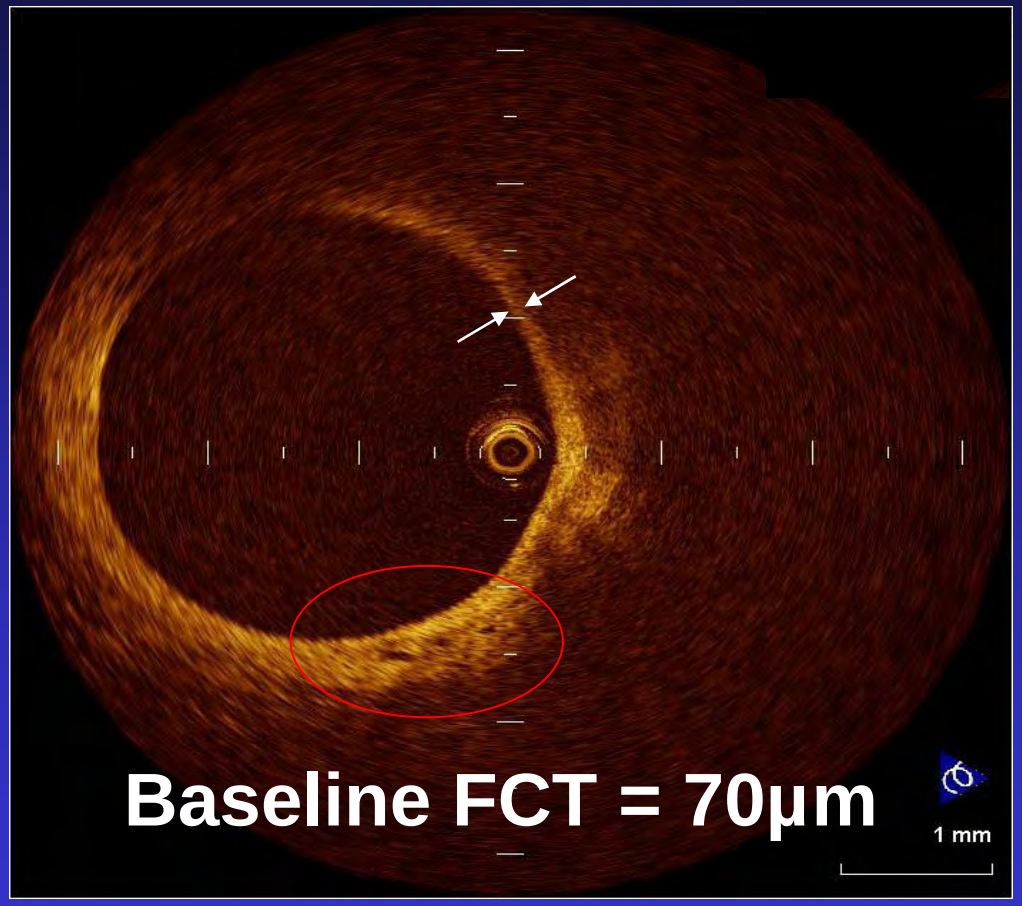


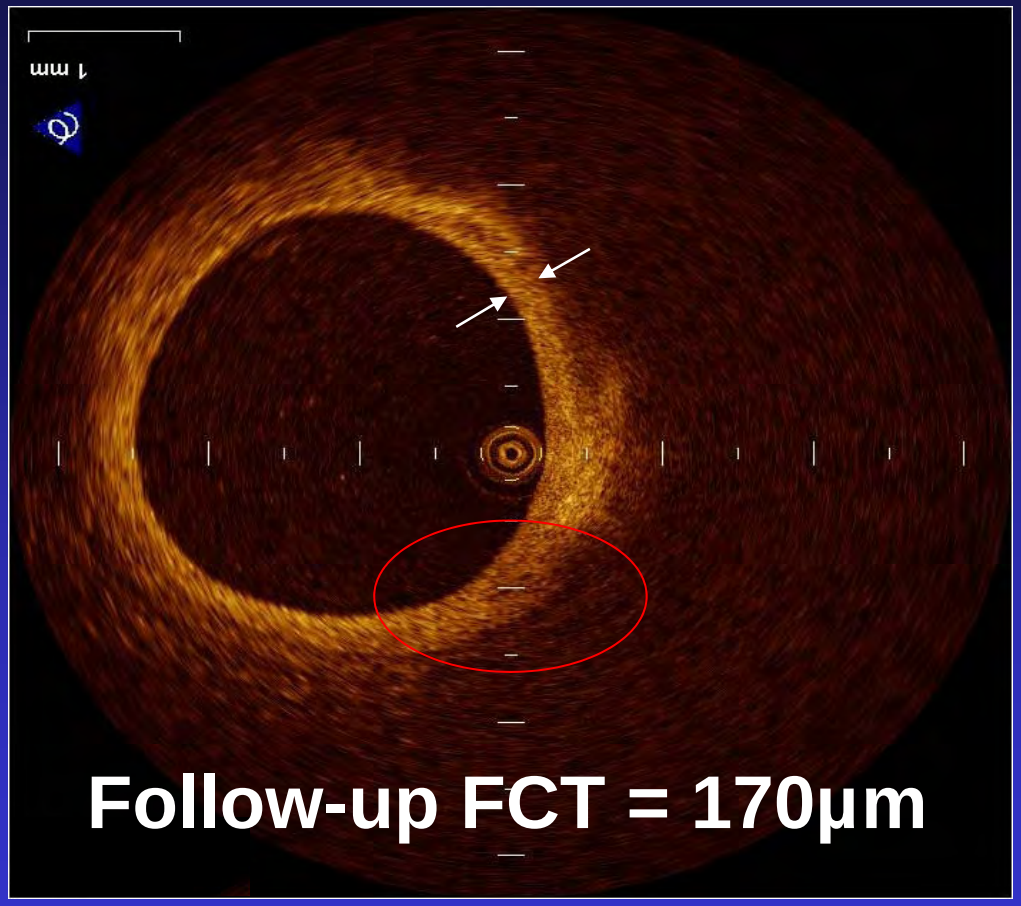
JUPITER trial

N Engl J Med 2008;359:2195-207.



These data demonstrated that hs-CRP provide the risk prediction better than LDL-C.

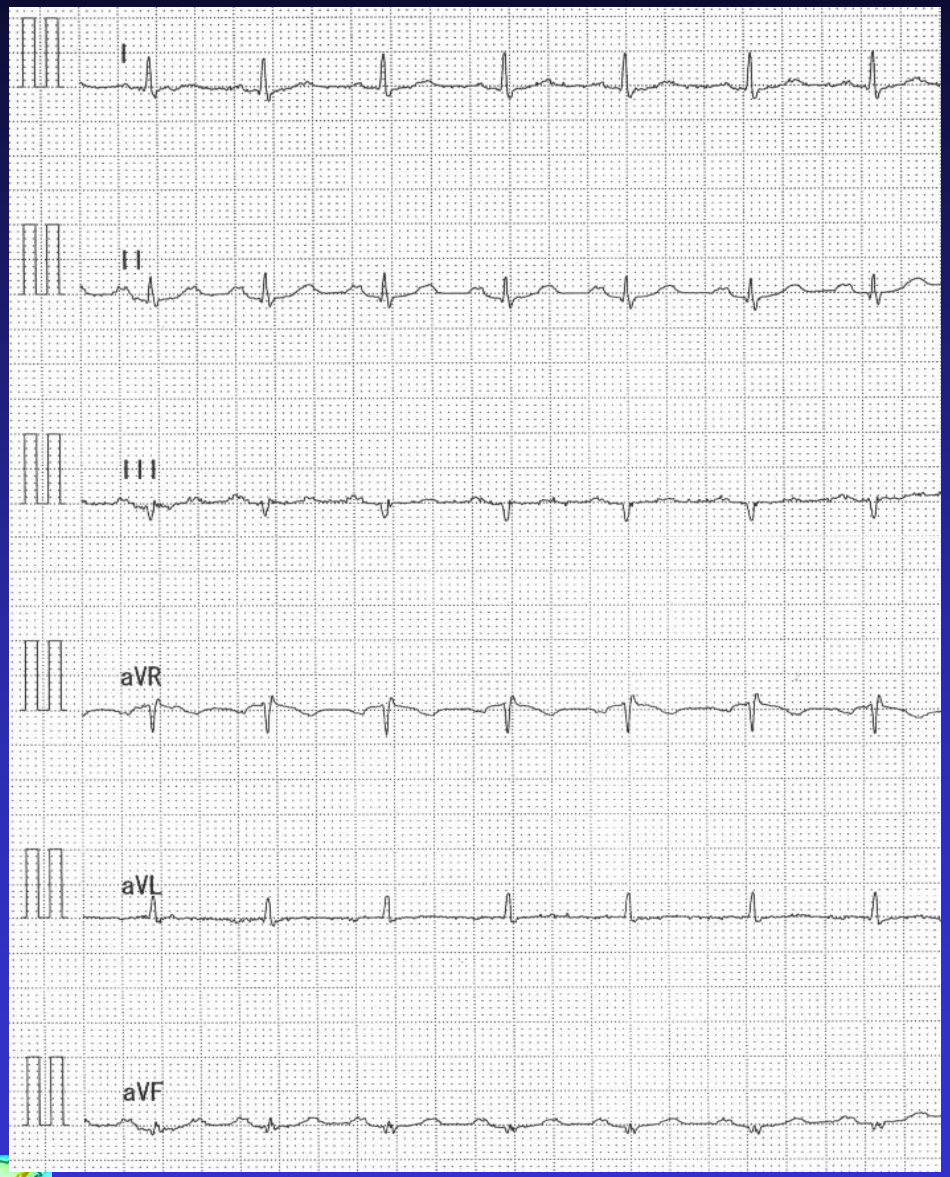

Baseline FCT = 70μm
1 mm

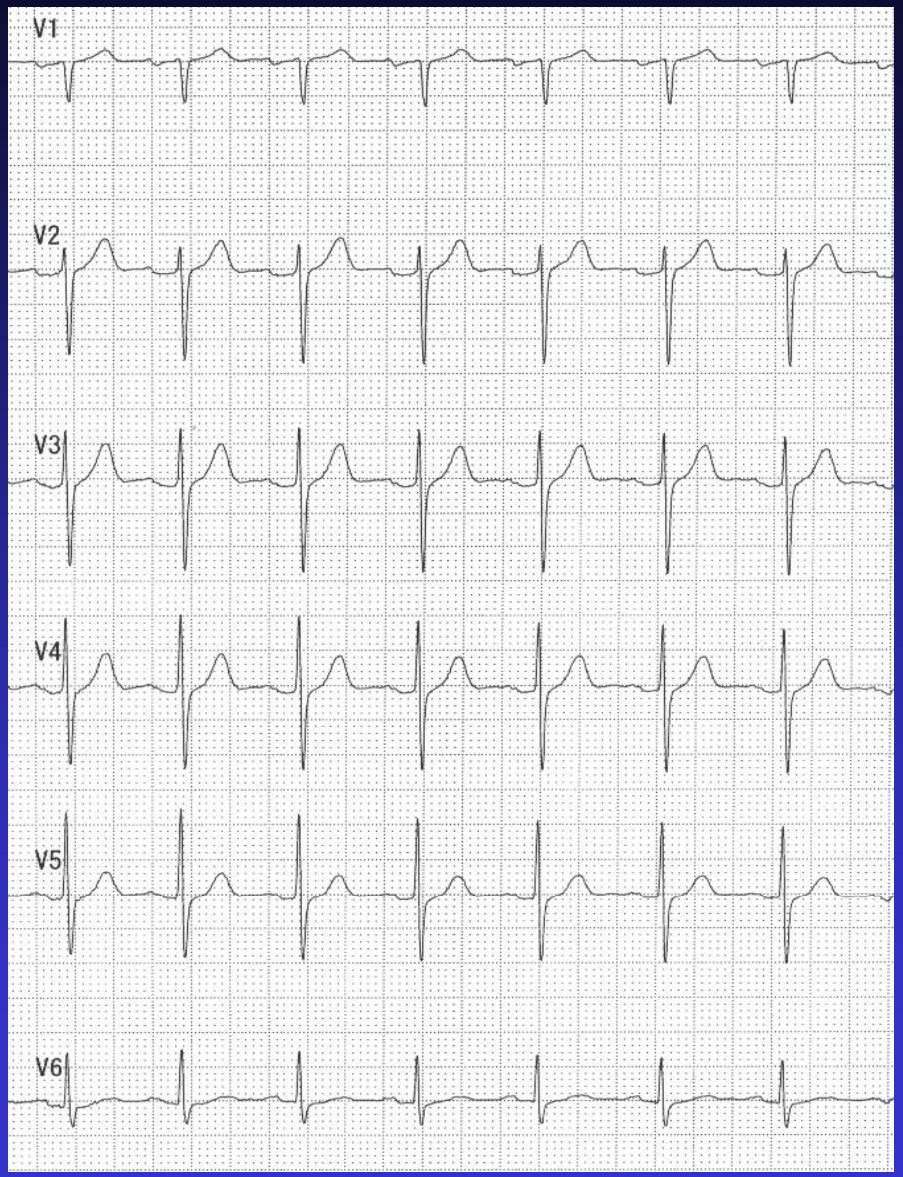

Follow-up FCT = 170μm
1 mm

Case 56 y.o. male

- This gentleman had chest pain on exertion from March 20, 2010.
- The frequency and severity of chest pain increased gradually .
- He was admitted to our hospital with a diagnosis of unstable angina (changing pattern) on April 12, 2010.
- He had multiple coronary risk factors such as hypertension, dyslipidemia, diabetes mellitus, family history and smoking.

ECG on admission (56 y.o. male)



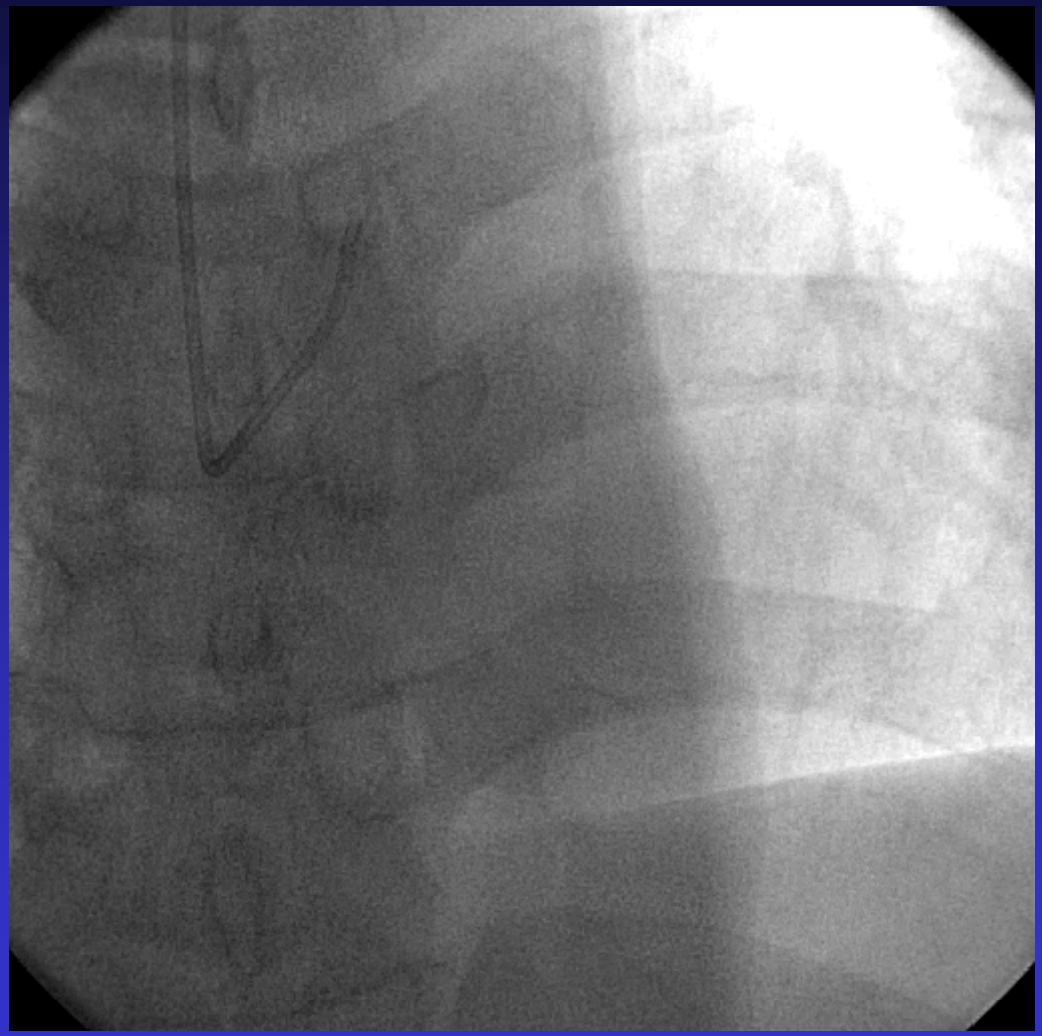


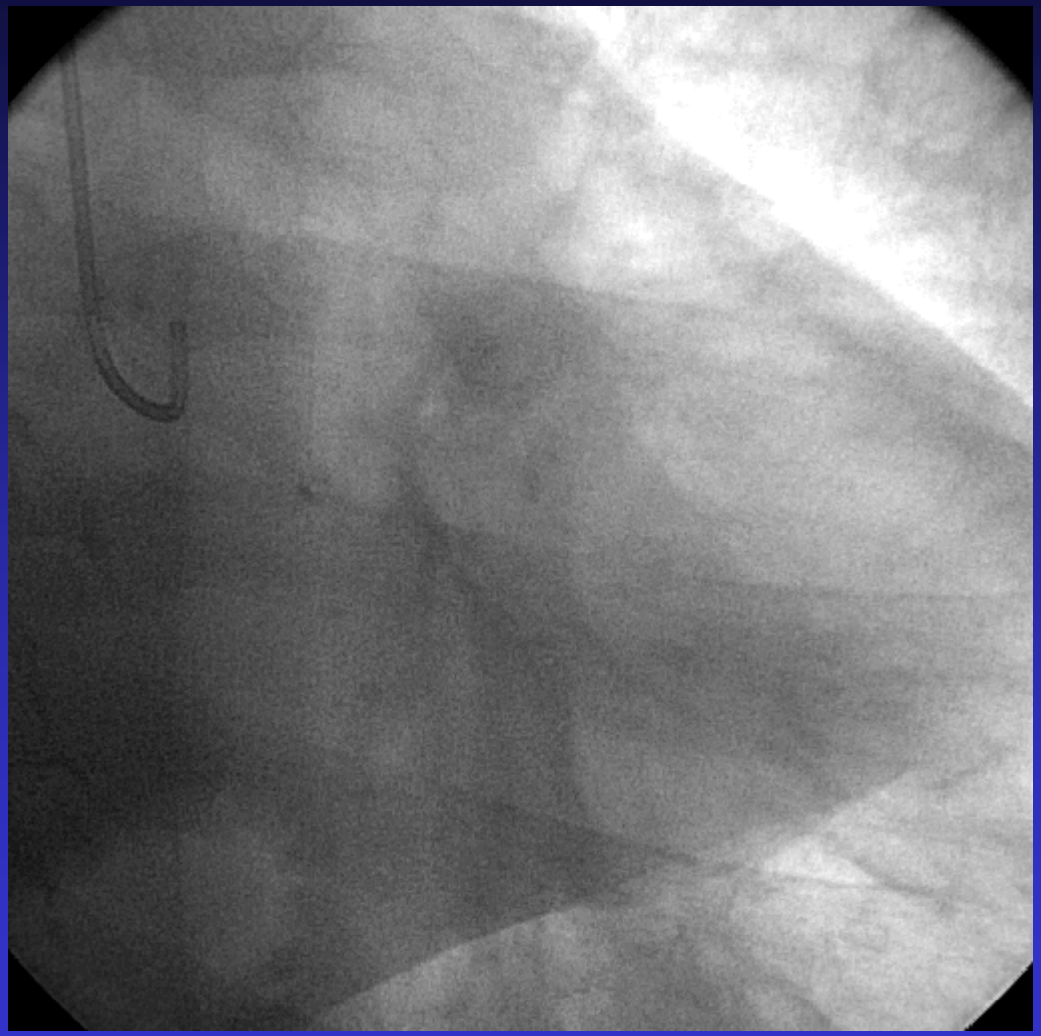
Case 1. 56 y.o. male

Labo data

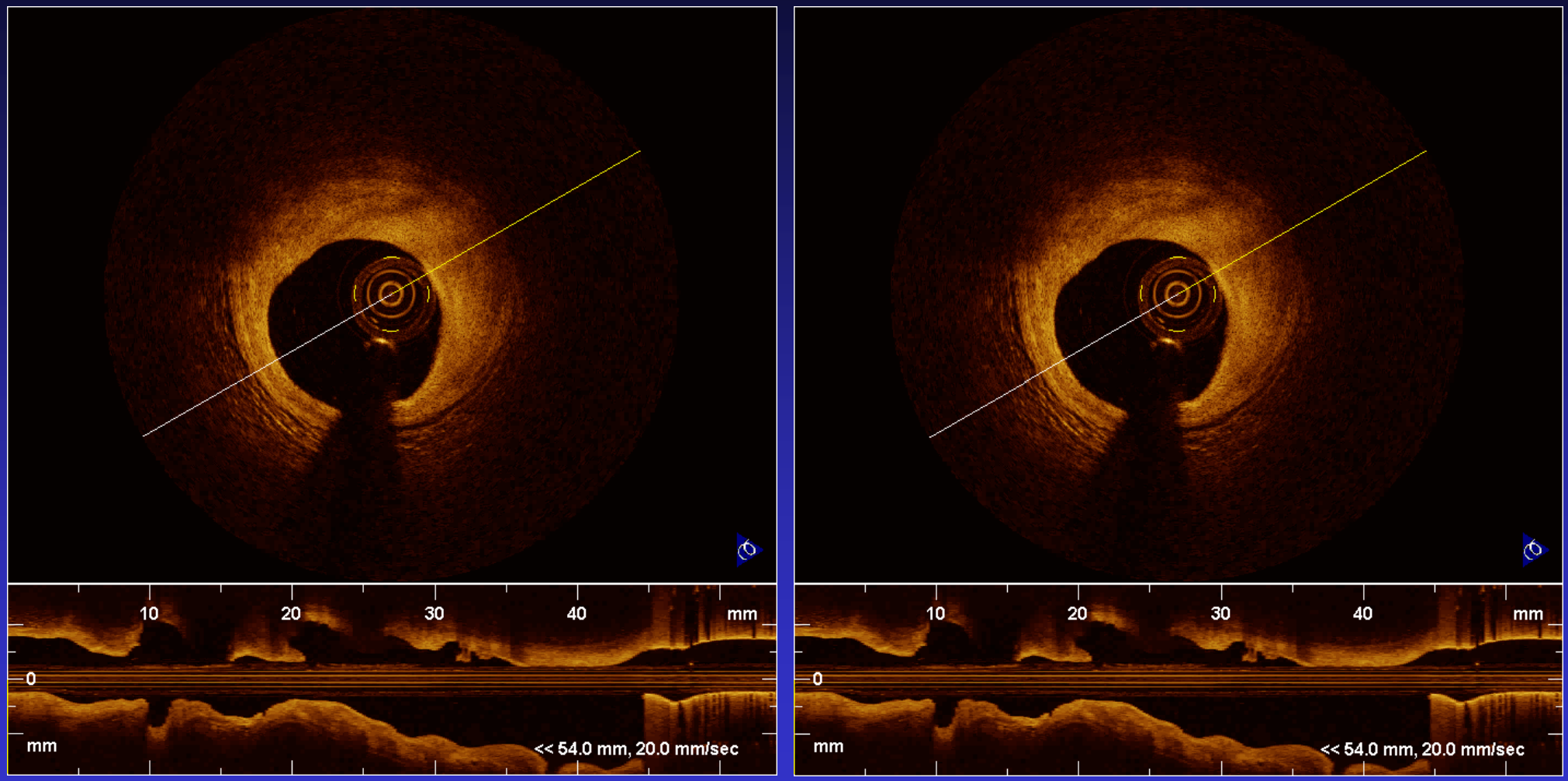
WBC:	**11070**	**LDL-C:**	**143**
CRP:	**0.42**	**HDL-C:**	**36**
CK:	**77**	**TG:**	**241**
CK-MB:	**5**	**BS:**	**298**
AST:	**30**	**HbA1c:**	**9.0**
ALT:	**33**	**Creat:**	**0.5**
LDH:	**156**	**e-GFR:**	**68.6**

UAP (56 y.o. male)

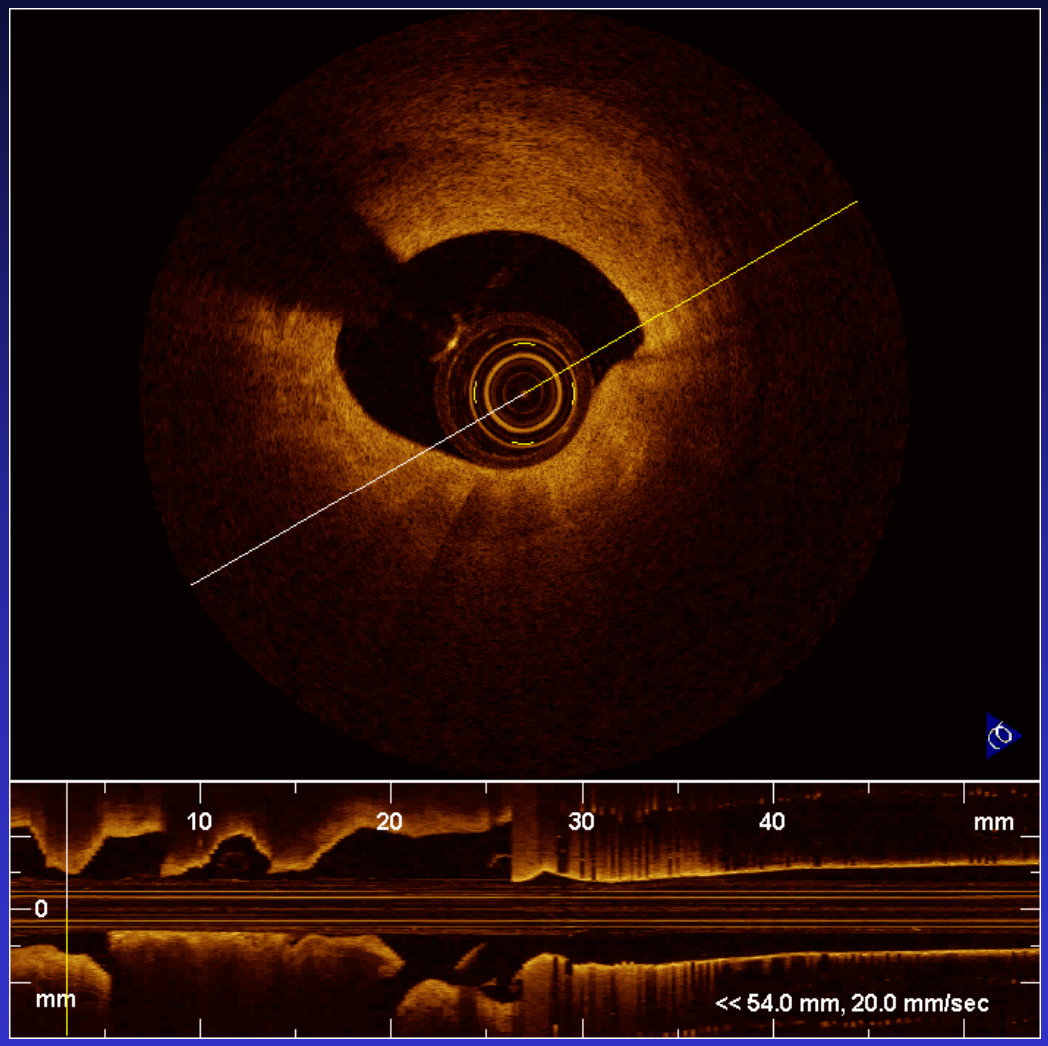


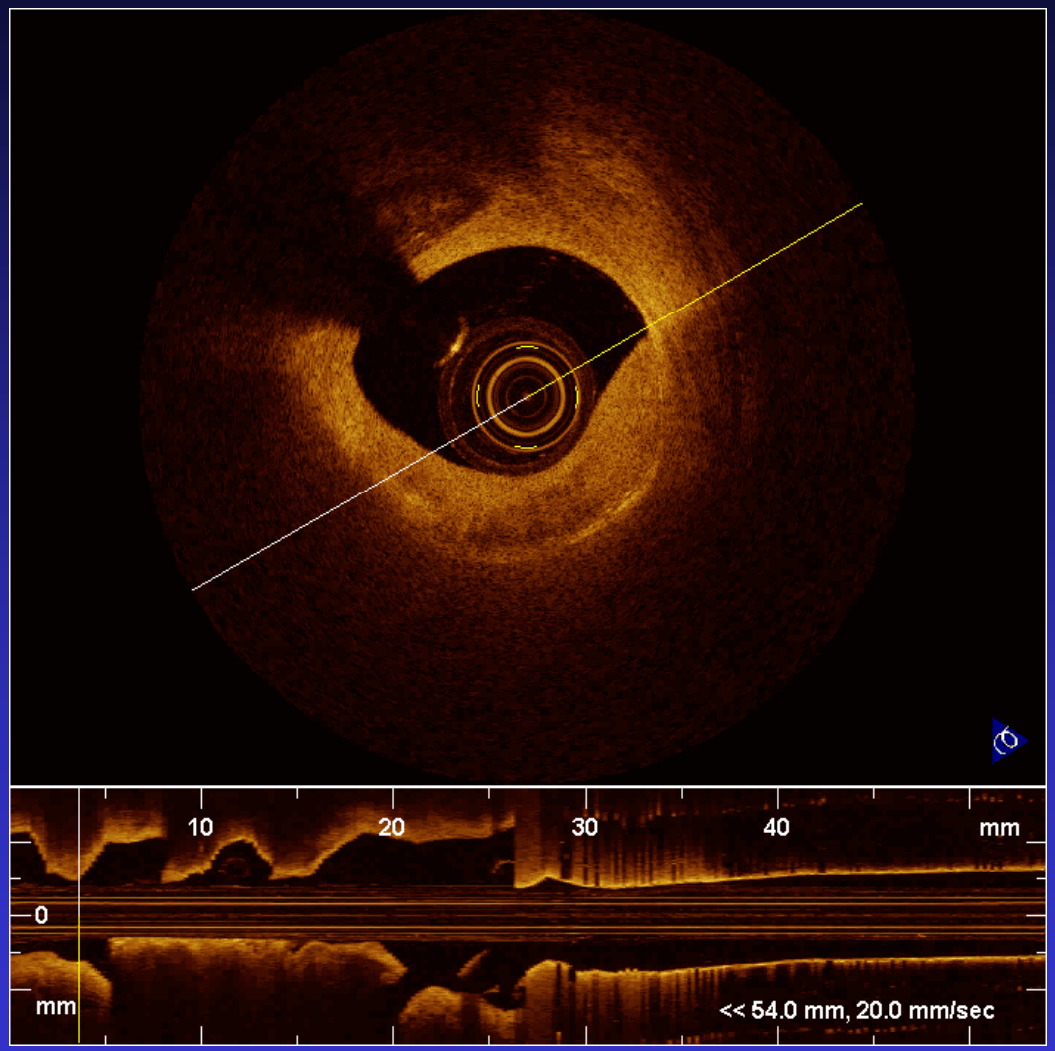


LAD in UAP (56 y.o. male)



LCx in UAP (56 y.o. male)





Case 1. 56 y.o. male

CAG (4/13)

#3: 50%, #6: 90%, #11:75%

PCI to the LAD lesion

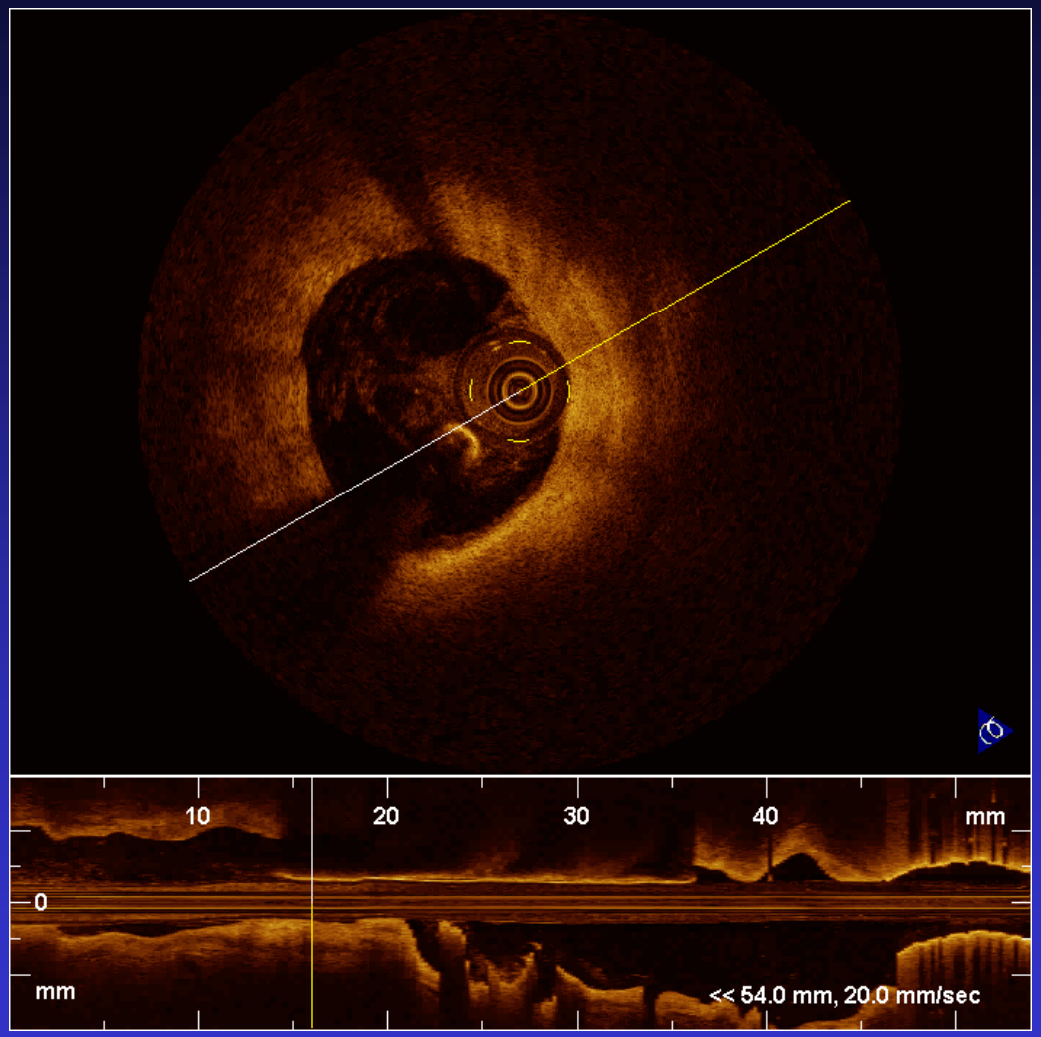
Guiding catheter: 6F Profit SS 3.5, Guide wire: Runthrough

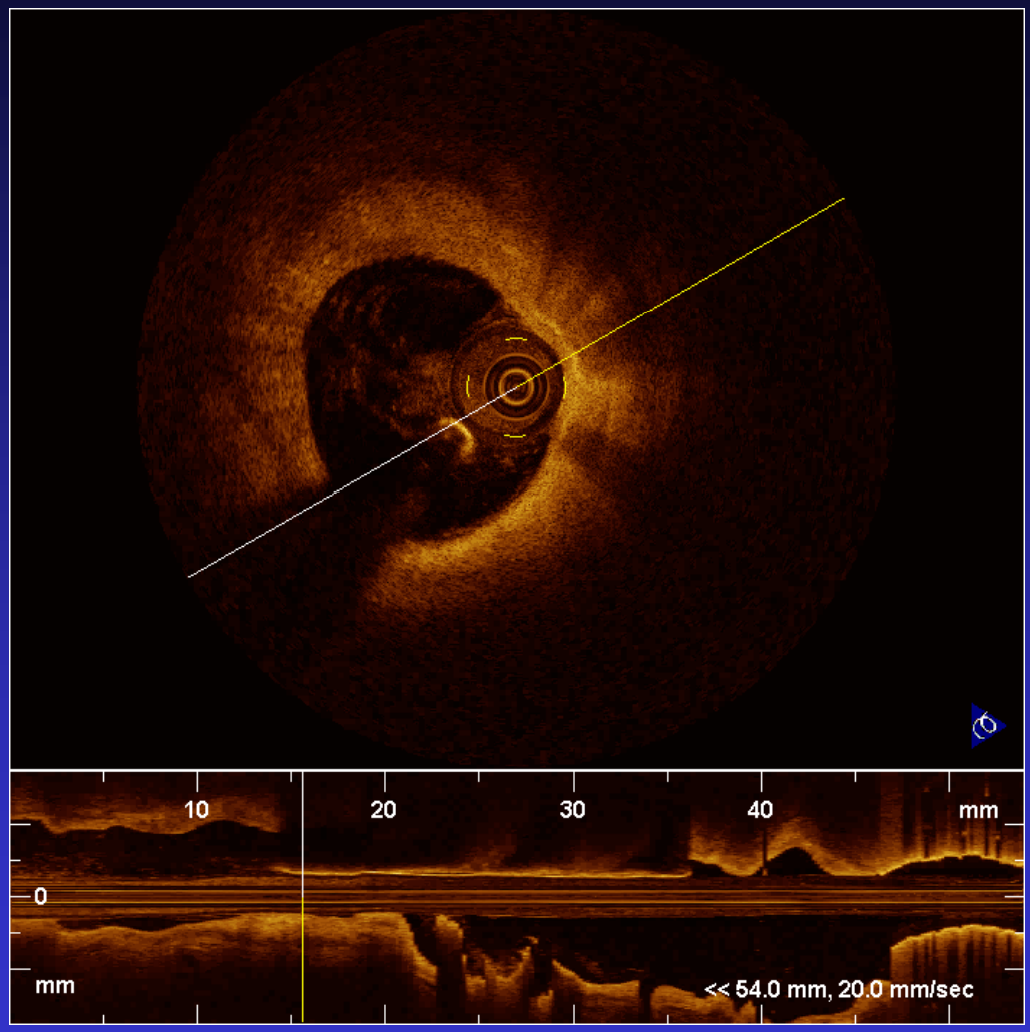
1. **OCT (C7) to the LAD**
2. **Pre-dilatation by a 3.5×12mm semi-compliant balloon**
3. **Stent implantation (3.5×25mm BMS)**
4. **Post-dilatation (18 atm)**
5. **OCT(C7) to the LAD & LCx**

Staged PCI to the LCX lesion (4/20)

1. **OCT (C7) to LCx**
2. **Stent implantation (3.5×18mm BMS)**
3. **Post-dilatation (18 atm)**

LCx one week later in UAP (56 y.o. male)





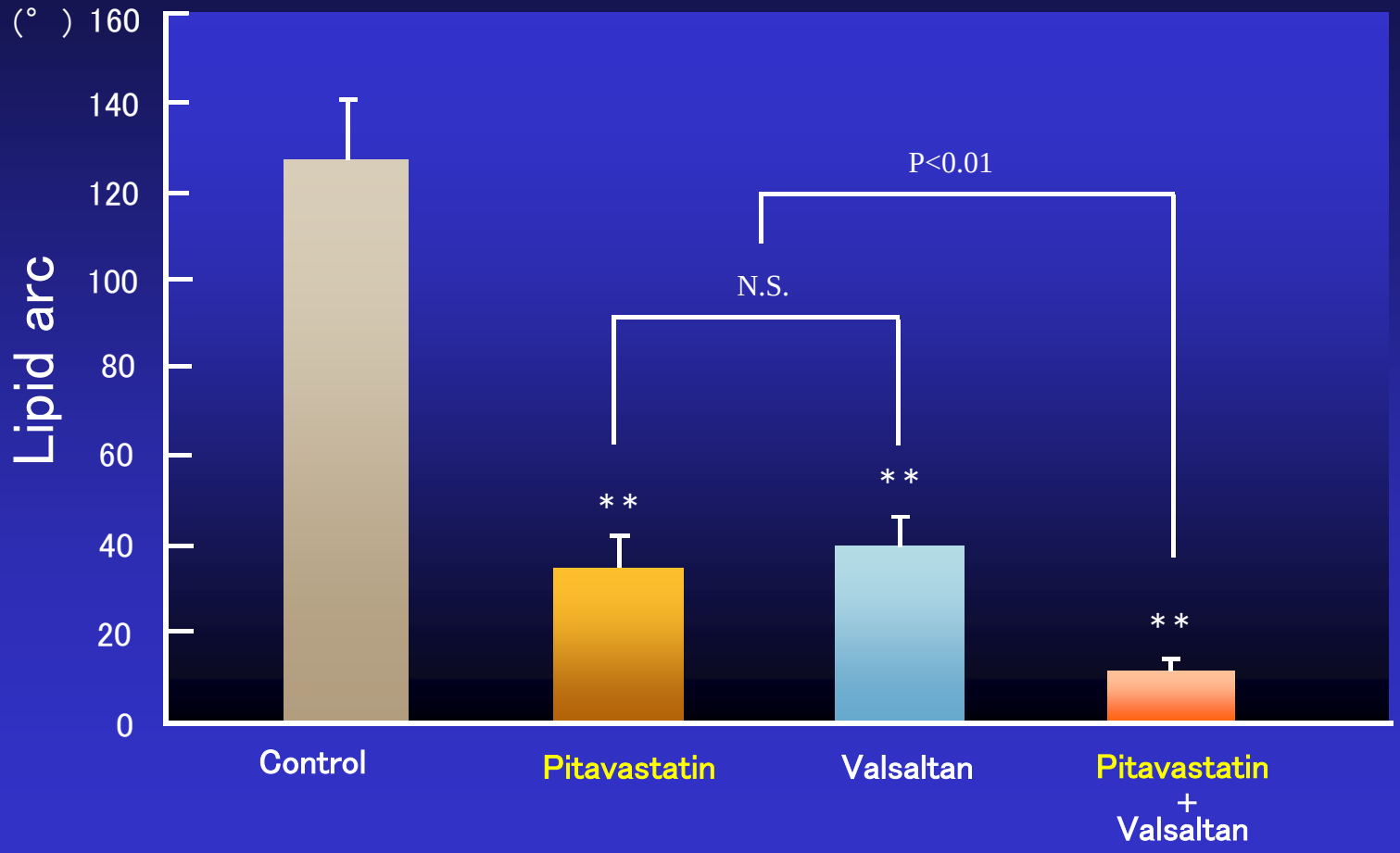
Conclusions

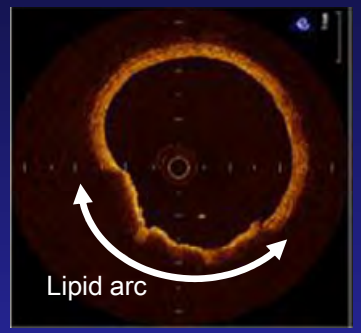
By higher resolution (10μm) and superior ability of tissue characterization, OCT may allow us to

- **assess coronary lesion morphology in ACS in detail.**
- **identify various types of vulnerable plaque correctly.**
- **estimate the effects of various drugs on plaque characteristics.**
- **assess the pathophysiology of coronary artery.**

Effect of pitavastatin on plaque morphology（WHHL-MI rabbit ）

Lipid arc assessed by OCT





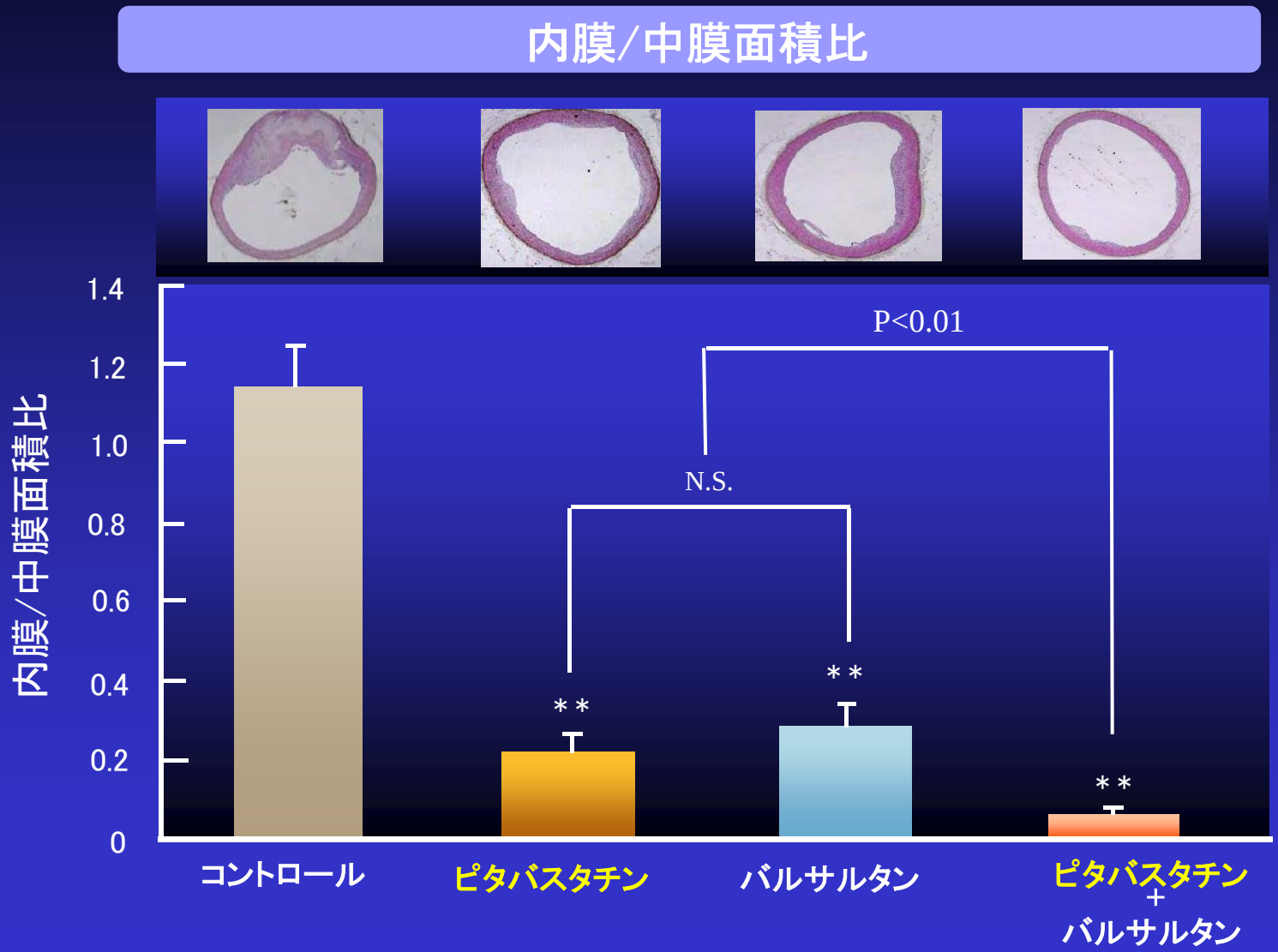
Lipid arc：

* * P<0.01 vs control Scheffie's test Mean±SEM

【Method】WHHL-MI rabbit, Pitavastatin 0.5mg/kg/day, Valsaltan 5mg/kg/day or both for 8 weeks.

Imanishi T, Akasaka T, et al.:Hypertens Res Vol. 31, No. 6 (2008)

ピタバスタチンのプラーク形成抑制作用（WHHL-MIウサギ）



＊＊ P<0.01 vs control Scheffie's test

Mean±SEM

【方法】WHHL-MIウサギにピタバスタチン0.5mg/kg/day、バルサルタン5mg/kg/dayおよび両者を8週間飲水投与した。

Imanishi T, Akasaka T, et al.:Hypertens Res Vol. 31, No. 6 (2008)

Wakayama Medical University

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Difference between IVUS and OCT

IVUS

OCT