Imaging Detection of Vulnerable Plaques
Invasive Imaging

Takashi Akasaka, MD, PhD, FESC
Department of Cardiovascular Medicine
Wakayama Medical University, Japan

TCTAP 2016

Wakayama Medical University

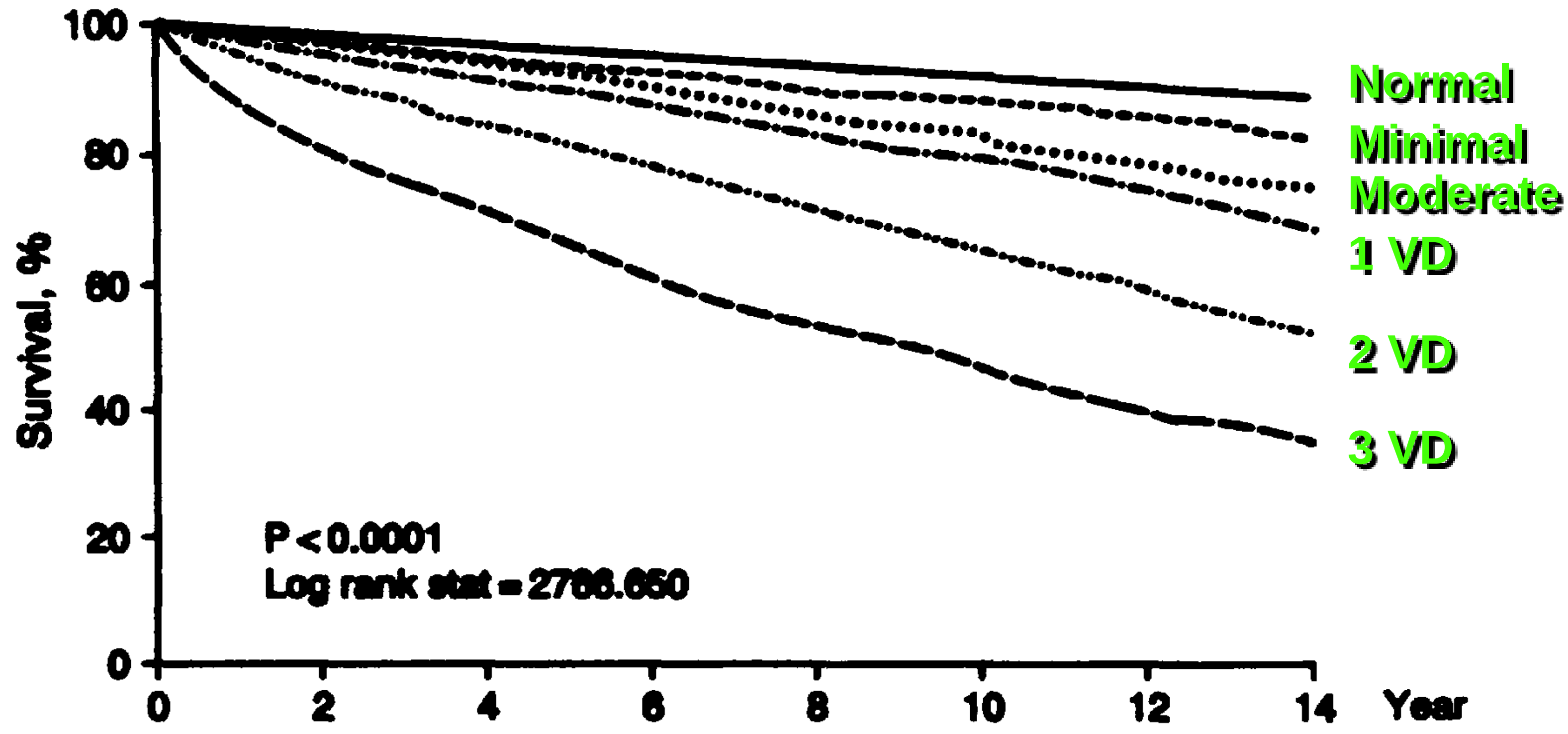
Declaration of Interest

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** : Daiichi-Sankyo Pharmaceutical Inc.
  Goodman Inc.
  St. Jude Medical Japan
  Terumo Inc.

CASS Registry

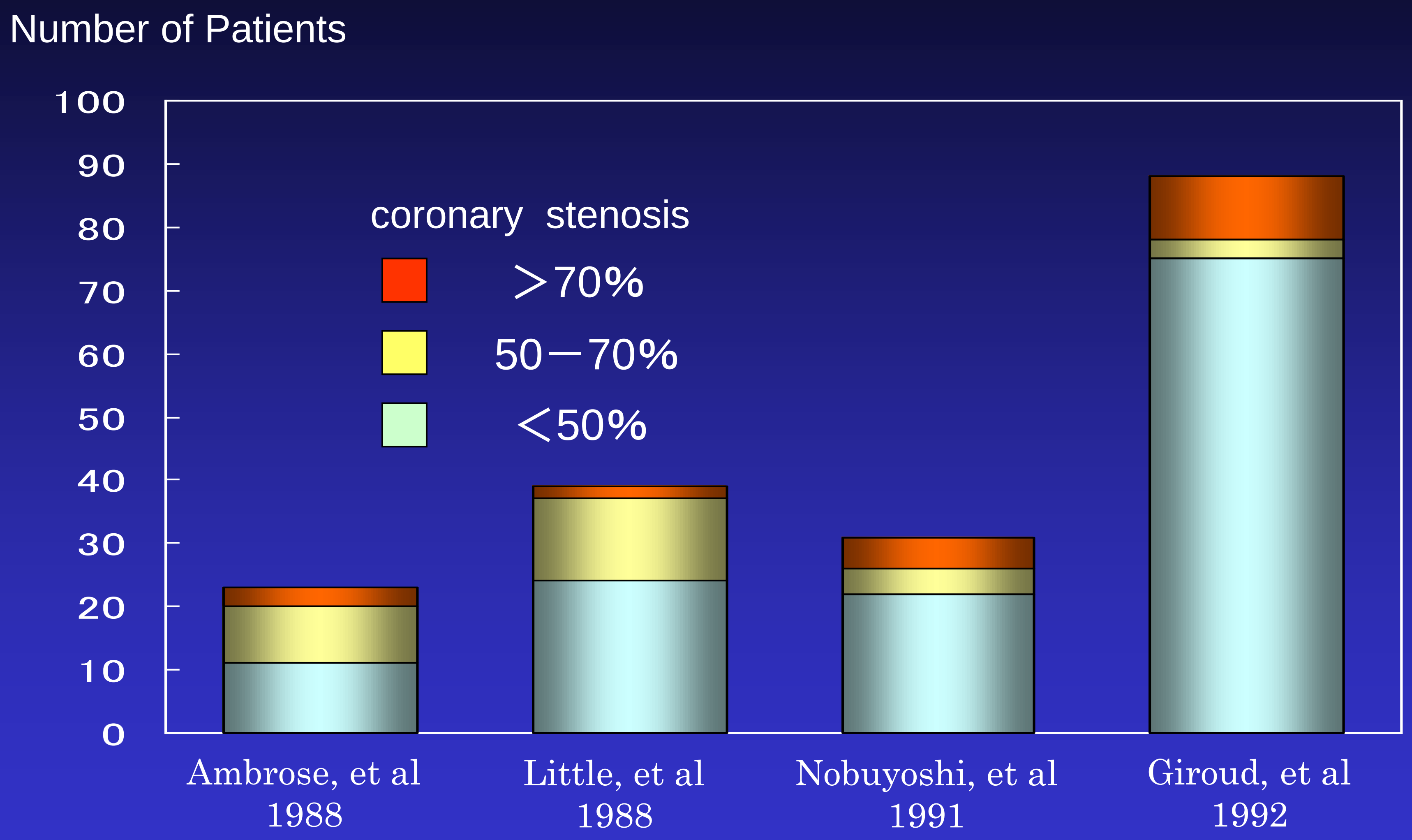


No.	%	No.	%	No.	%	No.	%		DISVES
4,463	100	4,352	98	4,196	95	3,202	91	———	0 (norm)
1,368	100	1,288	95	1,197	91	881	86	- - - - -	0 (min)
927	100	790	94	691	86	486	79	········	0 (mod)
4,818	100	2,868	92	2,385	84	1,559	74	—·—·—	1
5,286	100	1,897	85	1,410	72	784	59	-··-··-	2
6,536	100	1,384	71	917	54	490	40	— — —	3

Degree of stenosis & the number of diseased vessel might relate to future event.

Emond M, et al. Circulation 90:2645-2657, 1994

Previous coronary diameter stenosis at the culprit site of AMI pts.

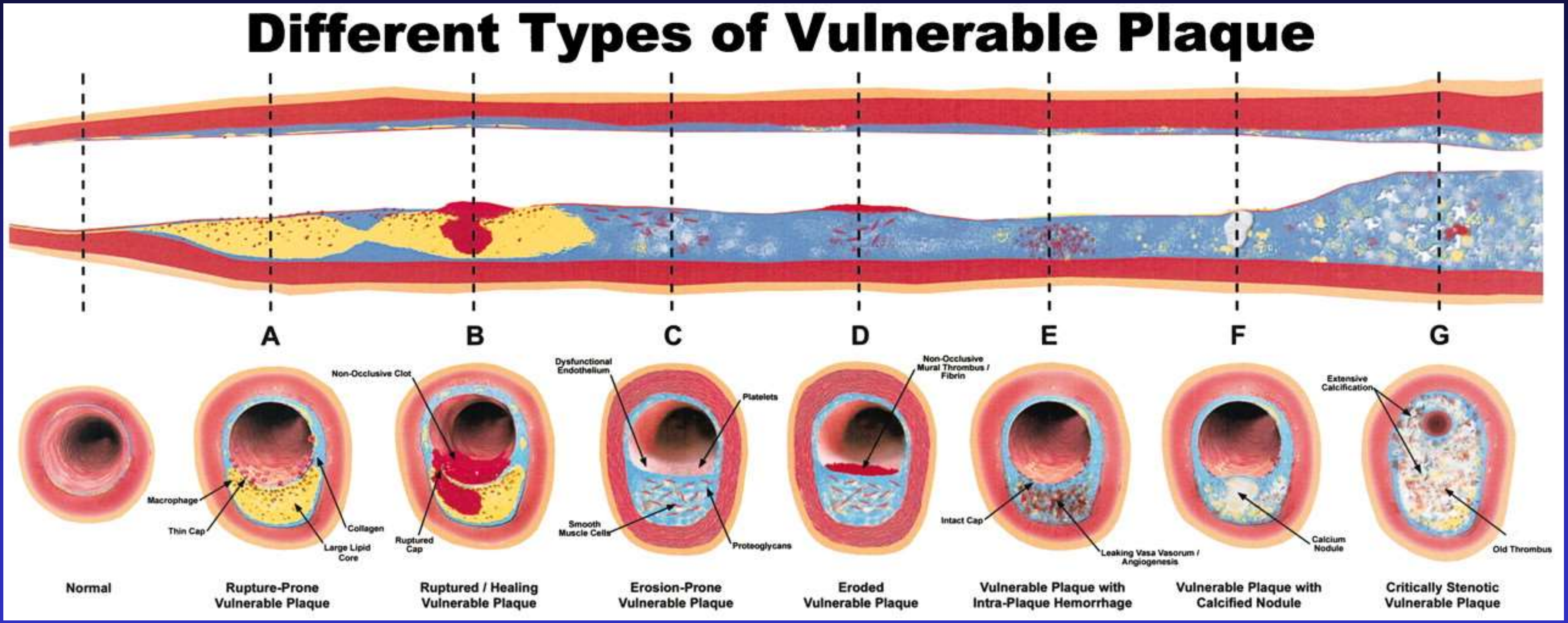


Degree of stenosis by angiography might not be enough to predict future event.

Wakayama Medical University

動脈硬化プラークの進展 P. Circulation 2001;104:365-372

Progression of atheroscrelosis & vulnerable plaques



(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

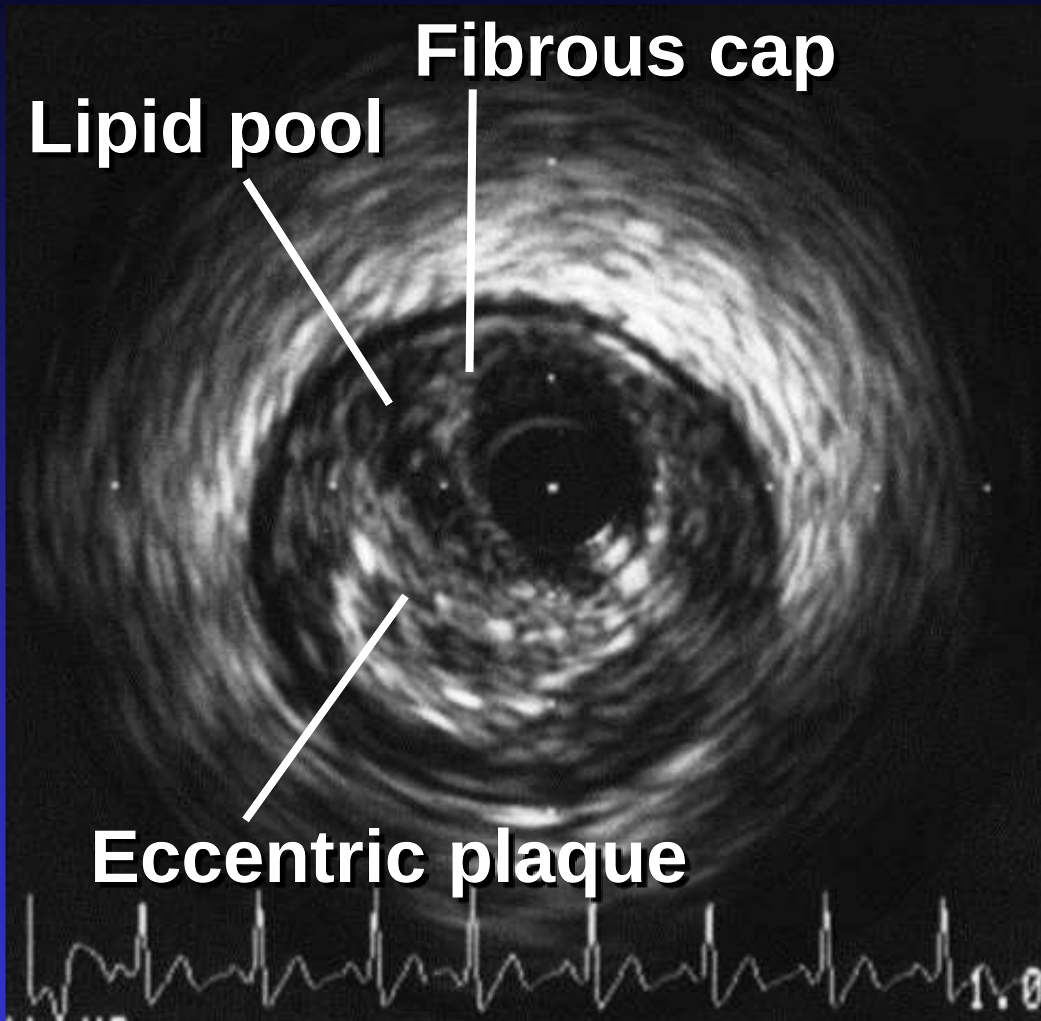
- Active inflammation
  (monocyte/macrophage and sometimes T-cell infiltration)
- Thin cap (< 65 μm) with large lipid core
- Endotherial denudation with superficial platelet aggregation
- Fissued plaque
- Stenosis > 90%

Minor criteria

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

Wakayama Medical University

Vulnerable plaque



① Positive remodering

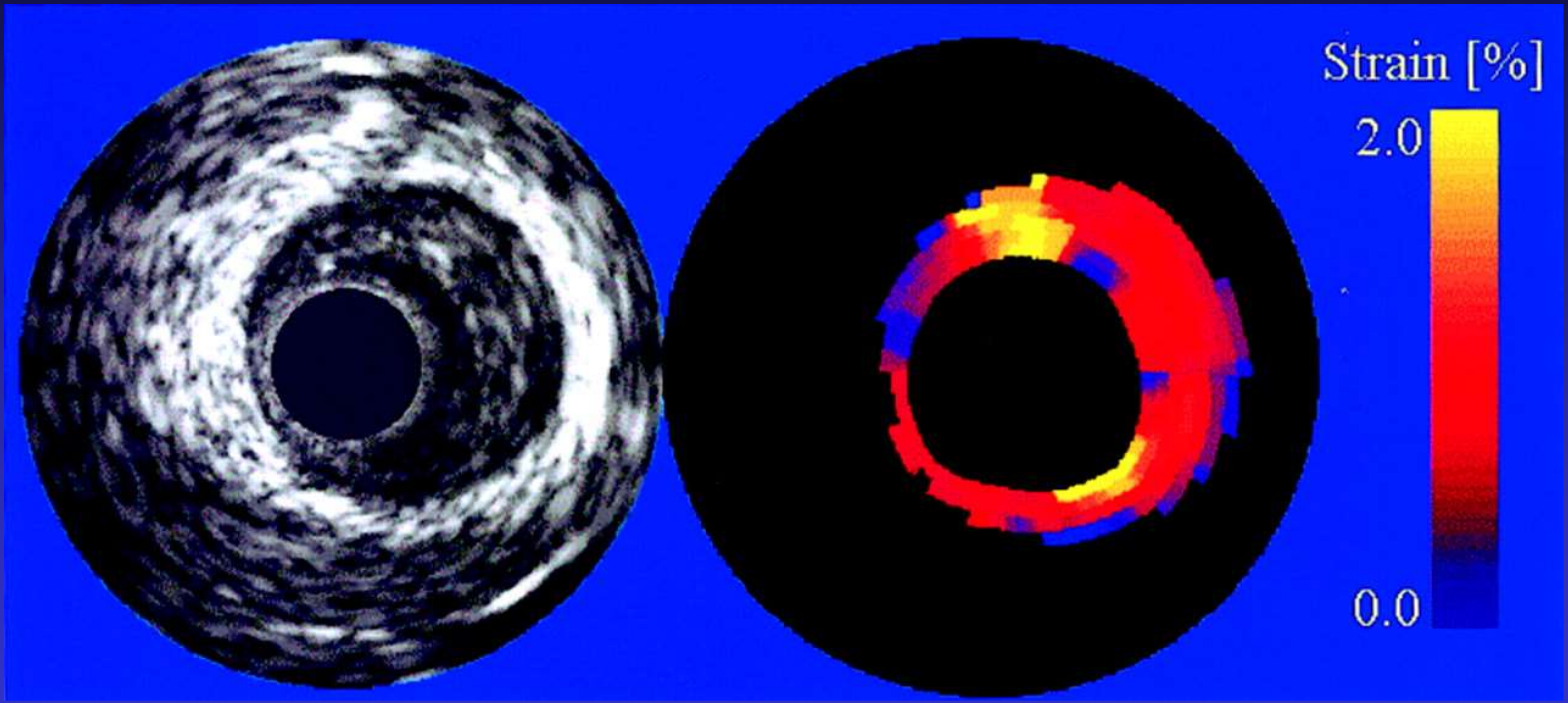
② Eccentric plaque

③ Low echoic area
(lipid pool)

④ Thin fibrous cap

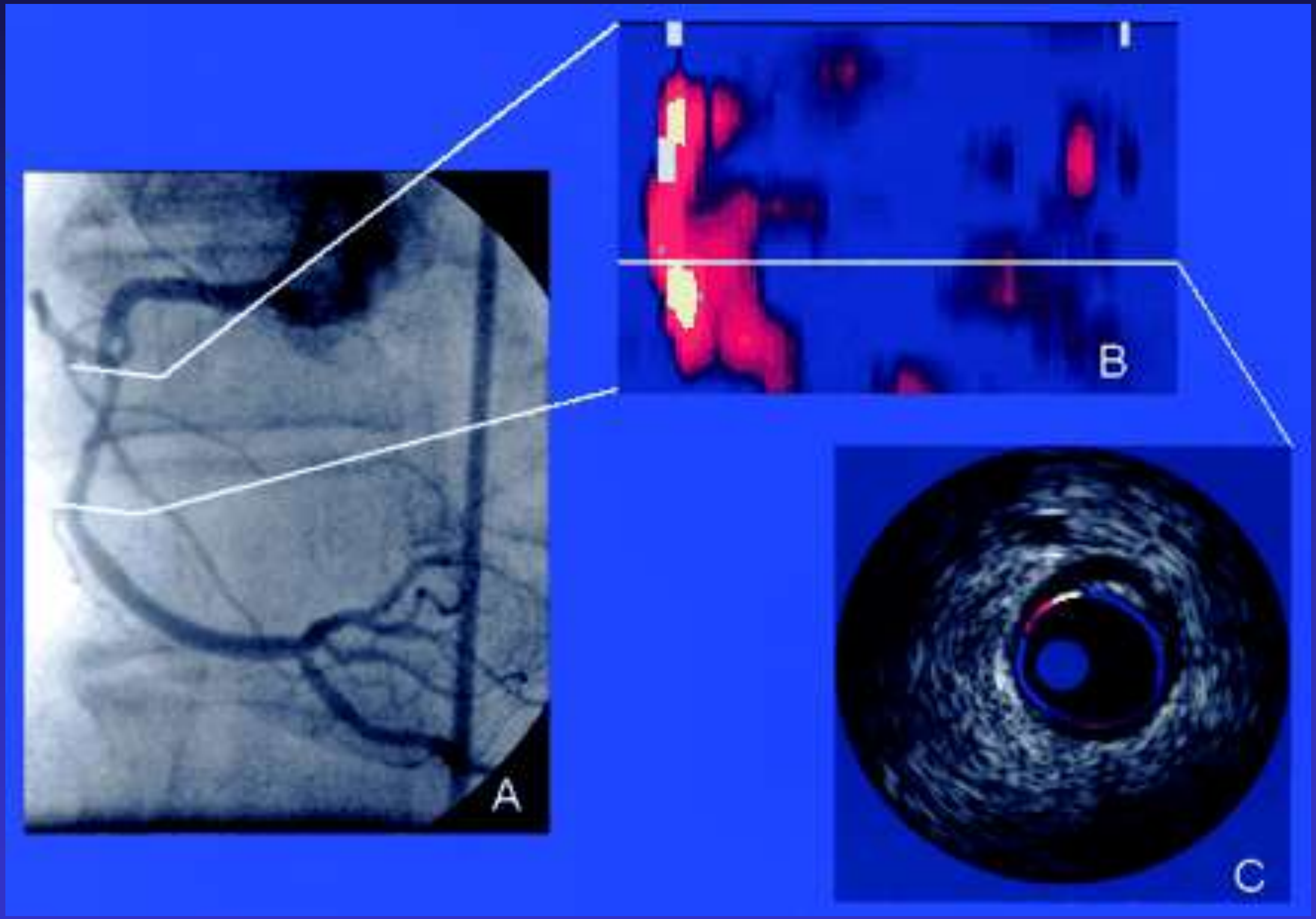
IVUS allow us to identify plaque characteristics, but it is not sufficient enough to detect VP.

IVUS elastography



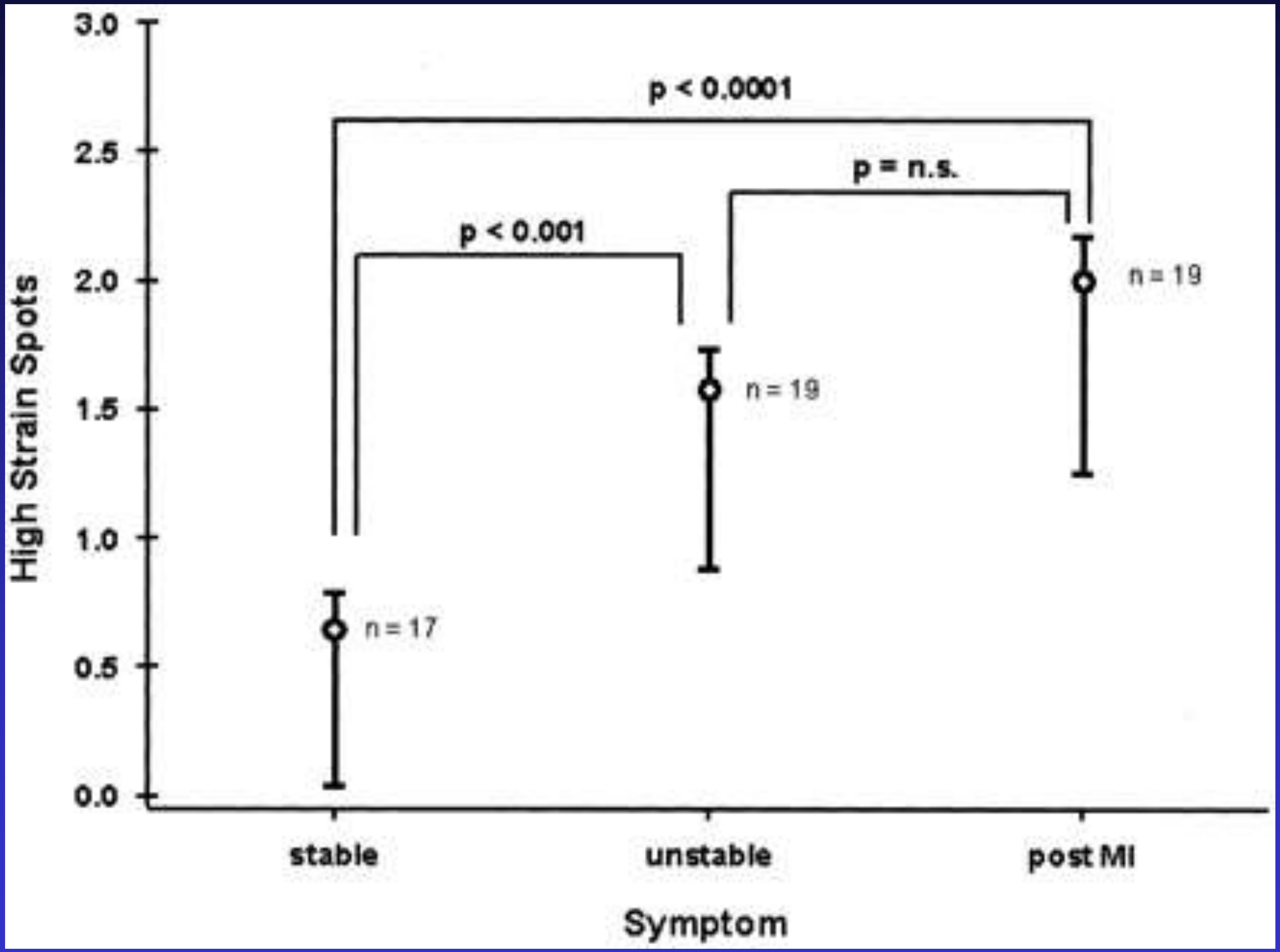
(Schaar JA, et al. Circulation 106: 2636 - 2641, 2003)

IVUS palpography



(Schaar JA, et al. Circulation 109: 2716 - 2719, 2004)

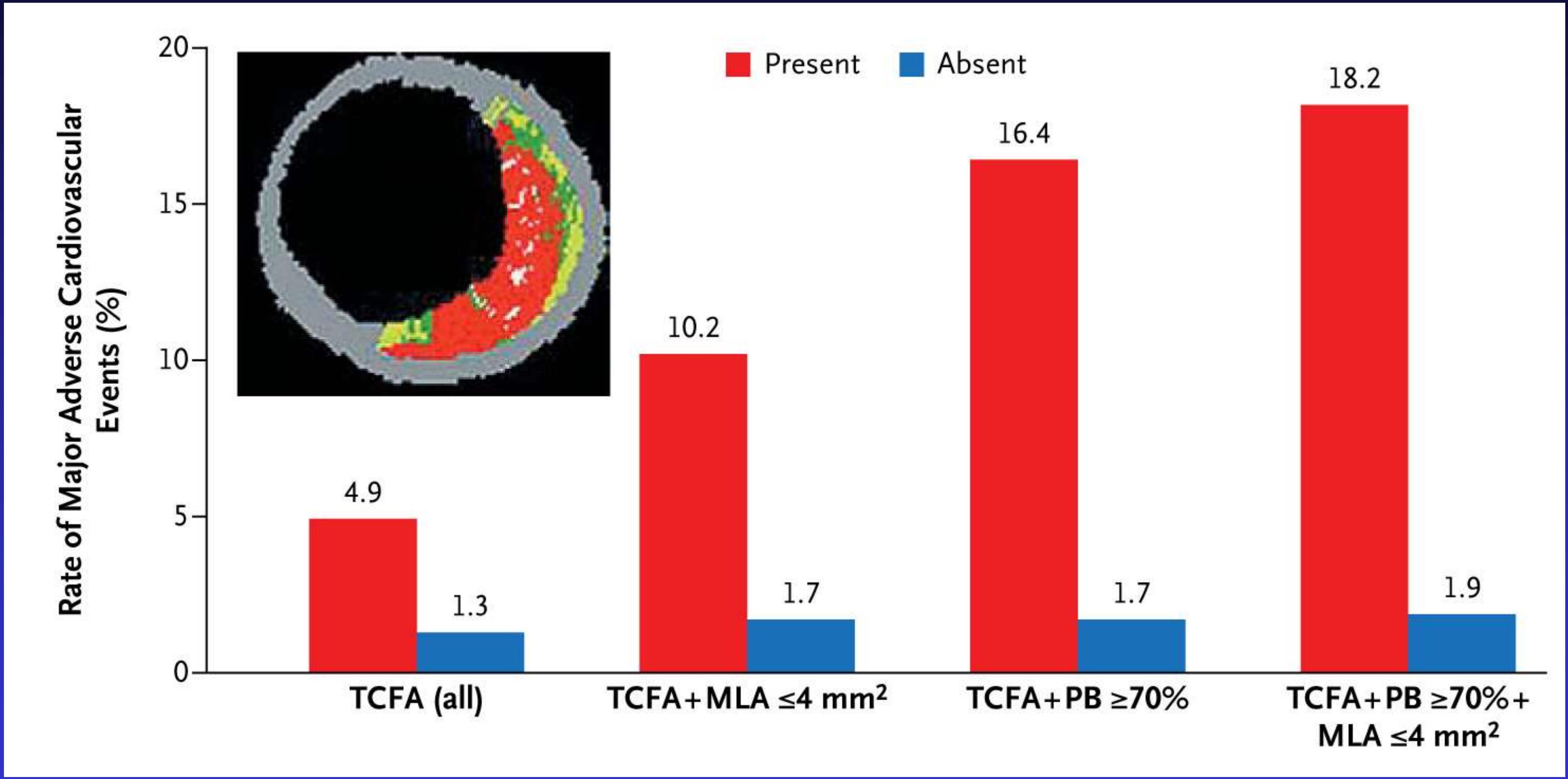
IVUS palpography



(Schaar JA, et al. Circulation 109: 2716 - 2719, 2004)

PROSPECT trial

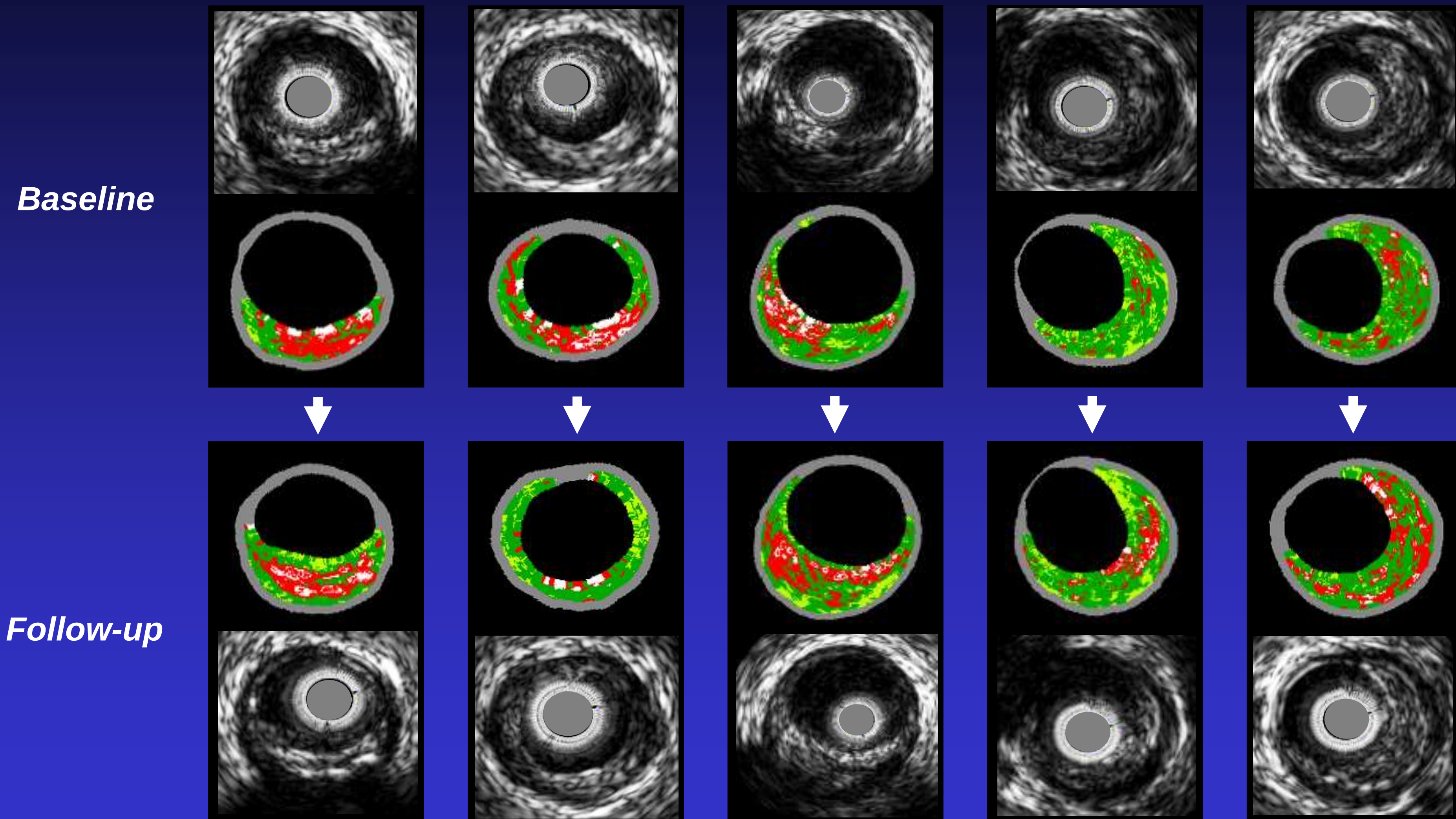
(Stone GW, et al. N Engl J Med 364:226-235, 2011)



Predictive value of IVUS tissue characterization is not so high compared with gray-scale IVUS information such as MLA & PB.

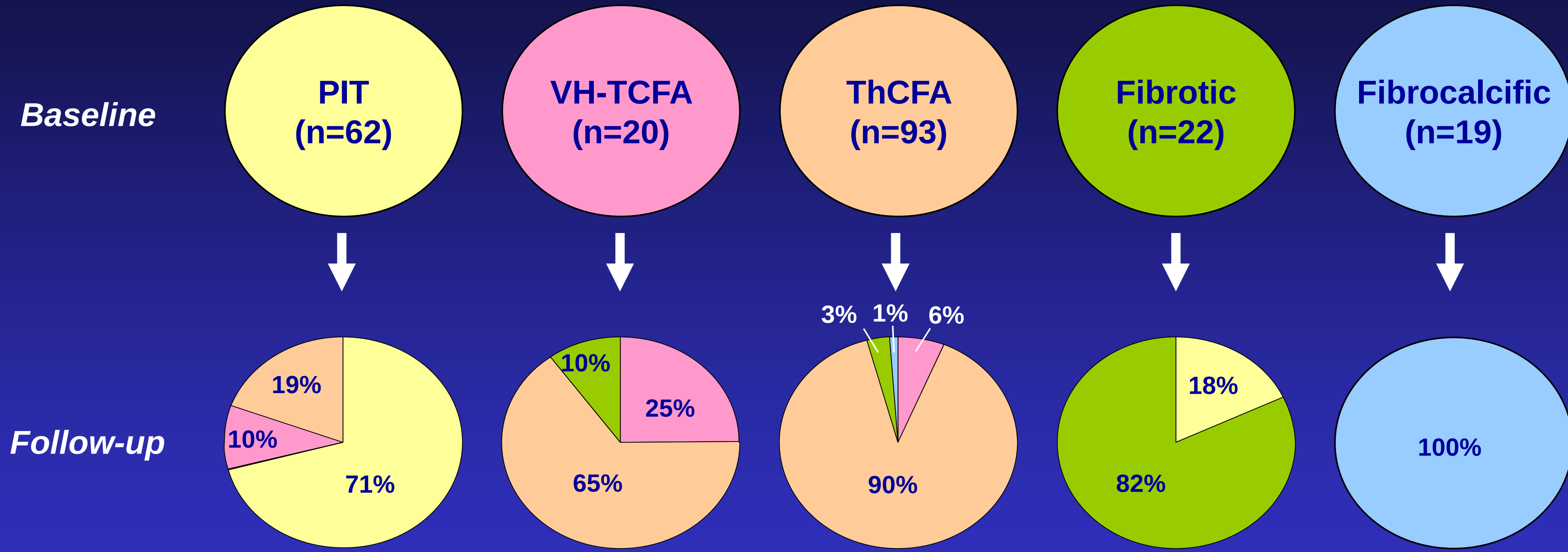
Wakayama Medical University

Representative images of serial VH-IVUS



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

Changes in plaque characteristics

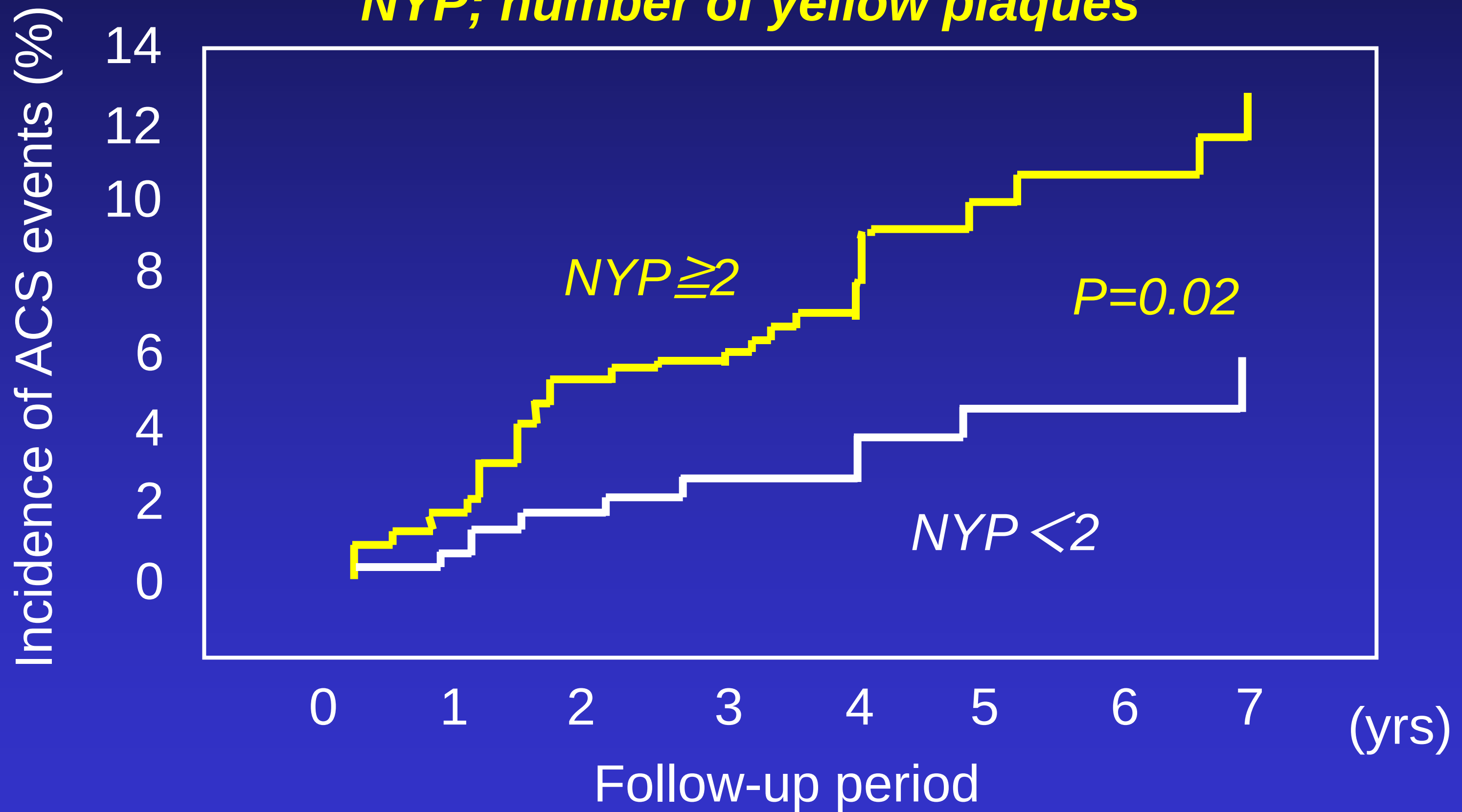


During follow-up, 75% of VH-TCFA evolved into a ThCFA or fibrotic plaque, and 25% remain unchanged. Conversely, 10% of PIT and 6% of ThCFA evolved into VH-TCFAs. No fibrotic plaque and fibrocalcific plaque evolved into fibroatheromas.

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

Incidence of ACS events in pts with multiple yellow plaques

NYP; number of yellow plaques



Ohtani T, Ueda Y, Mizote I et al. Number of yellow plaques detected in a coronary artery is associated with future risk of acute coronary syndrome: detection of vulnerable patients by angioscopy. J Am Coll Cardiol. 47(11):2194-2200, 2006

Wakayama Medical University

Demonstration of Multi-vessel Instability

Angioscopy

- Asakura M, et al. : J Am Coll Cardiol 2001;37:1284-1288
- Ohtani T, et al. : J Am Coll Cardiol 2006;47:2194-2200

Gray Scale IVUS

- Rioufol, et al. : Circulation 2002;106:804-808
- Hong MK, et al. : Circulation 2004;110:928-933

VH-IVUS

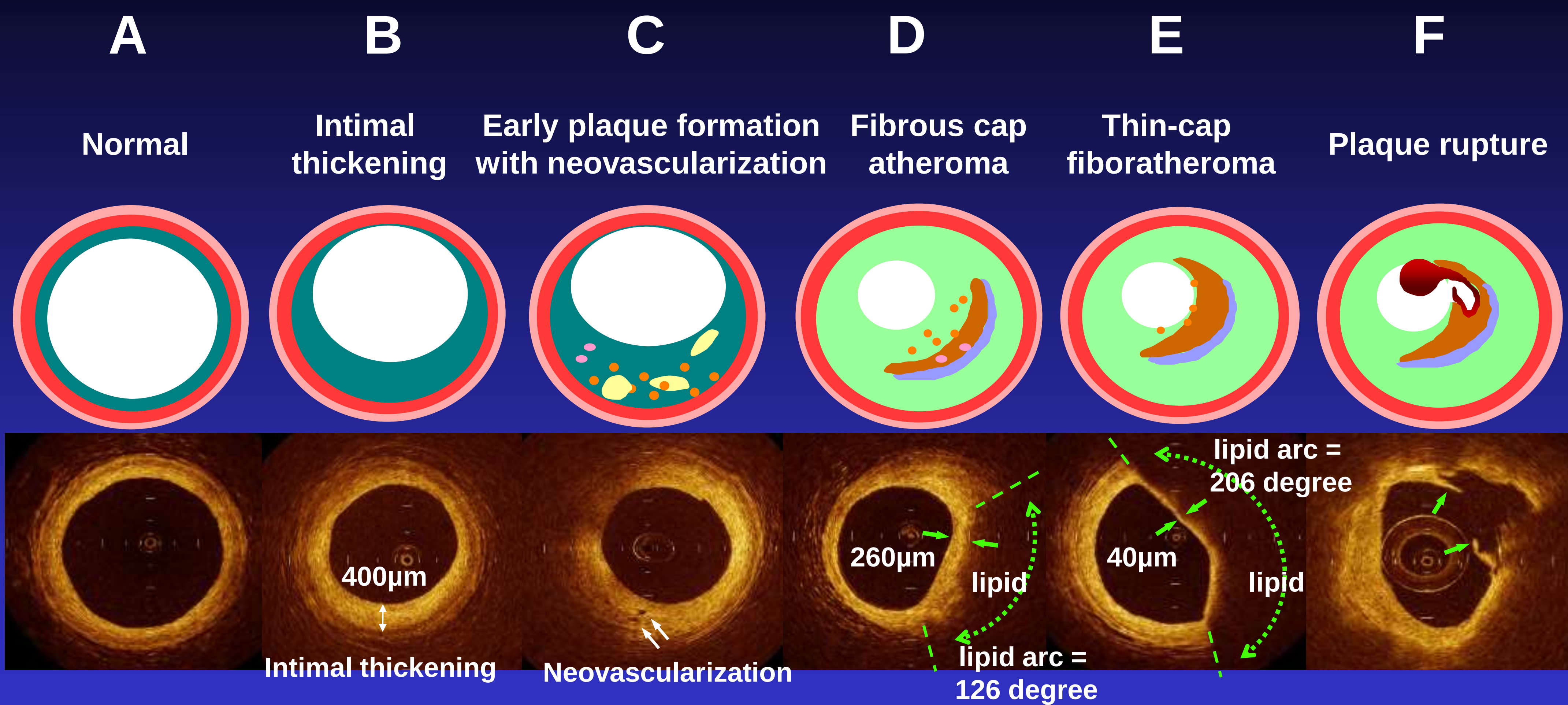
- Hong MK, et al. : Am J Cardiol 2008;101:568-572

OCT

- Kubo, et al. : Am J Cardiol 2010;105:318-322
- Fukunaga M, et al. : EuroInterv 2012;8:955-961

Multi-vessel & lesion instability could be useful to predict future events not for per each lesion or vessel but for per patient.

Progression of atherosclerosis & corresponding OCT Images

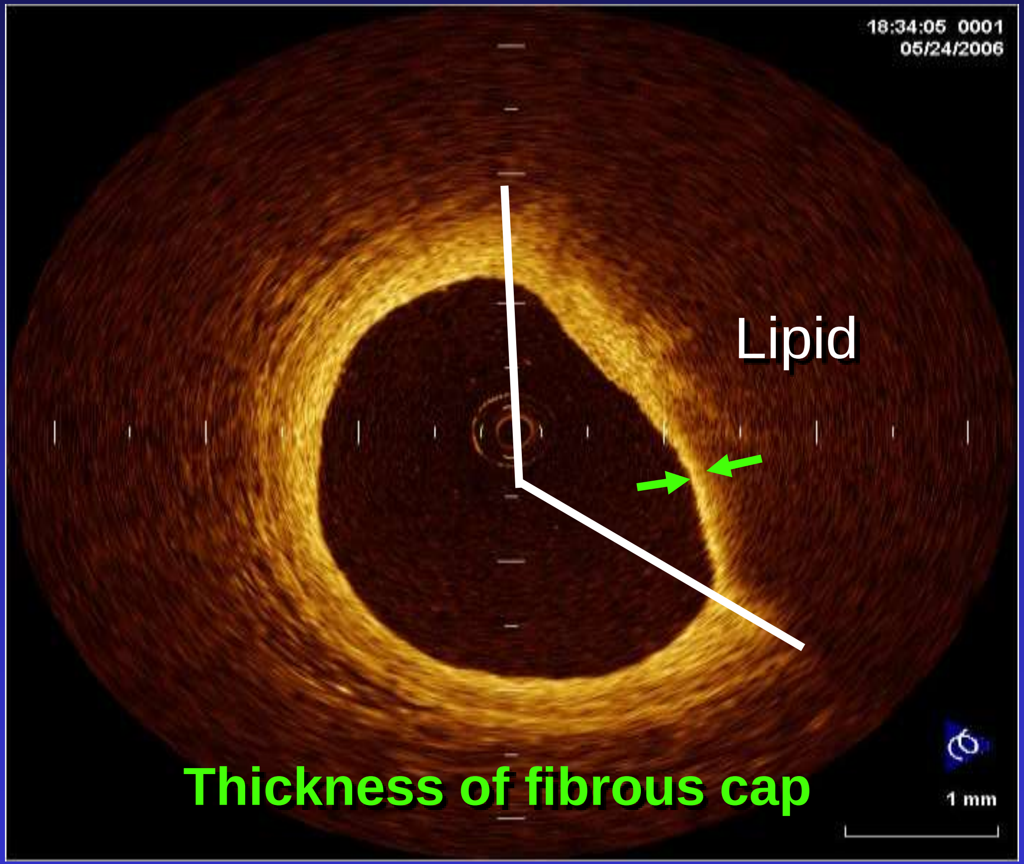


- Extracelluler lipid
- Machrophage form cells
- Smooth muscle cells
- Neovascular vessel
- Necrotic core
- Calcified plaque
- Thrombus
- Collagen

Wakayama Medical University

Thin-capped Fibroatheroma (TCFA)

TCFA is thought to be a plaque prone to rupture and vulnerable because 60% of ACS is developping by the rupture of TCFA.



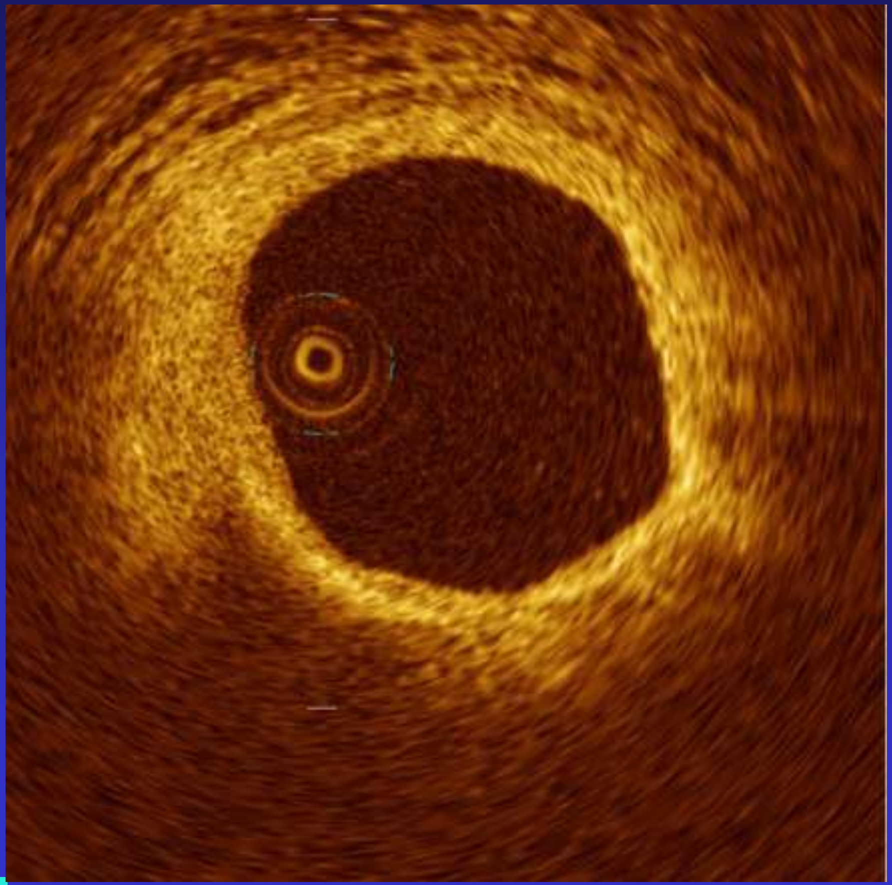
TCFA was defined as a plaque with lipid content in more than 2 quadrants and the thinnest part of a fibrous cap thickness less than 65 by histology and up to 150 μm by OCT.

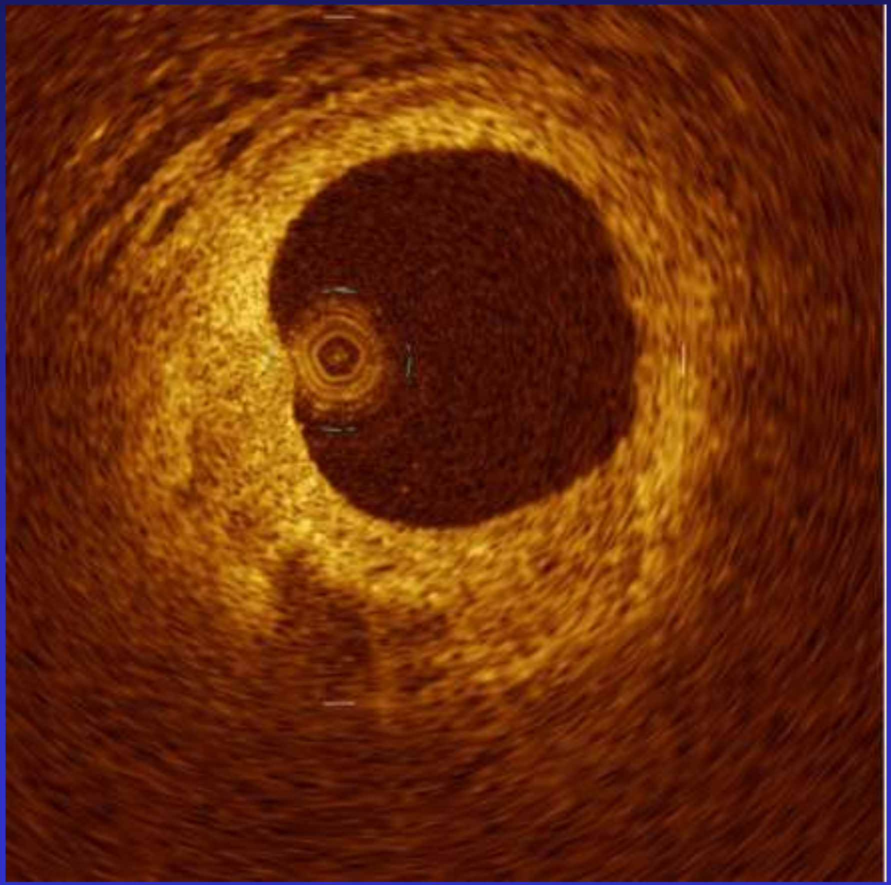
(Circulation. 2008,118: 2368-73)

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

Decrease of macrophage density during 20mg/day of Atorvastatin

Baseline — **12-month follow-up**

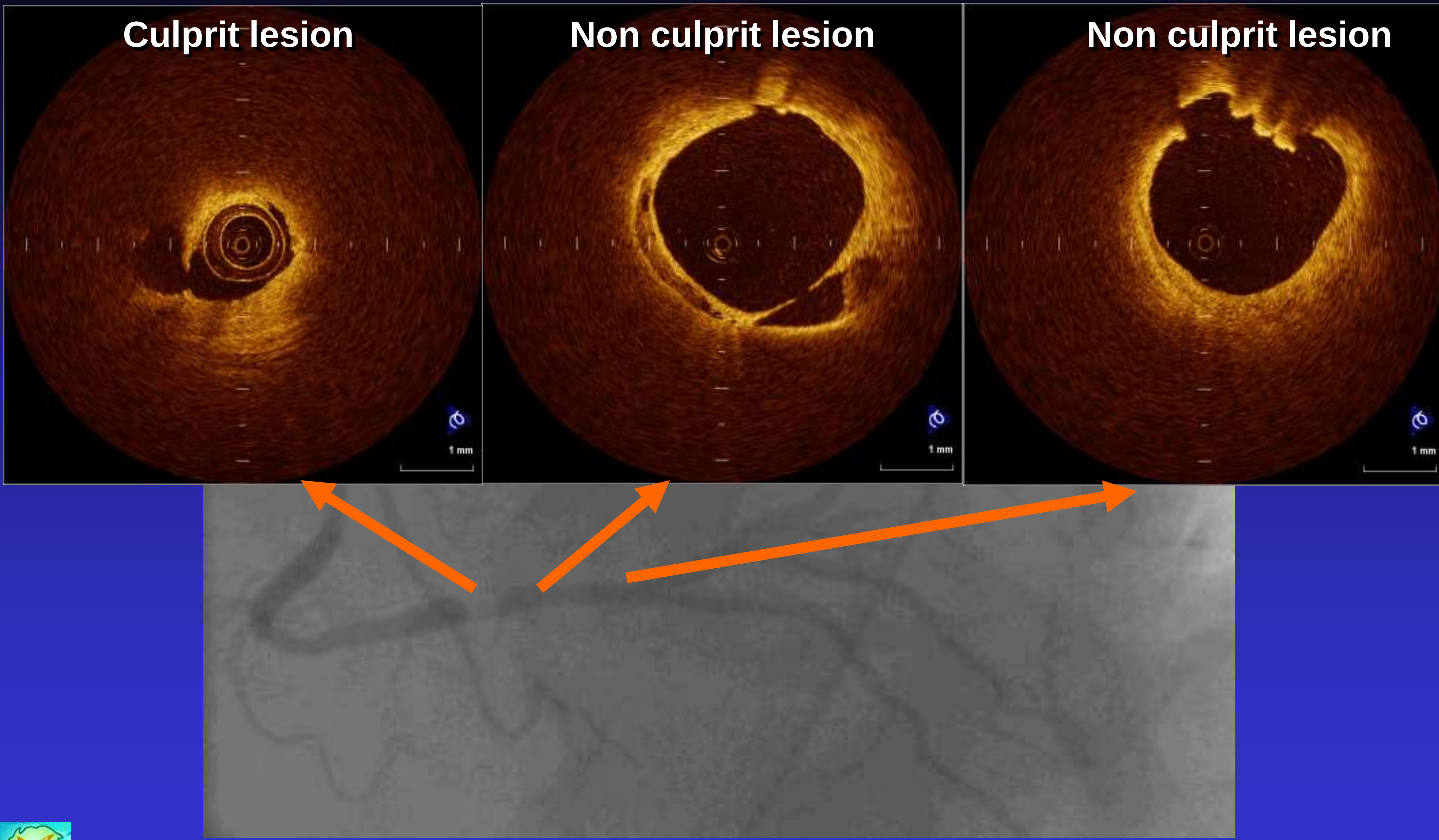




Komukai K, et al. J Am Coll Cardiol 2014 in press

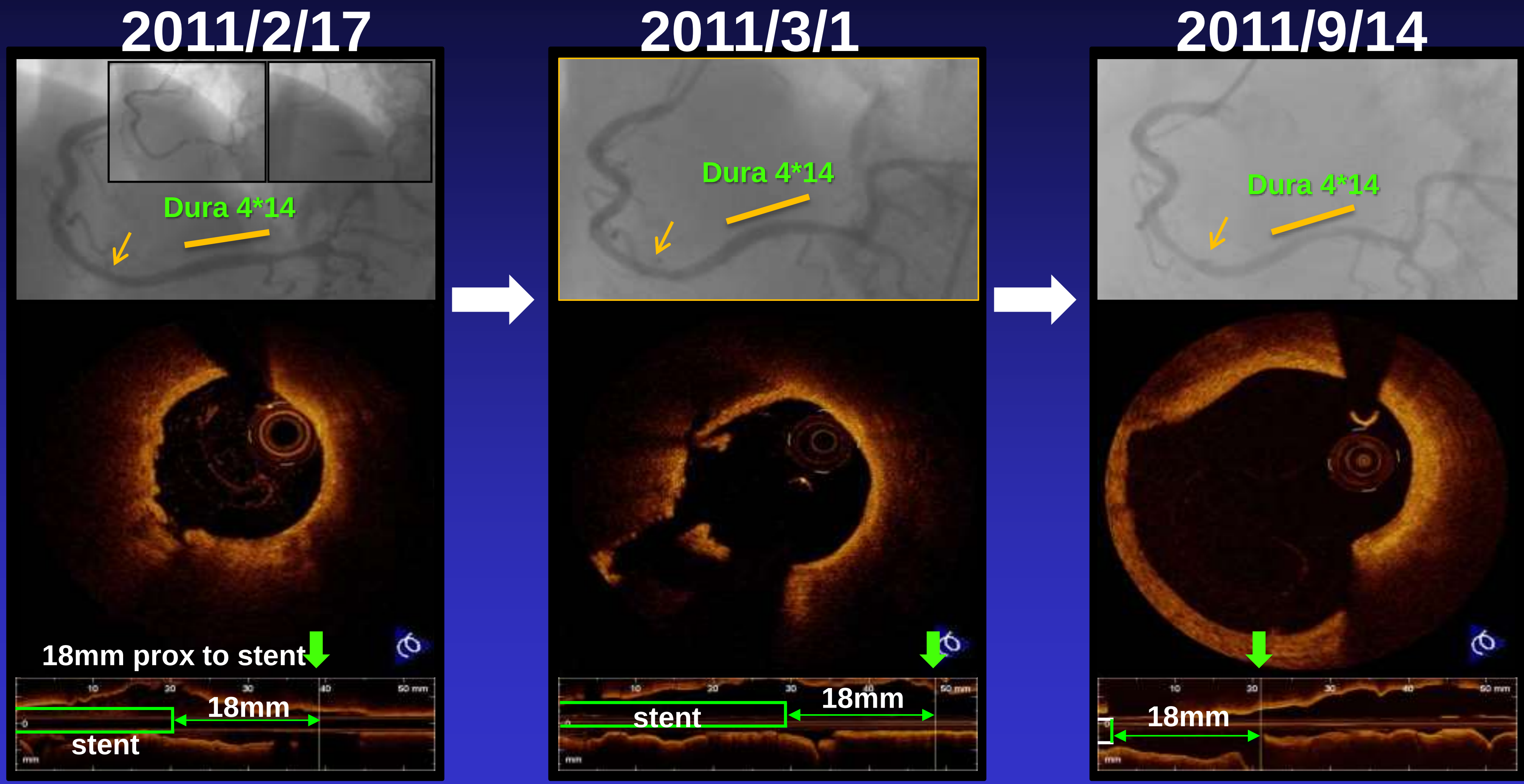
Wakayama Medical University

Unstable AP



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

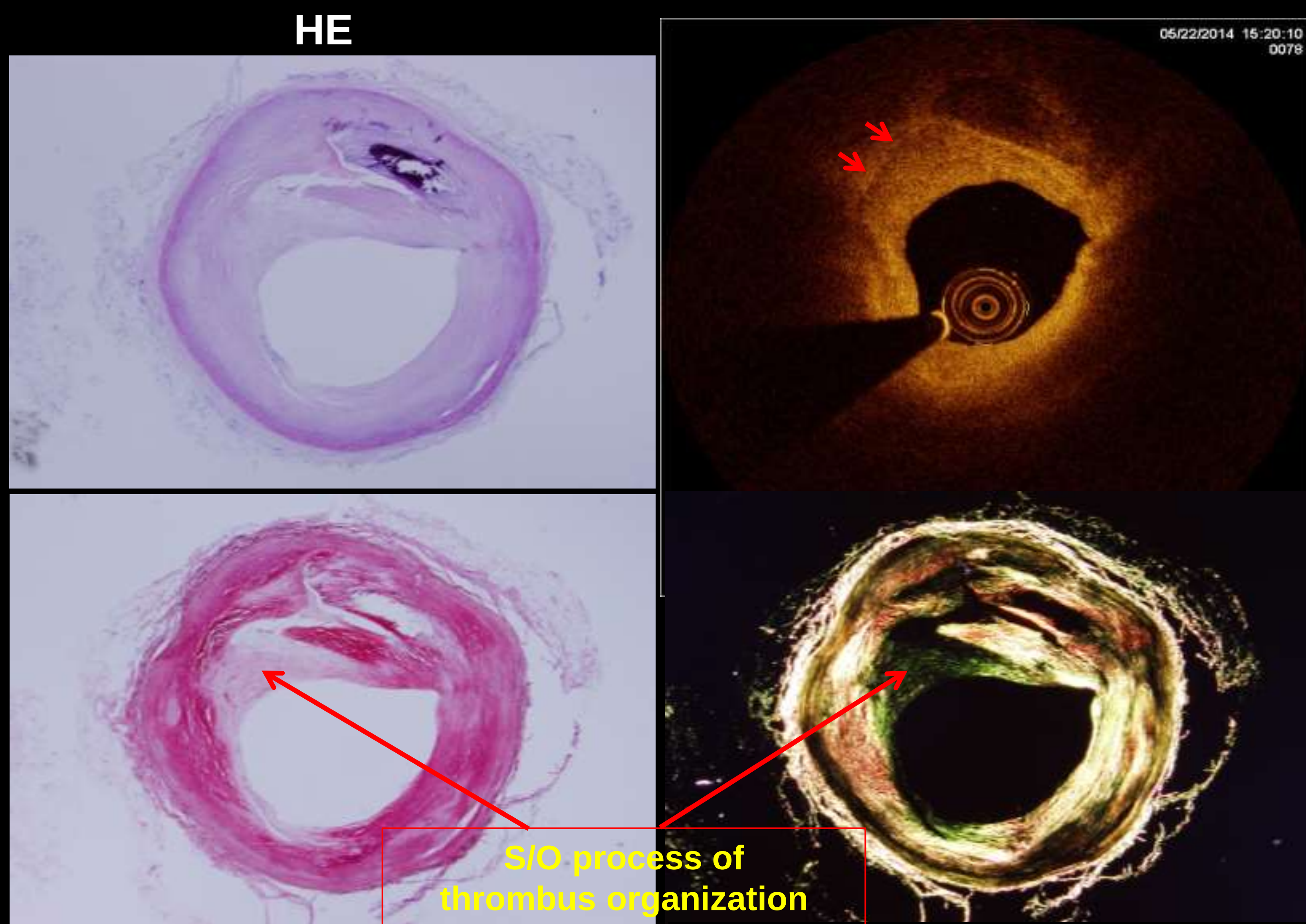
Plaque rupture; serial OCT



Wakayama Medical University

4406 4b

An Example of layered structure



Sirius red stain
(Collagen : red)

Sirius red stain with polarized
TypeⅢ(immature) collagen : green
TypeⅠ(mature) collagen: orange

niversity

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

CrossMark

Kunihiro Shimamura, Yasushi Ino*, Takashi Kubo, Tsuyoshi Nishiguchi, Takashi Tanimoto, Yuichi Ozaki, Keisuke Satogami, Makoto Orii, Yasutsugu Shiono, Kenichi Komukai, Takashi Yamano, Yoshiki Matsuo, Hironori Kitabata, Tomoyuki Yamaguchi, Kumiko Hirata, Atsushi Tanaka, Toshio Imanishi, Takashi Akasaka

Department of Cardiovascular Medicine, Wakayama Medical University, 811-1 Kimiidera, Wakayama 641-8509, Japan

ARTICLE INFO

Article history:
Received 14 November 2013
Received in revised form
29 April 2014
Accepted 3 May 2014
Available online 5 June 2014

Keywords:
Silent plaque rupture
Optical coherence tomography
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.

Summary of Target Lesions Morphology by OCT

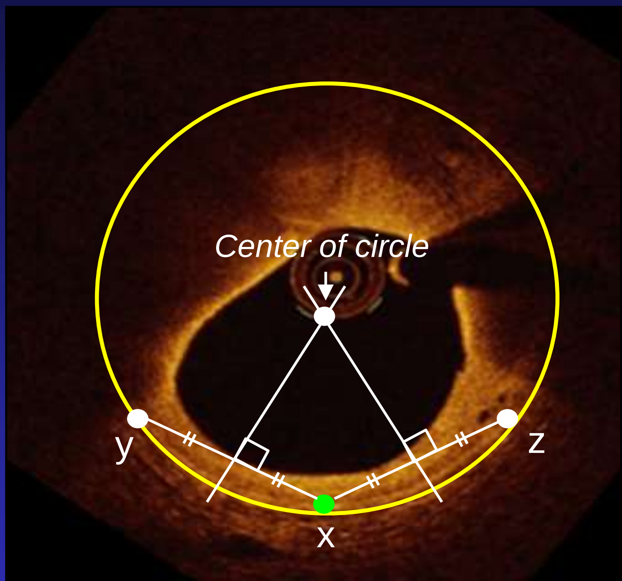
Kubo T, et al. J Am Coll Cardiol 50:933-939,2007
Ino Y, et al. JACC Cardiovasc Interv. 2011;4:76-82

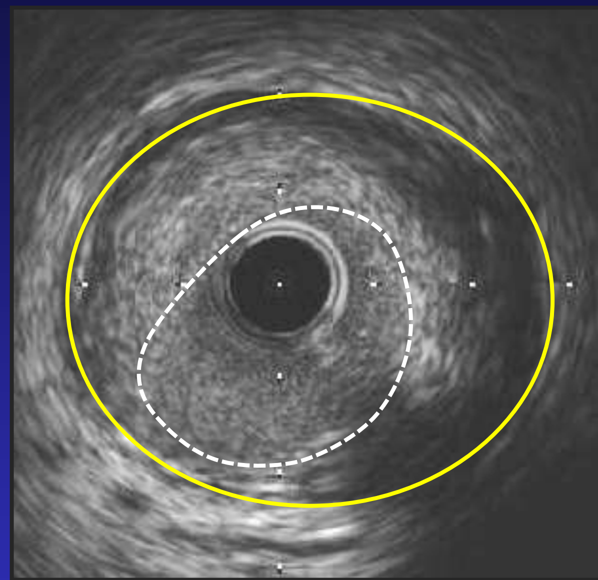
Mizukoshi M, et al. Am J Cardiol 2010, 106: 323-328
Shimamoto K, et al. Atherosclerosis 2014; 235:532-537

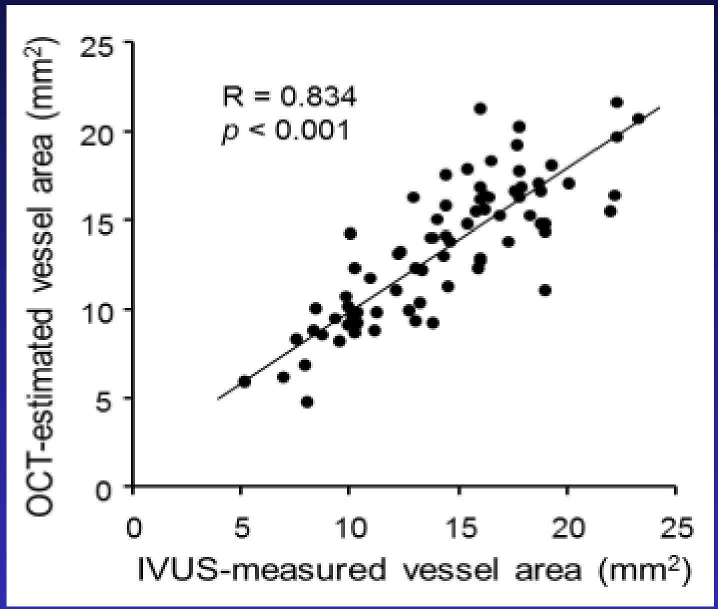
	STEACS		NSTEACS		Silent Plaque Rupture
Plaque rupture (%)	60-70	>	40-50		-
Lipid-rich plaque (>=2 quadrants), n(%)	80-90	>	70-80	>	50-70
Fibrous cap thickness, μm	30-140	<	40-160	<or =	40-100
TCFA, n(%)	70-80	>	40-50	>	-
Thrombus, n(%)	100	>	70-80	>	10-15
Red thrombus	70-80	>	20-30	>	<10
White thrombus	20-30	<	40-50	<	5-15
None	0	<	20-30	<	70-80
MLA (mm2)	0.5-2.0	<	0.5-4.0	<	1.5-4.0

Vessel circumference approximation in OCT

Feasibility of approximating algorithm of vessel circumference in OCT were evaluated in 80 coronary artery segments.







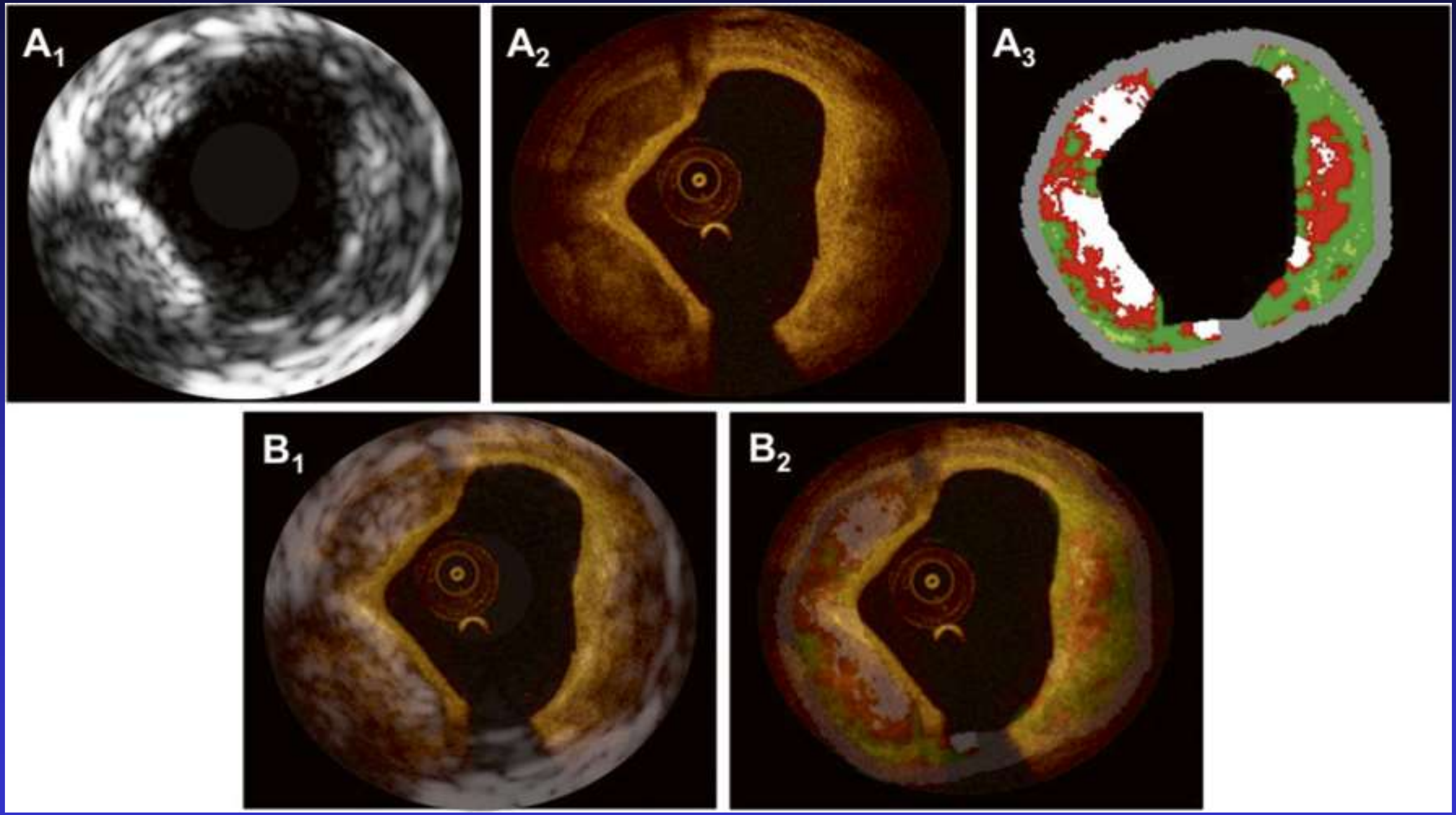
Three points (x, y, z) are placed on the visible circular arc. The central point (x) is connected with the other two points (y and z) by straight lines. Through the mid-point of each straight line, perpendicular line is drawn. Intersection of the two perpendicular lines is assumed to be the center of the circle. This makes circular approximation.

Conclusion: By approximating algorithm of vessel circumference, OCT can estimate vessel area even in coronary arteries with lipidic plaque.

Kubo T, Akasaka T et al, Circ J 2015:79;600-606

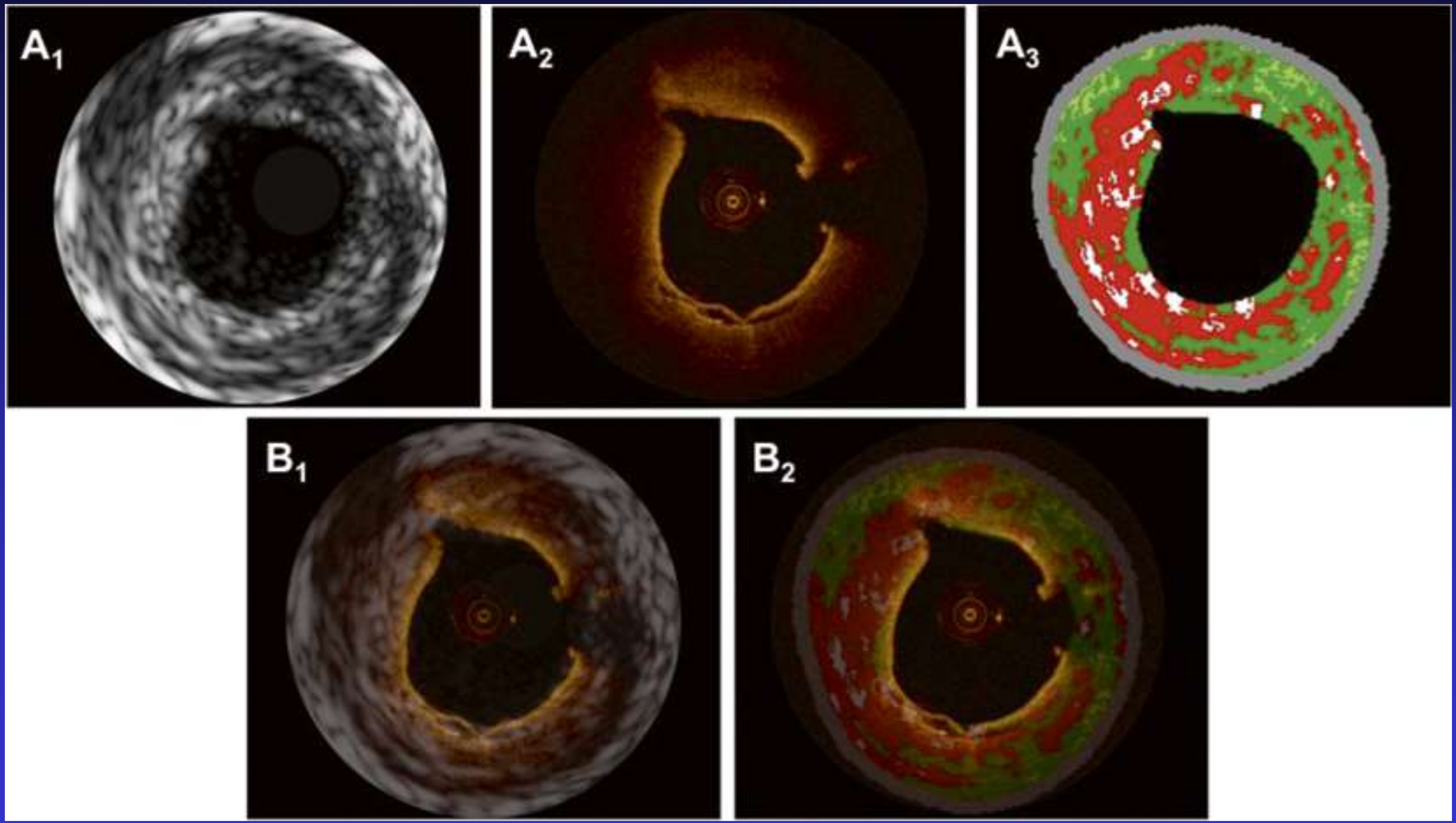
Wakayama Medical University

Fusion of co-registered IVUS & FD-OCT images for the analysis of human atherosclerotic plaques



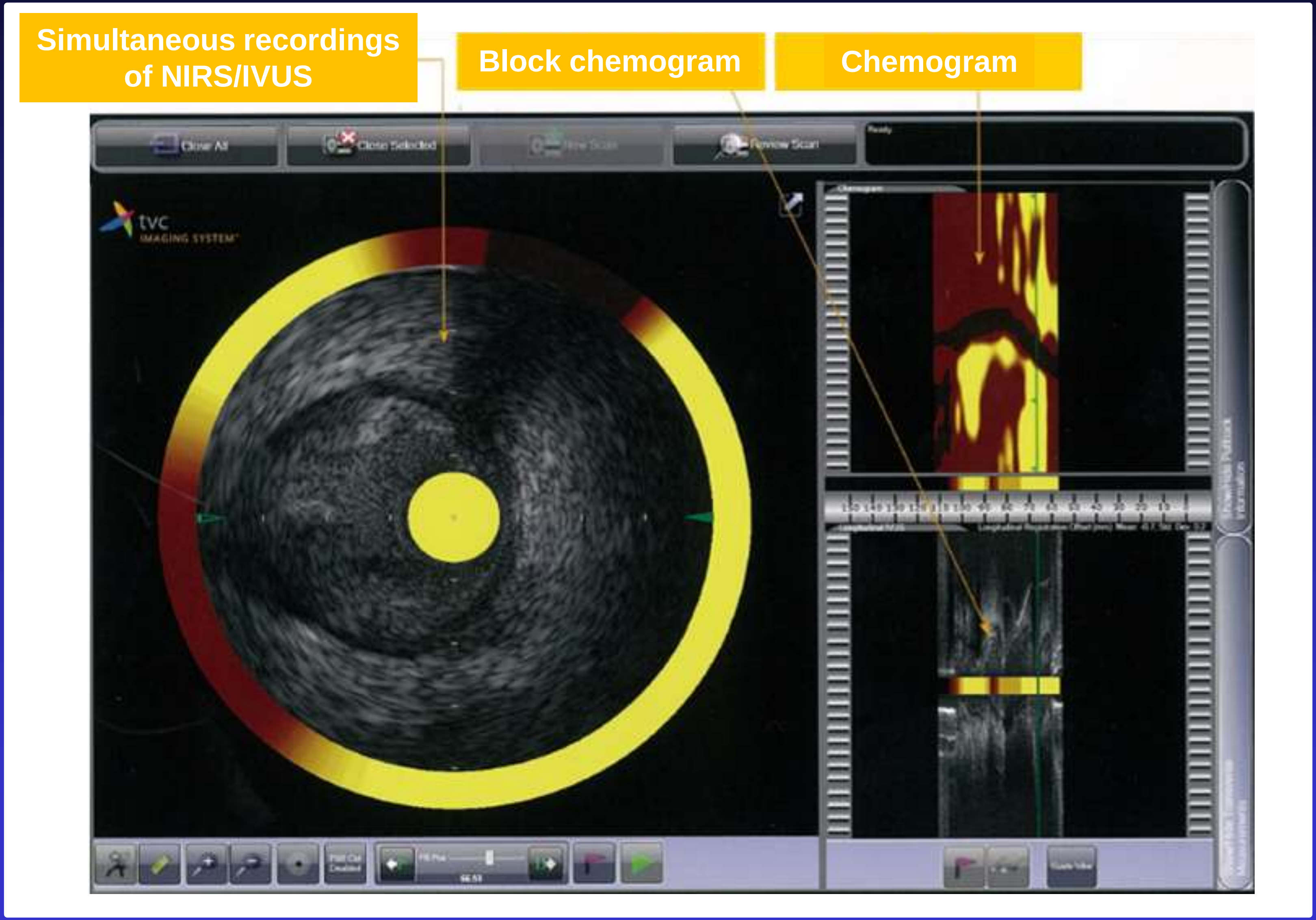
Raber L, et al. EuroIntervention 2012;8:98-108

Fusion of co-registered IVUS & FD-OCT images for the analysis of human atherosclerotic plaques

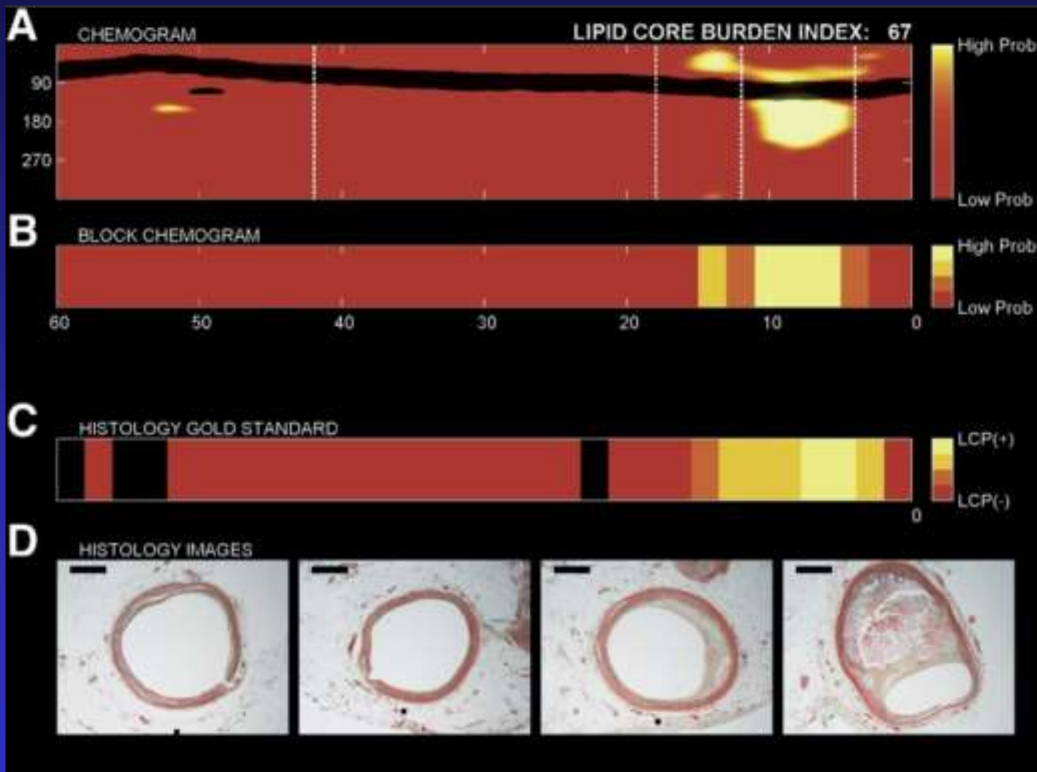


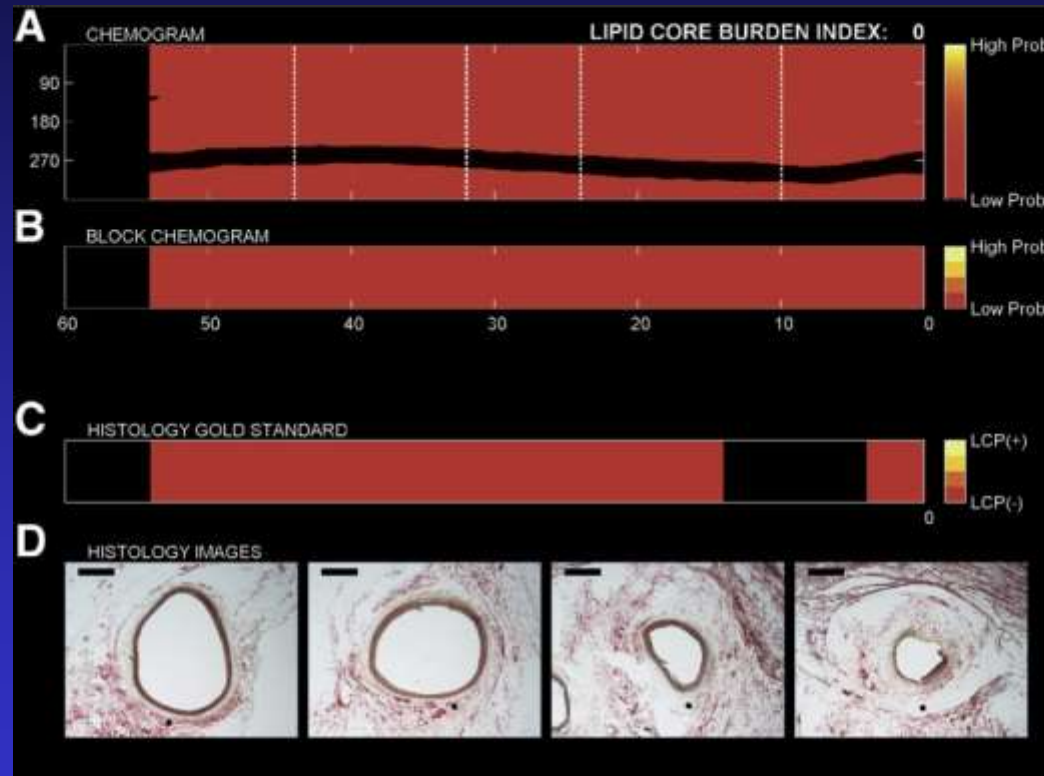
Raber L, et al. EuroIntervention 2012;8:98-108

NIRS-IVUS image



Near-infrared Spectroscopy
(Comparison with Histology)

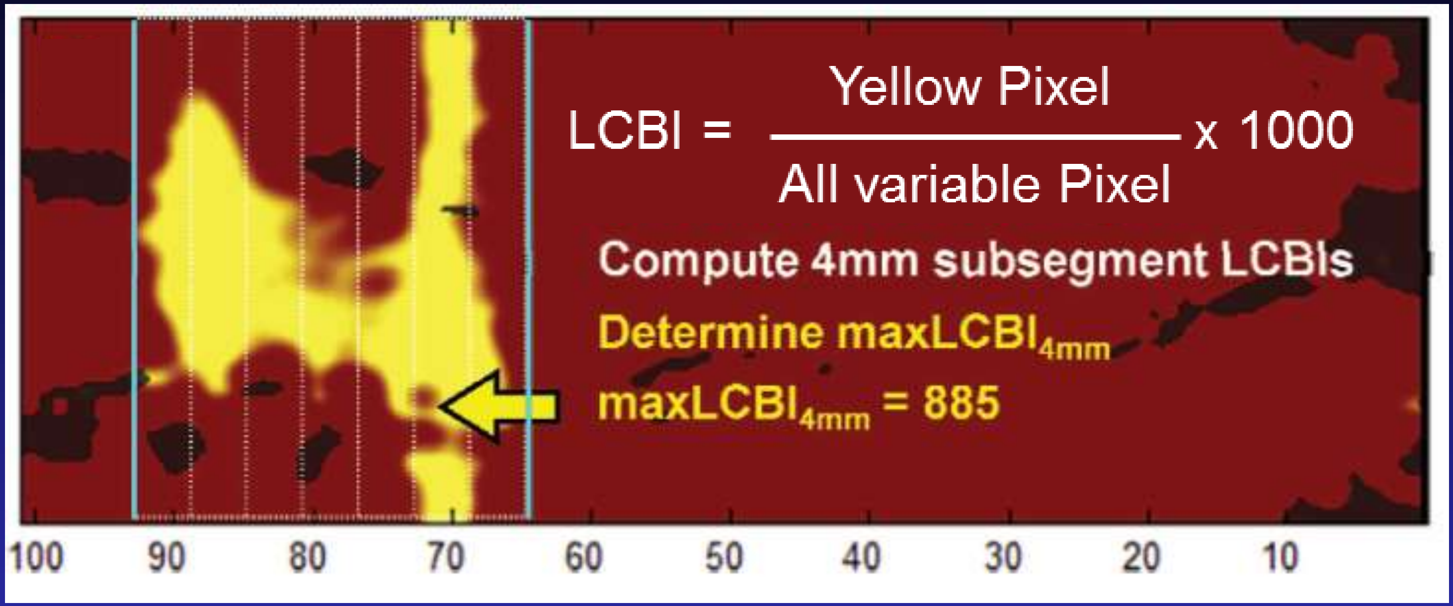




(Gardner CM, et al. J Am Coll Cardiol Img 2008;1:638-648)

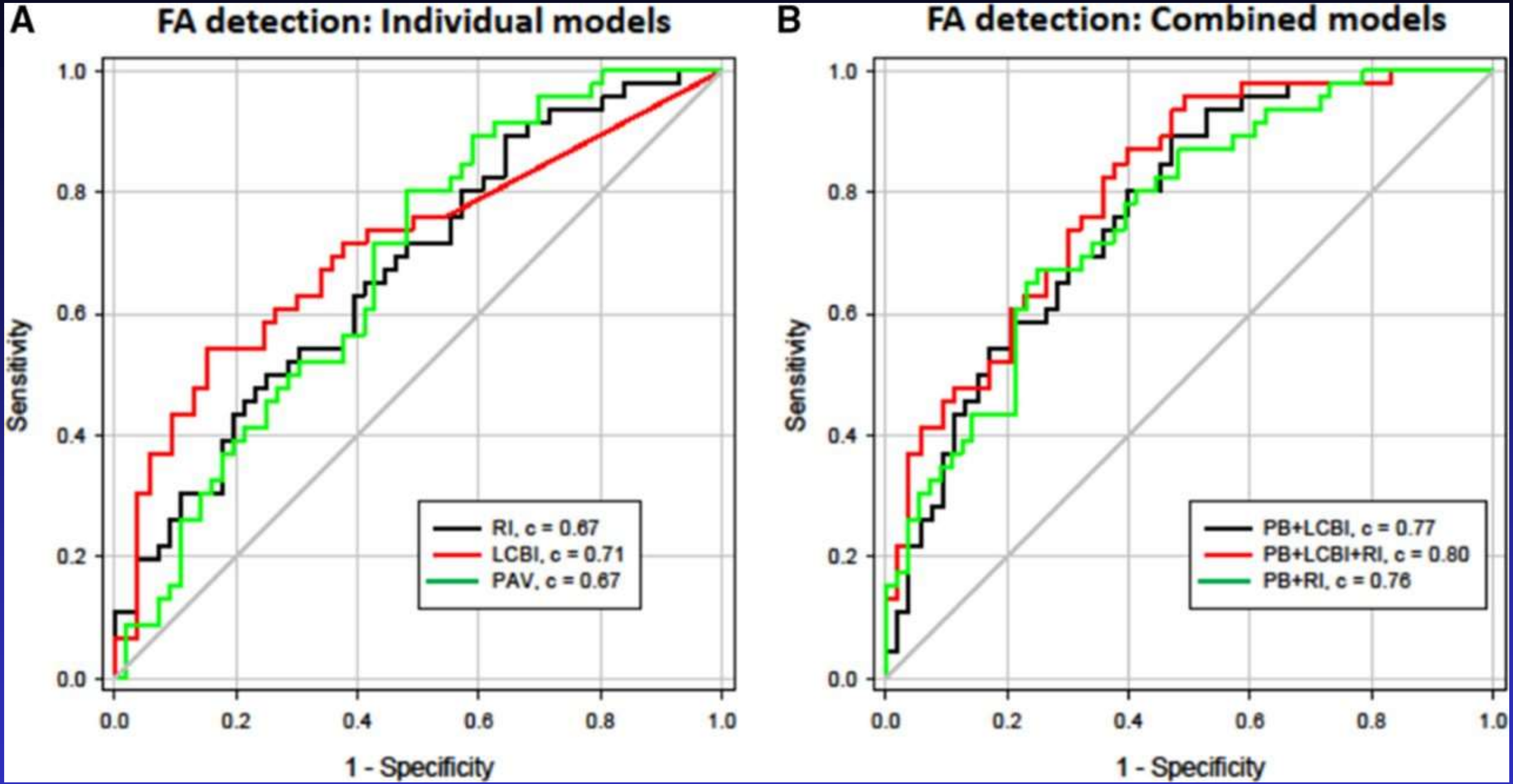
Wakayama Medical University

Lipid Core Burden Index (LCBI) & maxLCBI4mm



- LCBI can be obtained as the ratio of numbers of yellow pixels to all variable pixels in the limited segment.
- maxLCBI4mm demonstrates the maximum LCBI in each 4 mm segment in the limited segment.
- Median LCBI > 43 in non-culprit artery or maxLCMI4mm >500 in non-culprit plaque is thought to identify vulnerable plaque based on several previous investigations.

Receiver–operator curves for detecting autopsy-proven coronary fibroatheroma.



Lipid core burden index (LCBI) demonstrates better predictive capacity of coronary fibroatheroma (FA) by AUC compared with plaque burden (PB), remodeling index (RI) in individual models. Combination of PB, LCBI and RI demonstrates better prediction of coronary fibroatheroma (FA) by AUC in combined models .

Rishi Puri et al. Arterioscler Thromb Vasc Biol. 2015;35:2423-2431

NIRS-IVUS and OCT parameters

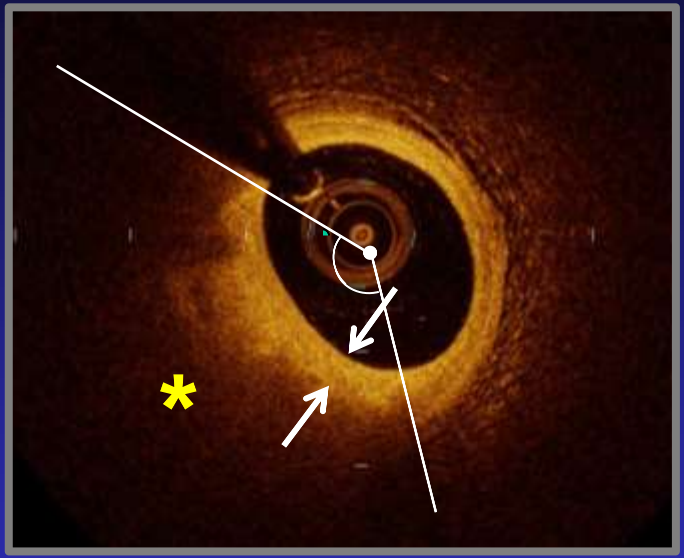
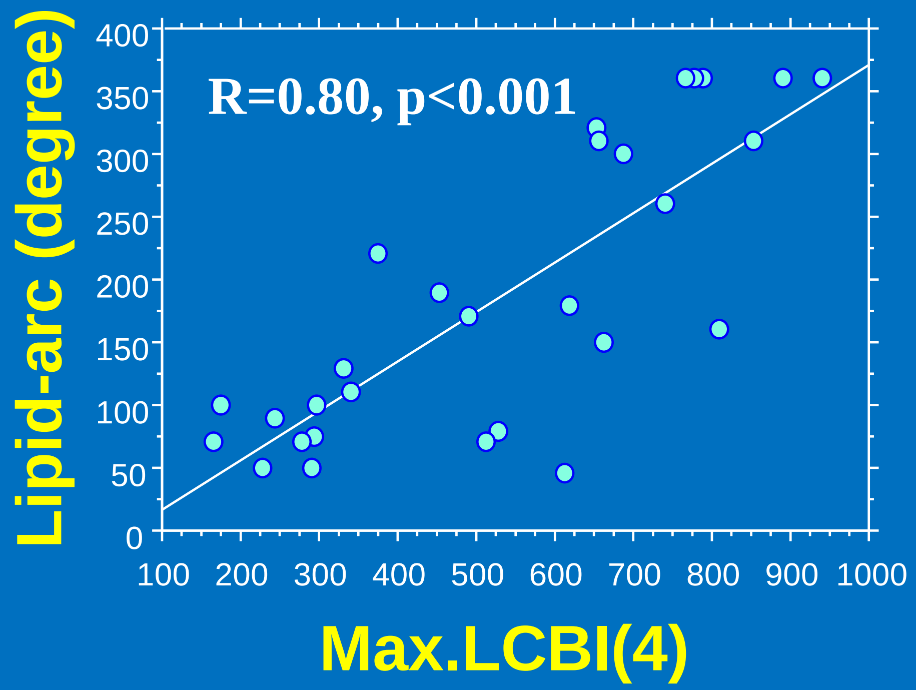


Figure. OCT image

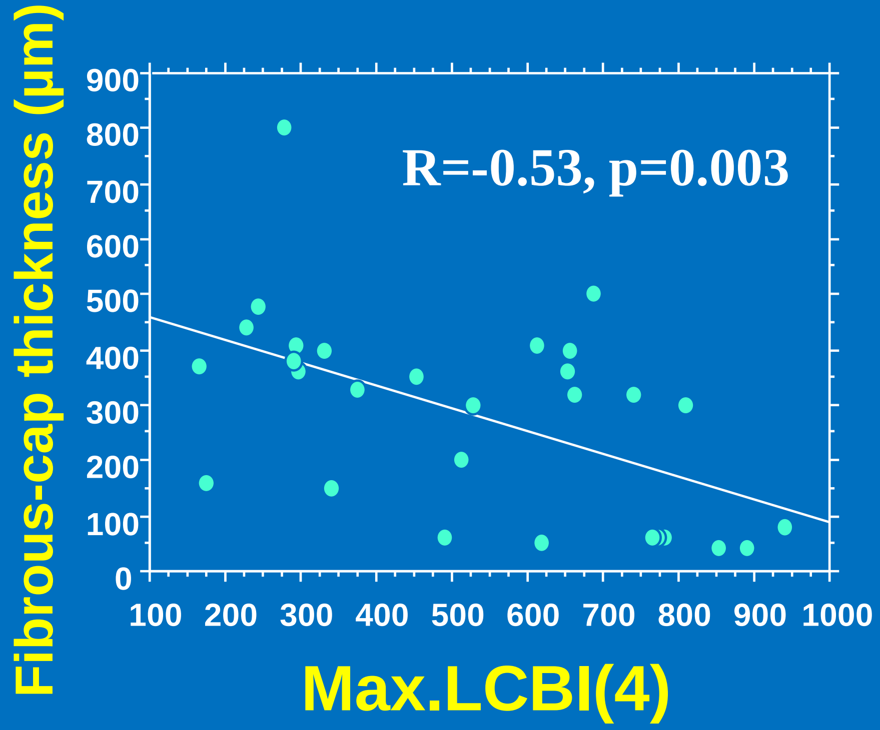
Lipid (asterisk):
Signal-poor, diffuse border
Fibrous-cap (arrows):
Homogeneous, signal-rich

Comparison between OCT and NIRS-IVUS

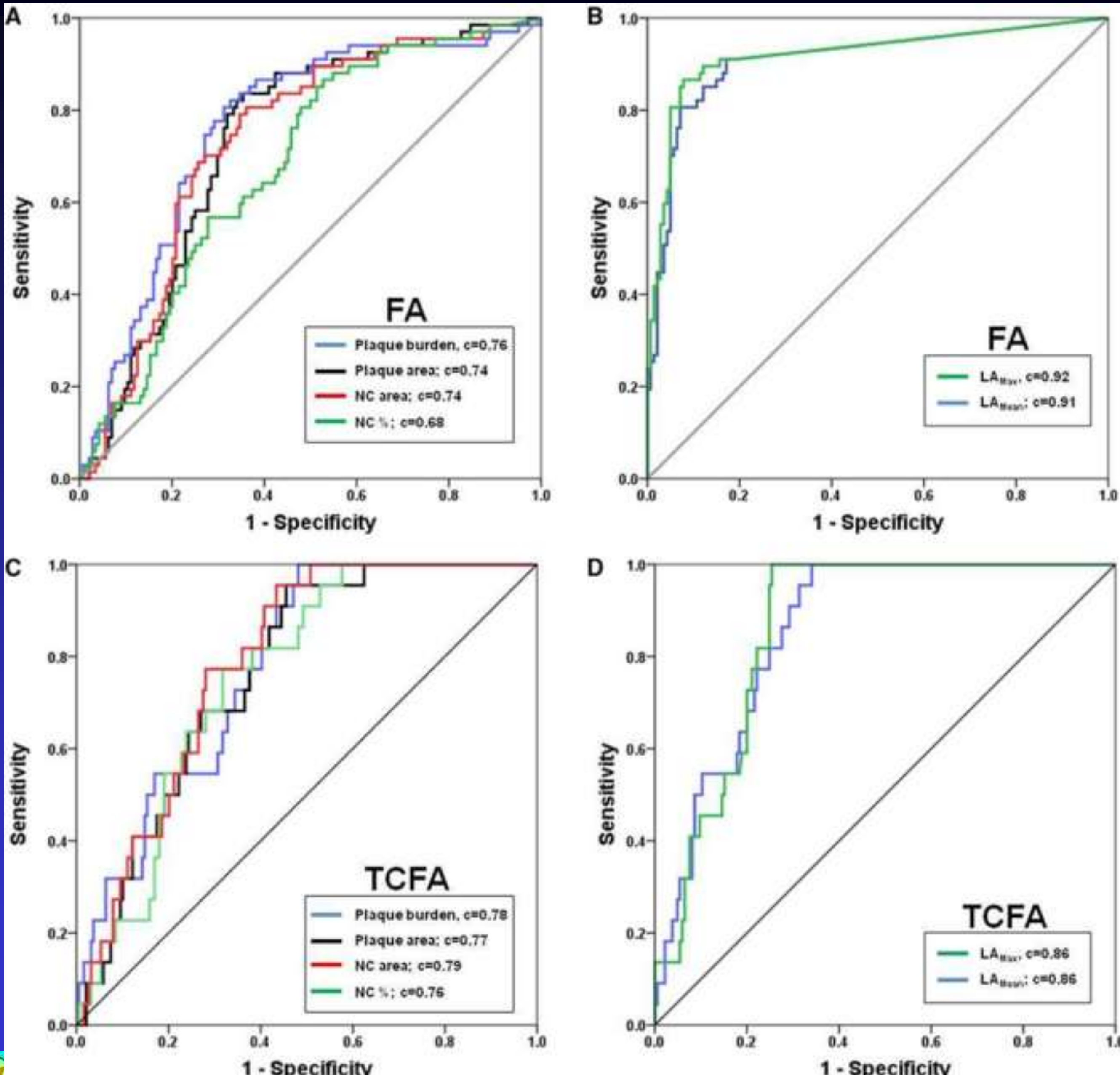
Max.LCBI(4) vs. lipid arc



MaxLCBI(4) vs. fibrous-cap thickness



Receiver-operating curves for identification of advanced coronary plaques.

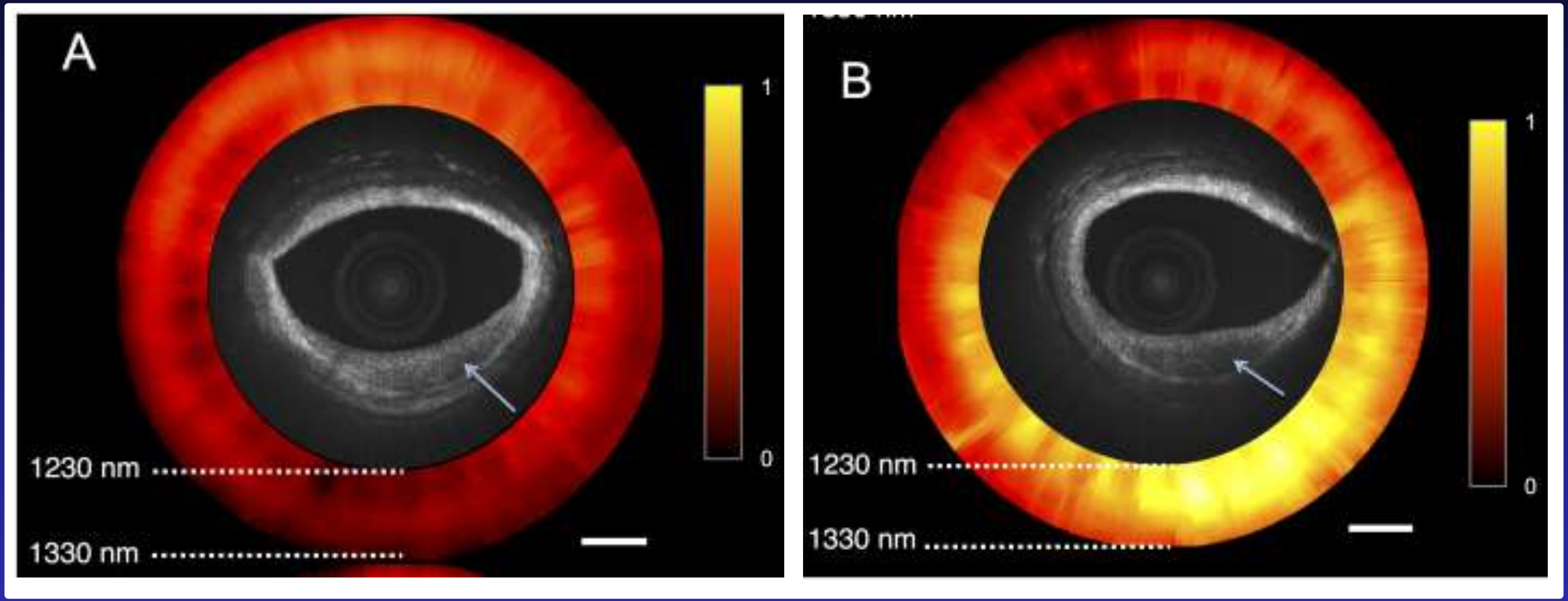


Plaque burden, Necrotic core and Lipid arc could predict for detecting advanced Fibroatheroma & TCFA.

Adam J. Brown et al. Circ Cardiovasc Imaging. 2015;8:e003487

NIRS-OCT

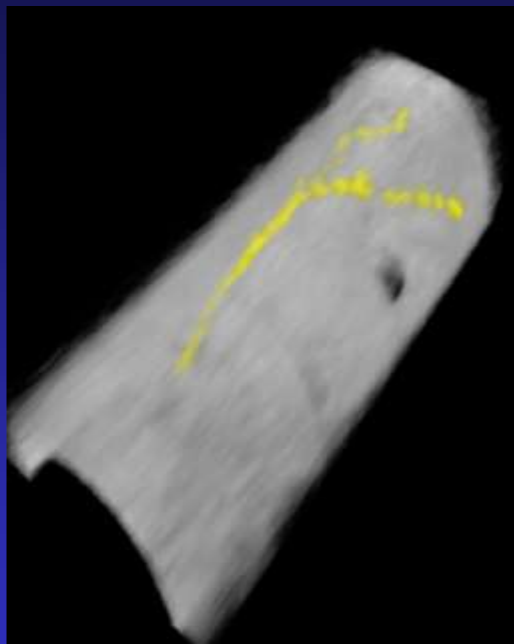
NIRS-OCT images of cadaver coronary artery ex vivo



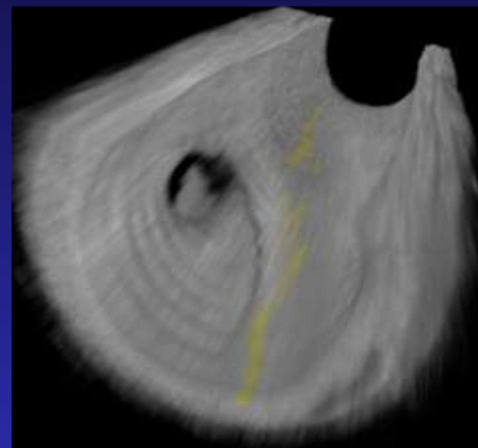
Both OCT images show lesions with reduced backscattering. NIRS image shows absorption spectra of tissue versus wavelength, representing the total attenuation normalized for the entire data set; '1' and '0' correspond to the maximum and minimum absorption within the data set, respectively.
The NIRS signal in (A) does not demonstrate a high lipid signal, while the NIRS signal in (B) shows the presence of abundant lipid. These findings suggest that the lesion in (A) does not contain much lipid whereas the lesion in (B) is lipid-rich. （Scale bars, 500 μm.）

3D structure of Vasa Vasorum

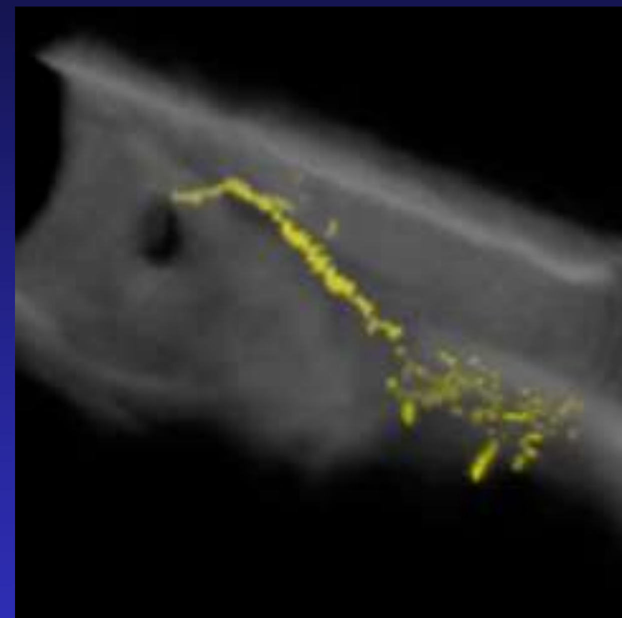
Adventitial VV | **Intraplaque neovessels**



External running



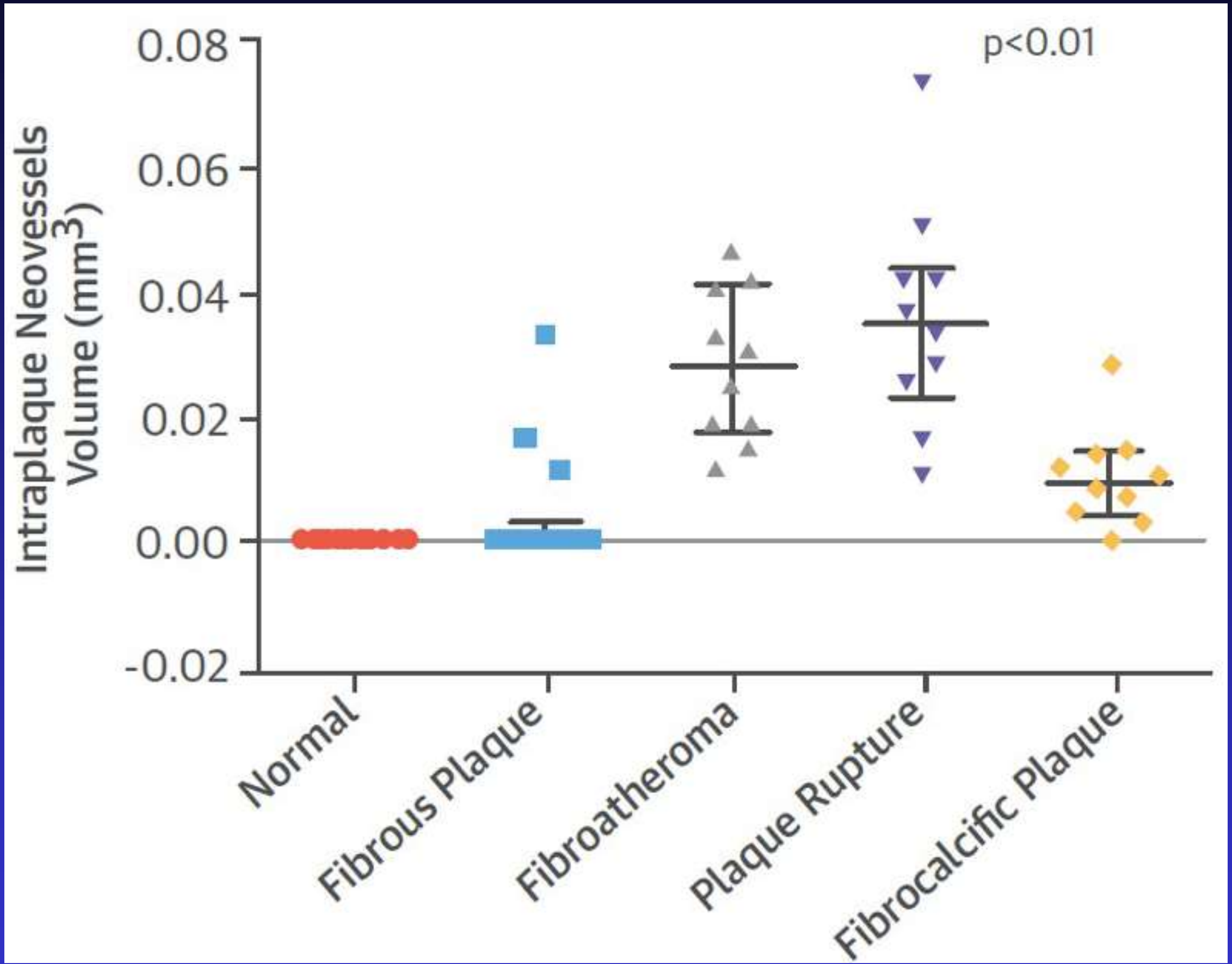
Internal running



Coral tree pattern

Taruya A, et al. J Am Coll Cardiol 2015

Intraplaque Neovessel Volume

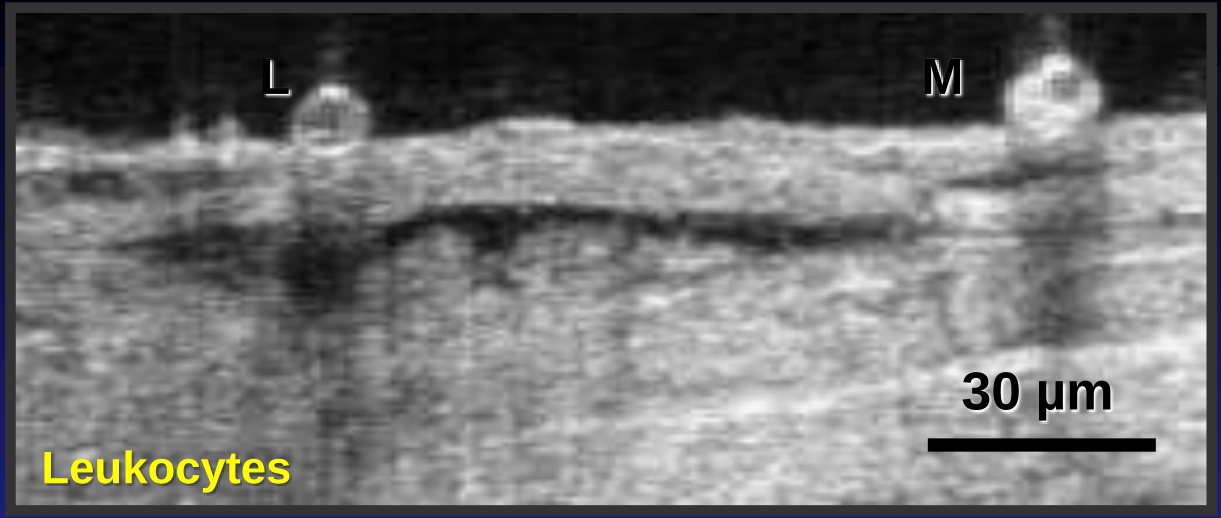


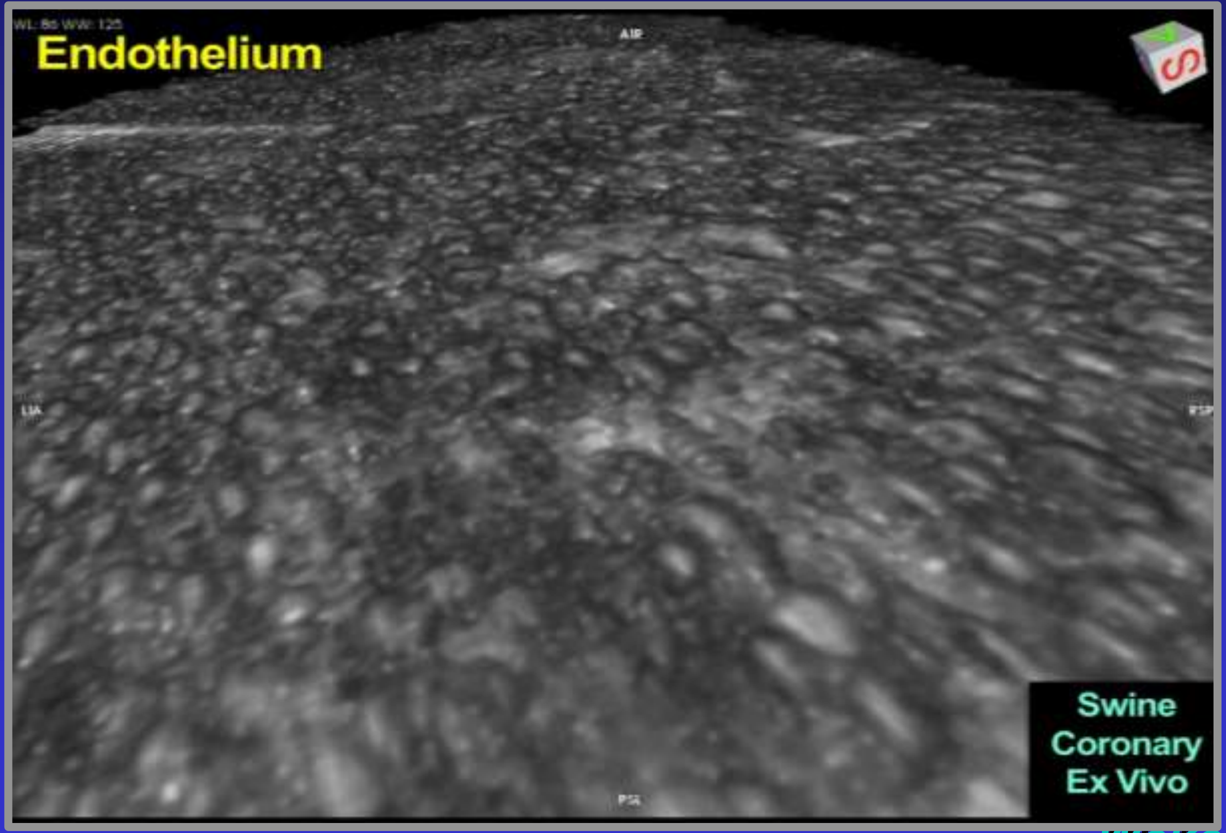
Taruya A, et al. J Am Coll Cardiol 2015

μOCT

- Cross-sectional imaging technology with order of magnitude resolution improvement compared to OCT

	Resolution (μm)		
	x	y	z
IVUS	250	250	100
Present OCT	30	30	10
μOCT	< 2	< 2	< 1



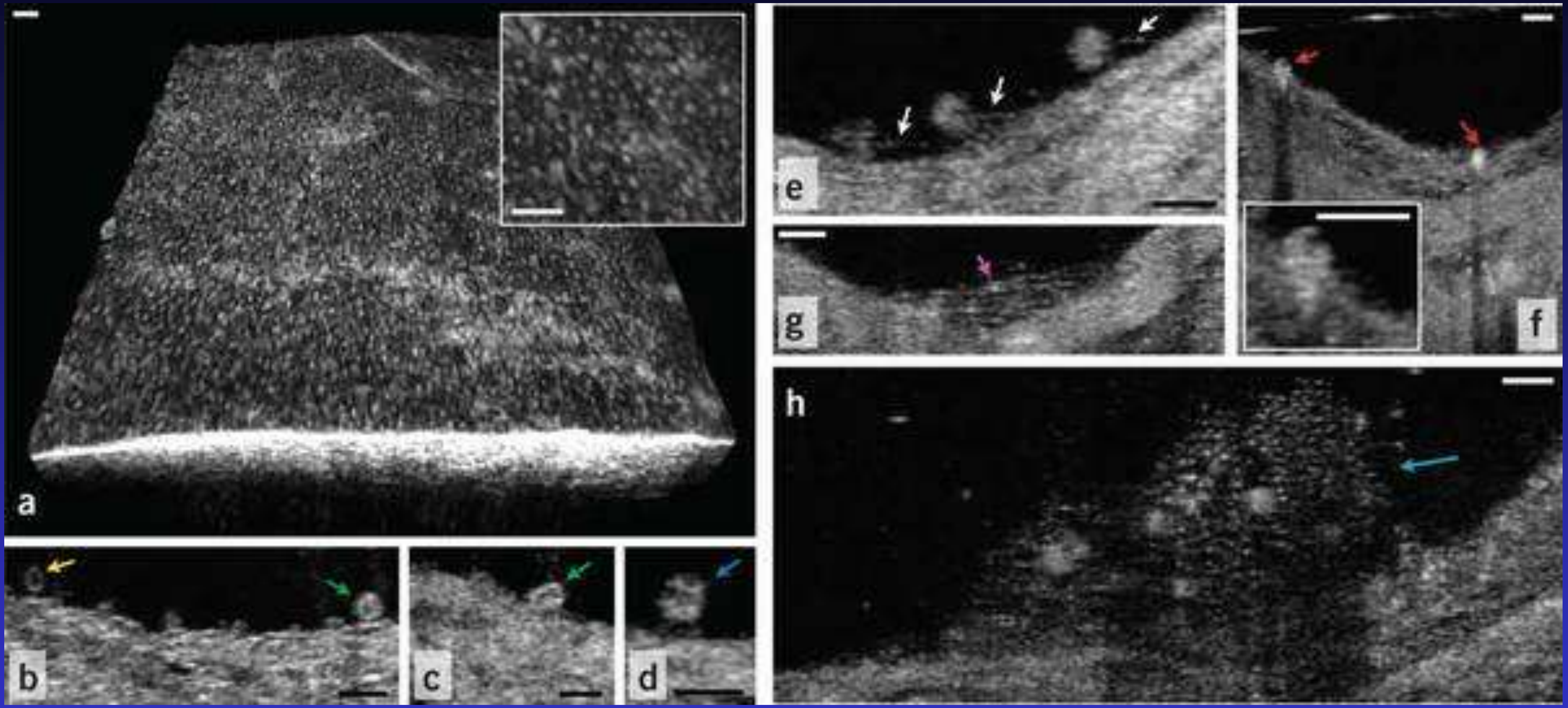


Courtesy by
Prof. Tearney G

Liu L, et al. Nat. Med. 2011;17:1010-1014

Wakayama Medical University

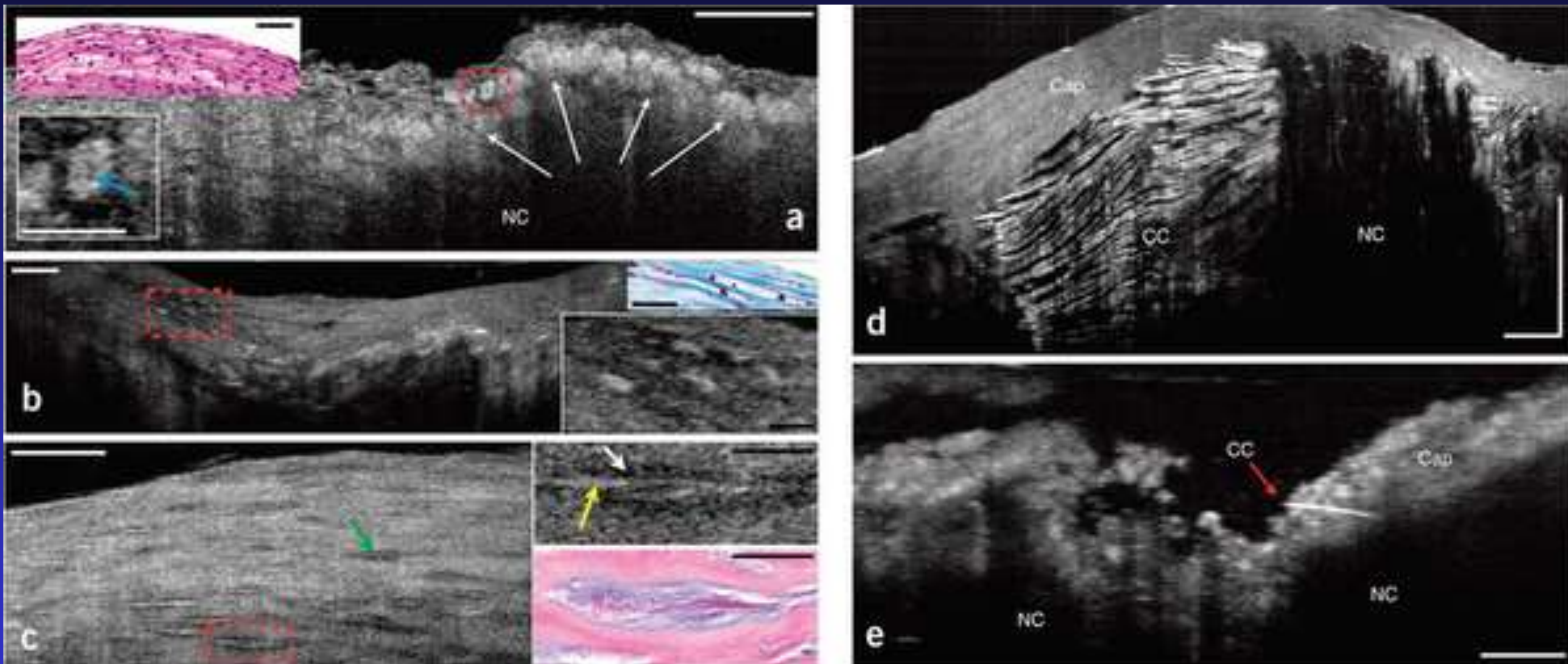
Platelet aggregation by µOCT



Courtesy by Prof. Tearney G

Liu L, et al. Nat. Med. 2011;17:1010-1014

Foam cell & cholesterol crystal by μOCT



Courtesy by Prof. Tearney G

Liu L, et al. Nat. Med. 2011;17:1010-1014

Summary

- Development of invasive imaging may allow us to assess the pathophysiology of ACS, vulnerable plaque in vivo.
- Although identification of non-flow limiting vulnerable plaque is thought to be difficult, MLA <3mm2, TCFA, large lipid core, positive remodeling, etc. might be important findings to speculate VP.
- It seems to be difficult to predict silent plaque rupture
- Lower event rate of TCFA may relate to secondary prevention of plaque stabilization using lipid lowering by statin, EPA, ezetimibe, (& PCSK9 inhibitor).
- Further advancement in the diagnosis of VP could be expected by the development of fusion image, μ-OCT, NIRS-IVUS, NIRS-OCT, etc.