Vulnerable Plaque Identification by OCT & NIRS-IVUS

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Disclosure Statement of Financial Interest

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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 Medical Japan**
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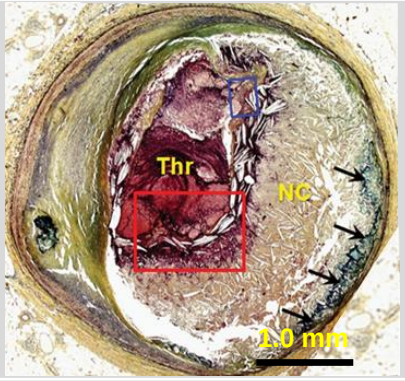
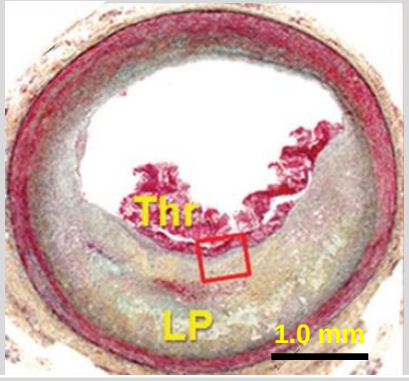
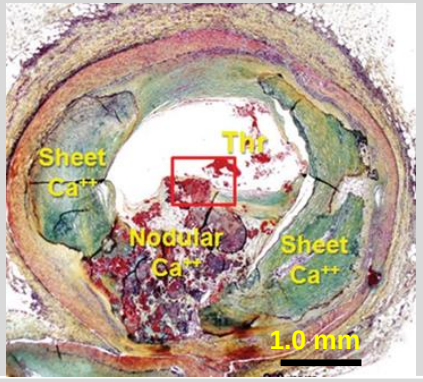
  Daiichi-Sankyo Pharmaceutical Corp.
  Nipro Corp.
  Terumo Corp.

- **Medical Advisor (Employed):Terumo Corp.**

Backgrounds

Plaque rupture (PR)	Plaque erosion (PE)	Calcified nodule (CN)
		
Disrupted fibrous cap	Intact fibrous cap	Disrupted luminal surface
Large lipid core	No/little lipid core	Eruptive nodular calcium

Most of ACS may occur from coronary thrombosis based on PR, PE, or CN, and OCT allows us to differentiate them accurately except for definite and probable PE. Although NIRS-IVUS may provide us the amount of lipid component, there are no data for differentiating PR, PE, or CN by NIRS-IVUS.

Falk E.. Eur Heart J. 2012;34(10):719-28

Plaque Classification Algorithm in ACS by OCT

Disrupted Fibrous Cap

- **Underlying plaque: Lipid** → **Plaque Rupture**
- **Underlying plaque: Calcium**
  - Protruding nodular calcium
  - Attached thrombus
  - Superficial calcium
  - Substantive calcium proximal and/or distal to lesion
  → **OCT-Calcified Nodule**

Intact Fibrous Cap

- **DEFINITE:**
  - Thrombus (+)
  - Intact underlying plaque visualized
- **PROBABLE:**
  - Thrombus (-)
    Irregular surface
  - Thrombus (+)
    Underlying plaque not visualized
    No superficial lipid or calcium proximal or distal to lesion

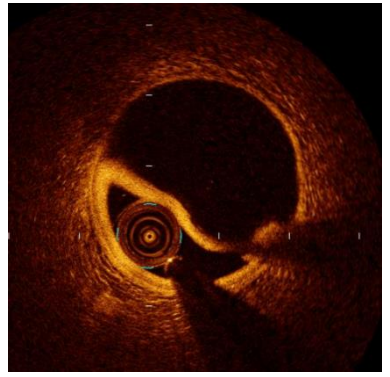
  → **OCT-Erosion**

Others

- Tight stenosis
- Dissection
- Hematoma
- Coronary spasm
- Fissure

→ **Others**

IPH (Hemorrhage)

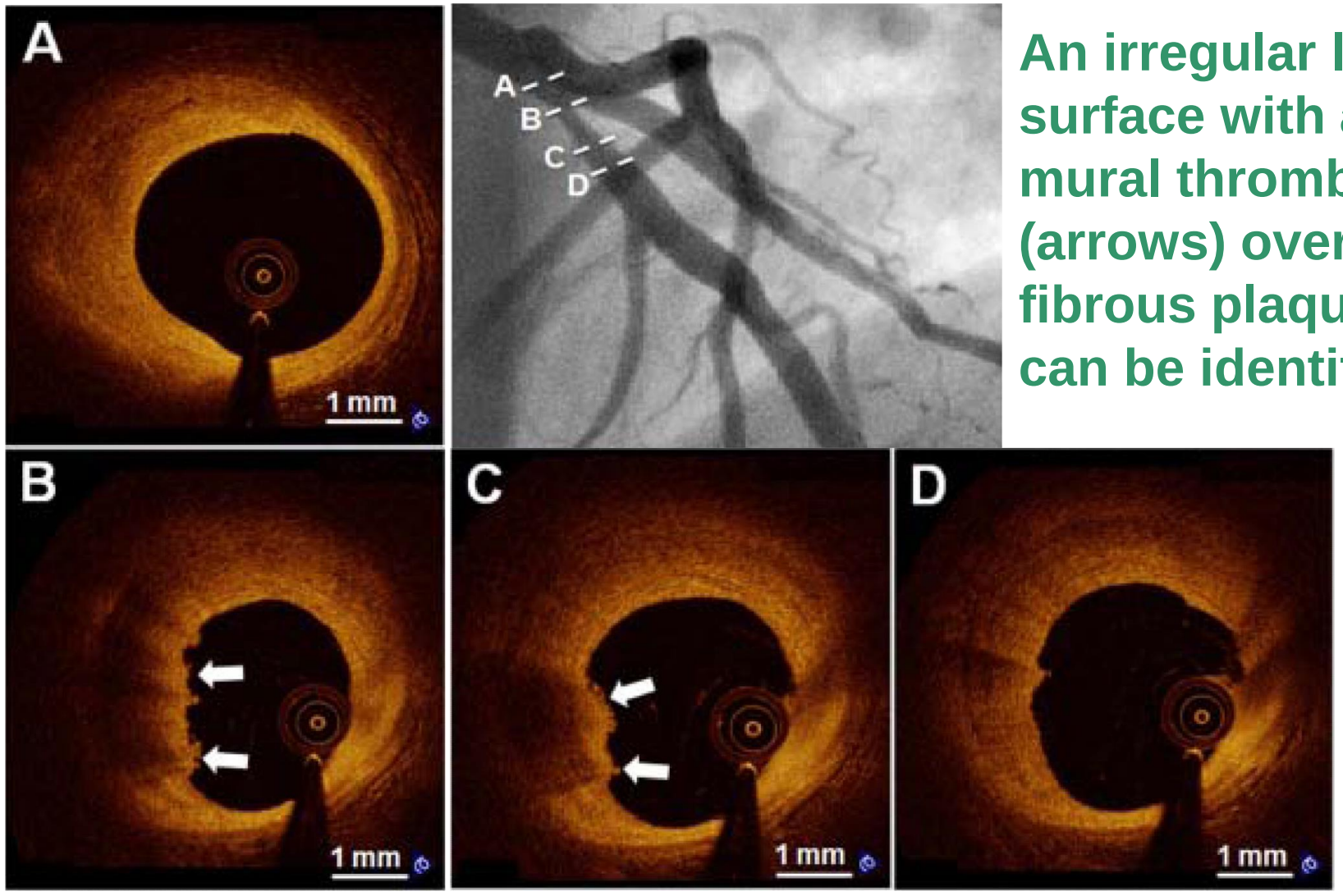


SCAD

Healed plaque

Jia H, et al. J Am Coll Cardiol 2013;62:1748–1758

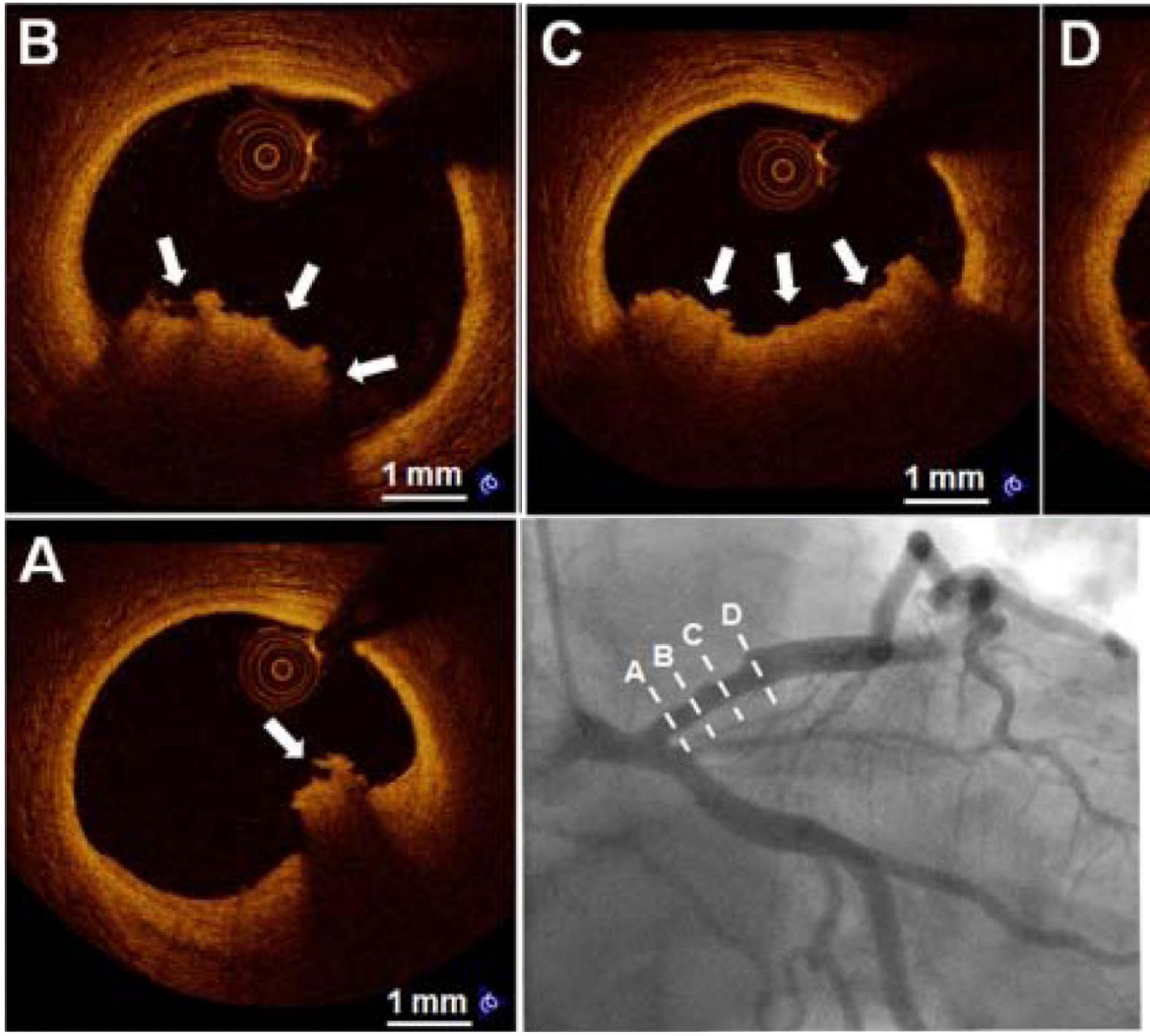
Representative case of definite OCT-erosion



An irregular lumen surface with attached mural thrombus (arrows) overlying a fibrous plaque (B,C) can be identified.

Jia H, et al. J Am Coll Cardiol 2013;62:1748–1758

Representative case of probable OCT-erosion



Underlying plaque morphology is not well visualized due to the presence of residual red thrombus (A, B and C, arrows) without any detectable rupture (A through D).

Jia H, et al. J Am Coll Cardiol 2013;62:1748–1758

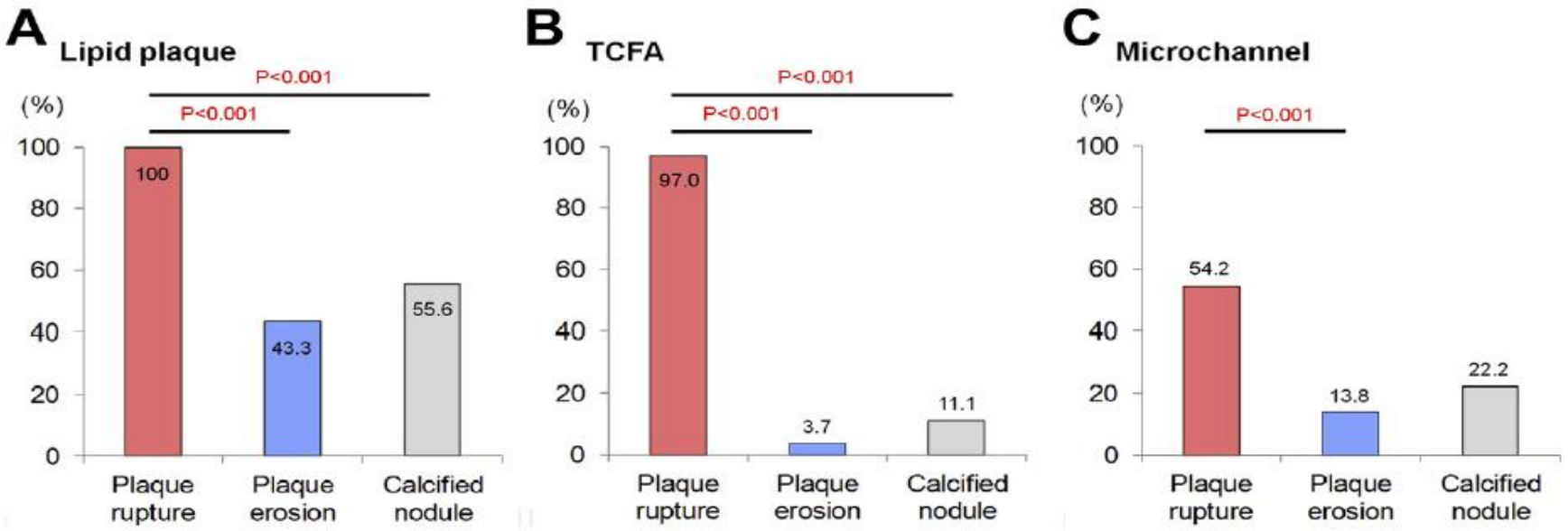
OCT Findings of 3 Underling Plaque Characteristics

	PR (n = 55)	OCT-Erosion (n = 39)	OCT-CN (n = 10)	p Value	p Value*		
					PR vs. OCT-Erosion	OCT-Erosion vs. OCT-CN	PR vs. OCT-CN
Fibrous plaque	0 (0.0%)	22 (56.4%)	10 (100%)	<0.001	<0.001	0.027	<0.001
Lipid plaque	55 (100%)	17 (43.6%)	0 (0.0%)	<0.001	<0.001	0.027	<0.001
TCFA	37 (67.3%)	3 (10.3%)	0 (0.0%)	<0.001	<0.001	1.000	<0.001
Calcification	22 (40.0%)	5 (12.8%)	10 (100%)	<0.001	0.016	<0.001	0.001
Microchannel	21 (38.2%)	7 (17.9%)	2 (6.7%)	0.083	N/A	N/A	N/A
Thrombus	45 (81.8%)	33 (84.6%)	10 (100%)	0.242	N/A	N/A	N/A
Red thrombus	39 (70.9%)	6 (15.4%)	4 (40.0%)	<0.001	<0.001	0.541	0.226
White thrombus	6 (10.9%)	27 (69.2%)	6 (60.0%)	<0.001	<0.001	1.000	0.005

Values are n (%). *The p values were calculated by Fisher exact test and adjusted by Bonferroni correction for multiple comparisons within 3 groups (PR, OCT-erosion, and OCT-CN) only if p value for the overall 3-group test <0.05.

Jia H, et al. J Am Coll Cardiol 2013;62:1748–1758

OCT Plaque Characteristics of 3 Underling Mechanisms of STEMI



Quantitative OCT Findings After Thrombectomy

	PR (n = 72)	PE (n = 30)	CN (n = 9)	p Value	p Value* PR vs. PE	p Value* PE vs. CN	p Value* PR vs. CN
Fibrous plaque	0 (0)	17 (56.7)	4 (44.4)	<0.001	<0.001	0.706	<0.001
Lipid plaque	72 (100)	13 (43.3)	5 (55.6)	<0.001	<0.001	0.706	<0.001
Minimum FCT, μm	50 (40, 59)	130 (95, 190)	170 (64, 320)	<0.001	<0.001	0.961	0.001
Maximum arc, degrees	360 (298, 360)	211 (168, 285)	154 (102, 312)	<0.001	<0.001	0.459	0.005
Length, mm	13.1 (9.1, 17.6)	8.1 (6.8, 9.8)	5.8 (5.0, 12.0)	0.002	<0.001	0.657	0.027
Calcification	50 (69.4)	15 (50.0)	9 (100)	0.014	0.074	0.007	0.105
Minimum depth,† μm	80 (50, 173)	160 (60, 270)	20 (10, 40)	<0.001	0.117	<0.001	<0.001
Maximum arc, degrees	56 (38, 93)	55 (42, 91)	251 (157, 360)	<0.001	0.889	<0.001	<0.001
Thrombus score	6.5 (3.0, 13.3)	9.0 (4.0, 15.0)	23.0 (5.5, 32.0)	0.117			

Values are n (%) or median (25th, 75th percentiles). *p < 0.017 was considered significant. †Minimum depth is measured from the luminal surface to calcification.

Higma T, et al. J Am Coll Cardiol Intv 2015;8:1166–1176

NIRS-IVUS for Differentiating Coronary Plaque Rupture, Erosion, and Calcified Nodule in Acute Myocardial Infarction

Kosei Terada, MD,[a] Takashi Kubo, MD, PhD,[a] Takeyoshi Kameyama, MD, PhD,[a] Yoshiki Matsuo, MD, PhD,[a] Yasushi Ino, MD, PhD,[a] Hiroki Emori, MD,[a] Daisuke Higashioka, MD,[a] Yosuke Katayama, MD,[a] Amir Kh.M. Khalifa, MD,[a] Masahiro Takahata, MD,[a] Kunihiro Shimamura, MD, PhD,[a] Yasutsugu Shiono, MD, PhD,[a] Atsushi Tanaka, MD, PhD,[a] Takeshi Hozumi, MD, PhD,[a] Ryan D. Madder, MD,[b] Takashi Akasaka, MD, PhD[a]

Objectives

This study sought to investigate the ability of NIRS-IVUS to differentiate among PR, PE and CN in AMI using an OCT diagnosis as the reference standard.

Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450
Doi.org/10.1016/j.jcmg.2020.08.030.

Objectives

To investigate the ability of NIRS-IVUS to differentiate among PR, PE and CN in AMI using an OCT diagnosis as the reference standard.

Method (1)

Study design:	**single center, intravascular imaging registry**
Patients:	***244*** **patients with AMI (186 STEMI, 58 NSTEMI)**
Target lesions:	***244*** **culprit lesions**
Procedures:	**OCT and NIRS-IVUS before PCI**
Definitions:	**OCT-PR / PE / CN based on the previous report by Jia H. et al. (J Am Coll Cardiol 2013;62:1748-1758)**

Method (2)

***244* patients with AMI**

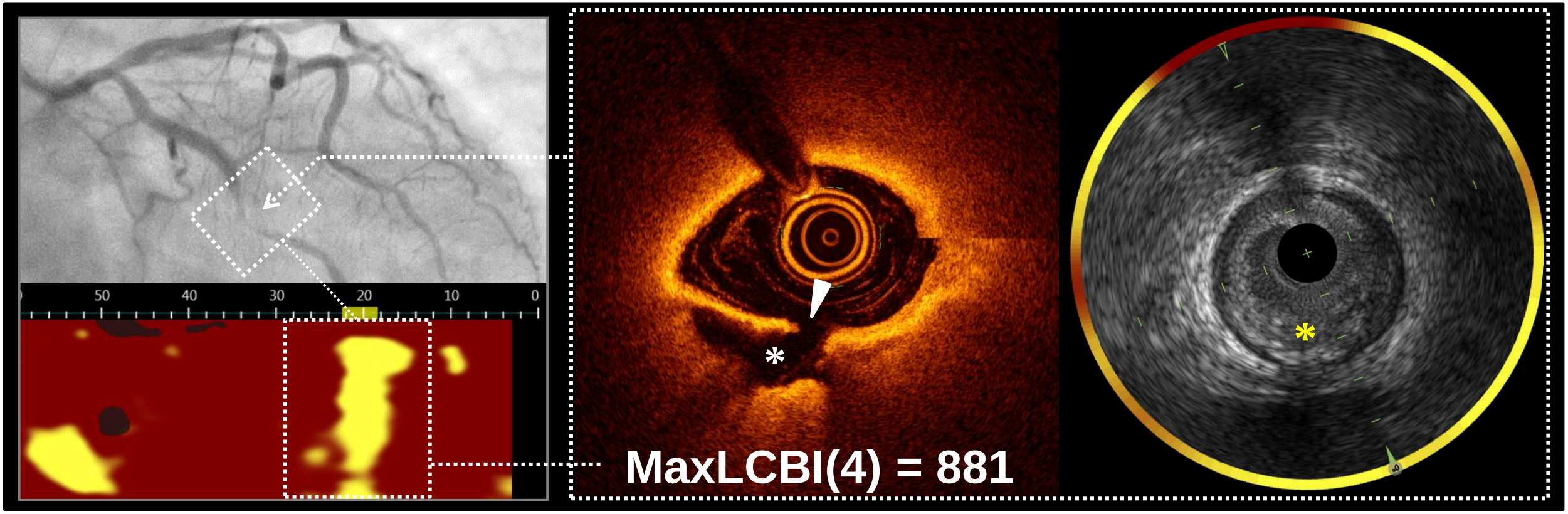
- ***Test cohort: 156 patients***

  We compared NIRS-IVUS findings among OCT-PR, OCT-PE, OCT-CN and developed the NIRS-IVUS classification algorithm for diagnosing PR, PE, and CN.

- ***Validation cohort: 88 patients***

  We investigated the accuracy of the NIRS-IVUS classification algorithm.

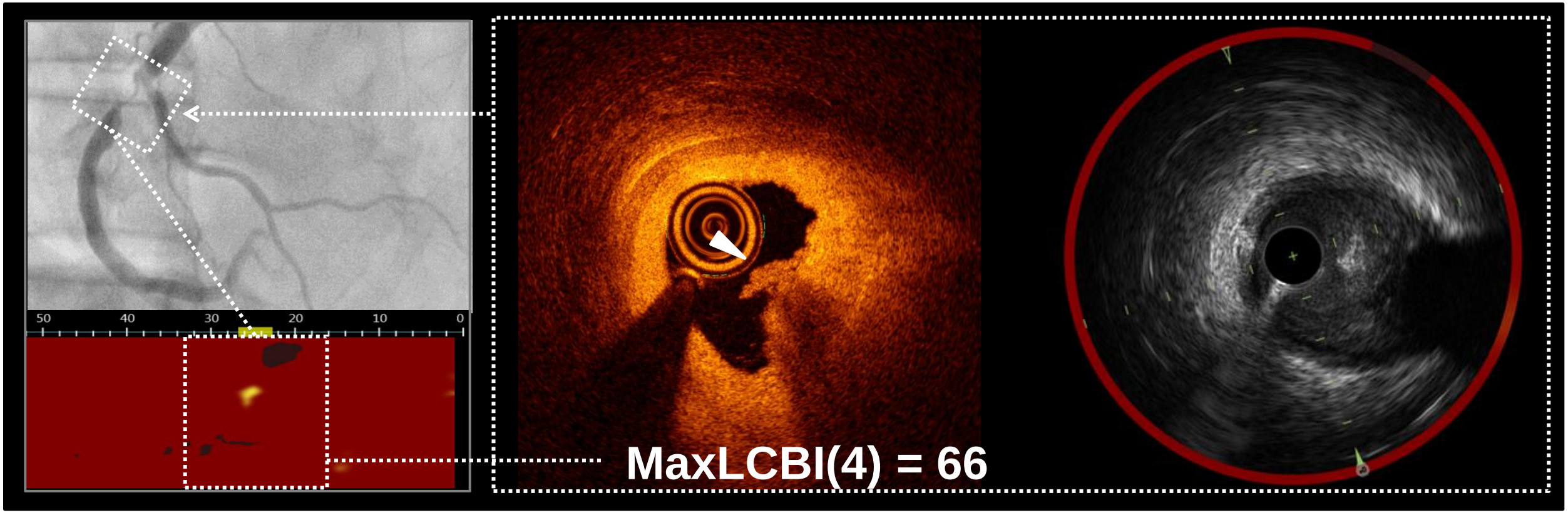
A representative case of OCT-PR (66 y.o., Male, STEMI)



- OCT demonstrates PR showing fibrous cap disruption & cavity formation within the plaque.
- IVUS reveals a plaque cavity.
- NIRS identifies a large lipid content in the culprit lesion.

Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

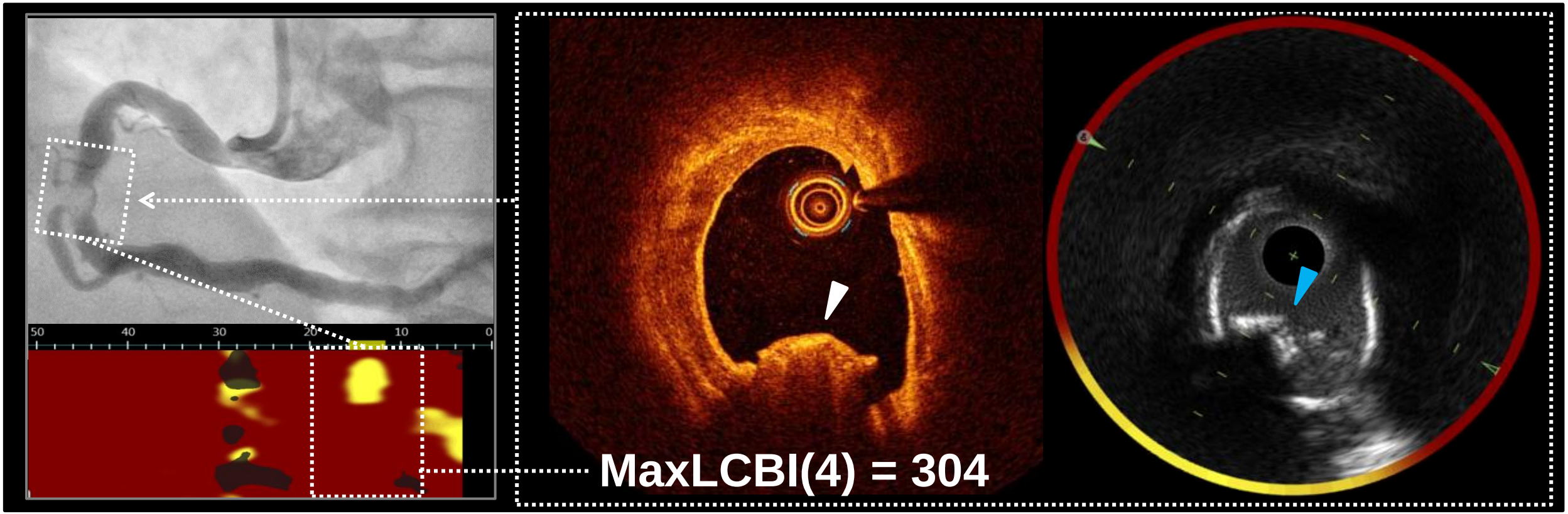
A representative case of OCT-PE (51 y.o. Male, STEMI)



- OCT demonstrates PE showing the thrombus overlying an intact FC.
- IVUS reveals the absence of plaque cavity.
- NIRS identifies a small amount of lipid in the culprit lesion.

Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

A representative case of OCT-CN (72 y.o. Male, NSTEMI)



- OCT demonstrates CN showing a protruding calcium with thrombi and near circumferential calcium.
- IVUS reveals a convex calcium with irregular surface and near circumferential superficial calcium.
- NIRS identifies a moderate lipid in the culprit lesion.

Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

Clinical Characteristics

	OCT-PR (n=112)	OCT-PE (n=29)	OCT-CN (n=15)	p Value
Age, y.o.	**72 (64-80)**	**65 (56-73)**	**80 (72-83)**	**0.002**
Male gender	88 (79)	19 (66)	11 (73)	0.316
HT	80 (71)	19 (66)	14 (93)	0.127
DM	33 (29)	8 (28)	7 (47)	0.367
DLP	56 (50)	12 (41)	9 (60)	0.488
Smoking	40 (36)	14 (48)	3 (20)	0.197
Obesity	24 (21)	7 (24)	2 (13)	0.770

Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

Angiographic findings

	OCT-PR (n=112)	OCT-PE (n=29)	OCT-CN (n=15)	p Value
LAD / LCX / RCA, %	54/ 8/ 38	45/ 10/ 15	67/ 13/ 20	0.466
Prox / Mid /Dis, %	46/ 44/ 10	34/ 52/ 14	67/ 33/ 0	0.319
Heavy calcification	**9 (8)**	**0 (0)**	**11 (73)**	**< 0.001**
TIMI flow grade, %	51/ 12/ 24/ 13	45/ 10/ 21/ 24	40/ 13/ 27/ 20	0.829
Diameter stenosis, %	100 (93-100)	96 (91-100)	91 (85-100)	0.286

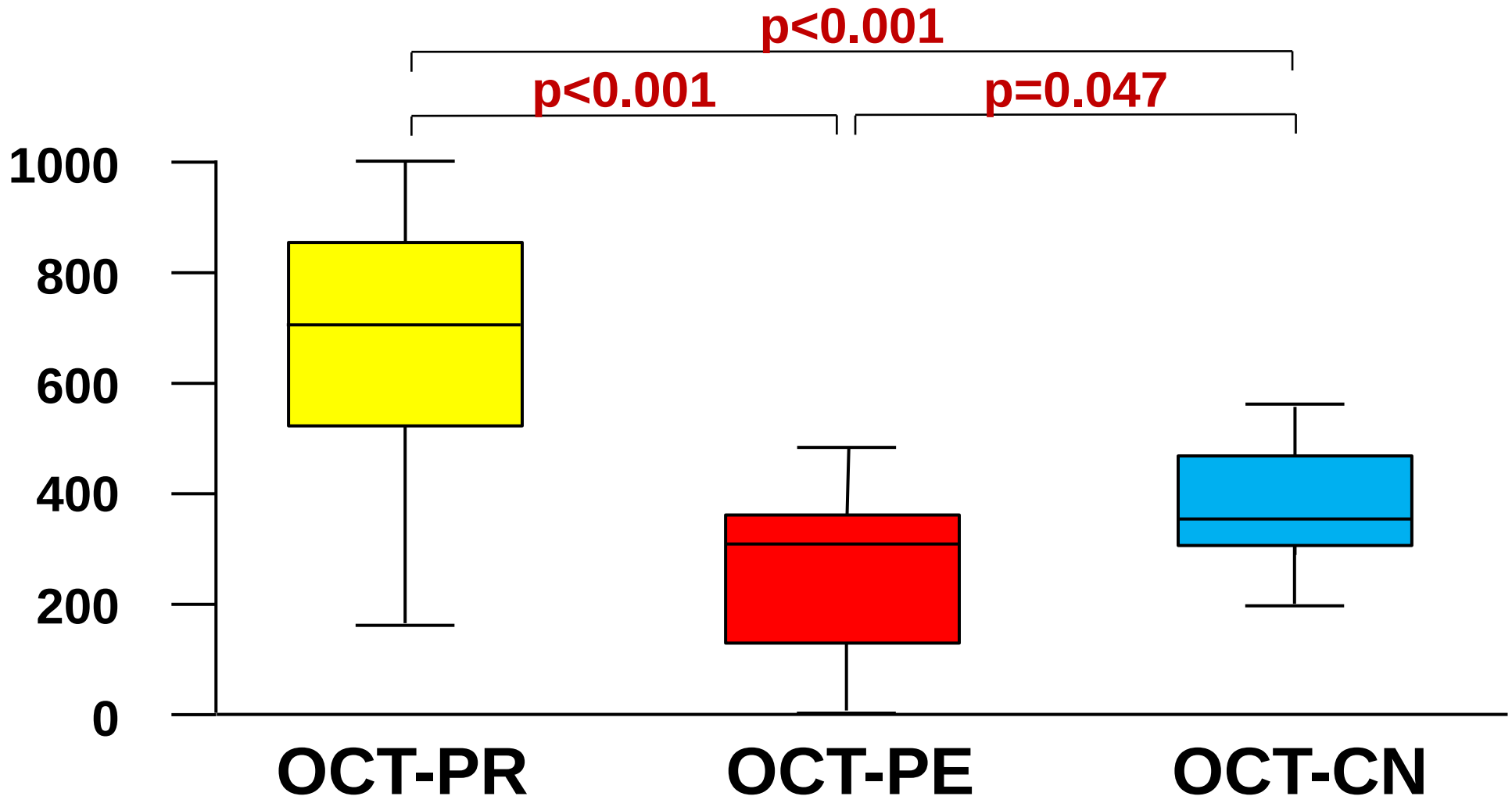
Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

IVUS findings at MLA site

	OCT-PR(112)	OCT-PE(29)	OCT-CN(15)	p Value
Plaque cavity, %	69 (62)	0 (0)	0 (0)	< 0.001
Convex calcium, %	0 (0)	0 (0)	14 (93)	< 0.001
Plaque burden, %	86 (82-98)	77 (72-84)	82 (77-87)	< 0.001
Positive remodel.,%	64 (57)	0 (0)	1 (7)	< 0.001

Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

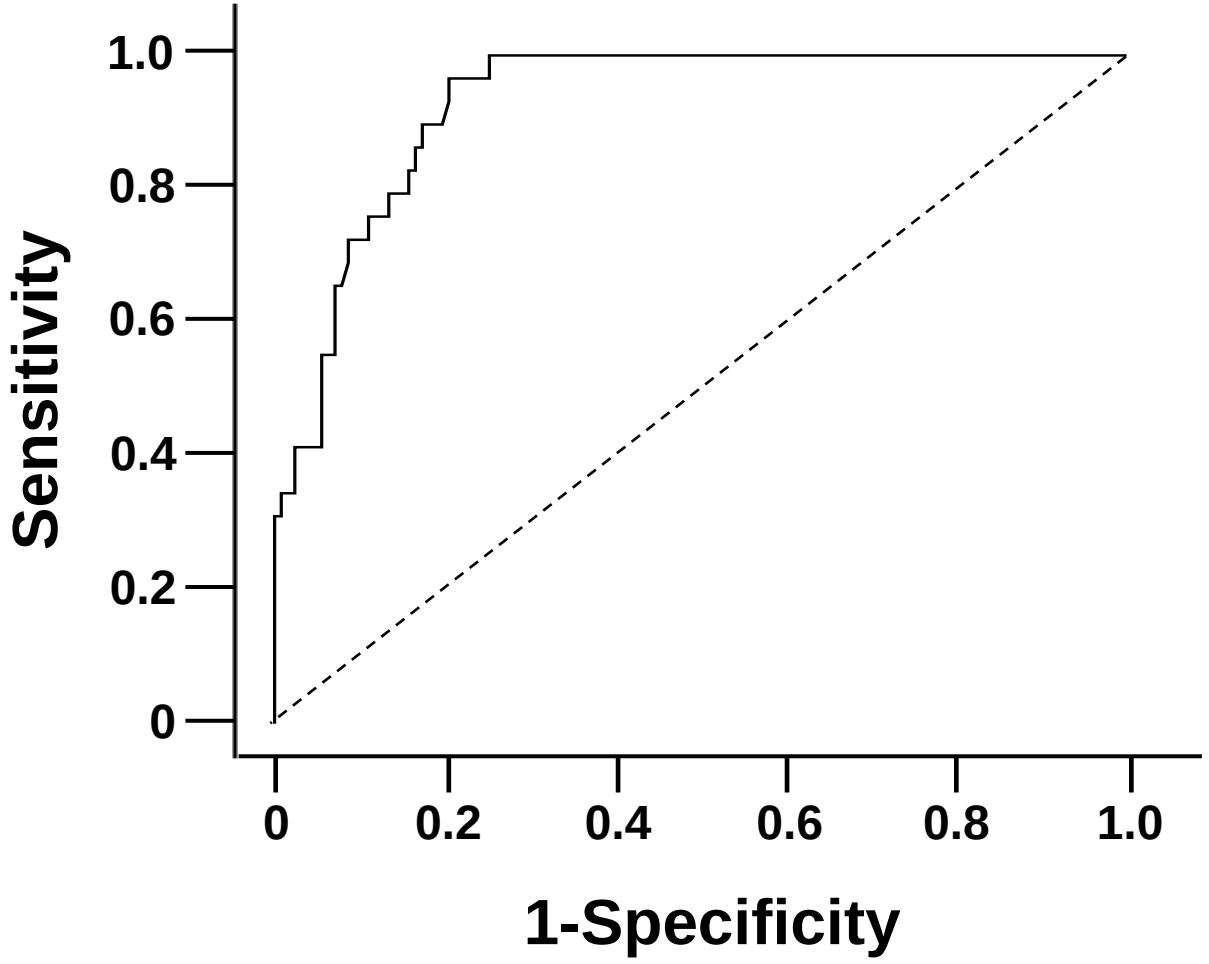
NIRS – maxLCBI4mm in OCT-PR, OCT-PE, OCT-CN



Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

ROC curve of MaxLCBI4mm

Differentiation between OCT-PR (probable PE) & OCT-PE (definite PE)



Cut off = 426

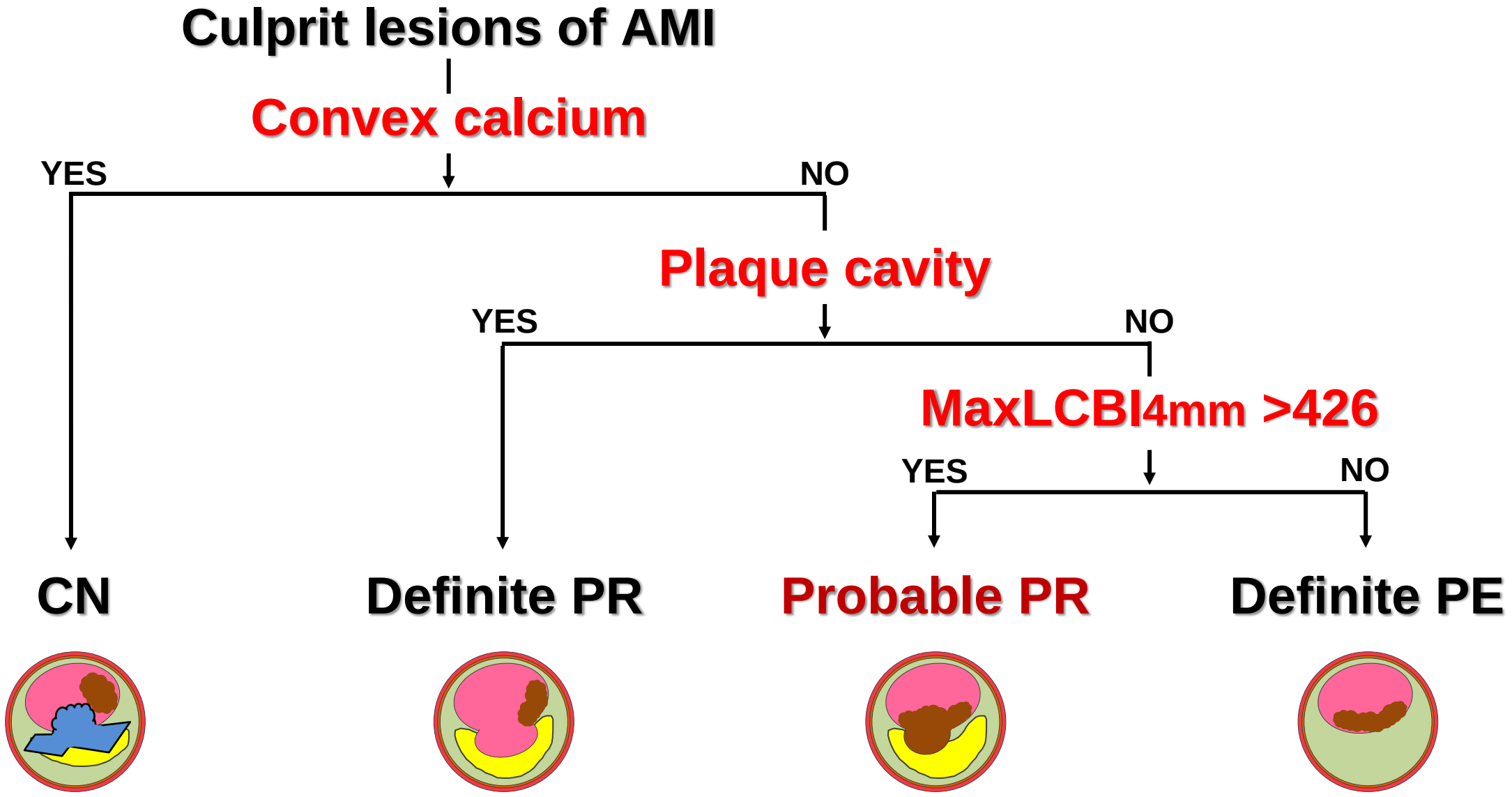
Sensitivity: 92%

Specificity: 97%

AUC = 0.96

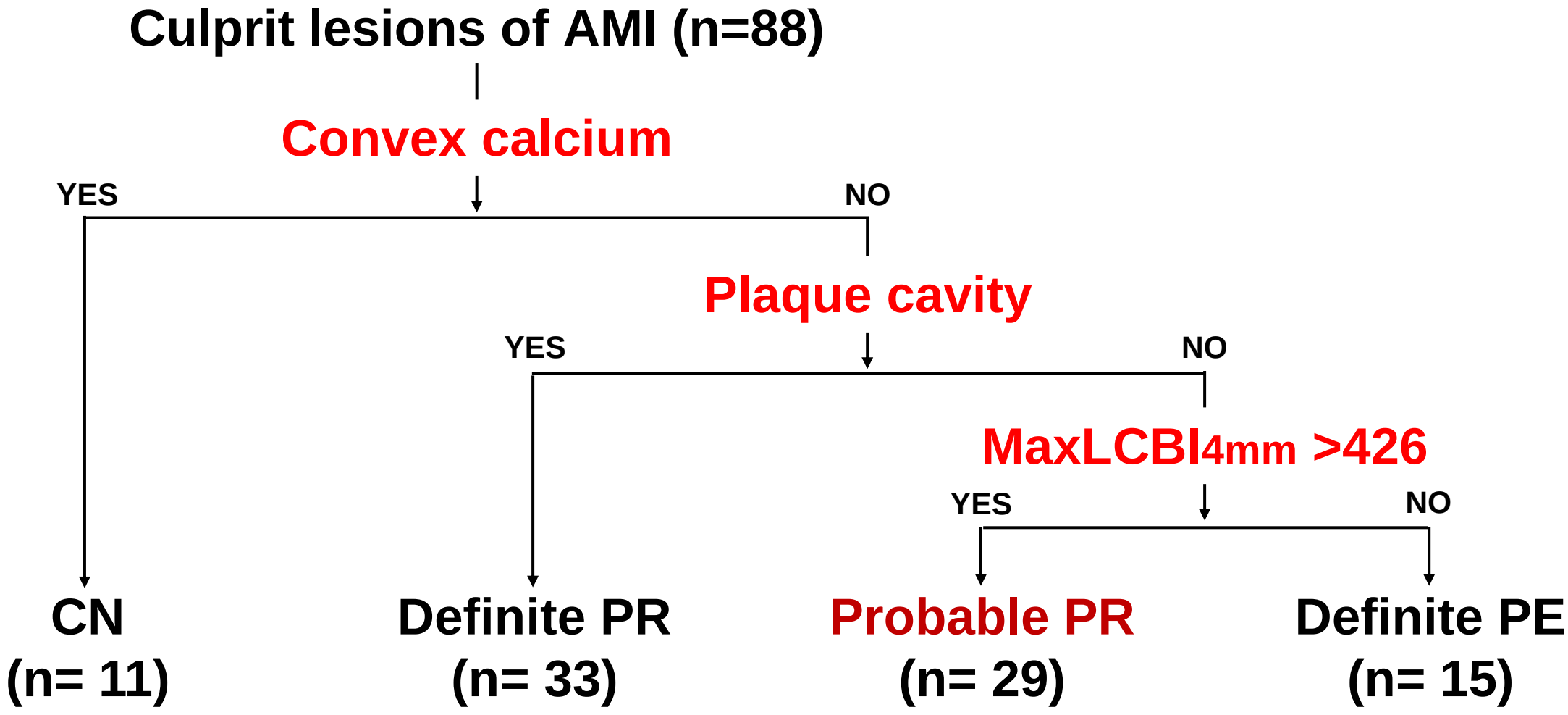
Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

NIRS-IVUS classification algorithm



Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

Validation cohort using NIRS-IVUS classification algorithm



Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

Ability of NIRS-IVUS for identifying OCT-PR, OCT-PE, and OCT-CN

	Accuracy	Sensitivity	Specificity	PPV	NPV
NIRS-IVUS-PR	97	97	96	98	92
NIRS-IVUS-PE	98	93	99	93	99
NIRS-IVUS-CN	99	100	99	91	100

By evaluating maxLCBI$_{4mm}$ in addition to plaque cavity, convex calcium, NIRS-IVUS can accurately differentiate among PR, PE, and CN.

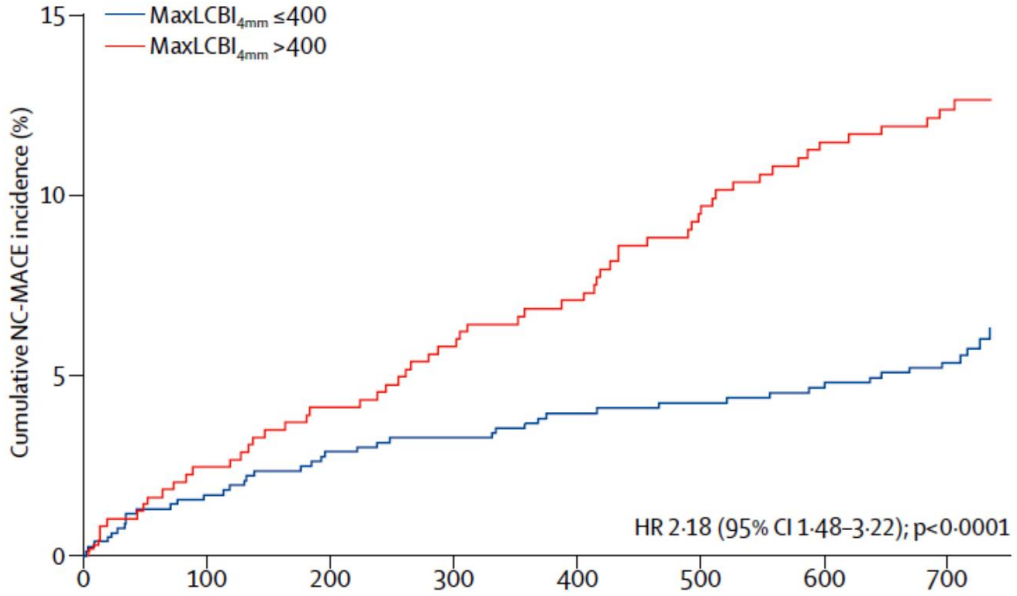
Terada K, et al. J Am Coll Cardiol Img 2021;14:1440-1450

Identification of patients and plaques vulnerable to future coronary events with near-infrared spectroscopy intravascular ultrasound imaging: a prospective, cohort study

*Ron Waksman, Carlo Di Mario, Rebecca Torguson, Ziad A Ali, Varinder Singh, William H Skinner, Andre K Artis, Tim Ten Cate, Eric Powers, Christopher Kim, Evelyn Regar, S Chiu Wong, Stephen Lewis, Joanna Wykrzykowska, Sandeep Dube, Samer Kazziha, Martin van der Ent, Priti Shah, Paige E Craig, Quan Zou, Paul Kolm, H Bryan Brewer, Hector M Garcia-Garcia, on behalf of the LRP Investigators**

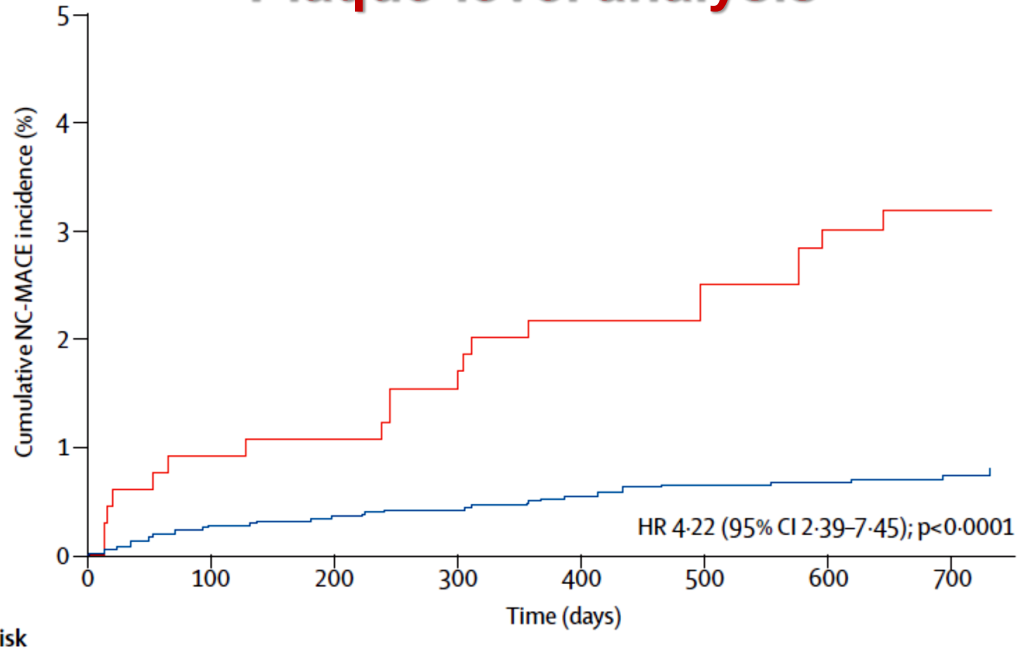
Cumulative incidence of non-culprit MACE

Patient-level analysis



Number at risk								
MaxLCBI$_{4mm}$ ≤400	778	748	733	728	689	682	676	664
MaxLCBI$_{4mm}$ >400	493	473	457	448	426	409	399	392

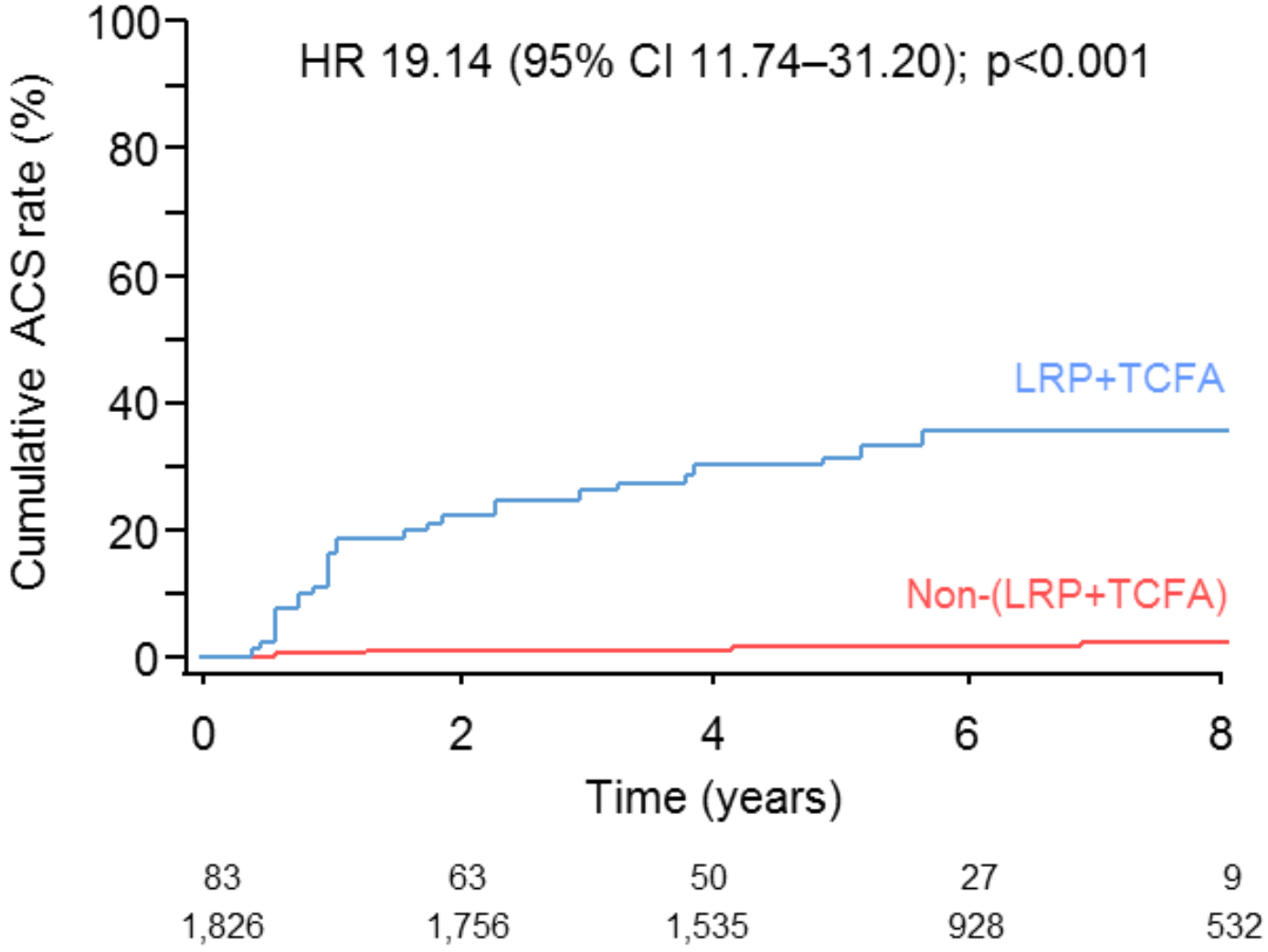
Plaque-level analysis

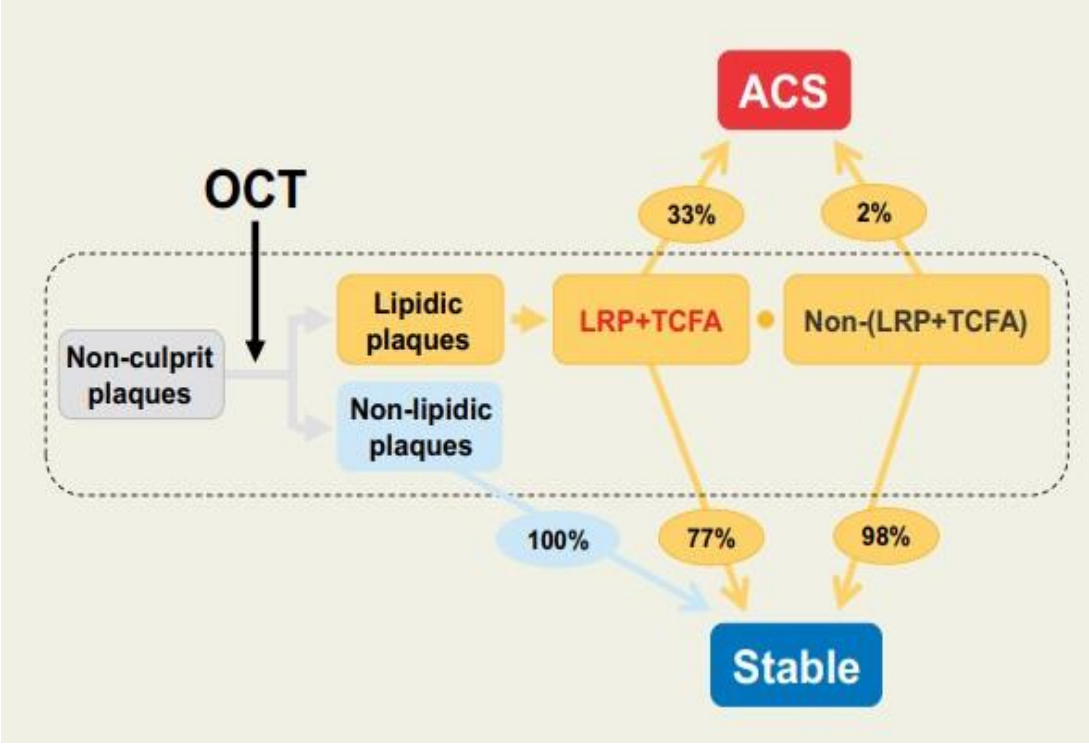


Number at risk								
MaxLCBI$_{4mm}$ ≤400	5091	4965	4903	4882	4681	4626	4583	4537
MaxLCBI$_{4mm}$ >400	664	644	634	626	600	581	568	563

Waksman R, et al. Lancet 2019；394:1629-1637

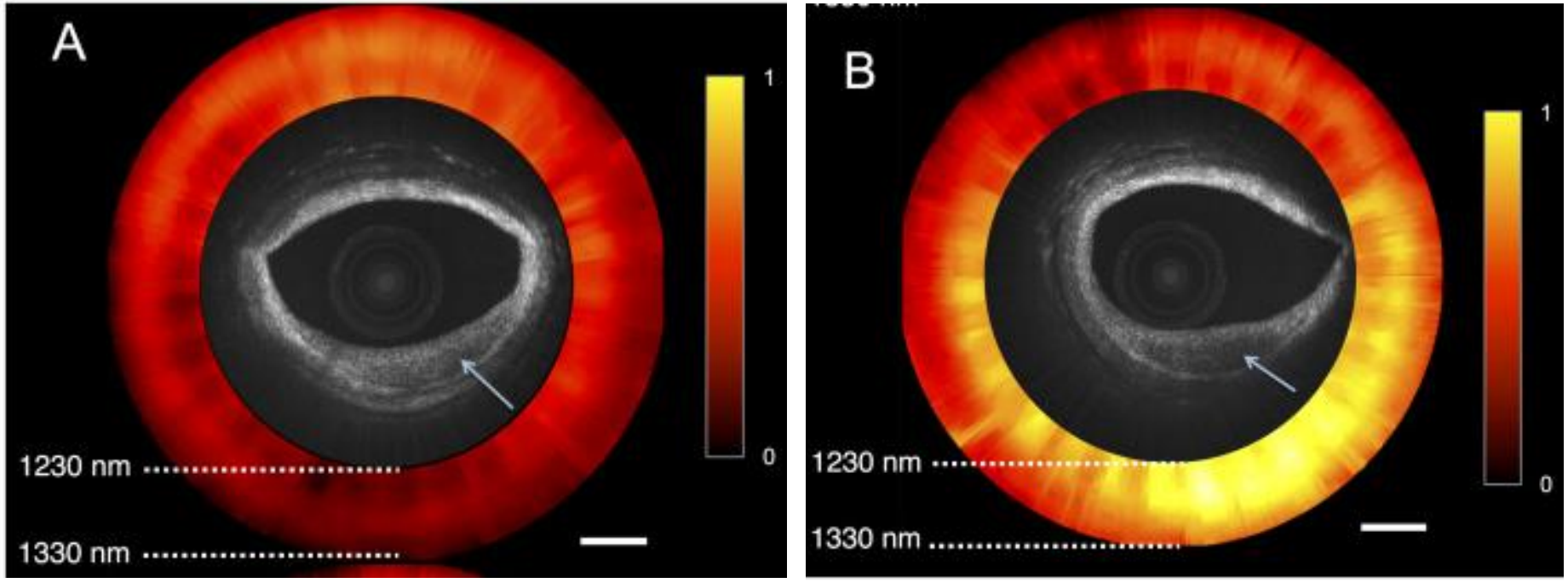
ACS event rate based on OCT findings





Kubo T, et al, Eur Heart J CV img, 2021;22:1376–1384

NIRS-OCT images (cadaver coronary artery ex vivo)



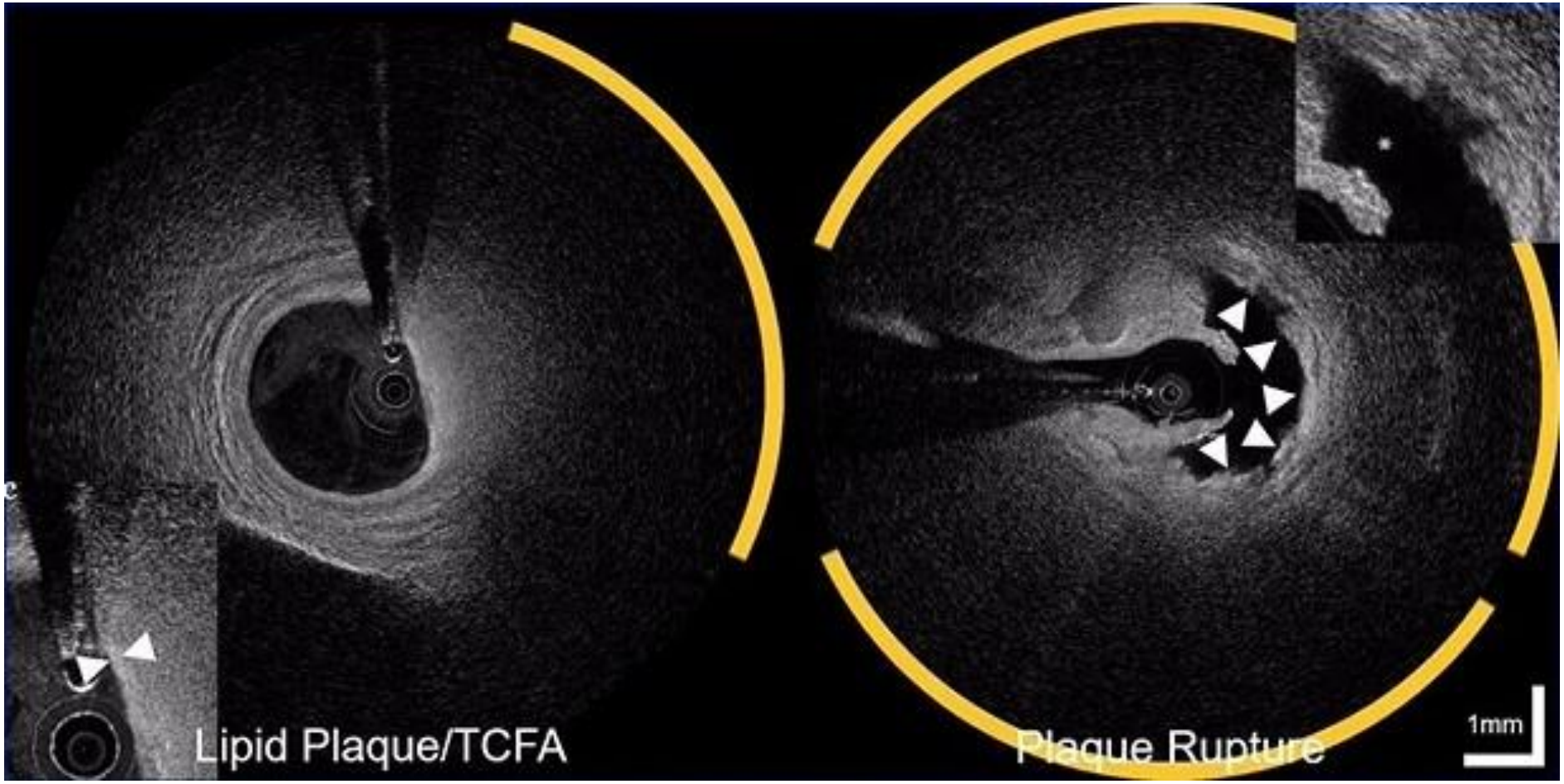
Scale bars;500 μm

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.

Deep-OCT with NIRS (HyperVue®･SpectraWAVE Inc.)

HyperVue®

Deep-OCT with NIRS images (First in human study)



Take home message

- It might be difficult to differentiate clearly between probable PE and PR by OCT alone because of huge red thrombus with signal attenuation on the culprit site.
- NIRS-IVUS may allow us to identified definite PE from probable PE and/or PR by evaluating maxLCBI$_{4mm}$ in addition to the findings of plaque cavity and convex calcium.
- Combined use of OCT and NIRS-IVUS may provide us to differentiate PR, PE and CN more accurately compared with separate use of each modality.
- NIRS-OCT might be an ideal modality to identify the mechanism of ACS caused by PR, PE and CN with easy and accurate.

Thank you for your kind attention !!

NIRS-IVUS for Differentiating Coronary Plaque Rupture, Erosion and Calcified Nodule in Acute Myocardial Infarction

Thank you for your kind attention !!

Kosei Terada, MD,[a] Takashi Kubo, MD, PhD,[a] Take
Yasushi Ino, MD, PhD,[a] Hiroki Emori, MD,[a] Daisuk
Amir Kh.M. Khalifa, MD,[a] Masahiro Takahata, MD,
Atsushi Tanaka, MD, PhD,[a] Takeshi Hozumi, MD,

OBJECTIVES This study sought to investigate the ability of combined near-infrared spectroscopy and intravascular ultrasound (NIRS-IVUS) to differentiate plaque rupture (PR), plaque erosion (PE), or calcified nodule (CN) in acute myocardial infarction (AMI).

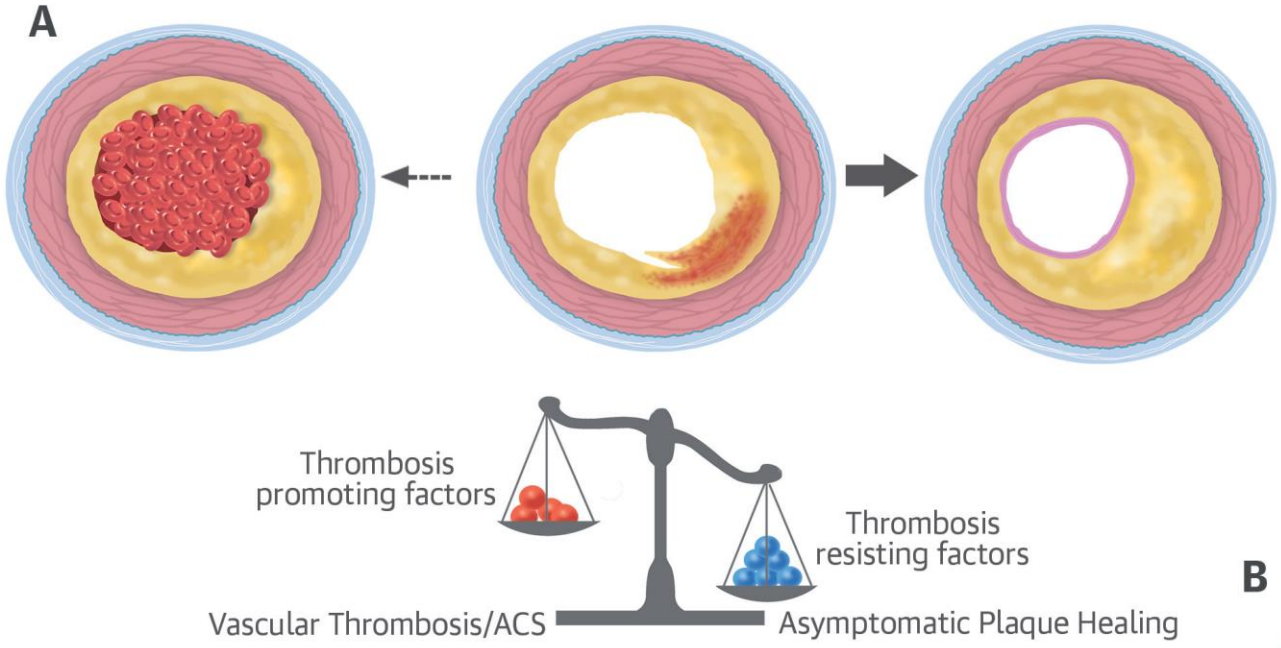
BACKGROUND Most acute coronary syndromes occur from coronary thrombosis based on PR, PE, or CN. In vivo differentiation among PR, PE, and CN is a major challenge for intravascular imaging.

METHODS The study enrolled 244 patients with AMI who had a de novo culprit lesion in a native coronary artery. The culprit lesions were assessed by both NIRS-IVUS and optical coherence tomography (OCT). Maximum lipid core burden index in 4 mm ($maxLCBI_{4mm}$) was measured by NIRS. Plaque cavity and convex calcium was detected by IVUS. The OCT diagnosis of PR (n = 175), PE (n = 44), and CN (n = 25) was used as a reference standard.

RESULTS In the development cohort, IVUS-detected plaque cavity showed a high specificity (100%) and intermediate sensitivity (62%) for identifying OCT-PR. IVUS-detected convex calcium showed a high sensitivity (93%) and specificity (100%) for identifying OCT-CN. NIRS-measured $maxLCBI_{4mm}$ was largest in OCT-PR (705 [interquartile range (IQR): 545 to 854]), followed by OCT-CN (355 [IQR: 303 to 478]) and OCT-PE (300 [IQR: 126 to 357]) ($p < 0.001$). The optimal cutoff value of $maxLCBI_{4mm}$ was 426 for differentiating between OCT-PR and -PE; 328 for differentiating between OCT-PE and -CN; and 579 for differentiating between OCT-PR and -CN. In the validation cohort, the NIRS-IVUS classification algorithm using plaque cavity, convex calcium, and $maxLCBI_{4mm}$ showed a sensitivity and specificity of 97% and 96% for identifying OCT-PR, 93% and 99% for OCT-PE, and 100% and 99% for OCT-CN, respectively.

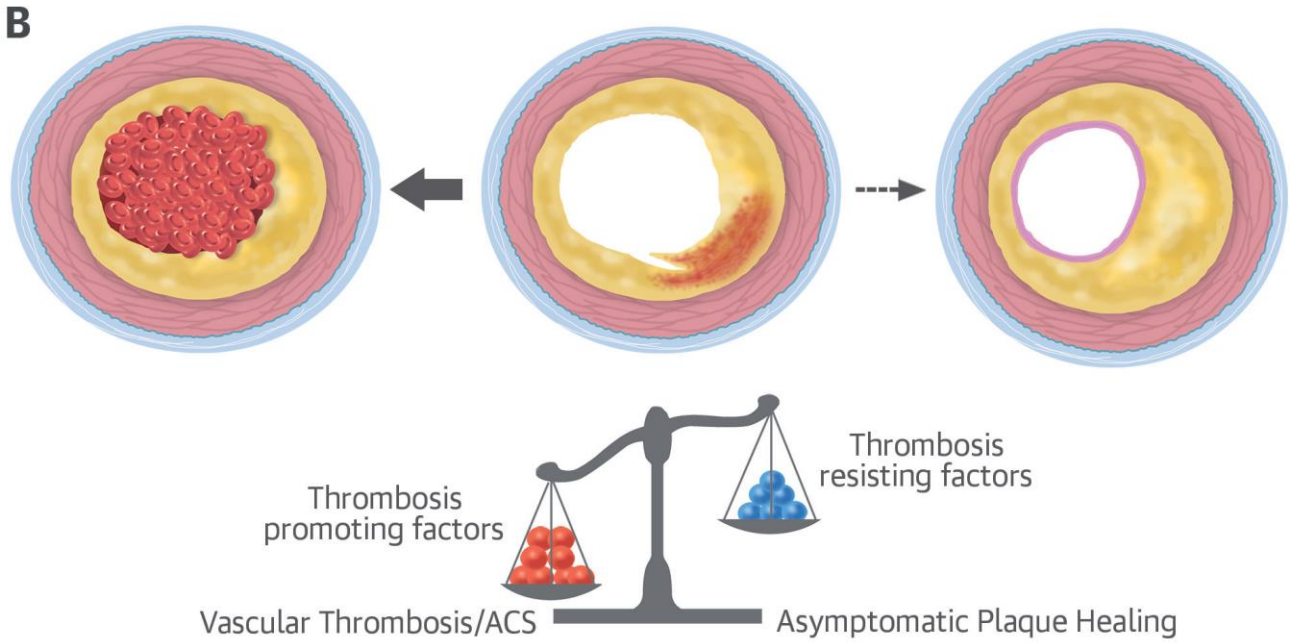
CONCLUSIONS By evaluating plaque cavity, convex calcium, and $maxLCBI_{4mm}$, NIRS-IVUS can accurately differentiate PR, PE, and CN. (J Am Coll Cardiol Img 2021;14:1440–50) © 2021 by the American College of Cardiology Foundation.

Fate of Ruptured Coronary Atherosclerotic Plaques According to Thrombotic Milieu



In the most common scenario, small thrombus formation associated with plaque rupture is contained and vascular occlusive thrombus is inhibited.

In the less common scenario of several prothrombotic factors coinciding (e.g., inflammatory state, large lesion plaque burden, vasoconstriction, circadian rheological changes), local thrombosis associated with plaque rupture cannot be contained, and clinically significant vascular thrombosis occurs, triggering an acute coronary syndrome (ACS).



Arbaba-Zadeh, A. et al. *J Am Coll Cardiol* 2015;65:846–855