"Detection and Prediction of Plaque Rupture Using OCT"

How Can We Predict and Prevent Adverse Ischemic Events?

So-Yeon Choi, MD., PhD.
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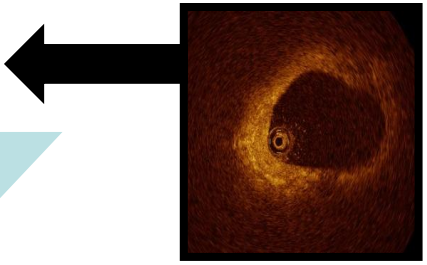
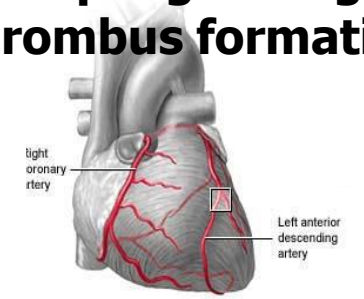
Can Invasive Imaging Predict and Prevent CV Events?

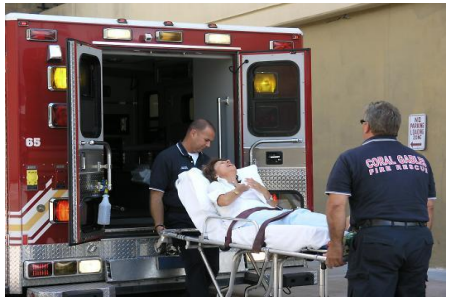
Vulnerable plaque



Invasive Imaging

Rapid growing Thrombus formation

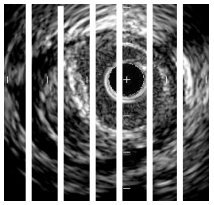
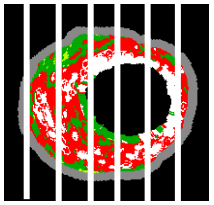
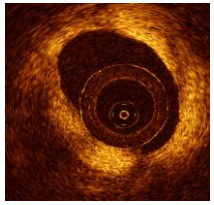
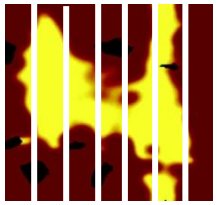
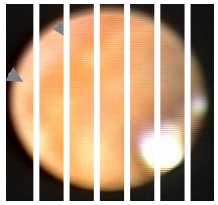




Revascularization, MI, SCD

Intracoronary Imaging Modalities

Ability of Detection for Vulnerable Plaque

	 Grey Scale IVUS	 RF-IVUS	 OCT	 NIR Spectroscopy	 Angioscopy
Axial Resolution (μm)	100	200	10-20	NA	10-50
PR	++	+	+++	-	+/-
TCFA	+/-	+++	++	+/-	+
Necrotic Core	+/-	++	+	++	+
Thrombus	+/-	-	++	+/-	++
Calcium	++	+	++	-	+/-
Thin cap	-	+	+++	-	+/-

What we already know about VPs from pathology and IVUS studies

VPs are characterized thin fibrous cap, extensive macrophage infiltration, paucity of smooth muscle cells, and large lipid core.

2/3 of lesions showed <75% cross sectional luminal narrowing (<50% DS).

VPs are prevalent in patients with high hs-CRP or ACS.

VPs distributes dominantly in proximal site in coronary tree.

VPs related with variable clinical presentation.

Symptomatic vs. silent (=secondary =innocent)

Luminal narrowing and thrombus formation

VPs are at the risk of immediate complications during PCI.

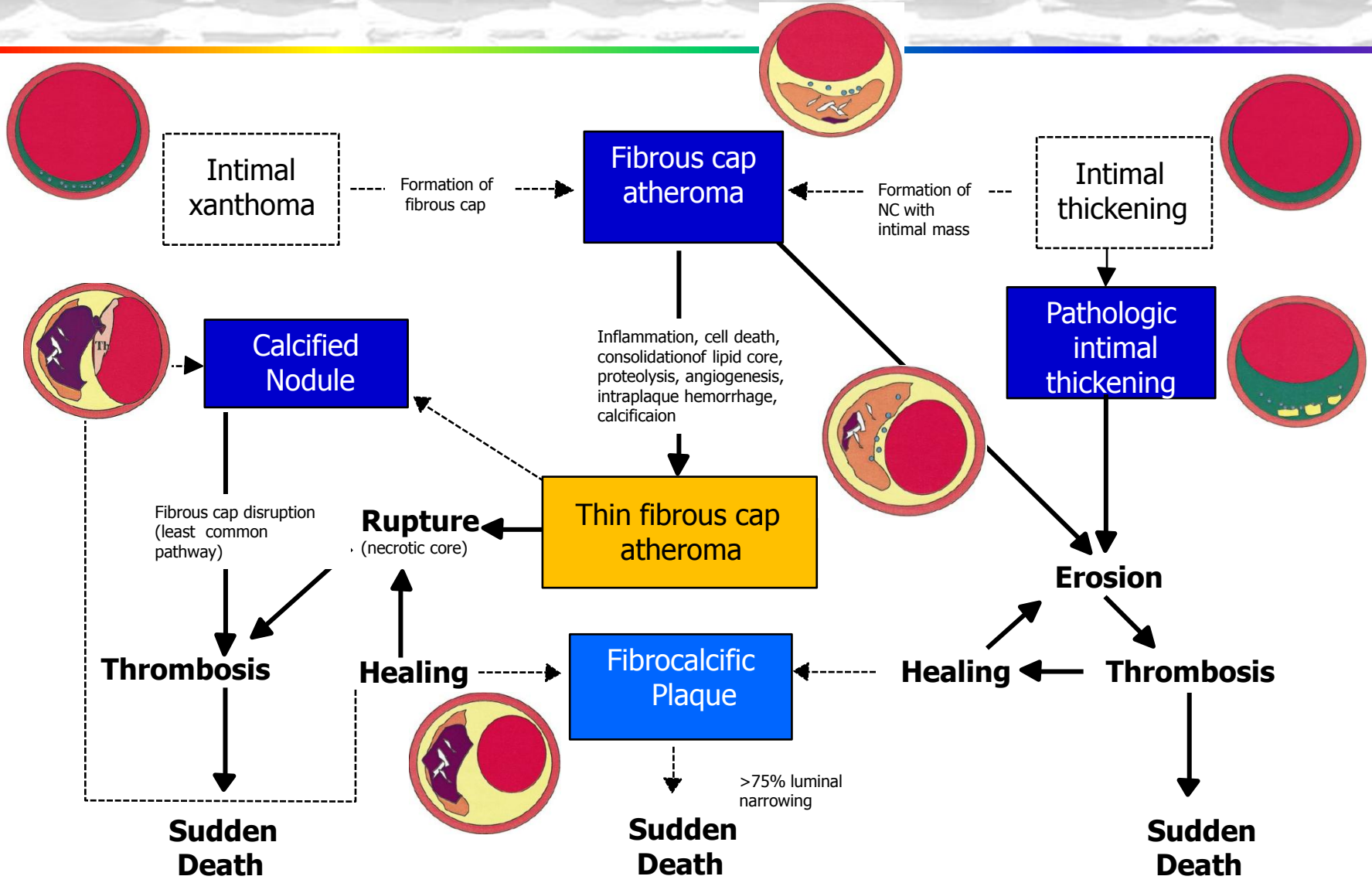
VPs might be related with clinical outcomes (lesion progression, CV events)

VPs could be stablized with statin.

What is OCT benefit for detecting VPs?
Compared with IVUS

- High resolution → better detection
- Differentiate phenotype of vulnerable plaques and other causes of CV events
- Understanding of mechanisms of plaque rupture
- Information of details: cap thickness, macrophage infiltration, microvessels, thrombus ...inflammation?

Scheme for AS Plaques Related to SCD

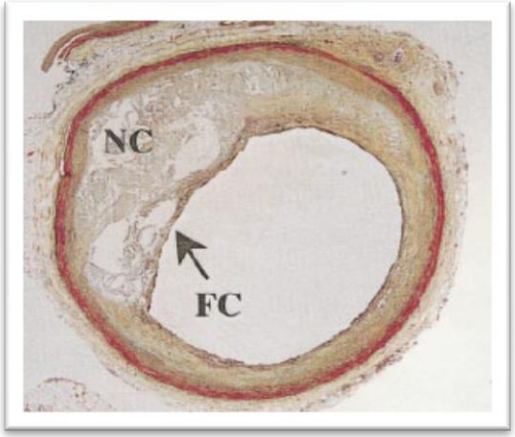


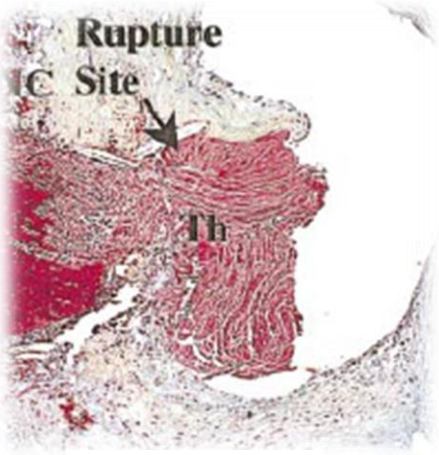
Distribution of Culprit Plaques by Sex and Age in 241 Cases of SCD
Virmani R et al, Arterioscler Thromb Vasc Biol 2000;20;1262-1275

Plaque features related with clinical events

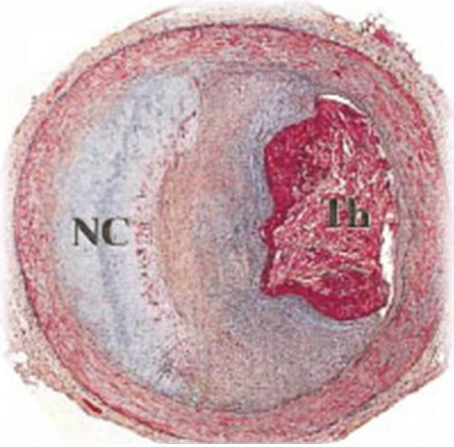
Pathology

TCFA

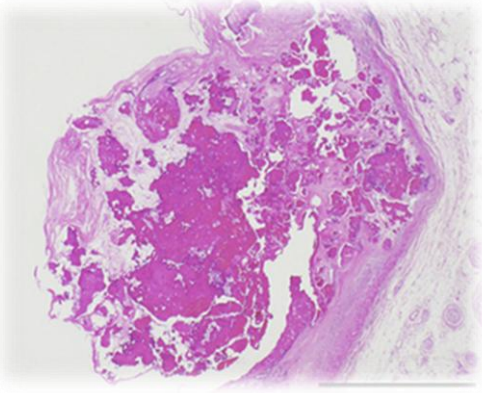




Rupture



Erosion

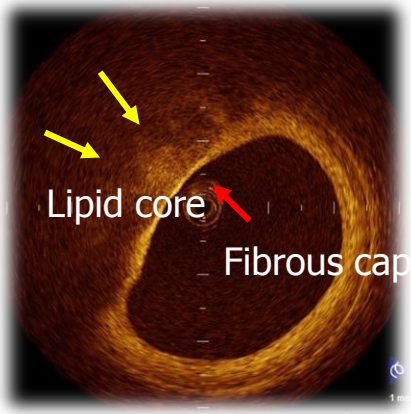


Calcific nodule

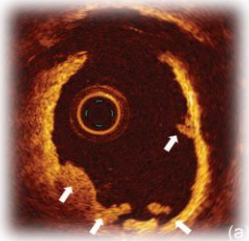
Plaque features related with clinical events

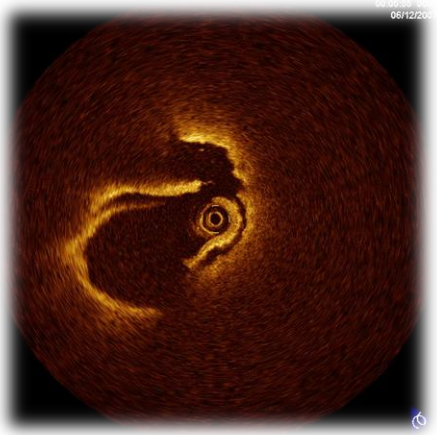
OCT

TCFA

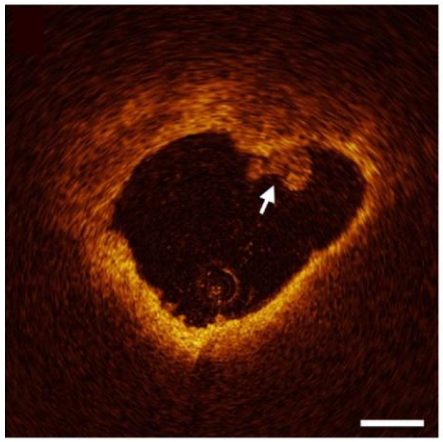


SCD

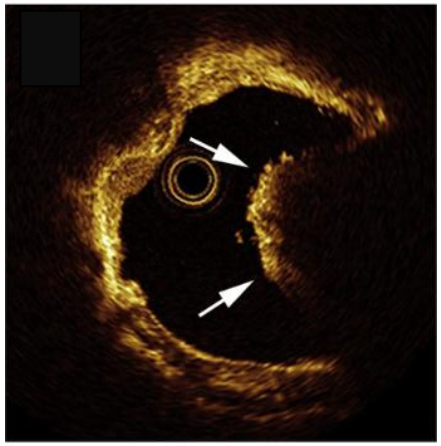




Rupture



Erosion



Calcific nodule

Direct comparison of VH-IVUS and OCT for "pathologic" TCFA

258 ROI were obtained from 14 autopsied human hearts, with plaque composition and classification assessed by histology and compared with coregistered ex vivo VH-IVUS and OCT

- **Maximum lipid arc** on OCT was an excellent discriminator of fibroatheroma (AUC 0.92, 95% CI 0.87-0.97) and TCFA (AUC 0.86, 95% CI 0.81-0.92), with lipid arc **≥80°** the optimal cut-off value.
- The sensitivity, specificity, and diagnostic accuracy for TCFA identification was 63.6%, 78.1%, and **76.5% for VH-IVUS** and 72.7%, 79.8%, and **79.0% for OCT.**
- Combining **VH-defined fibroatheroma and fibrous cap thickness ≤85 µm** over 3 continuous frames improved TCFA identification, with diagnostic accuracy of **89.0%**.

CONCLUSIONS: Both VH-IVUS and OCT can reliably identify TCFA, although OCT accuracy may be improved using lipid arc ≥80° and fibrous cap thickness ≤85 µm over 3 continuous frames. Combined VH-IVUS/OCT imaging markedly improved TCFA identification.

Brown et al, Circ CV Imaging 2015;8:e003487

Causes of STEMI/NSTEMI
In vivo OCT imaging study

Study	Pts	RFC =PR	IFC =Plaque erosion	Calcific nodules	Others	Findings
Prati, J Am Coll Cardiol Img 2013;6:283–7.	? STEMI In the OCT databases of 4 institutions		31			40% 에서 non-occlusive lesion으로 약물치료 no event
Jia, J Am Coll Cardiol 2013;62:1748–58.	126 STEMI/NSTEMI	55 (43.7%)	39 (31.0%)	10 (7.9%)	3 SCAD, 22 UD	병변차이는 있다. Erosion은 젊은 사람에서 생기고 임상양상이 NSTEMI로 더 잘 온다
Nishiguchi EHJ Acute CV Care 2013 e-pub	326 STEMI/NSTEMI	160 (49.1%)	135 non-PR/non-SCAD		13 (4.0%) SCAD	SCAD is not a rare, SCAD에서 여자빈도 높다
Guagliumi, JACC Intv 2014;7:958	140 STEMI age-matched men and women in OCTAVIA	69	35		2 SCAD, 34 UD	남녀 차이 없다
Saia, J Am Coll Cardiol Img 2015;8:566–75.	97 STEMI in OCTIVA	63	32		2 SCAD	병변차이는 있다. 임상양상은 좀 다르지만 치료 후에 반응은 유사하다.
Higuma JACC Intv 2015:8:1166	112 STEMI	72 (64.3%)	30 (26.8%)	9 (8.0%)		CN의 경우 neg remodelin과 연관된다. Erosion의 경우 PCI후 no-reflow가 PR보다 적다.

A Combined OCT and IVUS on PR, PE, and CN in Patients With STEMI

112 STEMI pts who underwent PCI within 12 h from symptom onset were included. Both OCT and IVUS were performed following aspiration thrombectomy.

- **The incidence of PR, PE, and CN was 64.3%, 26.8%, and 8.0%**, respectively.
- **PE and CN**, compared with PR, had **more fibrous plaque** ($p<0.001$ and $p<0.001$) **and less thin-cap fibroatheroma** ($p<0.001$ and $p<0.001$) as well as **smaller plaque burden** ($p=0.003$ and $p=0.001$) and **remodeling index** ($p=0.003$ and $p<0.001$).
- **PE** had **greater plaque eccentricity** index than PR and CN ($p<0.001$ and $p<0.001$).
- **CN** had greater calcified arc and shallower calcium than PR ($p<0.001$ and $p<0.001$) or PE ($p < 0.001$ and $p < 0.001$). More than one-half of CN had **negative remodeling**.

CONCLUSIONS: PE was the underlying mechanism in one-fourth of STEMI. PE was characterized by eccentric fibrous plaque. CN was characterized by superficial large calcium and negative remodeling. PE was associated with less microvascular damage after PCI.

Higuma JACC Intv 2015:8:1166

Eroded vs. Ruptured Plaques at the Culprit Site of STEMI (OCTAVIA)

In Vivo Pathophysiological Features and Response to Primary PCI

In a prospective study, 140 pts with STEMI underwent OCT of the IRA before PCI, after EES implantation and at 9-month follow-up

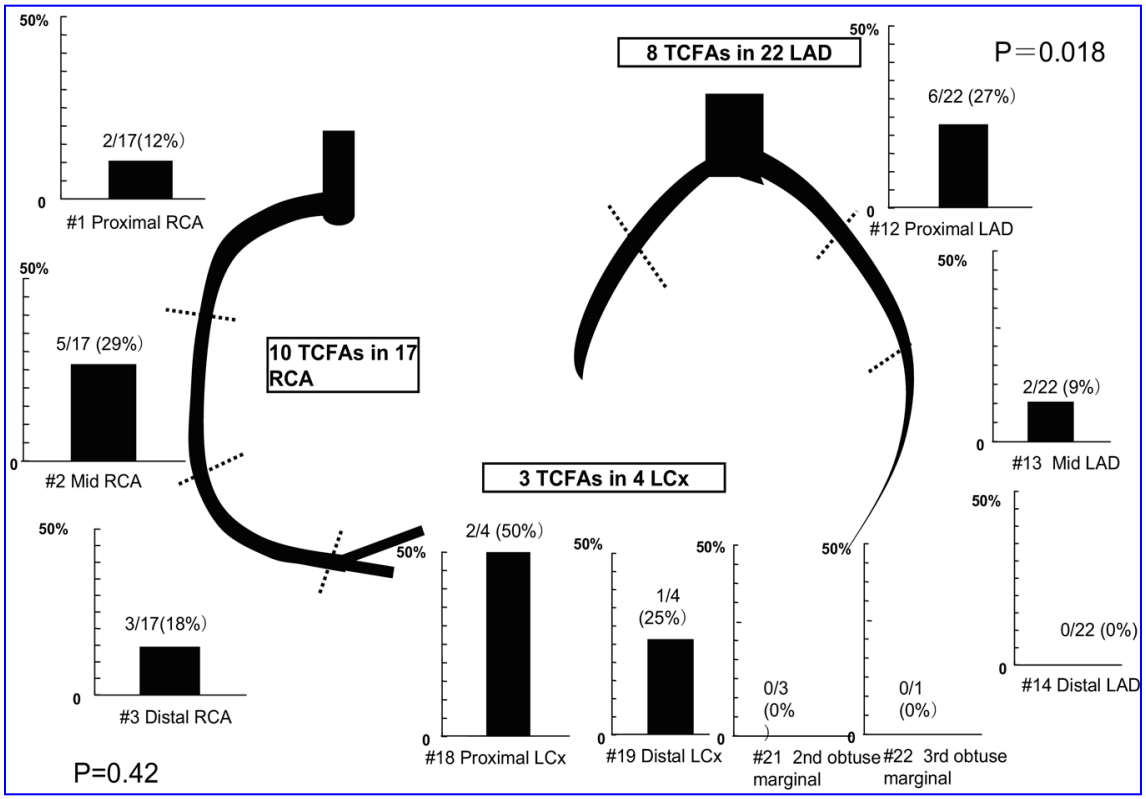
- Culprit plaque morphology was adjudicated in 97 pts: **32 plaques (33.0%) with an intact fibrous cap (IFC), 63 (64.9%) plaques with a ruptured fibrous cap (RFC), and 2 (2.1%) SCDs.**
- An **IFC** presented more frequently with a **patent IRA** (56.2% vs. 34.9%; p = 0.047), and had **fewer lipid areas** (lipid-rich areas: 75.0% vs. 100.0%; p < 0.001) and **less residual thrombus** before stenting (white thrombus: 0.41 mm^3 vs. 1.52 mm^3 ; p = 0.001; red thrombus: 0 mm^3 vs. 0.29 mm^3 ; p = 0.001) with a **lower peak of CKMB** (66.6 IU/l vs. 149.8 IU/l; p = 0.025).
- At the 9-month OCT, IFC and RFC had similar high rates of stent strut coverage (92.5% vs. 91.2%; p = 0.15) and similar percentage of volume obstruction (12.6% vs. 10.2%; p = 0.27). No significant differences in clinical outcomes were observed up to 2 years.

CONCLUSIONS: In the present study, an IFC was observed at the culprit lesion site of one-third of STEMIs. IFC, compared with RFC, was associated with higher rates of patent IRA at first angiography, fewer lipid areas, and residual endoluminal thrombus. However, no difference in vascular response to EES was observed.

Saia, J Am Coll Cardiol Img 2015;8:566–75.

Distribution and frequency of PR and OCT-TCFA

3V OCT study in 43 patients with ACS

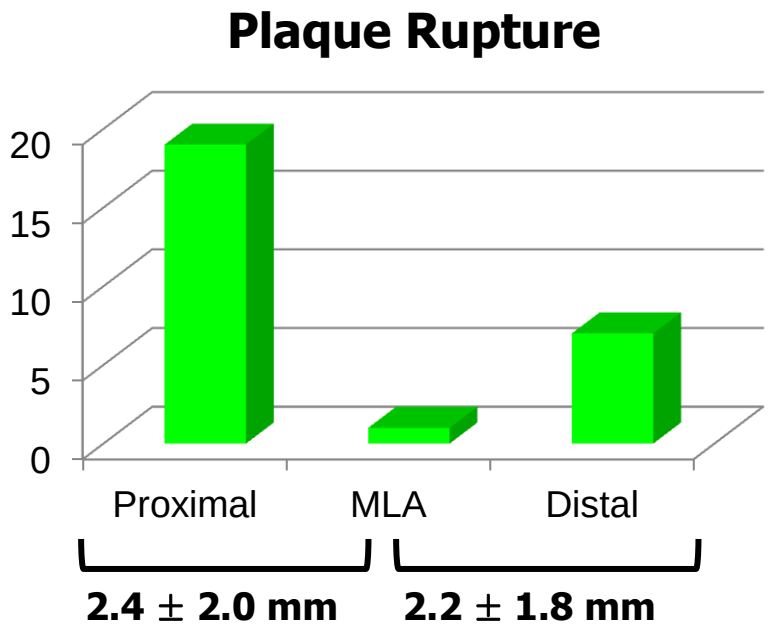


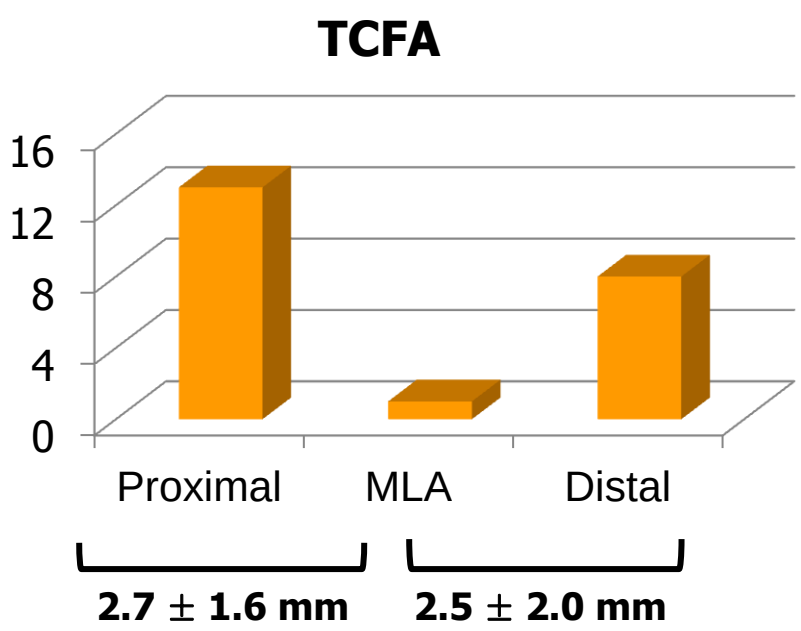
PR was found in 28 patients (65%) and multiple PRs in 5 patients (12%).
21 TCFA was found in 18 patients (42%) and multiple TCFAs were found in the same vessel in 3 patients (7%).

Tanaka et al. Am J Cardiol 2008;102:975–979

Axial Distribution of PR and TCFA

48 culprit lesions in 48 patients with ACS





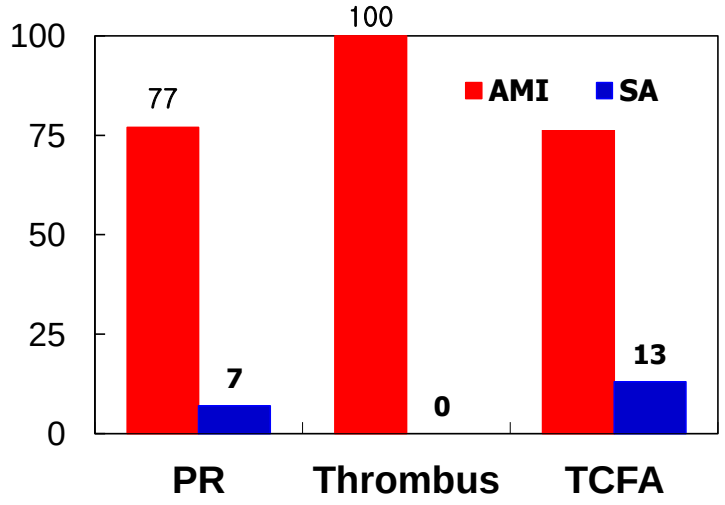
Conclusions: OCT showed that the MLA is rarely at the site of greatest instability (location of rupture and TCFA) and plaque instability sites are more common proximal to MLA site within the lesion in ACS.

Yang HM, Choi SY et al, TCT2009
Ajou OCT registry

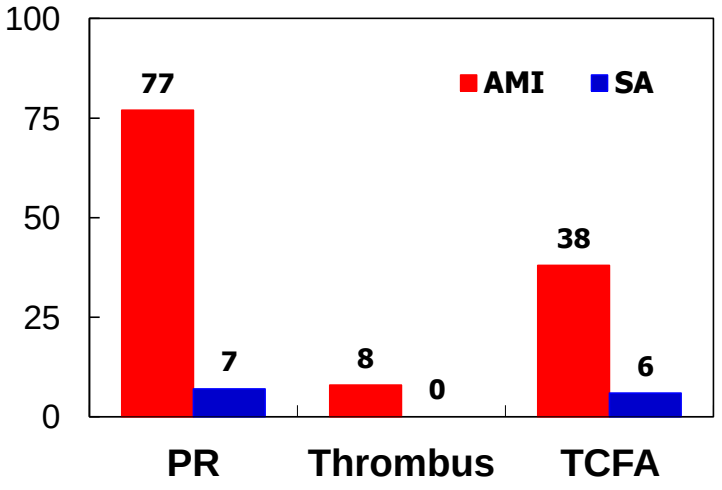
Multiple Coronary Lesion Instability in Pts with AMI

26 AMI pts and 16 SAP pts who had multivessel disease and underwent multivessel PCI

In the infarct-related/target lesion



In the non-infarct-related/non-target lesion



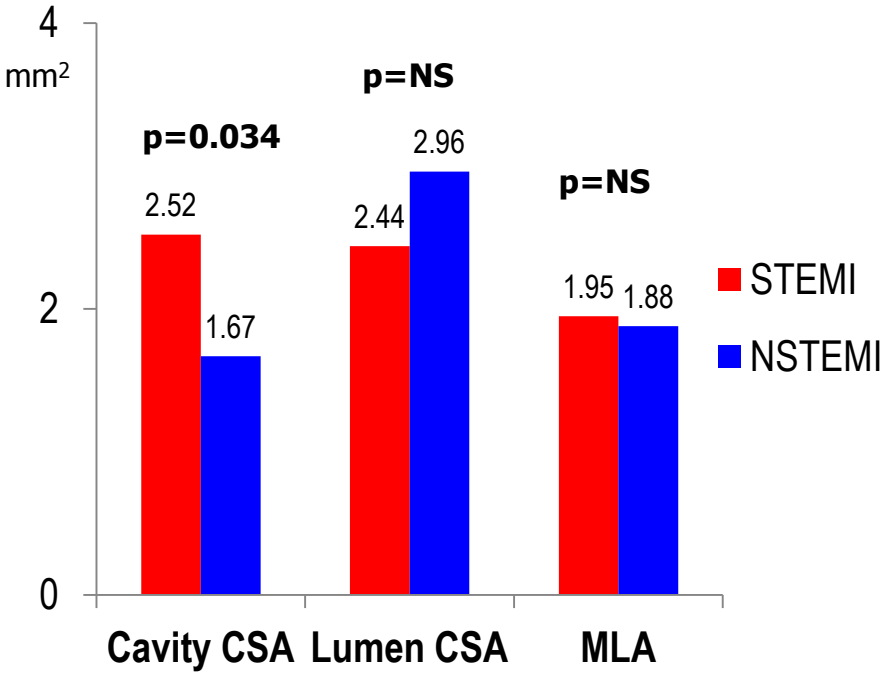
Multiple OCT-derived TCFAs in both the infarct-related/target and the noninfarct-related/nontarget lesions were observed in **38% of pts with AMI** but not in pts with SAP (p=0.007)

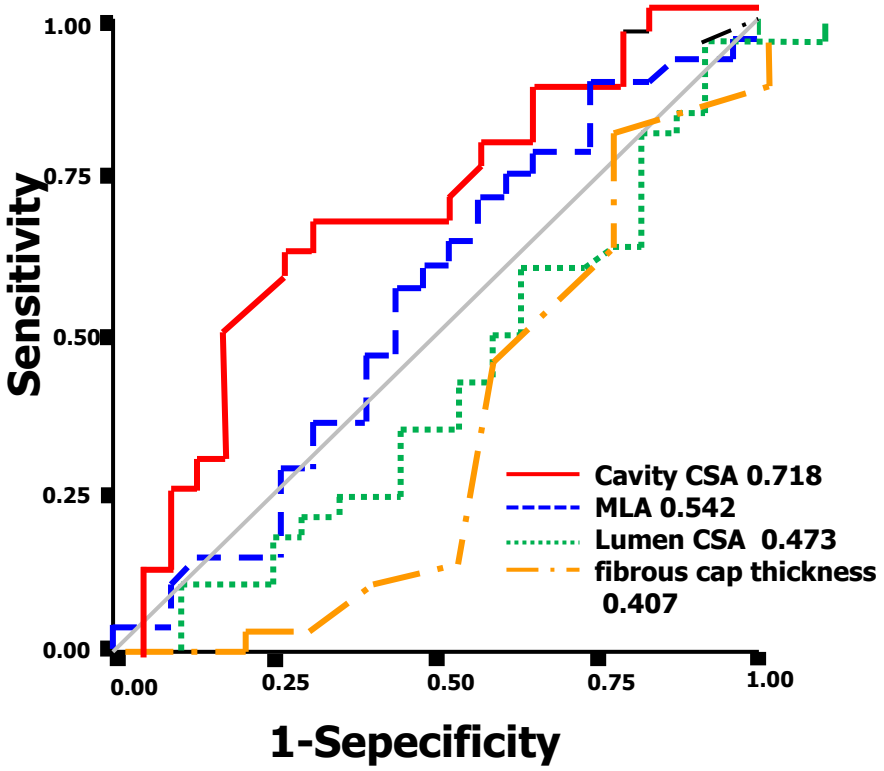
Conclusions The present OCT examination demonstrated multiple lesion instability in the presence of AMI.

Kubo et al. Am J Cardiol 2010;105:318 –322

Difference of culprit lesion morphologies: STEMI vs NSTEMI

- 89 culprit lesions in 89 pts (40 STEMI vs 49 NSTEMI)
- The incidence of **PR, TCFA and red thrombus** was significantly **higher in STEMI** compared with NSTEACS (70% vs. 47%, p = 0.033, 78% vs. 49%, p = 0.008, and 78% vs. 27%, p < 0.001, respectively).
- **PR of which aperture was open-wide against the direction of coronary flow** was more often seen **in STEMI** compared with NSTEACS (46% vs. 17%, p 0.036).

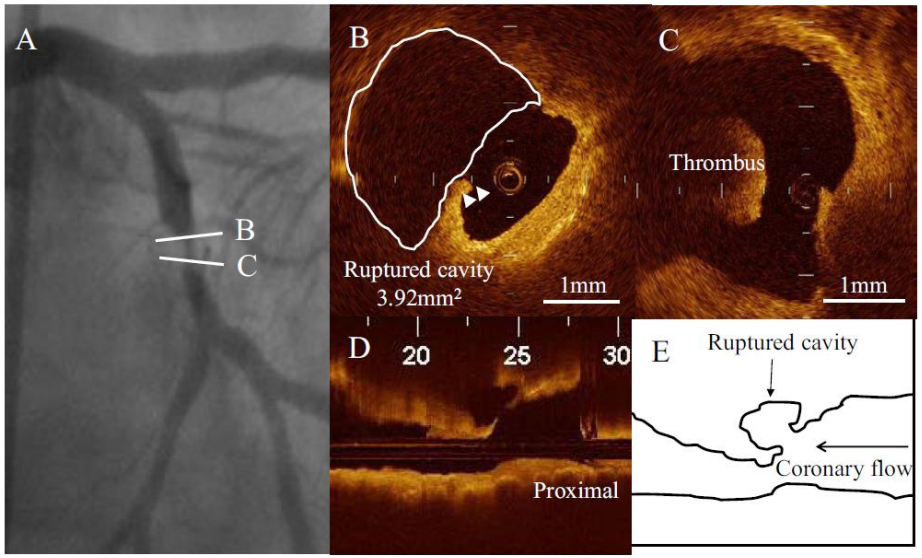




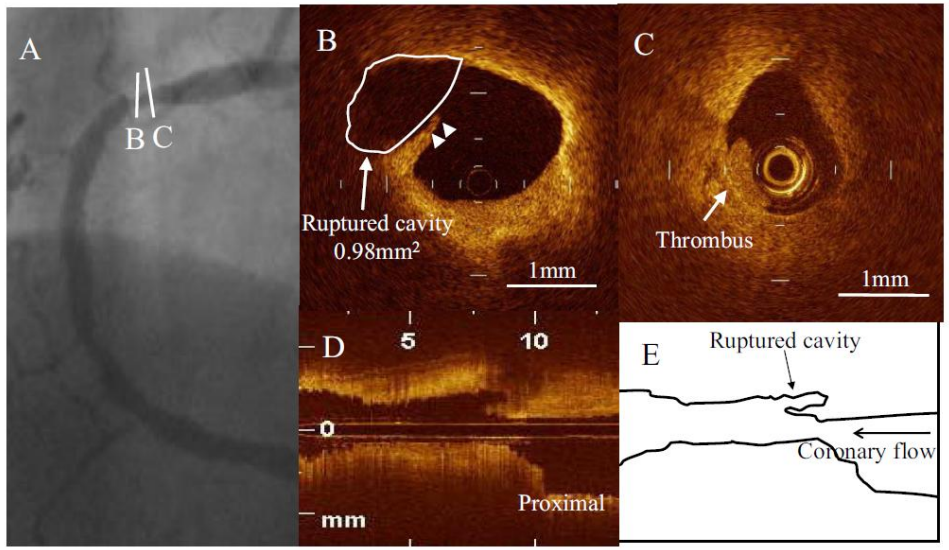
Ino et al., J Am Coll Cardiol Intv 2011;4:76–82

OCT Findings of PR STEMI vs NSTEMI

	STEMI	NSTEMI	P Value
Proximal location of ruptured cavity	18 (64)	8 (35)	0.036
Longitudinal morphological features of plaque rupture (proximal type)	13 (46)	4 (17)	0.039



STEMI

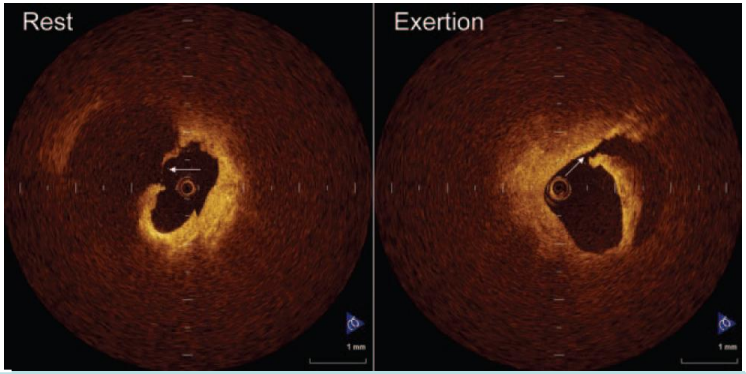


NSTEMI

Ino, et al., J Am Coll Cardiol Intv 2011;4:76–82

Exercise-triggered Plaque Rupture

43 consecutive ACS patients
Plaque rupture in 43 (60%)
Onset at rest vs onset with exertion



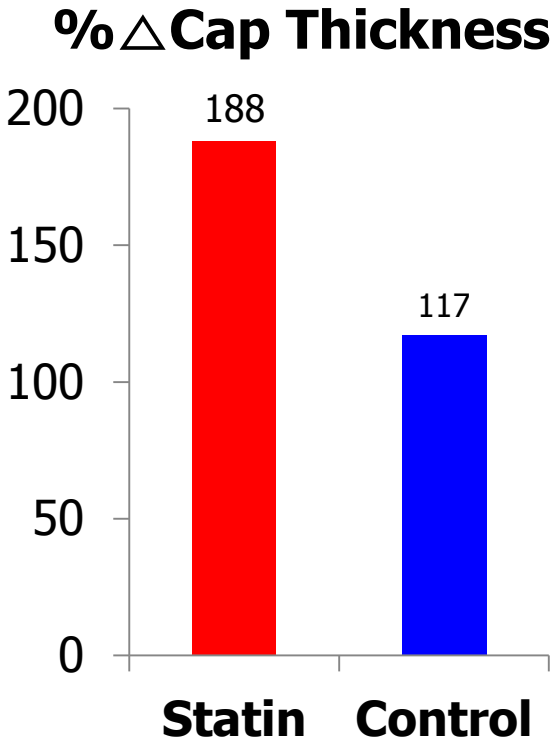
	Rest n=28	Exercise n=15	P
Thrombus	27 (96)	11(73)	0.04
Thin-cap fibroatheroma at culprit site	16 (57)	6 (40)	0.35
Broken at plaque shoulder	16 (57)	14 (93)	0.017
Thickness of broken fibrous cap, m	50 [median 15]	90 [median 65]	0.0017

Conclusion: The morphologies of exertion-triggered and rest-onset ruptured plaques differ in ACS patients. some plaque rupture may occur in thick fibrous caps depending on exertion levels.

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

Effect of statin therapy on coronary fibrous-cap thickness in pts with ACS

Forty AMI patients with hyperlipidemia were divided into statin treatment (n=23) vs control (n=17); serial OCT of a non-treated, lipid-rich lesion was performed at baseline and 9-month follow-up.



Conclusion: Statin therapy for 9 months after the onset of AMI increased fibrous-cap thickness in patients with hyperlipidemia.

Takarada S, et al. Atherosclerosis 2009;202(2):491–497

OCT based diagnosis makes treatment strategy in pts with AMI

Non-culprit, non-obstructing lesion pts with AMI could be stabilized with medical tx: antiplatelet agents

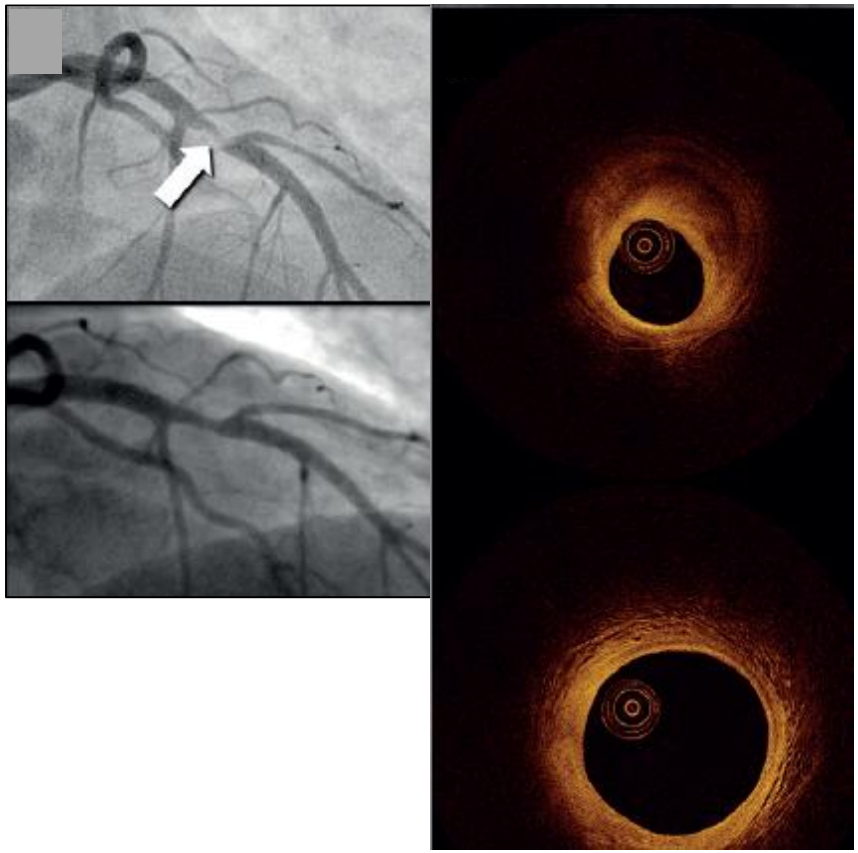
Plaque erosion as the cause in 31 pts presenting with STEMI.
At a median fu of 753 ds, all pts were asymptomatic, regardless of stent implantation

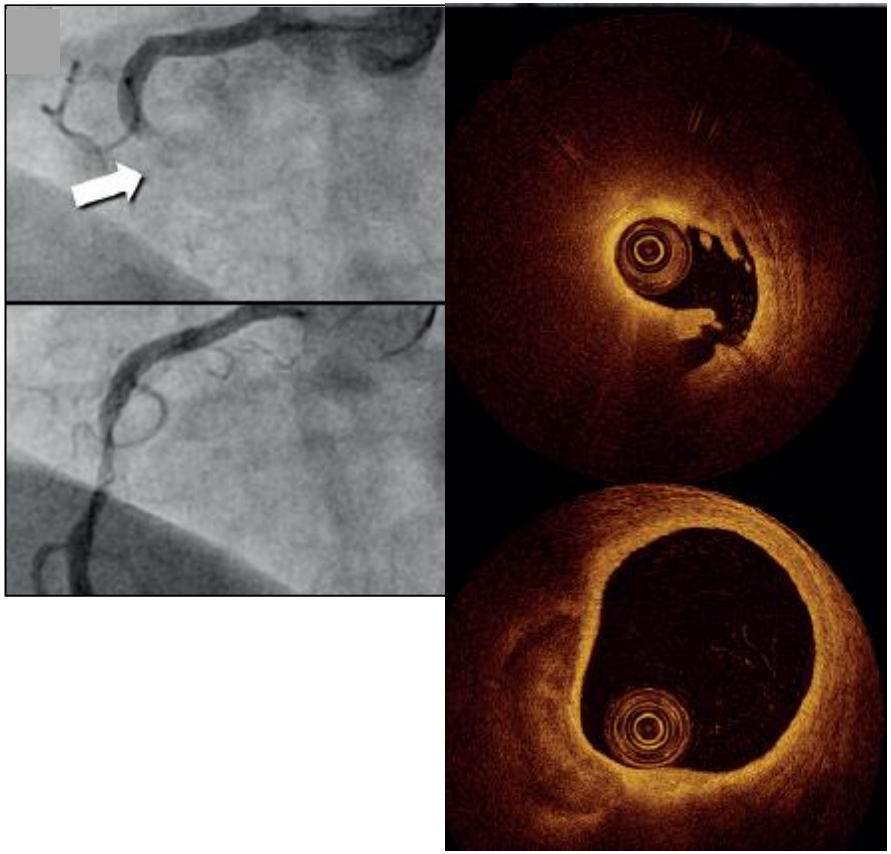
	Med Tx (n = 12)	**PCI (n = 19)**	p Value
Pre-aspiration DS, %	79.4 ± 33.3	87.9 ± 17.3	0.95
Post-aspiration DS, %	27.1 ± 19.4	32.0 ± 35.2	0.48
Pre-aspiration TIMI flow grade ≤2	9 (75)	15 (79)	0.85
Post-aspiration TIMI flow grade ≤2	1 (8)	0	0.81
Total ischemic time, h	3.5 ± 3.0	3.6 ± 2.3	0.82

Conclusion: These observations support an alternative treatment strategy for patients with acute coronary events and optical coherence tomography-verified intact fibrous cap (or plaque erosion), where nonobstructive lesions might be managed without stenting.

Prati F, et al. JACC Cardiovasc Imaging. 2013 Mar;6(3):283-7.

Representative Cases





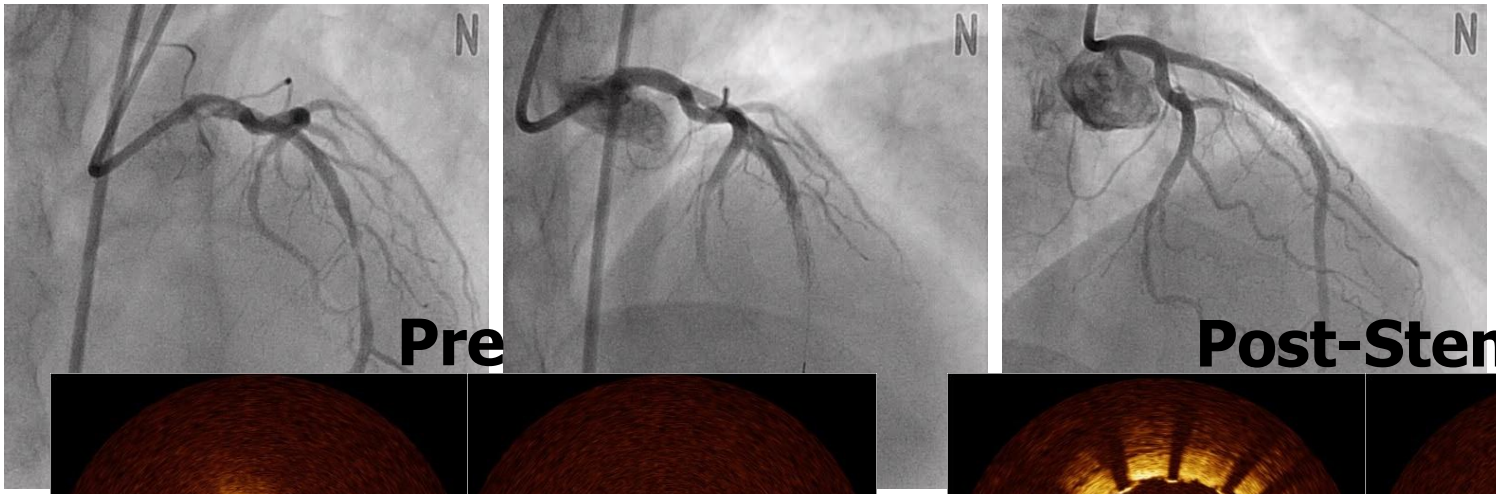
Thrombosuction only

Thrombosuction + stent

OCT features related with post-PCI myocardial injury

STUDY	PATIENTS	DEFINITION	FINDINGS
Tanaka, EHJ 2009;30:1348	83 NSTEMI pts (14 no-reflow vs 69 reflow) underwenting primary stenting	No relow Final TIMI blush	**OCT-TCFAs** (50% vs. 16%, P = 0.005) **Lipidic arc** (odds ratio 1.018; CI 1.004-1.033; P = 0.01)
Yonetsu, Int J Cardiol 2011;146:80	125 angina pt (35 CK vs 90 NCK)	CK-MB elevation	**OCT-TCFAs** (OR 4.68, 95% CI 1.88-11.64, p=0.001)
Lee, Circ Cardiovasdc Intv 2011;4:378	131 angina pts (31 vs 100 NPM)	cTnI >3x URL	**OCT-TCFAs** (odds ratio, 10.47; 95% confidence interval, 3.74 to 29.28; P<0.001)
Lee, JACC Cardiovasc Interv 2011;4:483	135 angina pts	CK-MB elevation	**OCT-PRs** (OR: 2.92; 95% CI: 1.21 to 7.06; p = 0.017) **plaques with echo attenuation** (odds ratio [OR]: 3.49; 95% confidence interval [CI]: 1.53 to 7.93; p = 0.003)
Prorto, Circ Cardiovasc Intv 2012;5:89	50 stable and NSTEMI pts	TnT elevation	**OCT-TCFAs** (OR 29.7, 95% CI 1.4 to 32.1)
Imola, Am J Cardiol 2013;111:526	30 (15 vs 15 control) pts without ongoing MI underwent PCI c stent OCT database	CK-MB elevation	**Proximal edge OCT lipid pools** (10 [66%] vs 2 [13%], p = 0.009) Lipidic arc
Ueda, Coron Artery Dis 2014;25:384	68 stable pts (25 MI)	TnT elevation	OCT-TCFAs 2.91 (0.68-13.55) p=0.1488 **Spotty calcium** (4.82 (1.51-16.85) p=0.0076) Both (odds ratio 21.00, 95% confidence interval 2.65-454.22, P=0.003).
Higuma JACC Intv 2015:8:1166	112 STEMI underwent PCI within 12 h	Myocardial blush grade ≤1 and no-relow	TMP: **PRs** 30.6% **Plaque erosion** 6.7% **CN** 22.2% p=0.010 No reflow: **PRs** 38.9% **Plaque erosion** 13.3% **CN** 22.2% p=0.011
Lee et al. Circ Cardiovasc Intv 2015, e-pub	206 Stable CAD pts	cTnI >5x UNL	**OCT-TCFAs** (odds ratio, 2.89; 95% confidence interval, 1.22-6.86; P=0.016)

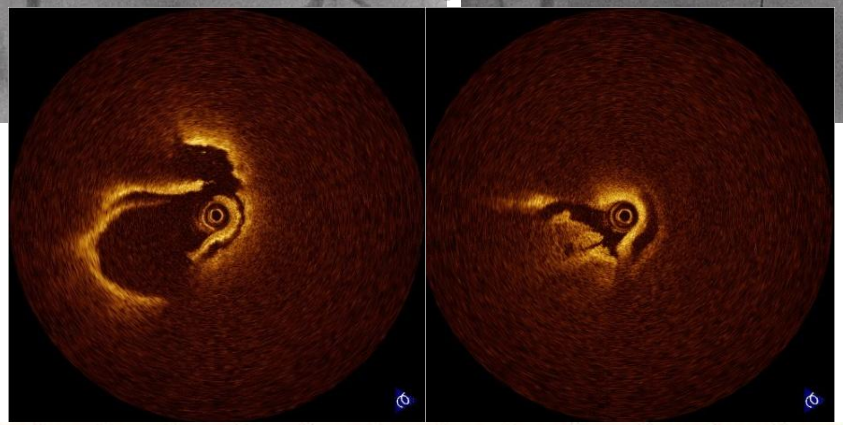
Case: high risk plaque

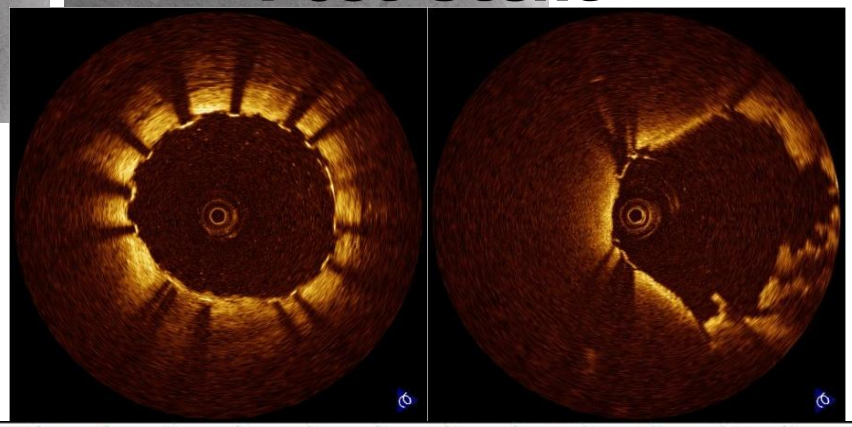


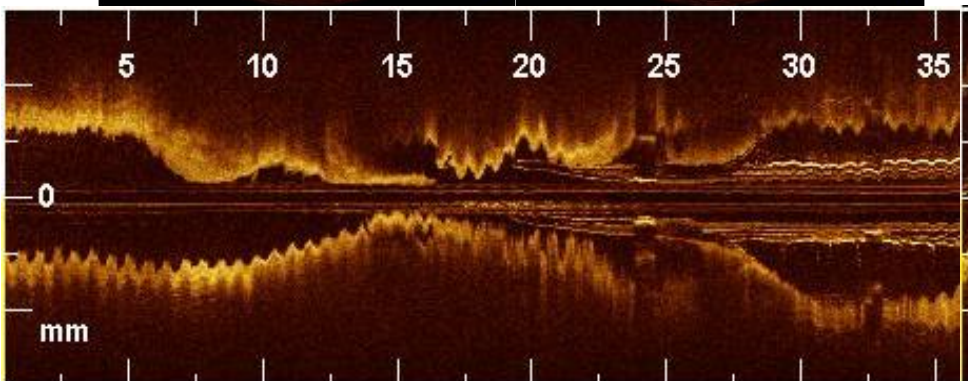
LPK M/66
STEMI

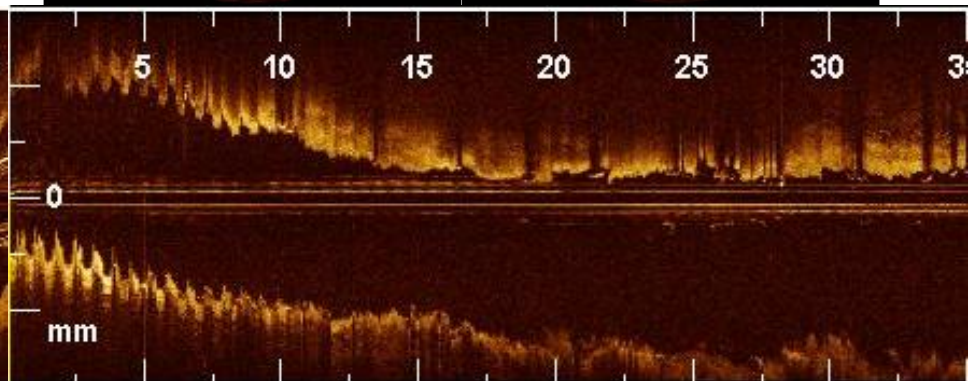
Pre

Post-Stent









Multimodality IV Imaging to Predict Periprocedural MI During PCI

110 patients who underwent OCT, IVUS, and NIRS
Periprocedural MI was defined as a post-procedural cTnI >3x URL
cTnI >3x URL was observed in 10 patients (9%)

		UNIVARIATE		MULTIVARIATE	
		OR(95% CI)	P value	OR(95% CI)	P value
OCT	**minimum cap thickness**	0.886(0.796-0.849)	<0.01	0.896(0.799-0.962)	0.02
IVUS	**plaque burden**	1.161(1.043-1.326)	0.01	1.040(0.927-1.195)	0.54
NIRS	**maxLCBI4mm**	1.004(1.001-1.007)	<0.01	1.001(0.997-1.005)	0.65

Kini et al. JACC Cariovasc Interv 2015;8:937

Imaging predictors in non-culprit lesion for clinical outcomes

Prospective observational studies

STUDY	PATIENTS	METHOD	OUTCOME	RESULTS
Ohtani, JACC 2006;47:2194	552 pts	**Angioscopy**	7.1% ACS events @ 57.3±22.1 mons	**Number of yellow plaques** (adjusted HR1.23[1.03-1.45], p=0.02)
PROSPECT Stone, N Engl J Med. 2011;364(3):226-35	697 ACS pts	**3-v VH-IVUS**	11.6% NCL-MACE (Cardiac death, cardiac arrest, MI, or rehospitalization due to unstable or progressive angina) @ 3.4 ys	**PB≥70%** (HR 5.03[2.51-10.11], p<0.001), **MLA ≤4.0 mm²** (HR3.21[1.61-6.42], p=0.001), **VH-TCFA** (HR3.35[1.77-6.36], p<0.001)
VIVA Calvert, JACC img 2011;4:894-90	931 non-culprit lesions in 170 pts (70 Tn (+) ACS)	**3-v VH-IVUS**	1.4% NCL-MACE (death, MI or unplanned revascularization) @ 625ds	**VHTCFA** (HR7.53, p=0.038) and **PB >70%** (HR 8.13, p=0.011) **remodeling index** (HR2686 [1.94 - 3.72×10^6], p=0.032
ATHEROREMO-IVUS Cheng, Eur Heart J 2014;35:639	Non-culprit artery(in 581 pts(318 ACS)		7.8 NCL-MACE(mortality, ACS, or unplanned coronary revascularization) @ 1yr	**VHTCFA** (adjusted HR1.98[1.09-3.60], p=0.026) and **PB ≥70%** (adjusted HR2.90[1.15-5.49], p=0.021)
ATHEROREMO-NIRS Rohit, JACC 2014;64:2510	Non-culprit artery(at least 40mm in length and <50% stenosis, preferred LAD>RCA>LCX) in 203 pts(47% ACS)	**1-v NIRS**	10.4% MACE (all-cause mortality, nonfatal ACS, stroke, and unplanned coronary revascularization) @ 1yr	**LCBI ≥ 43.0 (median)** (adjusted HR4.04[1.33-12.29], p=0.01)

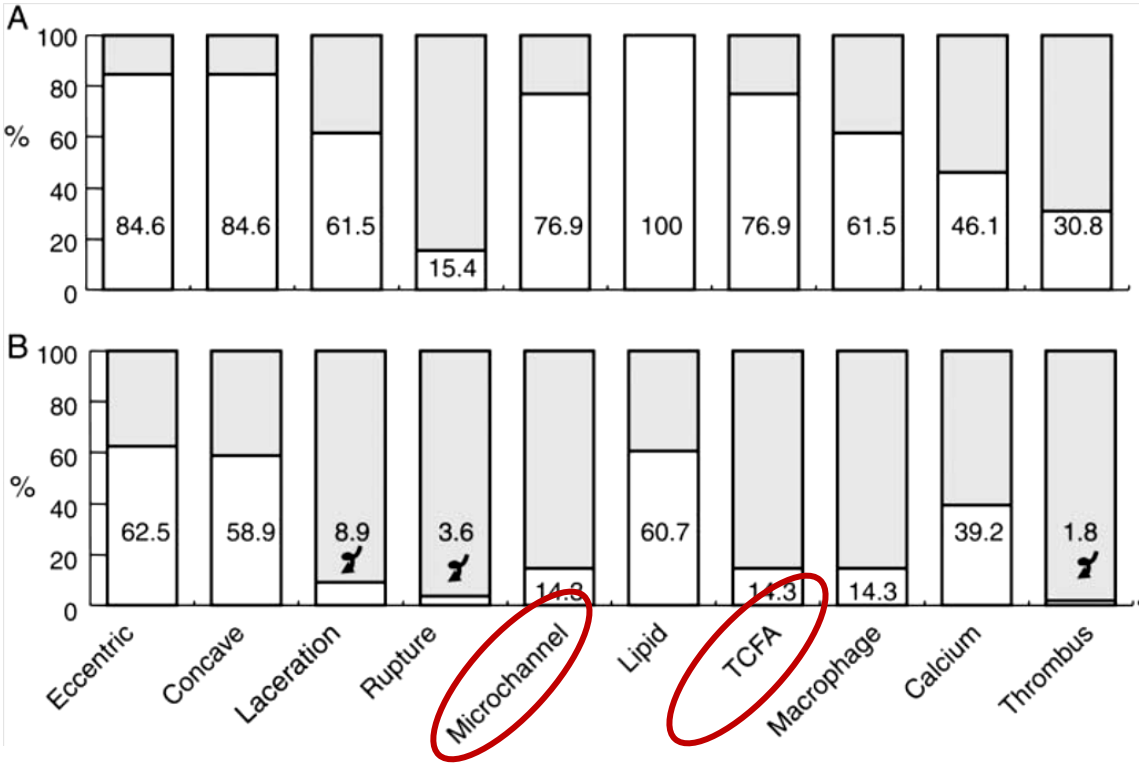
OCT Prediction of Plaque Progression

OCT was used to evaluate morphological characteristics of non-significant coronary plaques that develop rapid progression in 53 patients with coronary artery disease.

Progression (+)

Increase in MLD of >0.4 mm on QCA during 7-month follow-up

Progression (-)



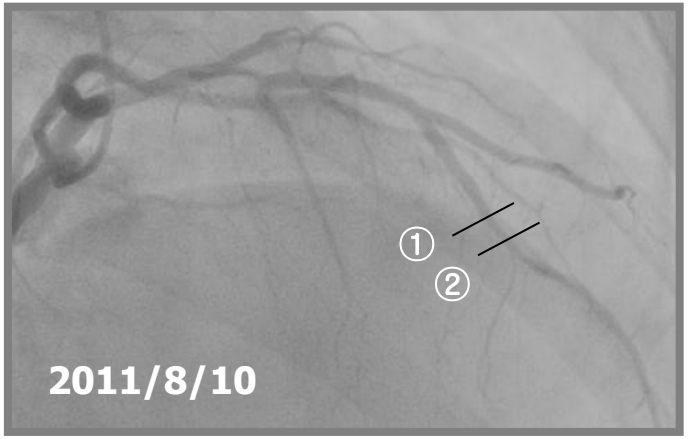
Conclusion: OCT-based complex characteristics of TCFA and microchannel were the potential predictors of subsequent plaque progression.

Uemura et al. Eur H J 2012;33:78-85

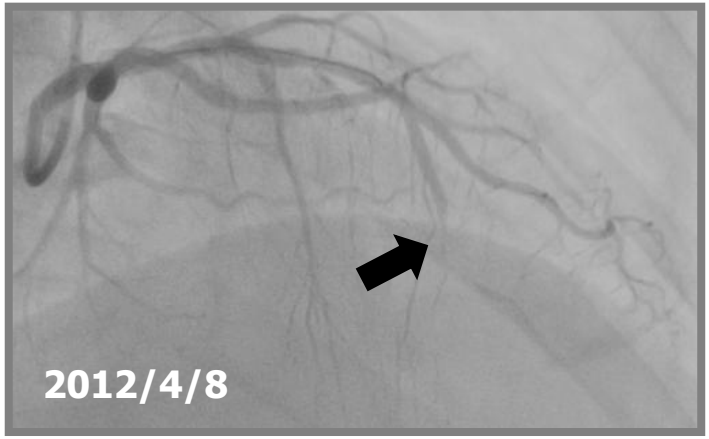
Case: Lesion progression

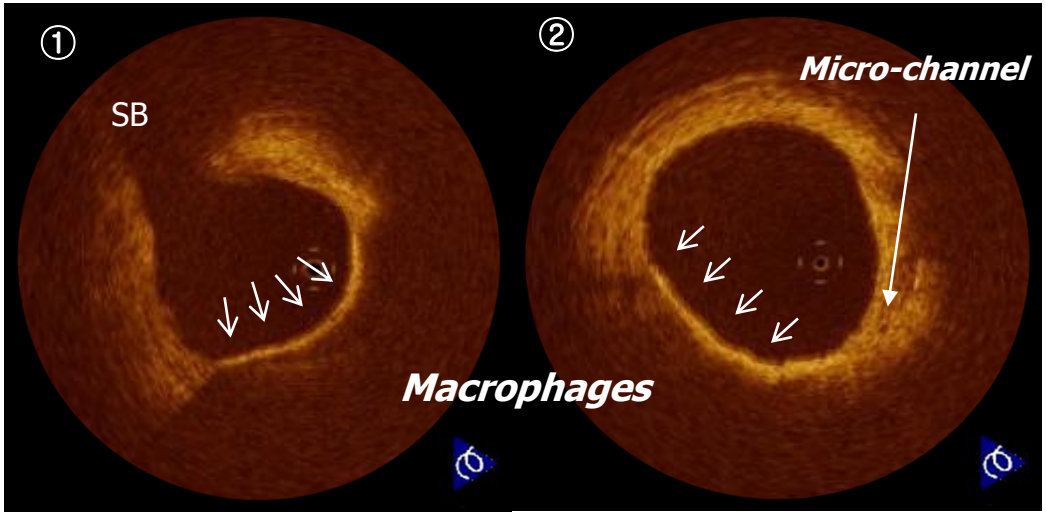
58/M

Baseline



8-month later





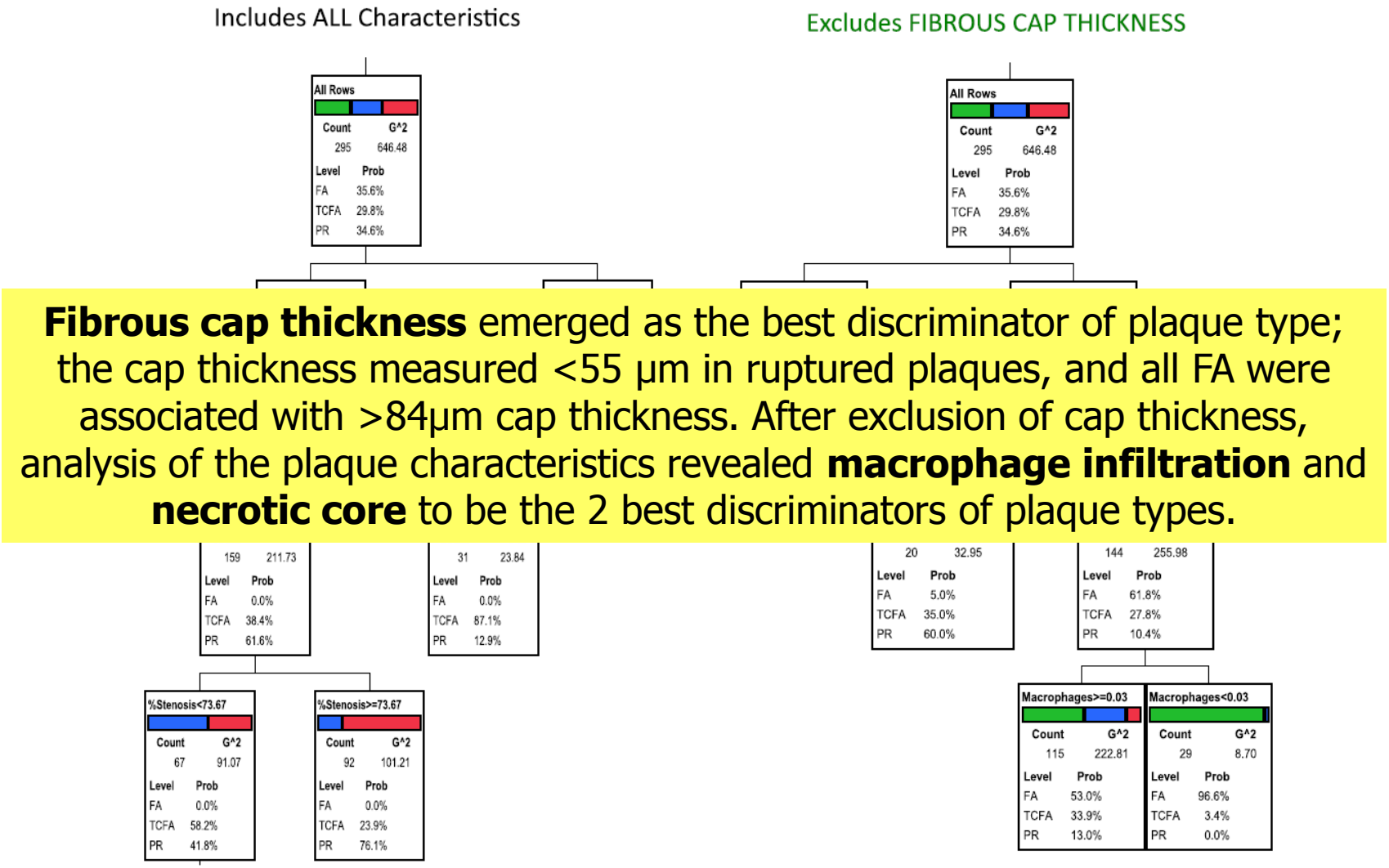
Courtesy of Dr Kubo T

Can We Predict Plaque Vulnerability by Invasive Imaging?

- Assessment of plaque burden
- Assessment of fibrous cap
- Necrotic core characterization
- Vessel remodeling
- Inflammation
- Endothelial function

Histopathologic Characteristics of ASCD and Implications of the Findings for the Invasive and Noninvasive Detection of VPs

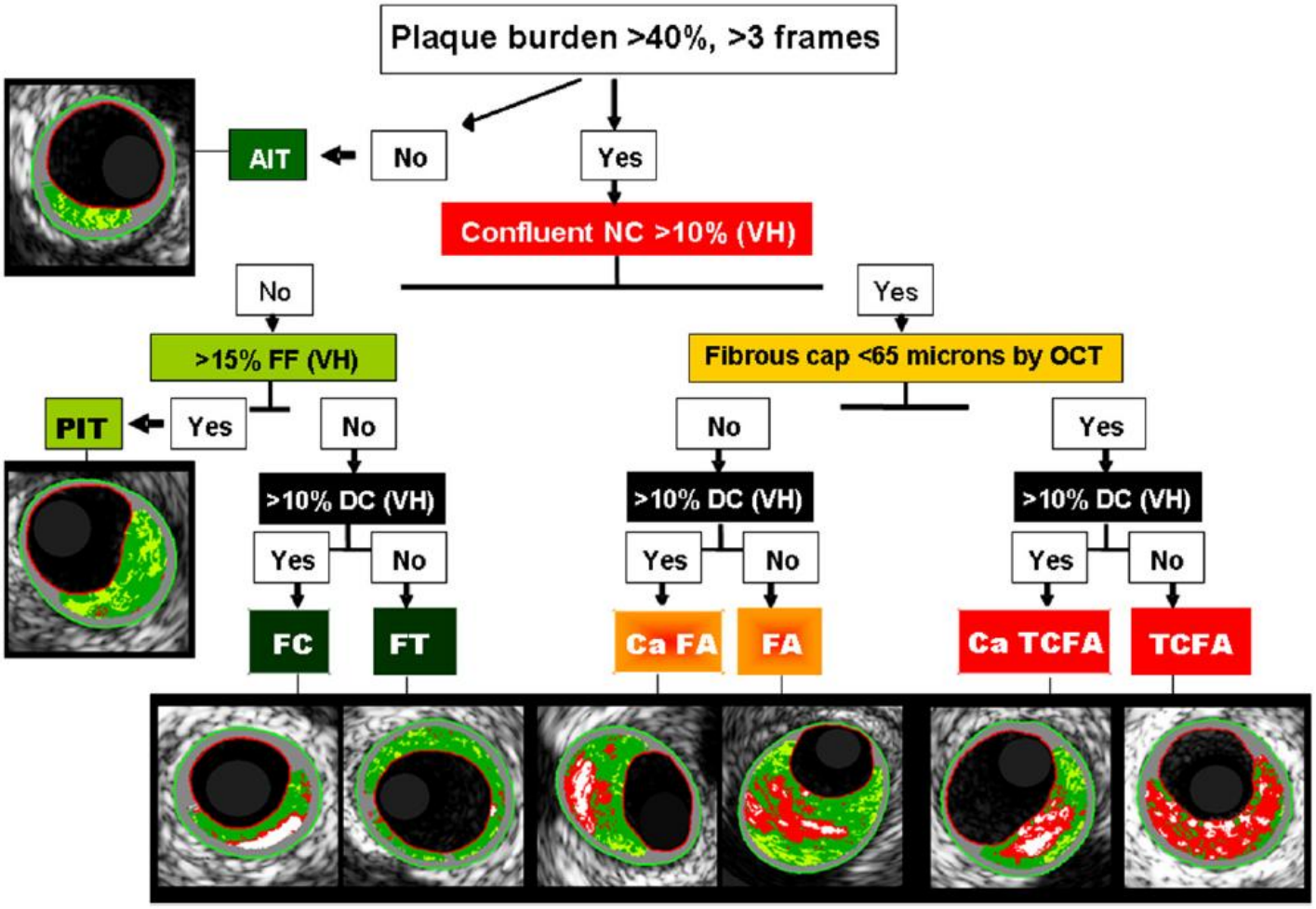
Multivariate RPA Model



Fibrous cap thickness emerged as the best discriminator of plaque type; the cap thickness measured <55 μm in ruptured plaques, and all FA were associated with >84μm cap thickness. After exclusion of cap thickness, analysis of the plaque characteristics revealed **macrophage infiltration** and **necrotic core** to be the 2 best discriminators of plaque types.

Narula et al, JACC 2013;61:1041

Imaging plaques to predict and better manage patients with acute coronary events



Garcia-Garcia et al. Circ Res 2014;114:1904

Take Home Massages

- OCT plays important role to detect VPs (other vulnerable plaque features as well).
- OCT provides detail morphologic information of VPs and help us to understand the mechanism of clinical events of VPs.
- OCT plaque vulnerable features are related with post-procedural MI.
- OCT plaque vulnerable features regarding future CV events should be investigated in the future.
- Combined intravascular imaging modality might be promising to detect and prevent future event .