Integration of Image-based Physiology and Plaque Vulnerability: Current and Future

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Disclosure

Speaker's name: Shengxian Tu

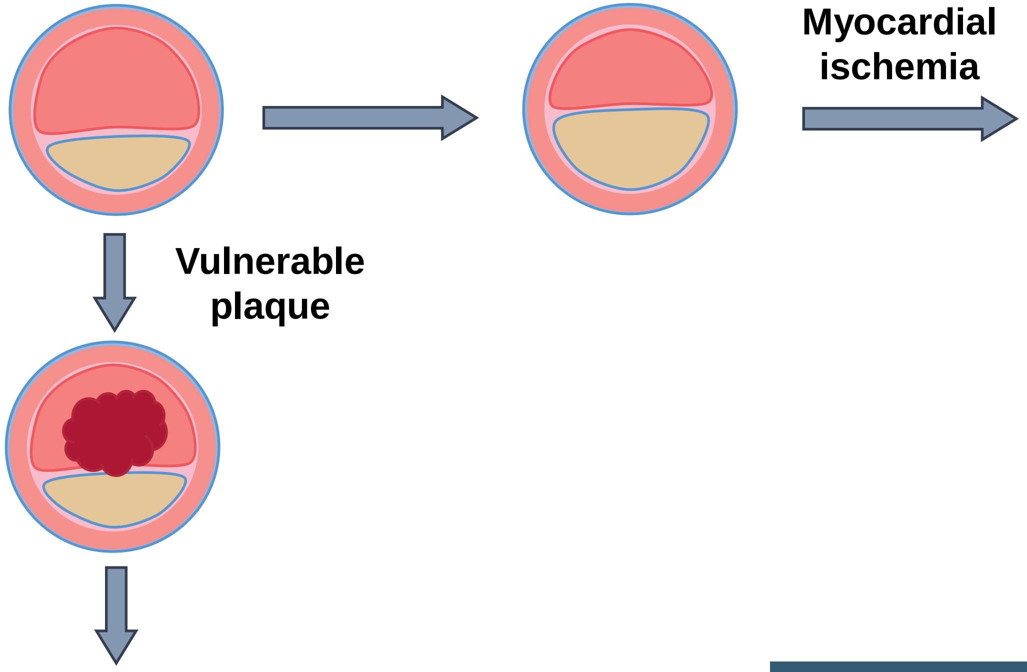
☑ I have the following potential conflicts of interest to declare:

Co-founder: Pulse Medical

Receipt of grants / research support: Pulse Medical

Consultancy: Pulse Medical

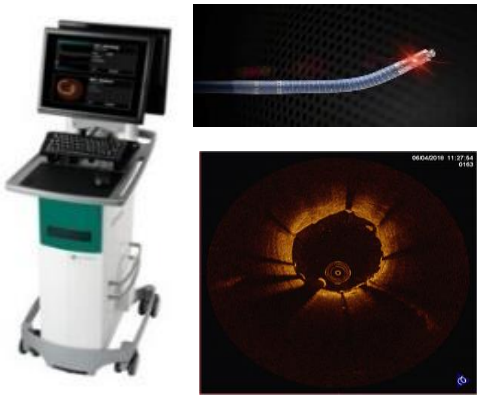
Available Tools for Precise Lesion Assessment



FFR

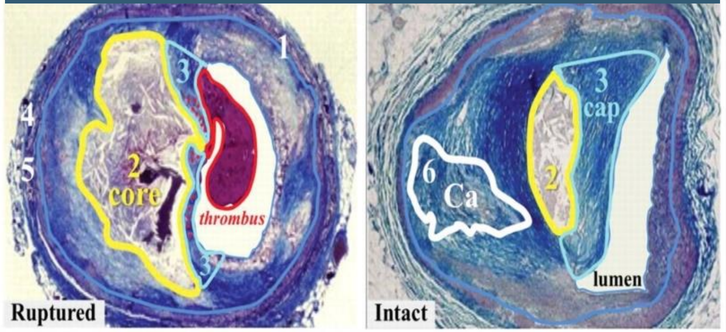
Coronary physiology

OCT



Plaque vulnerability

Autopsy finding

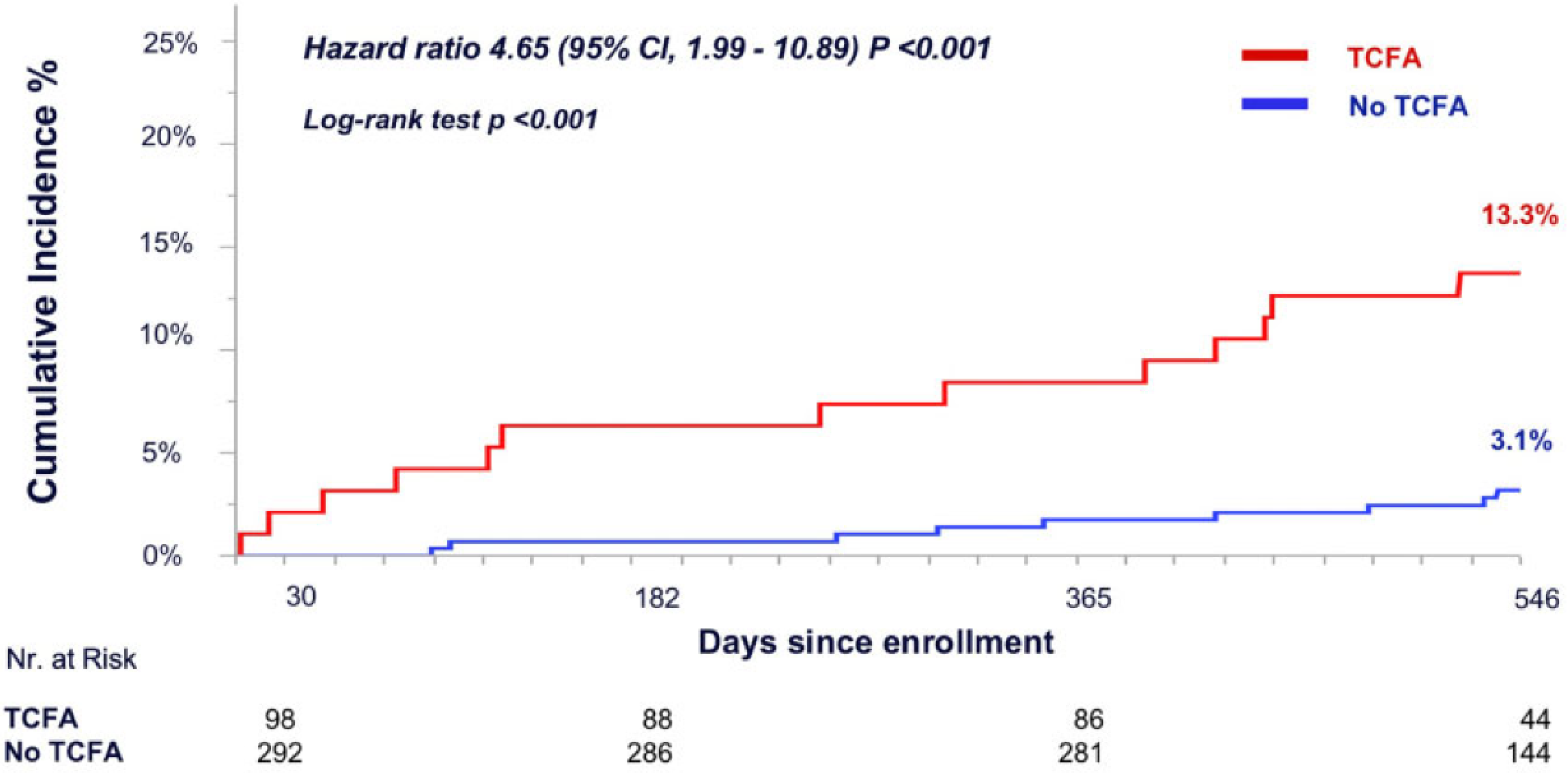


- A ruptured plaque responsible of cardiac death frequently appears as a **thin-cap fibroatheroma (TCFA)**, characterized by a large lipid core, a thin fibrous cap (<65 µm), and active inflammation

Falk E et al., Eur Heart J 2013;34(10):719-28   Libby P, Circulation 1995;91(11):2844-50

Safety Concern of Deferred Revascularization: Vulnerable Plaque

- **COMBINE OCT-FFR**: TCFA presented in **25%** of the patients with diabetes and ≥1 FFR-negative lesions and was associated with a nearly **five-fold higher** rate of MACE



Kedhi E et al., Eur Heart J 2021;42(45):4671-9

Novel AI-powered Methods to Compute FFR, IMR and Plaque Vulnerability From Coronary Angiography

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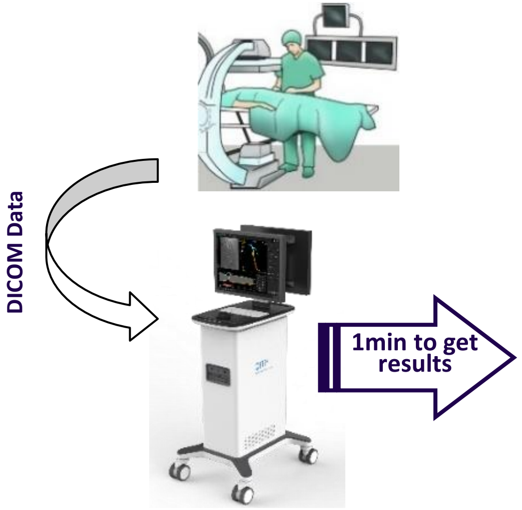
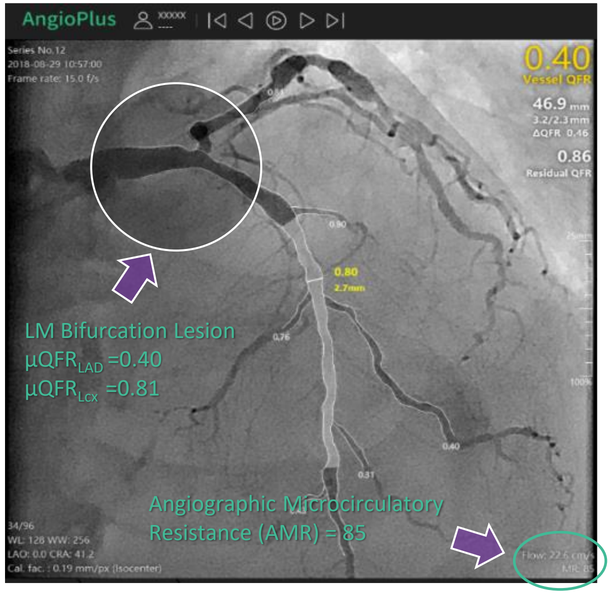
µQFR, AMR and RWS computed from a single angiographic view in 1 min

Standard angiogram

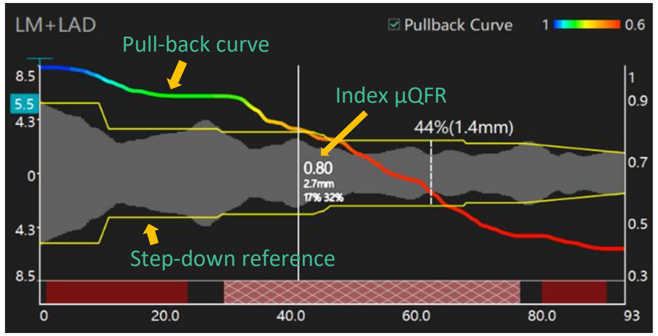


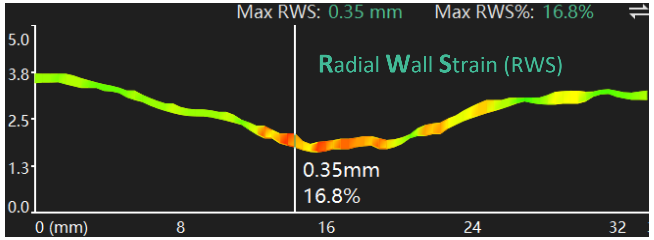
AngioPlus Core*

Coronary Tree µQFR & AMR



µQFR pull-back & RWS mapping





Use angio-based µQFR, AMR and RWS

You need

… **only angiography**, no need of costly disposables

… only software, **no additional invasive** procedure

… about **1 minute** to perform the computations

*Pulse Medical, Shanghai, China

Huang J and Tu S, EuroPCR 2022 Best Innovation & Jon DeHaan Grant

Murray Law-Based Quantitative Flow Ratio (μQFR/μFR)

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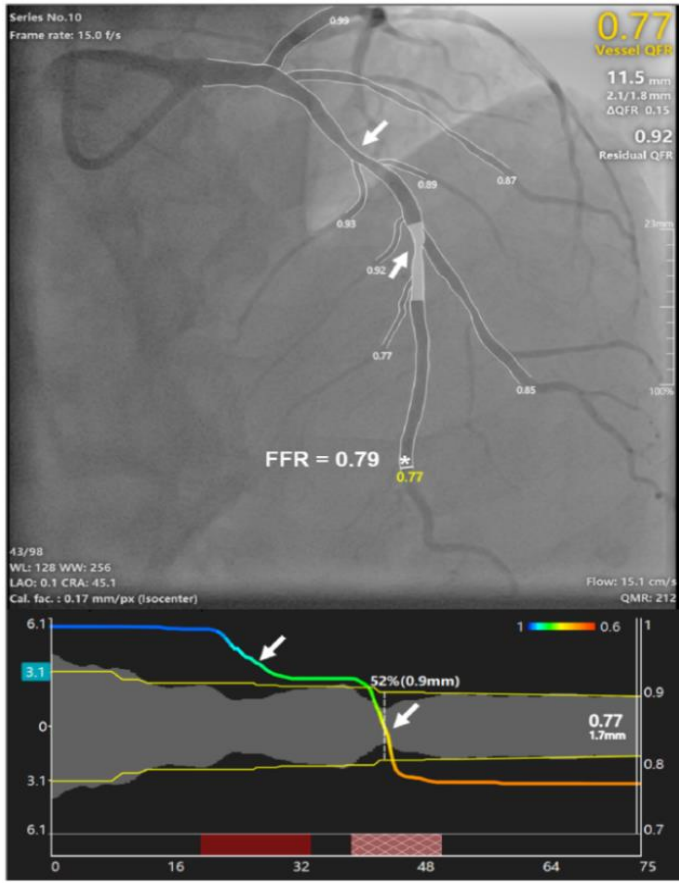


AngioPlus Core
(Pulse Medical)

Comparison between μQFR and DS% for the prediction of FFR≤0.80

	μQFR ≤0.80	DS% ≥50%
Accuracy %	93.0 (90.2, 95.8)	76.5 (71.9, 81.1)
Sensitivity %	87.5 (80.2, 92.8)	57.5 (48.1, 66.5)
Specificity %	96.2 (92.6, 98.3)	86.7 (81.3, 91.0)
PPV %	92.9 (86.5, 96.9)	71.1 (61.0, 79.9)
NPV %	93.1 (88.9, 96.1)	78.1 (72.2, 83.2)
+LR	23.0 (11.6, 45.5)	4.3 (3.0, 6.3)
-LR	0.13 (0.08, 0.20)	0.49 (0.40, 0.60)

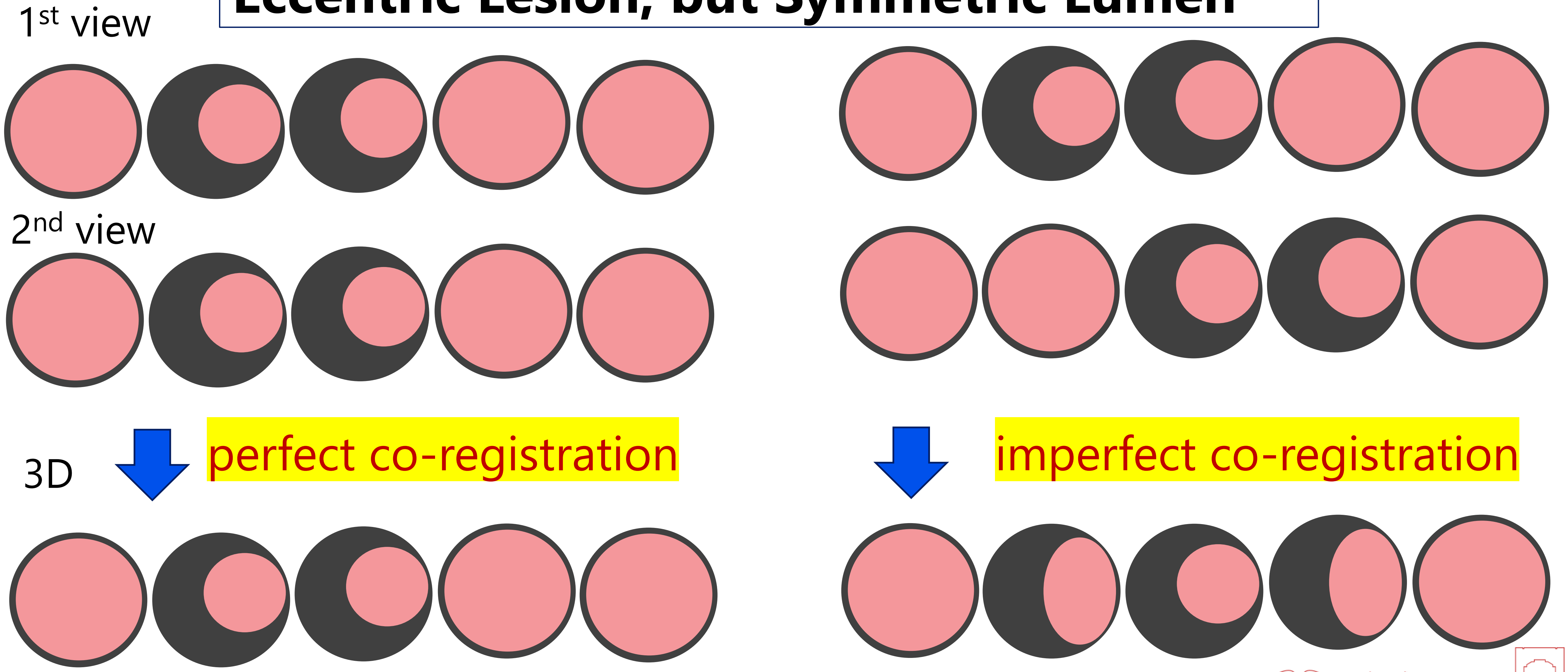
330 vessels, 306 patients

SJTU

Tu S et al., Catheter Cardiovasc Interv 2021;97(2):1040-7

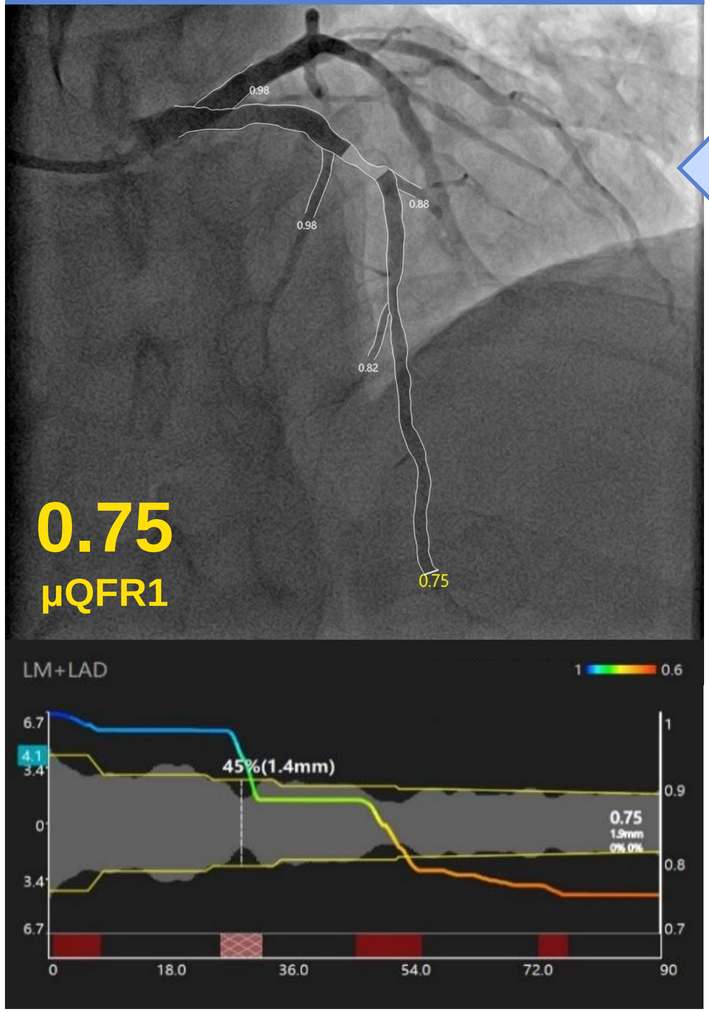
Two Views Is Not Always Better

Eccentric Lesion, but Symmetric Lumen

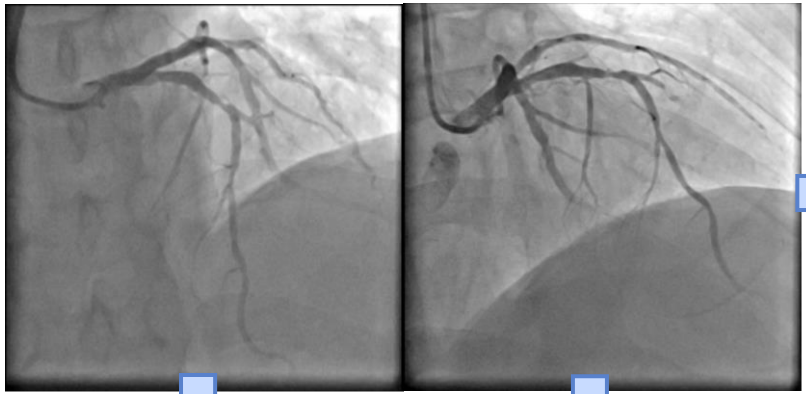


2D µQFR vs. 3D µQFR

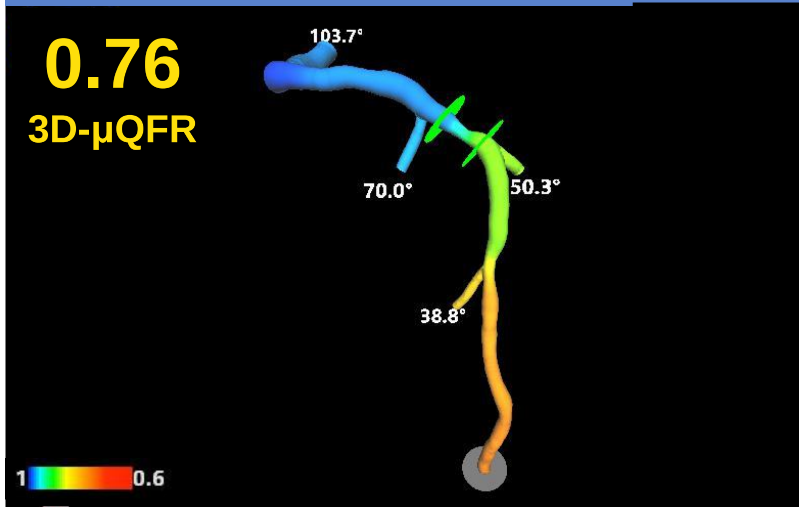
µQFR1



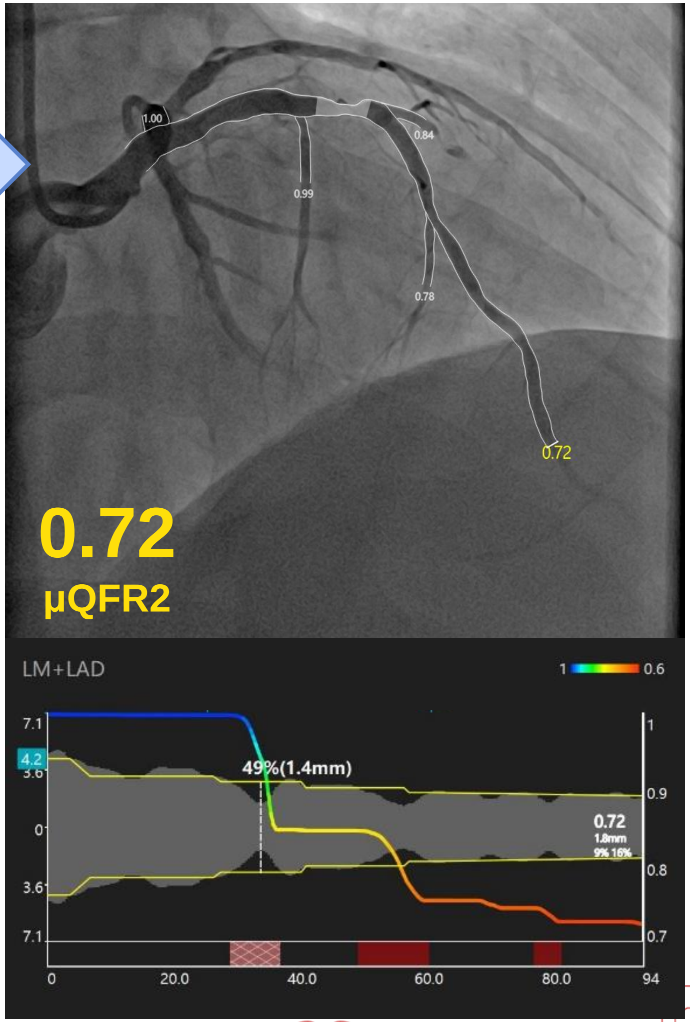
2 recommended projections



3D-µQFR



µQFR2



Ding, Tu, Wijns et al. *JSCAI* 2022; 1: 100399

2D µQFR vs. 3D µQFR

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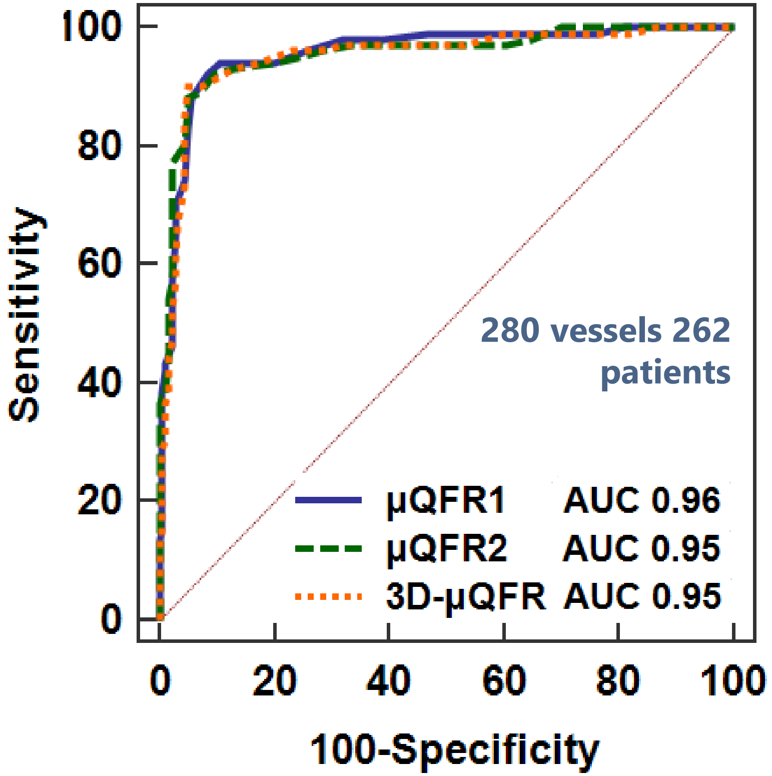

FFR ≤0.80 as reference

	µQFR1 ≤0.80	µQFR2 ≤0.80	3D-µQFR ≤0.80
Accuracy %	**92.1 (89.0, 95.3)**	**92.5 (89.4, 95.6)**	**93.2 (90.3, 96.2)**
Sensitivity %	88.1 (80.2, 93.7)	88.1 (80.2, 93.7)	90.1 (82.5, 93.7)
Specificity %	94.4 (90.0, 97.3)	95.0 (90.7, 97.7)	95.0 (90.7, 97.7)
PPV %	89.9 (82.2, 95.0)	90.8 (83.3, 95.7)	91.0 (83.6, 95.8)
NPV %	93.4 (88.7, 96.5)	93.4 (88.8, 96.5)	94.4 (90.0, 97.3)
+LR	15.8 (8.6, 28.9)	17.5 (9.2, 33.3)	17.9 (9.4, 34.0)
-LR	0.13 (0.07, 0.2)	0.13 (0.07, 0.2)	0.10 (0.06, 0.2)
AUC	0.96 (0.93, 0.98)	0.95 (0.92, 0.98)	0.95 (0.92, 0.97)

Single-view µQFR and two-view 3D-µQFR had comparable accuracy

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Ding, Tu, Wijns et al. *JSCAI* 2022; 1: 100399

Diagnostic Performance of μQFR

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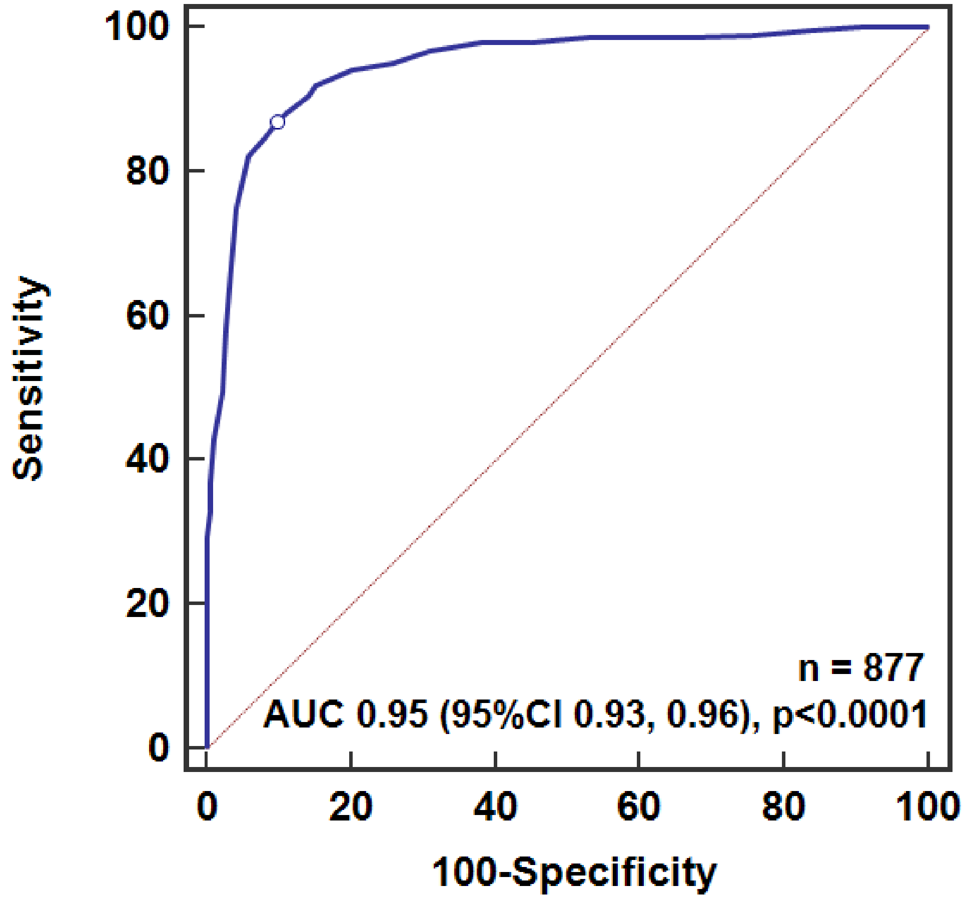
797 patients, 877 vessels (feasibility 95.4%) with paired μQFR and FFR core lab, blinded analysis using the FLAVOUR* study population



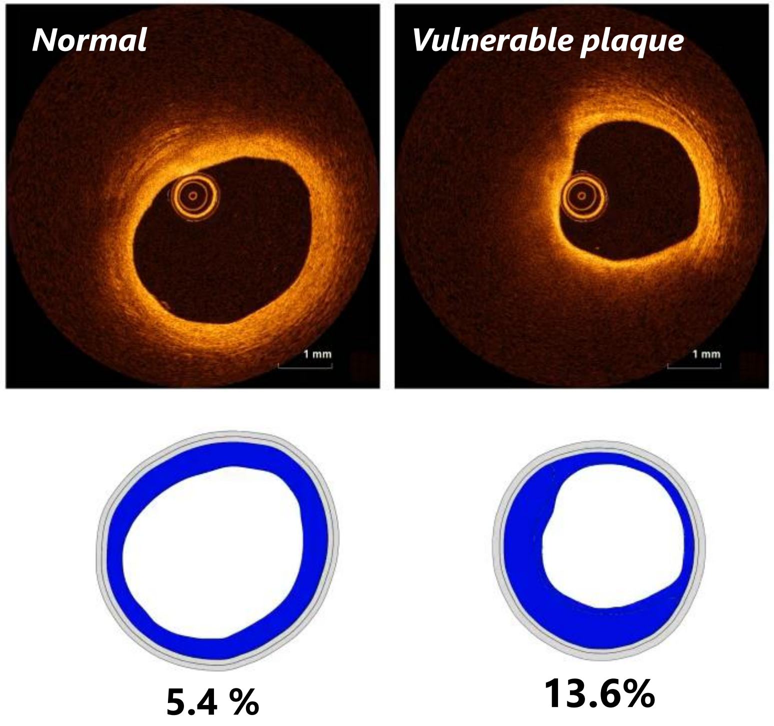
	Pre-PCI μQFR ≤0.80
Accuracy %	90 (88, 92)
Sensitivity %	82 (77, 86)
Specificity %	94 (92, 96)
PPV %	87 (83, 91)
NPV %	92 (89, 94)
+LR	14.3 (10.3, 19.9)
-LR	0.19 (0.1, 0.2)
AUC	0.95 (0.93, 0.96)

Pre-PCI FFR ≤0.80 as reference

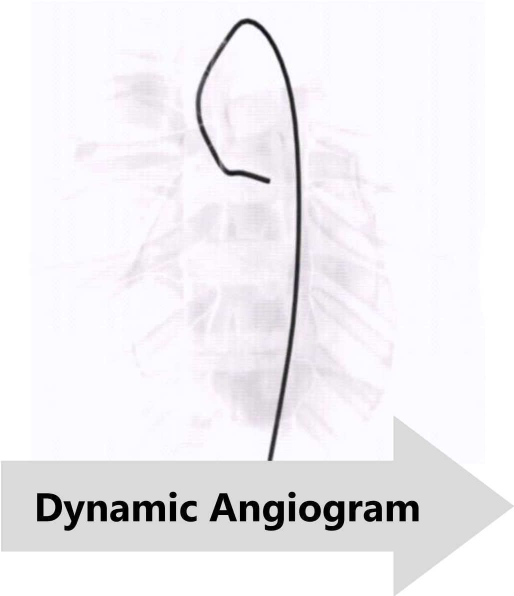
* Koo et al. N Engl J Med 2022;387:779-89

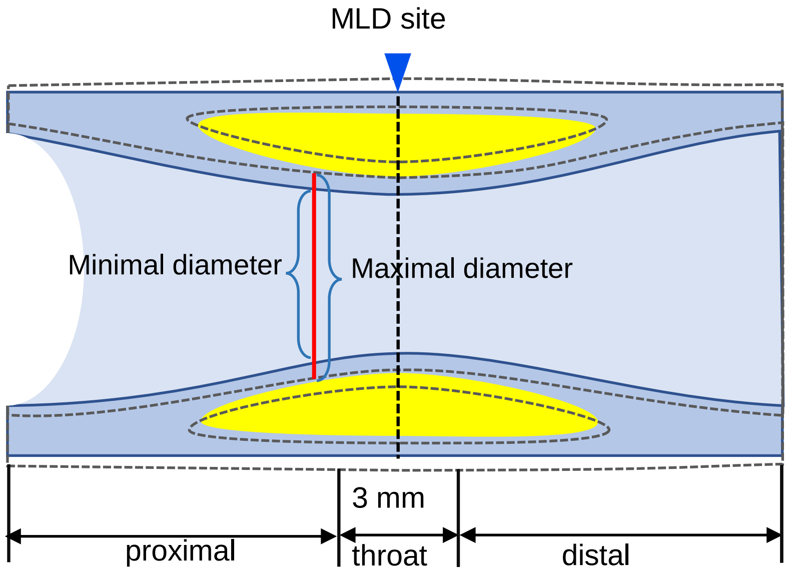
Ding et al, Manuscript under review

Concept of Radial Wall Strain (RWS)



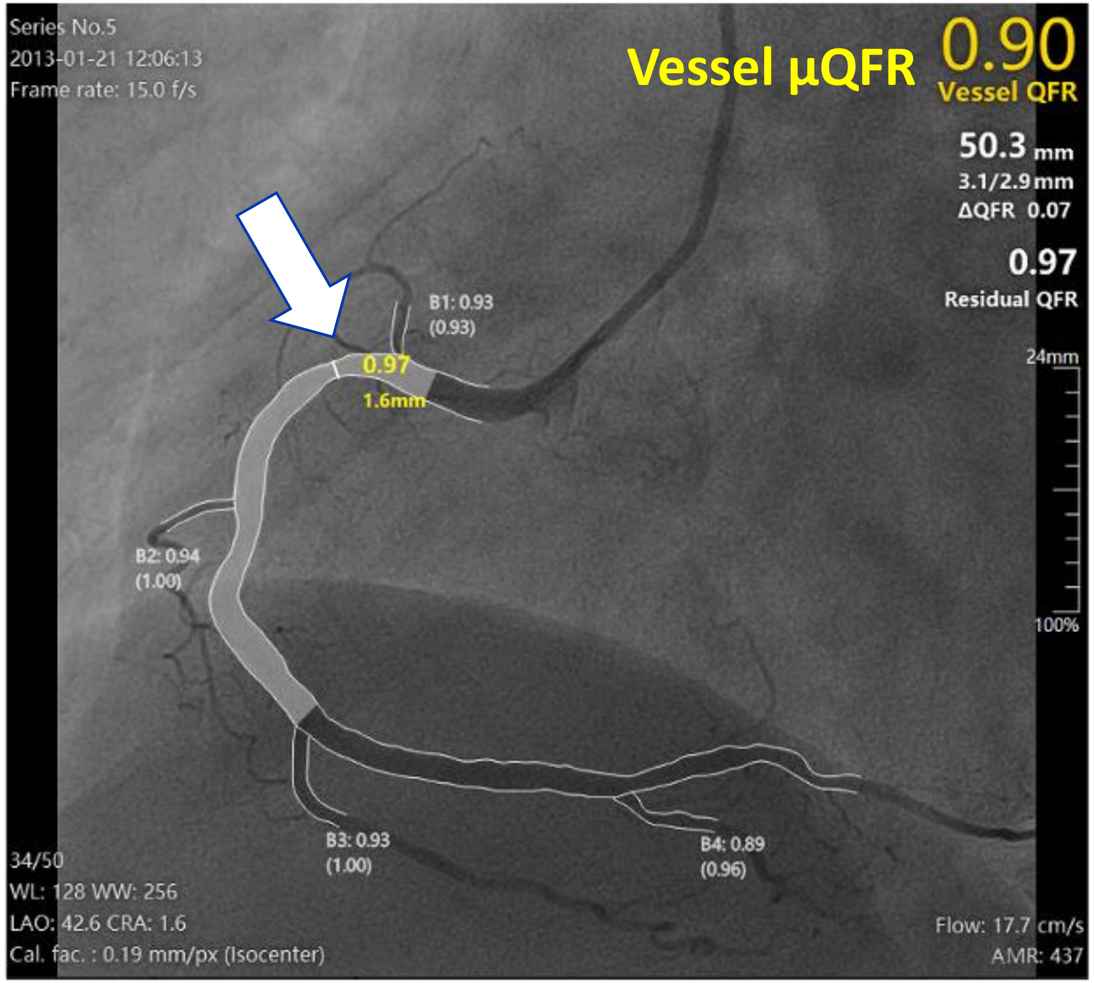
Max lumen deformation





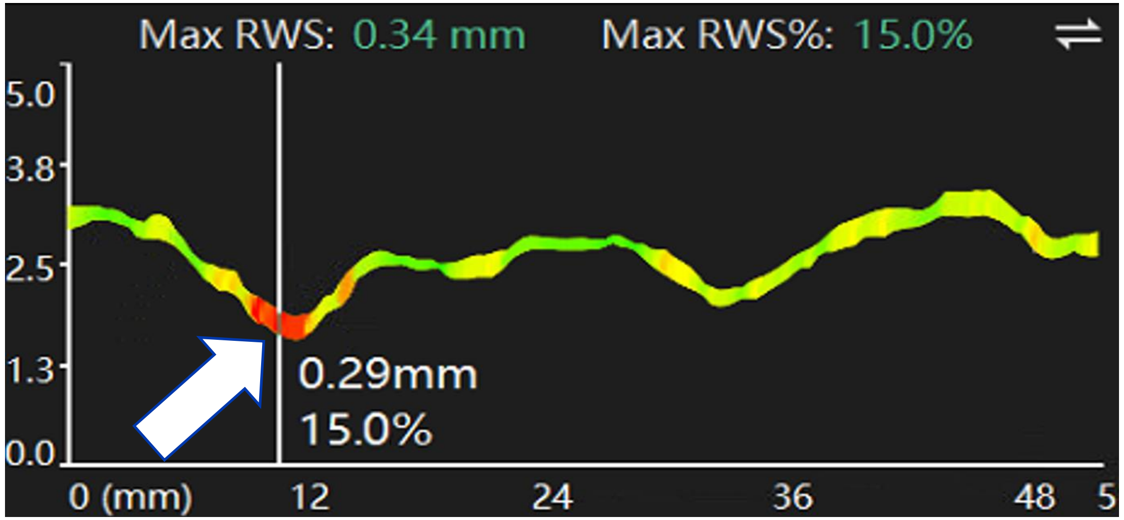
$$\text{Radial wall strain (RWS)} = \frac{max\ diameter - min\ diameter}{max\ diameter}$$

Implementation of RWS and μQFR



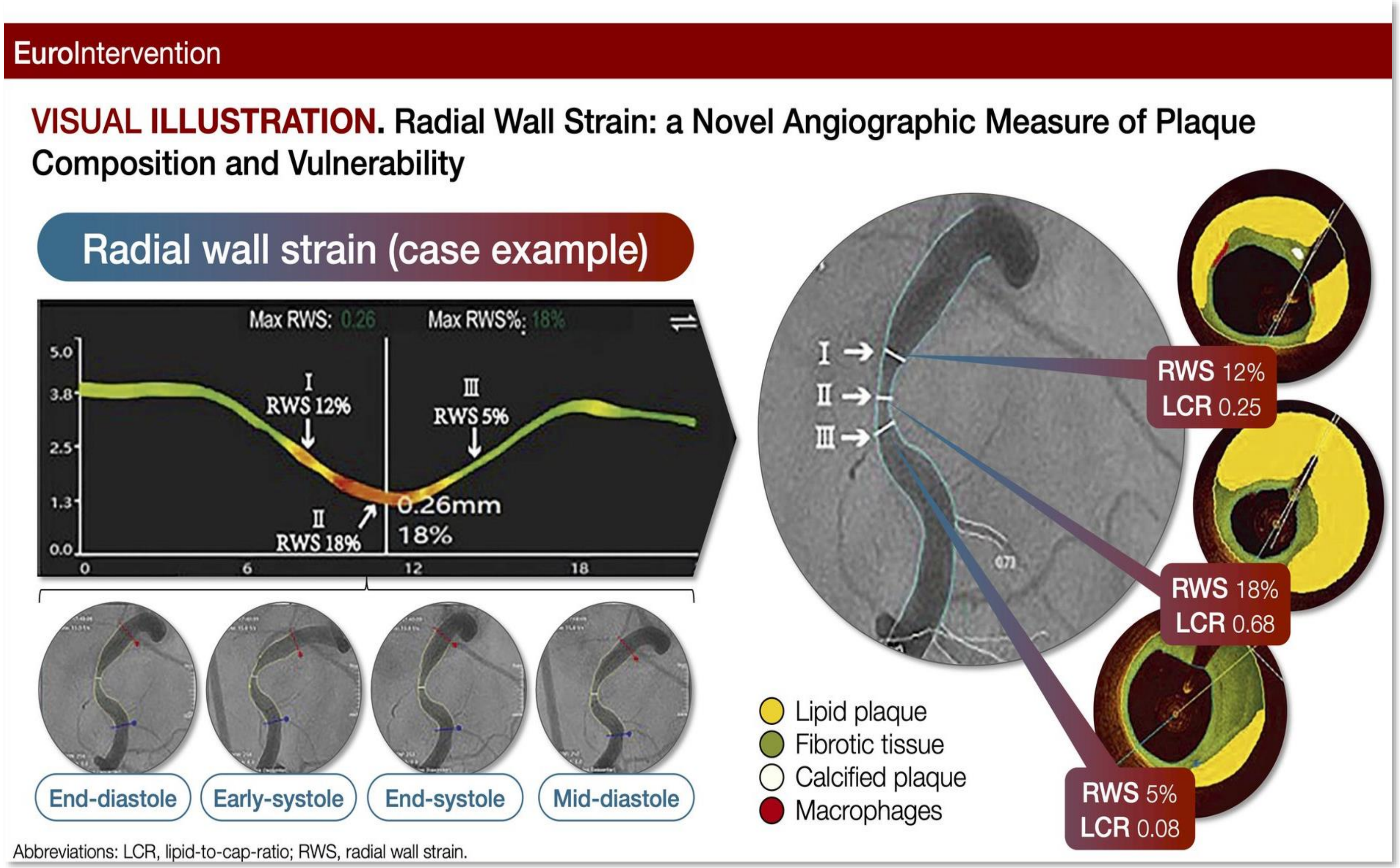
AngioPlus Core
(Pulse Medical, Shanghai)

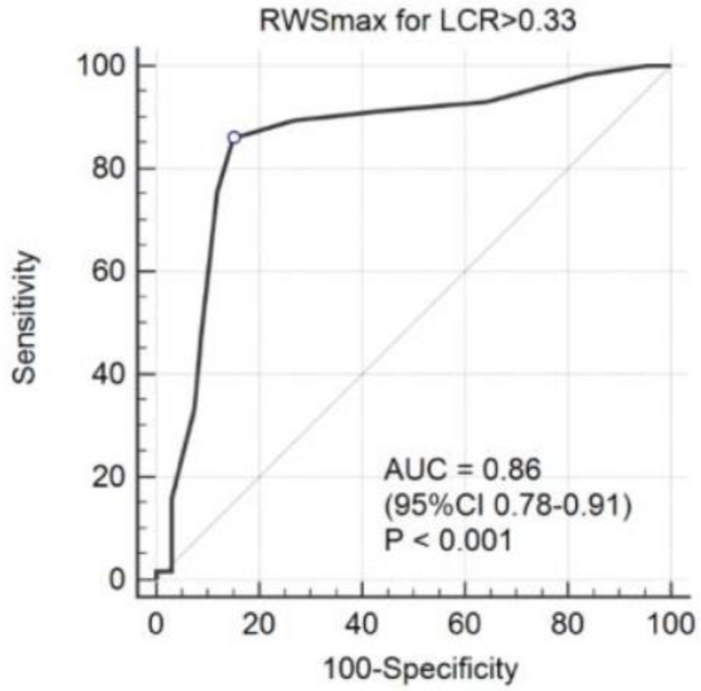
Radial Wall Strain (RWS)



RWS will be rapidly available after μQFR and co-registered with angiogram

RWS Identify Vulnerable Plaque Defined by OCT





Hong ,Tu, et al. EuroIntervention 2022; 18:1001-10

Hong, Tu et al., JACC:Asia 2022;2:460-472

RWS Predicts Subseqent AMI

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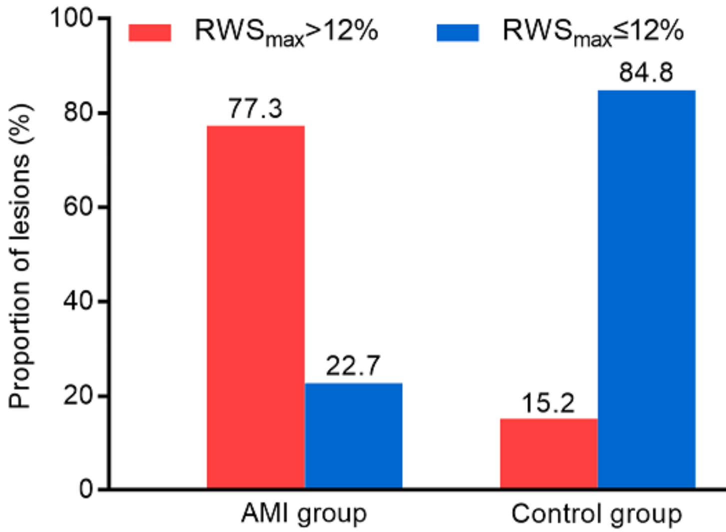
	All patients (n = 176)	AMI group (n = 44)	Control group (n = 132)	p value
Coronary artery location				1.000
LAD	52 (29.5)	13 (29.5)	39 (29.5)	
LCx	16 (9.1)	4 (9.1)	12 (9.1)	
RCA	108 (61.4)	27 (61.4)	81 (61.4)	
Coronary segment location				1.000
Proximal	60 (34.1)	15 (34.1)	45 (34.1)	
Middle	88 (50.0)	22 (50.0)	66 (50.0)	
Distal	28 (15.9)	7 (15.9)	21 (15.9)	
QCA-derived parameters				
MLD, mm	2.0 (1.7, 2.4)	1.9 (1.6, 2.4)	2.0 (1.7, 2.4)	0.409
DS%, %	34.0 (30.0, 40.0)	33.0 (29.0, 40.0)	34.5 (30.3, 40.0)	0.359
RVD, mm	3.0 (2.6, 3.6)	2.9 (2.5, 3.6)	3.1 (2.7, 3.6)	0.283
Lesion length, mm	13.0 (9.4, 16.9)	15.2 (10.4, 18.3)	11.9 (9.2, 16.5)	0.040
Vessel-level μQFR	0.91 (0.88, 0.94)	0.92 (0.88, 0.95)	0.91 (0.88, 0.94)	0.640
Lesion-level ΔμQFR	0.04 (0.02, 0.07)	0.04 (0.02, 0.07)	0.04 (0.02, 0.07)	0.725
RWS_{max}, %	10 (9, 13)	13 (13, 14)	10 (9, 11)	<0.001

44 lesion-related AMI patients with 132 matched controls



RWS_{max}>12%: 34/44 vs 20/132

Risk ratio (95% CI): 7.25 (3.94-13.37)

p value: <0.001

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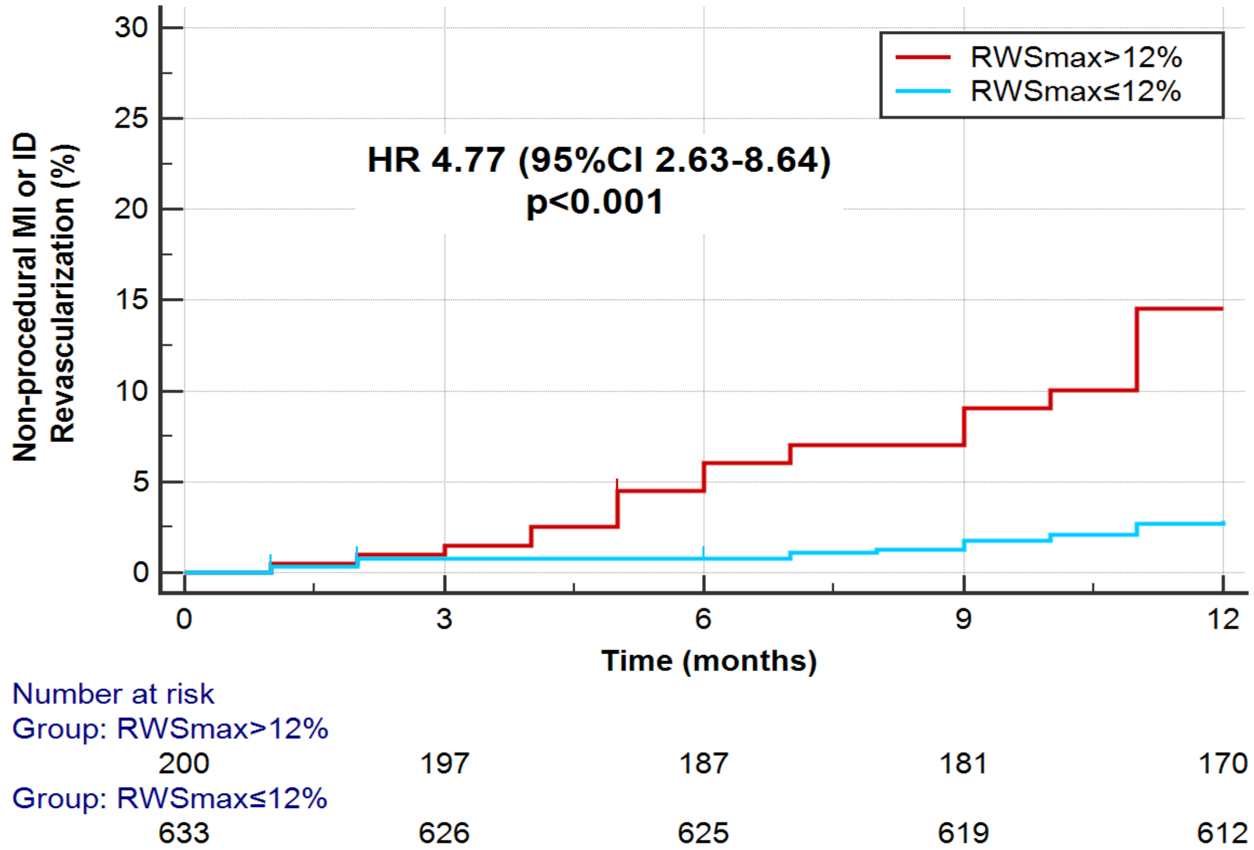
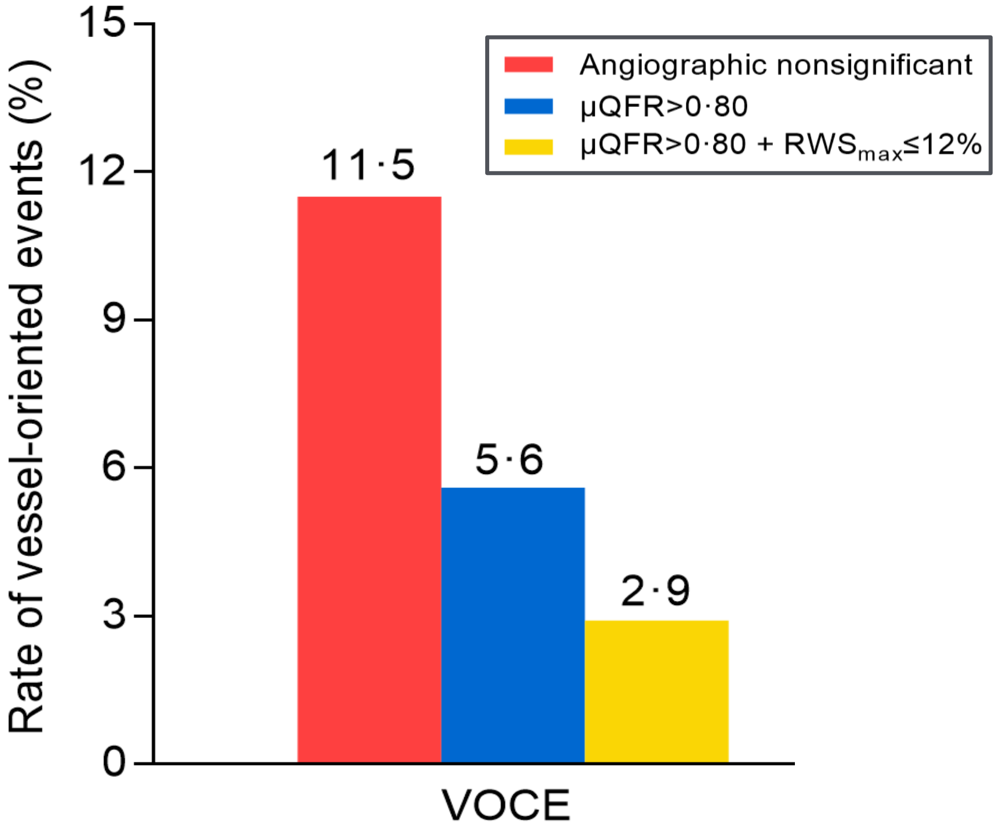
Li, ..., Tu, Ge. J Am Coll Cardiol Interv 2023; 16:1039-1049

Combined μQFR-RWS Significantly Improves the Safety of Deferred Revascularization



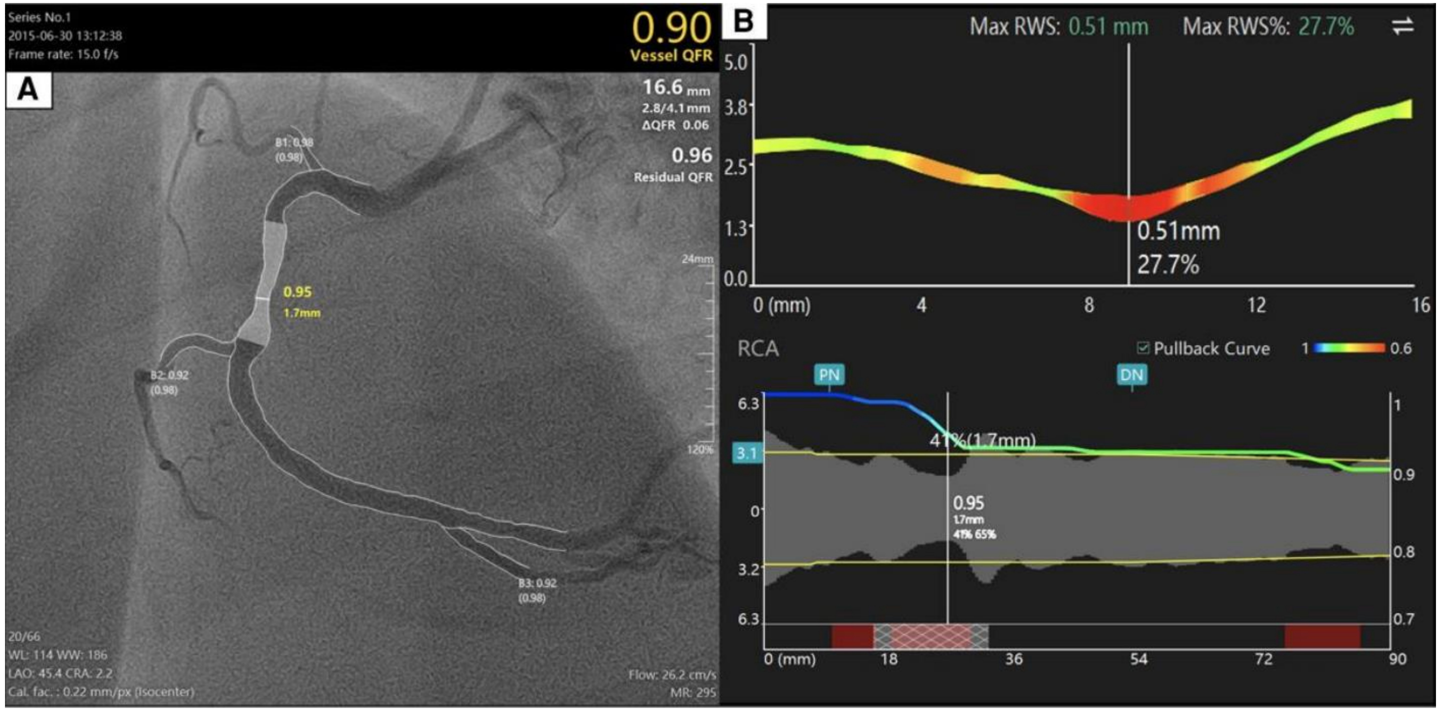


Tu S, Wijns W et al., J Am Coll Cardiol 2023; 81(8):756-67

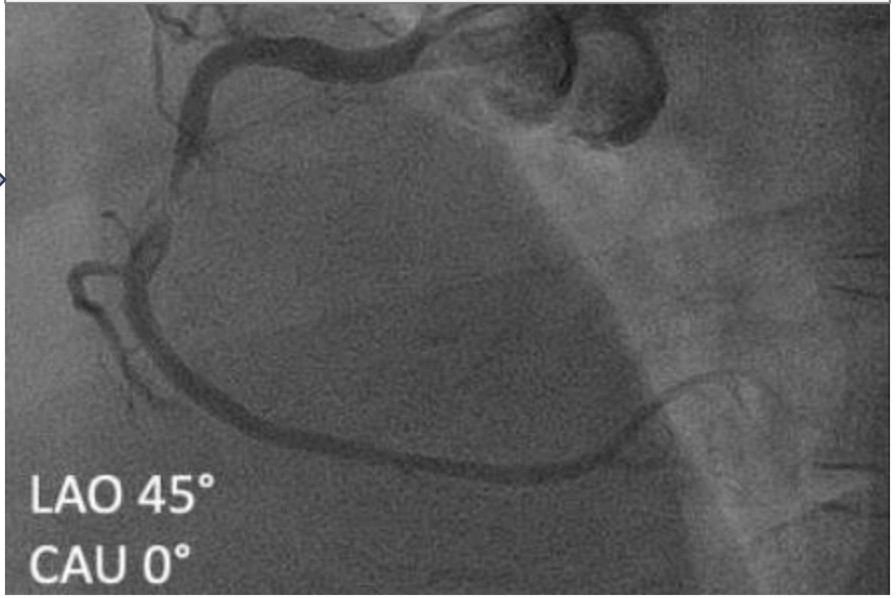
An Example Case

A 40-year-old patient presented with NSTEMI: the culprit sub-occlusive LCx stenosis was treated at the index procedure and the non-culprit RCA intermediate stenosis was deferred

Non-culprit RCA stenosis at the index procedure:
MLD = 1.7 mm, DS% = 41%, µQFR = 0.90, RWS_{max} = **27.7%**



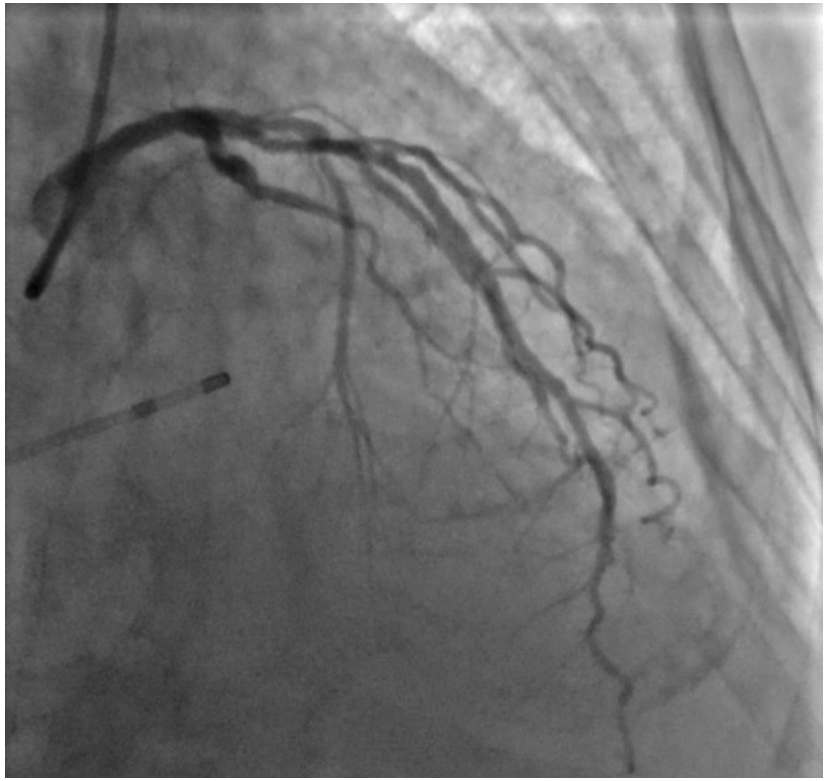
A severe progression of the deferred RCA lesion was found 9 months later

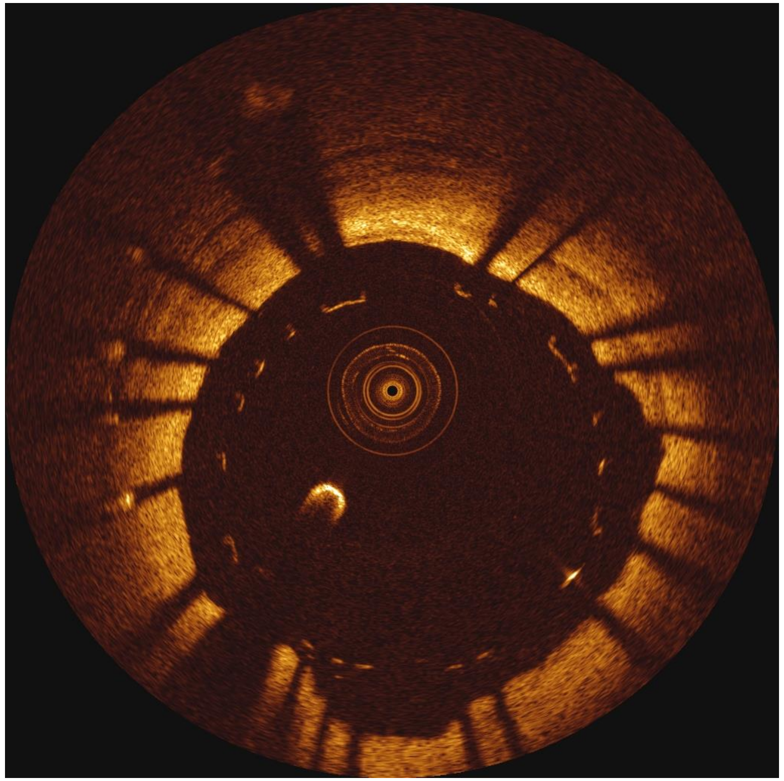


Fezzi, Tu, Wijns, Ribichini et al. *Eur Heart J Case Rep 2023; 7(8):ytad309*

Limitations in Angiography-based Solutions

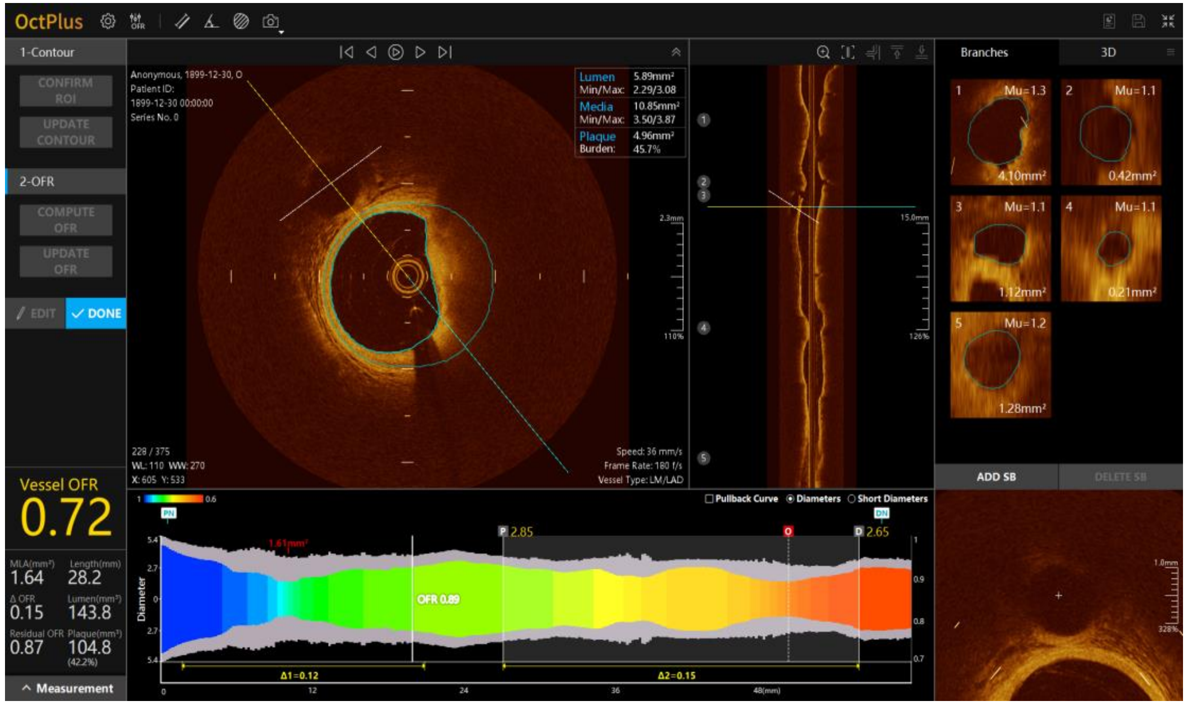
- Angiographic image overlap and significant foreshortening
- Post-PCI optimization: stent mal-apposition/under-expansion





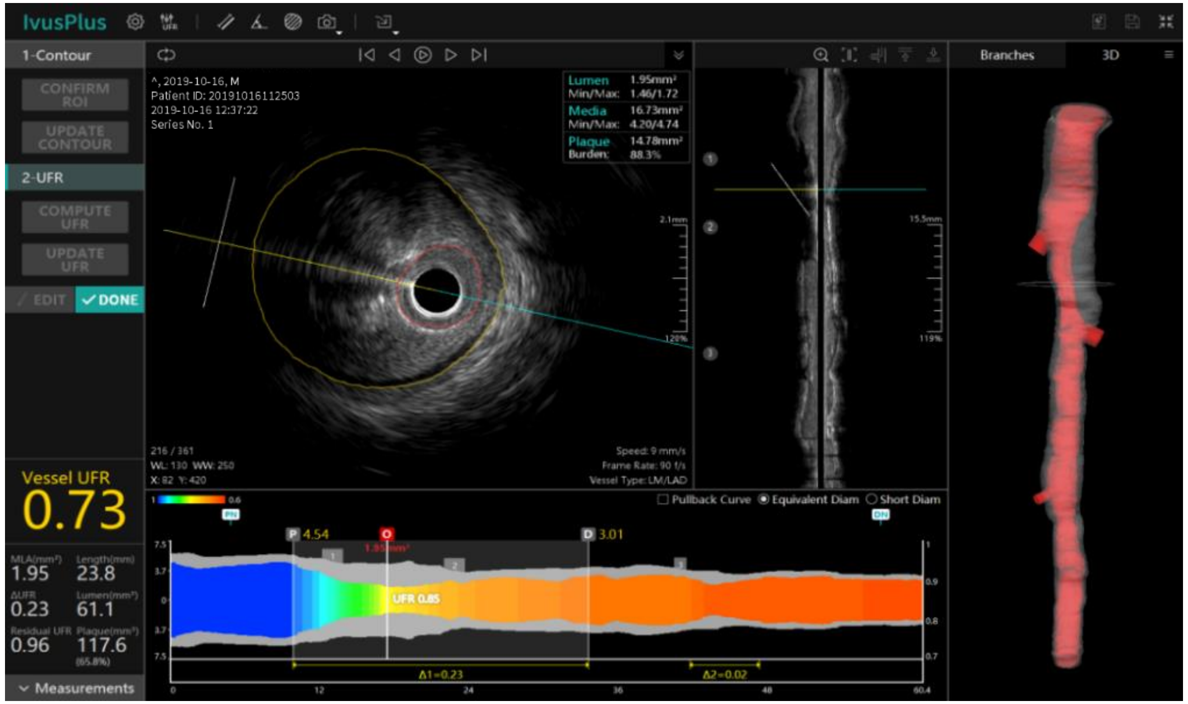
OCT/IVUS-based FFR (OFR and UFR)

OFR



OctPlus (Pulse Medical, Shanghai, China)

UFR



IvusPlus (Pulse Medical, Shanghai, China)

High Diagnostic Concordance between OFR and FFR

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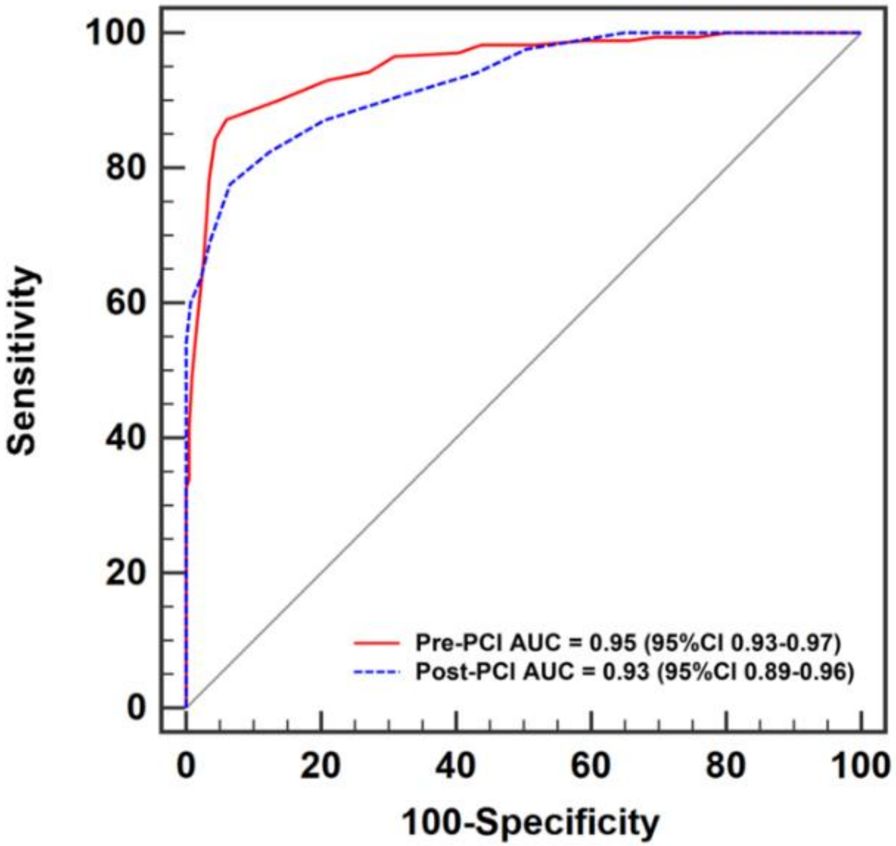

	Pre-PCI	Post-PCI
Accuracy, % (95% CI)	91 (88, 94)	87 (82, 91)
Sensitivity, % (95% CI)	88 (83, 93)	78 (67, 86)
Specificity, % (95% CI)	94 (90, 97)	93 (88, 97)
Positive predictive value, % (95% CI)	93 (88, 96)	88 (79, 93)
Negative predictive value, % (95% CI)	90 (86, 93)	87 (82, 91)
Positive likelihood ratio	15.11 (8.49, 26.88)	11.82 (6.22, 22.45)
Negative likelihood ratio	0.12 (0.08, 0.19)	0.24 (0.16, 0.36)

Hu, Wijns, Tu et al. *EuroIntervention* 2023:19(2):e145-54
Yu, Tu et al. *EuroIntervention* 2019;15:189-97
Huang, Tu et al. *EuroIntervention* 2020;16:568-76
Gutiérrez-Chico, Tu et al. *Cardiol J* 2020;27:350-61
Emori, Tu, Akasaka et al. *Circ J* 2020;84:2253-8
Ding, Wijns, Tu et al. *EuroIntervention* 2021;17:e989-98

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OCT-µFR from Co-registered Angiography and OCT

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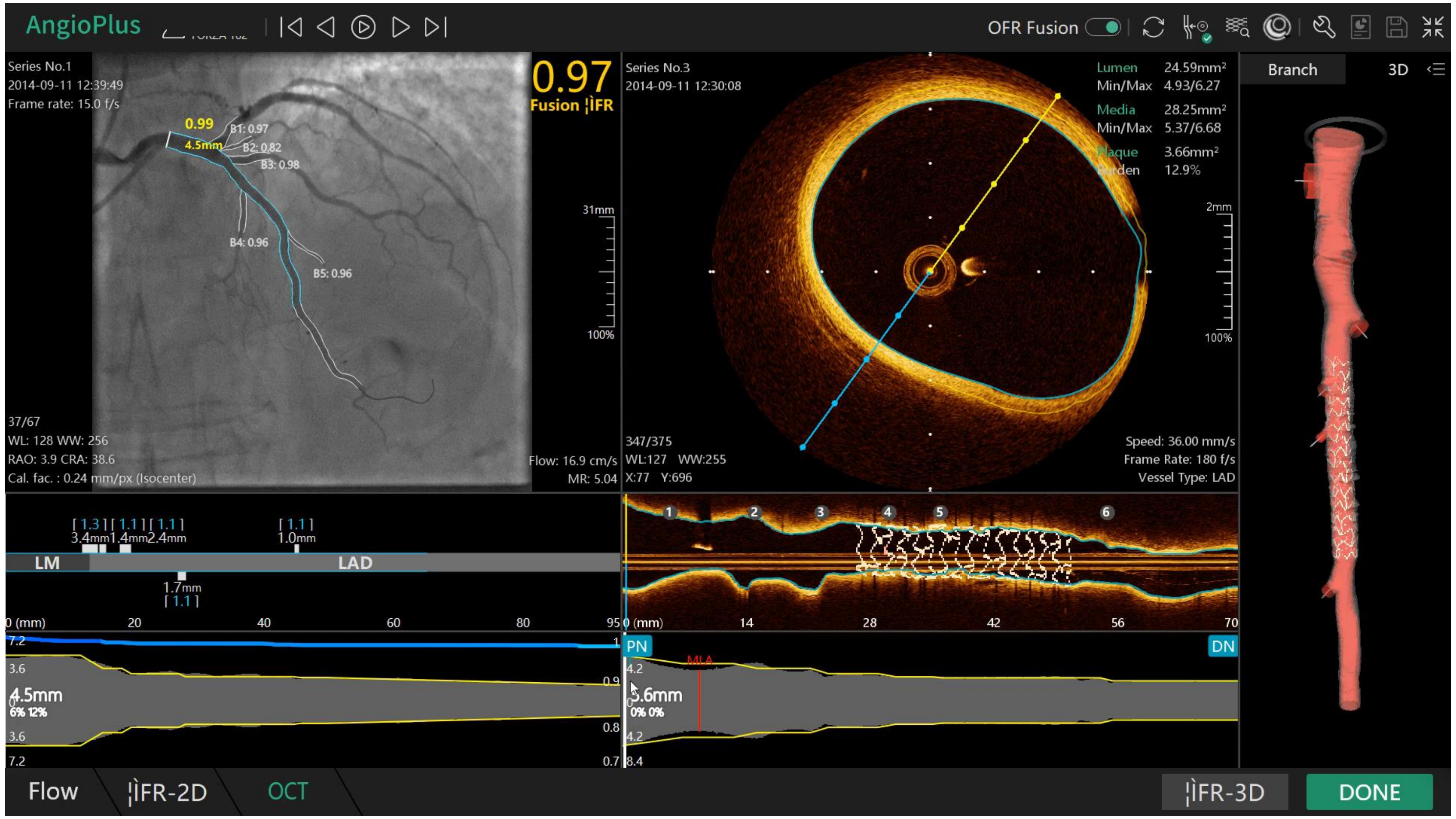
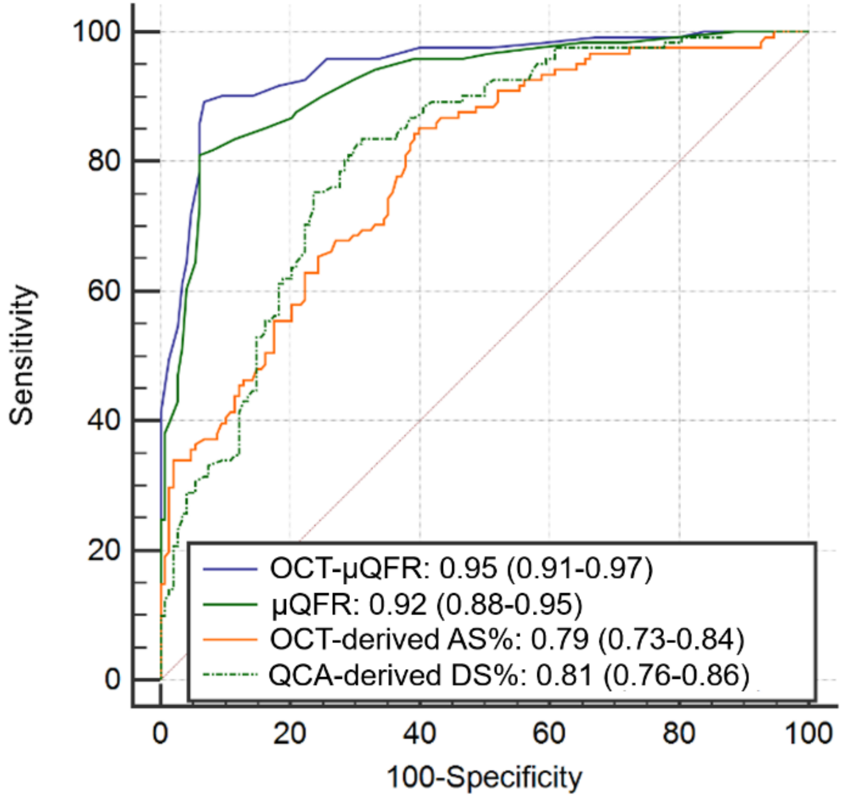
OCT-modulated Murray law-based QFR (OCT-µFR)



269 vessels from 218 patients with angio, OCT, and FFR measurement



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Xu, Tu et al. *JSCAI* 2023; 101043

OCT-μFR from Co-registered Angiography and OCT

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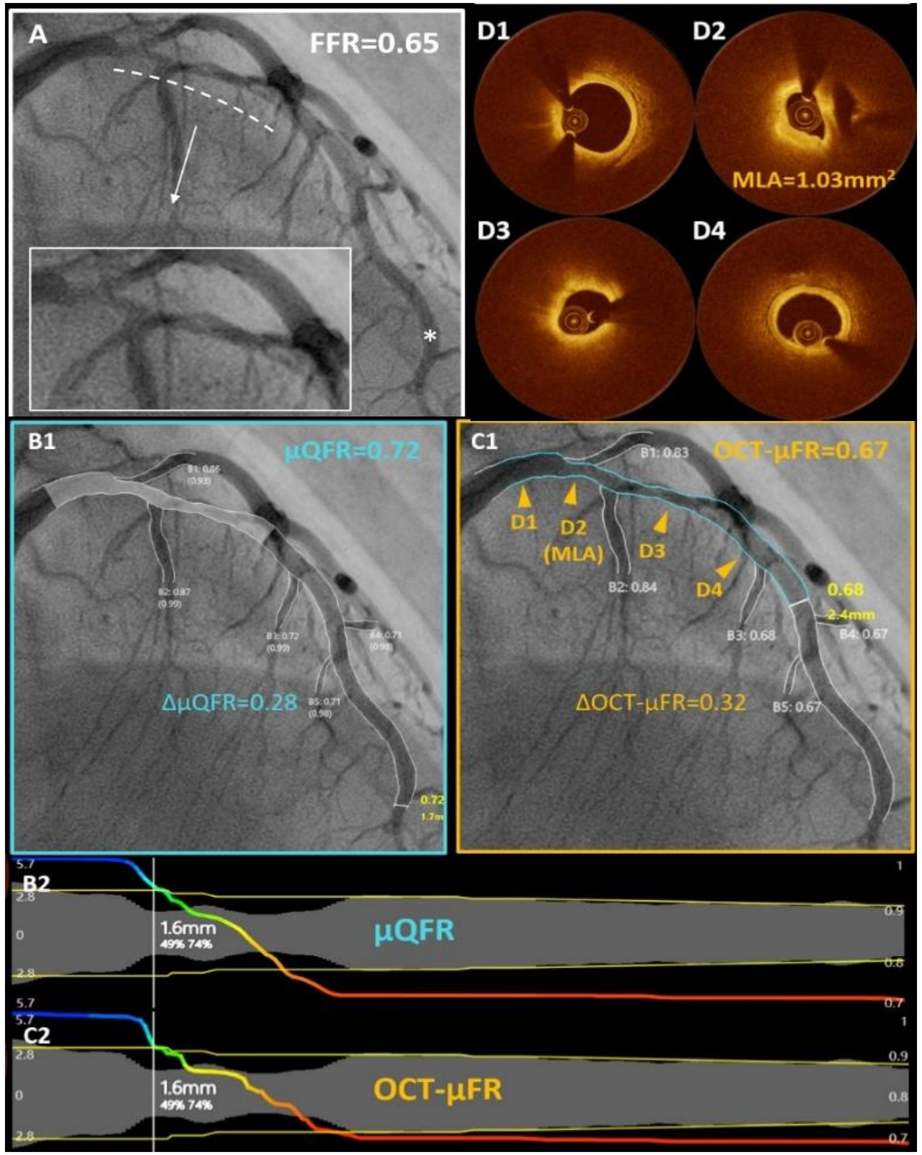

Suboptimal angiographic image quality (109 vessels)

	OCT-μQFR ≤ 0.80	μQFR ≤ 0.80	p
AUC	**0.93**	**0.87**	**0.028**
Accuracy	90%	81%	0.056

Optimal angiographic image quality (160 vessels)

	OCT-μQFR ≤ 0.80	μQFR ≤ 0.80	p
AUC	0.94	0.94	0.879
Accuracy	93%	93%	0.828

Xu, Tu et al. *JSCAI* 2023; 101043

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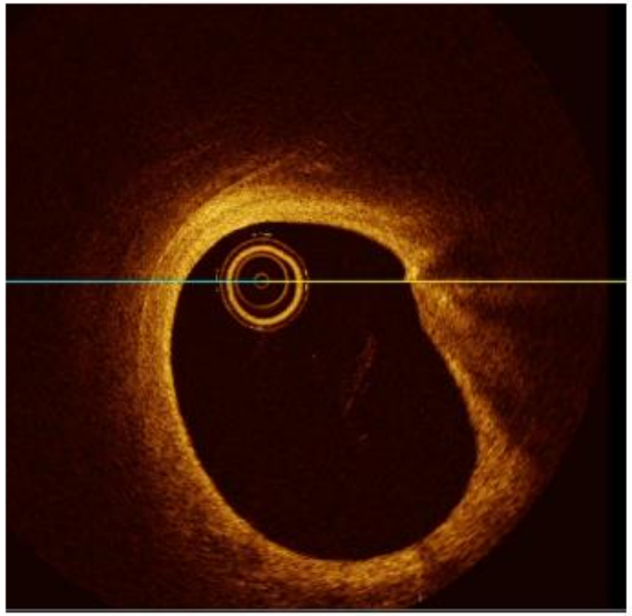
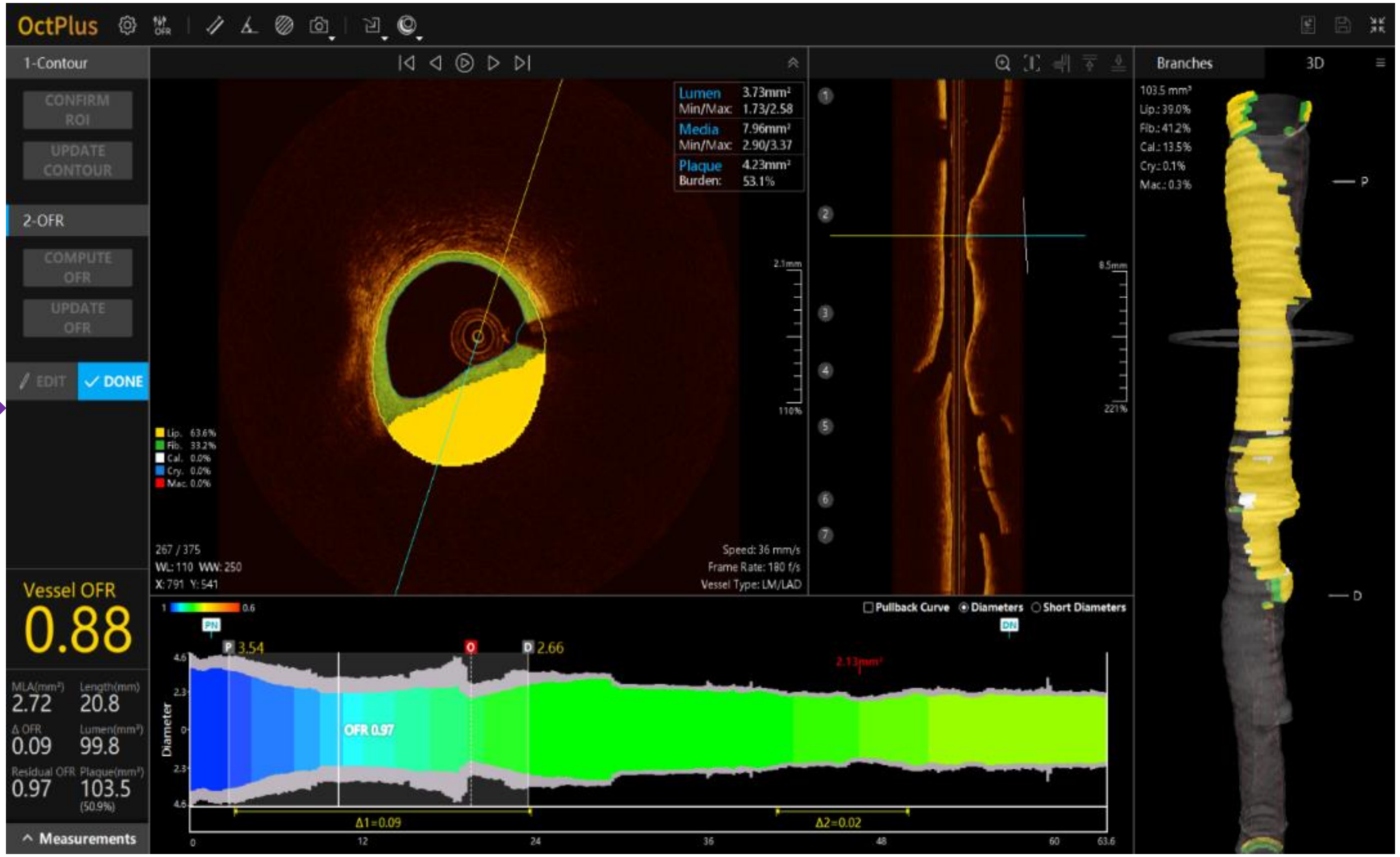
AI-powered OCT : Automated Plaque Characterization

OctPlus (version V2, Pulse Medical, Shanghai, China)



OCT-AI



Chu M, Tu S et al., EuroIntervention 2021;17:41-50

AI-powered OCT: Validation against Expert Annotation

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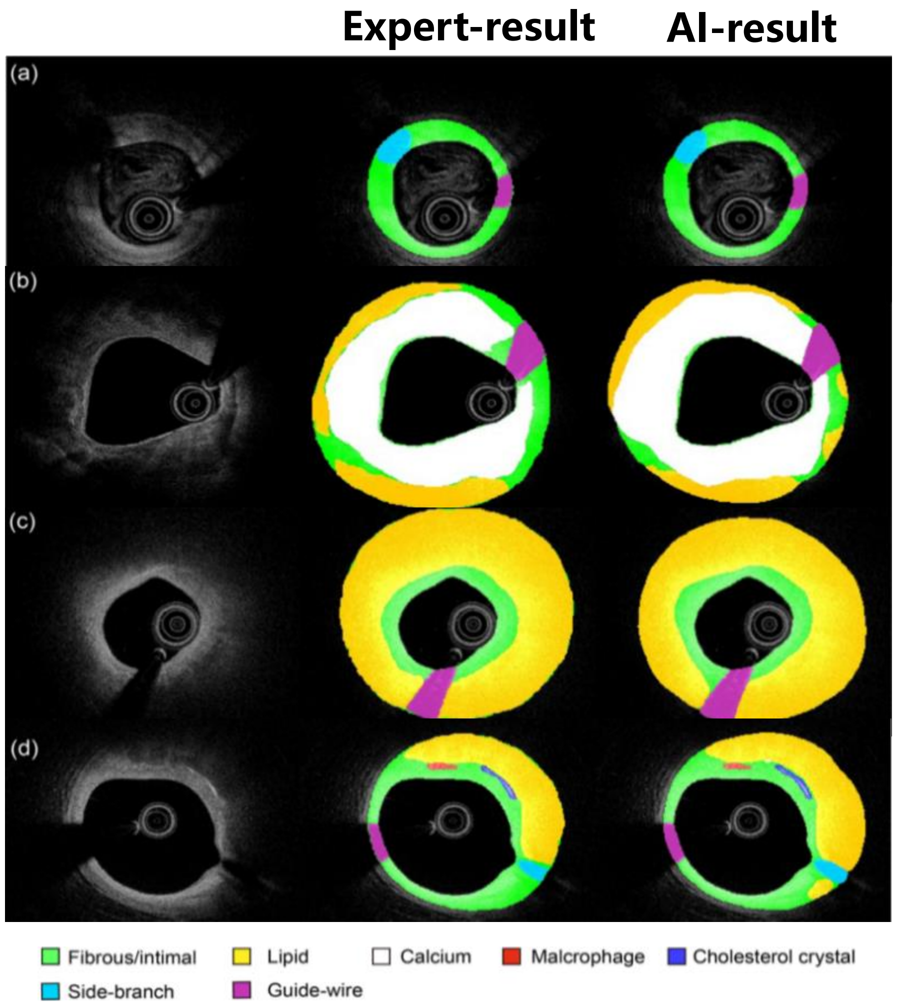

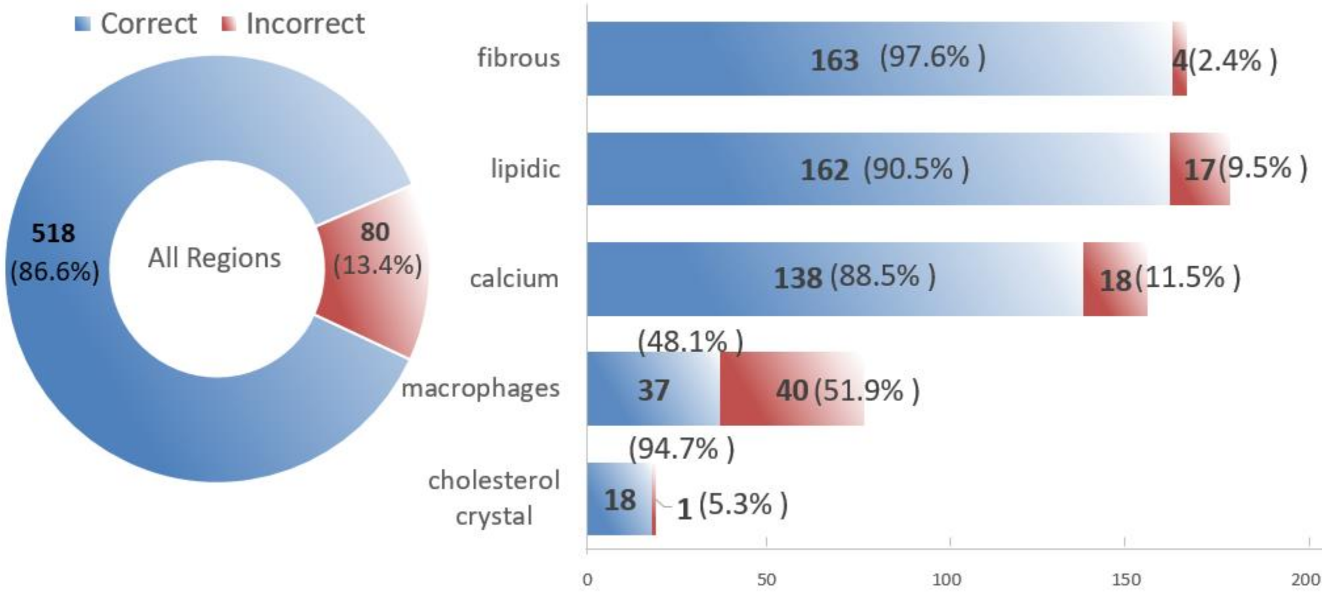

Diagnostic accuracy = 92.2% for basic plaque components

Chu M, Tu S et al., EuroIntervention 2021;17:41-50

Lipid-to-cap Ratio (LCR): A New Vulnerability Index

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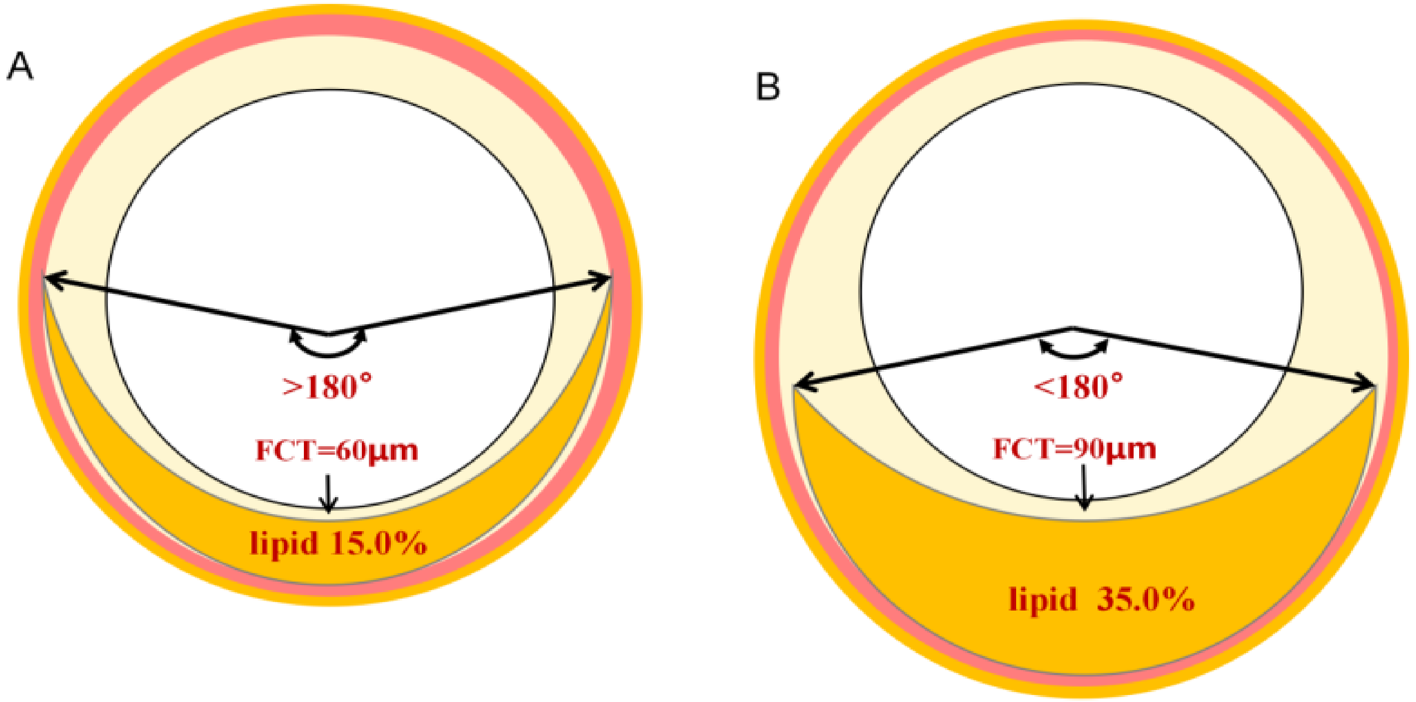
binary variable

TCFA = thin-cap fibroatheroma
Cap thickness<65um & lipid arc>180°

LCR = lipid-to-cap ratio
Lipid burden / cap thickness

continuous variable



TCFA(+)

$$LCR=\frac{15\%}{60\mu m}*100=0.25$$

TCFA(-)

$$LCR=\frac{35\%}{90\mu m}*100=0.389$$

Prediction of 2-year MACE for Non-culprit Vessels

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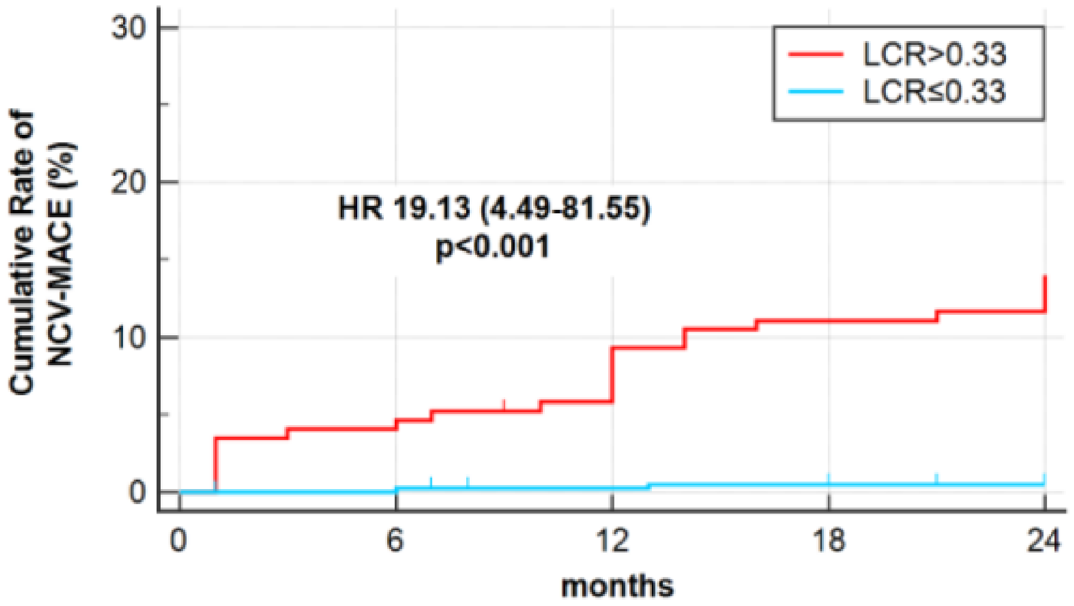
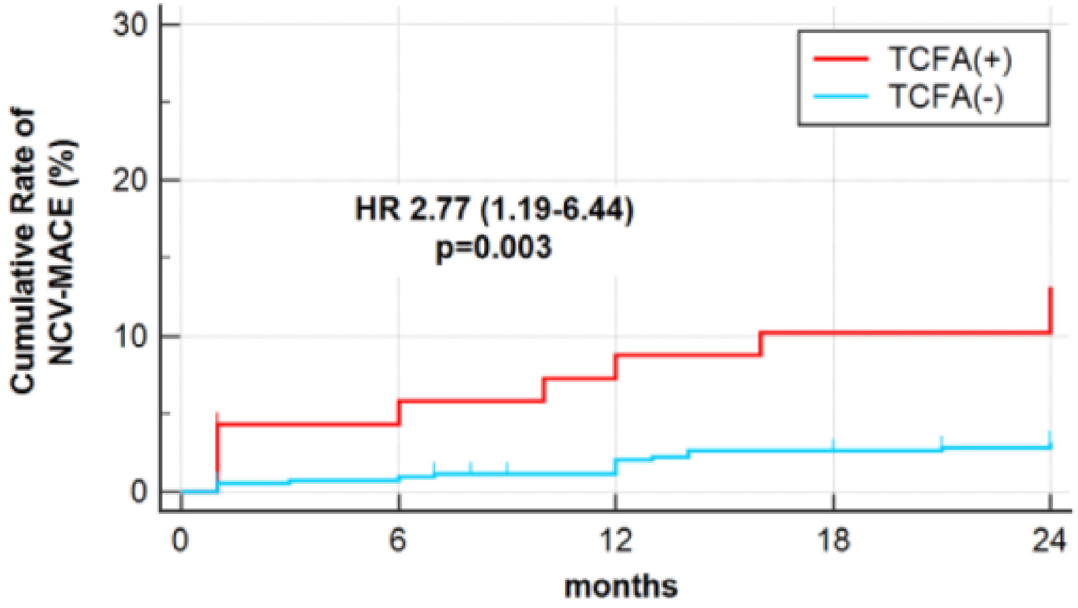
604 ACS patients (915 vessels)



Number at risk

	0	6	12	18	24
Group: LCR>0.33	172	164	155	152	147
Group: LCR≤0.33	432	429	427	425	422



Number at risk

	0	6	12	18	24
Group: TCFA(+)	69	64	62	61	59
Group: TCFA(-)	535	529	520	516	510

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Hong H, Tu S, et al., JACC: Asia 2022; 2:460-72

Prediction of 2-year MACE for Non-culprit Vessels

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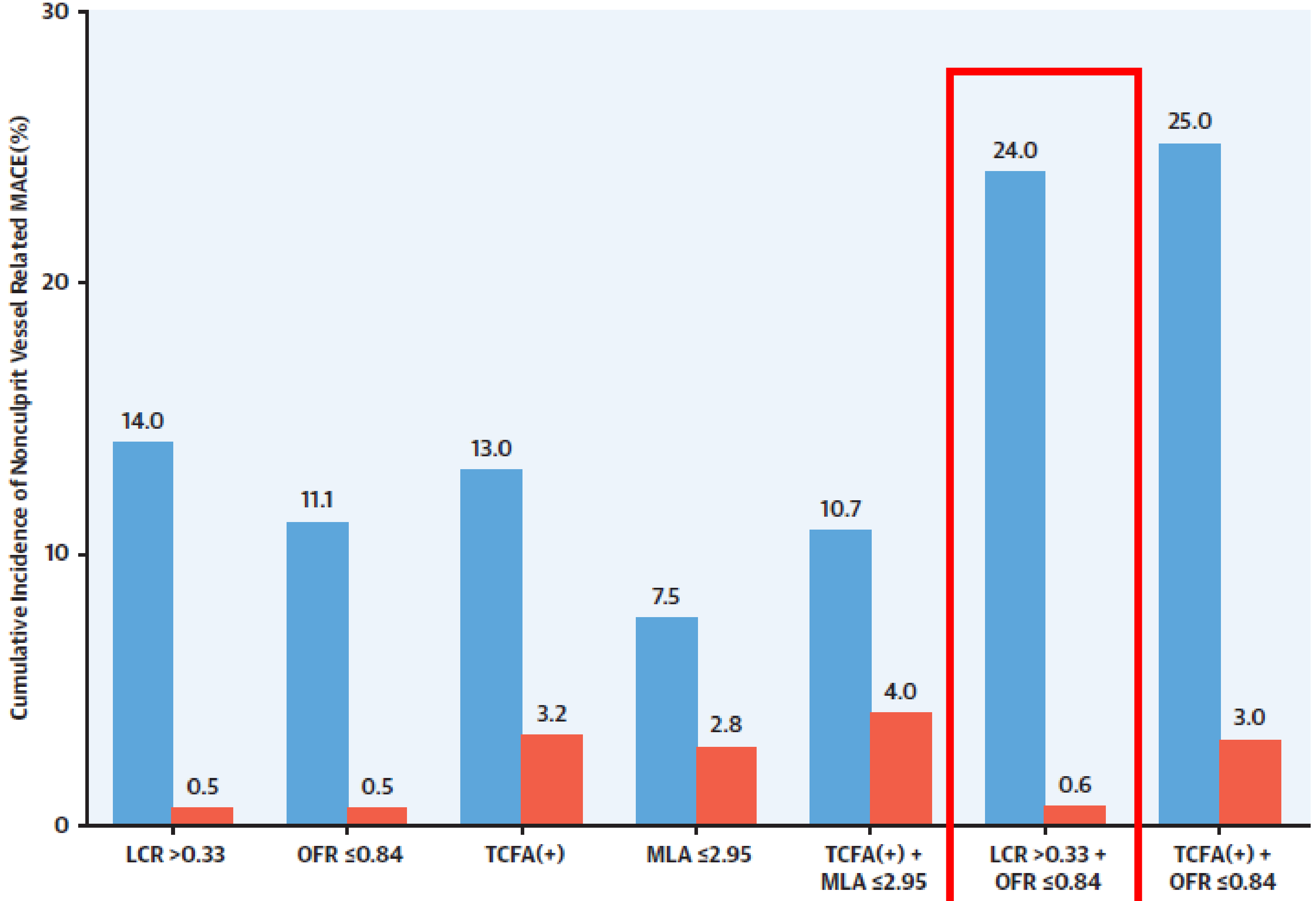

	LCR >0.33	OFR ≤0.84	TCFA(+)	MLA ≤2.95	TCFA(+) + MLA ≤2.95	LCR >0.33 + OFR ≤0.84	TCFA(+) + OFR ≤0.84
Events/Patients	24/172 2/432	24/217 2/387	9/69 17/535	15/200 11/404	3/28 23/576	23/96 3/508	9/36 17/568
Hazard Ratio (95% CI) *P* value	19.13 (4.49-81.55) < 0.001	11.52 (2.70-49.12) 0.001	2.77 (1.19-6.44) 0.003	2.63 (1.20-5.76) 0.016	1.95 (0.56-6.80) 0.295	42.73 (12.80-142.64) < 0.001	6.58 (2.83-15.33) < 0.001

Present Absent

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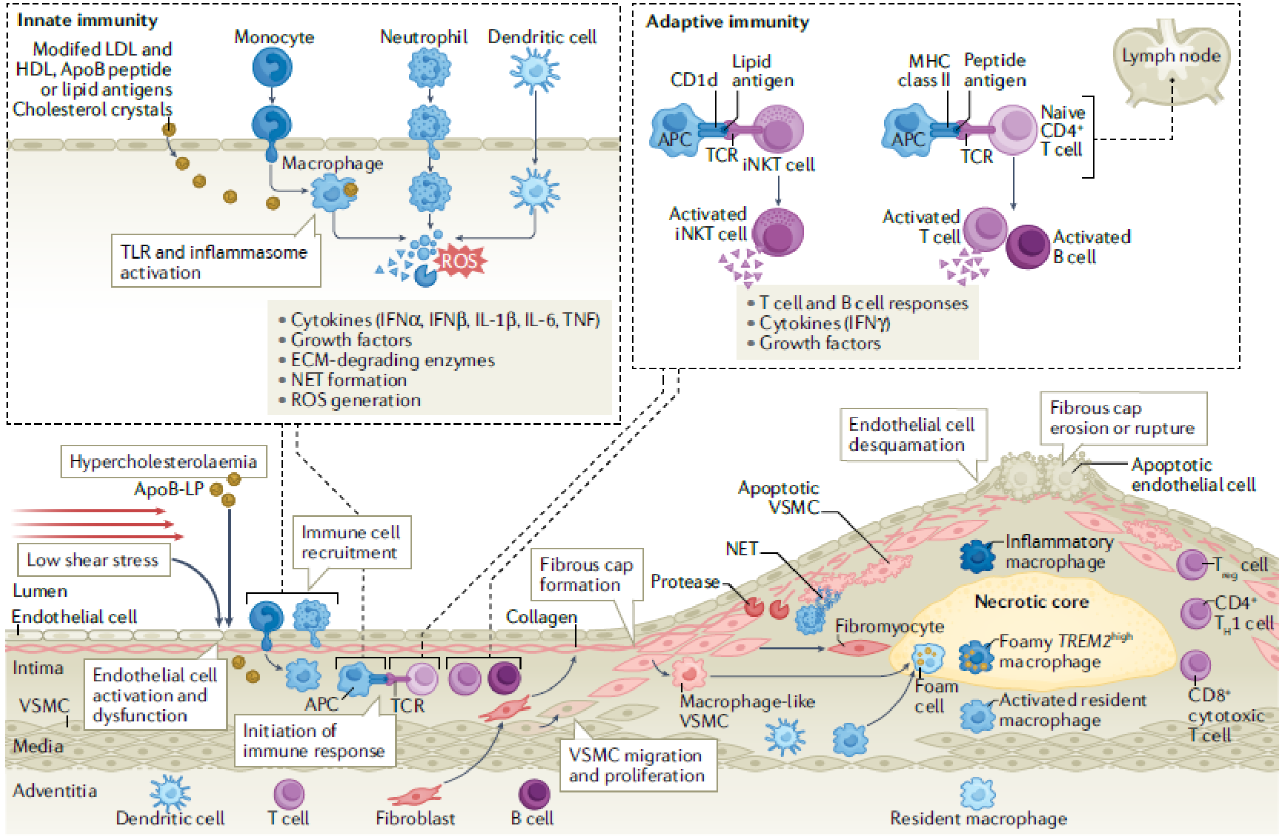
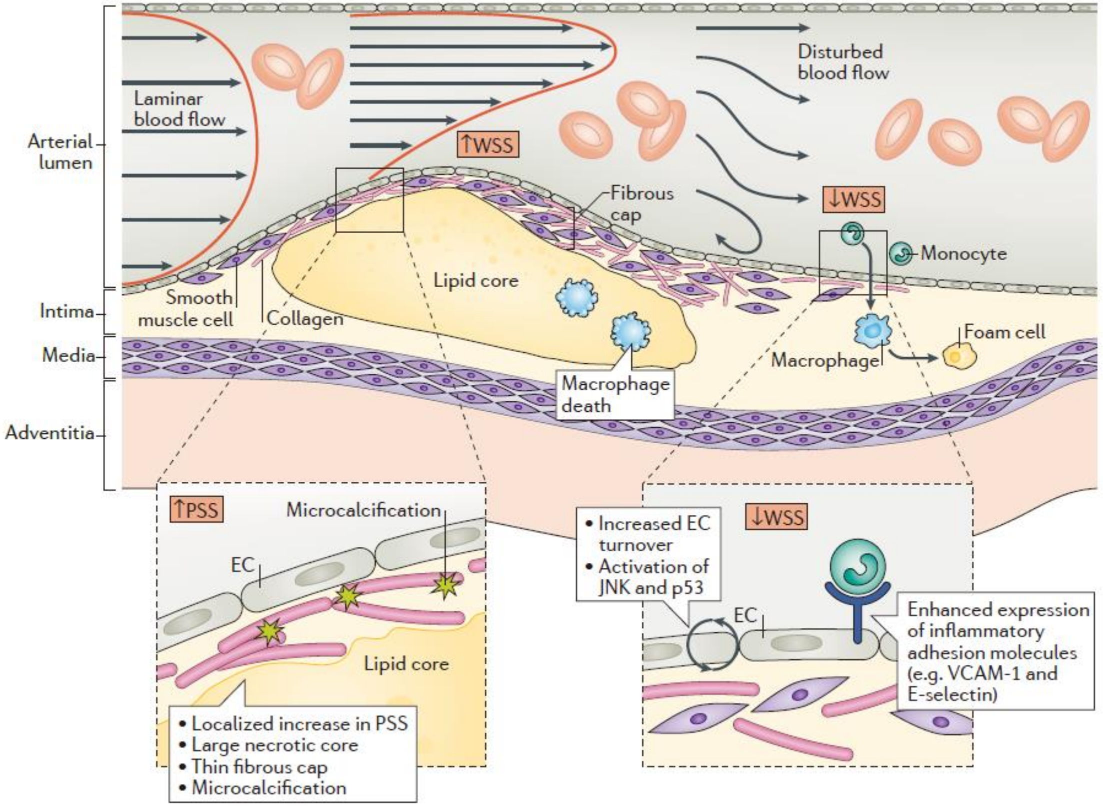
Hong H, Tu S, et al., JACC: Asia 2022; 2:460-72

Future: Inflammation and Biomechanics

- **Inflammation:** the major underlying mechanism of atherosclerosis
- **Biomechanical forces:** critical local factors affecting plaque initation, progression, and rupture





Engelen SE et al., Nat Rev Cardiol 2022;19(8):522-42

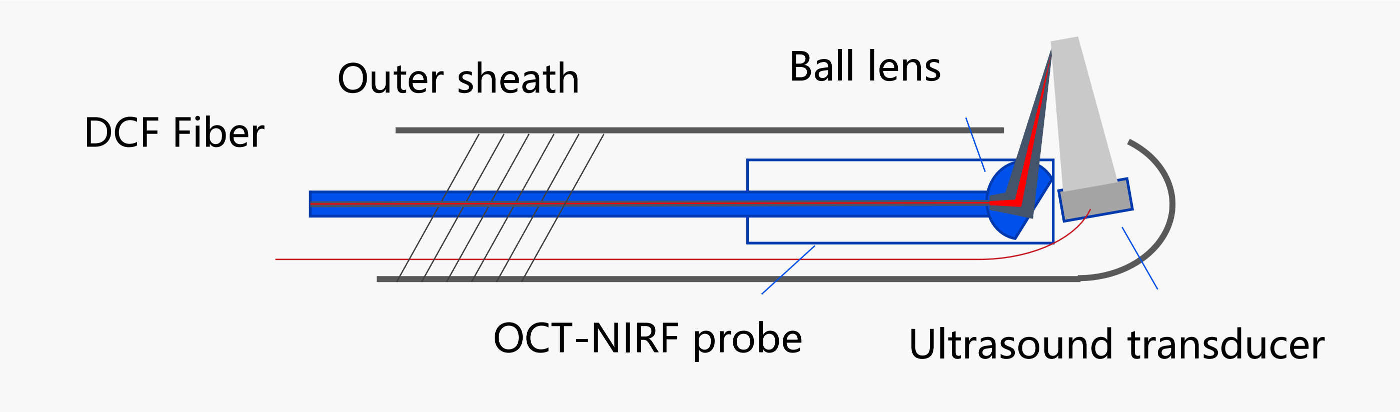
Brown AJ et al., Nat Rev Cardiol 2016;13(4):210-20

Integrated OCT, IVUS, NIFR, and PSS

OCT
superior spatial resolution

IVUS
high penetration depth

NIRF
molecular & biochemical imaging
especially for inflammation



NIRF = near infrared fluorescence

PSS = plaque stress

1 pullback=

Thank You!