Integrating Invasive Diagnostic Methods in Interventional Cardiology

Daniel Chamié, MD

Interventional Cardiologist, Instituto Dante Pazzanese de Cardiologia

Director, OCT Core Laboratory, Cardiovascuar Research Center

Sao Paulo, Brazil

CARDIOVASCULAR RESEARCH CENTER

Instituto DANTE PAZZANESE de Cardiologia

When Do I Think of an Adjunctive Method?

1. **To define which lesion to treat**
   - Physiology vs. Imaging
   - Defining the culprit
2. **To Guide/Optimize the PCI**
   - Pre-PCI
   - Post-PCI
3. **To understand the mechanisms of stent failure**

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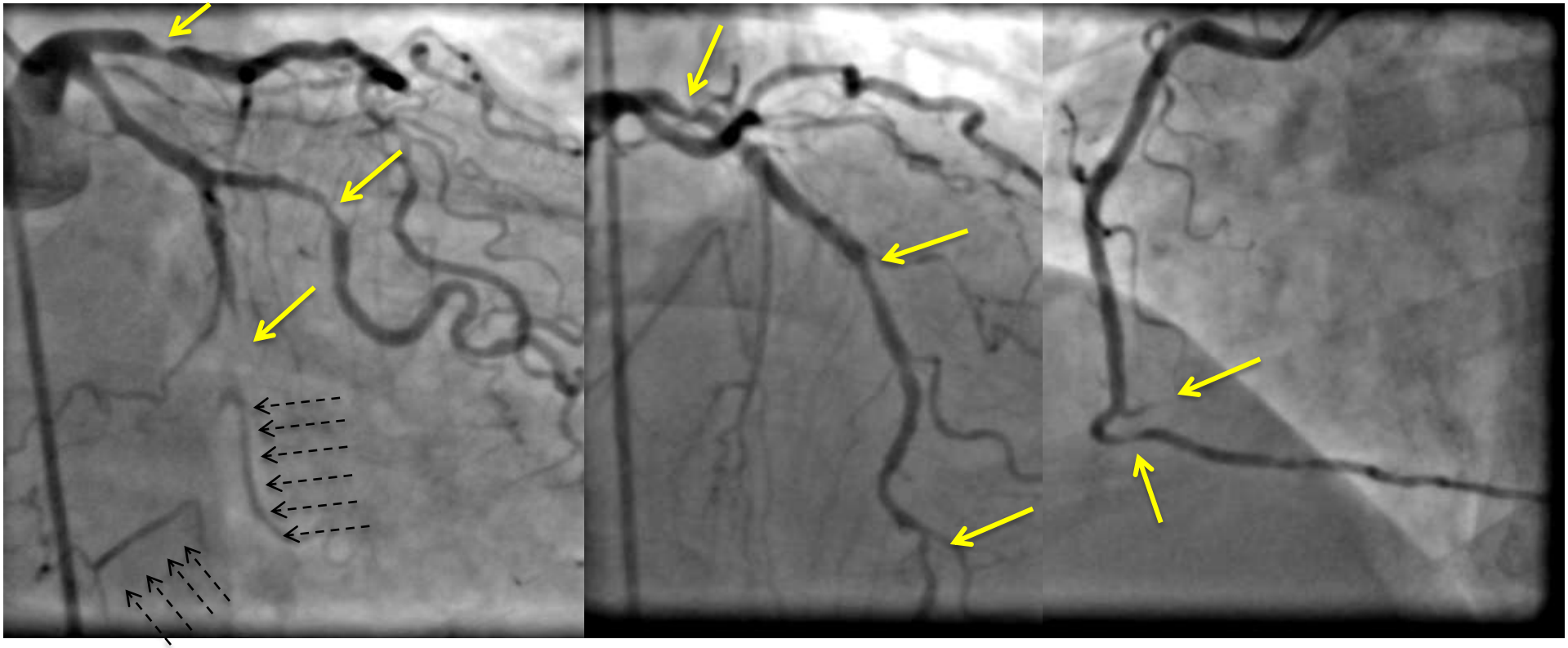
How to Approach This Patient?

64-yo female, HTN, Hypercholesterolemia, type II Diabetes Mellitus, prior MI
NSTEMI in the past 30 days, evolving w/ Stable Angina CCS II
Referred for coronary angiography w/o any non-invasive functional test assessment



Syntax Score: 27

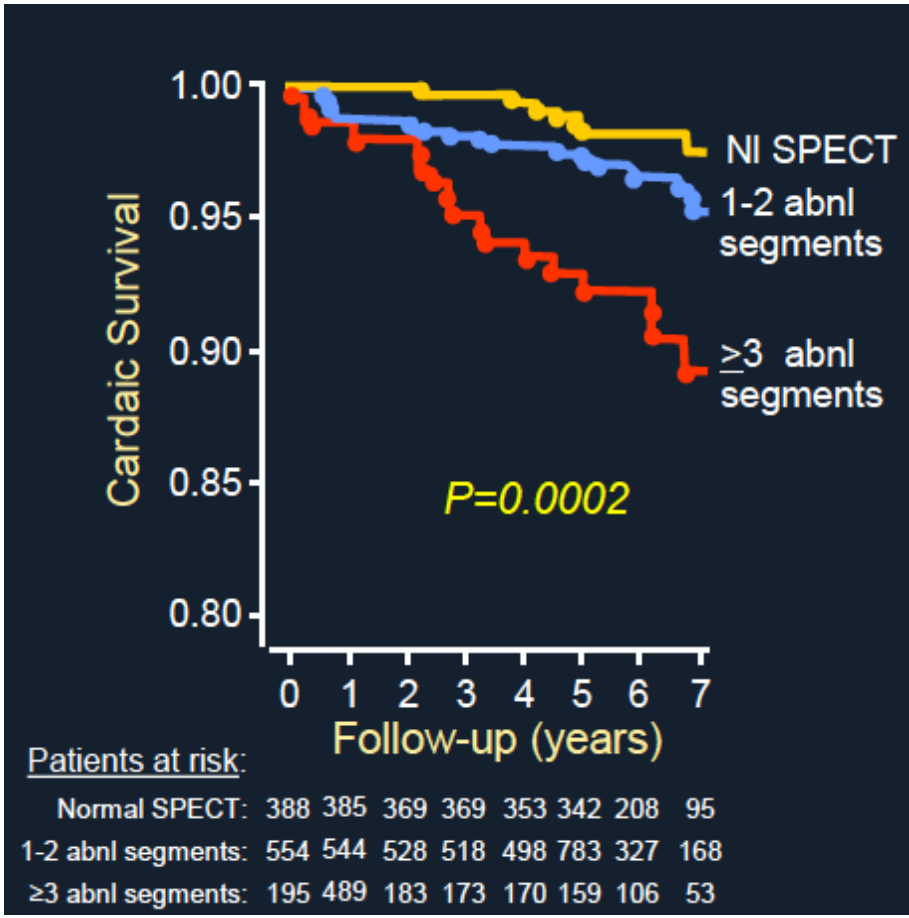
Two Goals of Tx in Pts with Stable CAD

1. **Improve Symptoms and Quality of Life**
   - Measured by “soft endpoints” (i.e. angina/QOL scales)

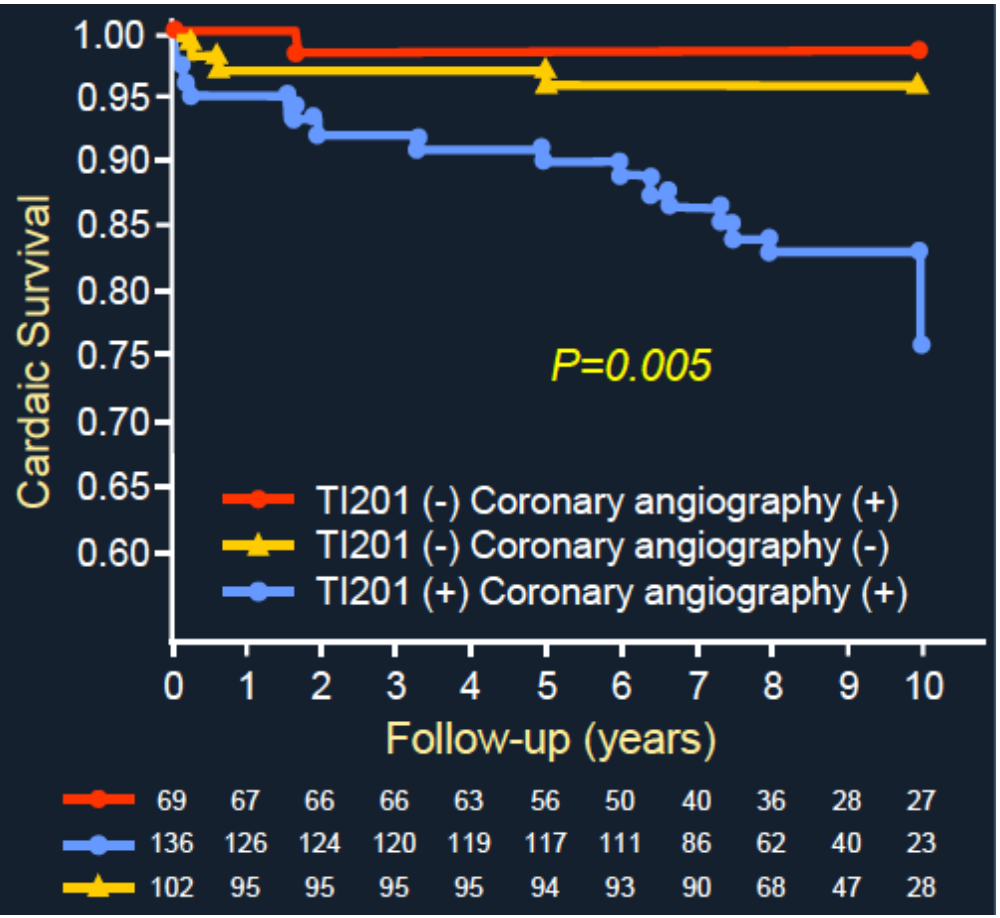
2. **Improve Prognosis**
   - Measured by “harder endpoints” (i.e. death, MI)

Multiple Studies have Shown a Powerful Relationship Between Ischemia and Survival

1,137 pts with chest pain or suspected CAD



10-yr survival in 307 pts according to CAD and Thallium-201

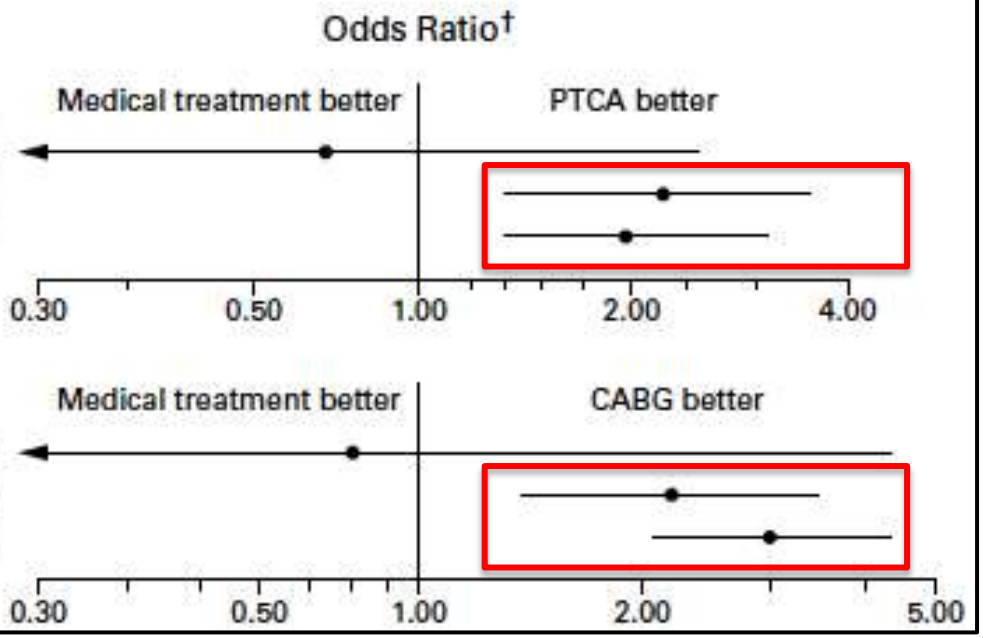


Vanzetto G, et al. Circulation 1999;100:1521-1527
Pavin D, et al. Eur Heart J 1997;18:69-77

Appropriateness of Revascularization and Outcomes in the UK

Prospective study of consecutive pts undergoing CAG at 3 London hospitals
Before pts were recruited, 9-member expert panel rated the appropriateness of revascularization according to the RAND method assigning pts a score [1: highly inappropriate; 9: highly appropriate]

Appropriateness Category	Angina at Follow-up		Odds Ratio (95% CI)
	Medical Treatment	Revascularization	
	no. with angina/total no.		
PTCA			
Inappropriate	56/110	9/14	0.73 (0.22–2.42)
Uncertain	172/317	67/142	2.15 (1.34–3.44)
Appropriate	143/205	114/210	1.97 (1.29–3.00)
CABG			
Inappropriate	49/70	6/8	0.82 (0.15–4.40)
Uncertain	189/348	60/136	2.23 (1.40–3.55)
Appropriate	137/208	213/547	3.03 (2.08–4.42)



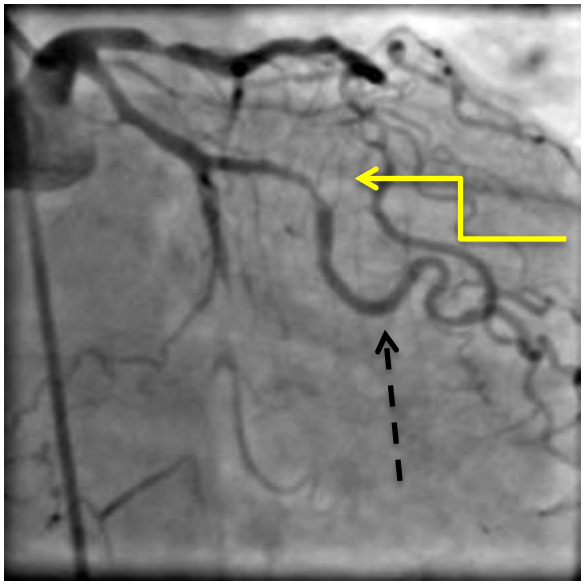
Hemingway H, et al. N Engl J Med 2001;344:645-654

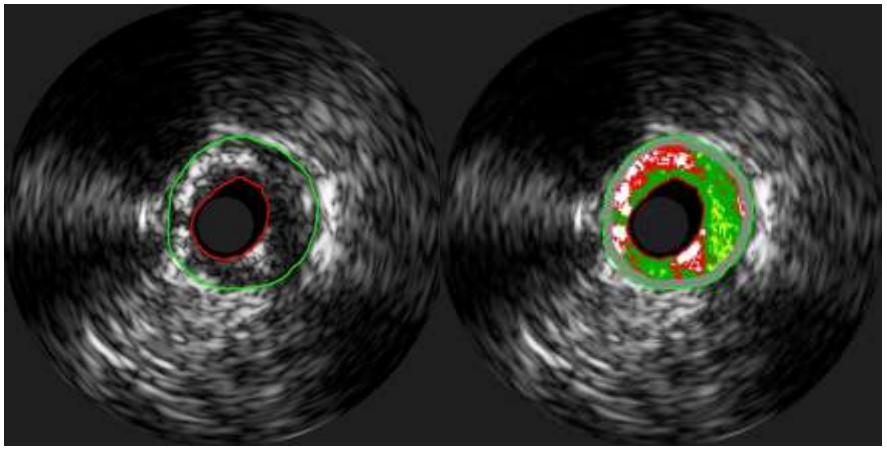
In Order for Revascularization to Provide a Benefit Perceived by Patients…

- The revascularization must be able to be done safely and with high quality and/or durability.

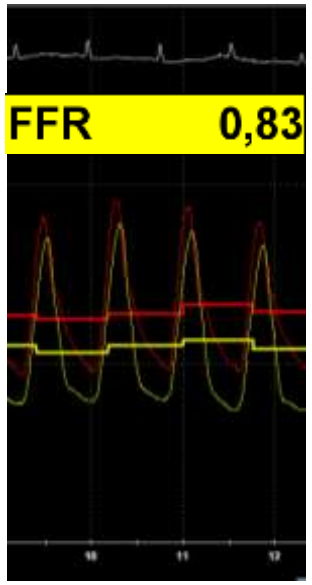
- The revascularization has to be performed on lesions that are actually causing symptoms or a reduction in quality of life (also possible in “asymptomatic” patients).
  - Ischemia-based lesion assessment

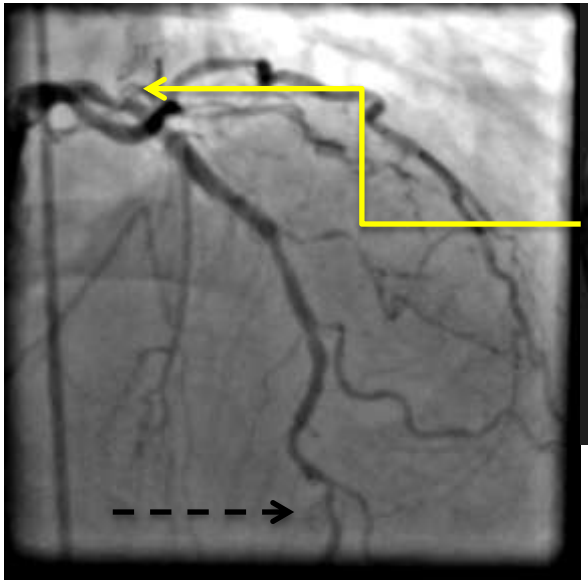
Anatomy vs. Physiology

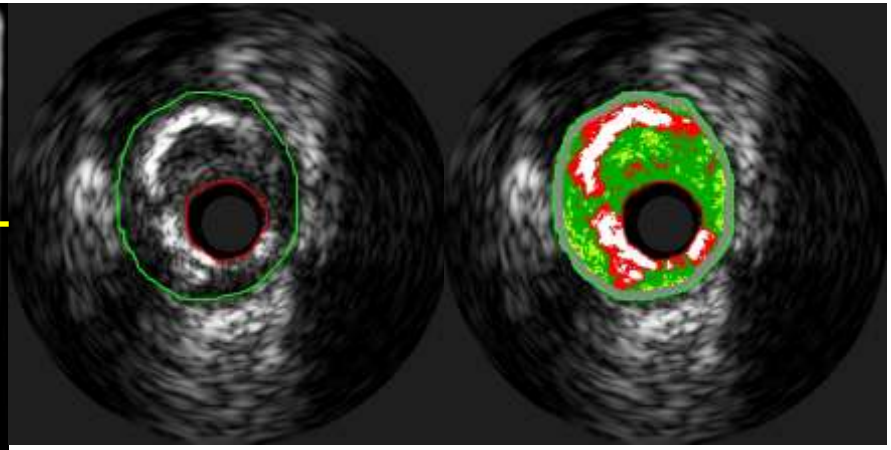




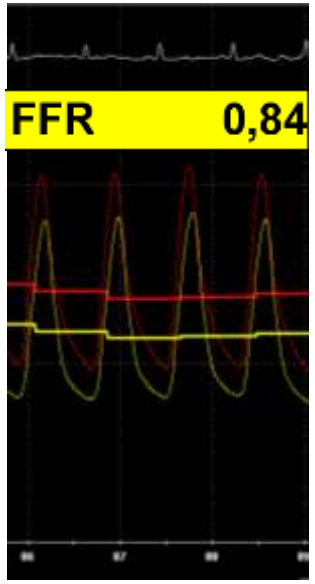
Vessel area: 9.1 mm^2
Lumen area: 2.1 mm^2
Plaque burden: 76.9%



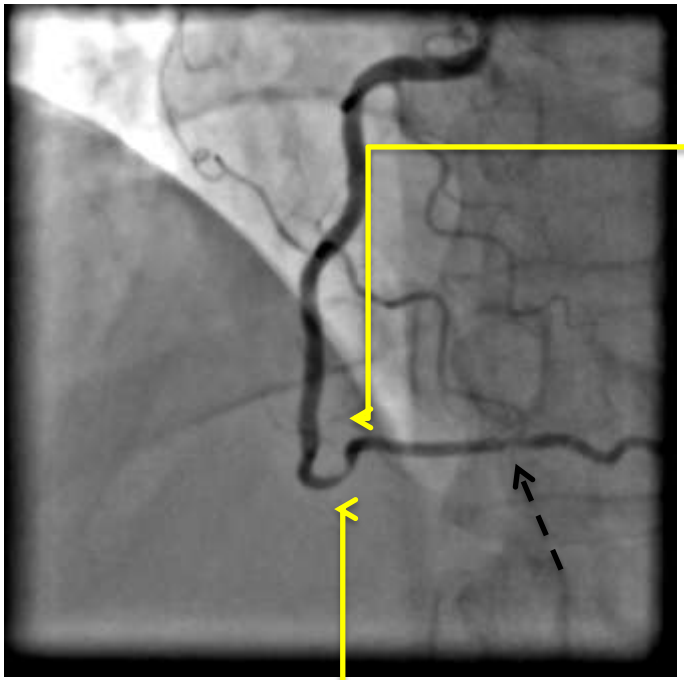


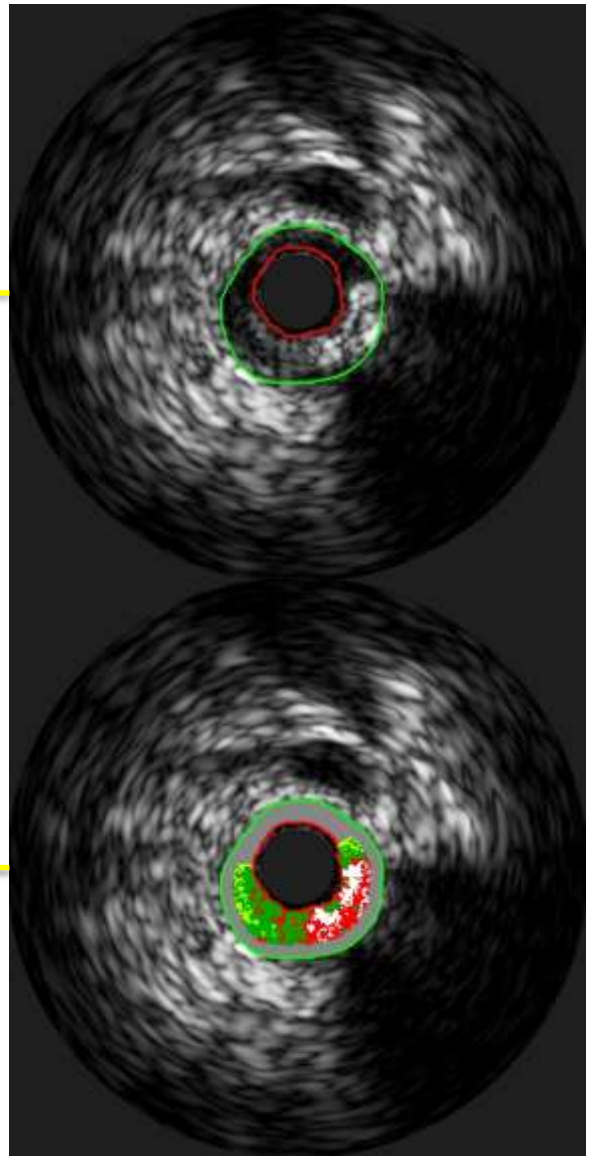


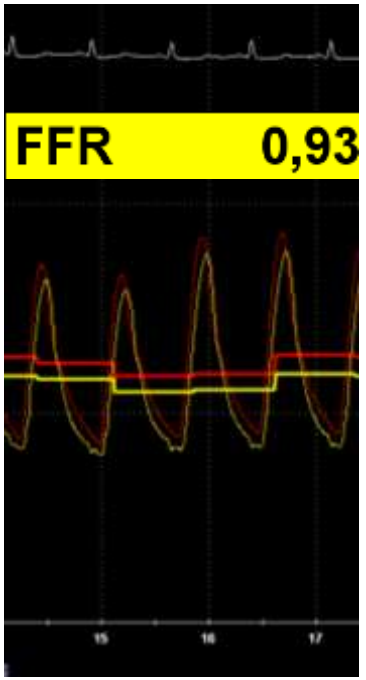
Vessel area: 14.5 mm^2
Lumen area: 2.4 mm^2
Plaque burden: 83.2%



Anatomy vs. Physiology







Vessel area: 6.2 mm^2
Lumen Area: 1.7 mm^2
Plaque Burden: 72.5%

Reclassification of the Patient's Risk

After FFR, Syntax Score = 5.0

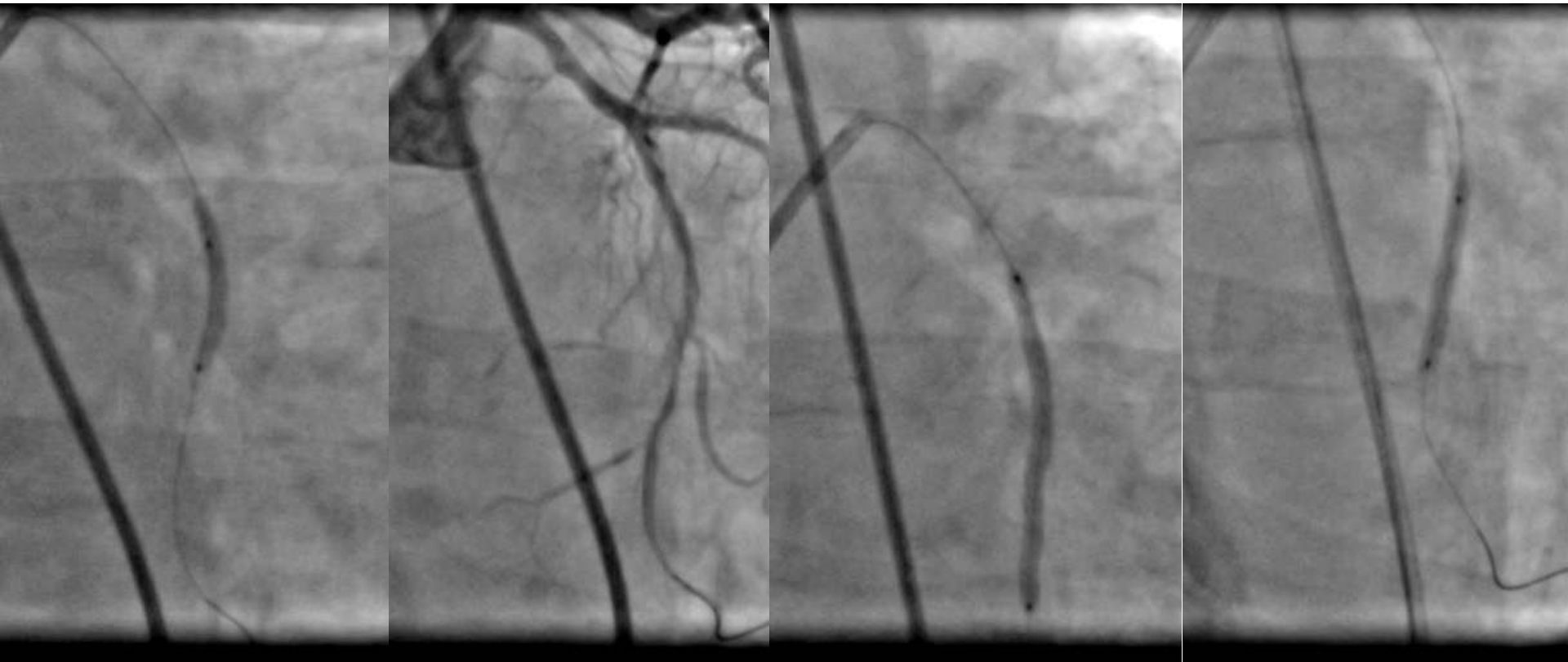
PCI of the LCx

Pre-Dil
Apex 2.0 x 15 mm

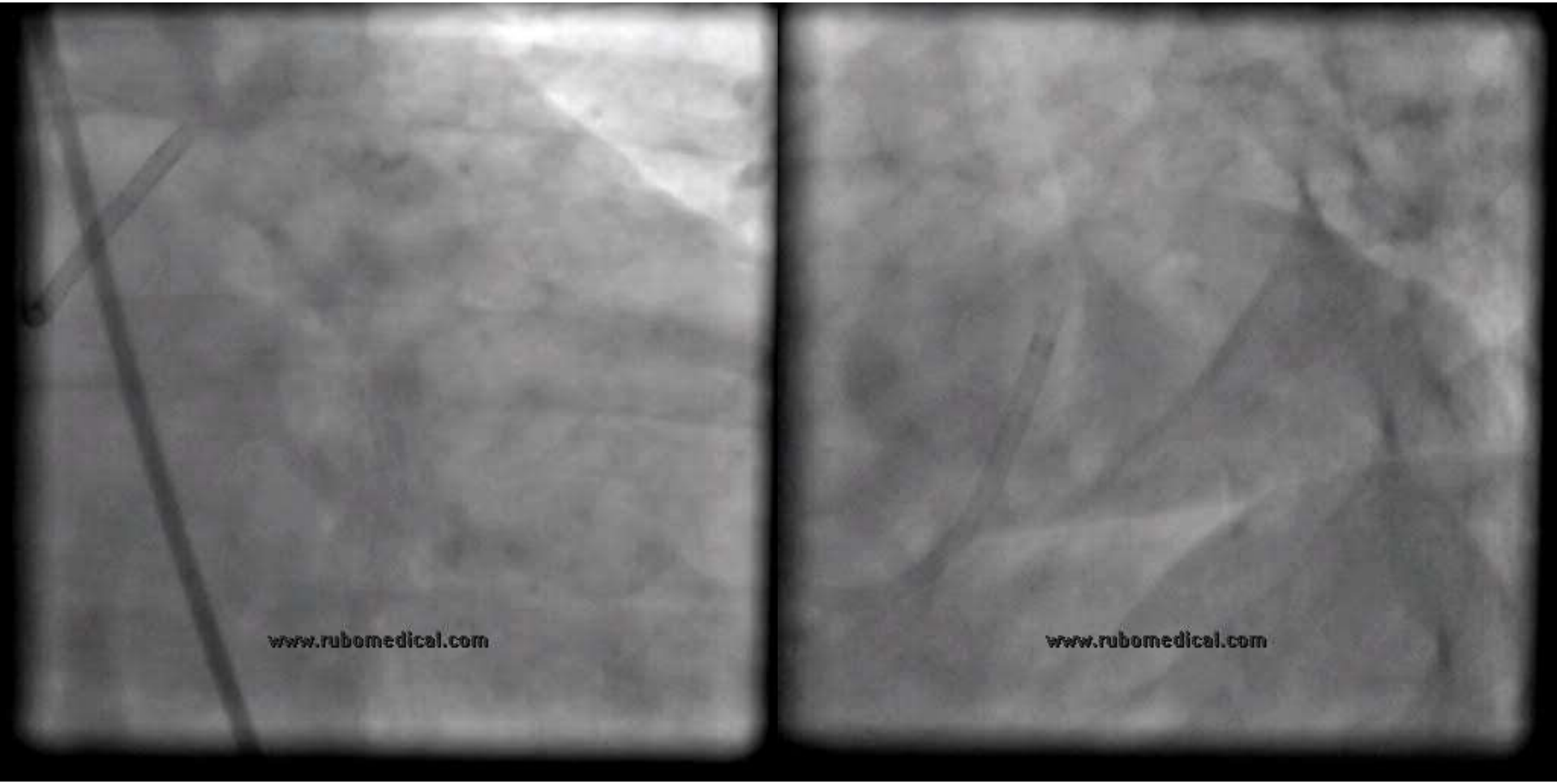
After Pre-Dil

Biomatrix Flex
2.5 x 36 mm

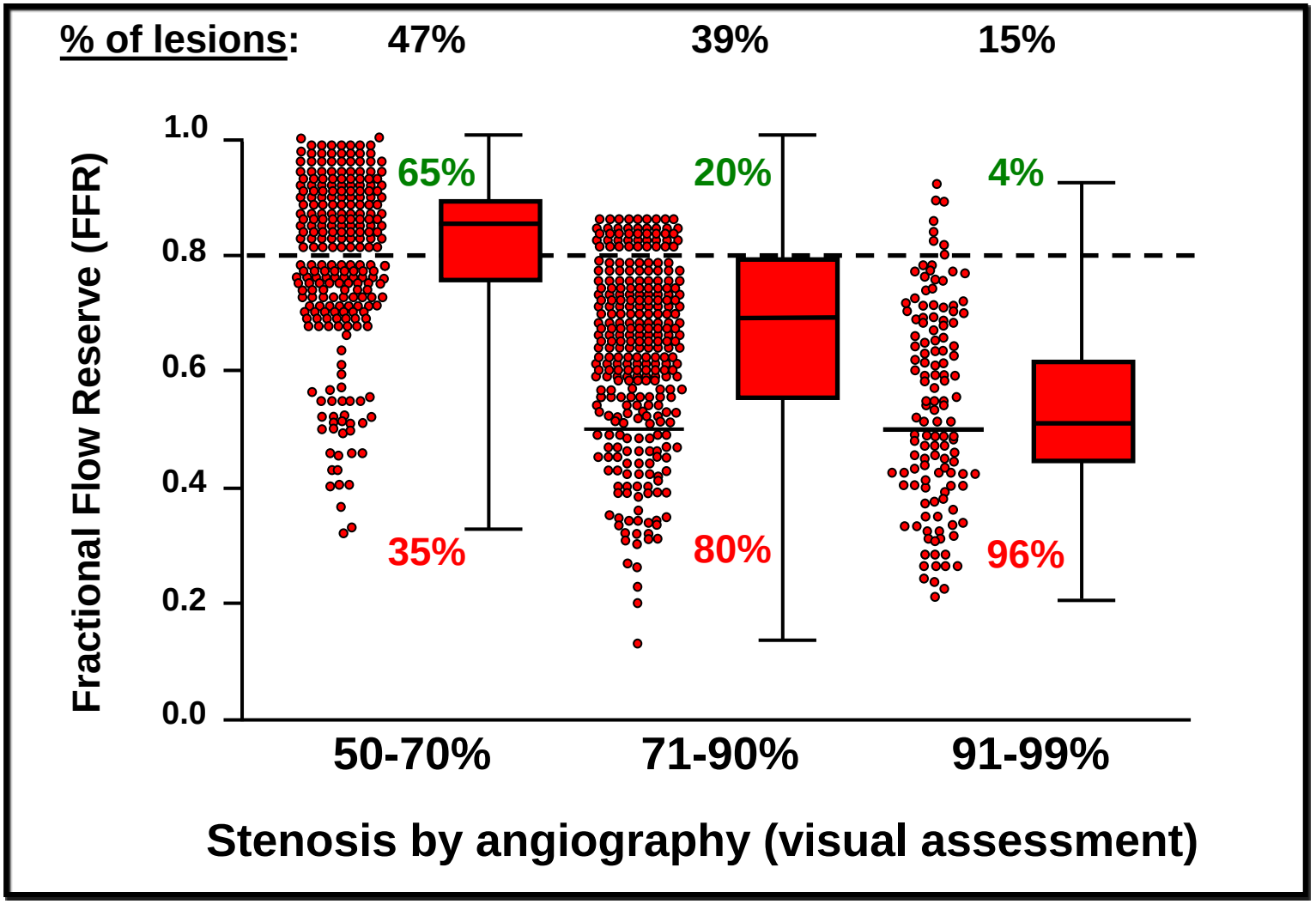
Post-Dil
Quantum 2.5 x 20 mm



Final Angiographic Result



Relation Between Angio %DS and FFR (n=1,329)



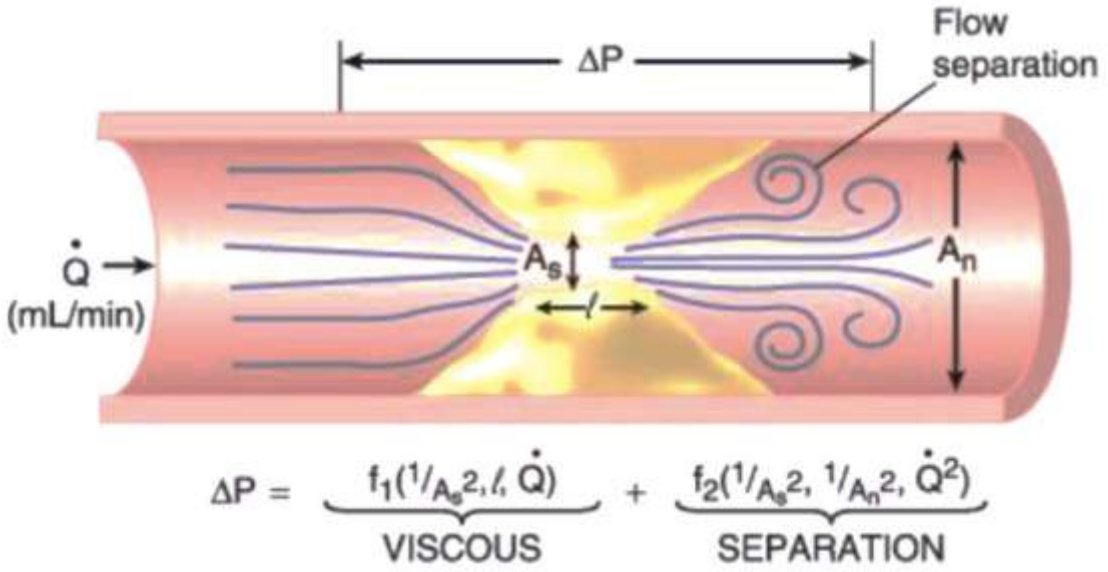
Torino PA, et al. J Am Coll Cardiol. 2010;55:2816-2821

IVUS MLA Cutoffs for Non-LM Stenosis

	N	FFR	MLA	AUC	Sens	Spec	PPV	NPV	Accuracy
Takagi [1999 Circ]	51	0.75	3.0	-	83%	92%	-	-	-
Briguori [2001 AJC]	53	0.75	4.0	-	92%	56%	38%	96%	64%
Ben-Dor [2012 Cardiovasc Revasc Med]	205	0.80	3.09	0.73	69%	72%	-	-	70%
Kang [2011 Circ Int]	236	0.80	2.4	0.80	90%	60%	37%	96%	68%
Kang [2012 AJC]	784	0.80	2.4	0.77	84%	63%	48%	90%	69%
Koo [2011 JACC Int]	267	0.80	2.75	0.81	69%	65%	27%	81%	67%
Gonzalo [2012 JACC]	47	0.80	2.36 IVUS	0.63	67%	65%	67%	65%	66%
Gonzalo [2012 JACC]	61	0.80	1.95 OCT	0.70	82%	63%	66%	80%	72%
Stone [TCT 2013]	544	0.80	2.9	-	66.3 %	65.9 %	46.7 %	81.3 %	66%

Influence of an Epicardial Stenosis in the Coronary Blood Flow Dinamics

Daniel Bernoulli
1700-1782

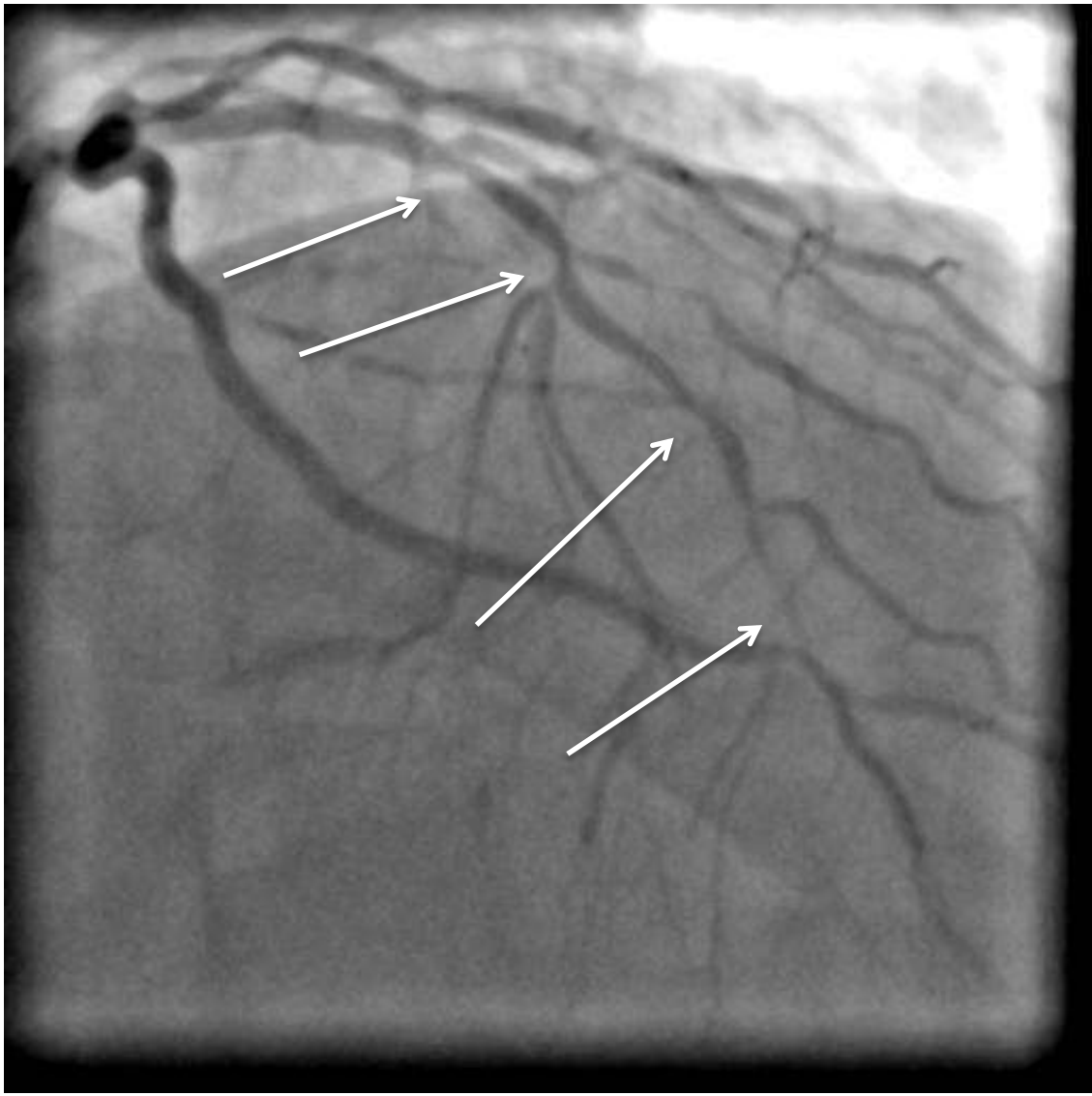


<u>Pression drops across the lesions:</u>

1. Increases with Longitudinal increase of the lesion (lesion length)
2. Increases with smaller lumen Area
3. Increases with Flow (which is not linear!)

FFR Guides You Where to Treat

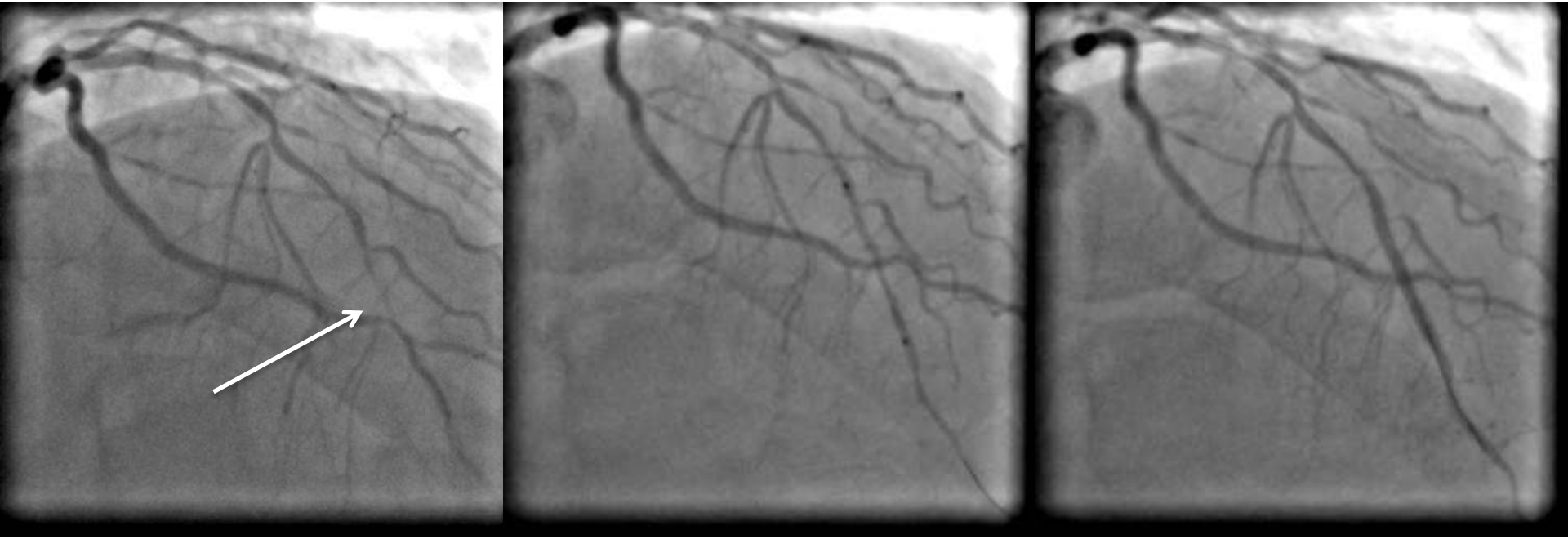
- 61-yo male
- HTN, dyslipidemia, prior MI
- Stable Angina (CCS III)
- SPECT w/ anterior wall ischemia
- Diffuse disease in the LAD



FFR Also Tells You Where to Treat

<u>Original Strategy</u>: stent the subocclusive distal LAD only

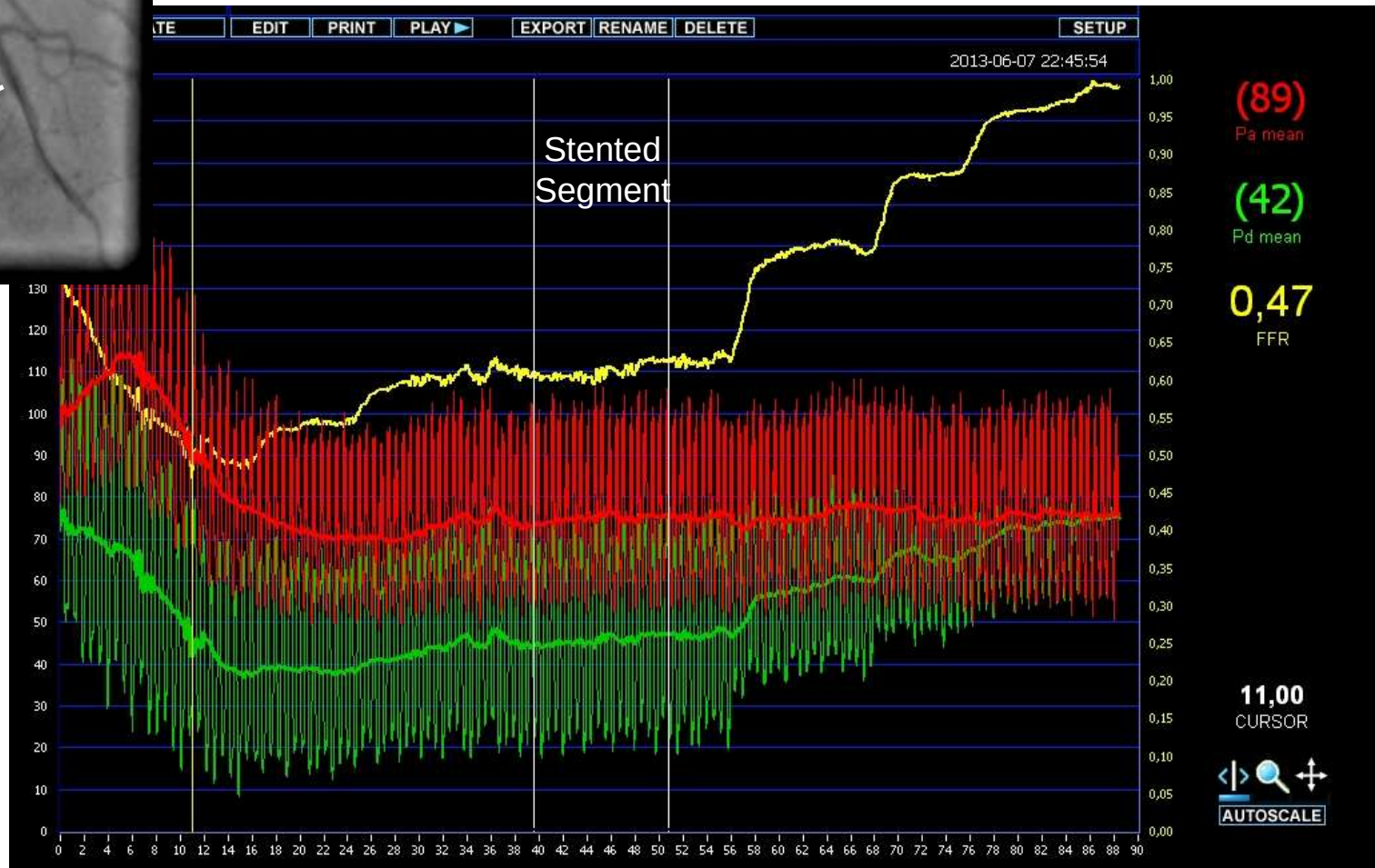
LAD Pre | 2.25/30 ZES Resolute | LAD After Stent



I was quite happy with the angiographic result, but…

FFR for Diffuse Disease Assessment

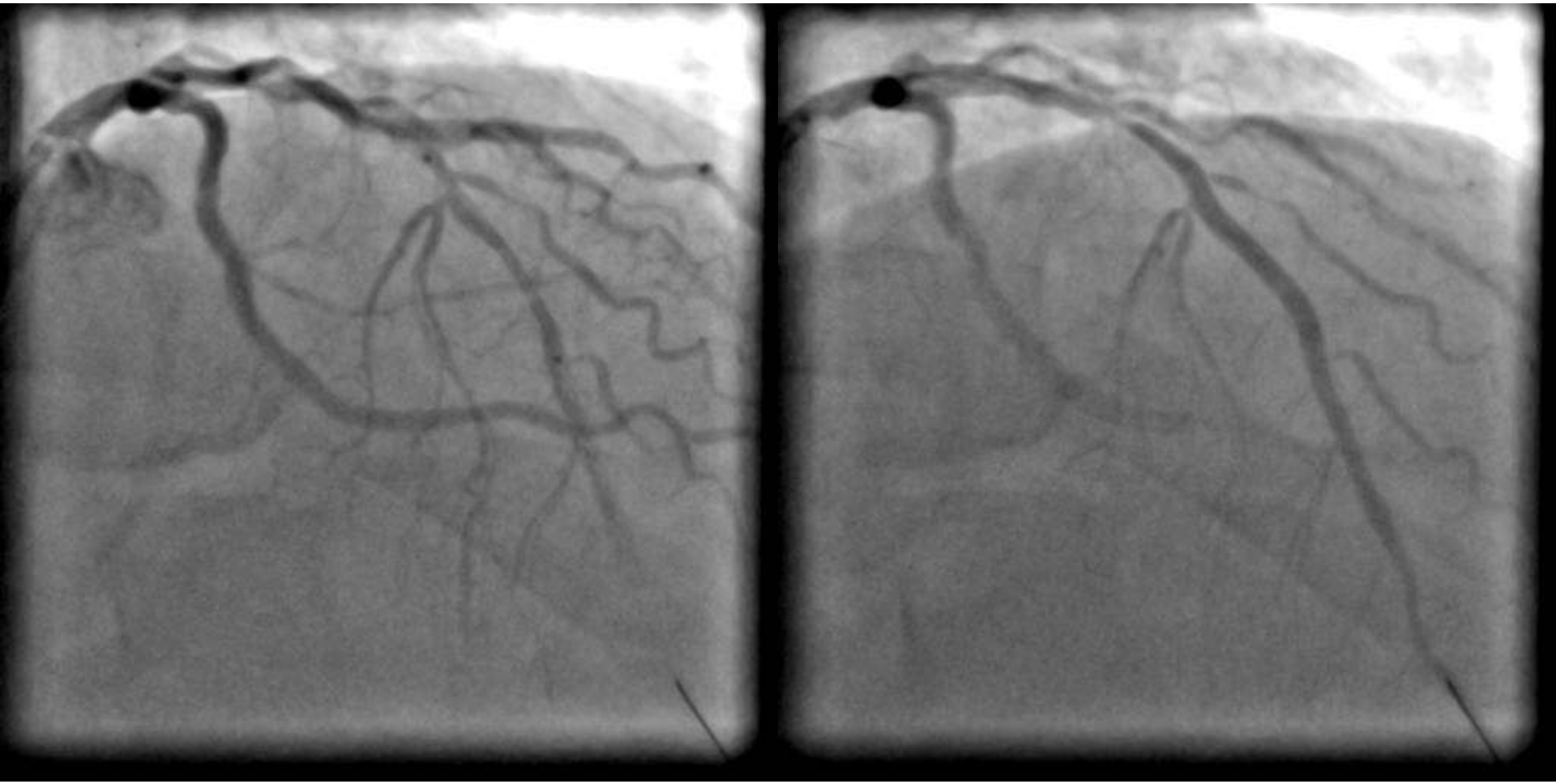
FFR After Distal LAD Stent Implantation



FFR for Diffuse Disease Assessment

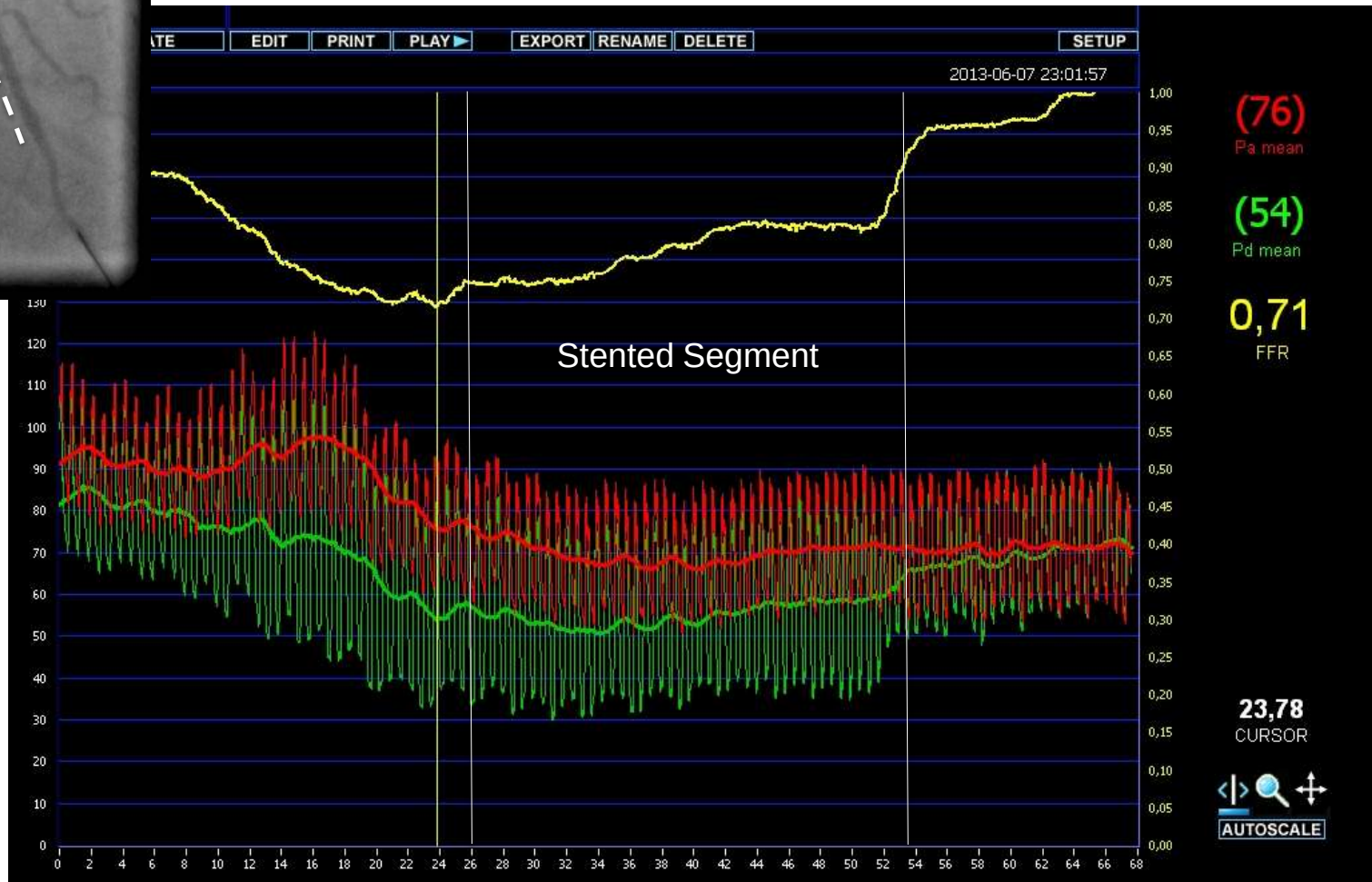
ZES Resolute 2.75/24 mm

Angio Control



FFR for Diffuse Disease Assessment

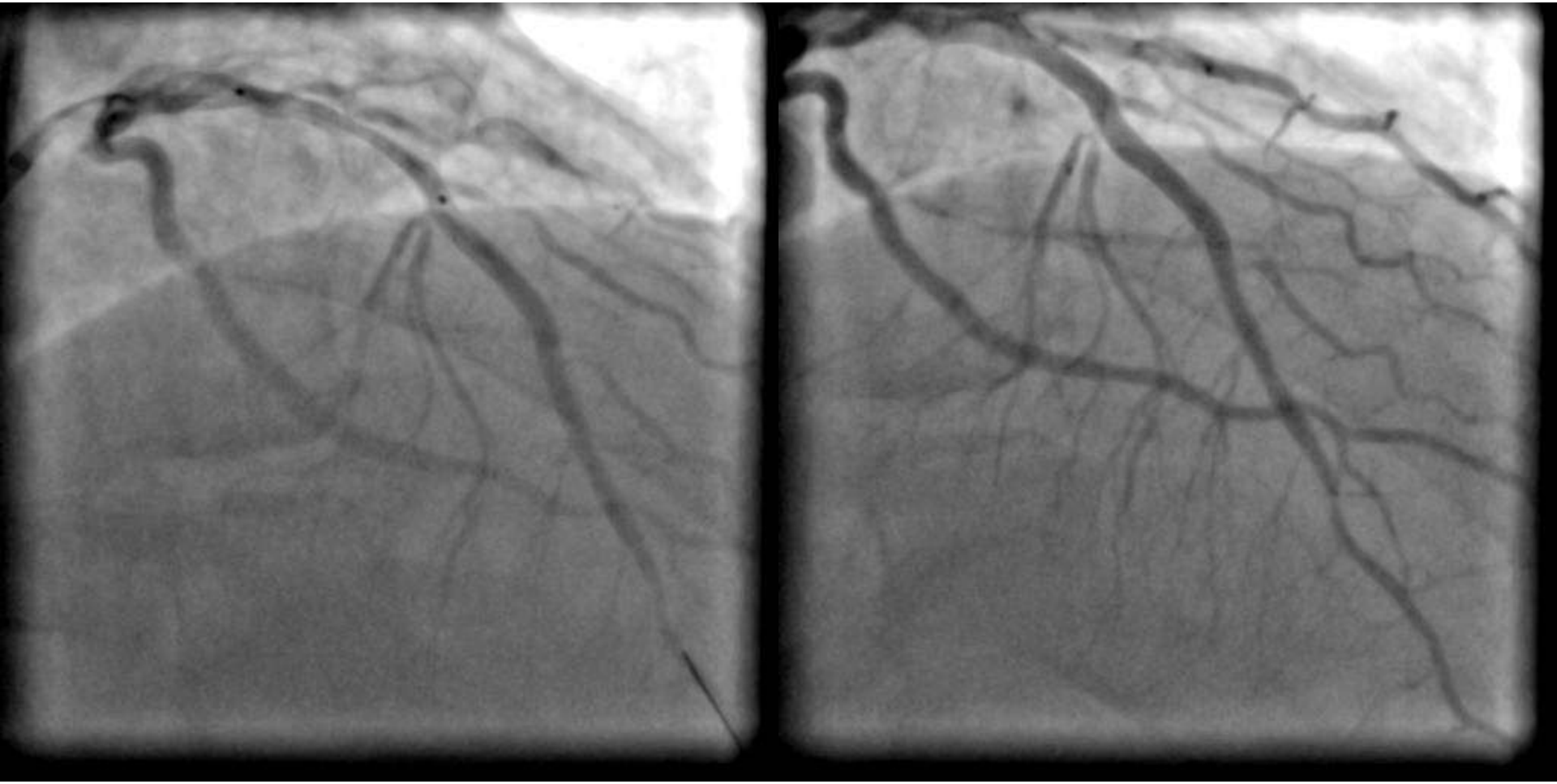
FFR After Mid LAD Stent Implantation



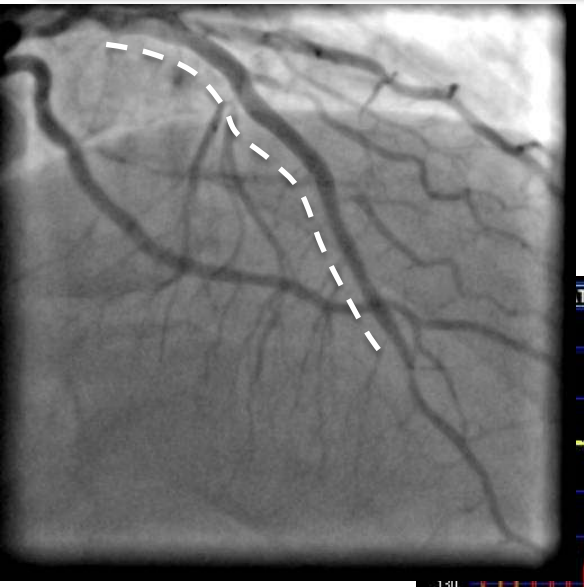
FFR for Diffuse Disease Assessment

ZES Resolute 3.0/24 mm

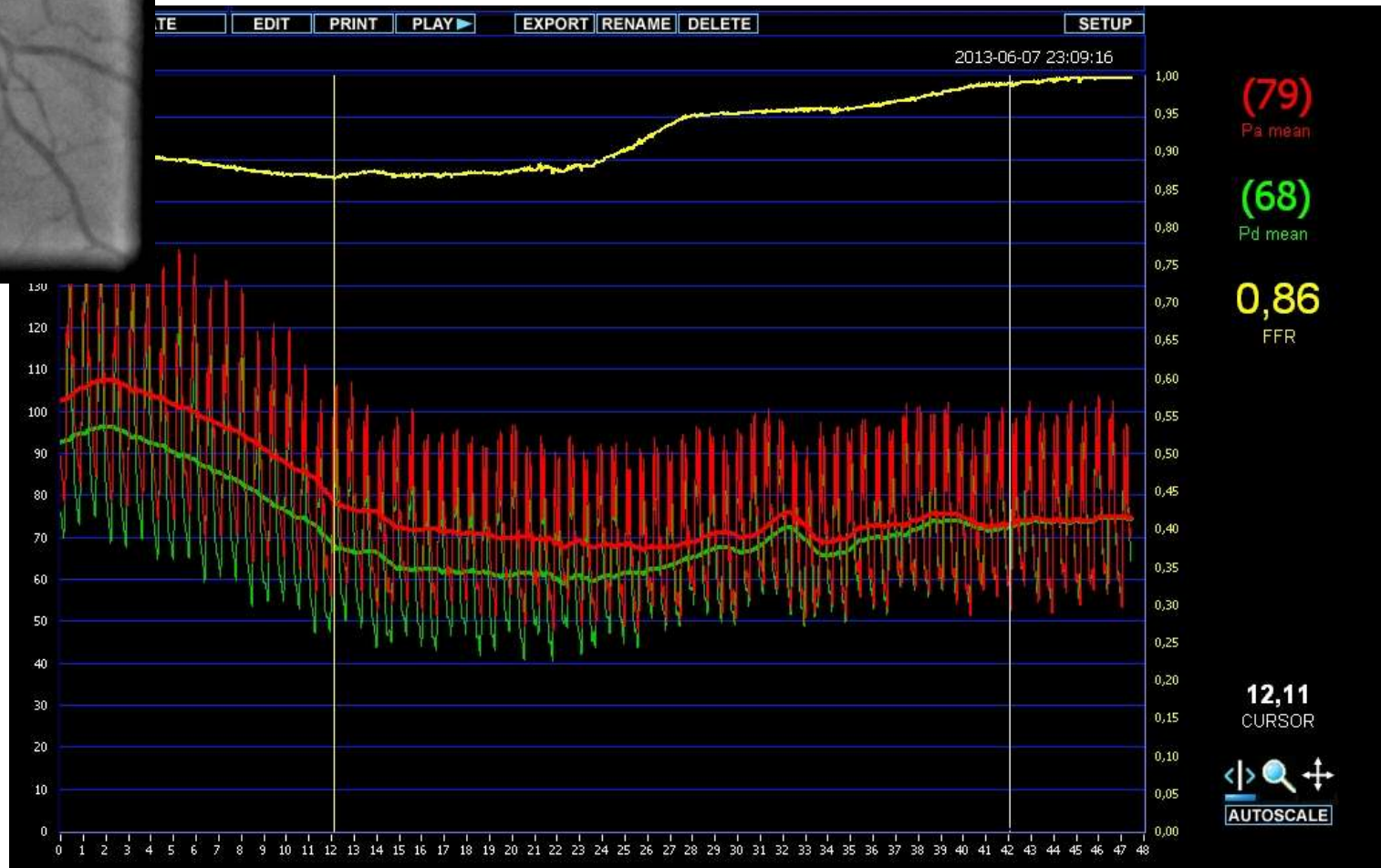
Angio Control



FFR for Diffuse Disease Assessment



FFR After Prox LAD Stent Implantation



2011 ACC/AHA/SCAI Guidelines for Percutaneous Coronary Intervention

5.4. Adjunctive Diagnostic Devices

5.4.1. FFR: Recommendation

Class IIa

1. **FFR is reasonable to assess angiographic intermediate coronary lesions (50% to 70% diameter stenosis) and can be useful for guiding revascularization decisions in patients with SIHD.[12,97,484–486] *(Level of Evidence: A)***

See Online Data Supplement 23 for additional data regarding FFR.

The limitations of coronary angiography for determination of lesion severity have been well described. Angiography

nism of stent thrombosis.[495] *(Level of Evidence: C)*

Class III: NO BENEFIT

1. **IVUS for routine lesion assessment is not recommended when revascularization with PCI or CABG is not being contemplated. *(Level of Evidence: C)***

IVUS provides a unique coronary artery assessment of lesion characteristics, minimal and maximal lumen diameters, cross-sectional area, and plaque area. Diagnostic uses for IVUS include the assessment of angiographic indeterminant coronary artery stenoses, determination of the mechanism of stent restenosis or thrombosis, and postcardiac transplantation surveillance of CAD.[488,490–492,499] For left main coronary artery stenoses, a minimal lumen diameter of <2.8 mm or a

European Heart Journal
doi:10.1093/eurheartj/ehq277

Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

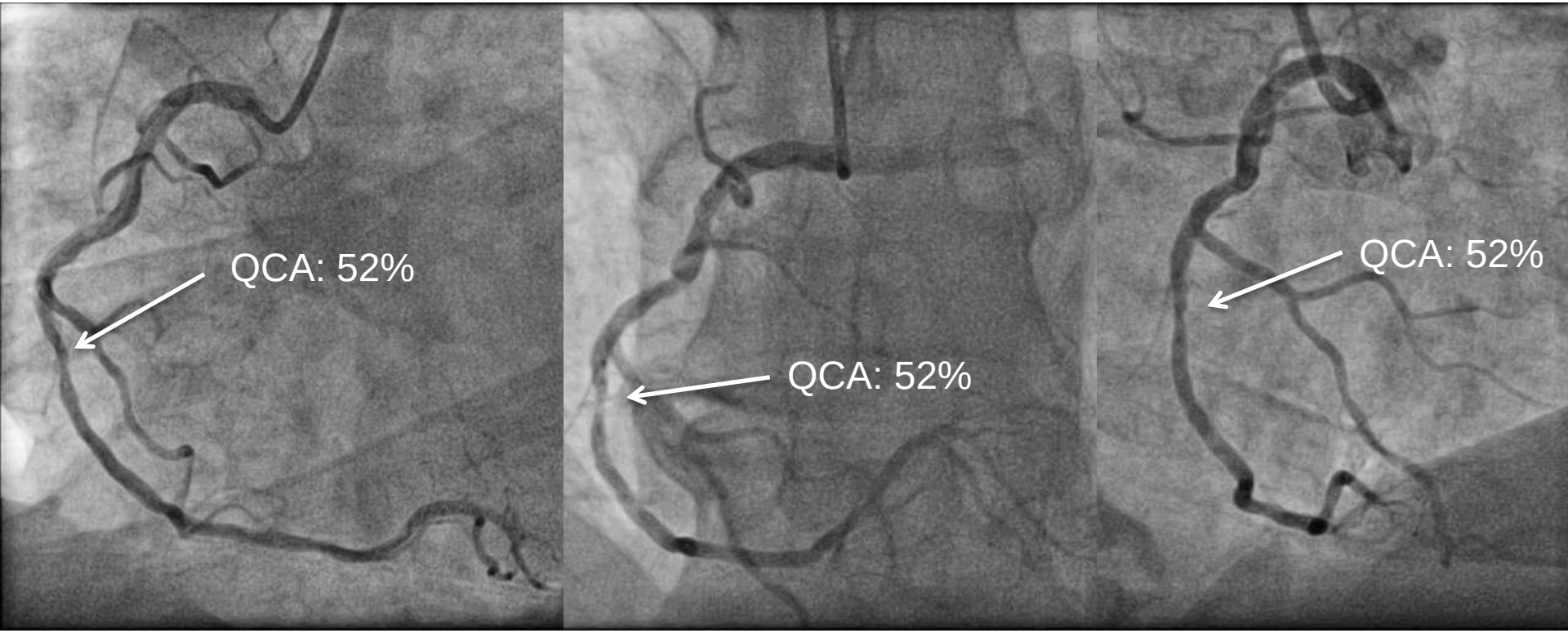
Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)†

Table 33 Recommendations for specific percutaneous coronary intervention devices and pharmacotherapy

	Class[a]	Level[b]	Ref.[c]
FFR-guided PCI is recommended for detection of ischaemia-related lesion(s) when objective evidence of vessel-related ischaemia is not available.	I	A	15, 28

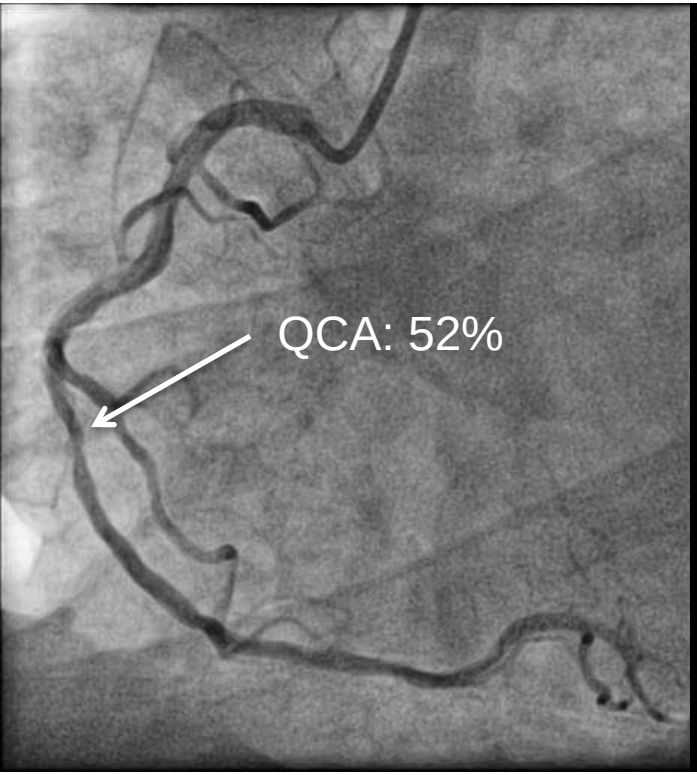
However, there Are Situations When Intravascular Imaging Is Preferred

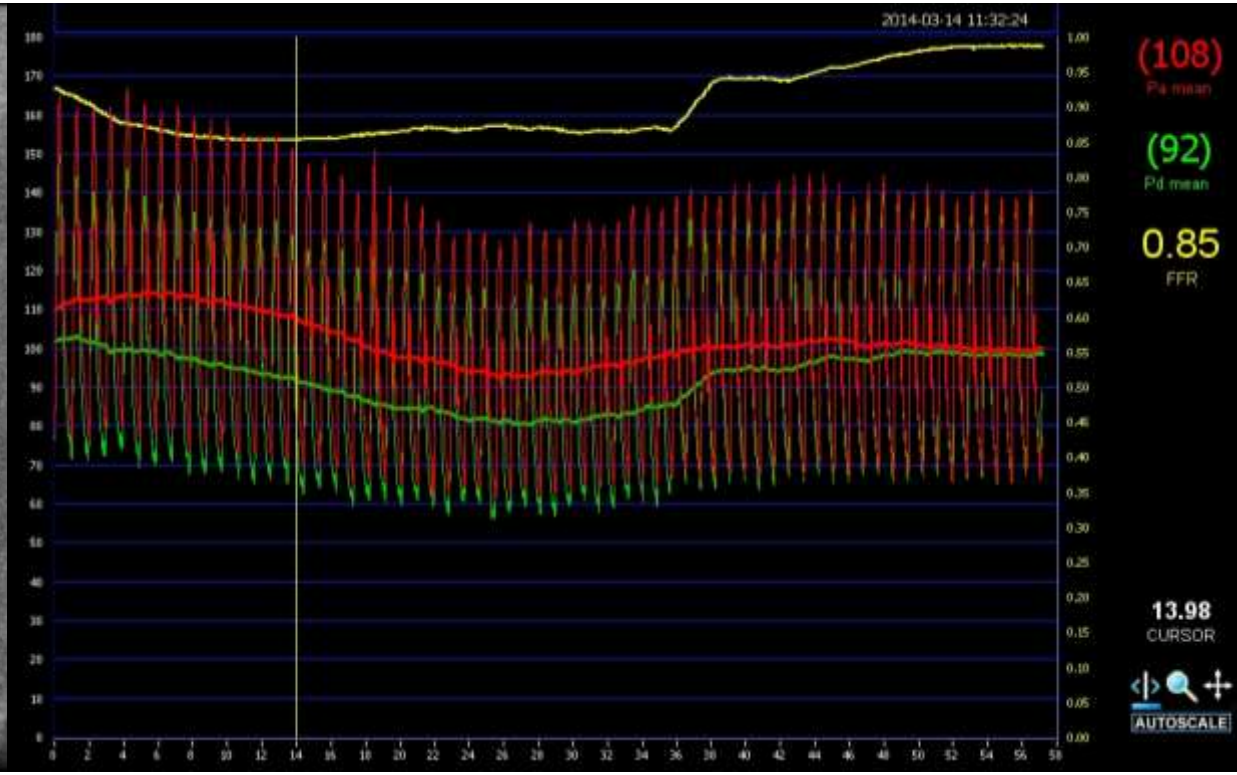
58-yo male, HTN, type II diabetic, active smoker
Inferior wall STEMI in the previous 4 days → tenecteplase w/ reperfusion criteria
Referred for coronary angiography



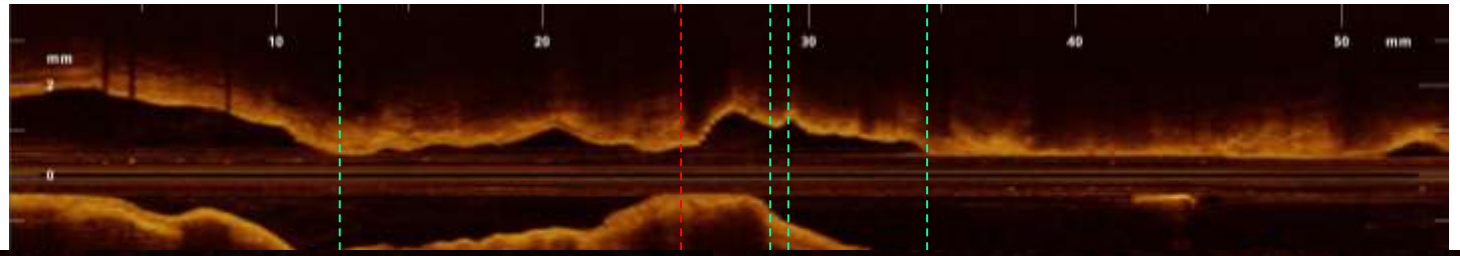
FFR has Limited Role in the Acute Phase of a Myocardial Infarction

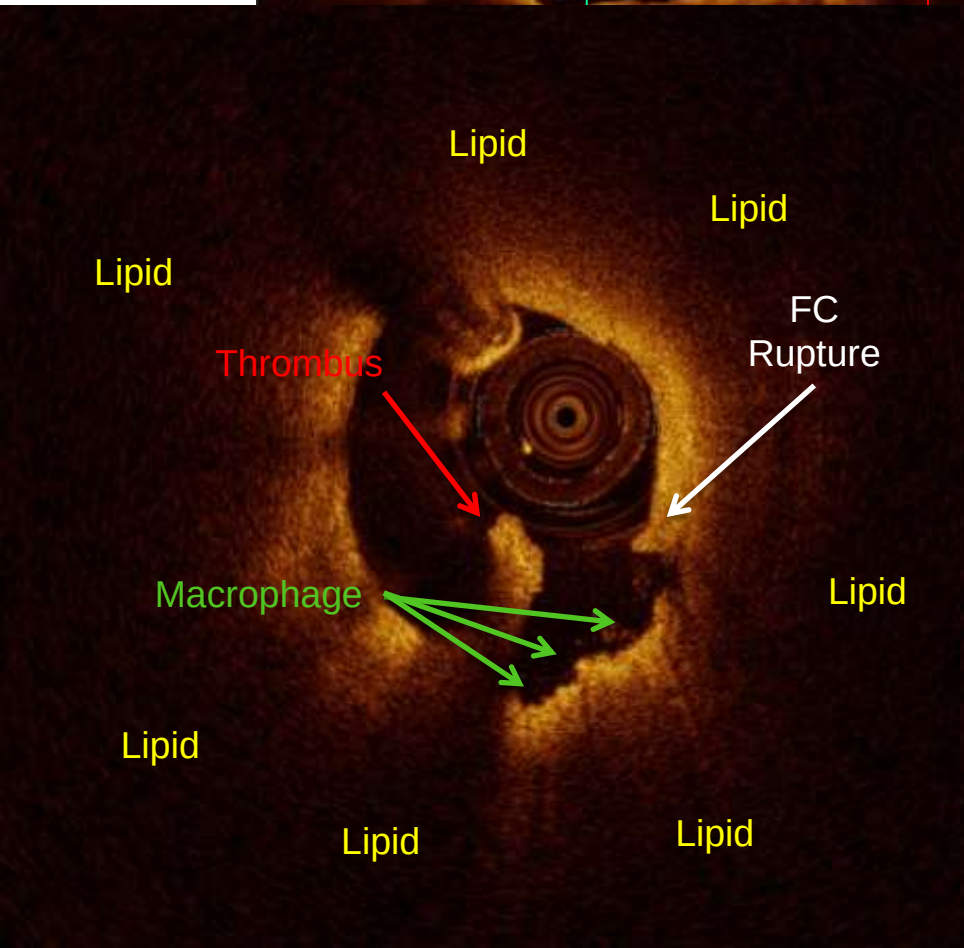
Transient edema and microvascular dysfunction in the acute phase of an MI (≤ 5 days) precludes maximal vasodilation of the infarcted territory, restricting coronary flow, and making the pressure drop across the stenosis during maximal hyperemia to be smaller than expected → underestimation of the FFR values

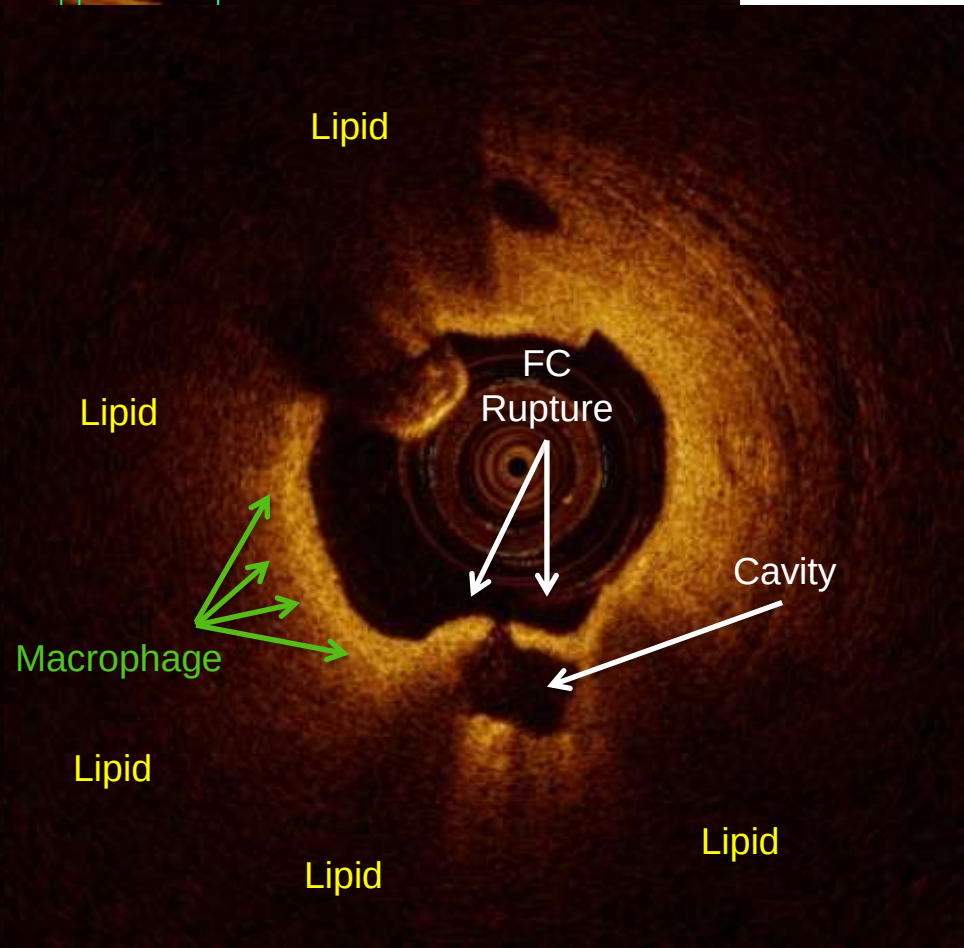




Defining the Culprit

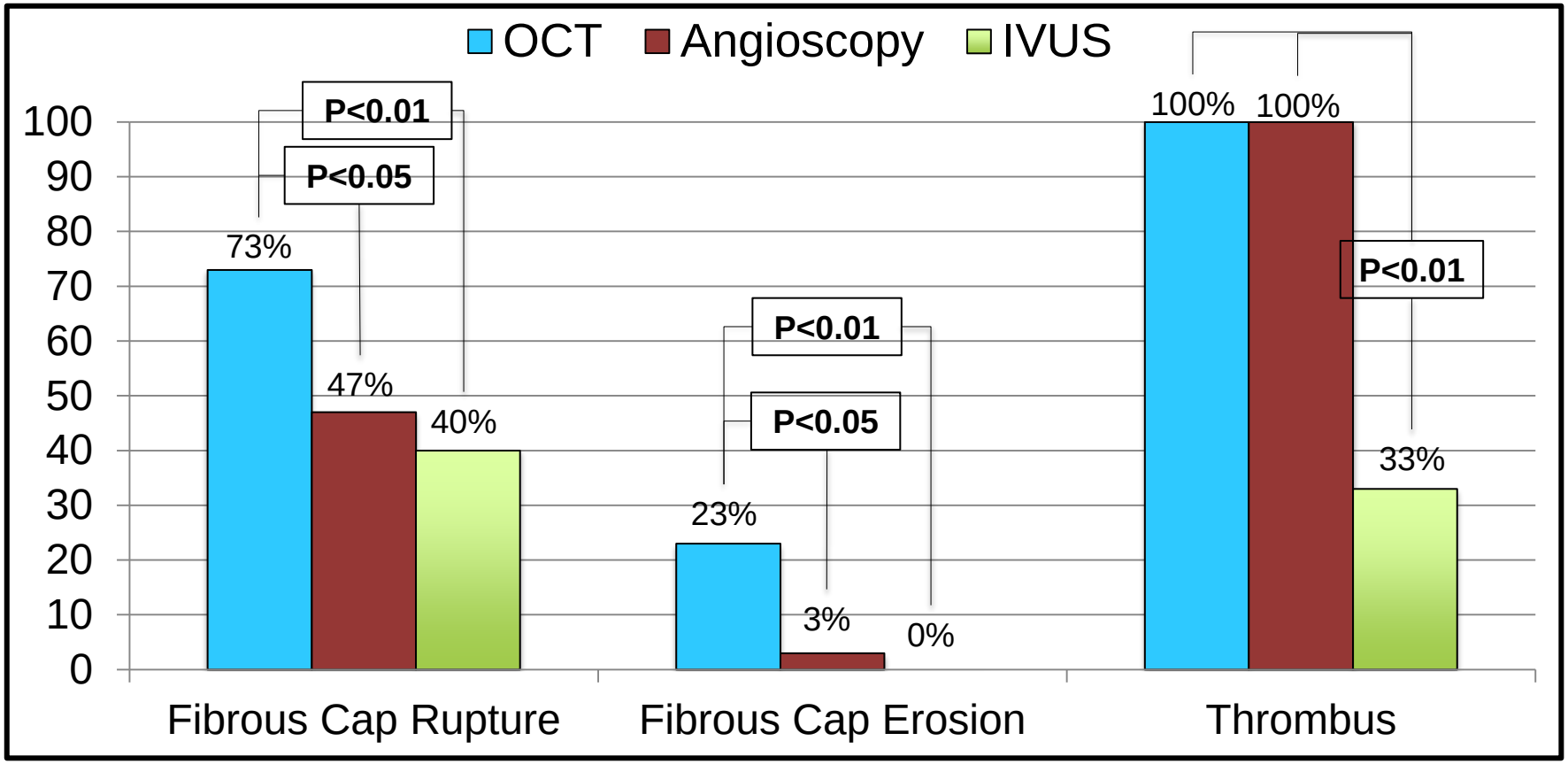






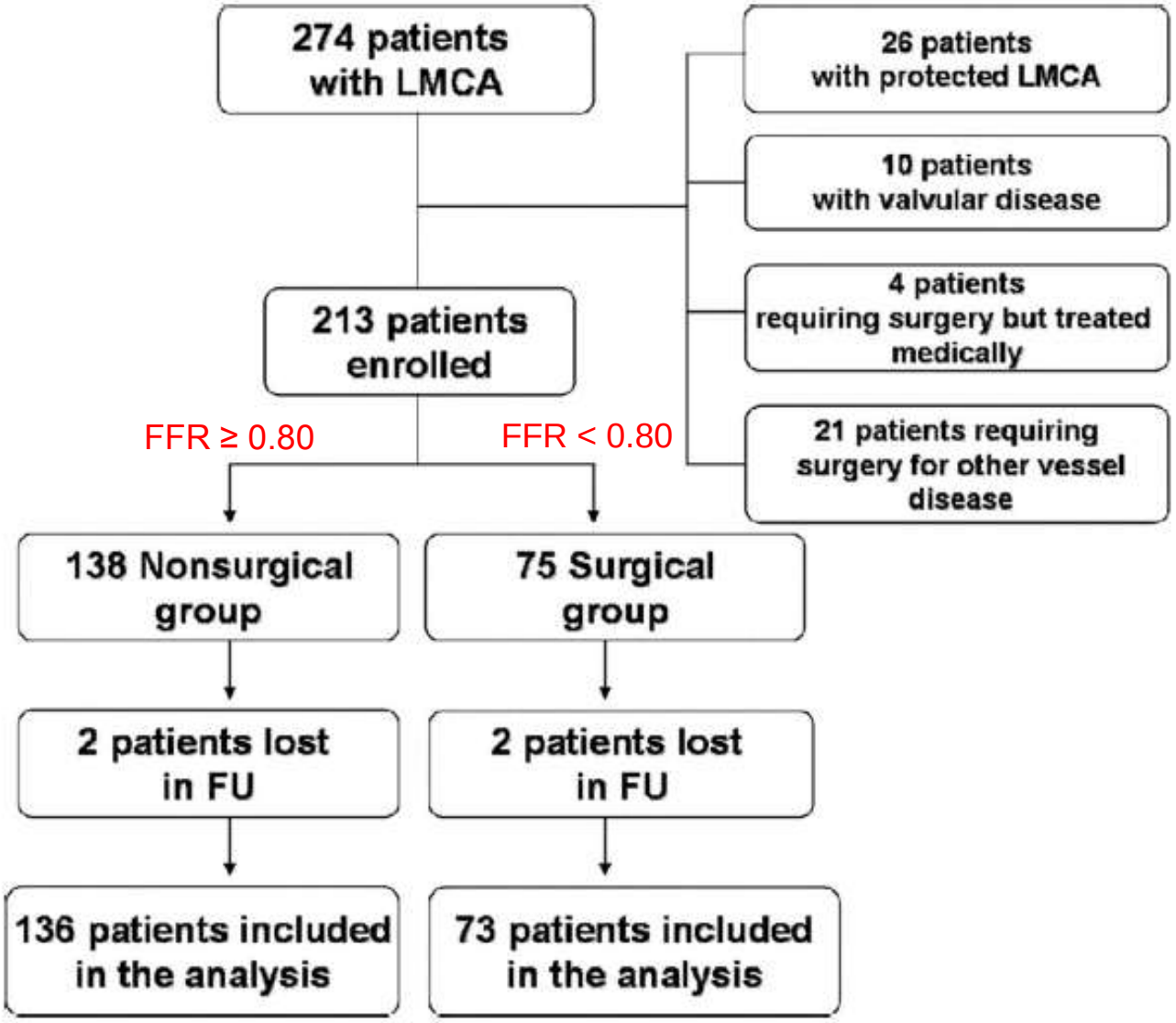
OCT has the Highest Sensitivity for Detection of Culprit Lesions

30 pts with AMI were assessed with OCT, angioscopy, and IVUS



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

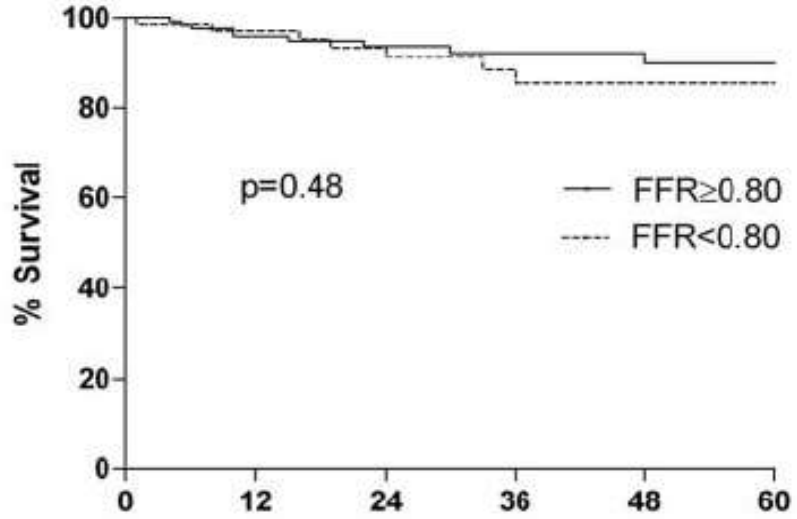
Intermediate LM Stenosis: FFR



Hamilos M, et al. Circulation 2009;120:1505-1512

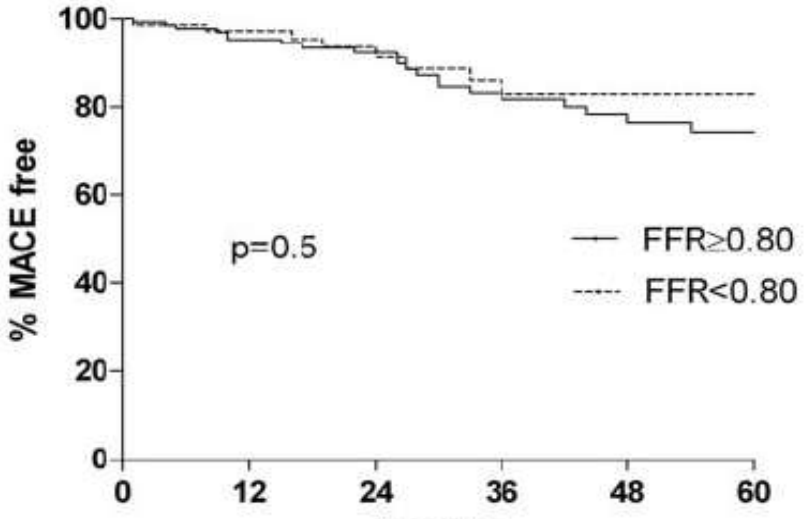
Intermediate LM Stenosis: FFR

Survival



No at risk						
FFR≥0.80	136	103	72	52	38	26
FFR<0.80	73	56	41	30	14	10

MACE



No at risk						
FFR≥0.80	136	106	77	57	42	30
FFR<0.80	73	56	40	29	15	10

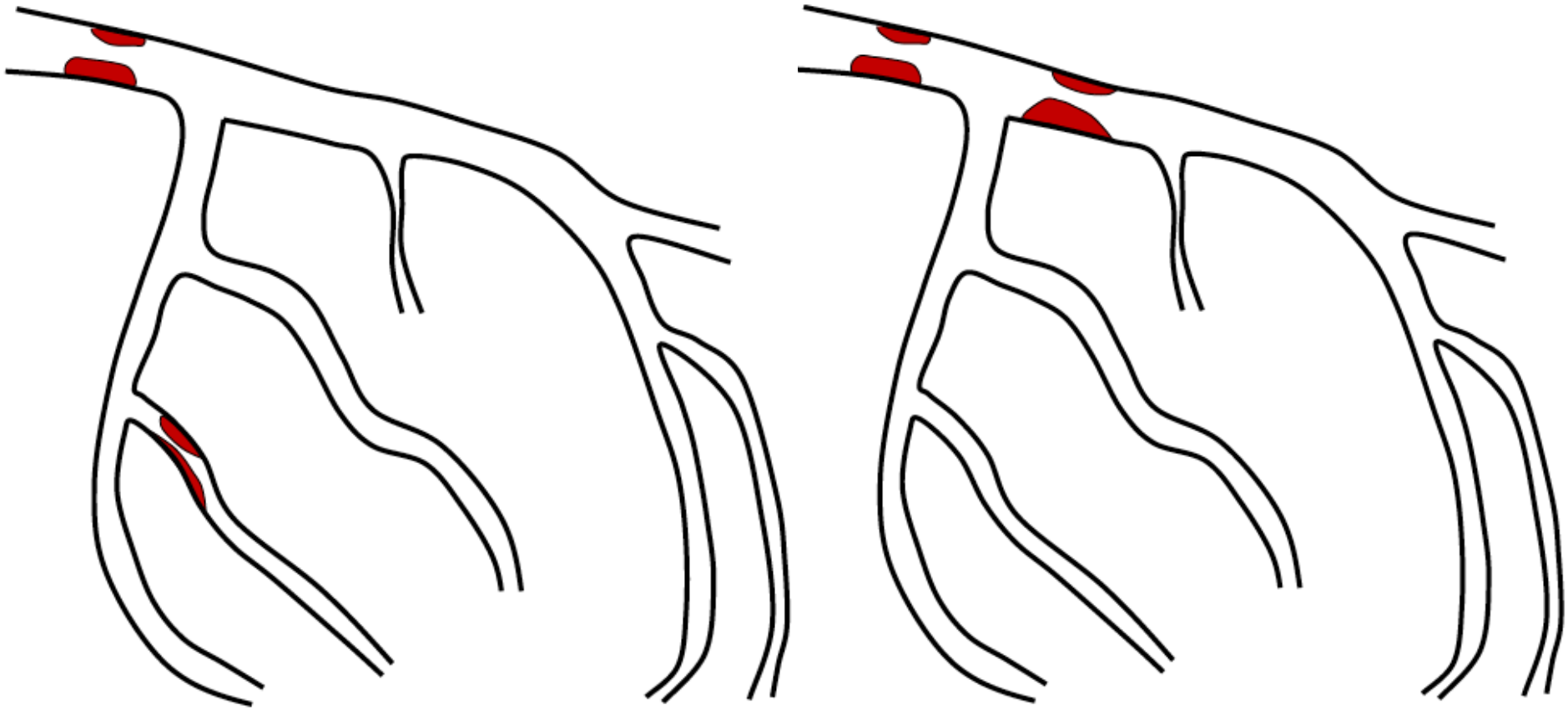
Hamilos M, et al. Circulation 2009;120:1505-1512

Intermediate LM Stenosis: FFR

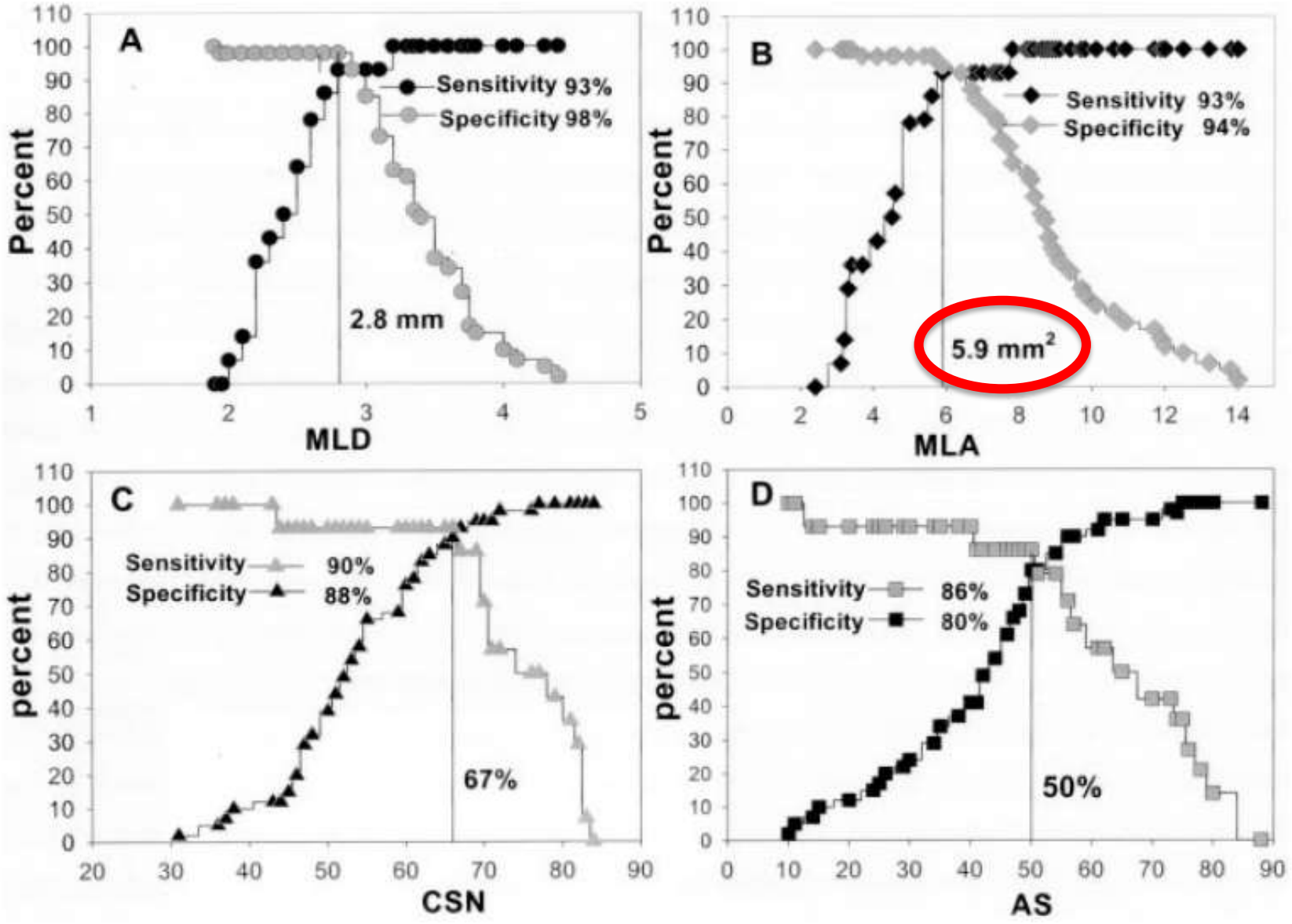
LM lesion rarely appear isolated (6-9%)

In the presence of a downstream stenosis, the FFR value across a LM lesion can be underestimated, depending on:

- *The severity of the distal stenosis*
- *Mass of myocardium at risk*

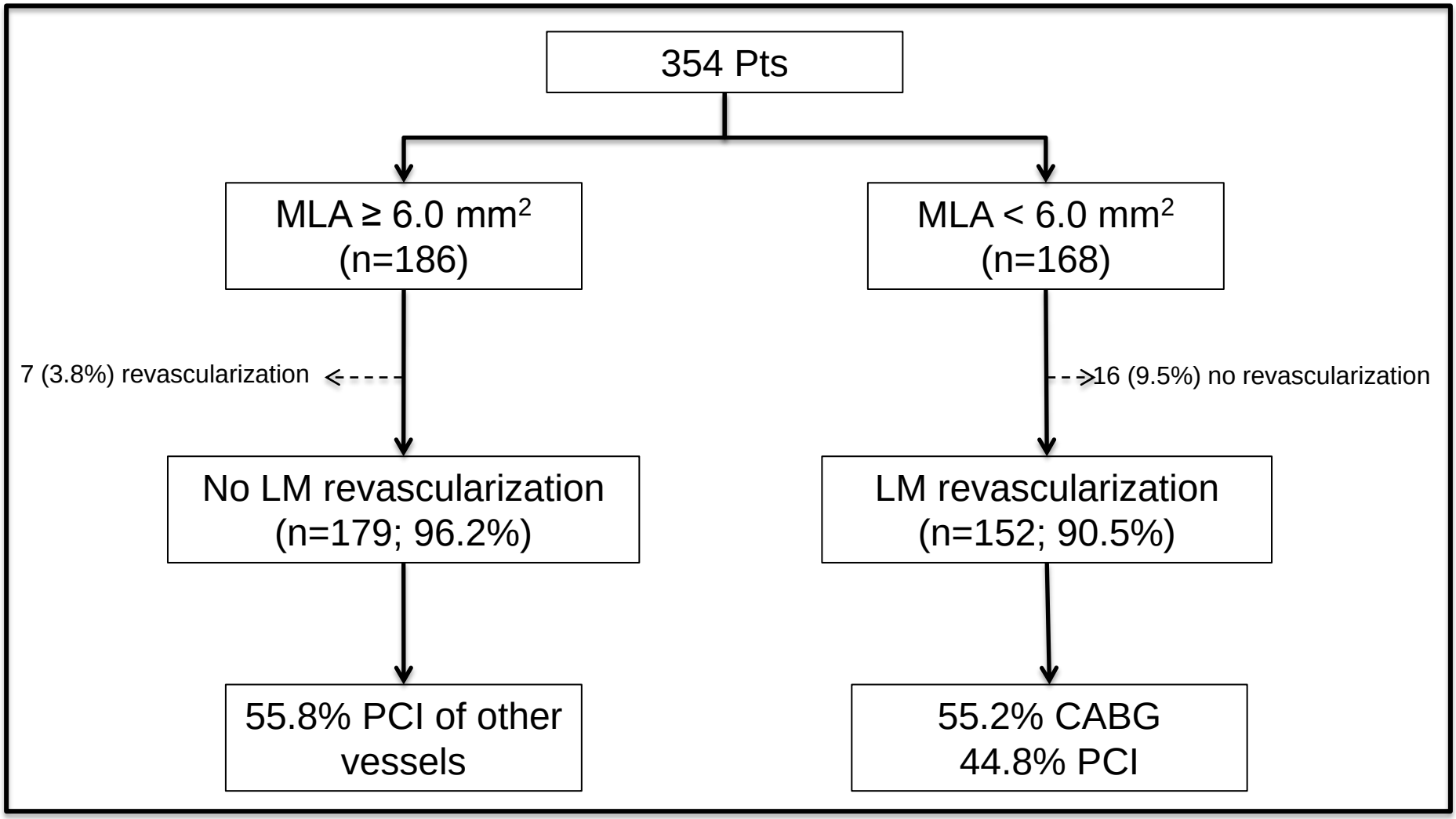


IVUS Determinants of LM FFR < 0.75



Jasti V, et al. Circulation 2004;110:2831-2836

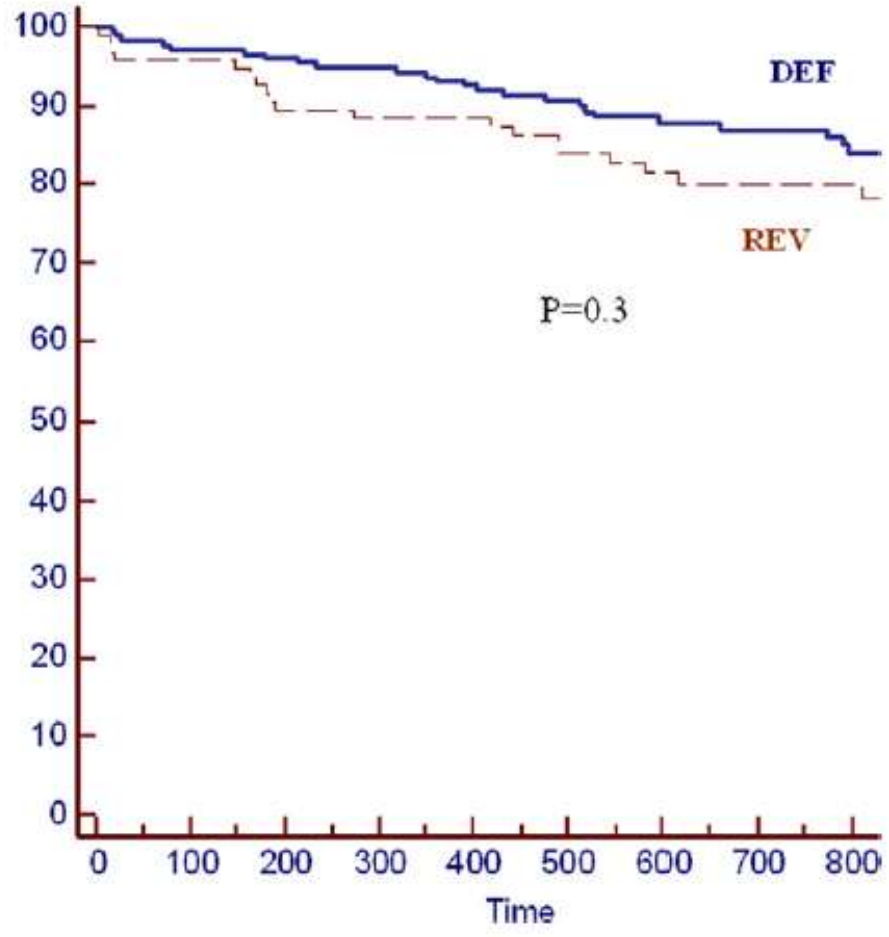
IVUS Criteria for Revascularization of Intermediate LM Stenosis – LITRO Study



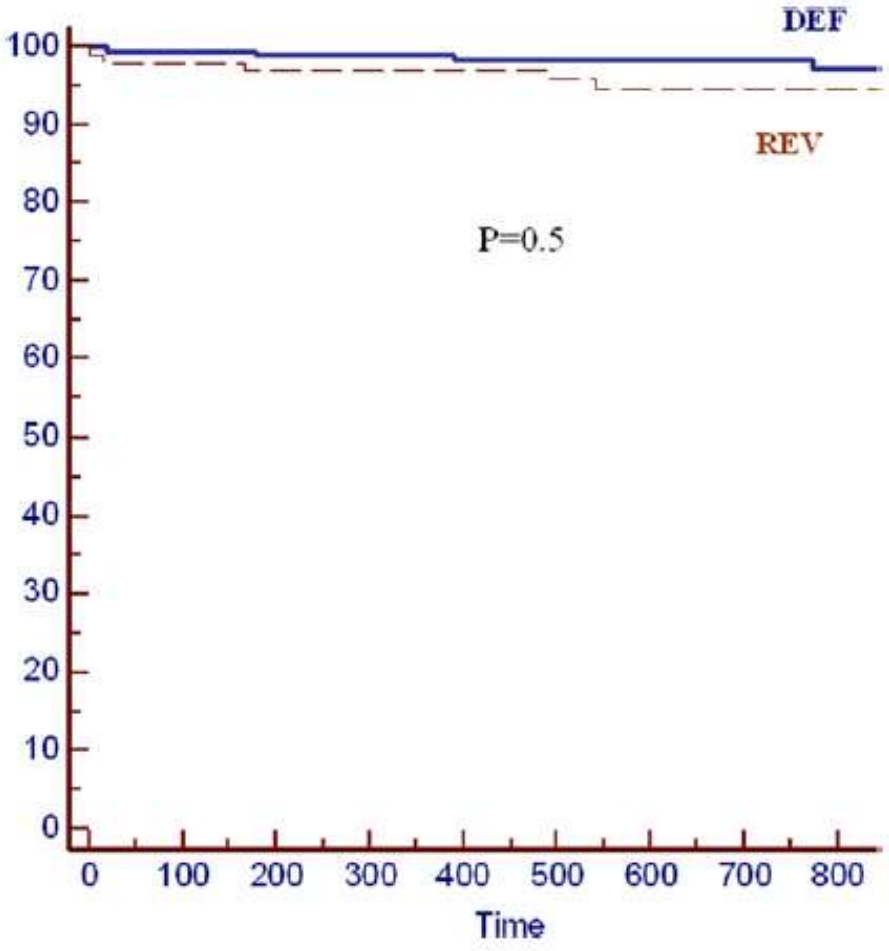
De La Torre Hernandez et al. J Am Coll Cardiol 2011;58:351-358

IVUS Criteria for Revascularization of Intermediate LM Stenosis – LITRO Study

Survival-Free of Death, MI, and Any Revascularization



Survival-Free of Cardiac Death



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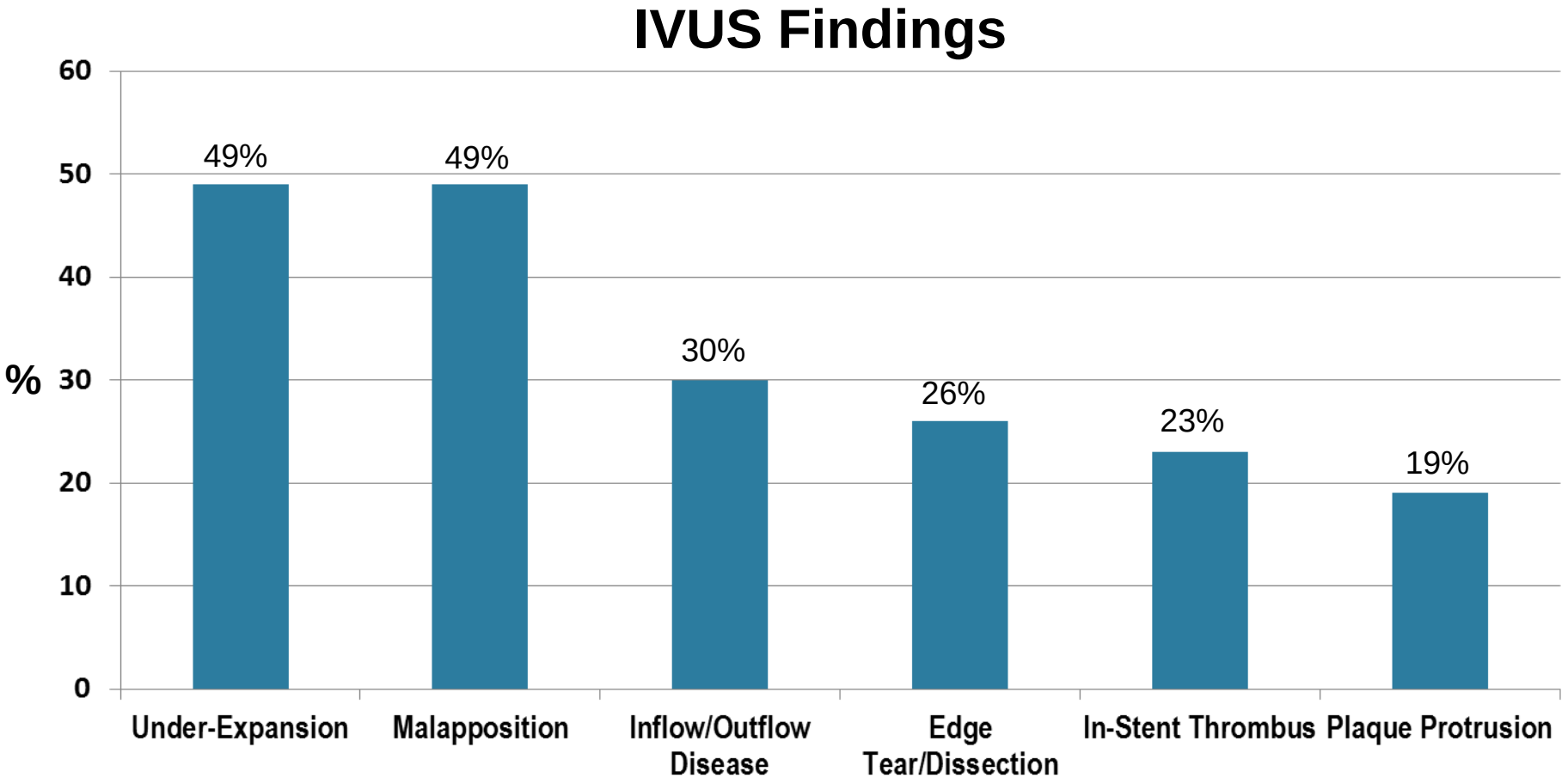
1. To define which lesion to treat
   - Physiology vs. Imaging
   - Defining the culprit
2. **To Guide/Optimize the PCI**
   - Pre-PCI
   - Post-PCI
3. To understand the mechanisms of stent failure

Predictors and Outcomes of ST

– An IVUS Registry –

53 Pts with Stent Thrombosis 132 ± 125 h following stent deployment under IVUS guidance

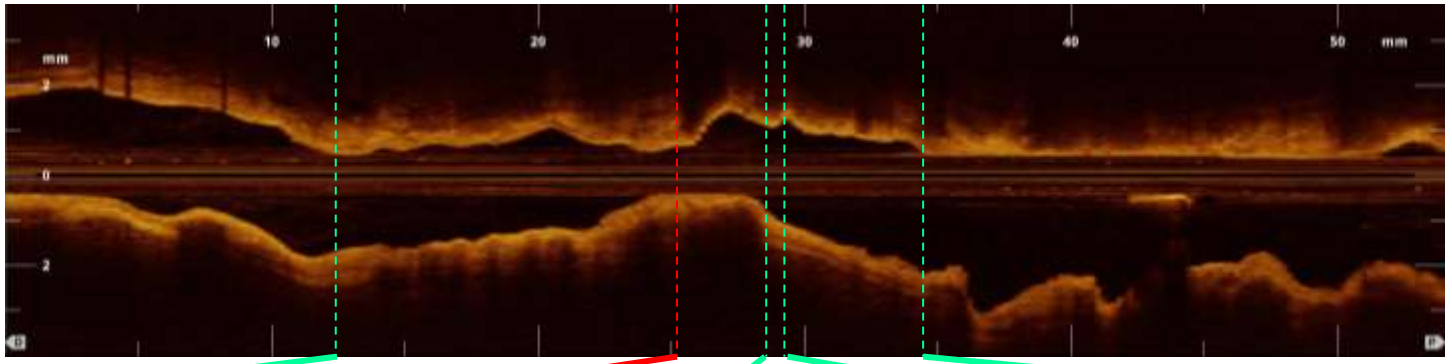


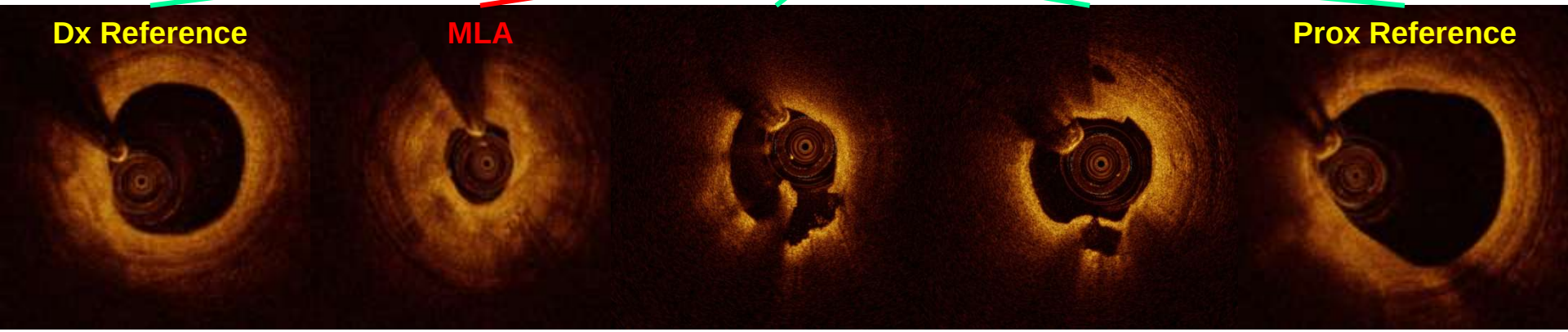
94% of the pts had at least 1 of these findings

Uren NG et al. Eur Heart J 2002;23:124-132

Use of Intravascular Imaging Pre-PCI

- Accurately measure vessel and lumen size to maximize stent dimensions.
- Identify proximal and distal reference segment landing zones and accurately select stent length.



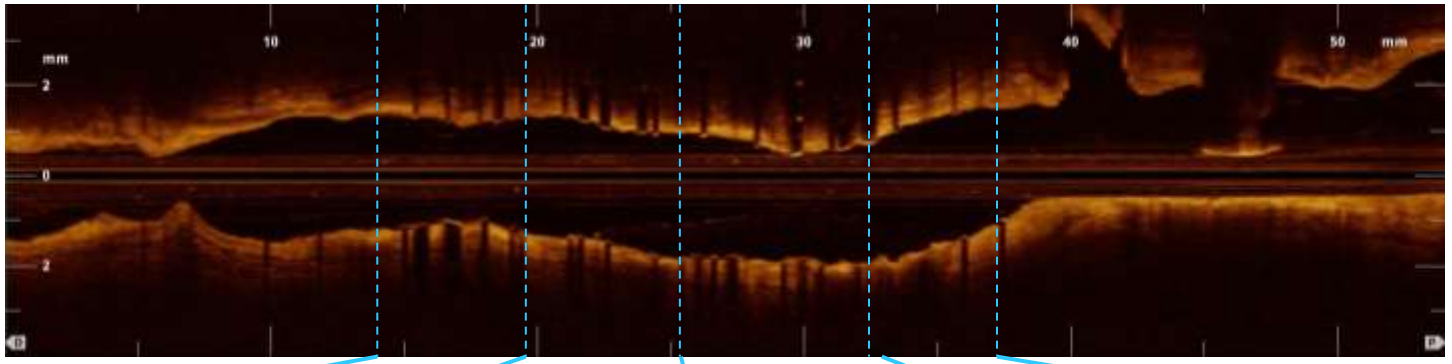


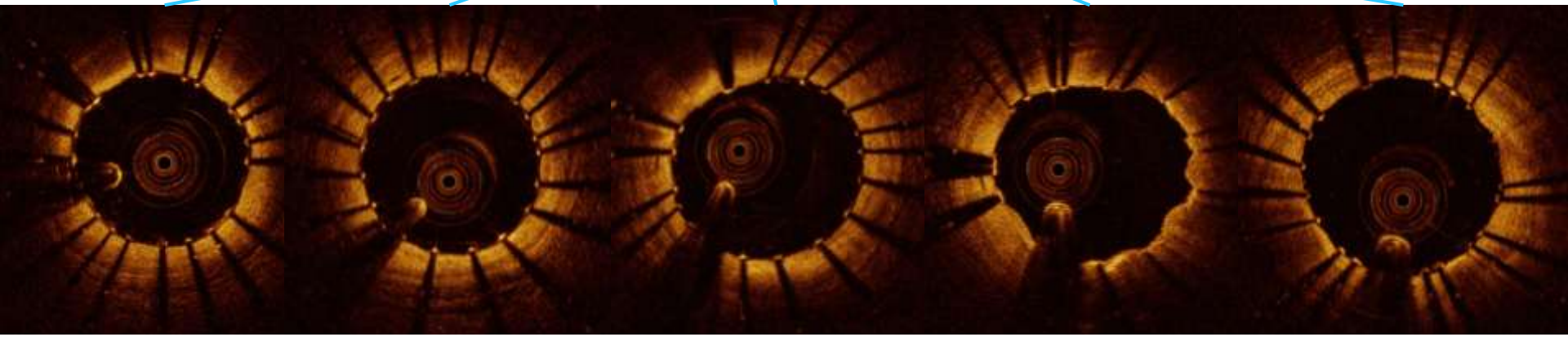
LA: 3.96 mm^2	LA: 1.04 mm^2	LA: 2.52 mm^2	LA: 2.73 mm^2	LA: 6.06 mm^2
Max. Diam: 2.68 mm	Max. Diam: 1.26 mm	Max. Diam: 2.12 mm	Max. Diam: 2.07 mm	Max. Diam: 2.96 mm

Lesion Length: 22.5 mm

Use of Intravascular Imaging Post-PCI

- Maximize stent CSA relative to the vessel references.
- Full lesion coverage.
- Recognize/diagnose/treat complications

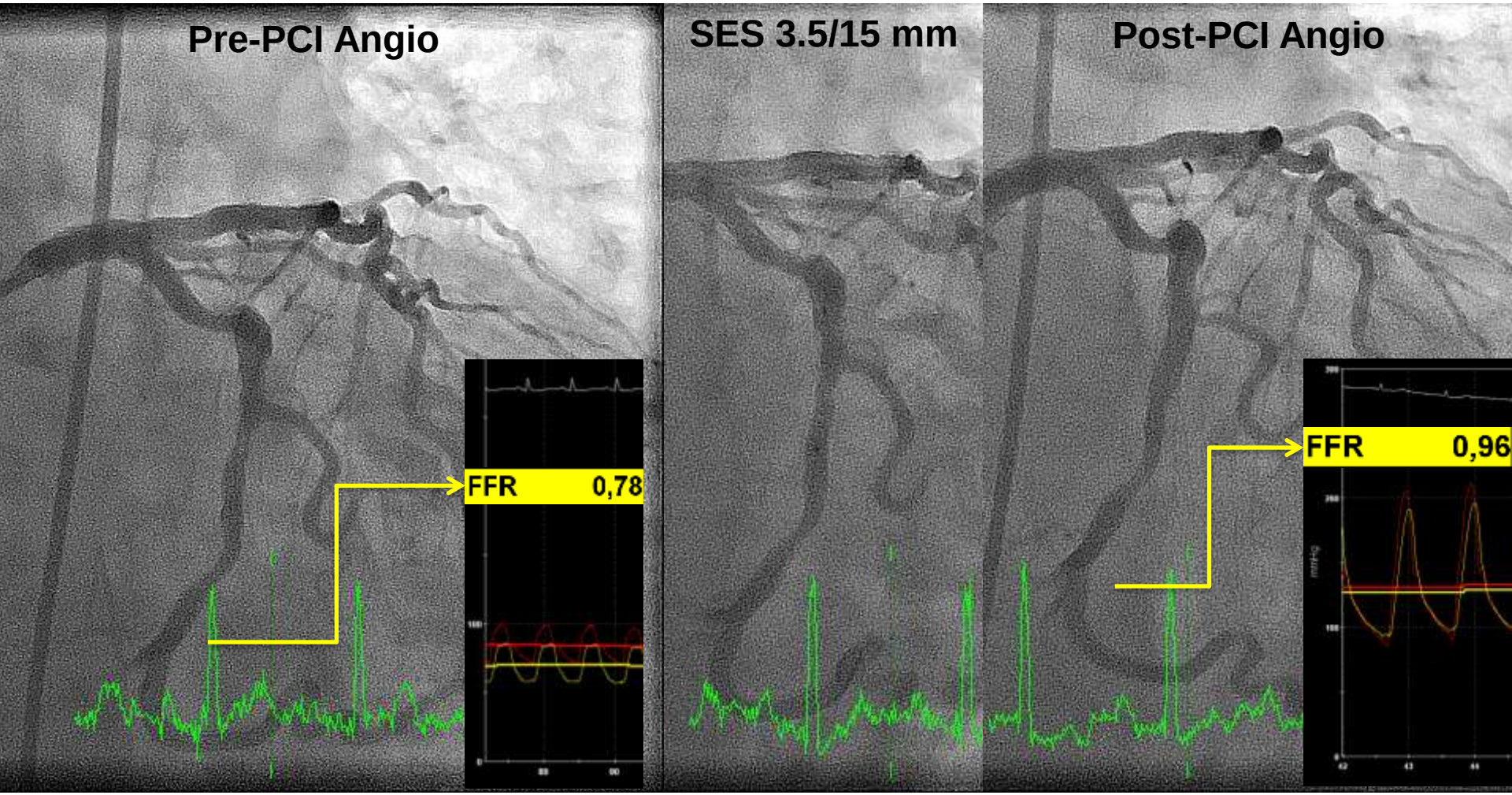




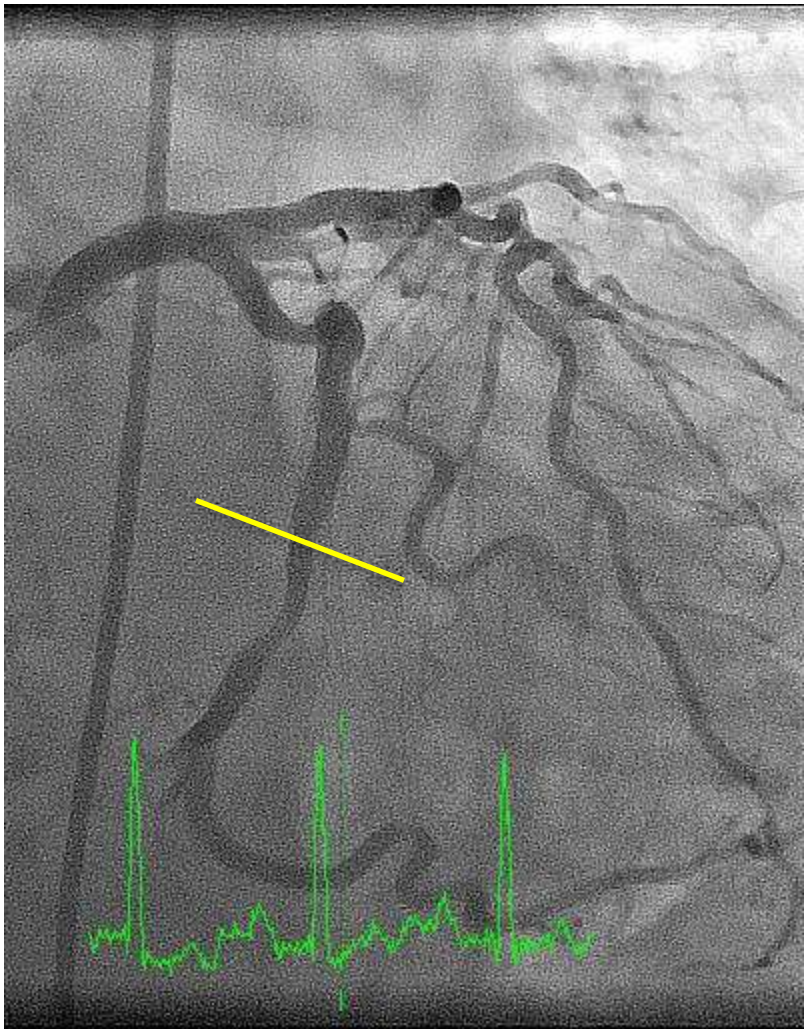
LA: 4.93 mm^2	**LA: 5.38 mm^2**	**LA: 5.78 mm^2**	**LA: 6.06 mm^2**	**LA: 6.42 mm^2**
Max. Diam: 2.57 mm	**Max. Diam: 2.64 mm**	**Max. Diam: 2.83 mm**	**Max. Diam: 2.98 mm**	**Max. Diam: 2.91 mm**

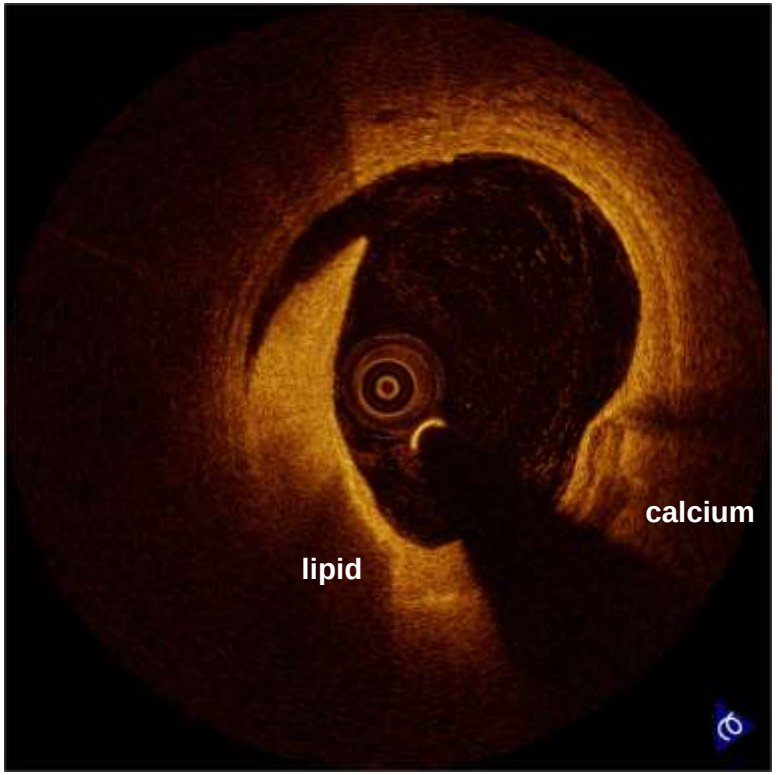
Use of Intravascular Imaging Post-PCI

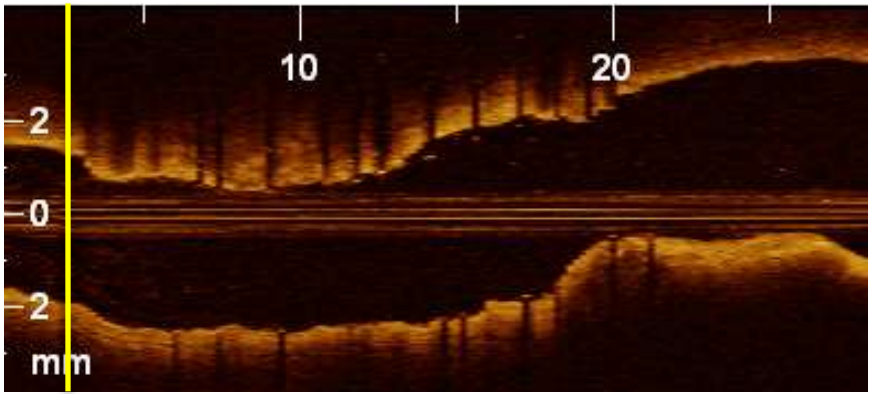
61 Year-old male, HTN, smoker, previous PCI. Presenting with stable angina (CCS II)



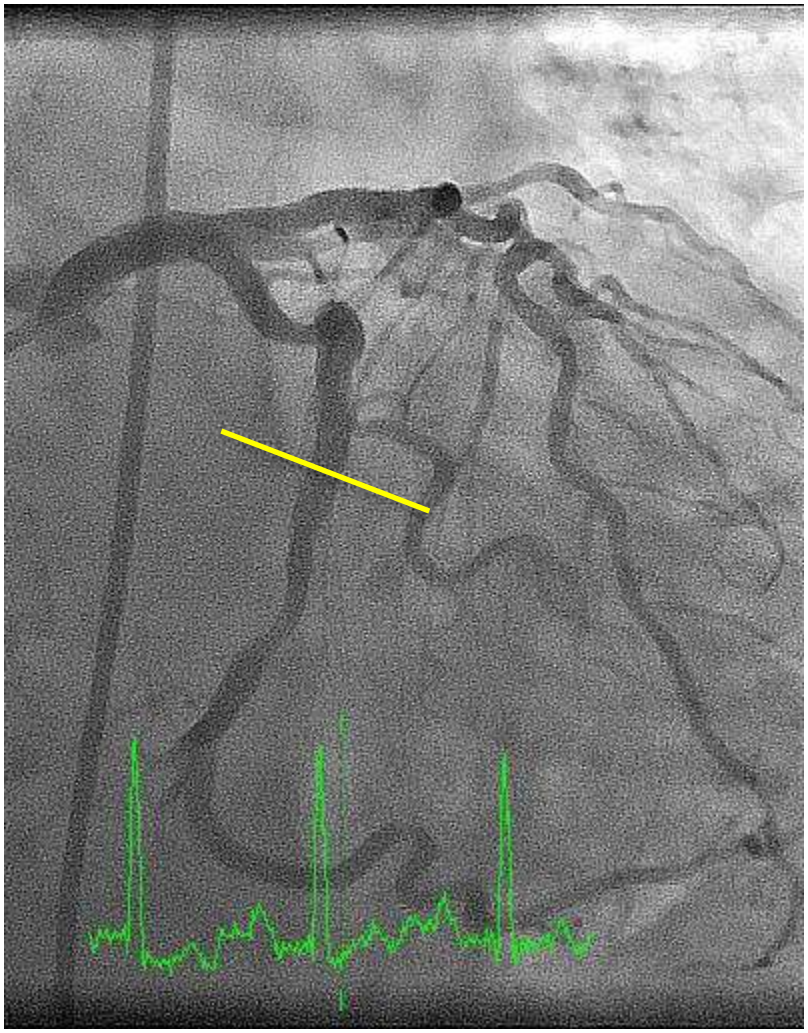
Acceptable Angiographic Result, Non-Ischemic FFR, but …

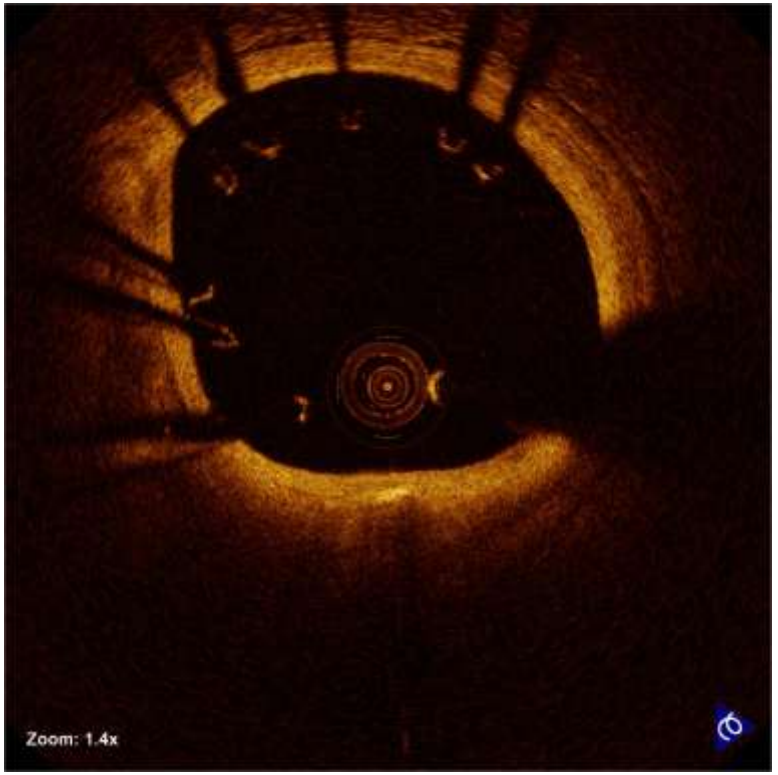


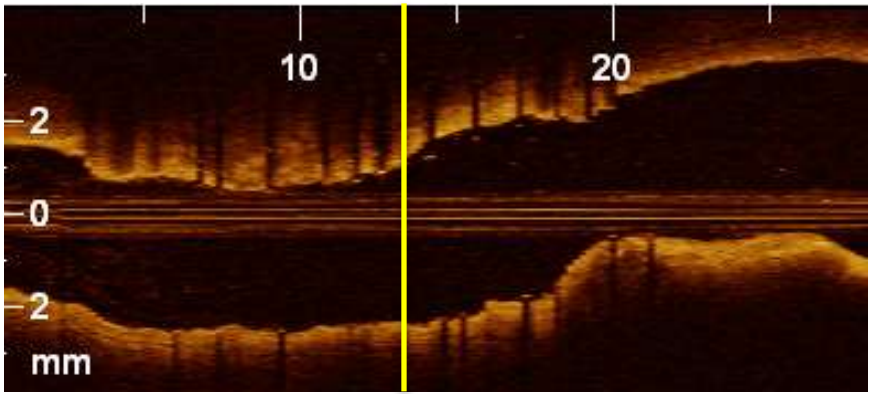




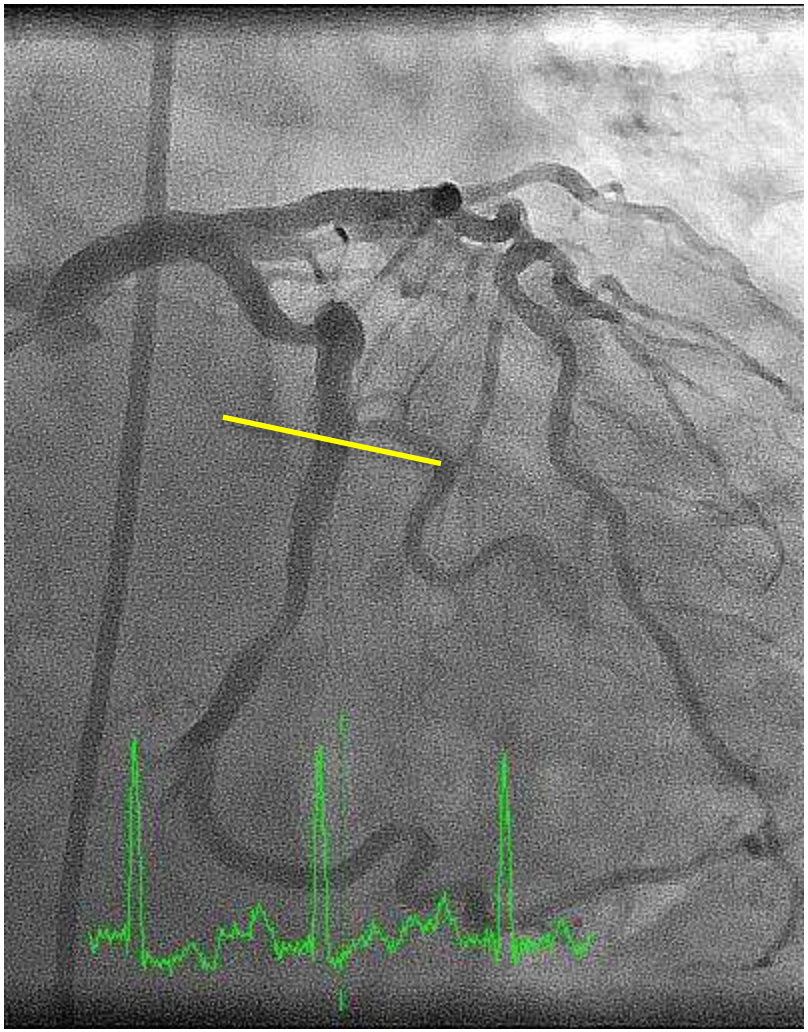
Acceptable Angiographic Result, Non-Ischemic FFR, but …

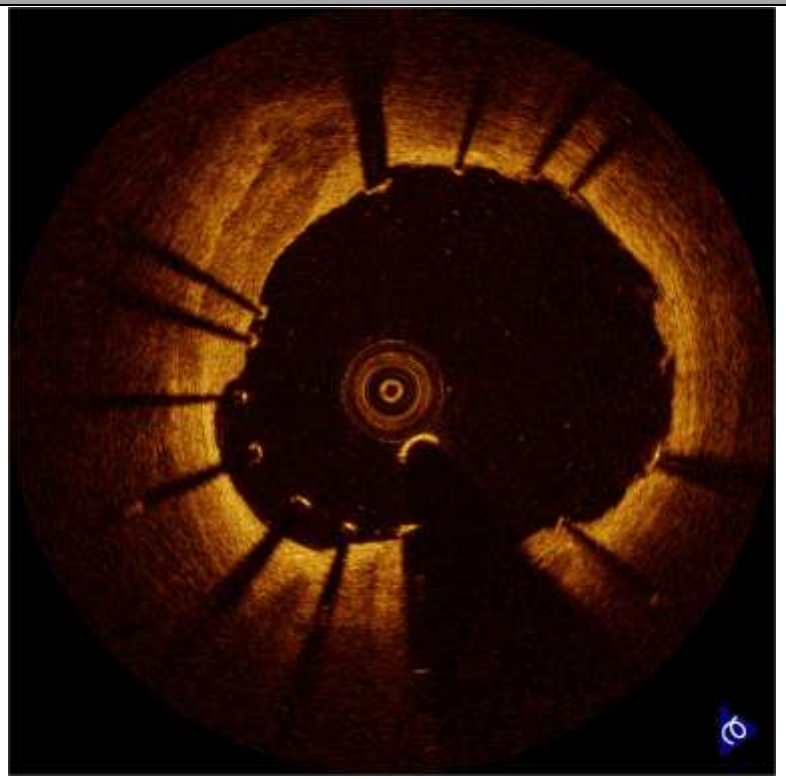


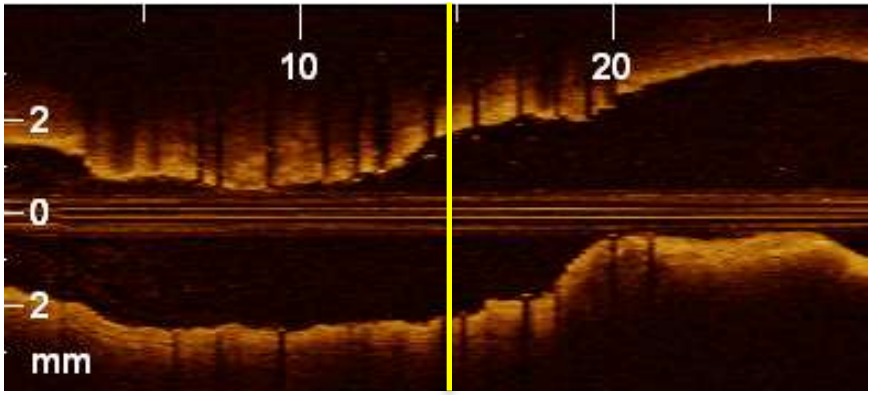




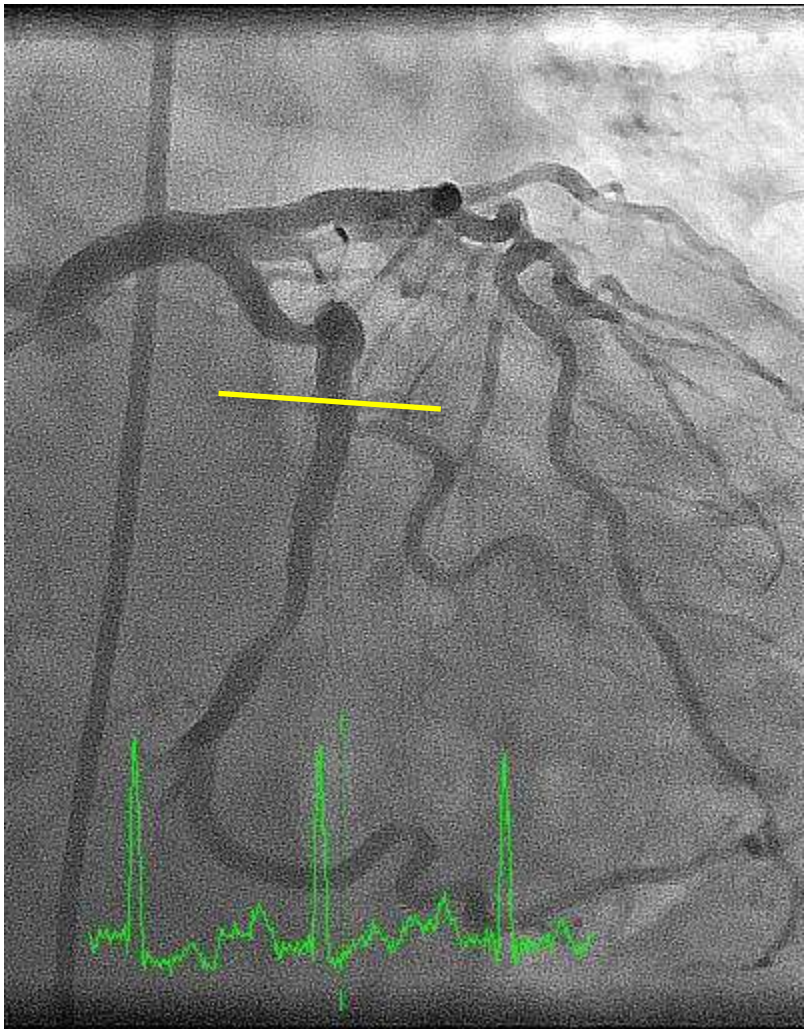
Acceptable Angiographic Result, Non-Ischemic FFR, but …

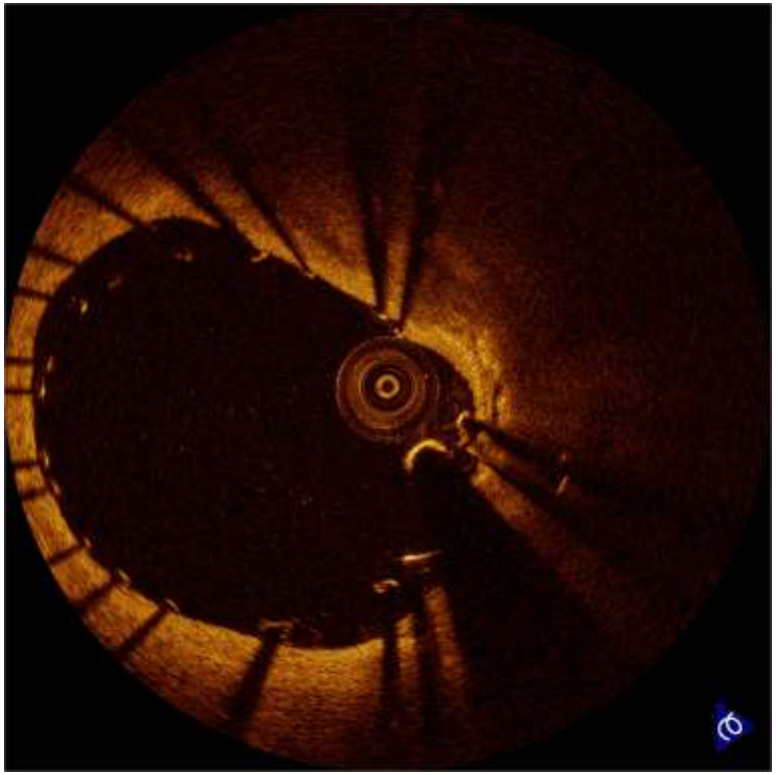


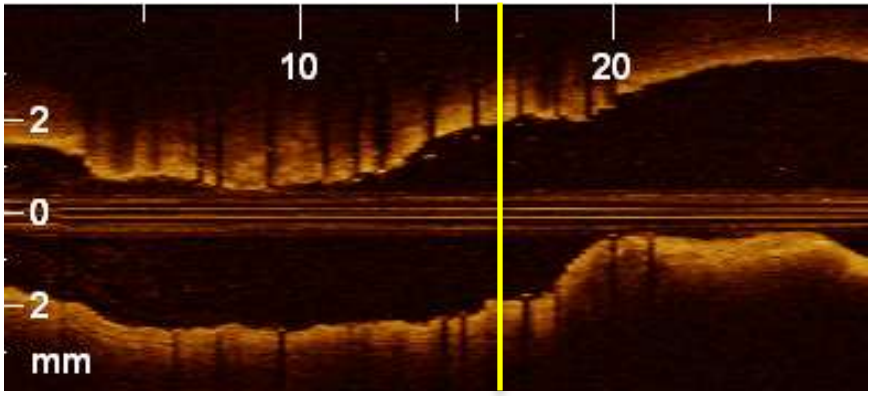




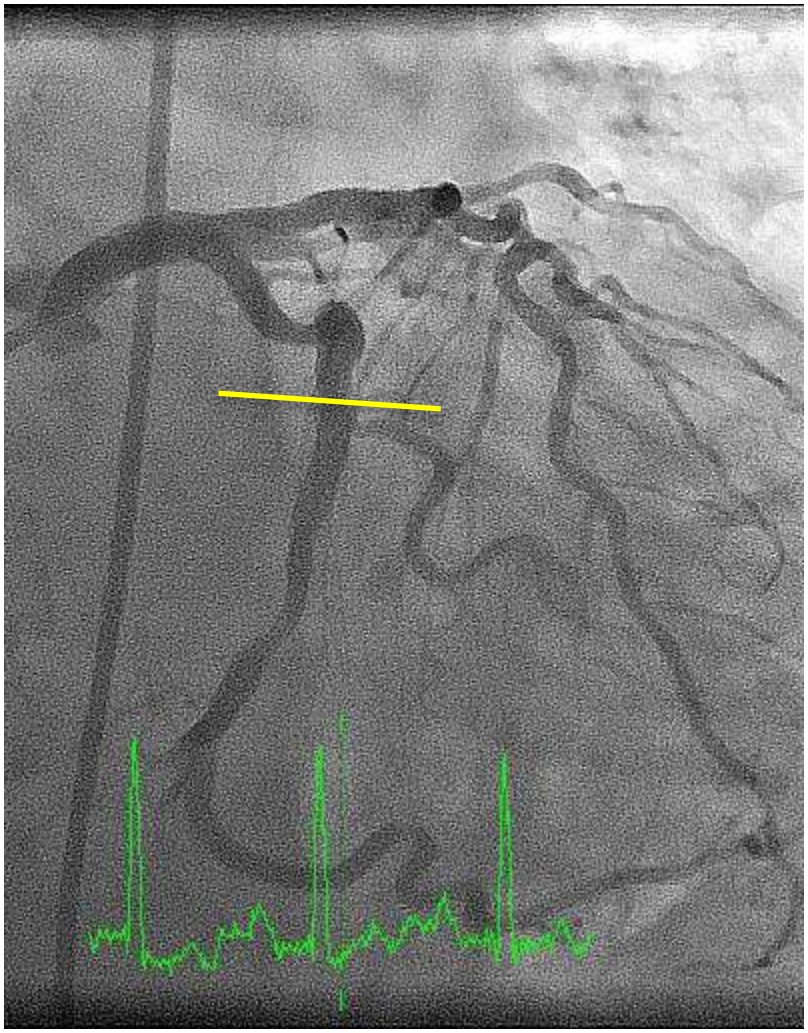
Acceptable Angiographic Result, Non-Ischemic FFR, but …

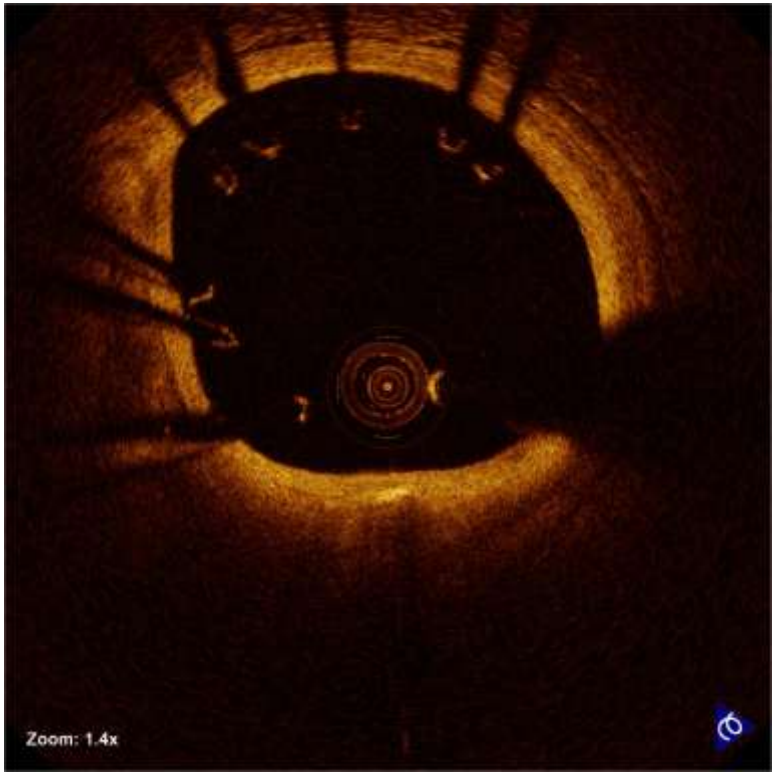


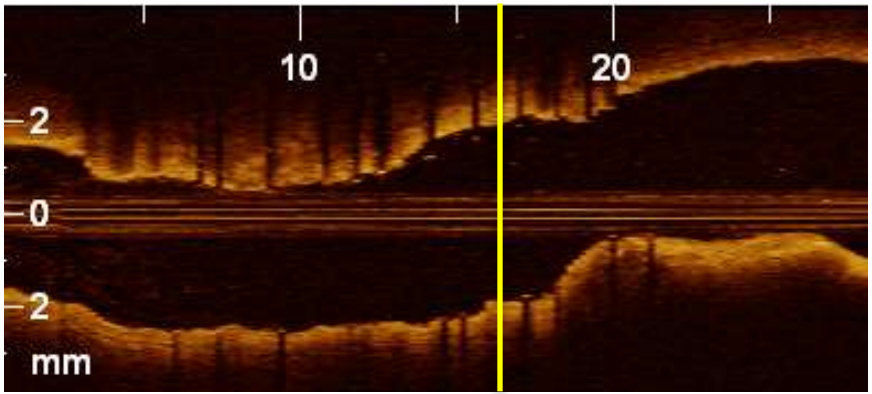




Acceptable Angiographic Result, Non-Ischemic FFR, but …







Meta-Analysis of DES Studies (n=17,570)

Compared with angiographic guidance, IVUS-guided DES implantation was associated with reduced rates of:

- **Death**

  HR 0.58 (0.47-0.71), p<0.001

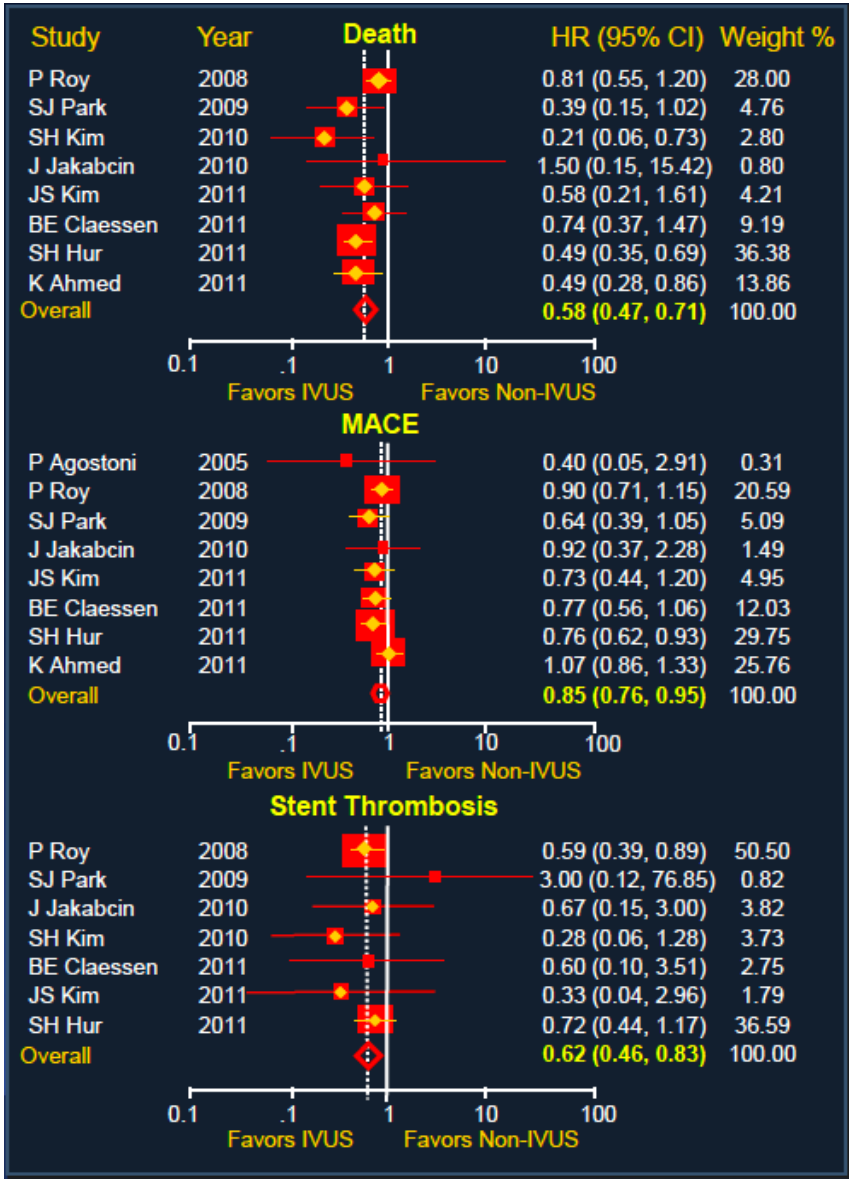
- **MACE**

  HR 0.85 (0.76-0.95), p=0.005

- **Stent Thrombosis**

  HR 0.62 (0.46-0.83), p=0.002

Note: TLR HR 0.90 (0.73-1.11) all studies; 0.63 (0.46-1.14) propensity-adjusted studies



Zhang Y, et al. EuroIntervention 2012;8:855-865

ADAPT-DES

Prospective, multicenter, real-world registry of 8,583 consecutive pts undergoing DES implantation to determine the frequency, timing, and correlates of early and late ST. During the index procedure, IVUS was used in 3,349 pts

	IVUS (n=3,349)	No IVUS (n=5,234)	P
Any ST within 1 year	0.52%	1.04%	0.011
Acute	0.06%	0.04%	0.66
Subacute	0.27%	0.56%	0.05
Late	0.25%	0.48%	0.10
All-cause death/MI within 1 year	3.96%	5.35%	0.004
Cardiac death within 1 year	0.84%	1.19%	0.12
Peri-procedural MI	1.26%	1.53%	0.29
ST-related MI	0.37%	0.59%	0.16%
Non-ST-related MI	0.87%	1.58%	0.0054
Ischemia-driven TVR	2.42%	3.95%	0.0001

Witzenbichler B, et al. Circulation 2014;129:463-470

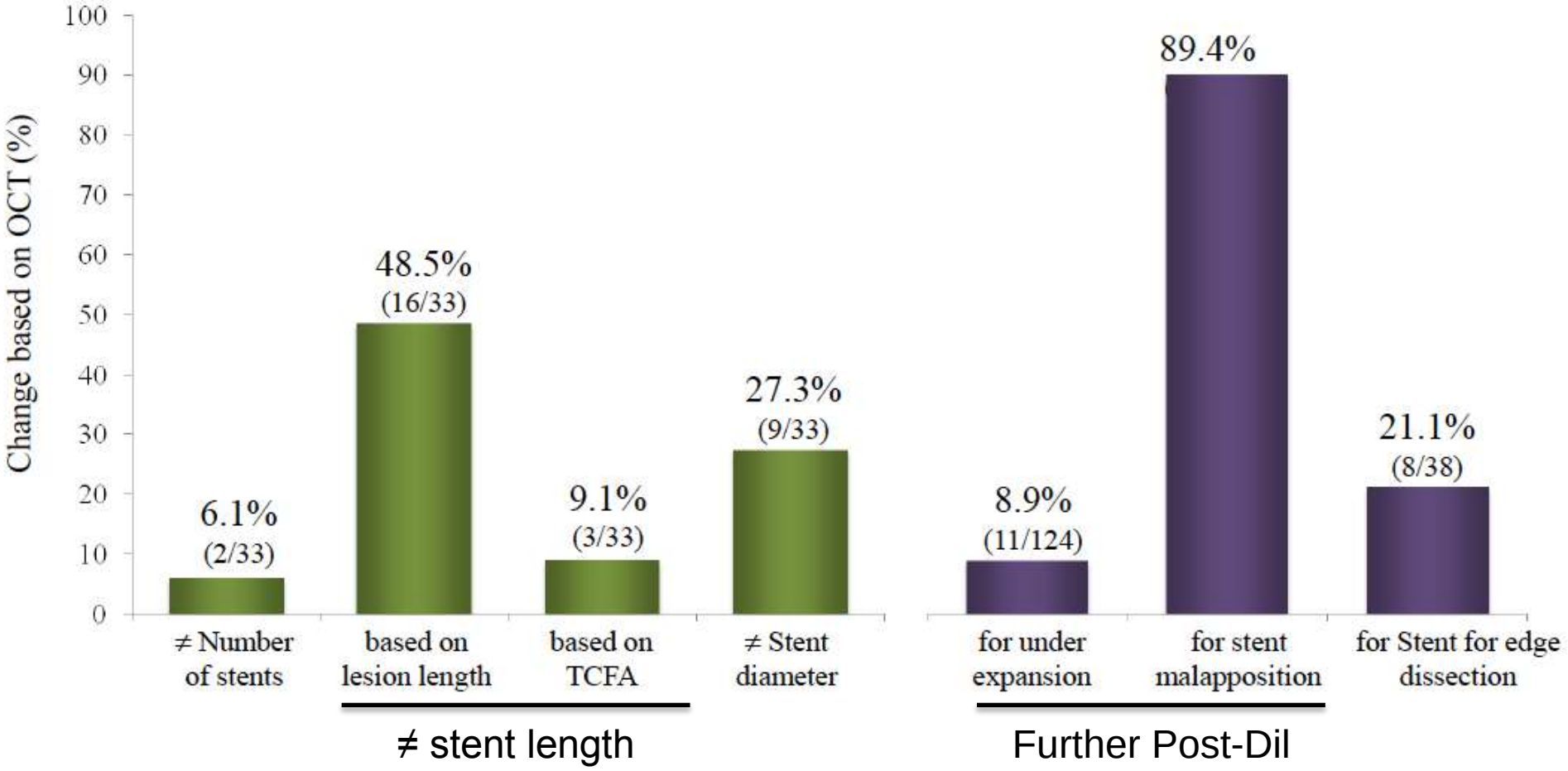
Impact of OCT on PCI Management

Pre-Intervention

Any Change Based on OCT: **81.8%**

Post-Intervention

Any Change Based on OCT: **54.8%**



Stefano GT, et al. Int J Cardiovasc Imaging 2013;29:741-752

OCT-Guided PCI

335 pts who underwent PCI guided by angiography + OCT were compared with a paired group of another 335 pts who underwent PCI under angiography guidance only during the same period (within 30 days)

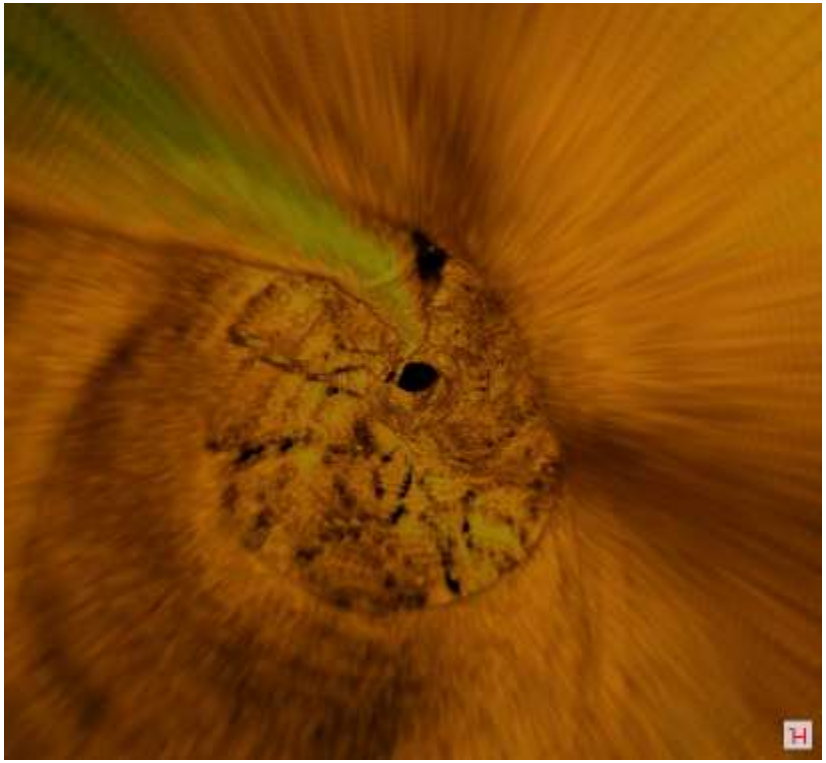
	Angiographic guidance group (n=335)	Angiographic plus OCT guidance group (n=335)	*p*-value
In-hospital events			
Cardiac death	3 (0.9%)	2 (0.6%)	1.0
Non-fatal myocardial infarction	22 (6.5%)	13 (3.9%)	0.118
Events at 1-year follow-up			
Death	23 (6.9%)	11 (3.3%)	0.035
Cardiac death	15 (4.5%)	4 (1.2%)	0.010
Myocardial infarction	29 (8.7%)	18 (5.4%)	0.096
Target lesion repeat revascularisation	11 (3.3%)	11 (3.3%)	1.0
Definite stent thrombosis	2 (0.6%)	1 (0.3%)	1.0
Cardiac death or myocardial infarction	43 (13.0%)	22 (6.6%)	0.006
Cardiac death, myocardial infarction, or repeat revascularisation	50 (15.1%)	32 (9.6%)	0.034

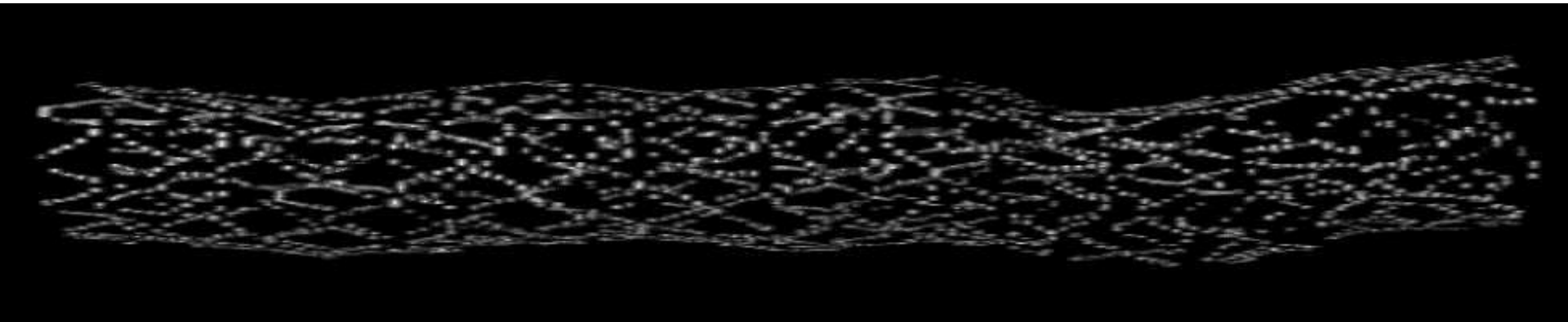
OCT-guided PCI independently associated with reduced risk of death and MI

- Multivariable logistic regression analysis: **OR: 0.49** [0.25-0.960, p=0.037
- Propensity score adjustment: **OR: 0.37** [0.10-0.90], p=0.050
- Cox proportional hazard analysis: **HR: 0.51** [0.28-0.93], p=0.028

Prati F, et al. EuroIntervention.2012;8:823-829

3D-OCT: Global Stent Geometry Assessment



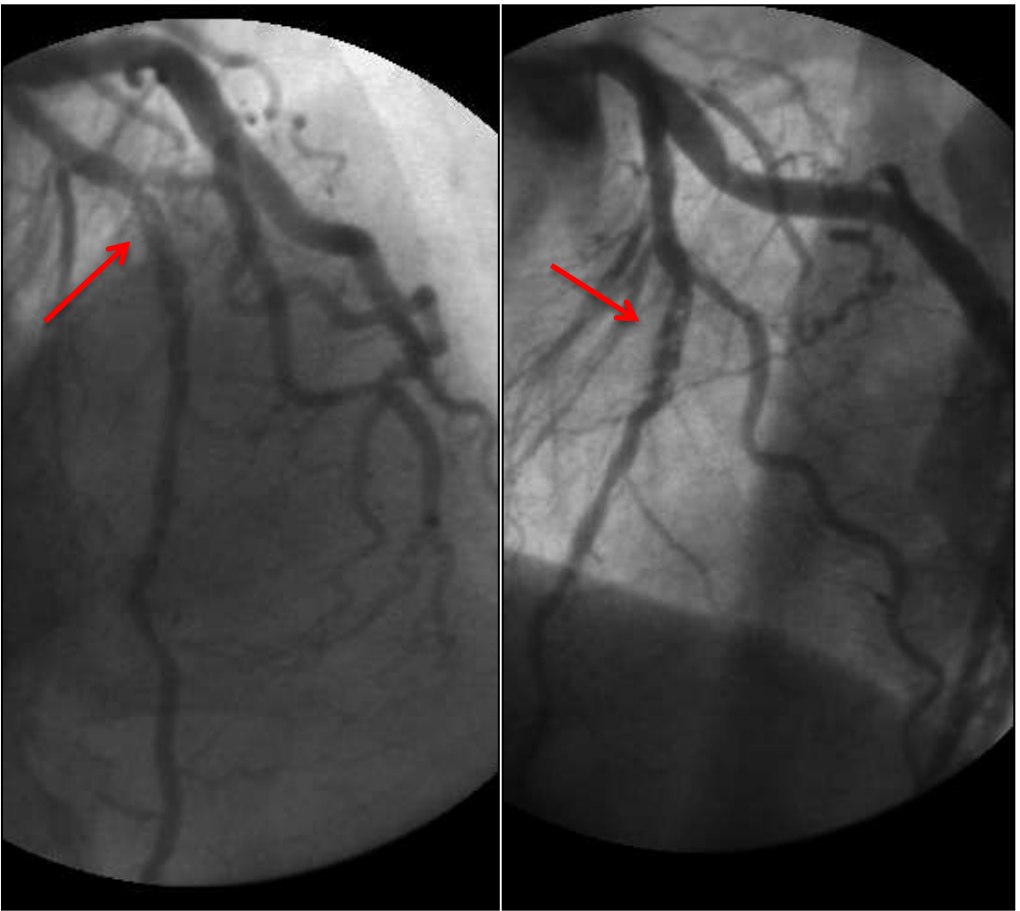


When Do I Think of an Adjunctive Method?

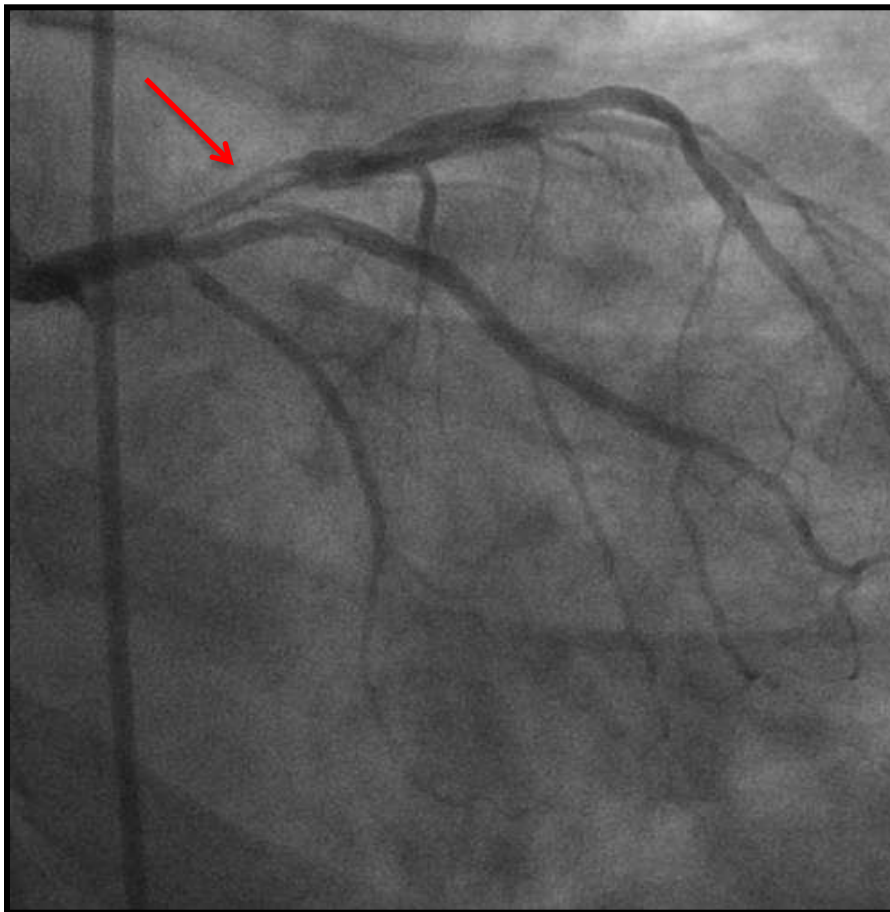
1. To define which lesion to treat
   - Physiology vs. Imaging
   - Defining the culprit
2. To Guide/Optimize my PCI
   - Pre-PCI
   - Post-PCI
3. **To understand the mechanisms of stent failure**

Understanding the Mechanisms of Stent Failure

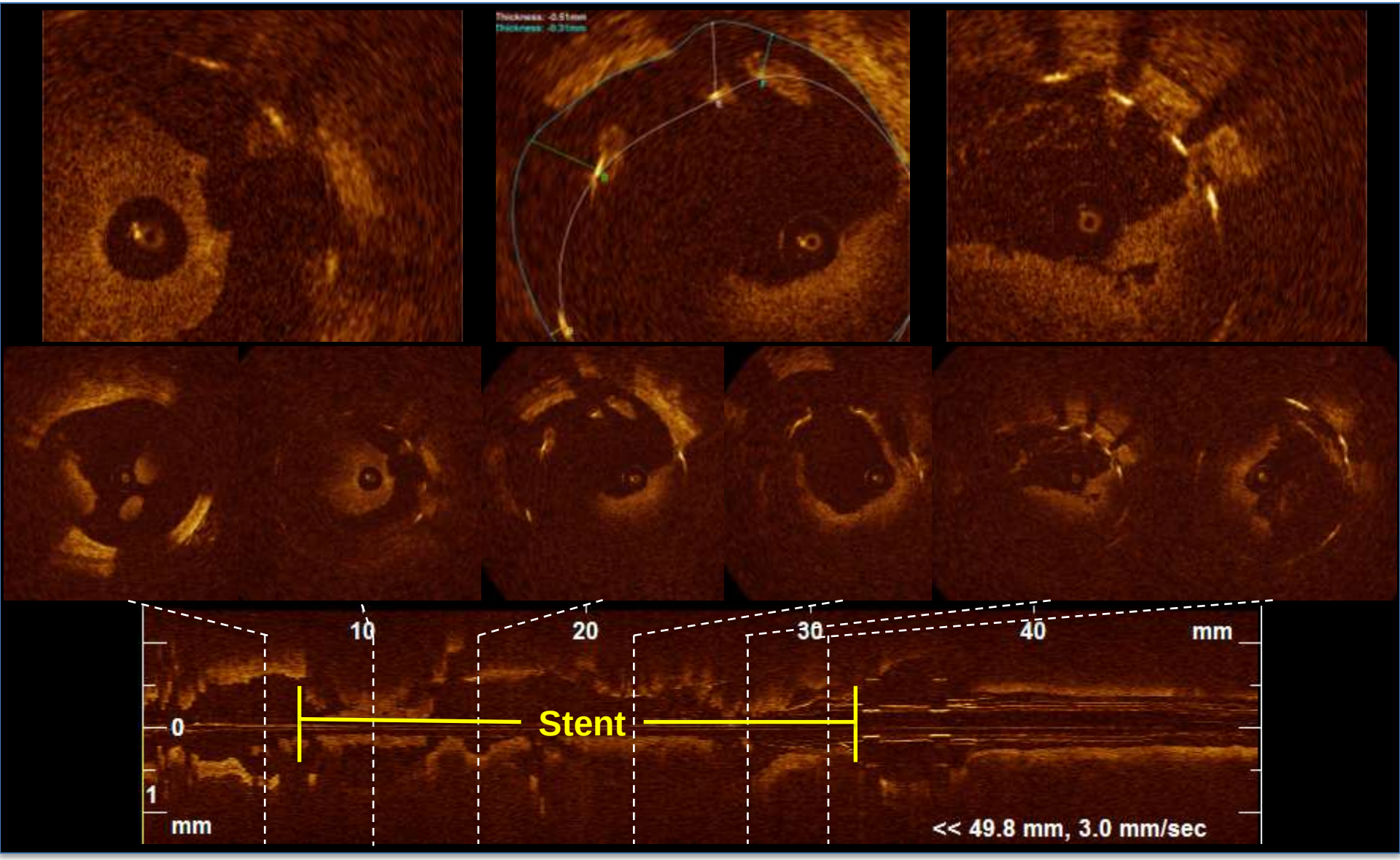
62-yo male, HTN, dyslipidemia
PCI to LAD w/ SES in Aug/2003
DAPT for 3 mos
Asymptomatic for 5 years
Jun/2008 → NSTEMI



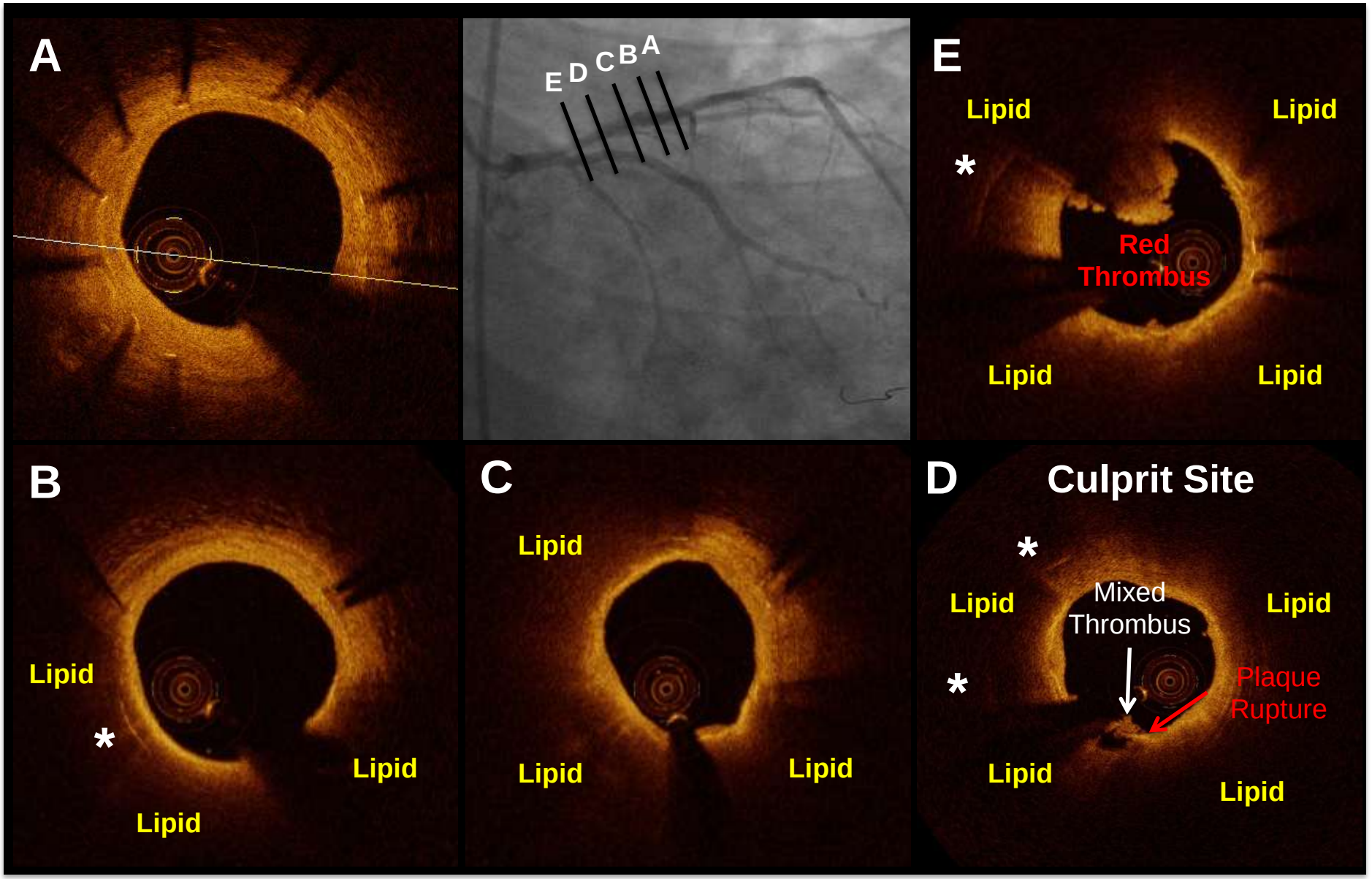
54-yo male, HTN, type II DM
Prior MI (May/2007); PCI to LAD w/ PES
DAPT for 12 mos
Asymptomatic for 3.9 years
Feb/2011 → Anterior wall STEMI



Understanding the Mechanisms of Stent Failure – Case 1: Incomplete Healing



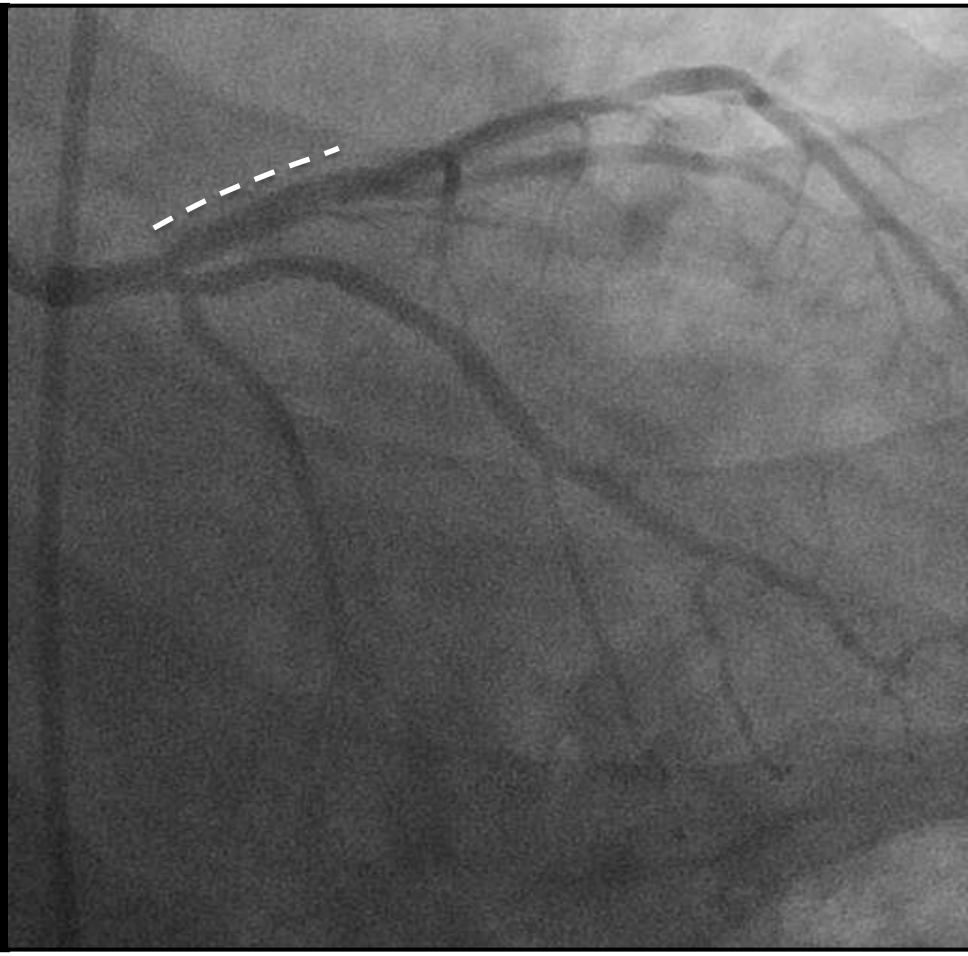
Understanding the Mechanisms of Stent Failure – Case 2: Neoatherosclerosis



Two Late DES Failures with the Same Clinical Impact; Two Different Mechanisms; Two Different Solutions

PCI with a 3.0x24 mm BMS Implantation

PCI with a 3.5x23 mm EES Implantation



Summary

1. Physiology should be the first choice for determining which lesion to treat.
   - Intravascular imaging (particularly OCT) may have a role in the ACS setting in identifying the culprit lesion.
   - For assessment of intermediate LM lesions, FFR and IVUS have demonstrated good prognostic applicability.
   - Due to the inherent limitations of FFR for assessment of LM lesions, IVUS-derived MLA cut-offs can be a more practical approach.
2. For Guidance/Optimization of PCI Results:
   - FFR has limited role.
   - IVUS and OCT can be used.
   - Large body of evidence with IVUS / Studies are ongoing with OCT.
   - OCT is more sensitive than IVUS for detection malapposition, dissections, plaque prolapse, and thrombus – clinical impact needs further studies.
3. For Identification of the Mechanisms of Stent Failure:
   - IVUS and OCT are useful in identifying regions of underexpansion and ISA.
   - OCT is more sensitive for ISA detection, and allows for:
     - strut level assessment – strut coverage and apposition
     - qualitative assessment of NIH – neoatherosclerosis, peri-strut infiltrates, etc

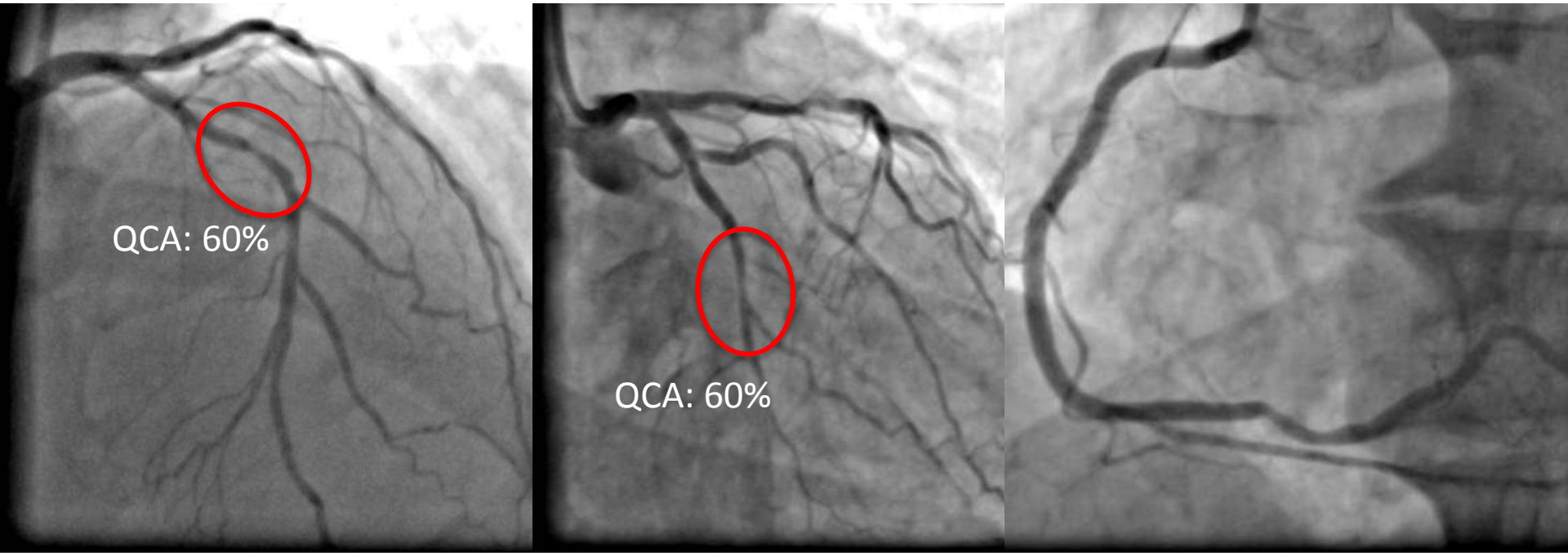
Conclusions

1. One of the legacies of coronary angiography is to assume that one technique will always answer all questions, but that is not the current state-of-the-art.
2. Barriers to implementing an intravascular imaging and physiology program:
   - Cost – unfortunately, the cost of these techniques can dwarf that of other materials used in PCI
   - Expertise
     - Interpretation is not intuitive, and requires training.
     - Understanding the artifacts, limitations, and confounders of the adjunct methods is critical for its proper use.
   - Being aware of the limitations of relying on coronary angiography alone for specific situations

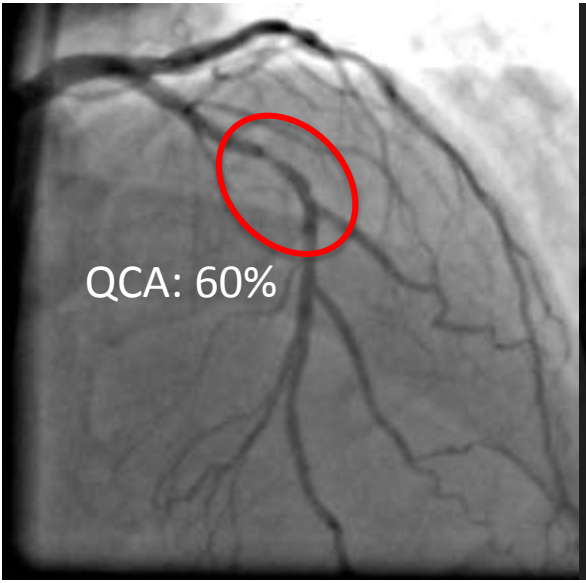
Instituto DANTE PAZZANESE
de Cardiologia

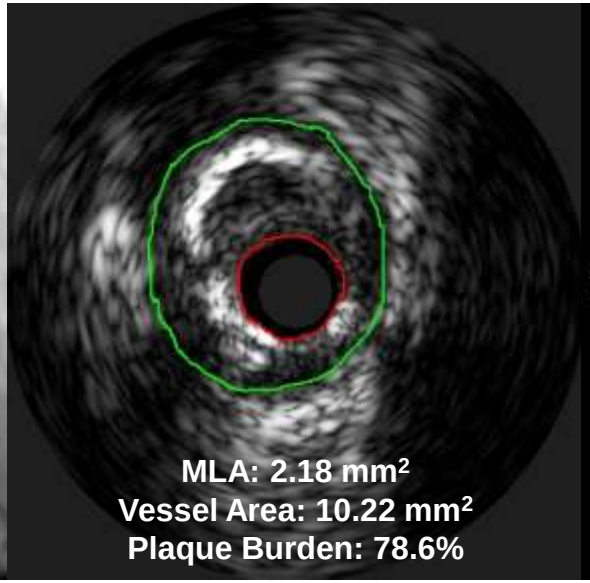
Do I Need to Treat These Lesions?

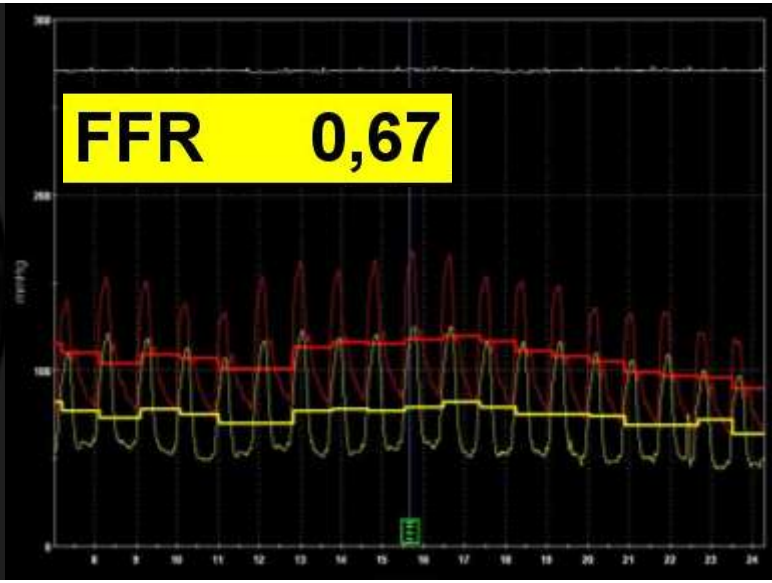
62-yo male, HTN, type II DM, Dyslipidemia, Former smoker
Stable Angina (CCS II) for 2 months
Referred to coronary angiography w/o any non-invasive functional test

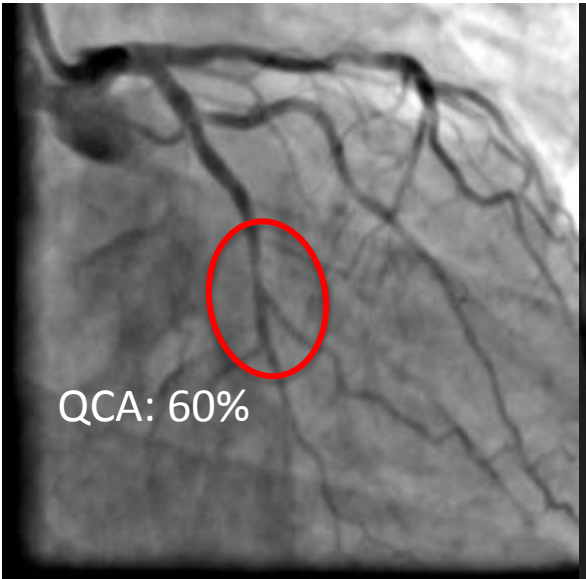


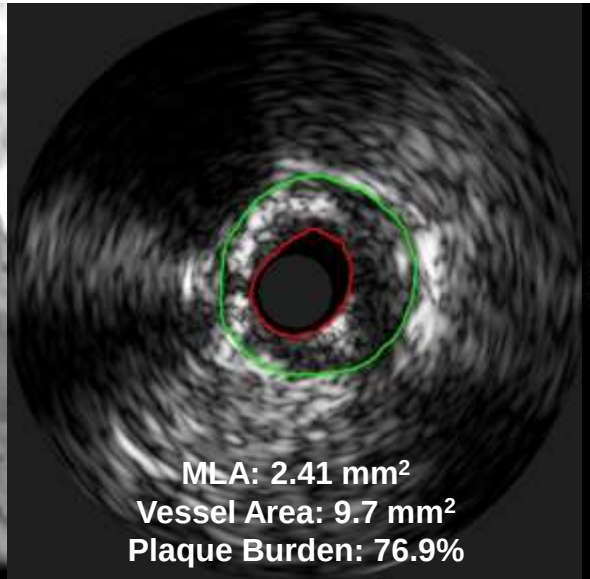
Two Lesions with the Same Anatomic Stenosis Severity, but Different Physiological Responses

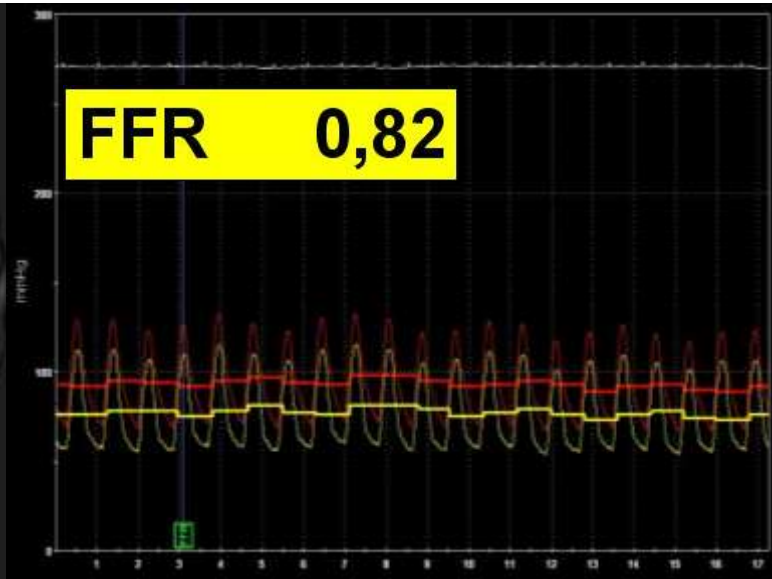








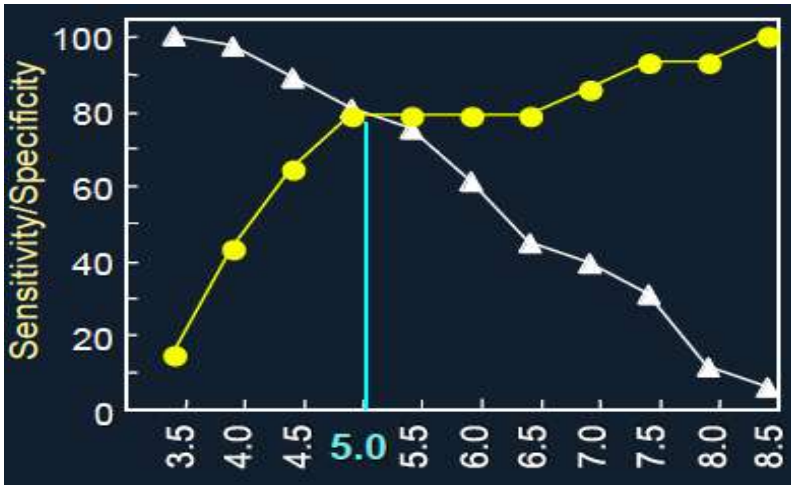




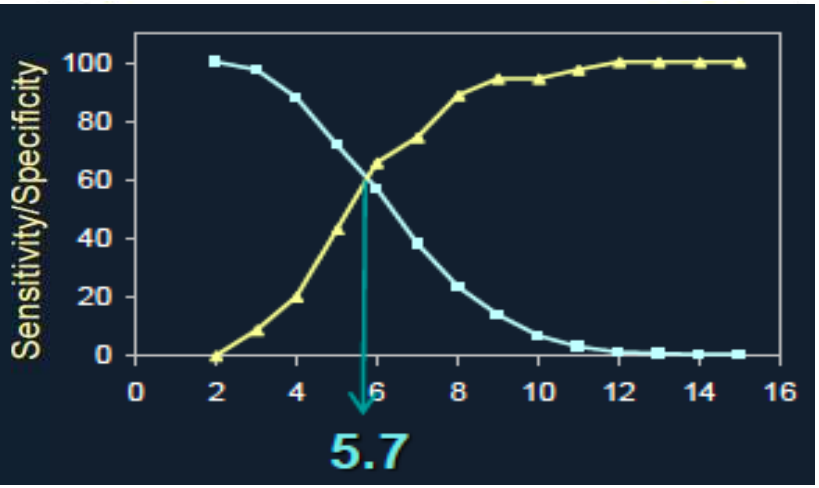
IVUS Criteria of "Optimal Stent Implantation"

− Drug-Eluting Stent Era −

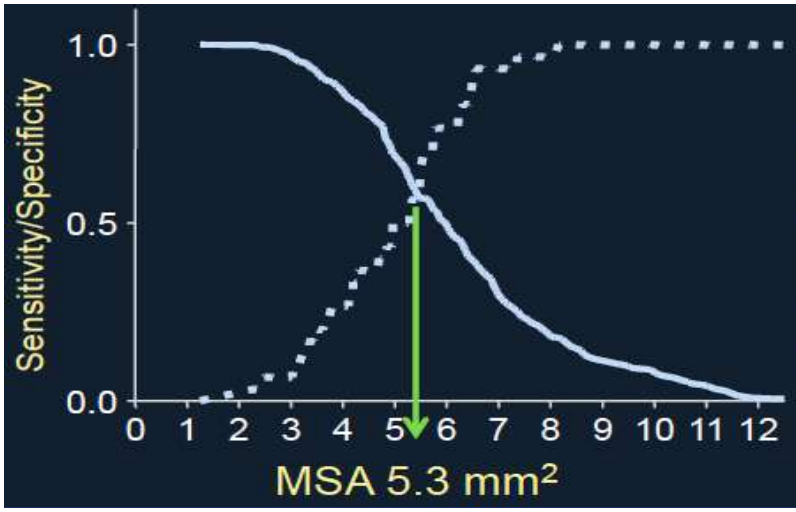
Cypher[1]



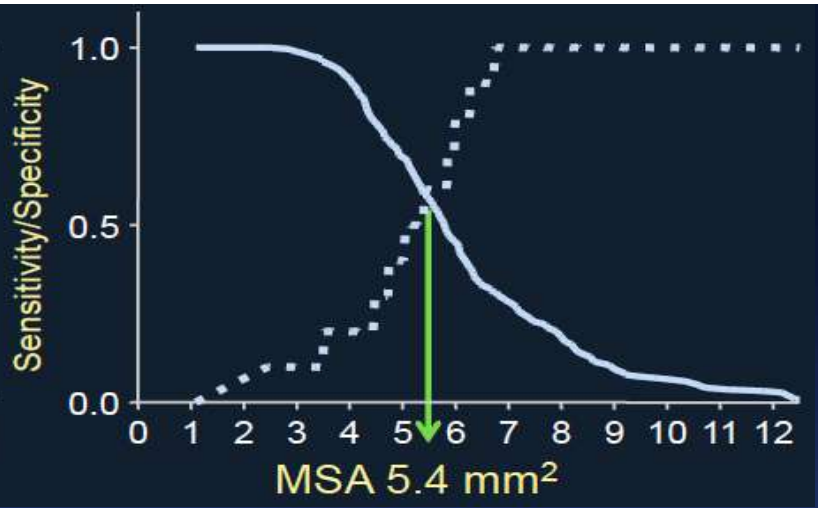
Taxus[2]



Endeavor[3]



Xience V[3]



[1]Sonoda S et al. JACC 2004;43:1959-1963 / [2]Doi H, et al. JACC Cardiovasc Interv 2009;2:1269-1275 / [3]Song HG, et al. Catheter Cardiovasc Interv 2012; pubmed ahead of print