IVUS assessment and DES-guided treatment of Left Main lesions

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VALDECILLA SANTANDER

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organizations listed below.

Affiliation/Financial Relationship	Company
Grant/Research Support	**Abbott vascular, Boston sci, Biotronik, Biosensors, St Jude**
Consulting Fees/Honoraria	**Medtronic, Abbott, Boston, Cordis, Biotronik, IHT, Lilly, Daychi Sankio, Astra Zeneca, Biosensors**
Major Stock Shareholder/Equity	
Royalty Income	
Ownership/Founder	
Intellectual Property Rights	
Other Financial Benefit	

Recommendations according to extent of CAD	CABG		PCI	
	Class[a]	Level[b]	Class[a]	Level[b]
Left main disease with a SYNTAX score ≤ 22.	I	B	I	B
Left main disease with a SYNTAX score 23–32.	I	B	IIa	B
Left main disease with a SYNTAX score >32.	I	B	III	B

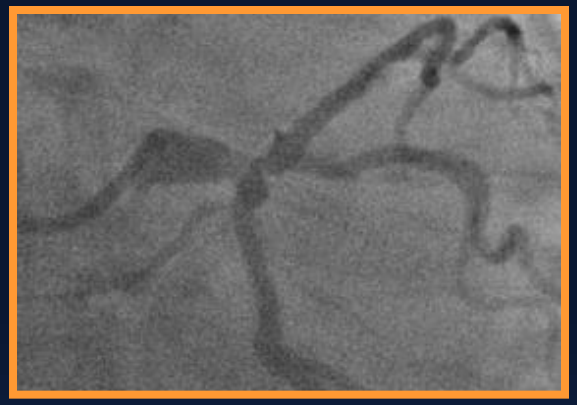
2014 ESC/EACTS Guidelines on myocardial revascularization

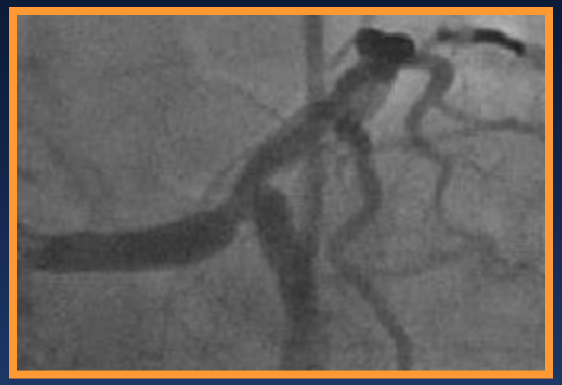
The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

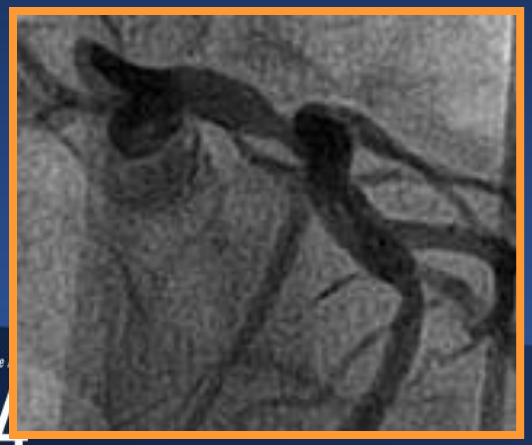
Recommendations	Class[a]	Level[b]
FFR to identify haemodynamically relevant coronary lesion(s) in stable patients when evidence of ischaemia is not available.	I	A
FFR-guided PCI in patients with multivessel disease.	IIa	B
IVUS in selected patients to optimize stent implantation.	IIa	B
IVUS to assess severity and optimize treatment of unprotected left main lesions.	IIa	B
IVUS or OCT to assess mechanisms of stent failure.	IIa	C
OCT in selected patients to optimize stent implantation.	IIb	C

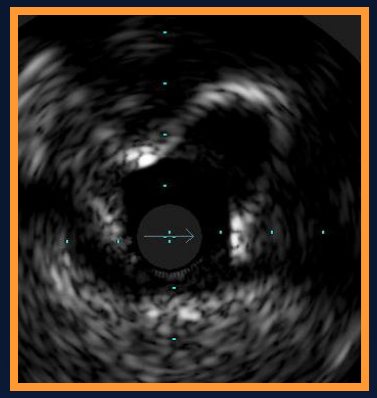
Significant ???

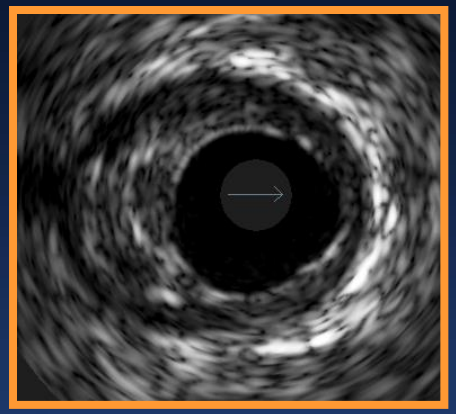
MLA cut-off ?

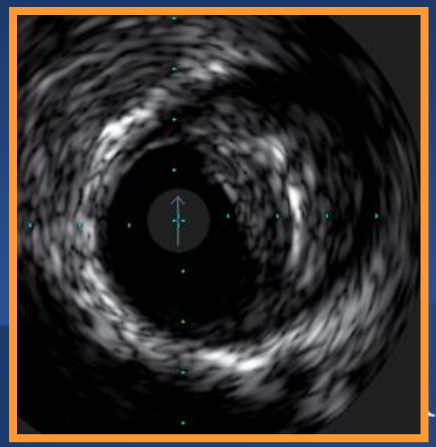












Proposed MLA cut-off values for LM

Park et al. 2014 **N= 112**	**IVUS vs FFR <0.8**	**4.5 mm²**
Jasti et al. 2004 **N= 55**	**IVUS vs FFR < 0.75**	**5.9 mm²**
LITRO **De la Torre et al.** 2011 **N = 354**	**Physics of flow / Jasti et al.**	**6 mm²**
Fassa et al. 2005 **N= 214**	**Inferred from normal pts.**	**7.5 mm²**

Clinical follow-up

LMCA

MLA = 6 mm²

Prospective Application of Pre-Defined Intravascular Ultrasound Criteria for Assessment of Intermediate Left Main Coronary Artery Lesions

Results From the Multicenter LITRO Study

De la Torre Hernandez, et al. J Am Coll Cardiol 2011; 58:351-8

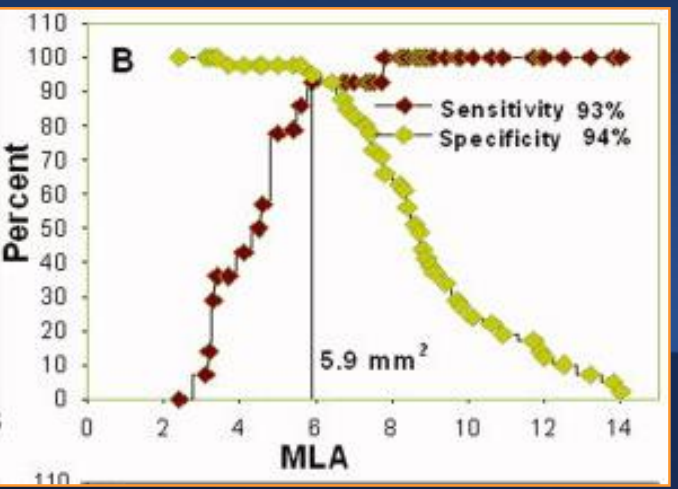
Proximal LAD

MLA = 3 mm²

Proximal LCx

MLA = 3 mm²

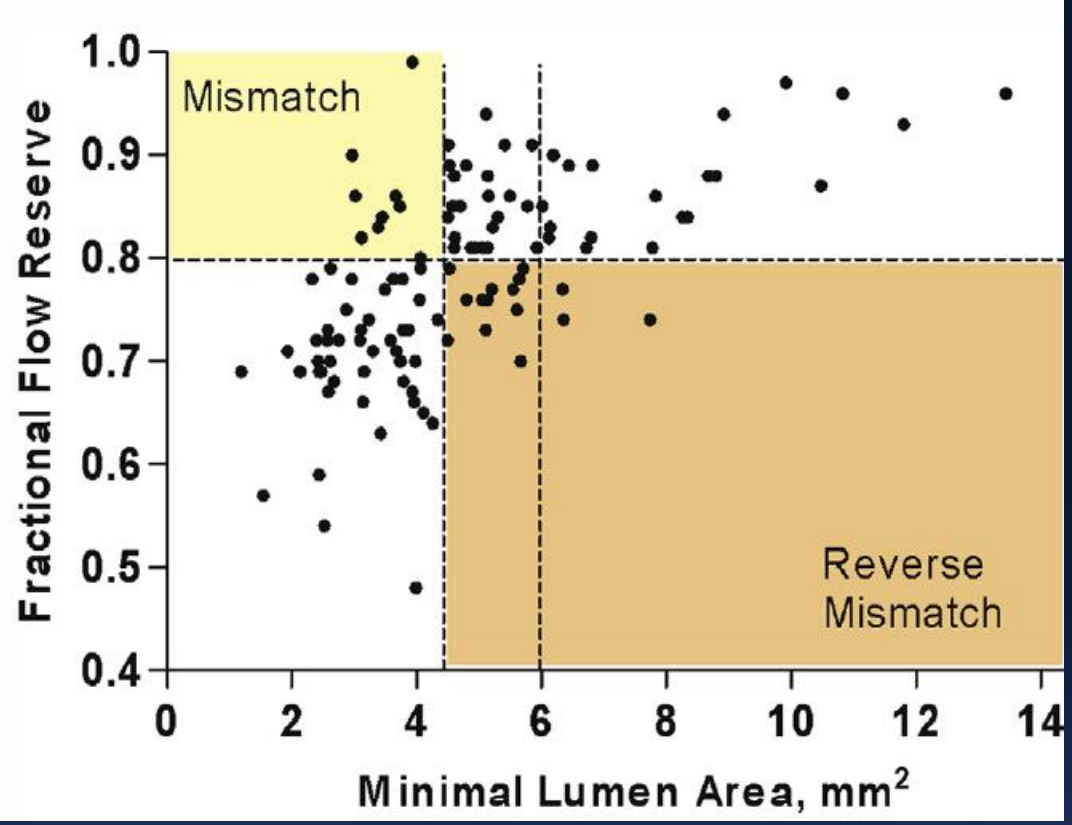
Jasti et al.
Circulation 2004;110:2831-6



Linear law (epicardial coronary artery)
Do = 0.678*(D1+D2)

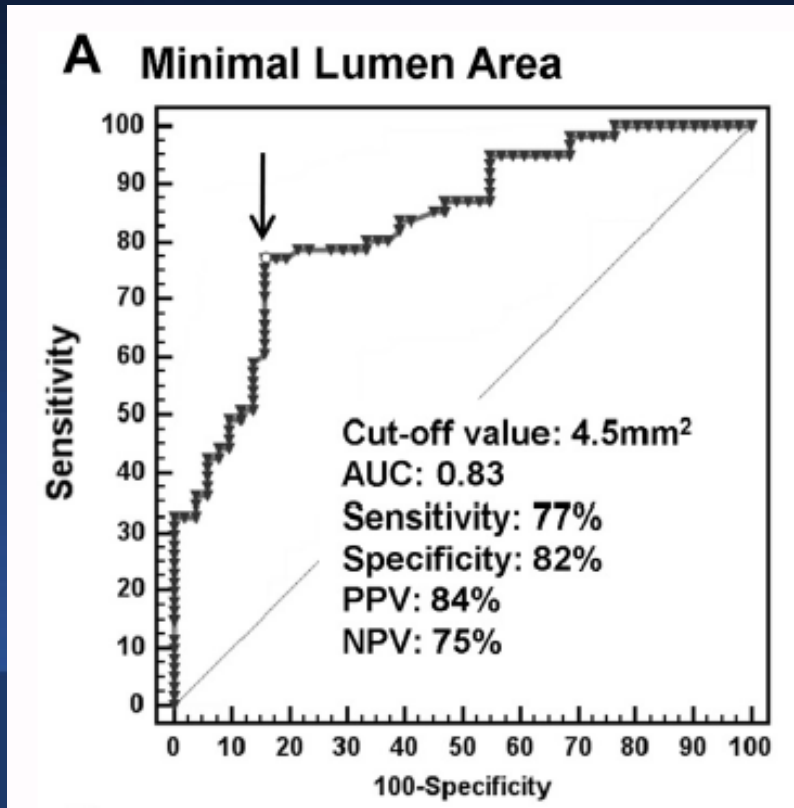
Finet G et al.
Eurointervention 2007;3:10-17

CRF CARDIOVASCULAR RESEARCH FOUNDATION
At the heart of innovation



New cut-off 4.5 mm^2

112 pts
Isolated LM ostial / shaft lesions
Correlation IVUS - FFR



Park et al. J Am Coll Cardiol Intv 2014;7:868-74

First,

The LM-MLA cut-off is population-dependent.

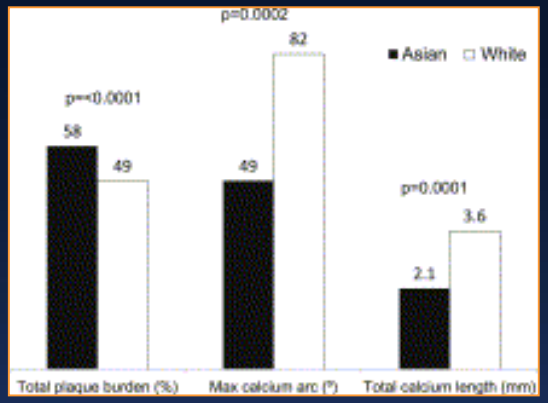
Differences between studies

	Asiatic	White Westerners	
	Park et al.	Jasti et al.	LITRO study
MLA, mm2	4.8	7.6	7.2
Method	**FFR** **IV** adenosine	**FFR** **IC** adenosine 42 - 56 µg	Clinical validation
Cut-off MLA	**4.5**	**5.9**	**6**

Intravascular ultrasound comparison of left main coronary artery disease between white and asian patients.

Rusinova RP, Mintz GS, Choi SY, et al. Am J Cardiol. 2013;111:979-84.

99 Asian patients (Japan and South Korea)
99 matched control United States white patients
with a stable clinical presentation and >30% LM stenosis

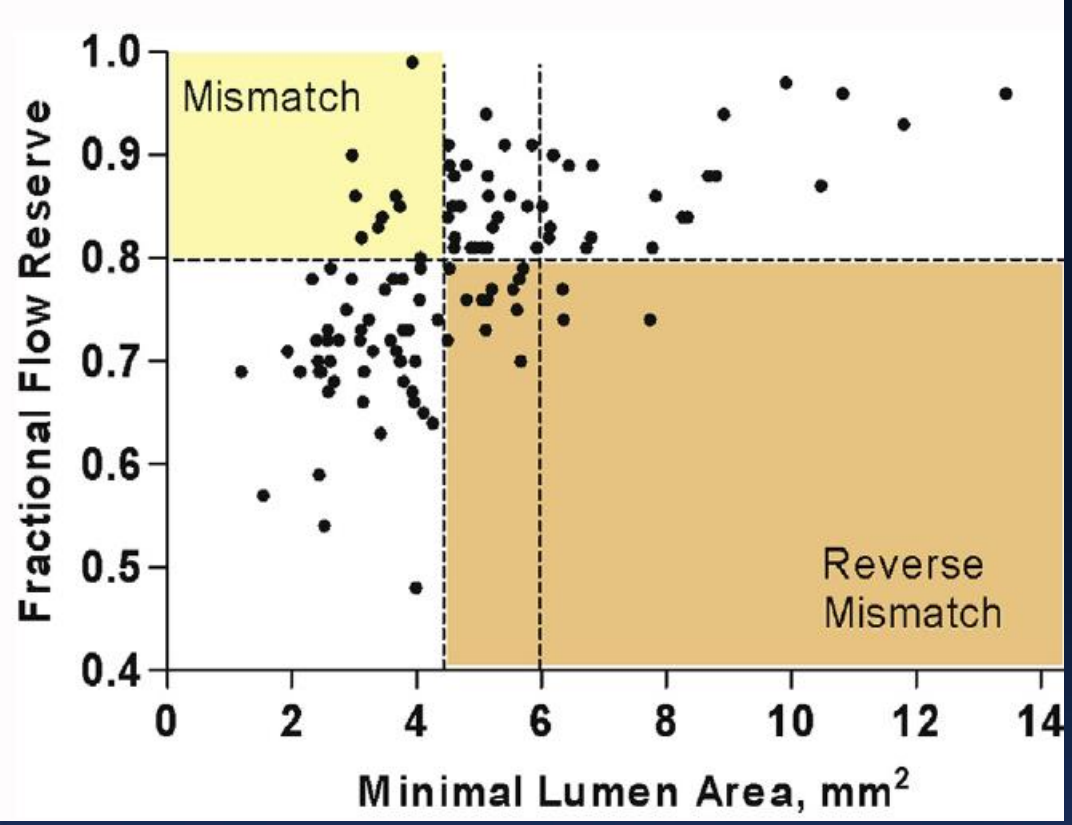


At the minimum lumen site and over the entire LMCA length
Asian patients had a smaller lumen area
(5.2 ± 1.8 vs 6.2 ± 14 mm^2; p <0.0001)

Second,

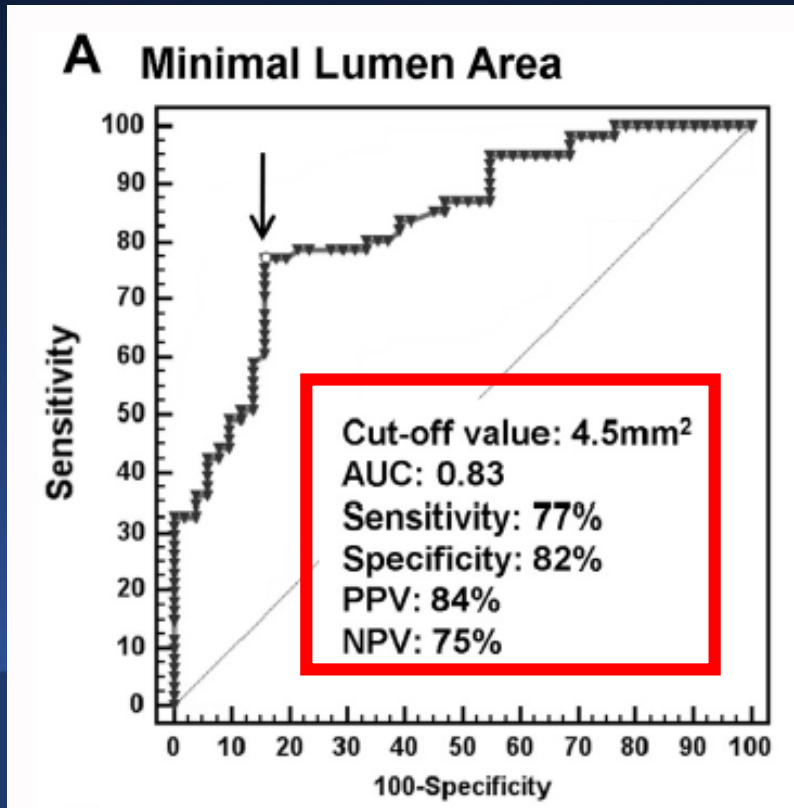
Given the unique prognostic implications of LM-derived ischemia, the optimal cut-off value must show very high sensitivity and negative predictive values

LM-MLA > cut-off MLA ≅ safe to defer



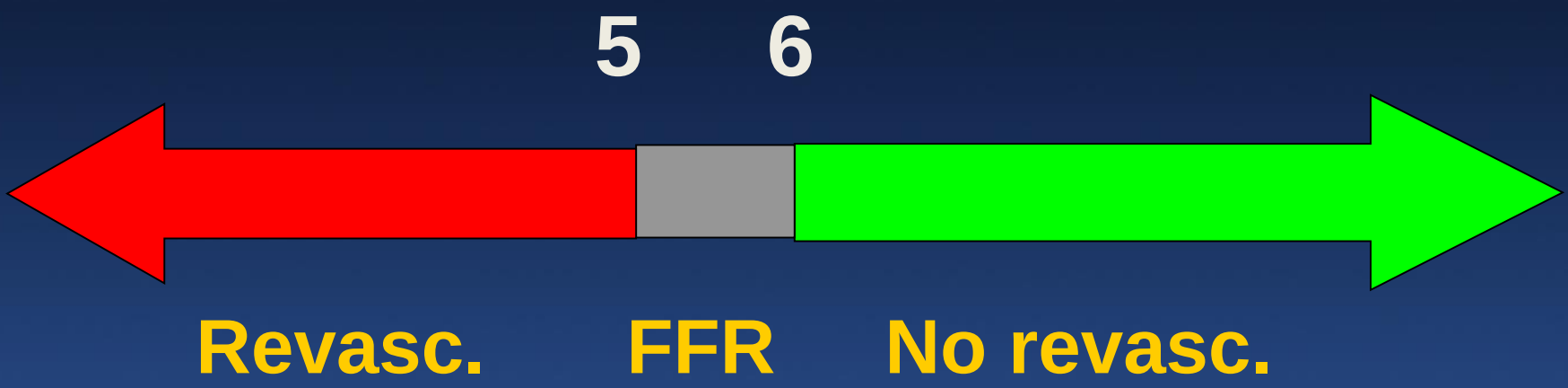
New cut-off 4.5 mm^2

Among 54 lesions with LM-MLA >4.5 mm^2 13 (24.1%) had an FFR of ≤0.80.



Park et al. J Am Coll Cardiol Intv 2014;7:868-74

LM - MLA mm^2



Third,

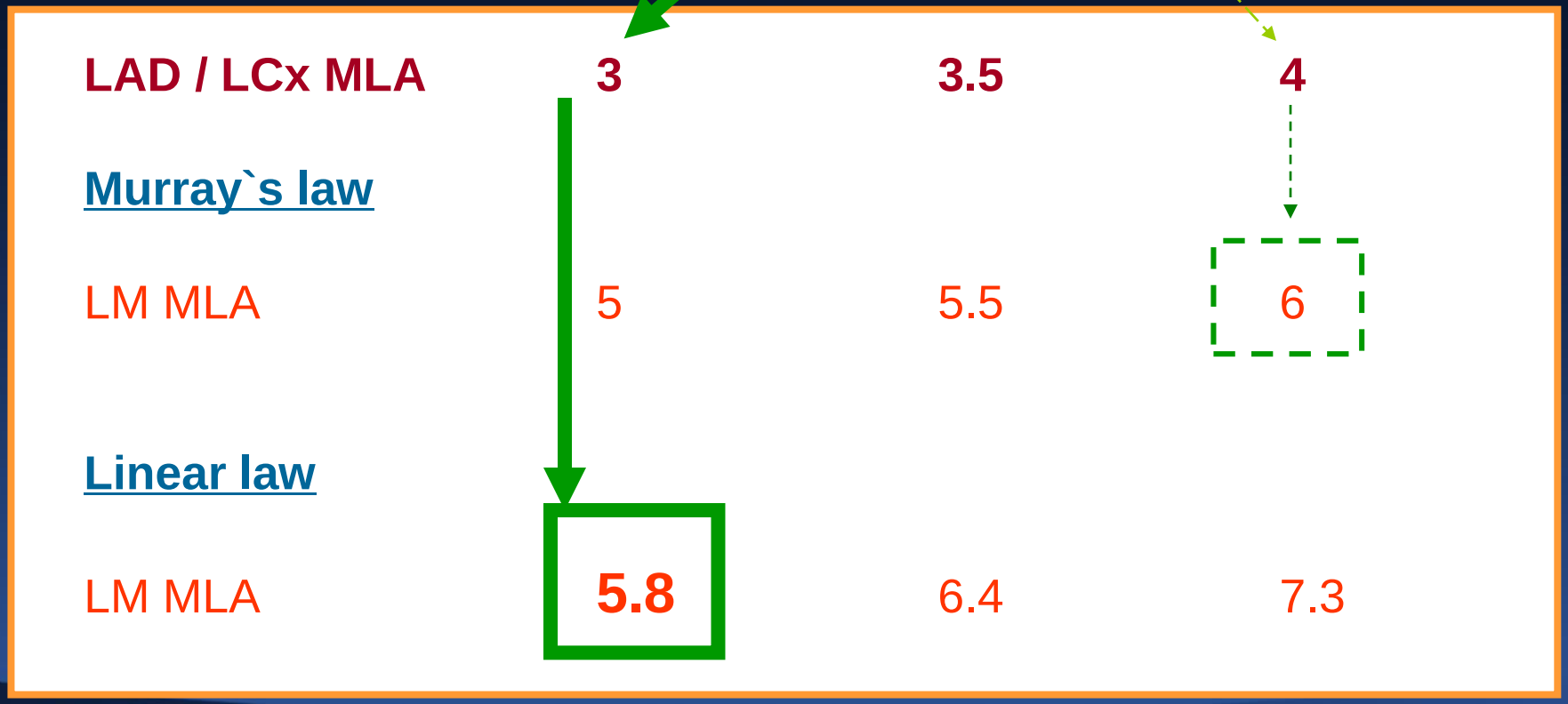
a theoretical LM-MLA cut-off value may be nicely derived from fractal geometry

-Linear law is more exact.
-Murray´s law underestimates calculated mother-vessel diameter.

Finet G et al. Eurointervention 2007;3:10-17

Threshold for MLA in LAD - LCx

Correlation FFR-IVUS in non-LM lesions in vessels of **3 - 3.5** mm in diameter



Fourth,

the optimal LM-MLA cut-off value should be prospectively validated

Validation of cut-off 6 mm^2 in multicenter prospective LITRO study

Prospective Application of Pre-Defined Intravascular Ultrasound Criteria for Assessment of Intermediate Left Main Coronary Artery Lesions

Results From the Multicenter LITRO Study

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on behalf of the LITRO Study Group (Spanish Working Group on Interventional Cardiology)
Santander, Madrid, Bilbao, Alicante, Oviedo, Vigo, Badalona, Toledo, and Valladolid, Spain

354 pts

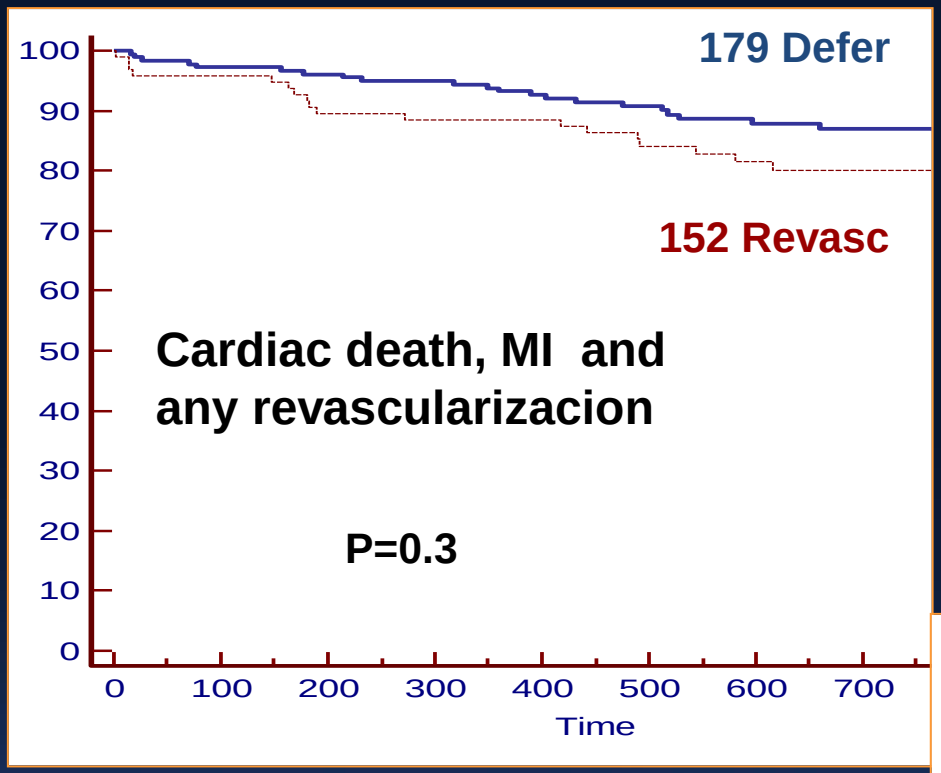
MLA ≥ 6 mm²
186 pts

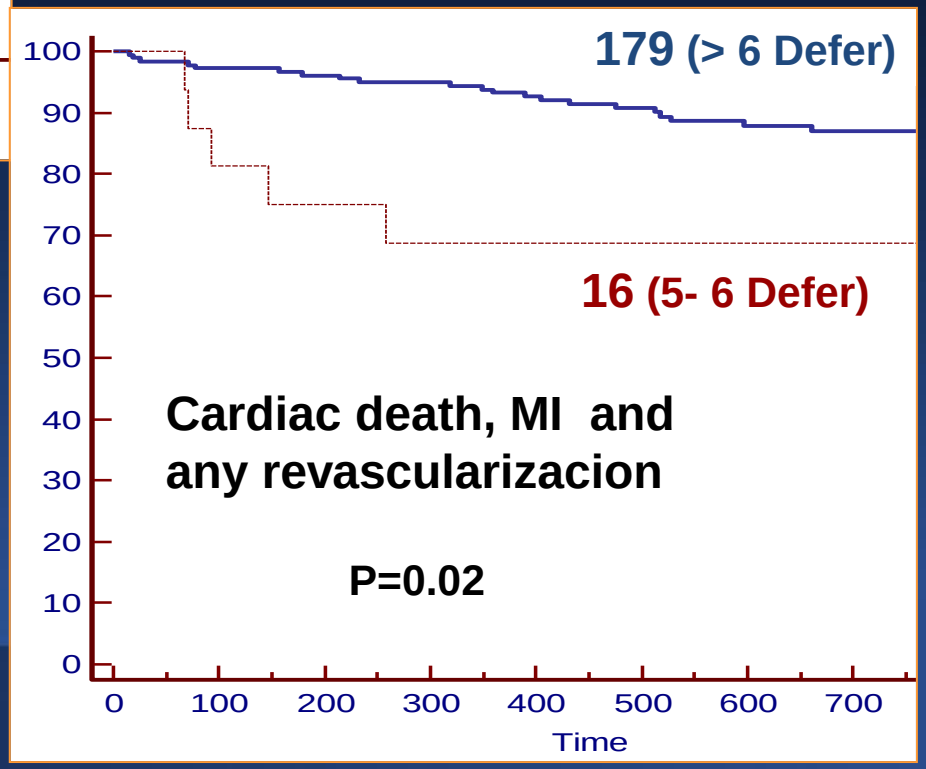
MLA < 6 mm²
168 pts

No Revascularización LM
179 pts (96%)

Revascularización LM
152 pts (90%)

De la Torre Hernandez et al,JACC 2011; 58:351-8





Safe approach up to 5 years

De la Torre Hernandez et al.
Am J Cardiol 2013;111 (7S):41B

FFR is more appropriate in assessing intermediate lesions
Why IVUS in ambiguous LM ?

An MLA cut off value of reference supported by:

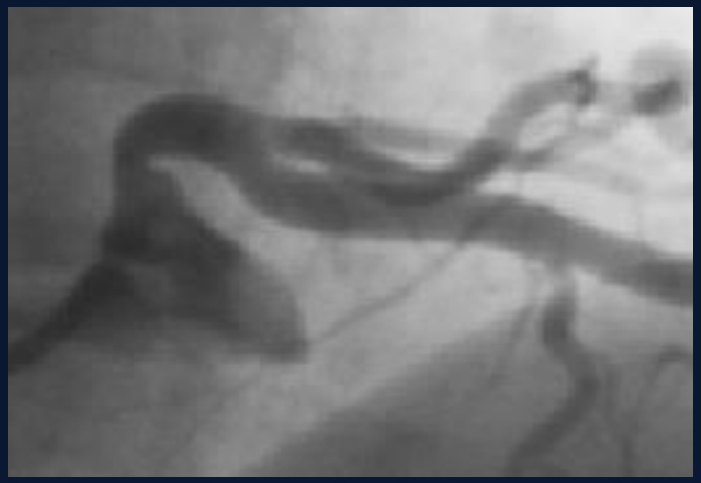
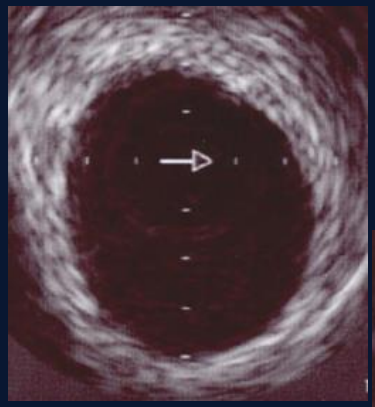
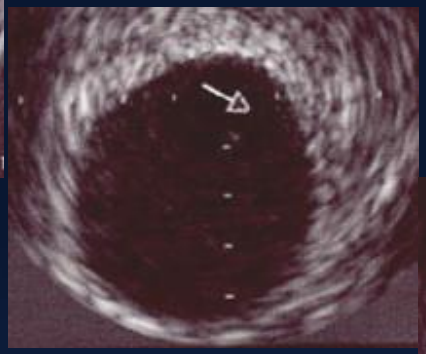
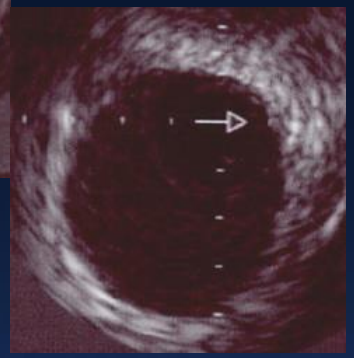
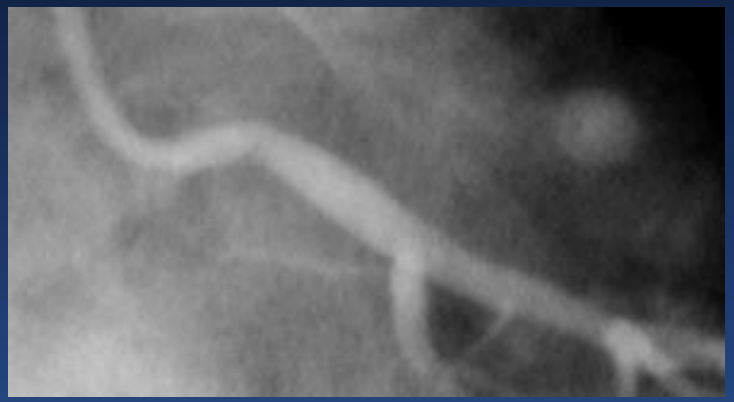
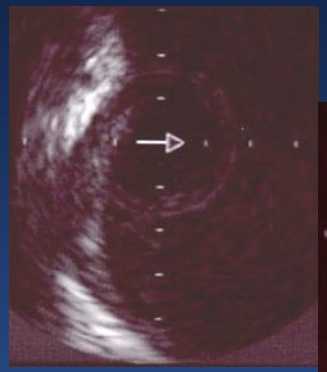
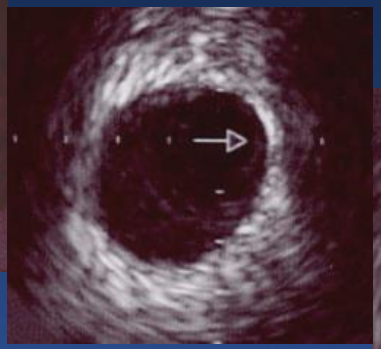
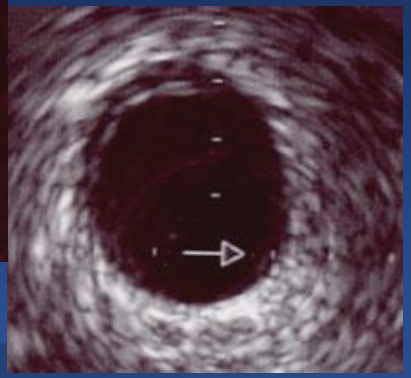
- Physics of vasculature (fractal linear law)
- FFR correlation (90 % S, 90%E; much better than in non-LM lesions)
- Prospective clinical validation (LITRO study)

Limitations for FFR:

-LAD and/or LCx significant disease (frequent 30-40%)
-Collaterals to an occluded (sub-occluded) RCA
-Inter-individual variation in hyperemic response
-More vulnerable to technical issues (false readings …)
-Gray zone 0.75 - 0.8

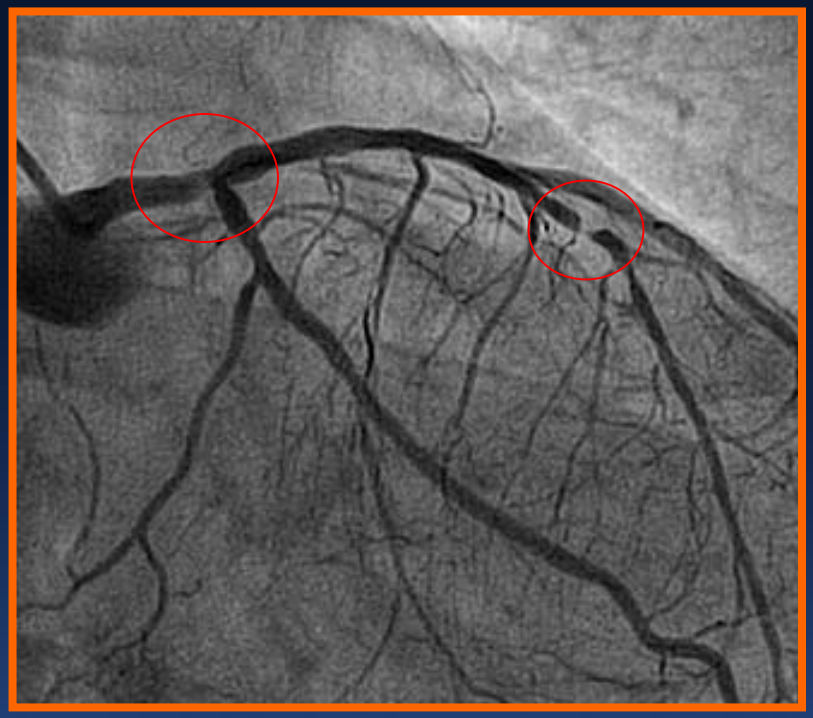
IVUS provides anatomic information not possible with FFR:

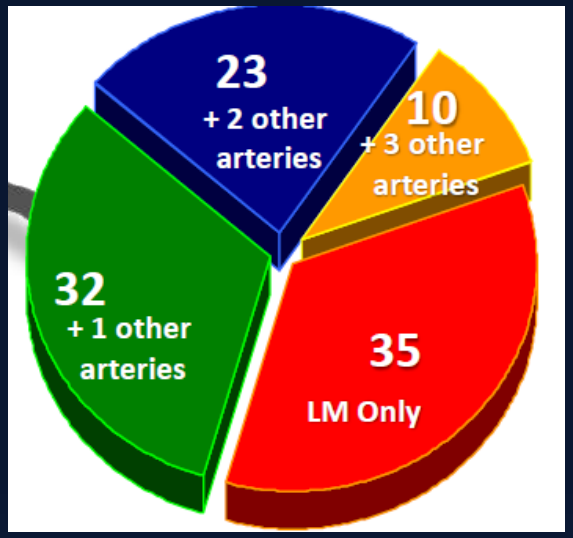
-Characterization of disease (LAD / LCx ostial involvement, Ca,.....)
-IVUS may be used to guide LM PCI = Improves outcomes

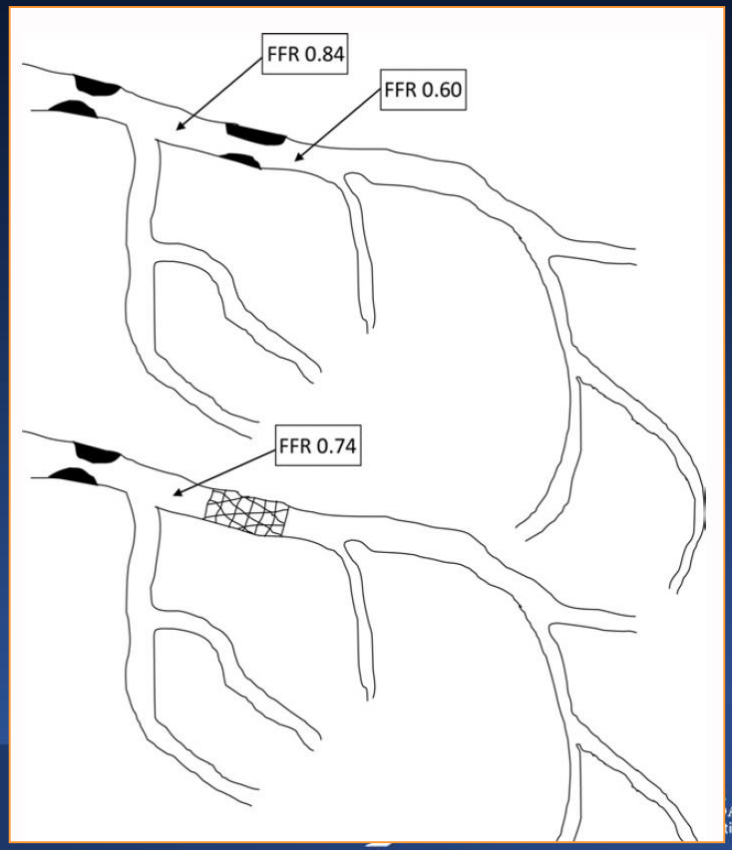









IVUS = No disease (artifact)
FFR = No significant lesion

No reliable FFR measurement for LM



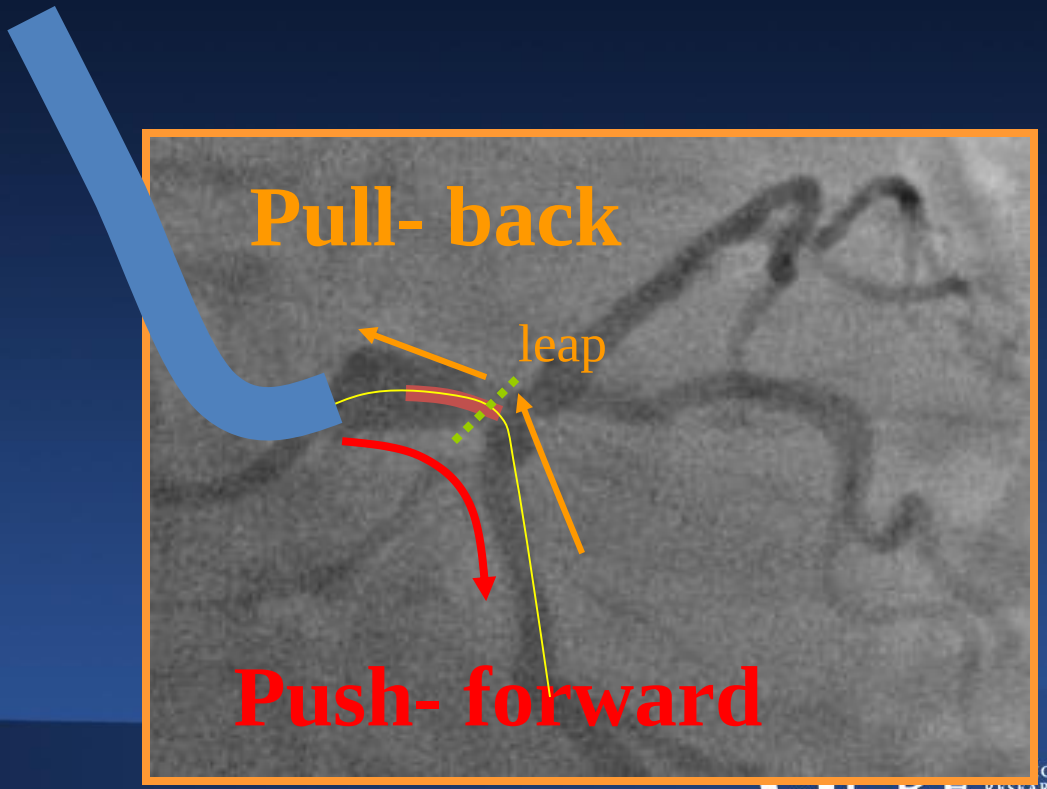




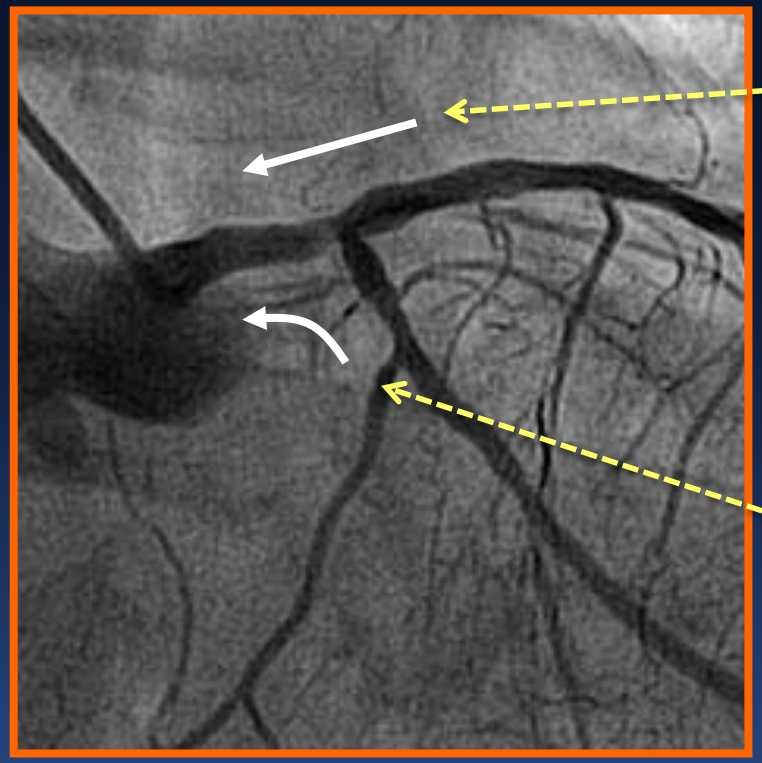
Yong AS, et al.
Circ Cardiovasc Interv C. 2013;6:161-5

¡ Missing the MLA in the automatic and manual pull-backs due to leaps ¡

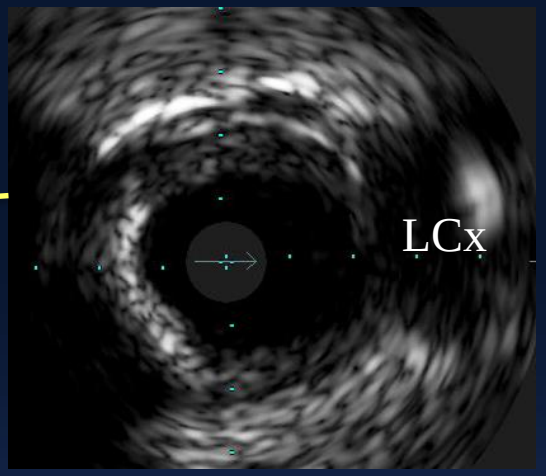
(Alternative gentle push-forward)

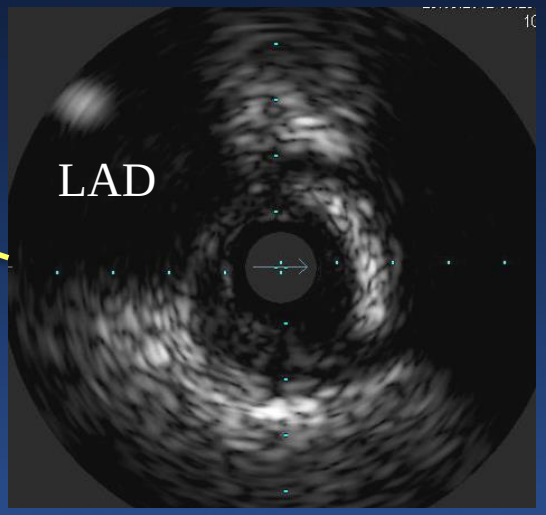


Perform both pull-backs (1)
-From LAD to LM
-From LCx to LM



Ostial LAD
MLA = 7 mm2





Ostial LCx
MLA = 3.2 mm2

(1) Oviedo et al. Am J Cardiol 2010;105:948-54

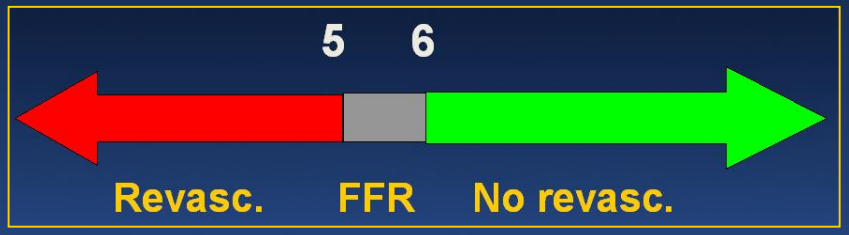
When IVUS and when FFR in basal LM assessment

Preference for FFR and secondarily IVUS in:

Isolated ostial or midshaft lesions in pts more appropriate candidates to CABG

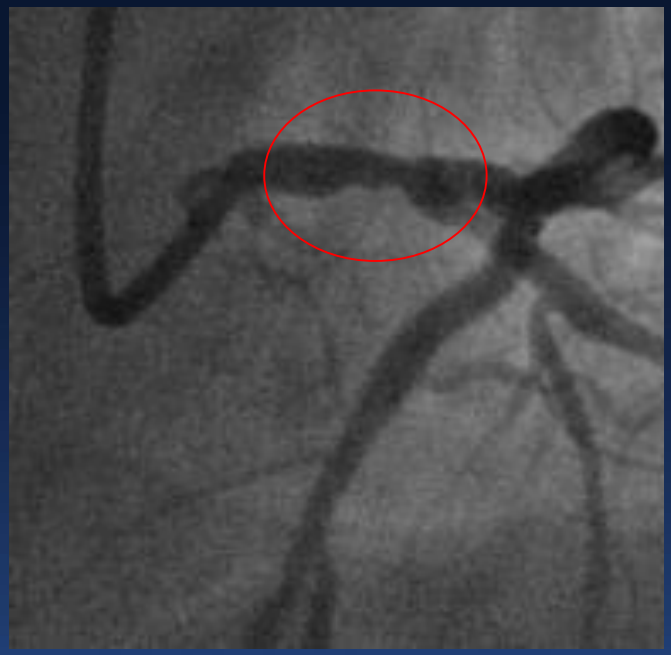
Preference for IVUS in:

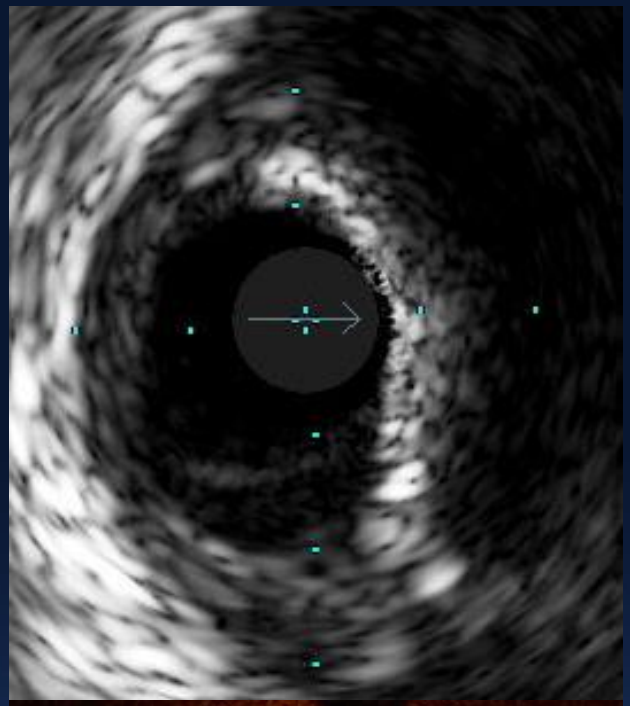
Distal-bifurcation lesions
Presence of significant lesions in LAD and/or LCx
Likely candidates to PCI



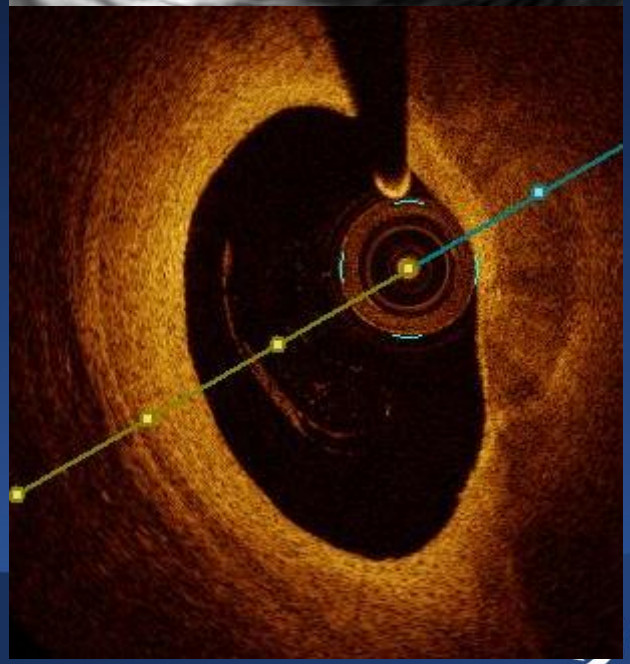
Patients are not numbers
MLA or FFR should be added to a multifactorial clinical decision process

¡ Cut-off to be defined by OCT ¡





MLA =6.3 mm2



MLA = 5.1 mm2

The “double value” of IVUS

LM

intermediate lesion

Severe lesion

IVUS

Significant

FFR

CABG

PCI

IVUS

Indication for plaque modulation techniques

Calcification in angiography:

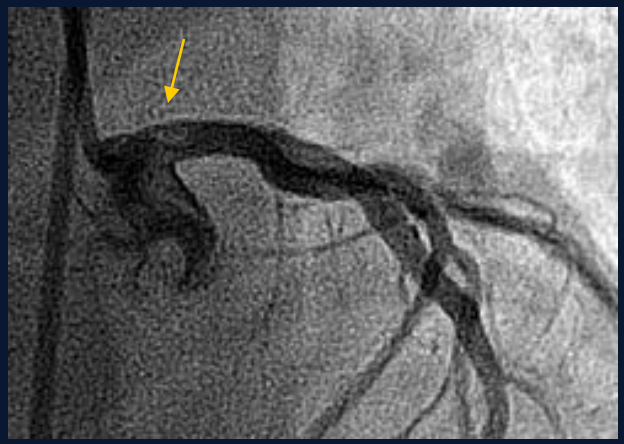
Assessement of extension, distribution and severity

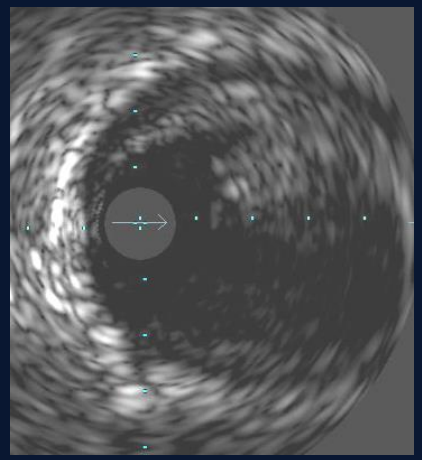
-Need for Rotational ablation

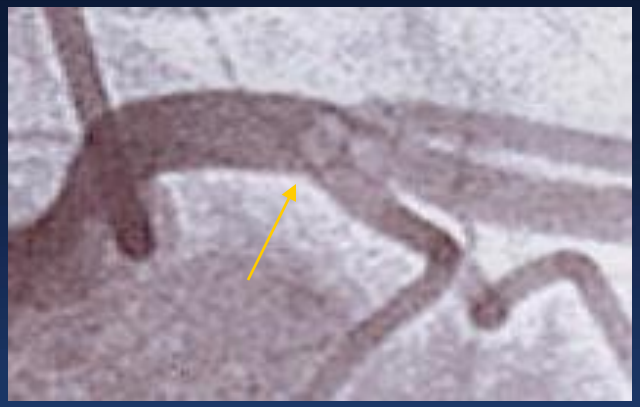
Contrast filling defects in unstable patients:

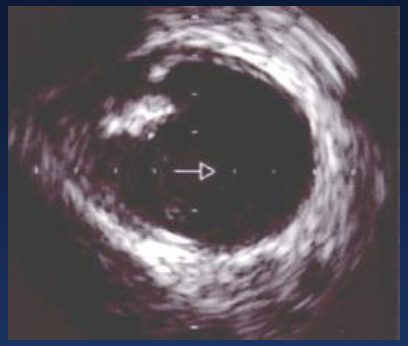
Diferential diagnosis between calcium, thrombus, plaque rupture

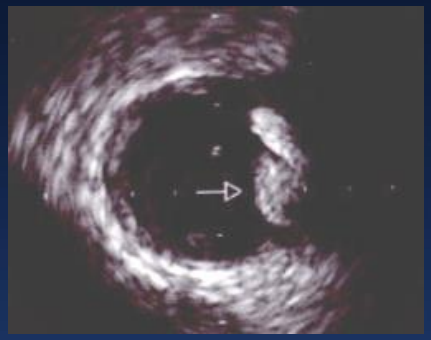
-Need for aspiration thrombectomy

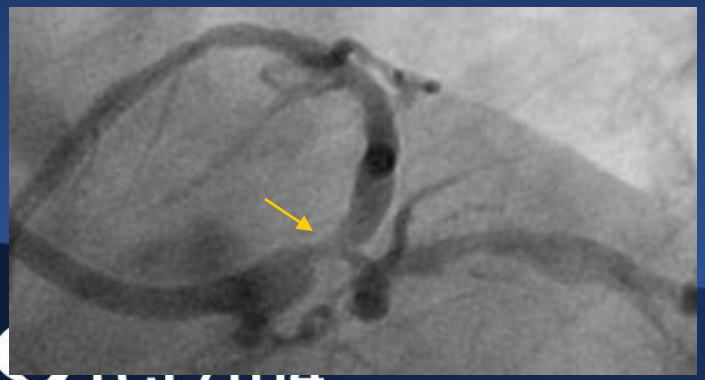


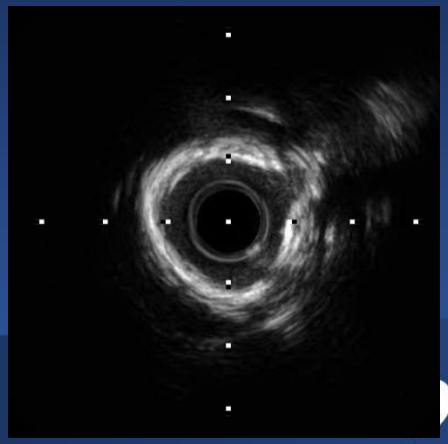




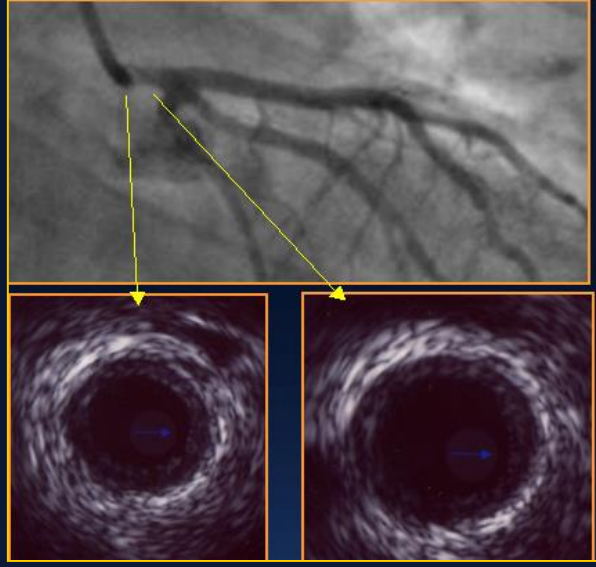








Ostial and mid-shaft lesions



Stent length and diameter selection

Lesion: Focal in angiopghraphy and diffuse in IVUS.

Appropiate indication of stent landing sites (preventing stent edges problems: dissection, hematoma, large residual plaque,....)

Some ostial stenosis can be related with pathologic and extreme constrictive remodelling (IVUS allows safe stent sizing or indicates CABG)

In mid-shaft lesions is adequate to know the LM lenght to be covered by the stent

- -To reach aorto ostial junction or not depending on plaque burden at ostium
- -To reach ostial LAD or not depending on plaque burden at distal LM

Distal lesions: *(more frequent and more challenging)*

Provisional stenting vs. 2 – stents technique:

-**Assessment of ostial LAD and ostial LCx compromise**

-**If MLA in LCx is > 3.5 - 4 mm² then provisional could be done safely**
Kang et al. Cath Cardiovasc Interv 2014;83:545-52

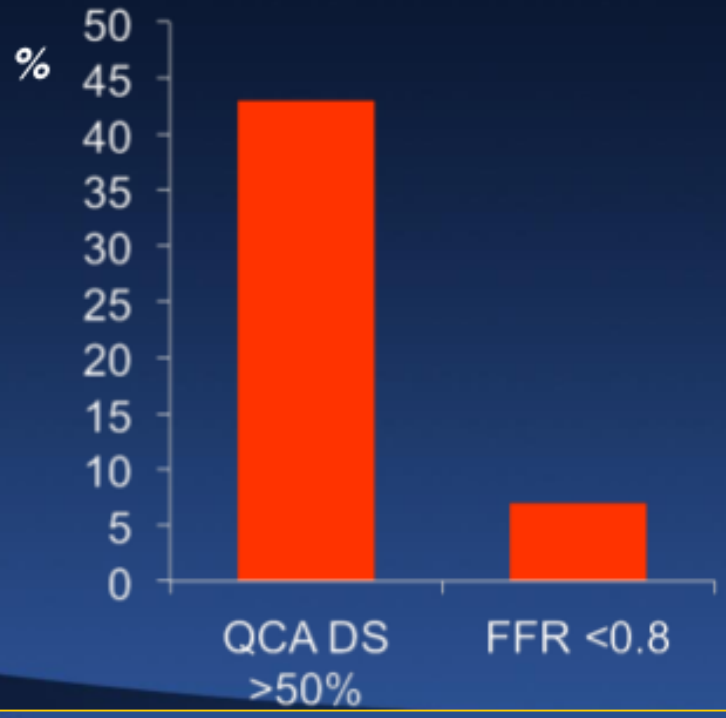
-**Lumen loss at the LCX ostium frequently occur after crossover stenting from LAD to LM (median ↓1.4 mm²)**
Kang SJ et al. Circ Cardiovasc Interv. 2011;4:355-61

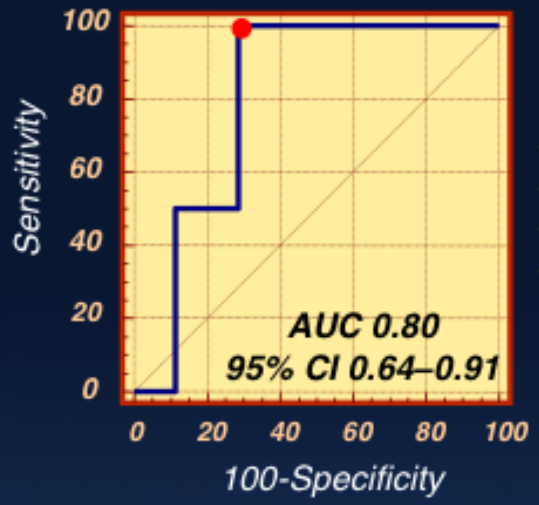
-**Stent sizing** (stent landing sites and lesion to be covered)

What 2-stents technique is more suitable and stents sizing:

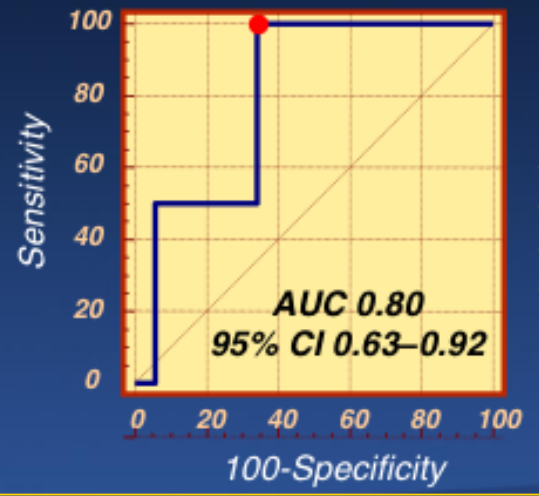
-Wide lumen in shaft, both ostial LAD and LCx significantly diseased: ***V kissing***
-Angulation of LCx respect to LAD: ***T or Culotte stenting***

43 LMCA bifurcation lesions with a pre-PCI LCX ostial DS<50% were treated by single-stent cross-over





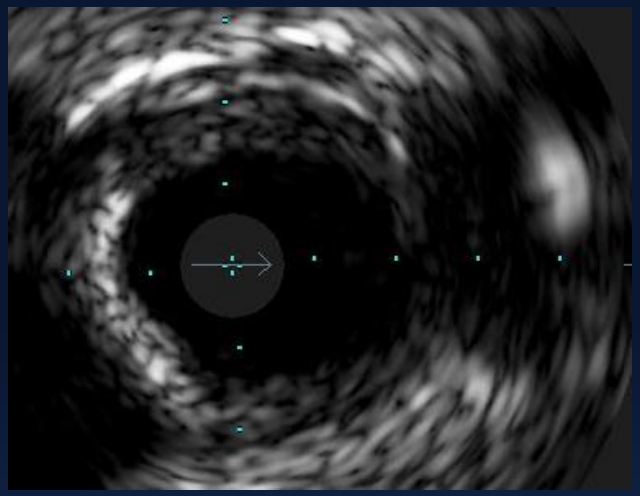
MLA <3.7mm²
- Sensitivity 100%
- Specificity 71%
- PPV 16%
- NPV 100%

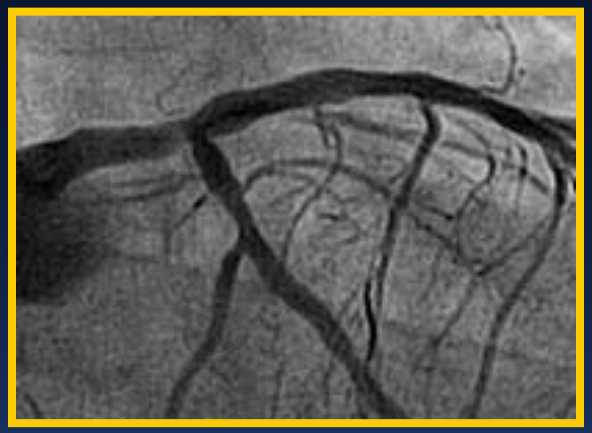


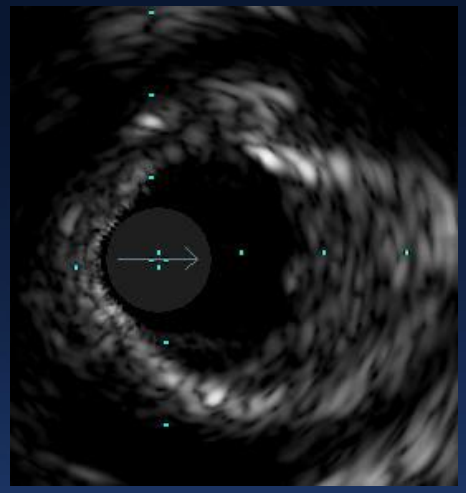
Plaque Burden >56%
- Sensitivity 100%
- Specificity 65%
- PPV 14%
- NPV 100%

Kang et al. Cath Cardiovasc Interv 2014 ;83:546-52

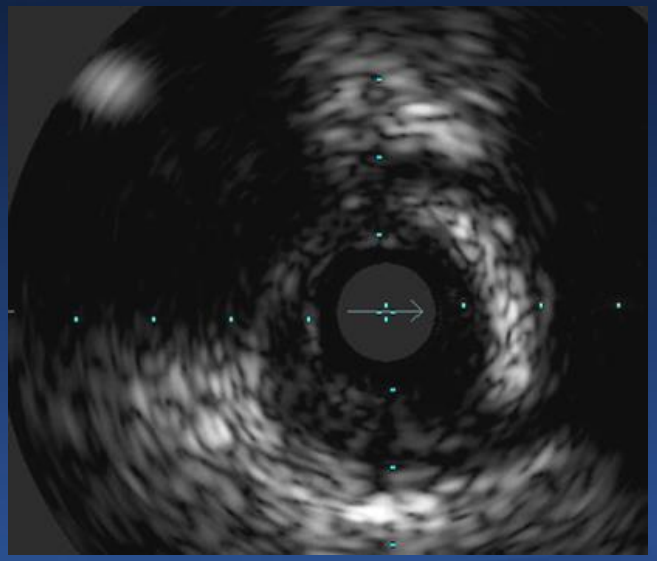
ostial LAD
MLA = 7 mm^2







LM-MLA = 4.7 mm^2



ostial LCx
MLA = 3.2 mm^2

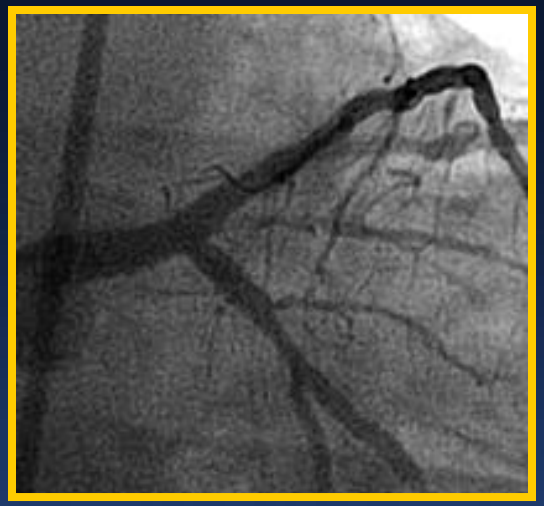
Two stents - T stenting

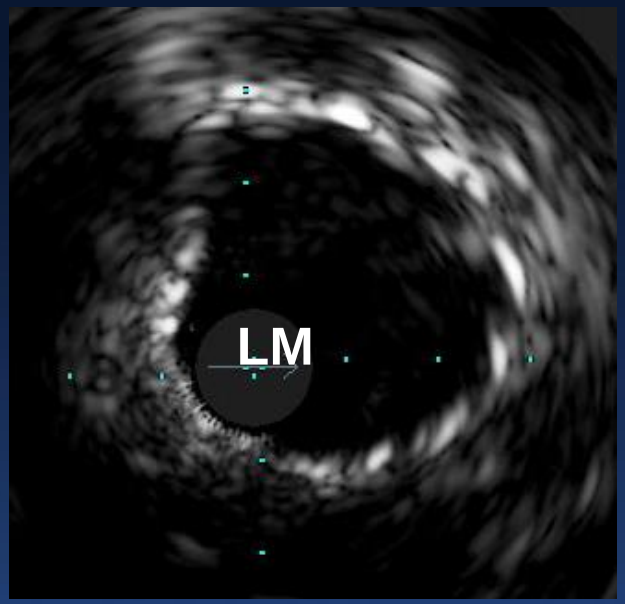
LM-LAD DES 3.5 / 15

LCx DES 3 / 12

Final kissing balloon

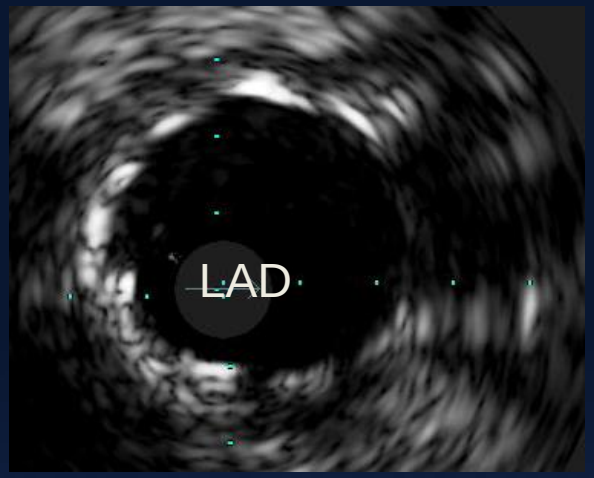
LM ostium-mid shaft dilated 4 mm

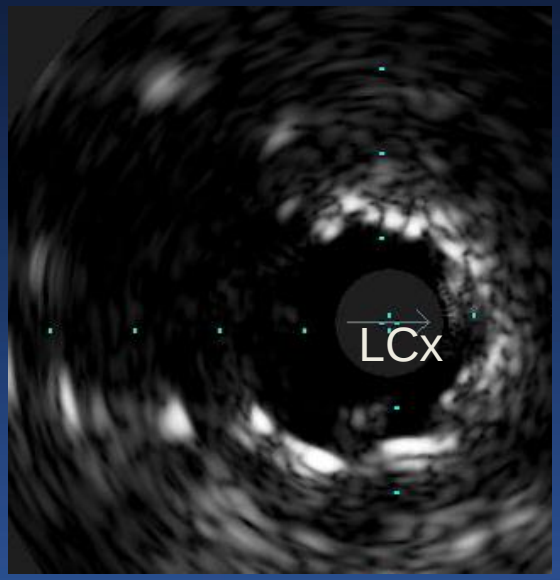




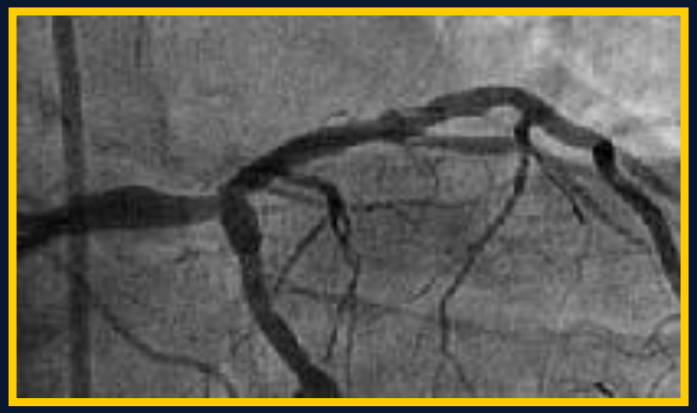
LM-MSA = 11.3 mm^2

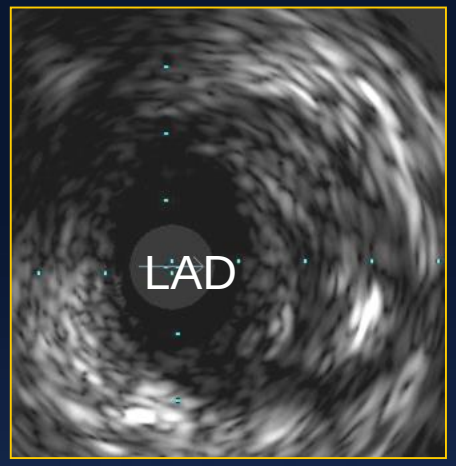
LAD-MSA = 9 mm^2

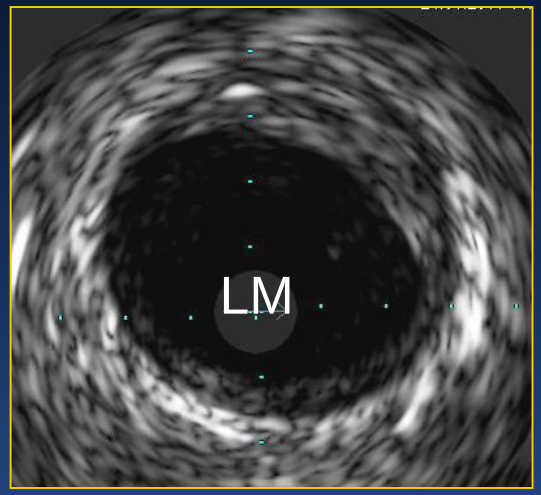


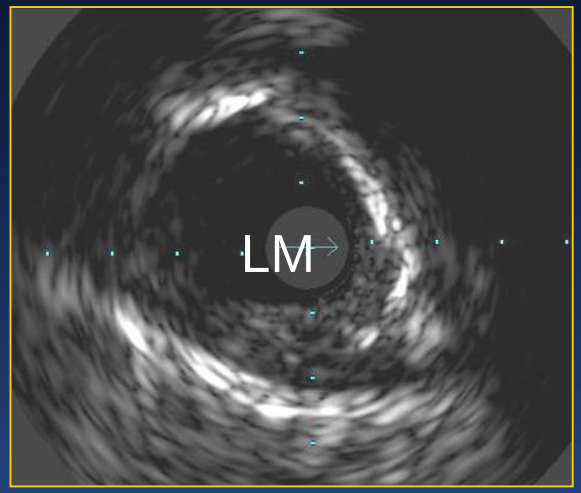


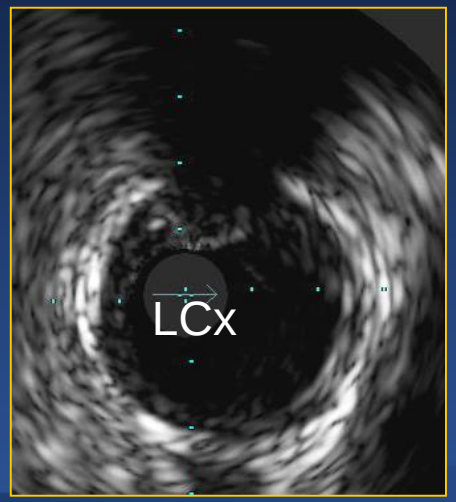
LCx MSA = 6 mm^2

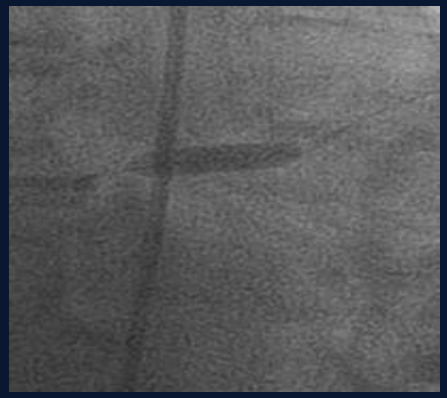



LAD


LM


LM

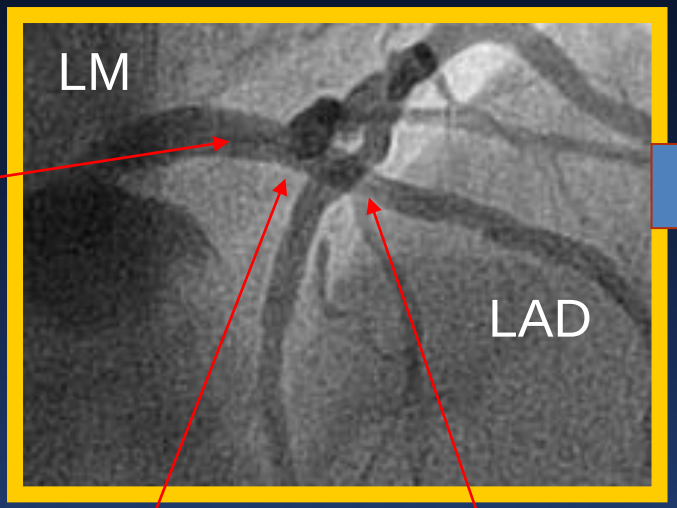

LCx



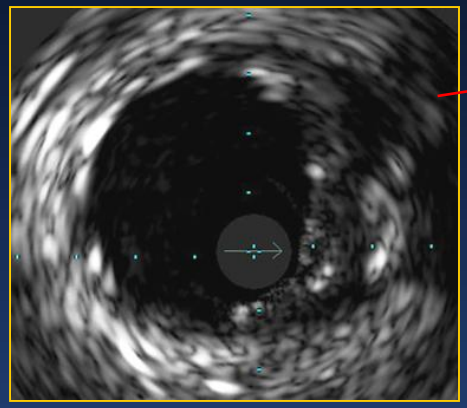
DES from LAD to LM

3.5 / 20 mm

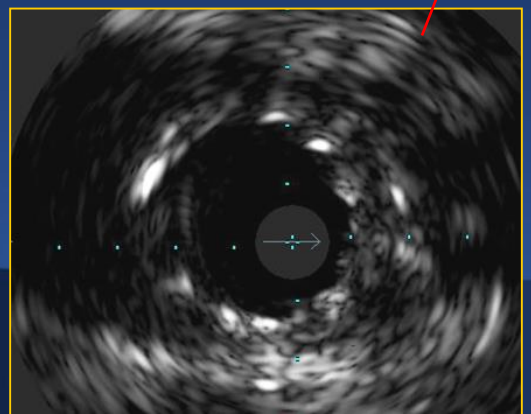
Post dilated proximally 4 mm

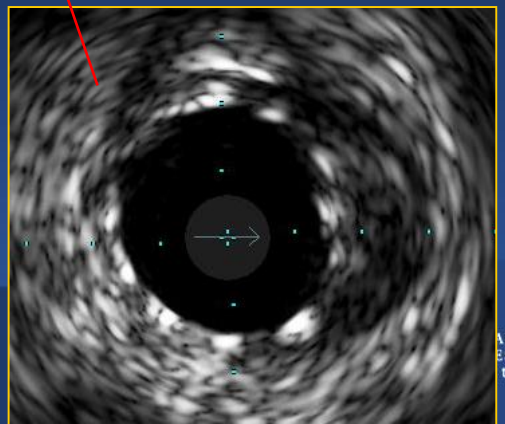


FFR > 0.9 in LCx

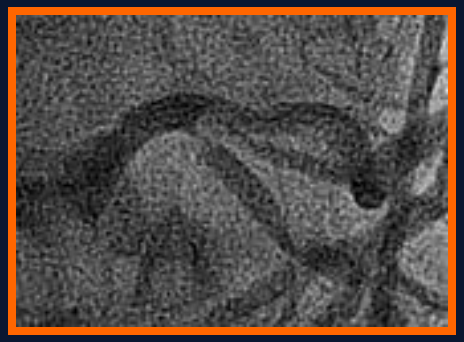


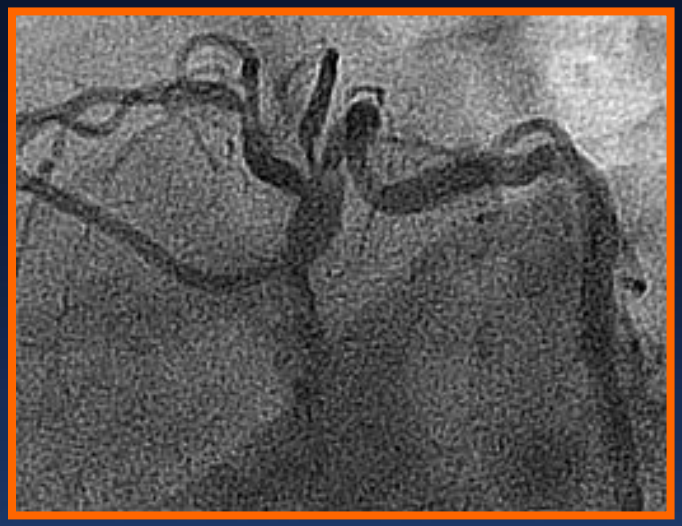
MLA 12.2 mm^2





MLA 8.3 mm2

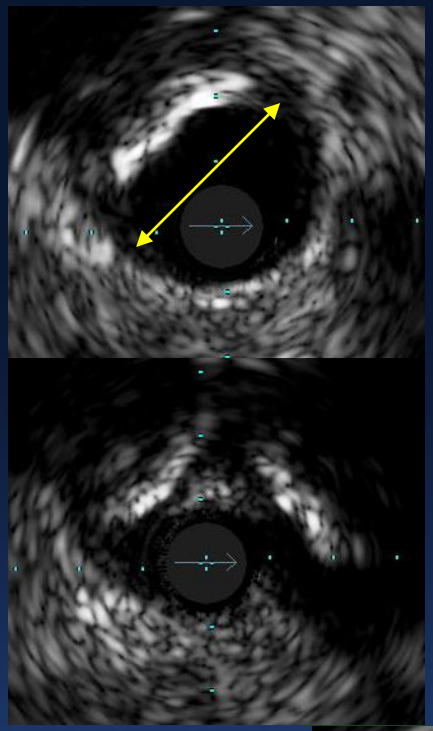




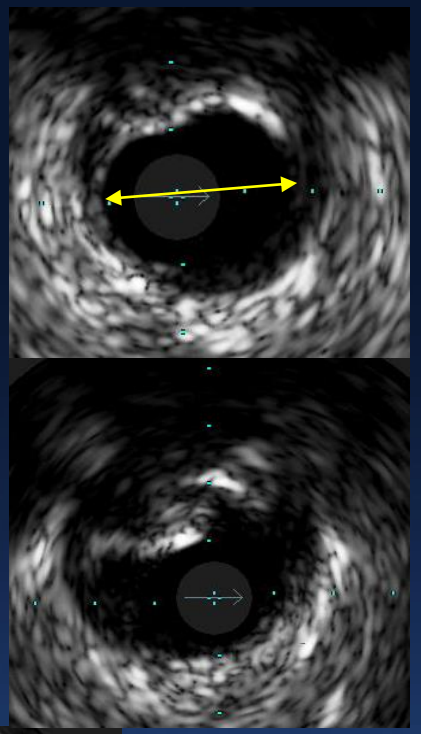
“Landing zones”

LAD

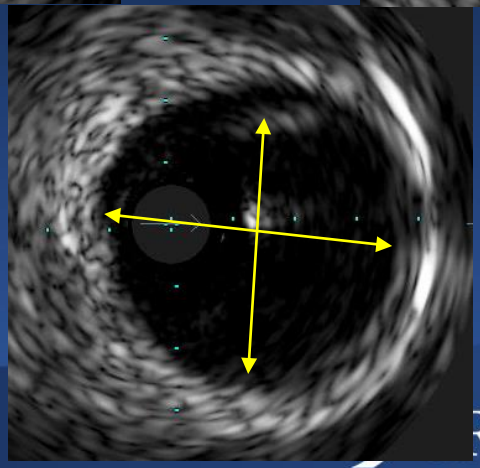
LCx



3 mm

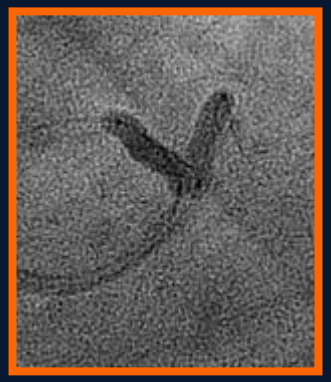
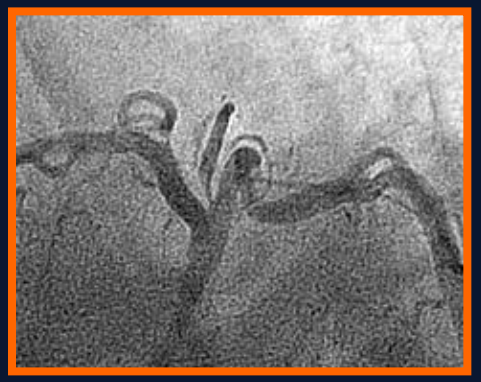
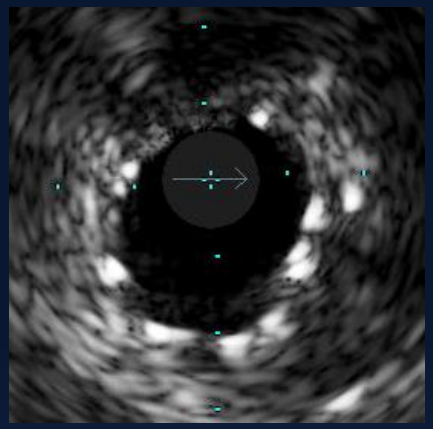
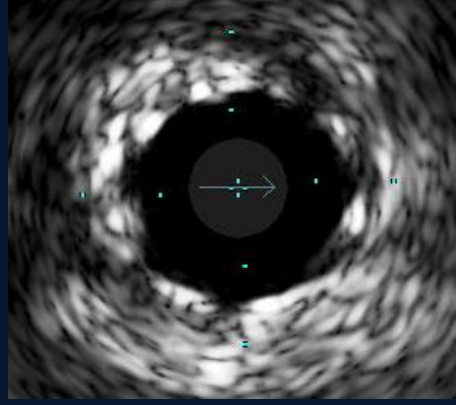
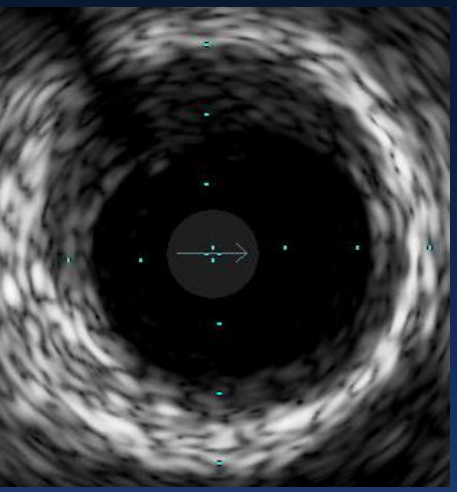
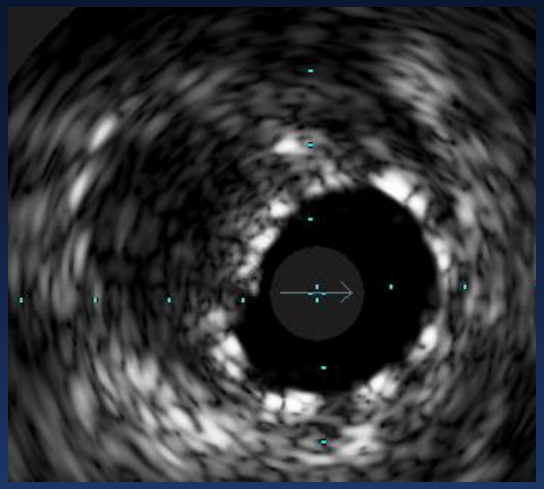
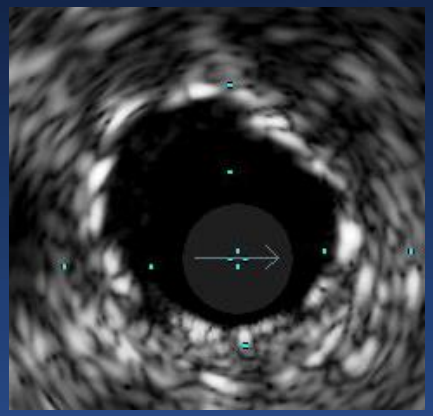
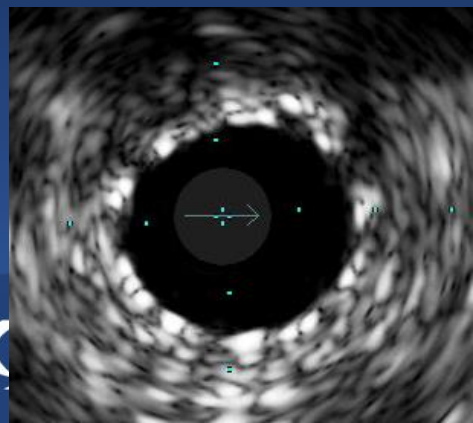


LM



“Landing zone”

4 - 4.5 mm

LM-LAD DES 3/18 mm
LM-LCx DES 3/15 mm

Evaluation and optimization of stenting

Adequate lesion coverage (i.e. to reach aorta in ostial lesions)

Edge problems:

Incomplete apposition (common in cross-over stents from LAD to LM), hematoma, dissection or large plaque burden

Stent expansion

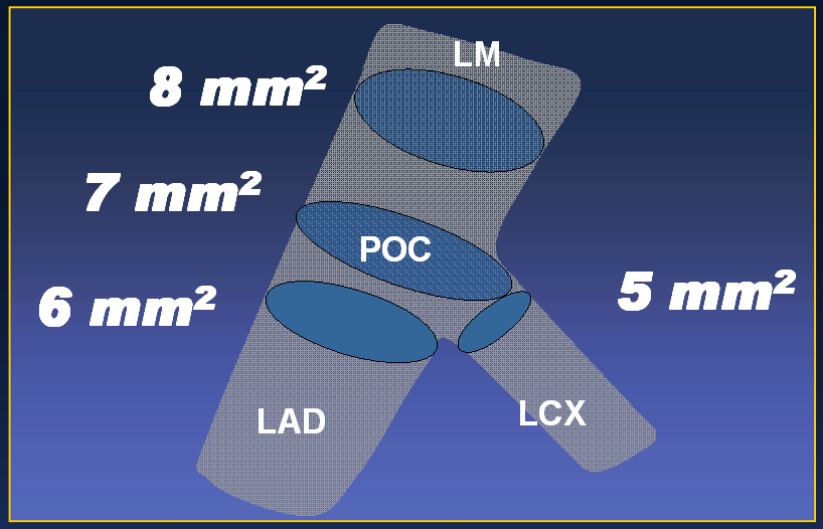
Subexpansion frequent in heavily fibrotic ostial lesions.
In distal lesions:
The MSA cutoffs that best predict ISR on a segmental basis are *:
5.0 mm^2 (ostial LCX), 6.3 mm^2 (ostial LAD), 7.2 mm^2 (POC) and 8.2 mm^2 in prox LM

LCx ostium in provisional stenting (from LAD to LM)

If FFR > 0.8 or MLA > 3.5-4 mm^2, no additonal stenting needed

*Kang SJ. Circ Cardiovasc Interv. 2011;4:562-9.

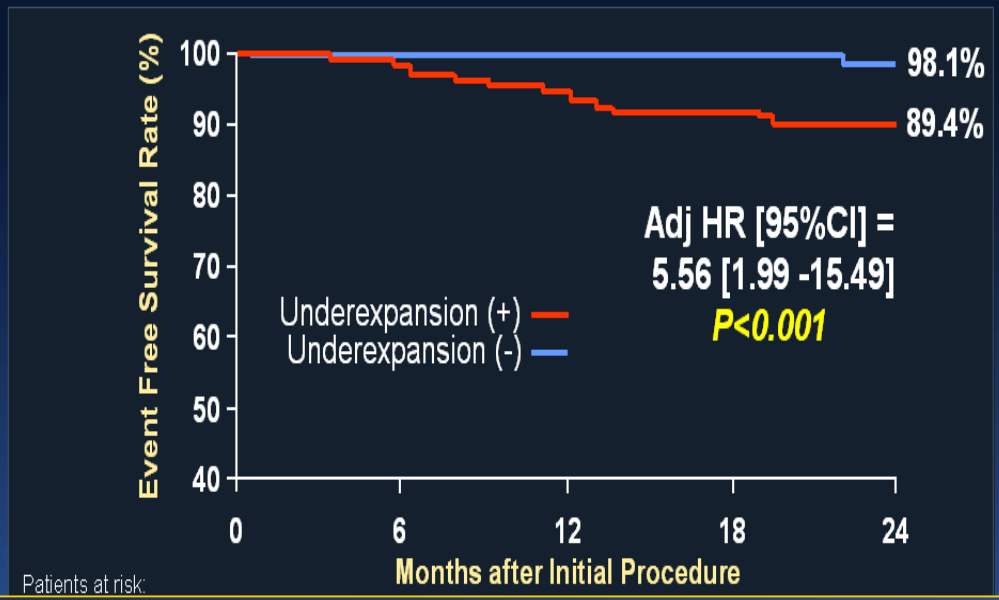
The MSA cutoffs that best predict ISR in LM



403 pts
9 months angio follow up

TLR-free survival was lower in pts with underexpansion vs. no underexpansion (90.9% vs 98.5%)

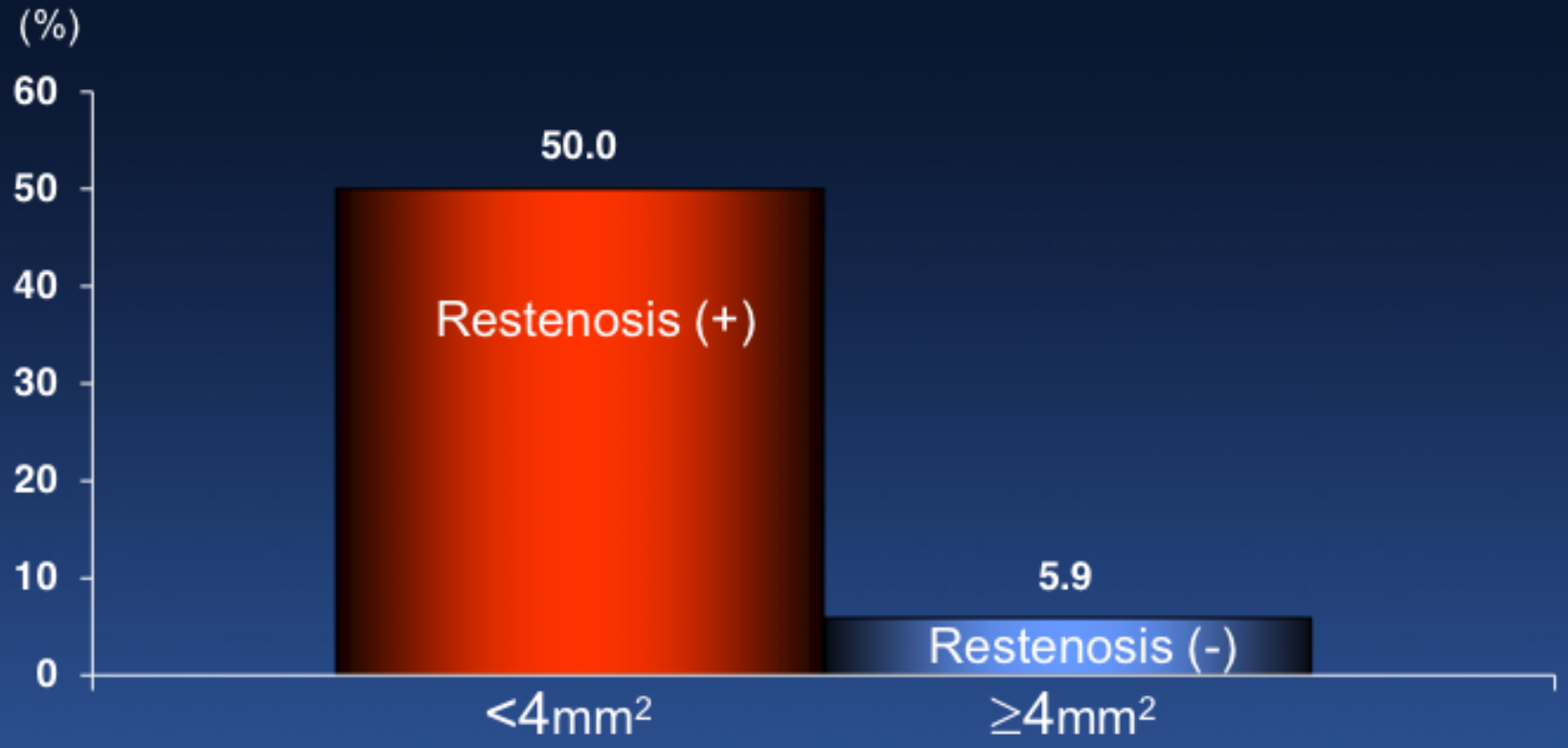
133 pts (33.8%) had underexpansion of ≥1 segment



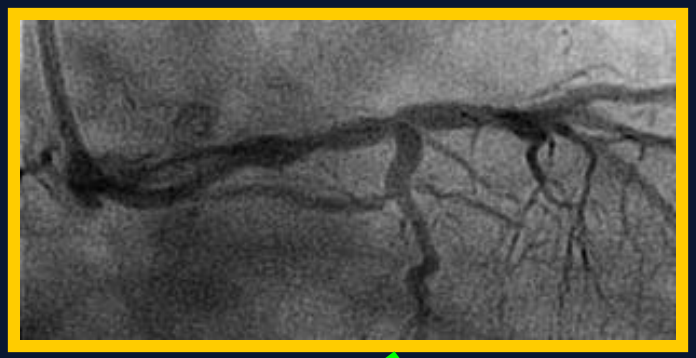
Kang SJ. Circ Cardiovasc Interv. 2011;4:562-9.

Predictor of Restenosis in Ostial LCX with both LAD/LCX IVUS Evaluation

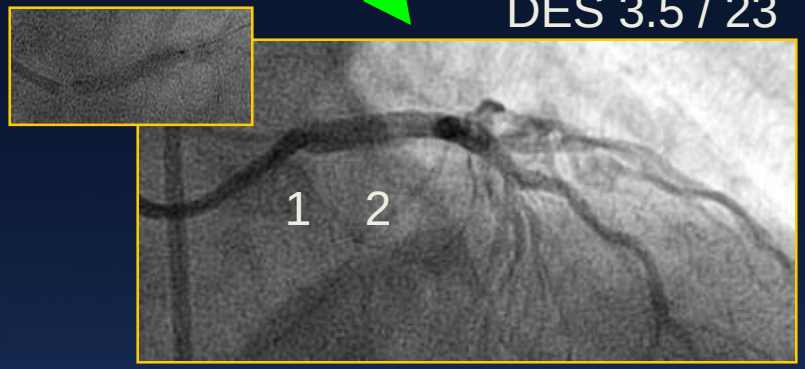
Post LCX Minimum Lumen Area

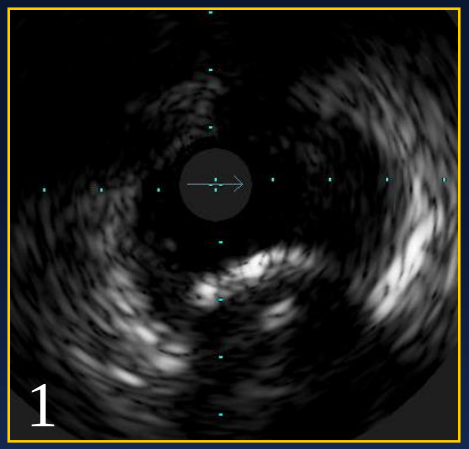


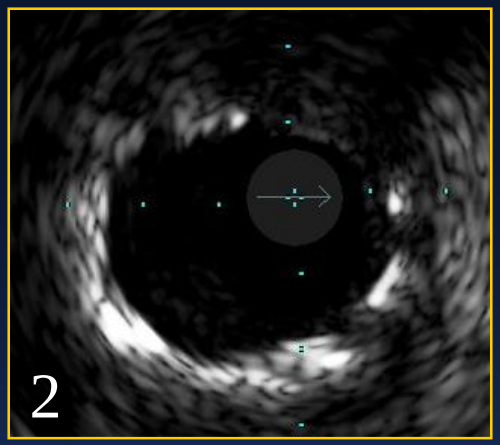
He Y et al. AHA 2009



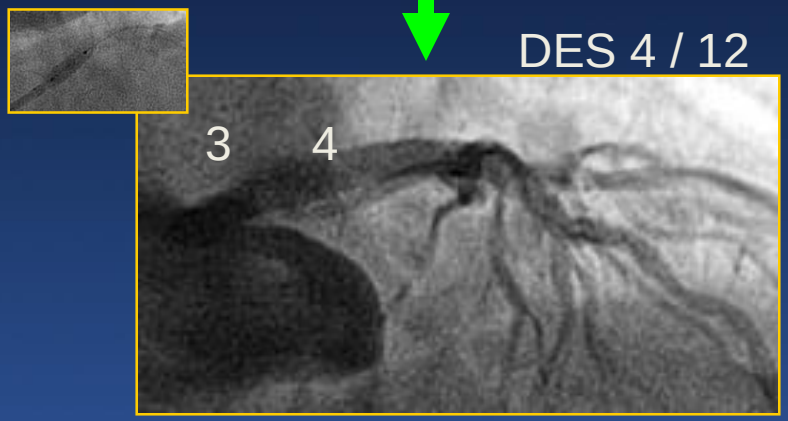
DES 3.5 / 23

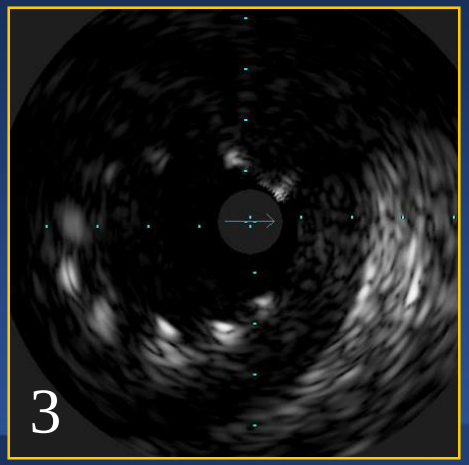


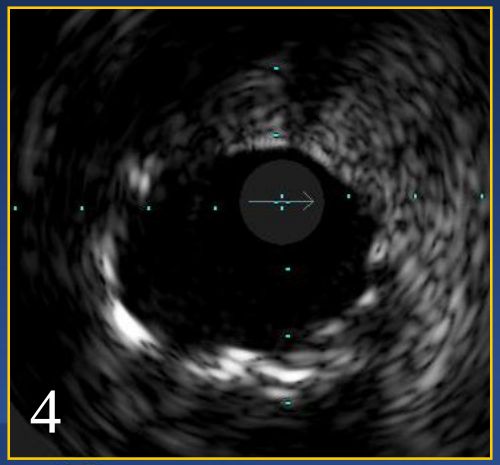




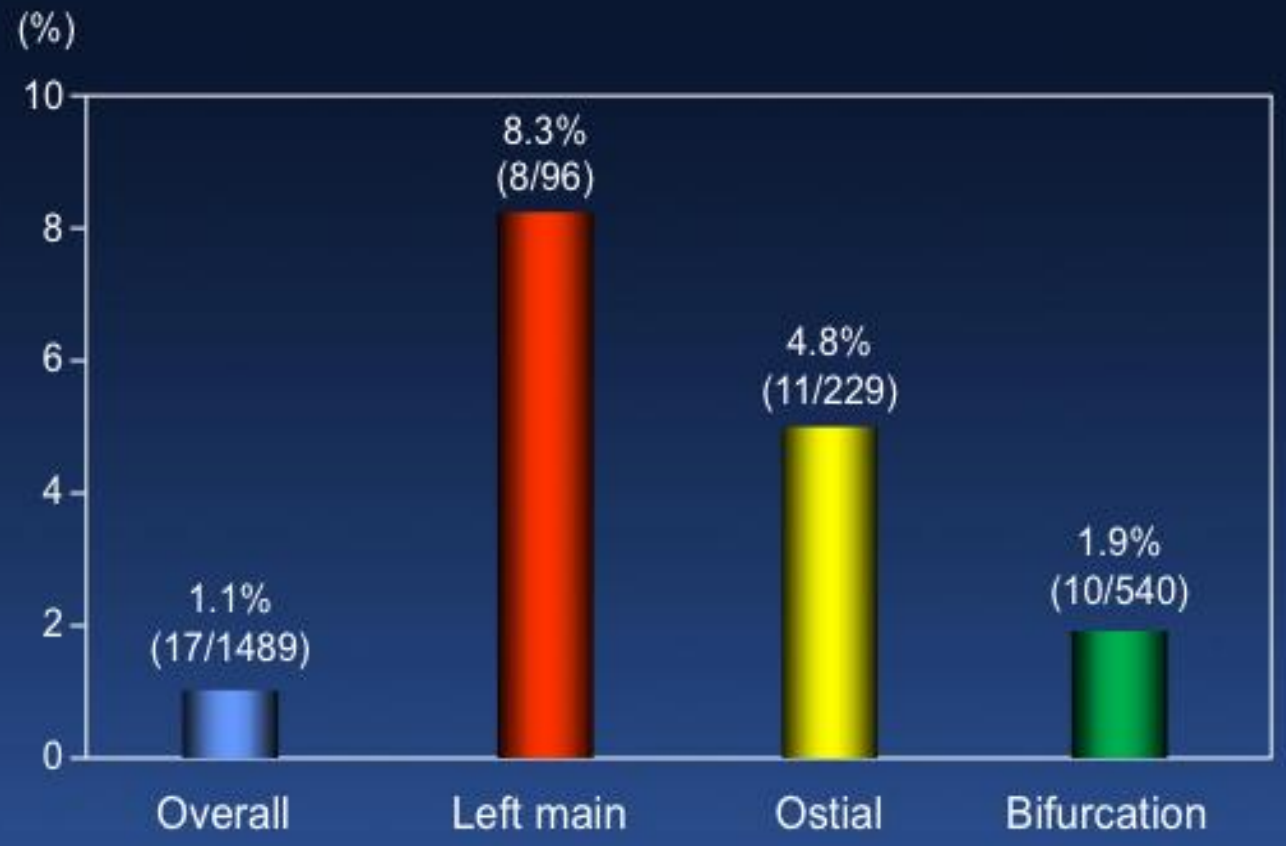
DES 4 / 12



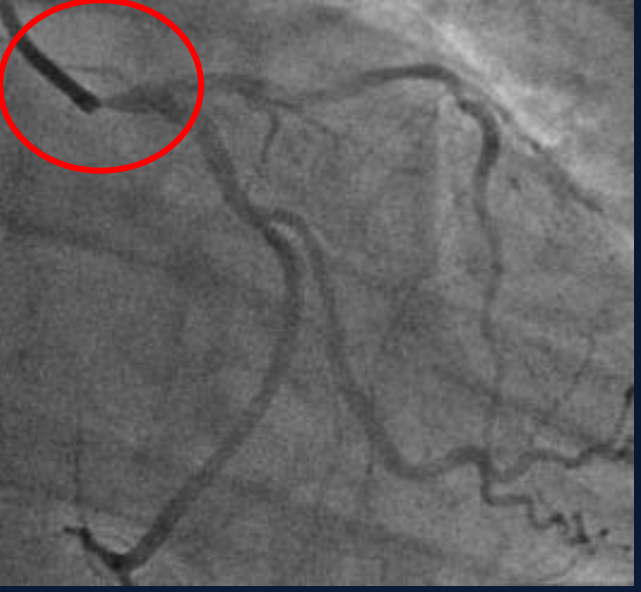




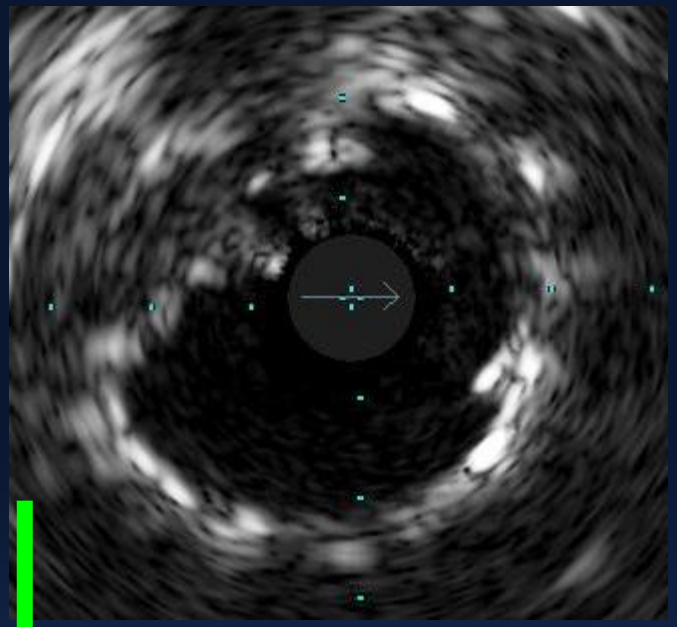
Incidence of Stent Deformation

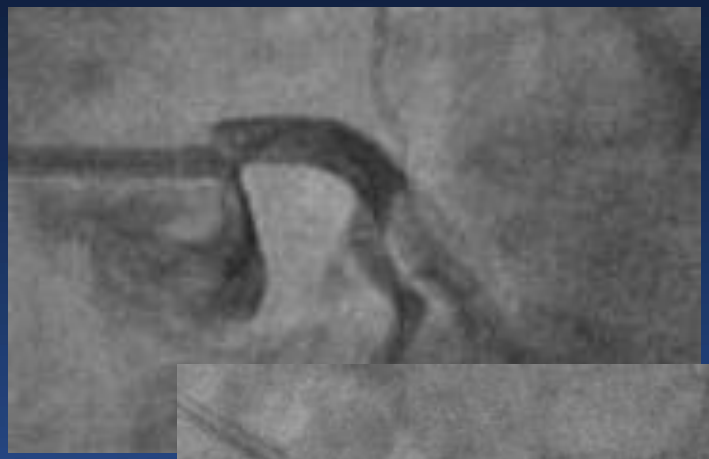


Inaba S, et al. CCI 2014

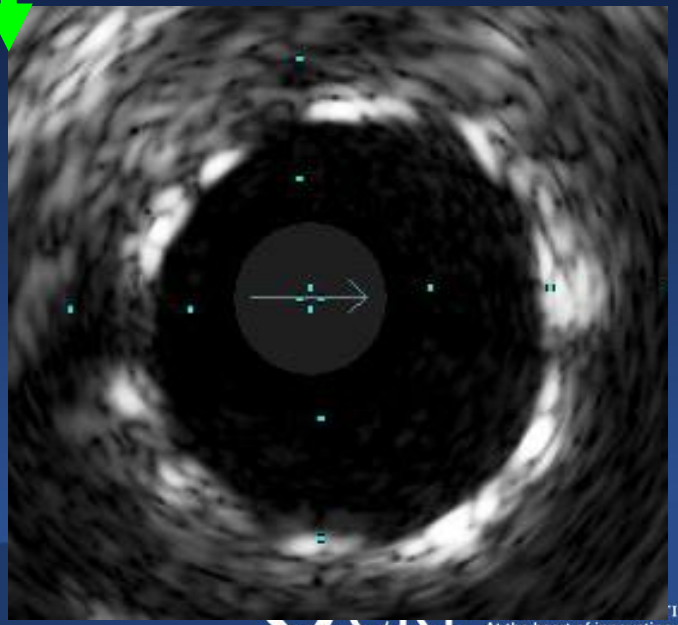


DES 3.5 / 12

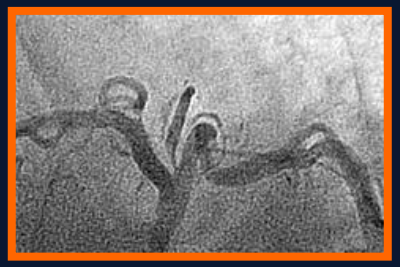


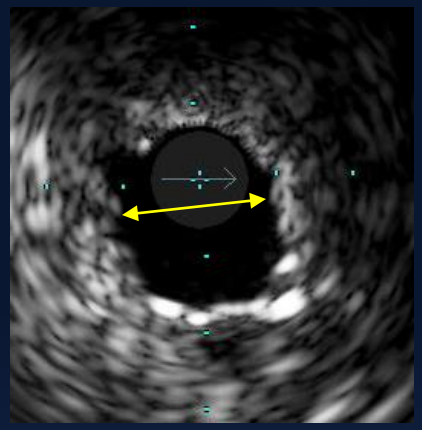


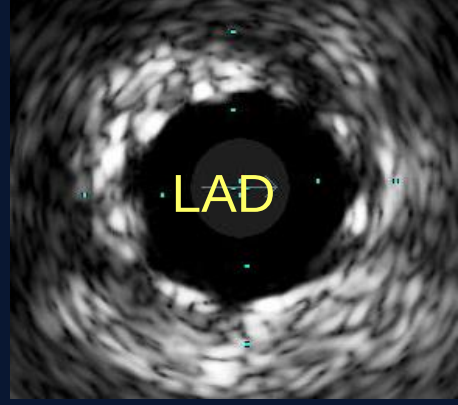
Postdilatation
4 mm

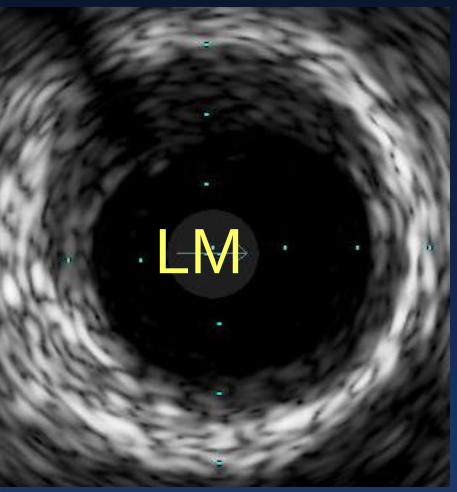


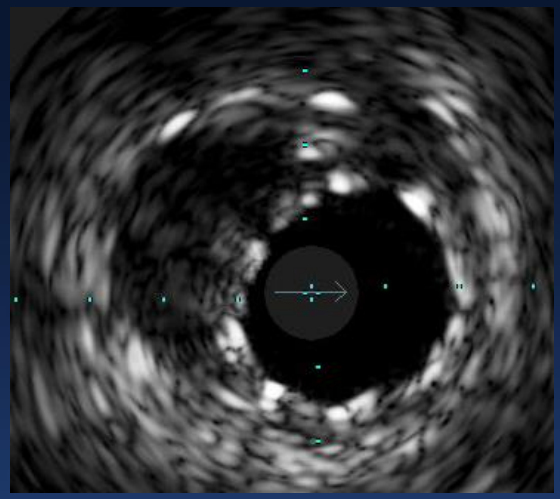
After stent implantation



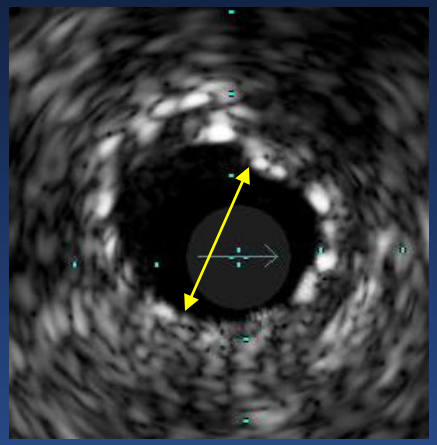




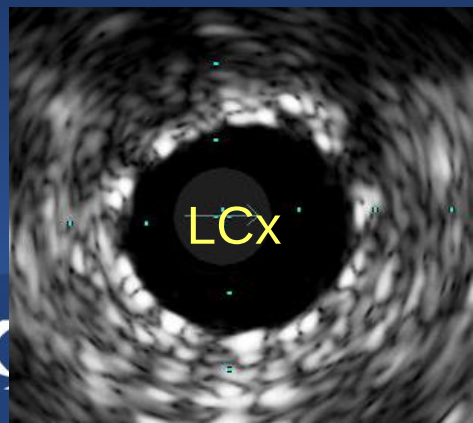




MLD = 2.3 - 2.5 mm

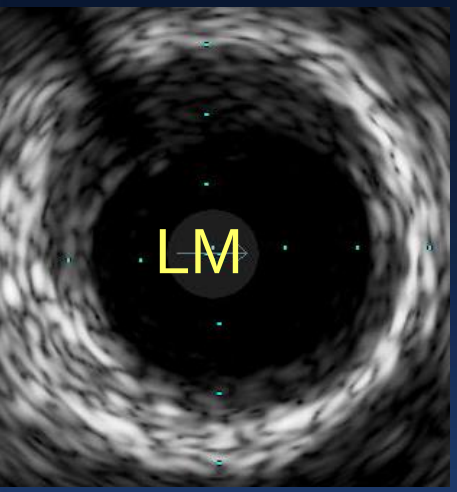


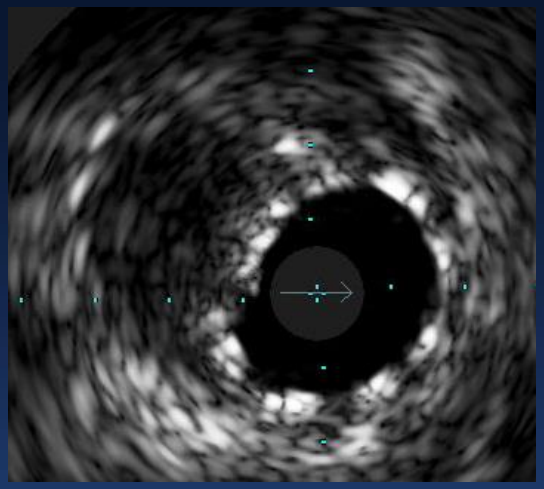
LM-LAD DES 3/18 mm
LM-LCx DES 3/15 mm

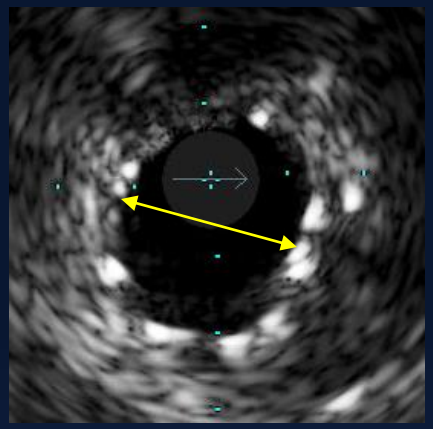


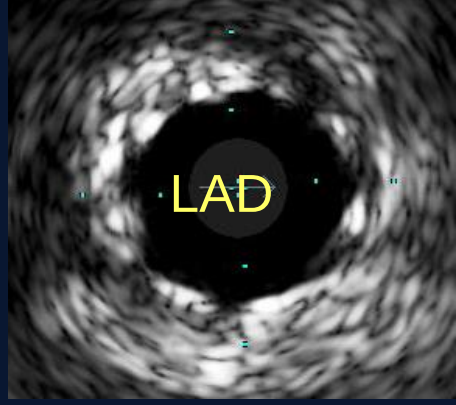
Postdilatation

Twin layer balloon 3 mm
at 24 atm sequential and
final kissing

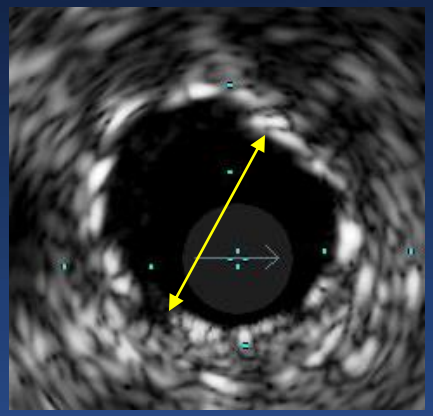


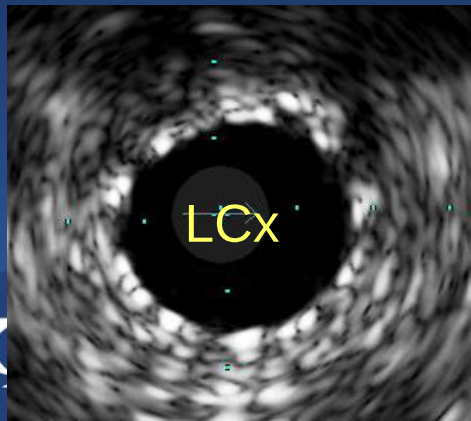






MLD = 2.7 - 2.9 mm

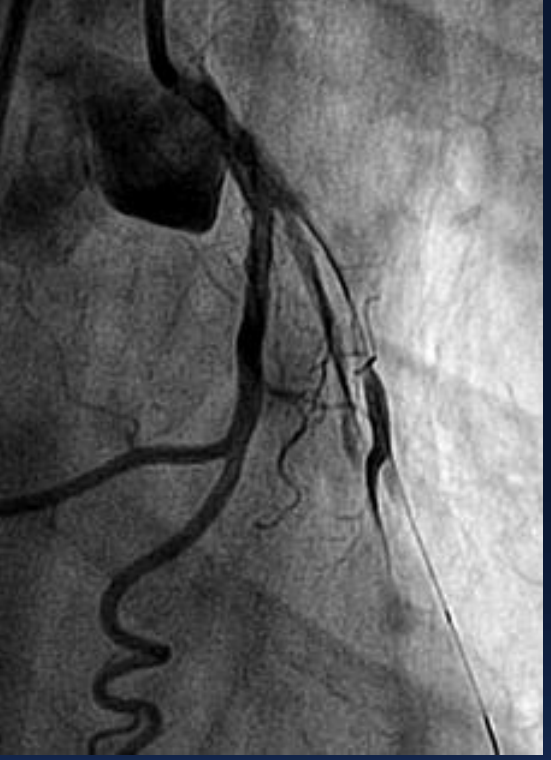


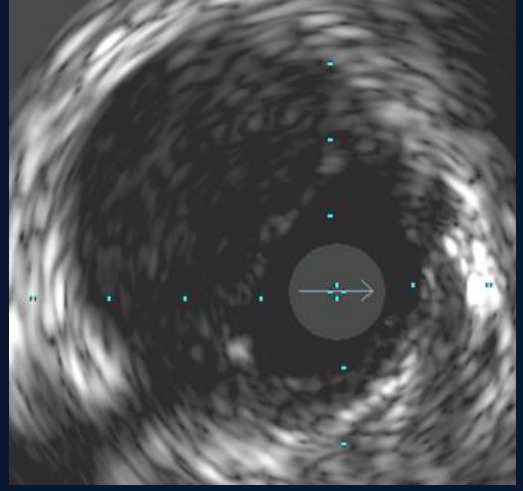


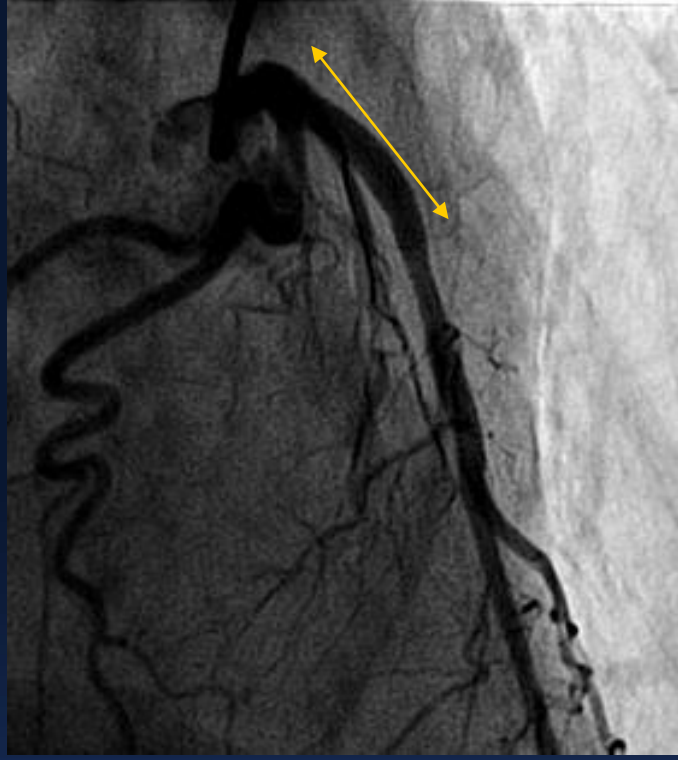
Complications

IVUS

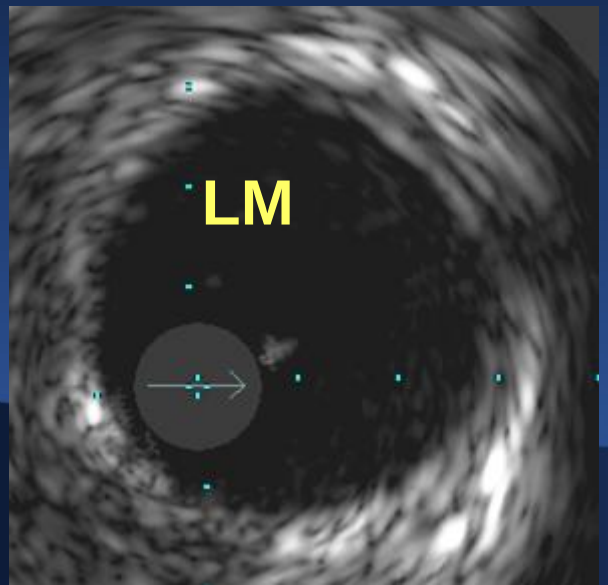
identifying and solving

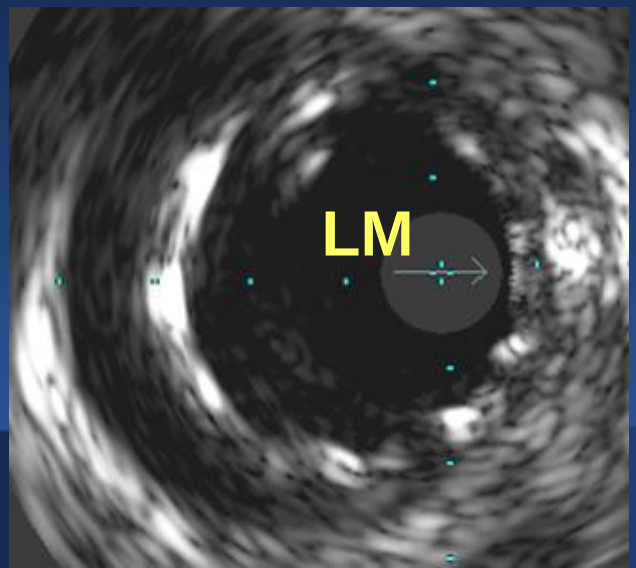




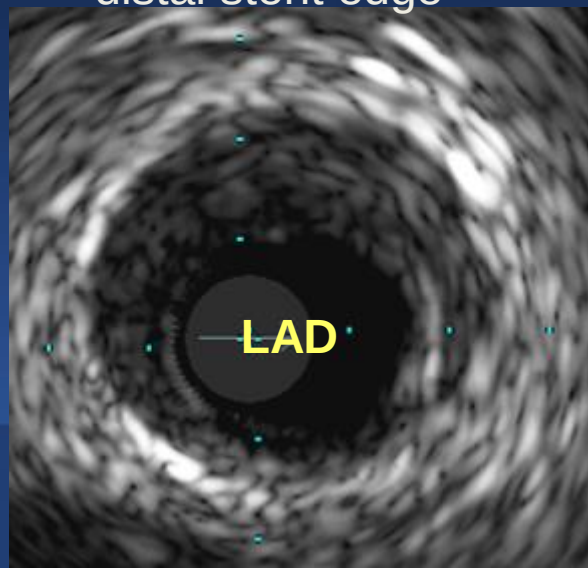


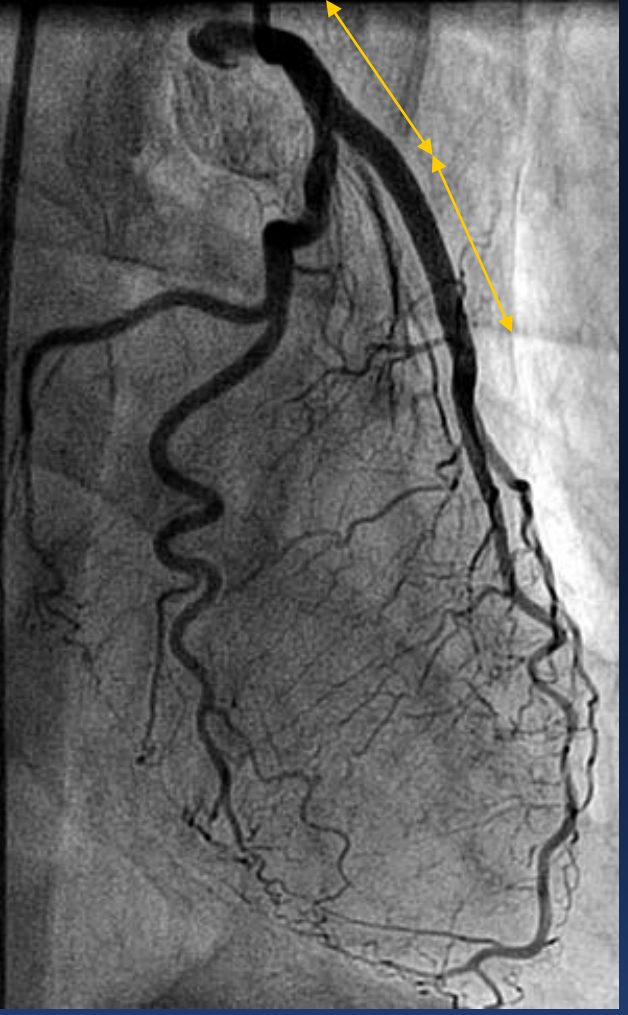
DES 3.5 / 24 in LM





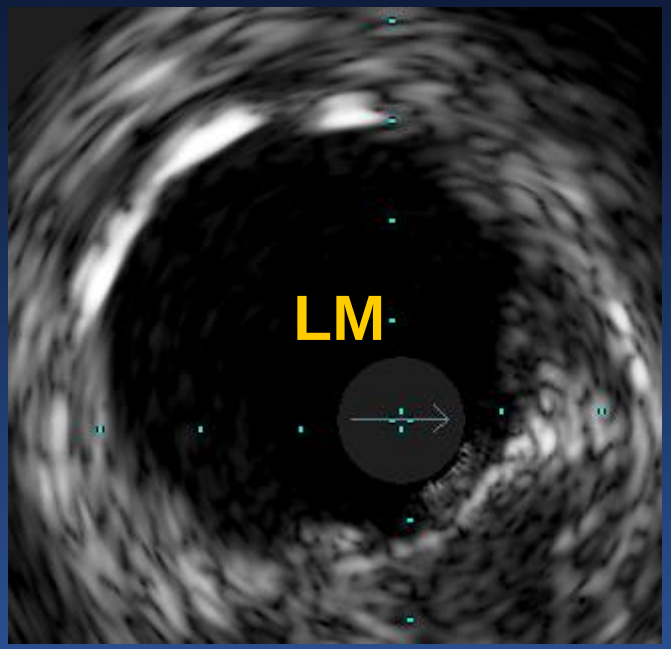
distal stent edge



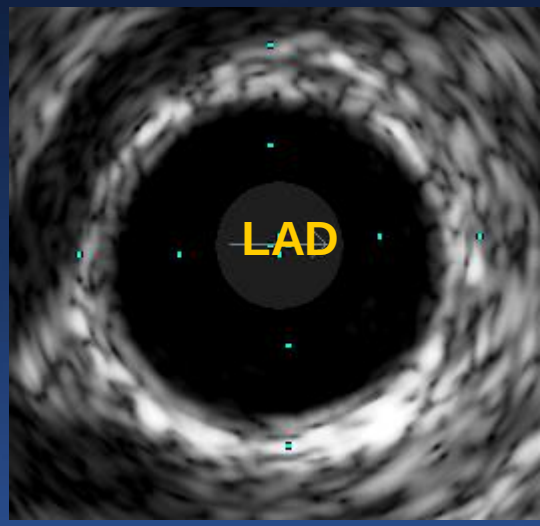


DES 3 / 18 mm in LAD just distal to the 1st stent
Postdilatation with 3.5 mm in the gap.

Postdilatation at LM level with 4.5 mm^2

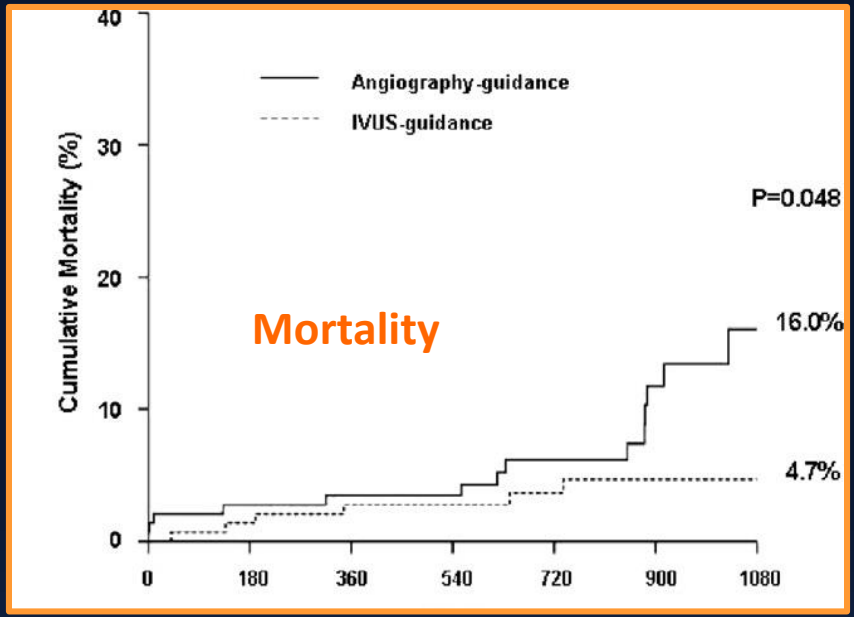


distal stent edge

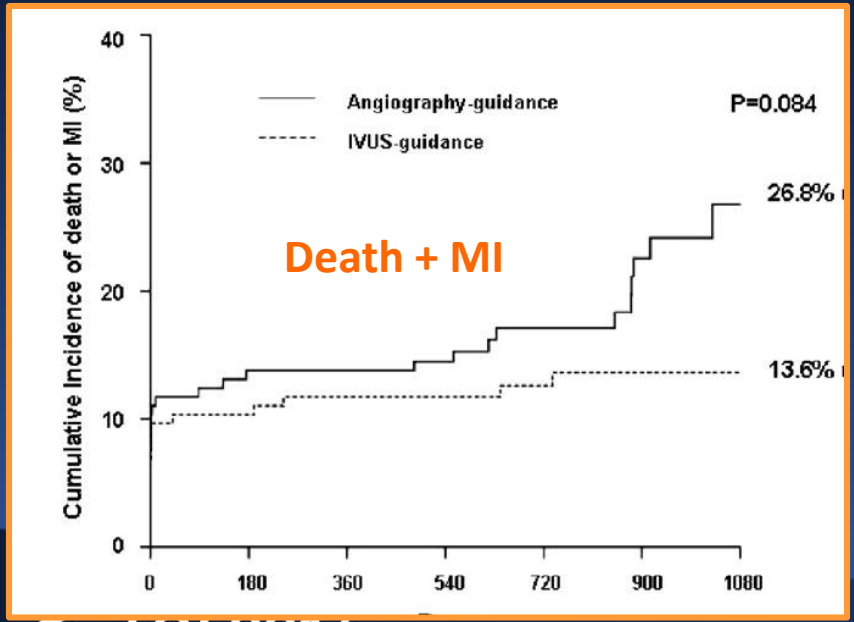


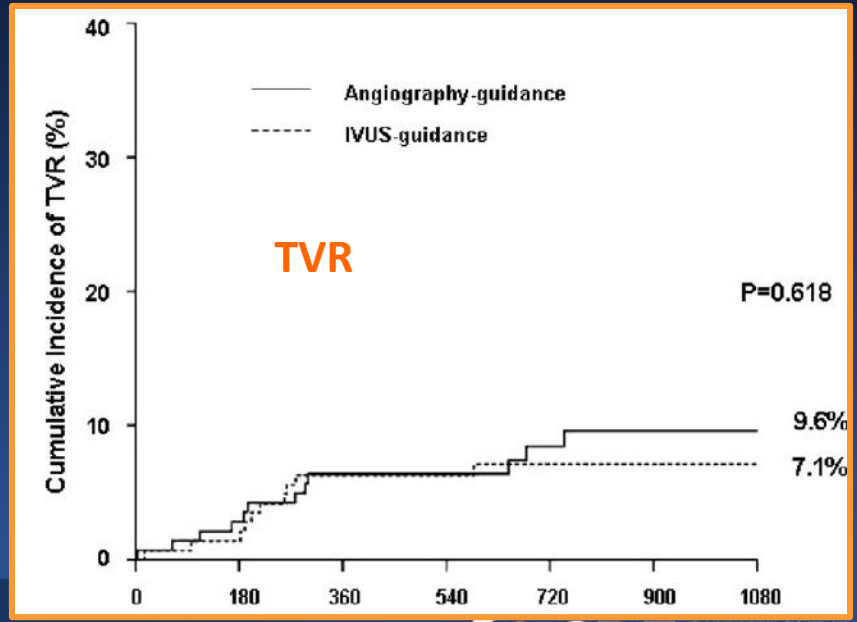
The Korean experience

Outcomes in 145 propensity-matched pairs of patients receiving DES with and without IVUS guidance



IVUS guidance associated to lower long-term mortality





Park S et al. Circ Cardiovasc Interv 2009;2:167-177

Limitations

Small groups (145 pts vs. 145 pts)

Very high use rate of IVUS in LM PCI (77%)

Difference in *late all-cause mortality* (beyond the 3rd year)

-High probability for unmeasured confounders

No cardiac mortality data

No stent thrombosis data

Clinical Impact of Intravascular Ultrasound Guidance in Drug-Eluting Stent Implantation for Unprotected Left Main Coronary Disease

Pooled Analysis at the Patient-Level of 4 Registries

Jose M. de la Torre Hernandez, MD, PHD,* José A. Baz Alonso, MD,†
Joan A. Gómez Hospital, MD, PHD,‡ Fernando Alfonso Manterola, MD, PHD,§
Tamara Garcia Camarero, MD,* Federico Gimeno de Carlos, MD, PHD,‖
Gerard Roura Ferrer, MD,‡ Angel Sanchez Recalde, MD,¶
Íñigo Lozano Martínez-Luengas, MD, PHD,# Josep Gomez Lara, MD,‡
Felipe Hernandez Hernandez, MD,** María J. Pérez-Vizcayno, MD,§
Angel Cequier Fillat, MD, PHD,‡ Armando Perez de Prado, MD,††
Agustín Albarrán Gonzalez-Trevilla, MD,** Manuel F. Jimenez Navarro, MD, PHD,‡‡
Josepa Mauri Ferre, MD,§§ Jose A. Fernandez Diaz, MD,‖‖
Eduardo Pinar Bermudez, MD, PHD,¶¶ Javier Zueco Gil, MD,*
on behalf of the collaborative IVUS-TRONCO-ICP Spanish study

Santander, Vigo, Barcelona, Madrid, Valladolid, Oviedo, Leon, Malaga, Badalona, and Murcia, Spain

De la Torre Hernandez et al. JACC Intv 2014;7:244-254

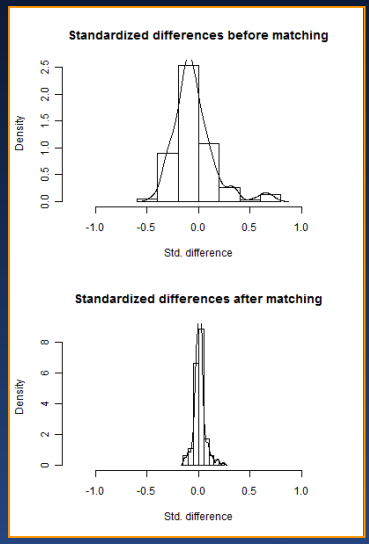
Registries pooled:	Pts with DES in LM:	F up:
ESTROFA-LM*	(770 pts in 21 centers)	3 yrs
RENACIMIENTO	(596 pts in 30 centers)	1 yr
Bellvitge	(189 pts in 1 center)	3 yrs
Valdecilla	(200 pts in 1 center)	3 yrs

1,670 patients with PCI with DES in LM
(pts. with shock and duplicated inclusions excluded)

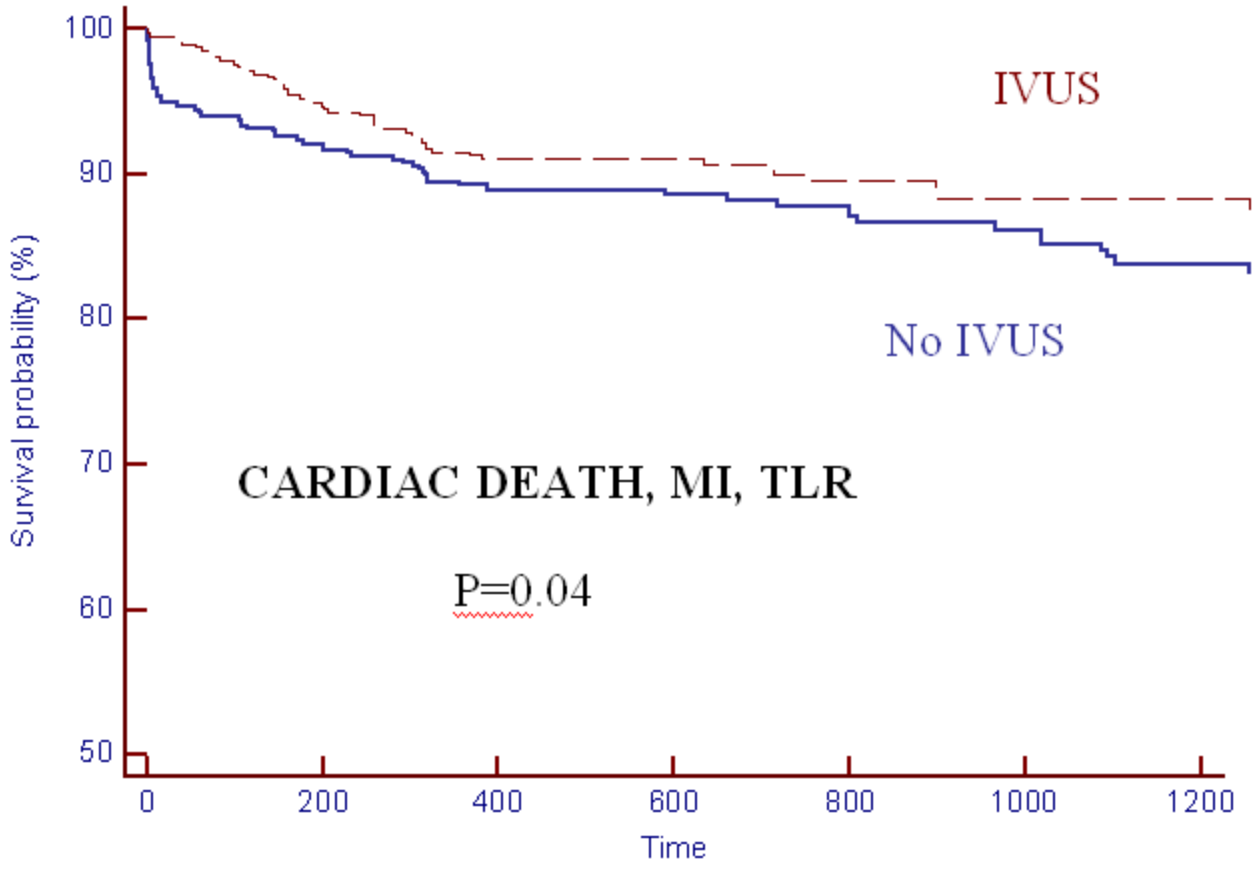
505 patients under IVUS guidance:***IVUS group***

Propensity score matched to:

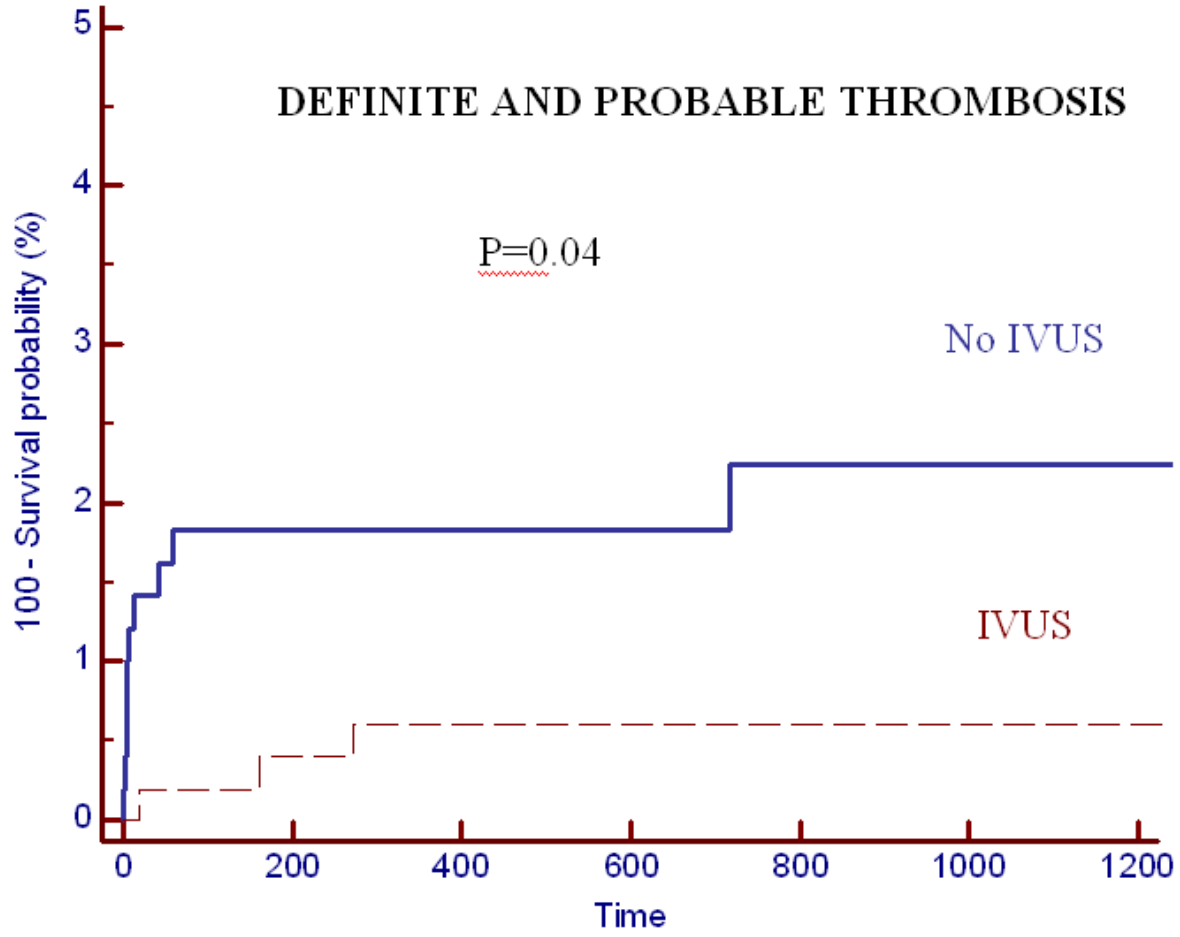
505 patients without the use of IVUS:***no-IVUS group***



*De la Torre et al. Am J Cardiol. 2013;111(5):676-83

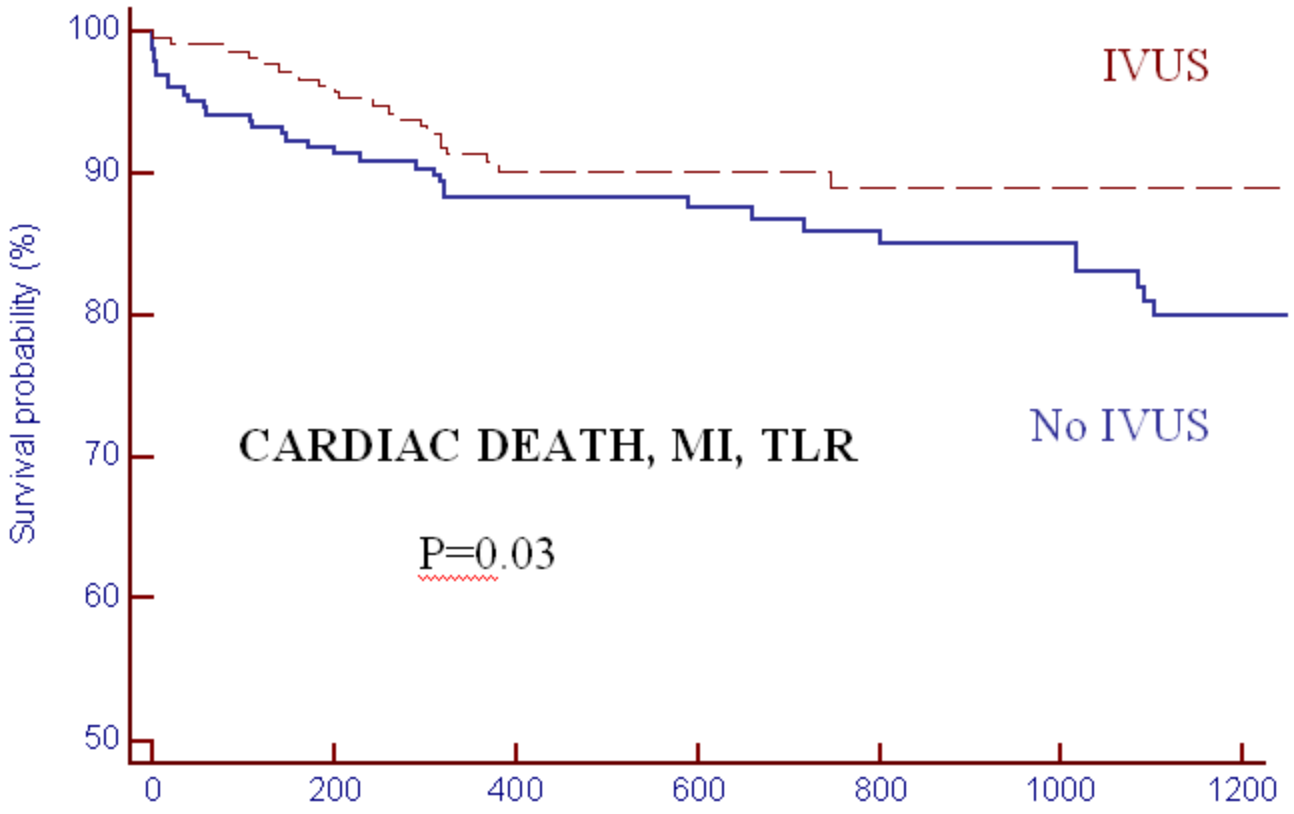


Pts. at risk	365 days	730 days	1095 days
IVUS	485	286	203
No IVUS	470	275	201



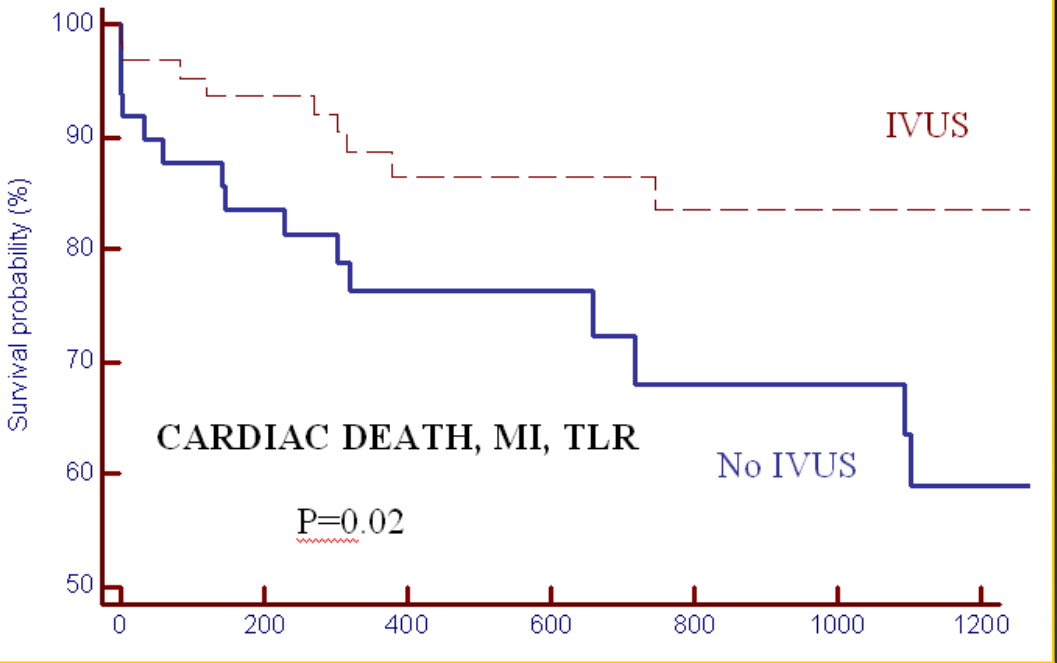
Pts. at risk	365 days	730 days	1095 days
IVUS	485	286	203
No IVUS	470	275	201

LM distal subgroup

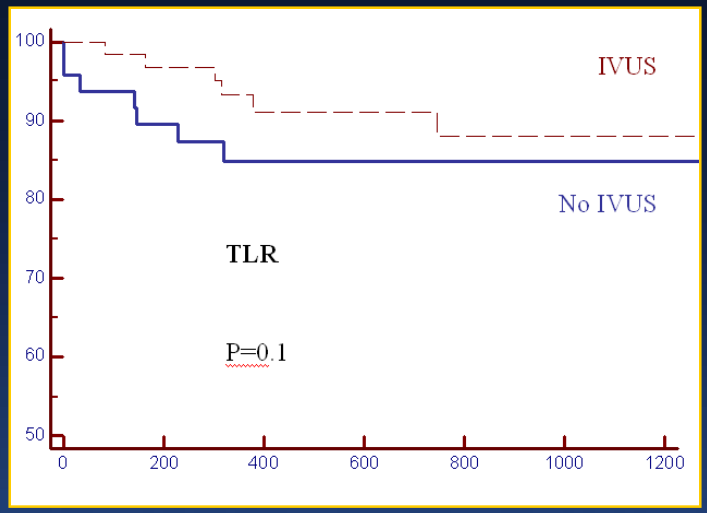


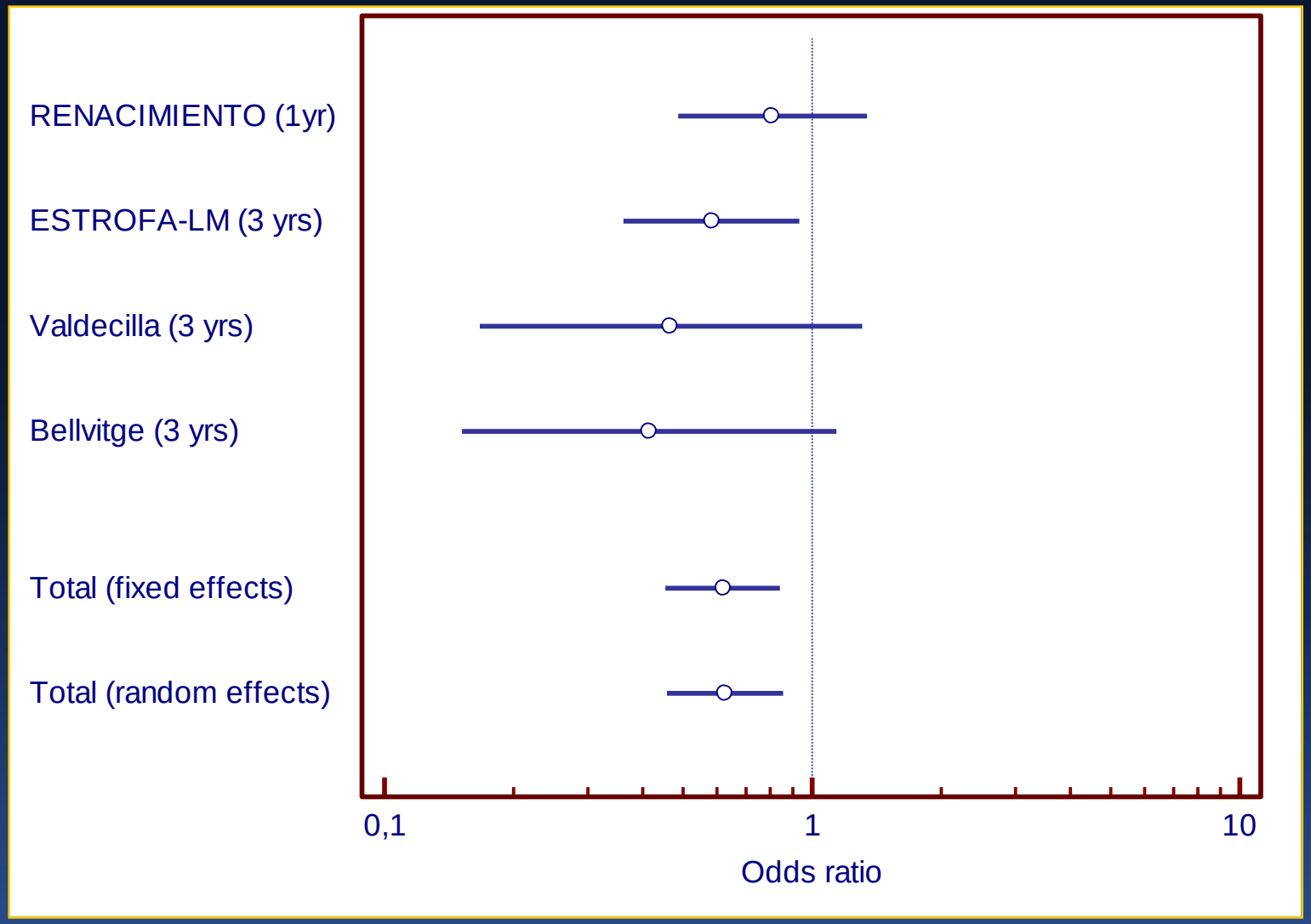
Pts. at risk	365 days	730 days	1095 days
IVUS	212	111	90
No IVUS	219	112	97

LM distal-2 stents subgroup



Pts. at risk	365 days	730 days	1095 days
IVUS	60	41	23
No IVUS	57	24	20





IVUS better **Angio better**

Predictors of MACE (Cardiac death, MI, TLR)

Overall population	HR	95% CI	p
IVUS	0.70	0.52 – 0.99	0.04
Age	1.03	1.01 – 1.05	0.0001
LVEF	0.98	0.97 – 0.99	0.01
Diabetes	1.81	1.32 – 2.47	0.0002
Distal LM with 2 stents	2.23	1.44 – 3.48	0.0004
ACS	1.84	1.30 – 2.60	0.0006
Subgroup with distal LM disease			
IVUS	0.54	0.34 – 0.90	0.02
Age	1.02	1.004 – 1.05	0.02
Diabetes	1.62	1.02 – 2.59	0.04
Distal LM with 2 stents	2.86	1.71 – 4.77	0.0001
ACS	1.95	1.14 – 3.31	0.01
Subgroup with ostial-mid LM disease			
Age	1.04	1.02–1.05	<0.0001
ACS	1.68	1.17–2.40	0.004
IVUS	0.85	0.55–1.15	0.2

Limitations

Despite propensity-score matching it still remains possible that some unmeasured confounders could favor the IVUS-guided arm, explaining its better outcome.

None of the registries was specifically designed to evaluate the influence of IVUS in outcomes. Therefore, there were not specific IVUS criteria for device sizing, identification and treatment of malapposition and/or underexpansion.

This is a limitation in order to know how did IVUS affect the procedure that lead to improved outcomes. The decisions taken after IVUS examination were left up to the operator.

Conclusions

The use of IVUS to assess intermediate LM lesions results safe to defer revascularization

The use of IVUS to guide PCI and to identify and solve complications has a positive impact on clinical outcomes

But,
be careful and precise in the IVUS examination of the LM