

Optimal Cut-off of Minimal Lumen Area to Predict Fractional Flow Reserve

Soo-Jin Kang, MD., PhD.

Department of Cardiology, University of Ulsan College of Medicine
Asan Medical Center, Seoul, Korea

Disclosure

I have nothing to disclose

Optimal Minimal Lumen Area to Predict Functional Significance of

- Non-LM Stenosis
- Pure LM Stenosis

IVUS-MLA 4.0mm²

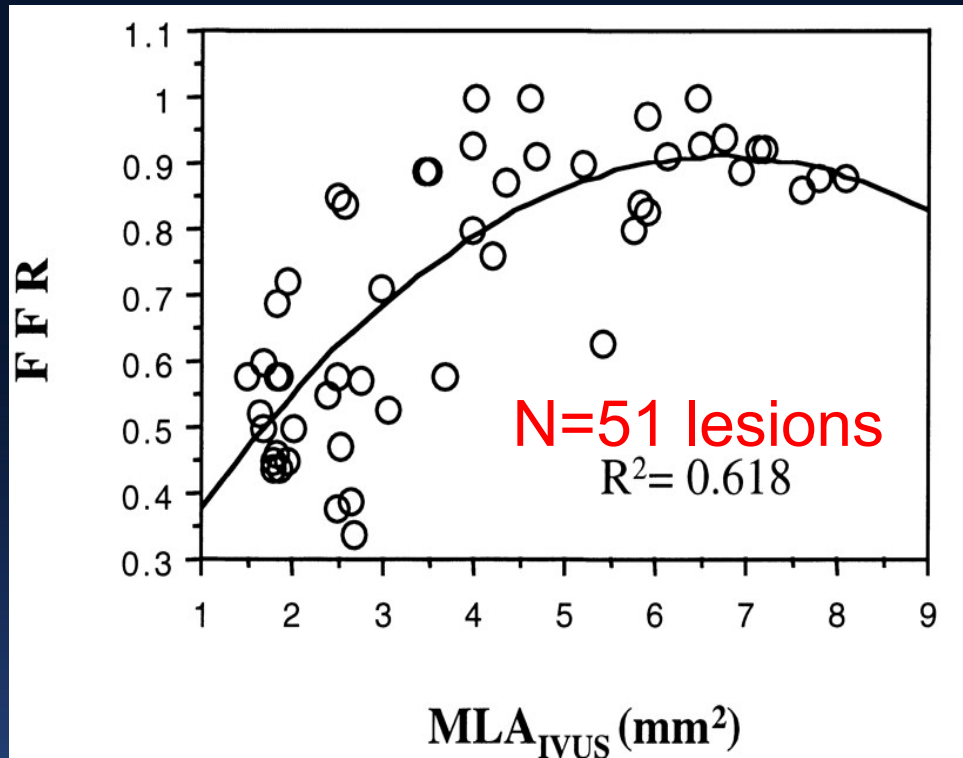
Ischemia-Producing Stenosis
-Validated by CFR, Thallium, FFR

Abizaid et al. AJC 1998;82:42-8

Nishioka et al. JACC 1999;33:1870-8

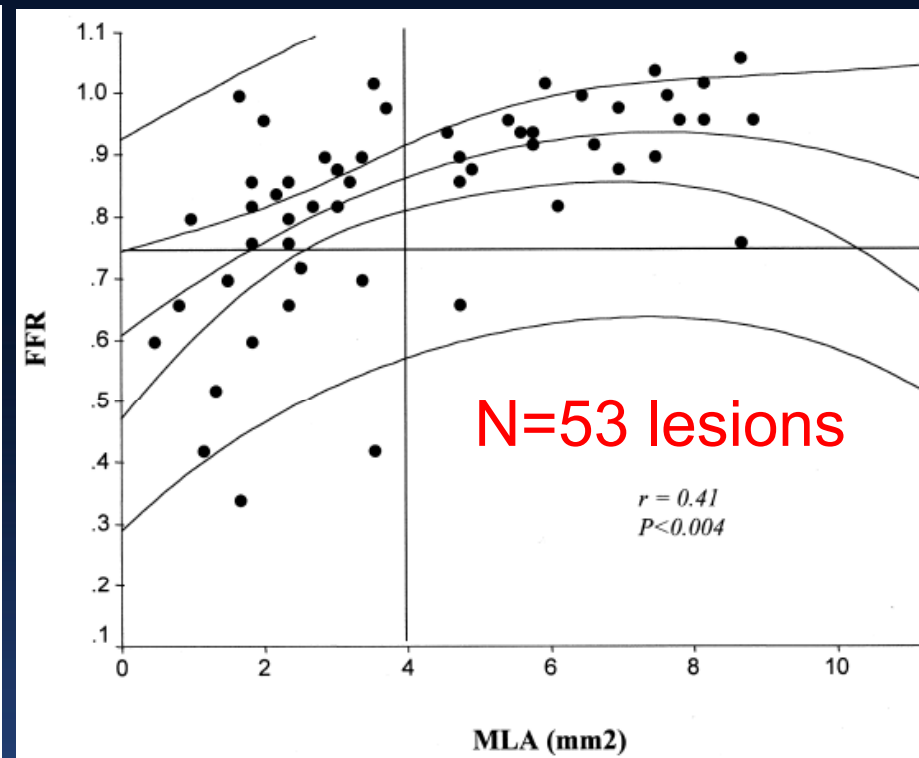
Abizaid et al. Circulation 1999;100:256-61

Validation of IVUS-MLA with FFR<0.75



MLA < 3.0 mm²

sensitivity 83%



MLA < 4.0 mm²

sensitivity 92%

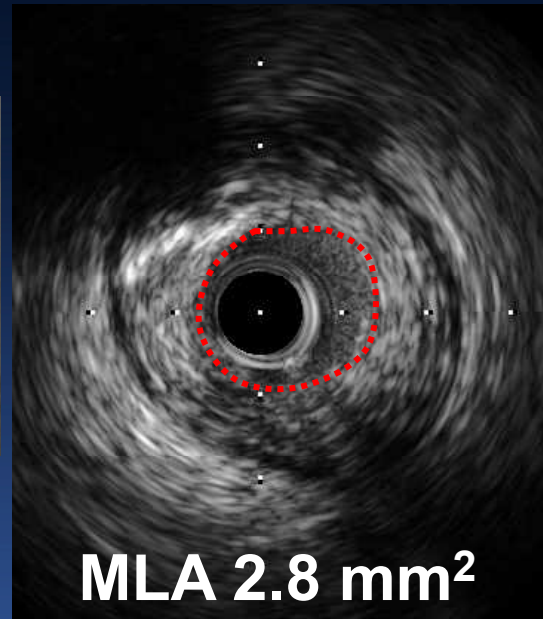
The accuracy of MLA criteria still remains debatable

Takagi et al. *Circulation* 1999;100:250-5

Briguori et al. *AJC* 2001;87:136-41

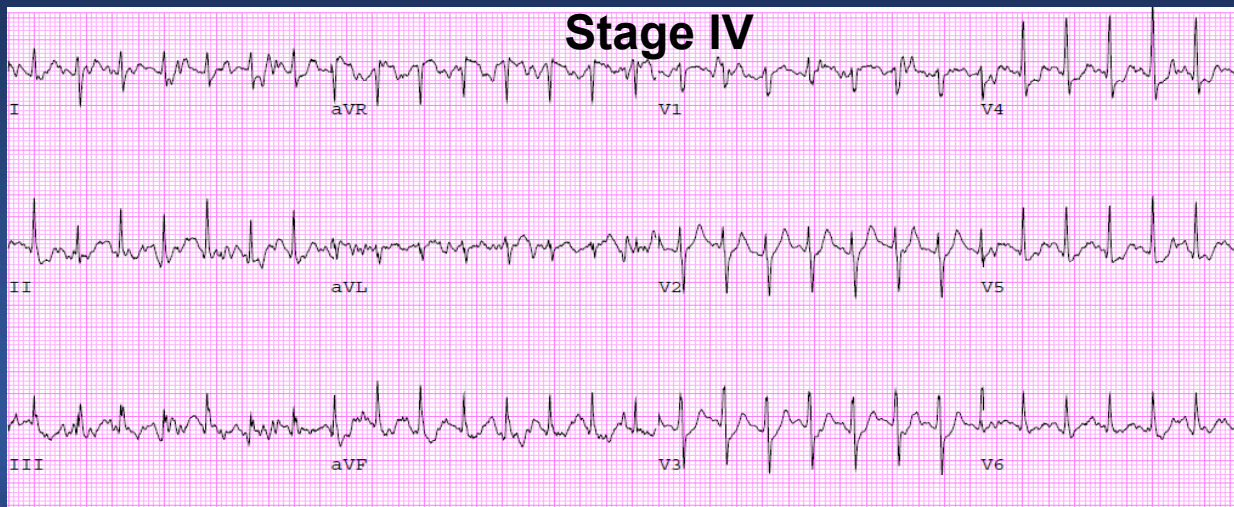
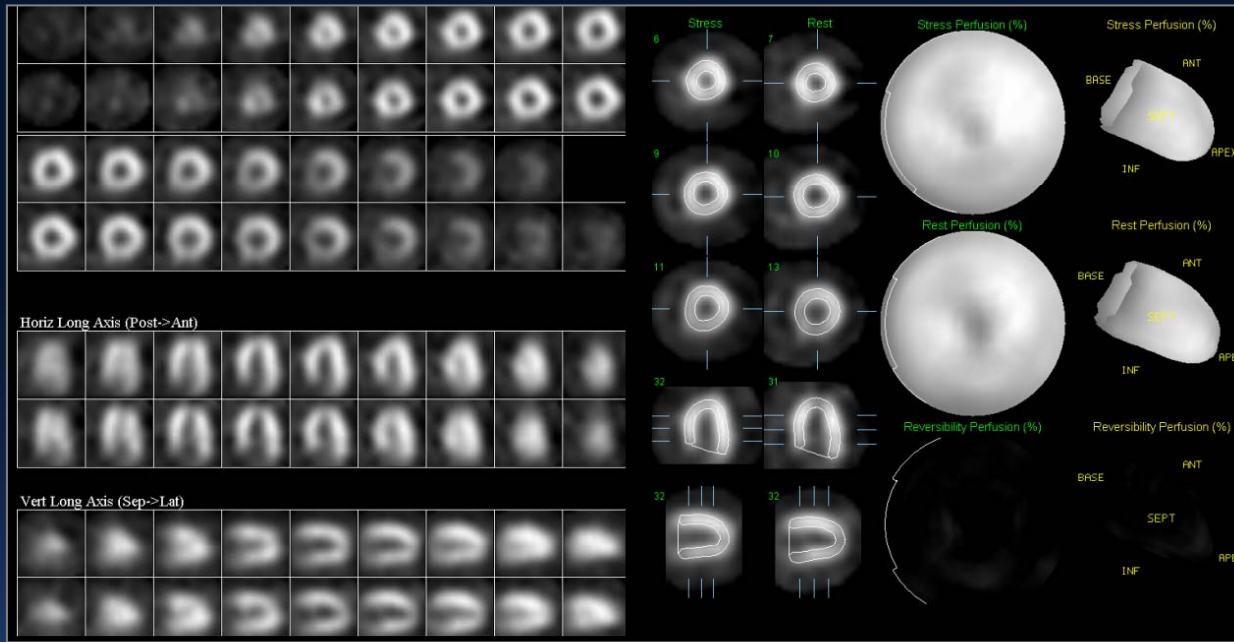
Anatomical-Functional Mismatch

- 55 year-old male
- Effort-related chest pain for 6 months



What Would You Do?
PCI vs. Medical

Anatomical-Functional Mismatch



Validation of IVUS-Derived Parameters With FFR for Stenosis Severity in Non-LM Disease

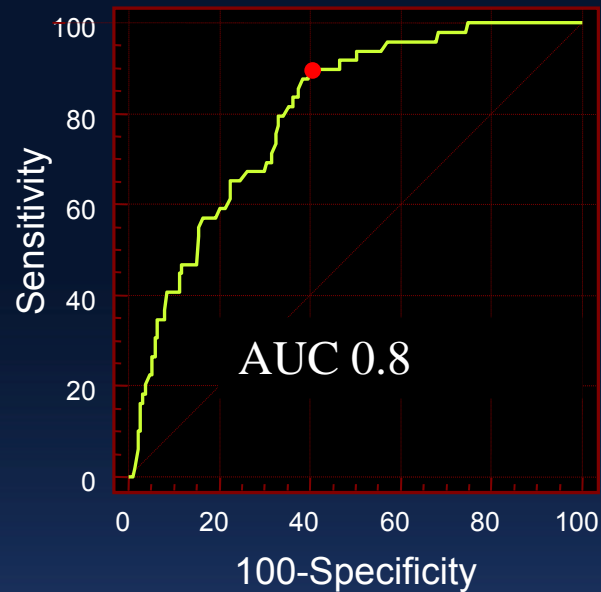
236 Lesions with 30%-75% of Angiographic DS

Independent determinants of FFR as continuous variable			
	β	95% CI	P value
MLA	0.269	0.010-0.035	<0.001
Plaque burden	-0.204	-0.003--0.001	0.001
Lesion length	-0.237	-0.006 - -0.001	0.001
Independent determinants for FFR<0.8			
Male gender	4.2	1.546-11.384	0.005
MLA	0.21	0.098-0.432	0.001
Plaque burden	1.06	1.010-1.116	0.019
LAD lesion	4.37	1.608-11.88	0.004

Age, male gender, DM, reference lumen diameter, LAD lesion location, MLA, PB, area stenosis and lesion length with a lumen area <3.0mm²

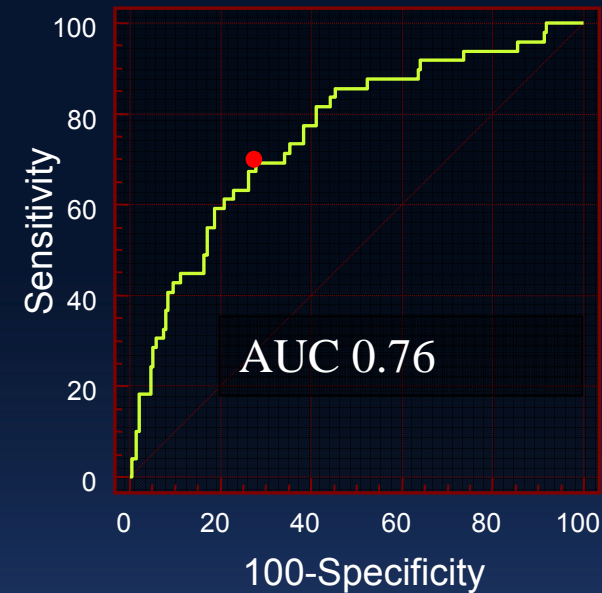
Kang et al. Circ Cardiovasc Interv 2011;4:65-71

MLA 2.4mm²



Sensitivity=90%
Specificity=60%
PPV=37%
NPV=96%
Accuracy=68%

Plaque Burden 78%



Sensitivity=69%
Specificity=72%
PPV=40%
NPV=90%
Accuracy=70%

Kang et al. Circ Cardiovasc Interv. 2011;4:65-71

Total 236 intermediate lesions

117 with $MLA \geq 2.4mm^2$

119 with $MLA < 2.4mm^2$

112/117 (96%)
FFR ≥ 0.8

5/117 (4%)
FFR < 0.8

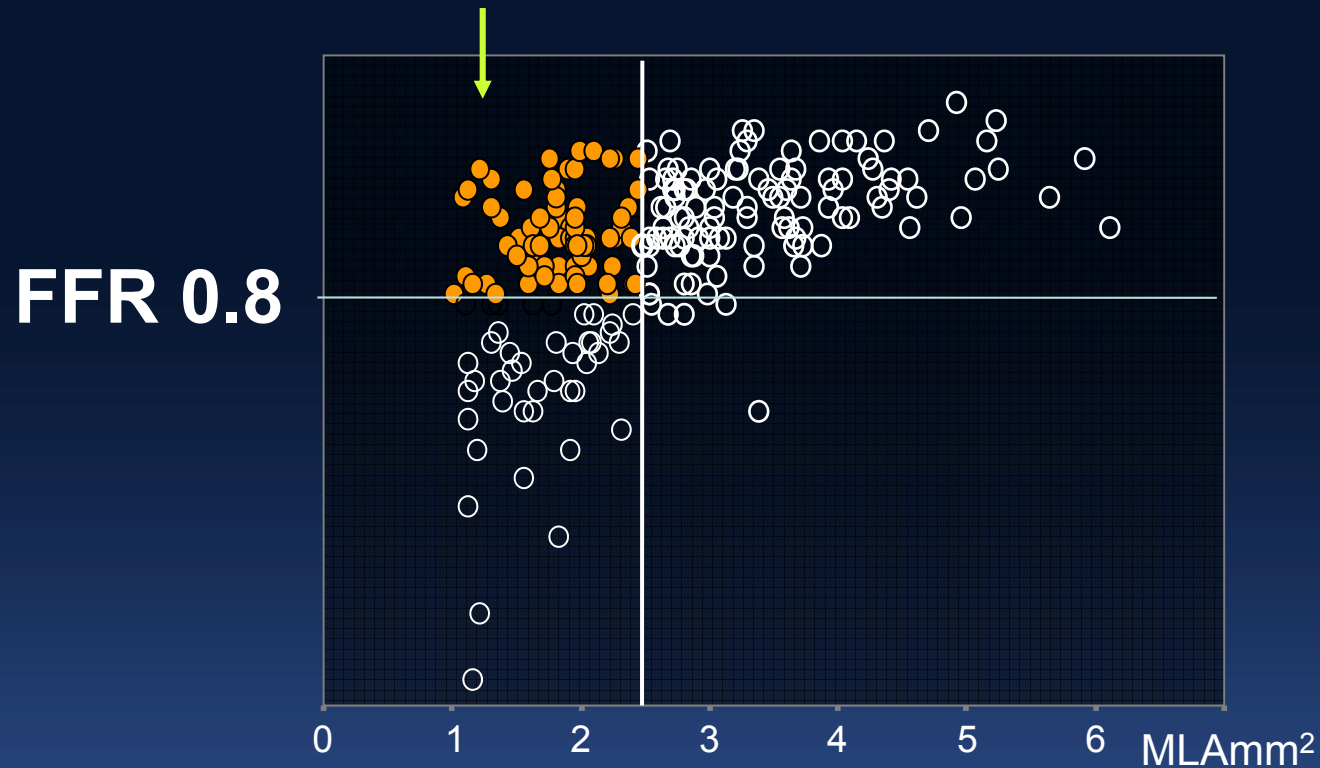
75/119 (63%)
FFR ≥ 0.8

44/119 (37%)
FFR < 0.8

119 with $MLA < 2.4mm^2$	Cut-off	Sensitivity	Specificity	Accuracy	AUC	95% CI
Length, lumen area < 3.0	11.7mm	36%	84%	66%	0.567	0.473-0.657
Length, lumen area < 2.4	4.1mm	55%	68%	63%	0.609	0.516-0.697
Plaque burden	81.2%	66%	68%	67%	0.686	0.595-0.768
Area stenosis	77.2%	50%	81%	69%	0.647	0.554-0.732

In lesions with an $MLA < 2.4mm^2$, there was no IVUS parameter having additive value to improve the accuracy predicting FFR

40% were targets for unnecessary PCI

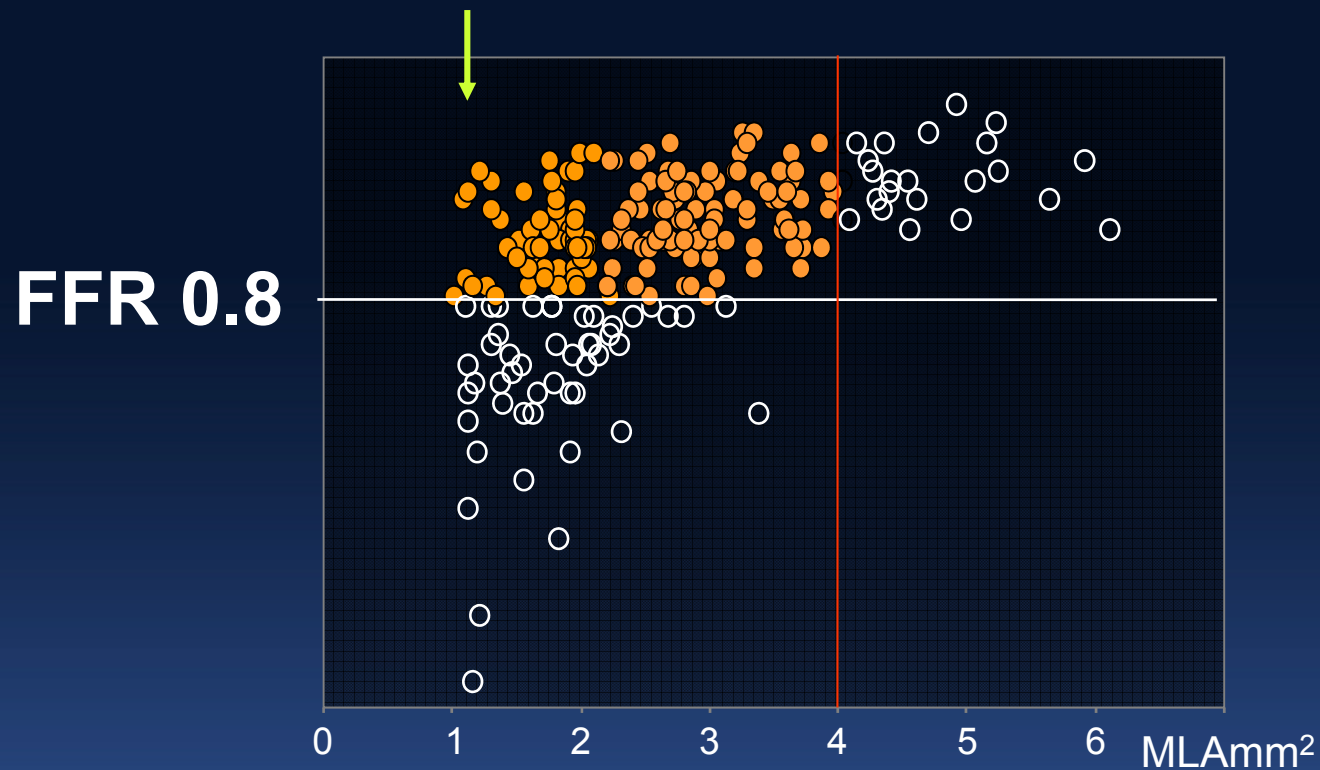


MLA < 2.4mm²

Specificity 60%

Kang et al. Circ Cardiovasc Interv 2011[Epub]

87% were targets for unnecessary PCI



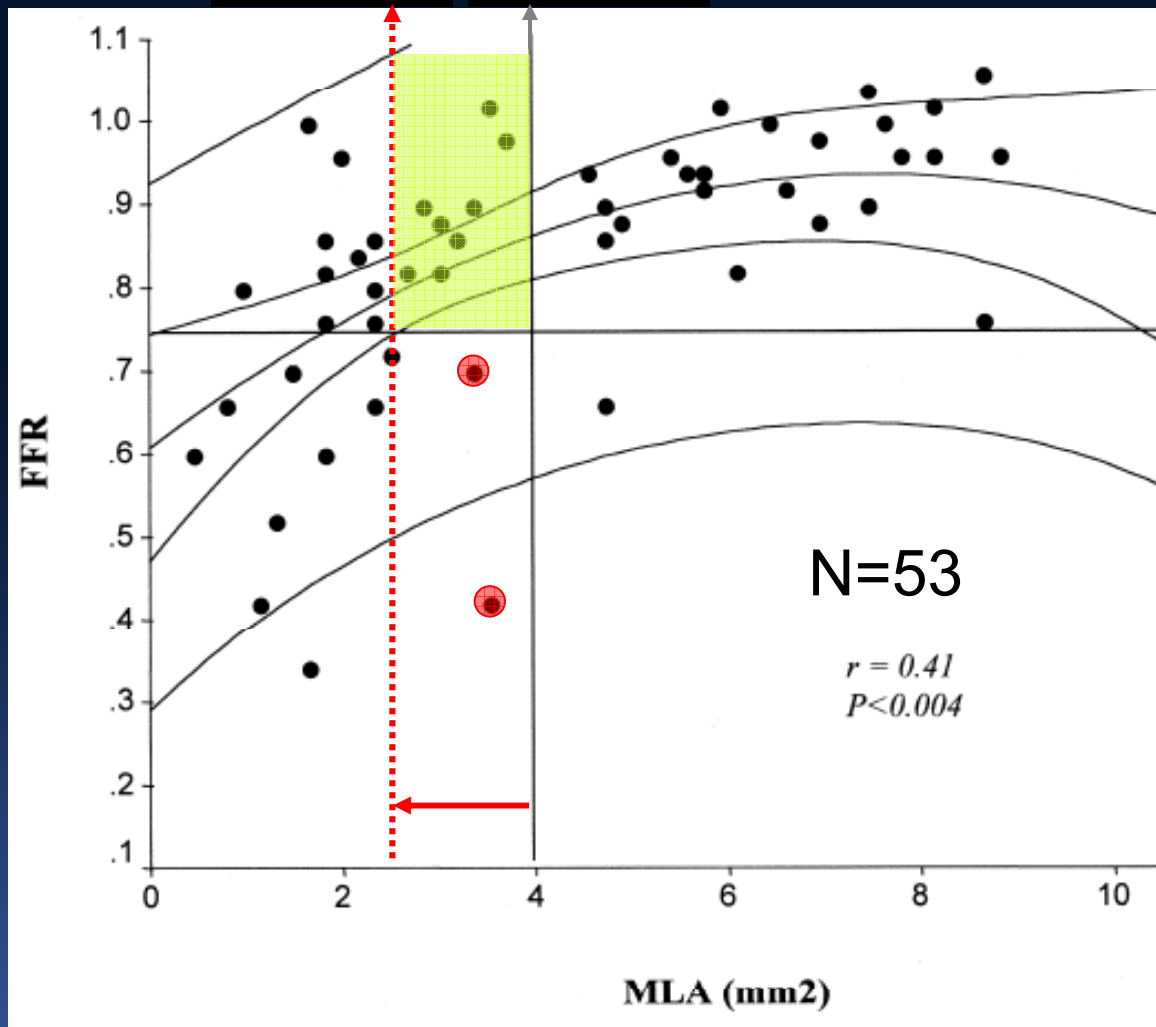
MLA < 4.0mm²

Specificity 13%

Kang et al. Circ Cardiovasc Interv 2011[Epub]

2.4 mm²

4.0 mm²



MLA 4.0mm²
predicted FFR <0.75

Sensitivity 92%
Specificity 56%

Accuracy
76%

>

Accuracy
64%

Briguori et al. *Am J Cardiol* 2001;87:136-41

MLA Criteria in Small Vessel Lesions with Reference Lumen Diameter < 3mm

to predict a FFR<0.75

- **MLA <2.0mm²** (sensitivity 82%, specificity 80%)
- **Plaque burden >80%** (sensitivity 88%, specificity 79%)
- **Lesion length >20mm** (sensitivity 63%, specificity 79%)

Lee et al. AJC 2010

According to Vessel Diameter at MLA Site

	FFR <0.8	Cut-off	Sensitiv	Specific	PPV	NPV	Accuray	AUC
Vessel < 3.0mm (n=38)								
MLA	7/31	1.5	71	77.4	42	92	76	0.730
PB	7/31	75.4	43	94	60	88	85	0.654
Vessel 3.0-3.5mm (n=53)								
MLA	13/40	1.8	61.5	87.5	61	88	81	0.769
PB	13/40	74.5	84.6	67.5	46	93	71	0.765
Vessel 3.5-4.0mm (n=72)								
MLA	18/54	2.2	83	75	54	93	77	0.841
PB	18/54	80.2	83	75	54	93	77	0.850
Vessel > 4.0mm (n=73)								
MLA	11/62	2.4	91	83	50	98	84	0.874
PB	11/62	80.7	100	61	31	100	67	0.855

Optimal Minimal Lumen Area to Predict Functional Significance of

- Non-LM Stenosis
- Pure LM Stenosis

What is the Best IVUS Criteria for LM?

To identify Functionally Significant LM Stenosis

	IVUS Criteria	To predict	Outcomes
Jasti¹	MLD 2.8mm MLA 5.9mm²	FFR 0.75	38-month Survival / MACE-free
Fassa²	MLA 7.5mm²	3-yr MACE	MACE-free 88% with medical Tx 79% with revasculariz
Fassa²	MLA 9.6mm²	3-yr MACE	The best cut-off value on ROC based on MACE in deferred lesions
Abizaid³	MLD 3.0mm	1-yr MACE	60% in MLD<2.0mm 3% in MLD>3.0mm

The cut-off and its accuracy still remains debatable

¹Circulation 2004;110:2831–6, ²JACC2005;45:204–11, ³JACC 1999;34:707-15

IVUS vs. FFR vs. Outcomes

	IVUS Criteria	To predict	Outcomes
Jasti¹	MLD 2.8mm MLA 5.9mm²	FFR 0.75	38-month Survival / MACE-free

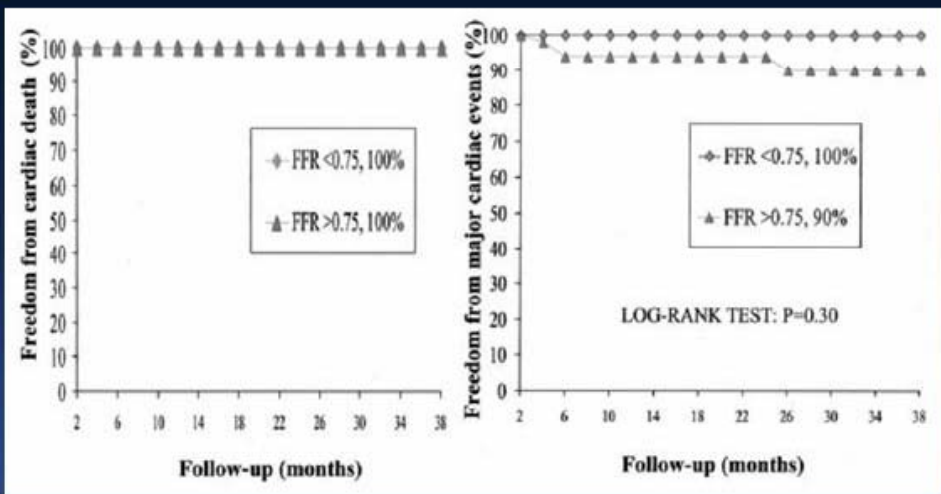
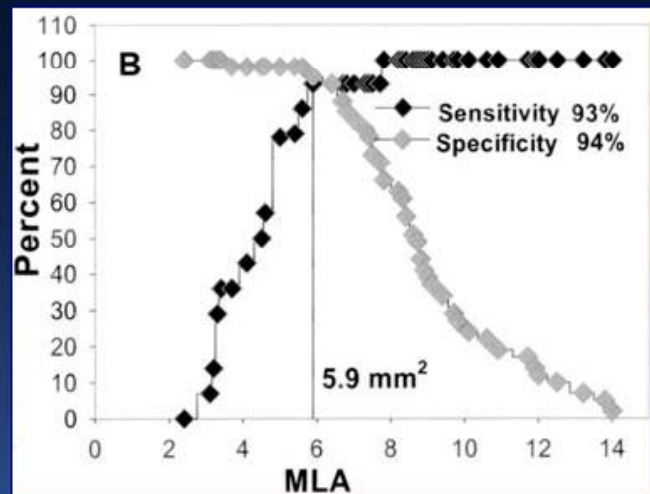
Fassa²

MLA < 6.0mm² Predicts LM FFR<0.75

Fassa²

- Sum of lumen areas of two daughter vessels (Each of LAD and LCX should be 4.0mm²)= 150% of the parent LM
- Murray's Law ($LM r^3 = LAD r^3 + LCX r^3$)

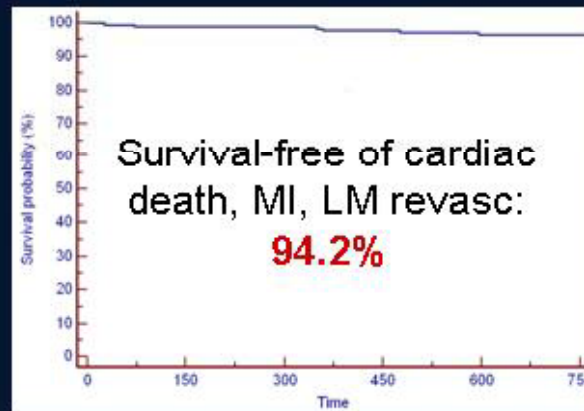
Abizaid³



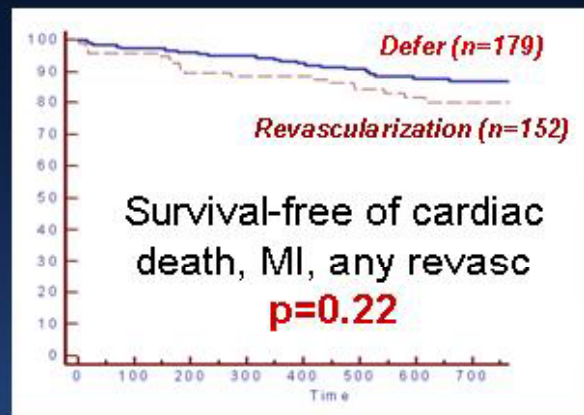
LITRO Study

Prospective application of predefined IVUS criteria for revascularization of intermediate LM lesions:

2-Year Outcome of Deferred Lesions with $MLA > 6mm^2$



2-Year Outcome of Deferred vs. Revasc

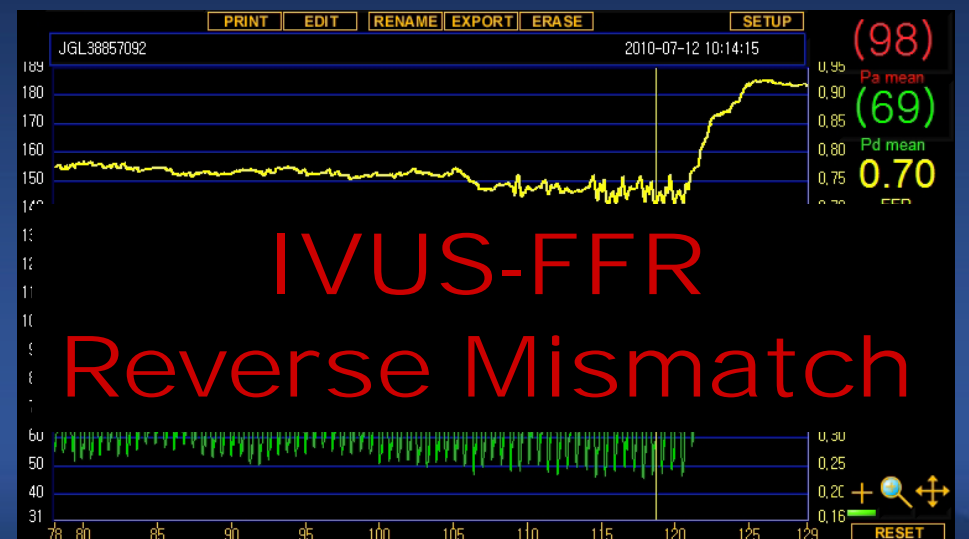
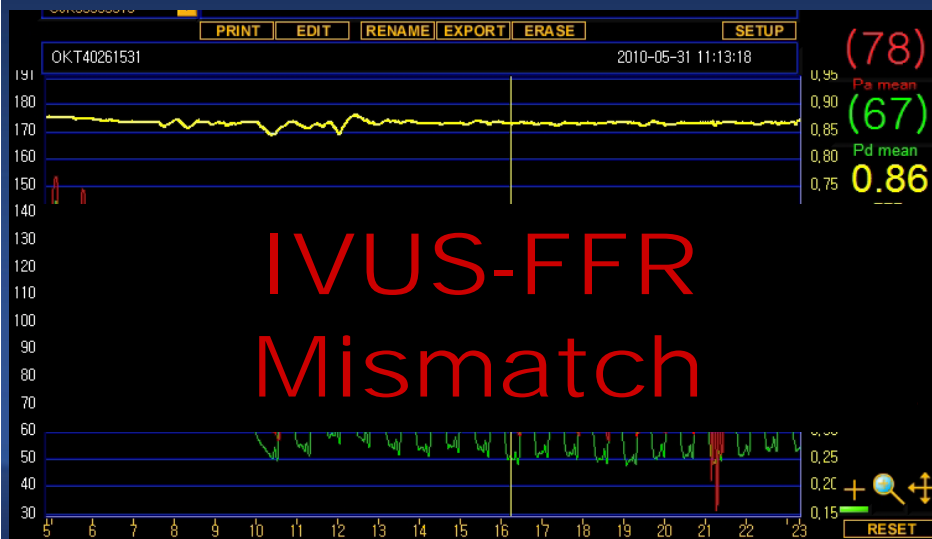
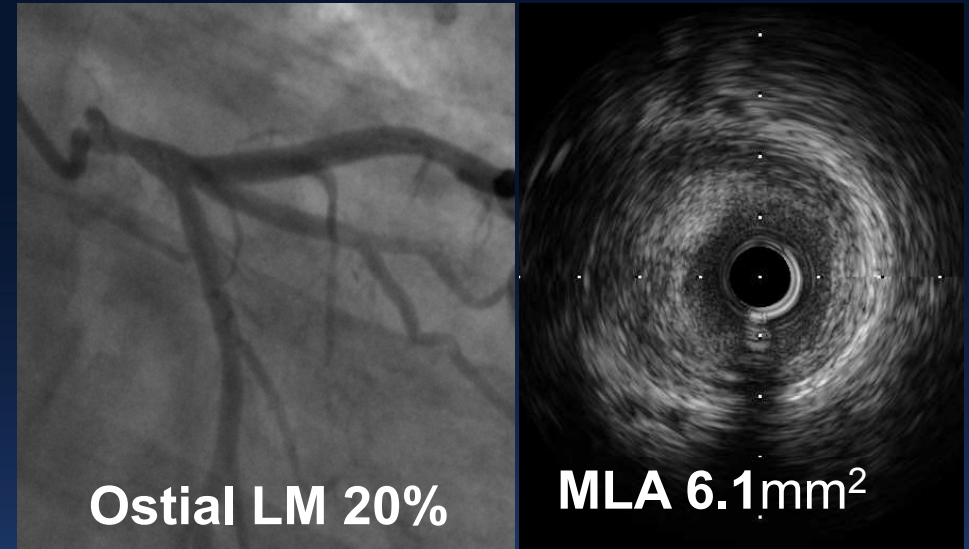
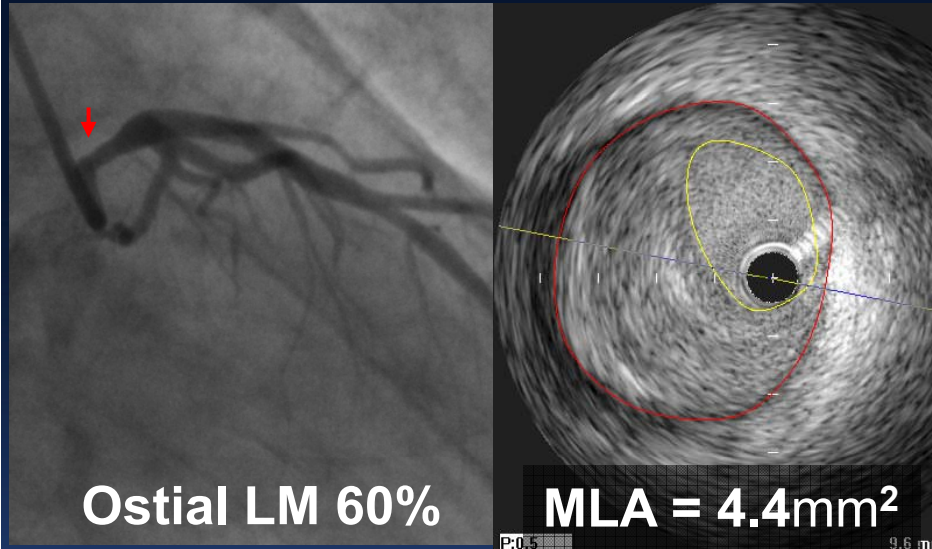


An $MLA \geq 6mm^2$ is a safe value for deferral

QCA = IVUS \neq FFR

47/M Stable angina

50/M Stable angina



Pitfalls of LM FFR

- Combined LAD/LCX stenosis is so common, which may increase the LM FFR
- The influence of SB lesion on LM FFR will depend on stenosis severity of distal lesion, even more, on the vascular territory supplied by the distal stream lesion

True LM FFR



LM FFR ↑↑



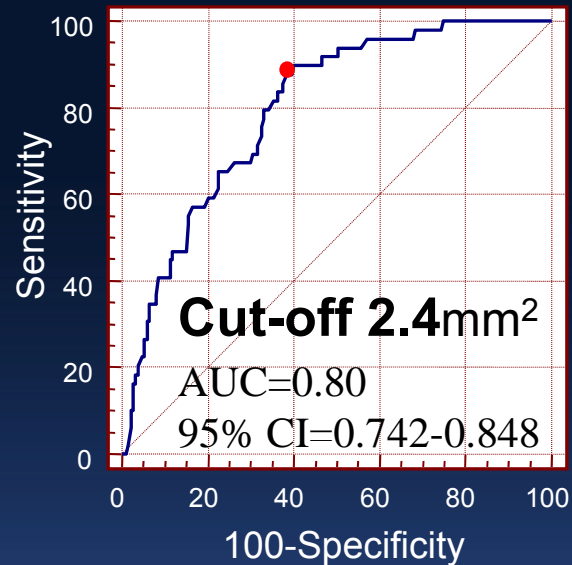
LM FFR ↑



Bruyne et al. Heart 2008;94:949-59

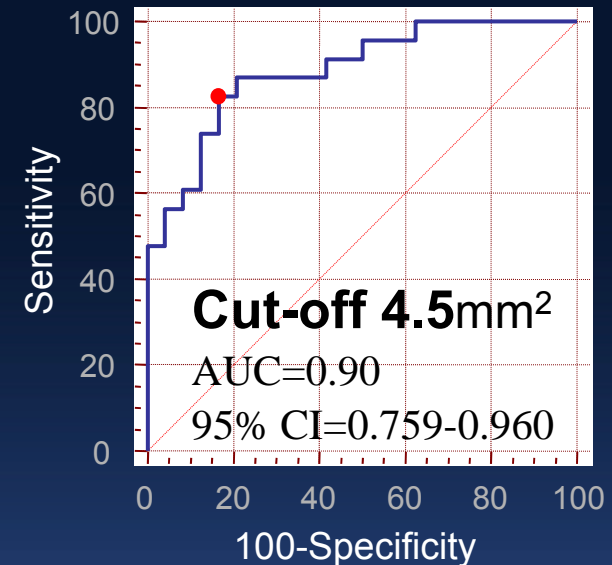
MLA Predicting FFR < 0.80

Non-LM



Sensitivity=90%
Specificity=60%
PPV=37%

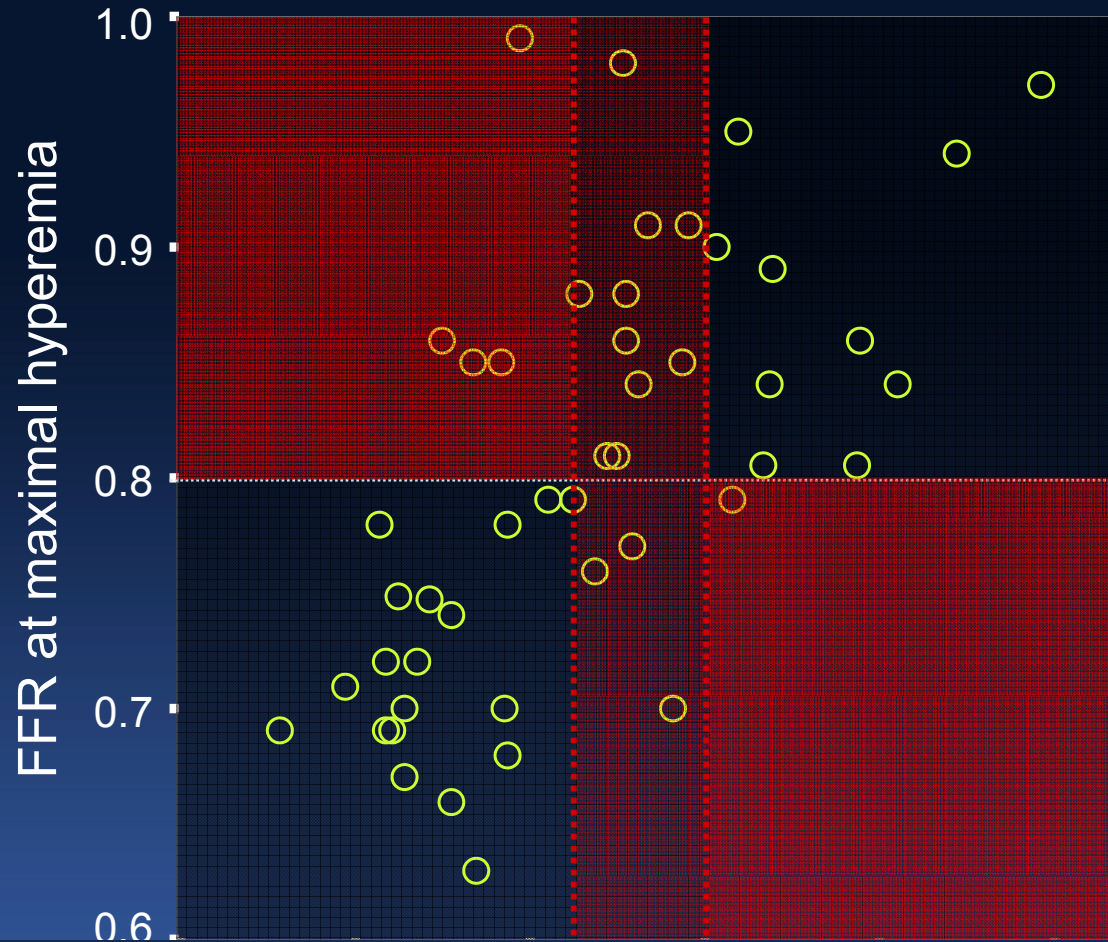
Pure LM Disease



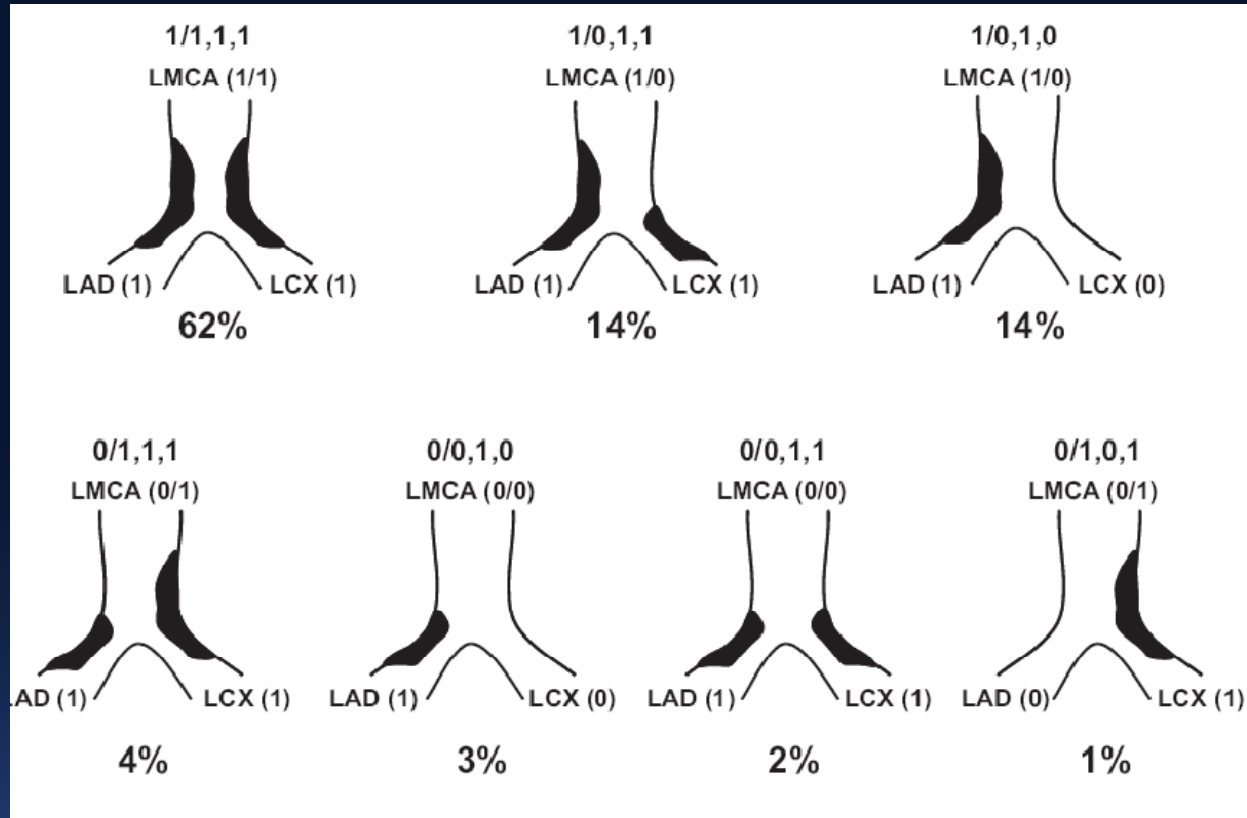
Sensitivity 83%
Specificity 83%
PPV 83%

Morphologic Simplicity of Pure LM Lesion
uniformly large vessel, short lesion length, lack of sidebranch

MLA-FFR Mismatch in 32%



With a lower specificity, 60% of patients may undergo unnecessary revascularization procedure



Oviedo et al. Circ Cardiovasc Interv 2010;3:105-12

MLA criteria in isolated LM disease cannot be applied to all LM bifurcations. It defines functional impact of **LM MLA**, were it not for the distal stream disease or if the distal stenosis were fixed

Conclusions

- As IVUS-MLA is only one of various factors affecting FFR, functional significance should be based on direct FFR measurement
- While **MLA \geq 2.4mm²** was a useful criterion to exclude FFR $<$ 0.8, MLA $<$ 2.4mm² does not always equate with functional significance
- In pure LM disease, the best criteria to predict an FFR $<$ 0.80 was an **IVUS-MLA of 4.5mm²**
However, 17% still remains misdiagnosed