How to Physiologically Interpret IVUS Parameters?

Soo-Jin Kang, MD., PhD.

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

Disclosure Statement of Financial Interest

I, Soo-Jin Kang DO NOT have a financial interest /arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation

How to Physiologically Interpret IVUS Parameters?

- IVUS MLA
- Plaque Morphology
- Side Branch Stenosis
- In-stent Restenosis

Why Mismatch

Nov 2009-Jun 2011, 1000 consecutive patients (1129 lesions with DS >30%) who underwent pre-PCI IVUS and FFR

(ClinicalTrials.gov NCT01366404)

Factors Affecting FFR

	Beta	p-value	95% CI
Age	0.008	<0.001	0.004 - 0.011
LAD location	-0.386	<0.001	-0.462 - 0.311
Lesion length	-0.006	<0.001	-0.009 - 0.003
Minimal lumen area	0.185	<0.001	0.149 - 0.222
Plaque burden	-0.006	<0.004	-0.009 - 0.003
Plaque rupture	-0.165	0.020	-0.302 - 0.027

Park et al. JACC interv 2012;5:1029-36

	N	FFR	RLA	MLA	AUC	Sens	Spec	PPV	NPV	Accu
Takaki (1999 Circ)	51	0.75	9.3	**3.0**	–	83%	92%	–	–	–
Briguori (2001 AJC)	53	0.75	7.8	**4.0**	–	92%	56%	38%	96%	**64%**
Ben-Dor (2012 *)	205	0.80	8.6	**3.09**	0.73	69%	72%	–	–	**70%**
Kang (2011 Circ int)	236	0.80	7.6	**2.4**	0.80	90%	60%	37%	96%	**68%**
Kang (2012 AJC)	784	0.80	8.2	**2.4**	0.77	84%	63%	48%	90%	**69%**
Koo (2011 JACC int)	267	0.80	6.8	**2.75**	0.81	69%	65%	27%	81%	**67%**
Gonzalo (2012 JACC)	47	0.80	7.1	**2.36** IVUS	0.63	67%	65%	67%	65%	**66%**
Gonzalo (2012 JACC)	61	0.80	7.1	**1.95** OCT	0.70	82%	63%	66%	80%	**72%**

Meta-analysis of 11 Clinical Trials

1759 patients with 1953 lesions

To predict FFR <0.80

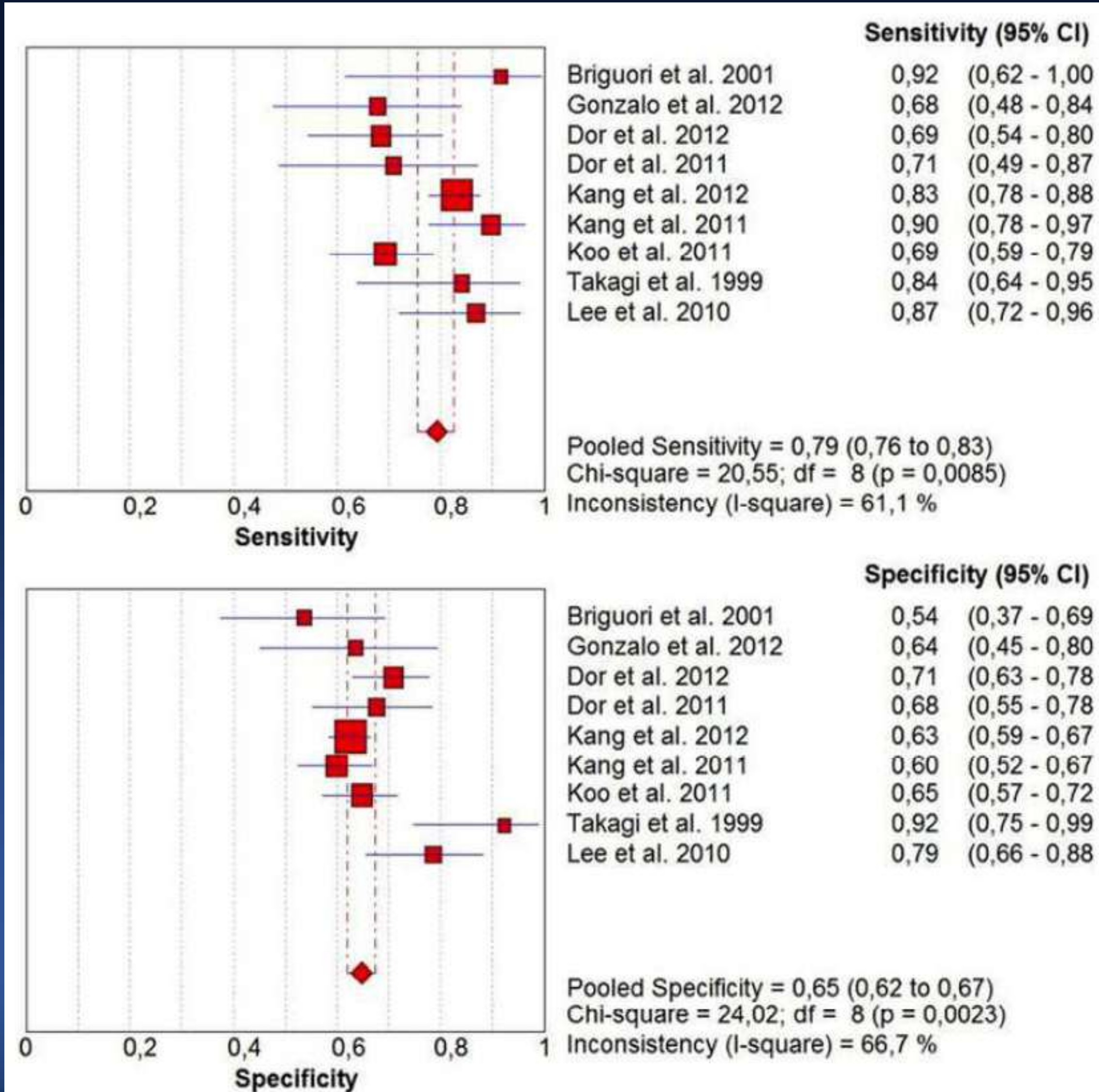
Weighted **MLA 2.61**mm^2

Pooled sensitivity **79%**

Pooled specificity **65%**

Smaller Cut-off than Used

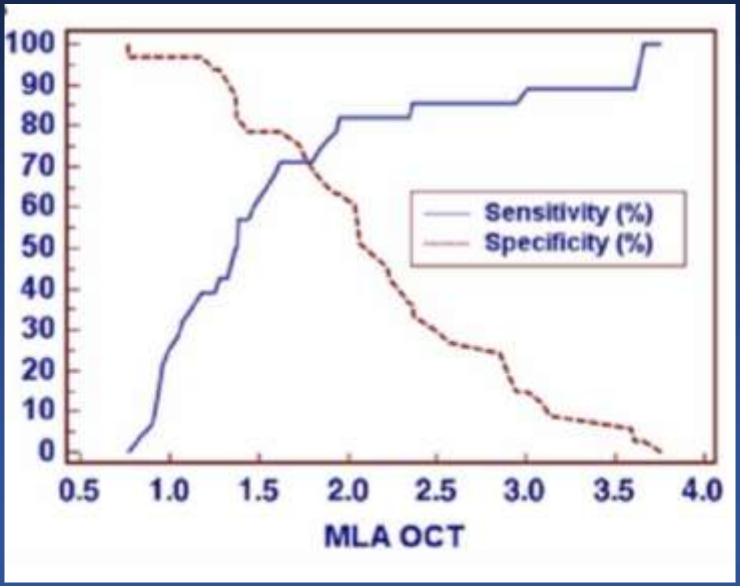
Poor Accuracy

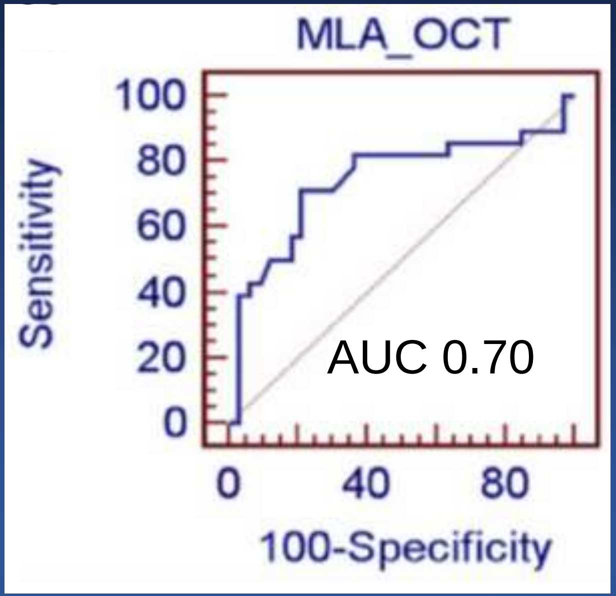


Nascimento et al. Catheter Cardiovasc Interv 2013 (in press)

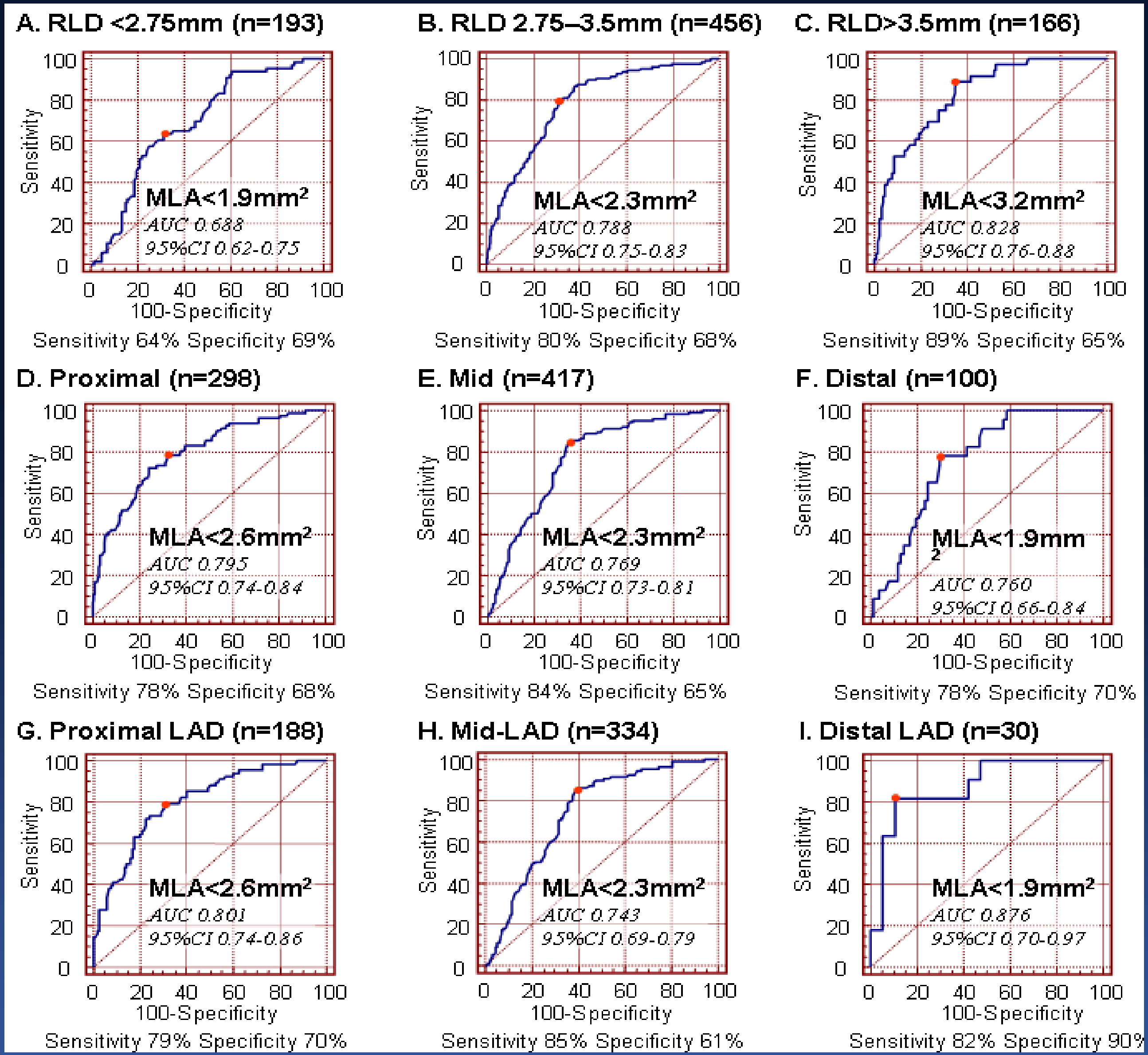
Is OCT-MLA More Accurate?

	FFR	MLA	AUC	Sens	Spec	PPV	NPV	Accuracy
IVUS	0.80	**2.36**	0.63	67%	65%	67%	65%	**66%**
OCT		**1.95**	0.70	82%	63%	66%	80%	**72%**





Gonzalo et al. J Am Coll Cardiol 2012;59:1080-9



Subgroup-specific MLA, accuracies <70-75%

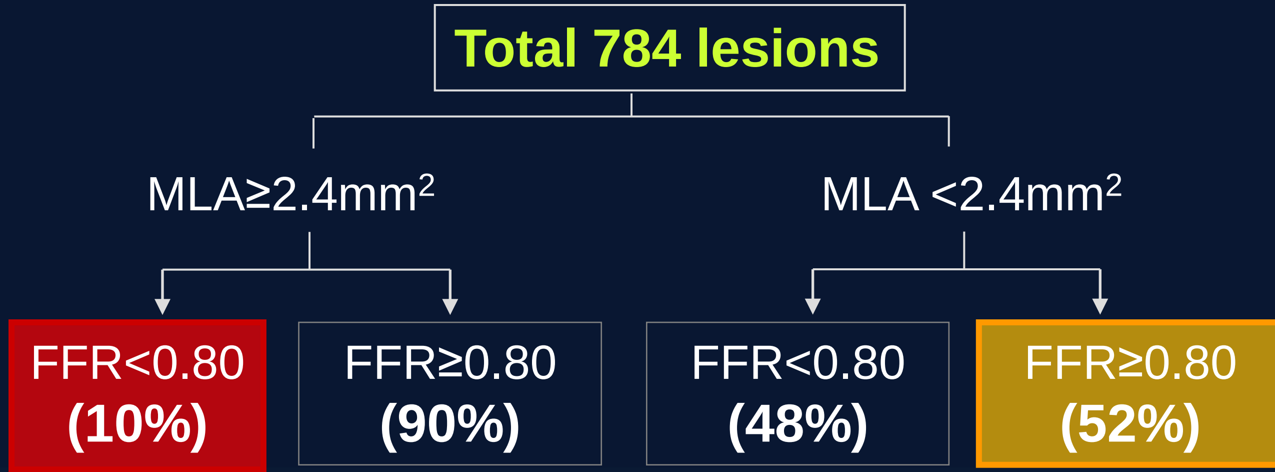
Kang et al. Am J Cardiol 2012;109:947-5

Subgroup-specific MLA

544 intermediate lesions assessed in 516 pts from 24 centers

FFR ≤0.80 in 169/544 lesions (31.1%) and 167/516 pts (32.4%)

	N	MLA cutoff	C-statistic	Accuracy
All lesions	544	2.9 mm^2	0.66	66.0%
LAD	296	2.9 mm^2	0.64	63.5%
LCX	110	2.4 mm^2	0.72	77.3%
RCA	138	2.8 mm^2	0.75	77.5%
Proximal	259	3.0 mm^2	0.76	74.9%
Mid	195	2.6 mm^2	0.63	65.6%
Distal	90	3.0 mm^2	0.63	51.1%
RVD <3.0 mm	322	2.6 mm^2	0.65	66.1%
RVD ≥3.0 mm	219	3.0 mm^2	0.71	72.6%
Length ≤12.3 mm	272	3.0 mm^2	0.67	64.7%
Length >12.3 mm	269	2.8 mm^2	0.69	68.8%



	Beta	p-value	Adjusted OR	95% CI
MLA<2.4 *but* **FFR≥0.8** ***"Mismatch"***				
Women	0.371	0.048	1.450	1.003 – 2.095
LAD location	-0.406	0.027	0.666	0.465 – 0.954
Reference lumen ø	-1.209	<0.001	0.298	0.204 – 0.437
Distal segment	0.704	0.002	2.021	1.293 – 3.159
MLA≥2.4 *but* **FFR<0.8** ***"Rev-mismatch"***				
Age	-0.062	<0.001	0.940	0.909 – 0.972
LAD location	0.813	0.071	2.256	0.932 – 5.460
Plaque rupture	2.410	<0.001	11.138	4.886 – 25.39

Multivariable Analysis Predicting FFR

in 700 LAD lesions of 700 patients

**Including age, female, body surface area, smoking, angiographic DS, minimal lumen diameter, lesion length, IVUS-MLA, plaque burden, averaged reference EEM area and %area stenosis, †addition of left ventricular mass*

	Total (700 patients)*			608 patients with echo data†		
	ß	p value	95% CI	ß	p value	95% CI
Age	0.119	0.001	0.000–0.002	0.192	<0.001	0.001–0.002
BSA	**-0.111**	**0.002**	-0.101– -0.024			
LV mass				**-0.121**	**<0.001**	-0.001 – 0.000
Angiographic DS	-0.185	<0.001	-0.002 – -0.001	-0.190	<0.001	-0.002 – -0.002
Lesion length	-0.110	0.001	-0.001 – 0.001	-0.077	0.027	-0.001 – 0.000
IVUS-MLA	0.312	<0.001	0.022 – 0.035	0.294	<0.001	0.019 – 0.032
Plaque burden	-0.115	0.002	0.001 – 0.000	-0.157	<0.001	-0.002 – -0.001

Kang et al. JACC Cardiovasc Interv 2013 in press

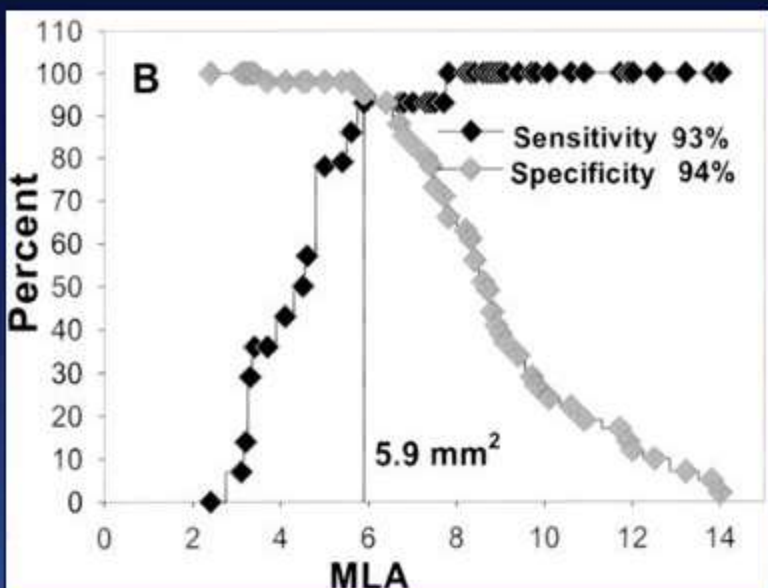
Isolated LMCA Disease: Ostial - Shaft

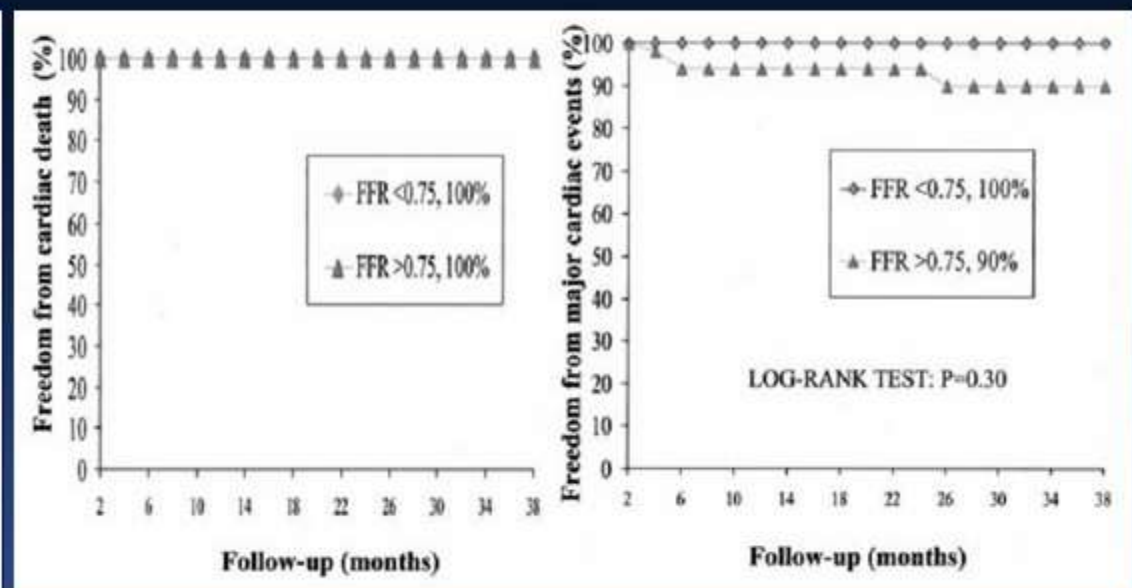
47/M Stable angina

50/M Stable angina

Cut-off for Predicting LM FFR<0.75
LM MLA 6.0mm²

- 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)

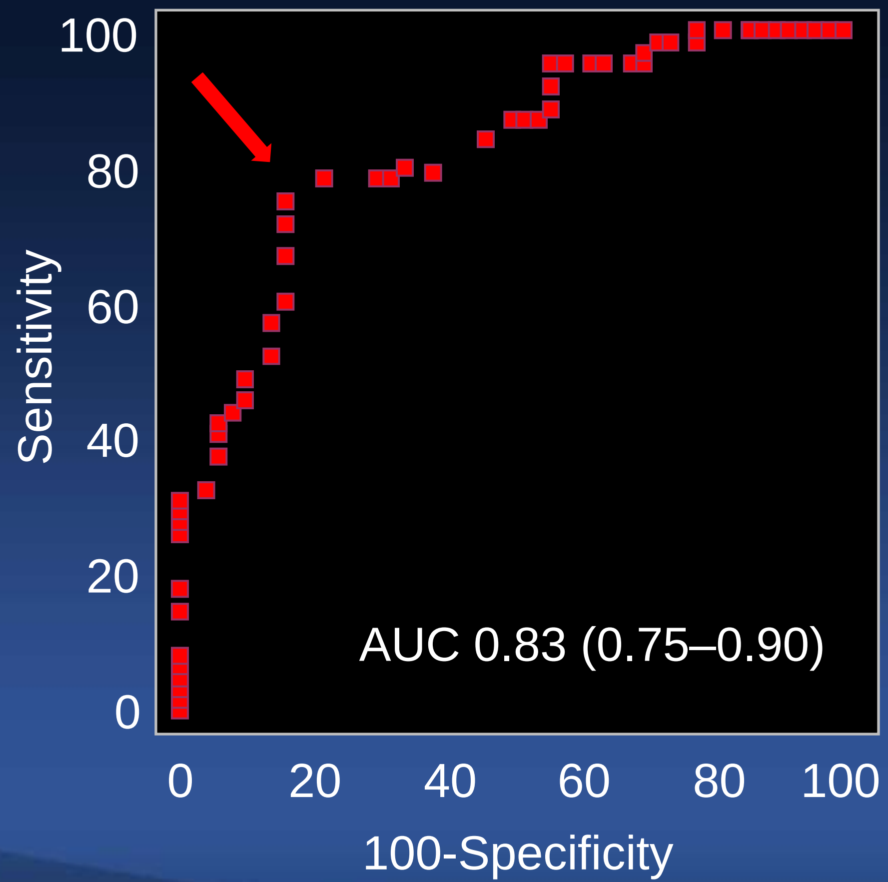




Jasti et al. Circulation 2004;110:2831-6

New LM MLA 4.5 mm^2

Matched with FFR <0.80
Ostial and Shaft LM Disease (N=112)



Sensitivity	79%
Specificity	80%
PPV	83%
NPV	76%

LM MLA can be alternatively used in pure LM lesions

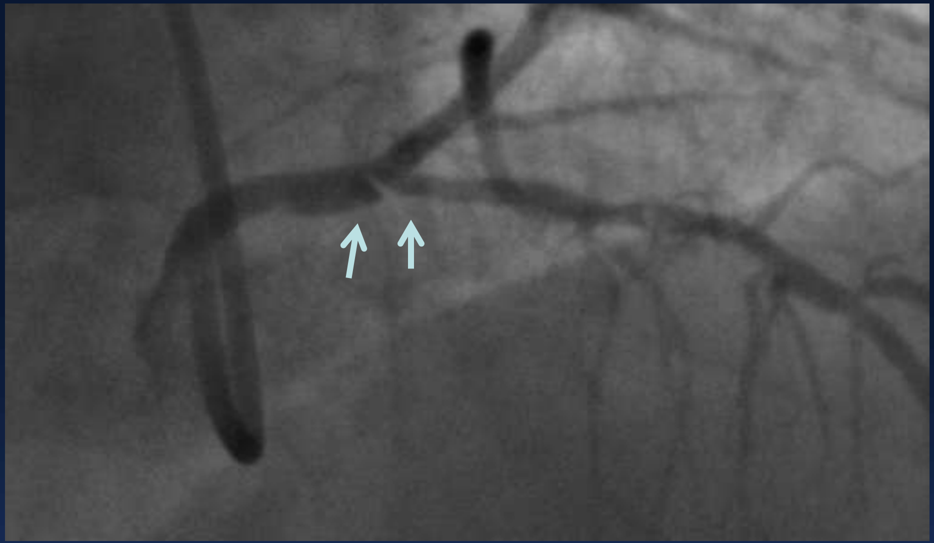
Park SJ, Ahn JM et al. JACC Interv (in press)

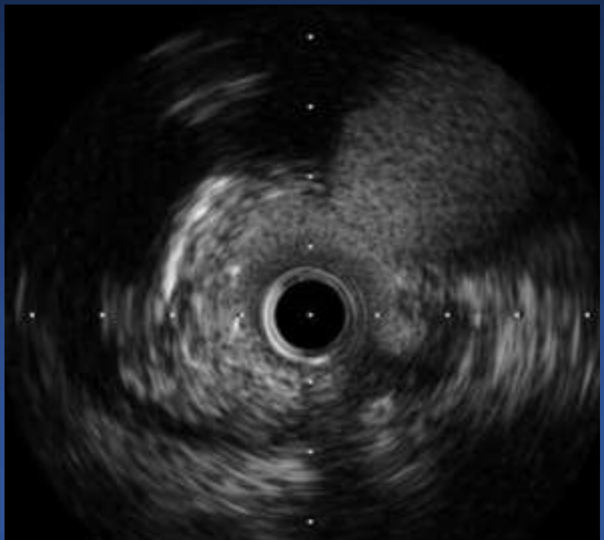
How to Physiologically Interpret IVUS Parameters?

- **IVUS MLA**
- **Plaque Morphology**
- **Side Branch Stenosis**
- **In-stent Restenosis**

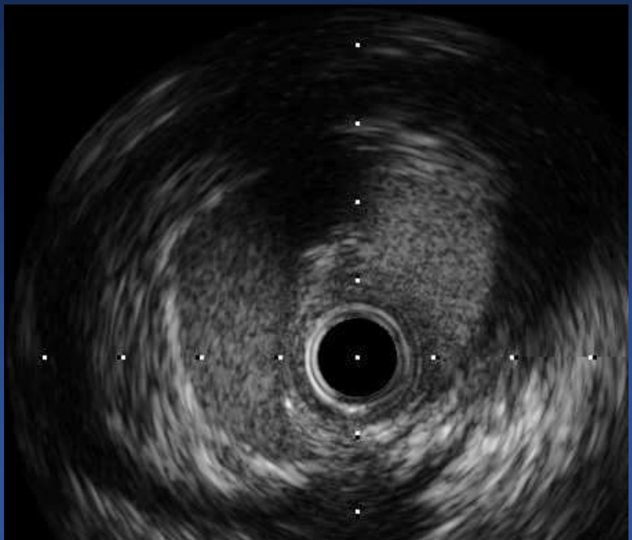
80-Year Old Male

- Resting chest pain
- Normal EKG
- Normal CK-MB, TnI

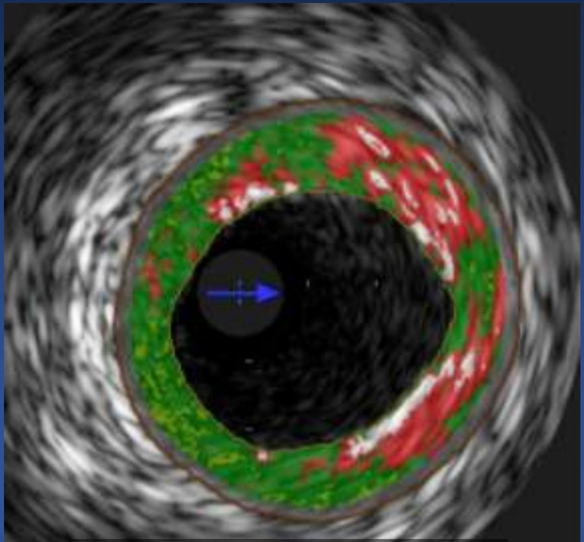




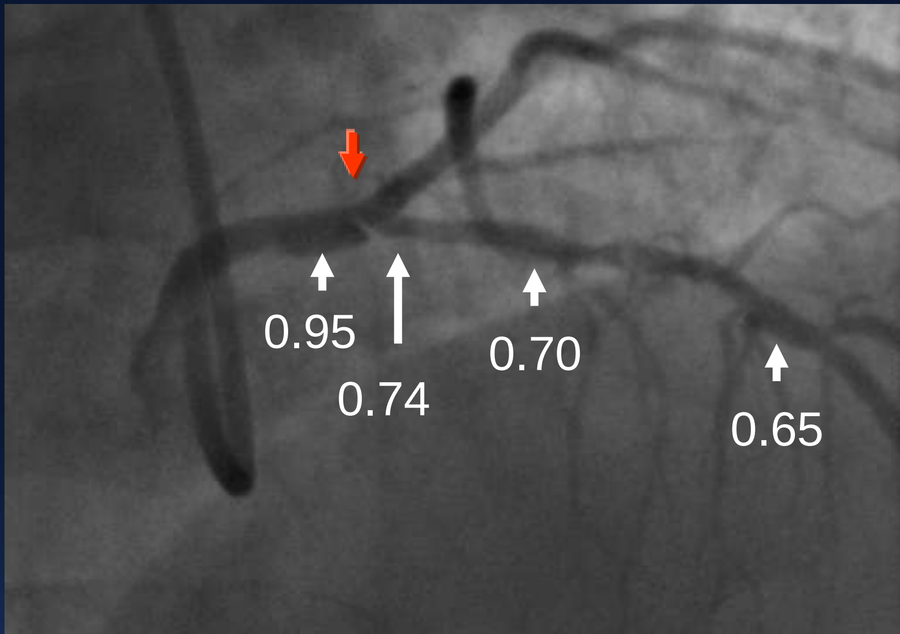
LAD MLA 3.7mm^2



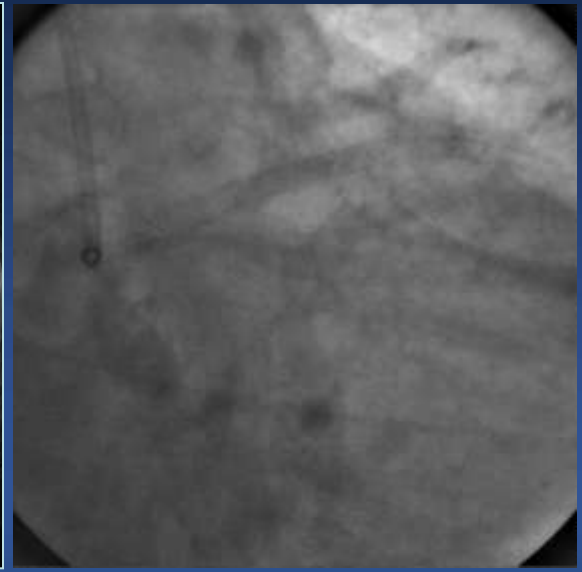
LM MLA 6.2mm^2



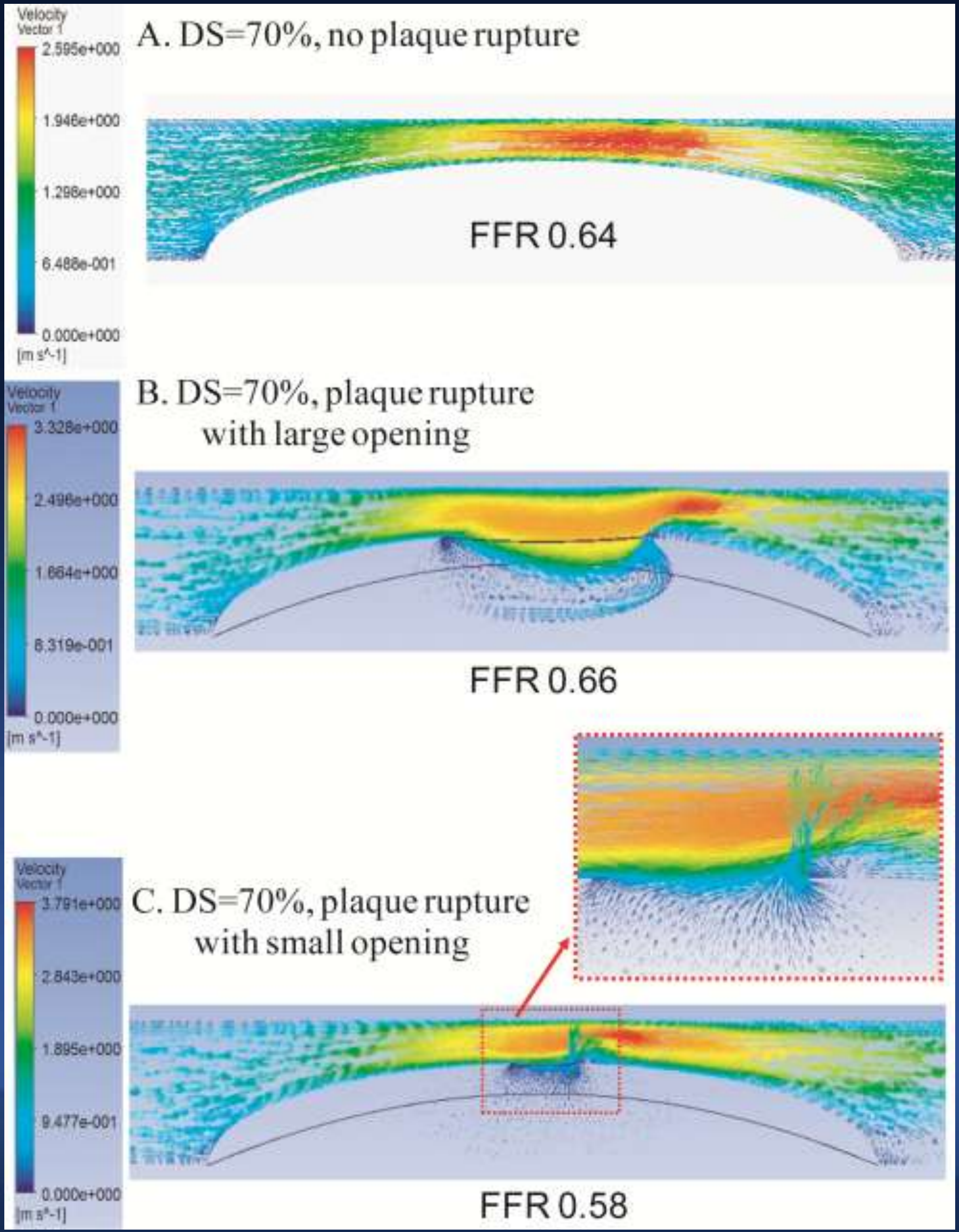
LM TCFA



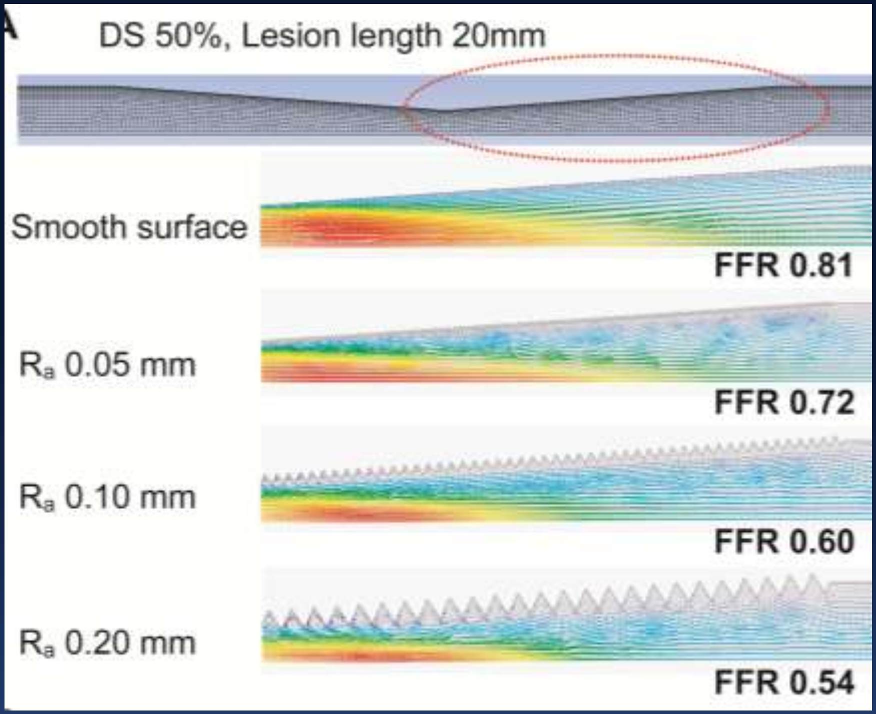
0.65 0.70 0.74 0.95



Impact of Plaque Rupture



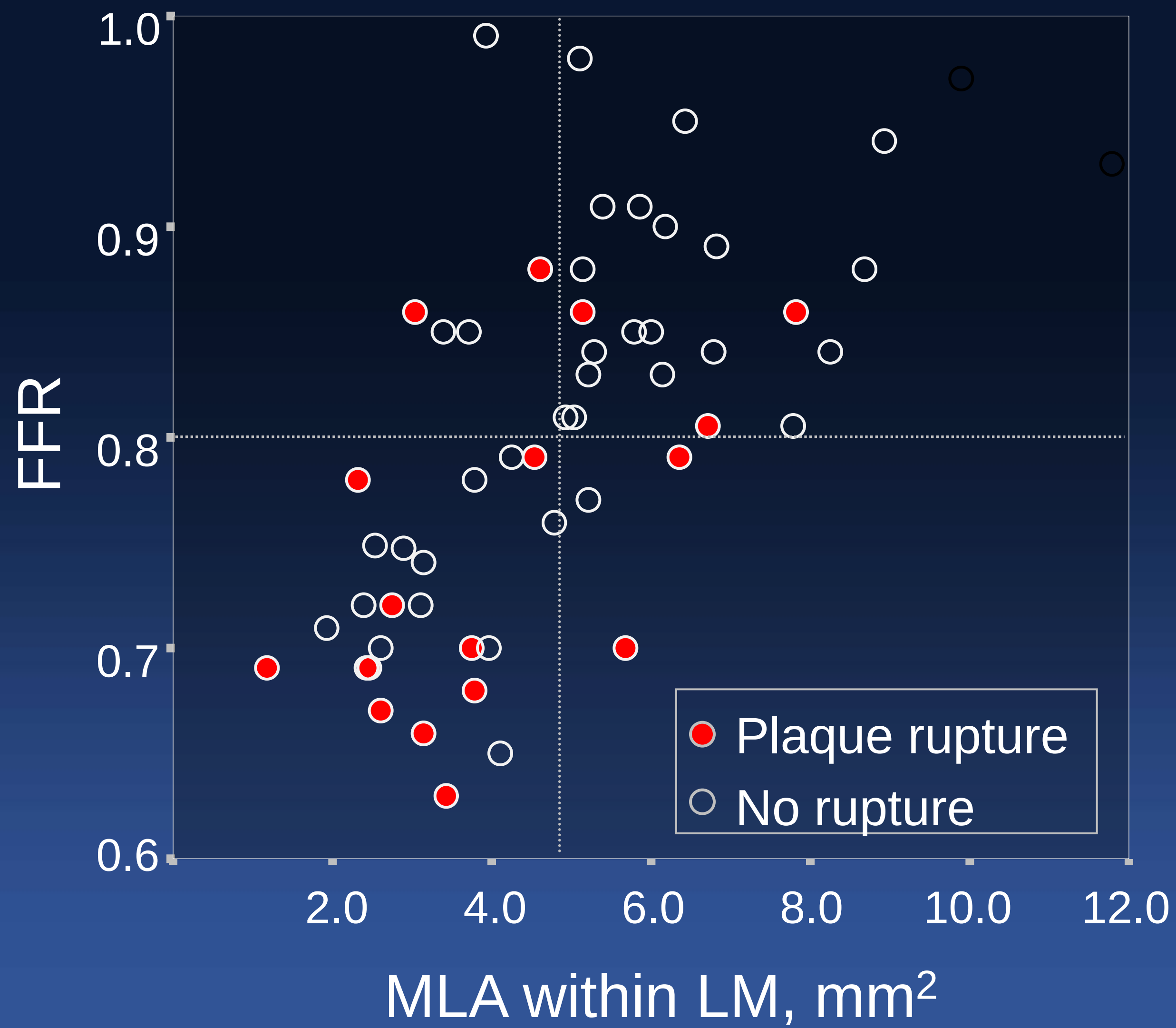
Impact of Roughness



Complex or irregular lumen produces greater flow resistance and energy loss of fluid, thus resulting in pressure drop and FFR↓

Park et al. JACC interv 2012;5:1029-36

Impact of Plaque Rupture on Ischemia



Kang et al. JACC Interv 2011;4:1168-74

FIRST: Fractional Flow Reserve and Intravascular Ultrasound Relationship Study

Ron Waksman, MD,* Jacek Legutko, MD,† Jasvindar Singh, MD,‡ Quentin Orlando, DO,§ Steven Marso, MD,|| Timothy Schloss, MD,¶ John Tugaoen, MD,# James DeVries, MD,** Nicholas Palmer, MD,†† Michael Haude, MD,‡‡ Stacy Swymelar, BS,* Rebecca Torguson, MPH*

Table 3 Virtual Histology Findings by Fractional Flow Reserve

VH IVUS Variable	Overall (N = 343)	FFR <0.8 (n = 92)	FFR ≥0.8 (n = 251)	r* Value	p Value
Plaque burden, %	68.7 ± 11.2	72.1 ± 8.7	67.4 ± 11.7	−0.220	<.001
Plaque area, mm	8.8 ± 3.8	8.8 ± 3.7	8.8 ± 3.9	0.028	0.903
Necrotic core tissue, %	21.7 ± 9.3	21.9 ± 7.9	21.7 ± 9.9	−0.037	0.809
Necrotic core tissue, mm^2	1.4 ± 0.6	1.4 ± 0.9	1.4 ± 1.0	0.002	0.676
Fibrofatty tissue, %	13.1 ± 9.3	13.3 ± 8.1	13.0 ± 9.7	0.006	0.787
Fibrofatty tissue, mm^2	0.9 ± 0.9	0.9 ± 0.8	0.9 ± 0.9	−0.015	0.861
Fibrous tissue, %	52.5 ± 15.6	54.3 ± 12.6	51.8 ± 16.5	−0.020	0.205
Fibrous tissue, mm^2	3.2 ± 2.0	3.3 ± 1.8	3.2 ± 2.0	0.011	0.723
Dense calcium, %	11.1 ± 10.7	10.5 ± 8.1	11.4 ± 11.5	−0.008	0.469
Dense calcium, mm^2	0.7 ± 0.7	0.7 ± 0.7	0.7 ± 0.7	0.013	0.992

Waksman et al. JACC 2013;61:917-23

Morphology of coronary artery lesions assessed by virtual histology intravascular ultrasound tissue characterization and fractional flow reserve

Salvatore Brugaletta · Hector M. Garcia-Garcia · Zhu Jun Shen ·

	FFR > 0.80 (*n* = 38 lesions)	FFR ≤ 0.80 (*n* = 17 lesions)	*P* value
IVUS-VH data			
Necrotic core tissue (mm^2)	0.9 ± 0.5	0.7 ± 0.4	0.2
Necrotic core tissue (%)	19.2 ± 10.2	14.2 ± 8.0	0.08
Dense calcium (mm^2)	0.5 ± 0.4	0.3 ± 0.3	0.1
Dense calcium (%)	11.0 ± 8.3	6.8 ± 4.8	0.1
VH plaque distribution			0.7
PIT, *n* (%)	6 (15)	3 (17)	
FC, *n* (%)	2 (8)	0 (0)	
FA, *n* (%)	4 (10)	3 (17)	
CaFA, *n* (%)	5 (13)	1 (8)	
TCFA, *n* (%)	6 (15)	3 (17)	
CaTCFA, *n* (%)	15 (39)	7 (41)	

Brugaletta et al. Int J Cardiovasc imaging;2012;28:221-8

Independent Predictor of TCFA

	Beta	SE	p value
Age	0.30	0.36	0.121
Gender	-0.04	7.65	0.825
Hypertension	0.02	8.11	0.934
Diabetes	0.14	6.53	0.400
Body mass index	-0.02	0.59	0.914
Smoking	-0.25	6.58	0.177
Log hs-CRP	-0.11	6.32	0.567
Microvascular dysfunction (CFR<2.0)	**0.42**	**6.90**	**0.033**

Microvascular dysfunction is associated with higher hs-CRP and predicts more TCFA, a marker of plaque vulnerability

Dhawan et al. Ahterosclerosis 2012;223:384-8

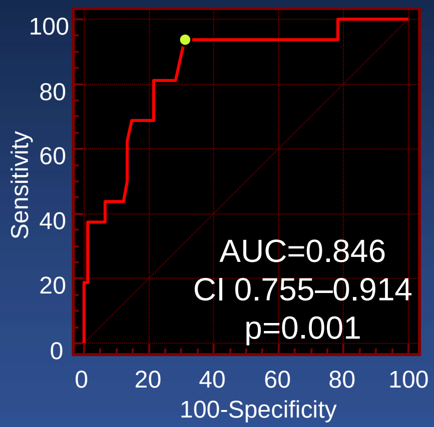
How to Physiologically Interpret IVUS Parameters?

- IVUS MLA
- Plaque Morphology
- Side Branch Stenosis
- In-stent Restenosis

Does Pre-PCI SB-IVUS Predict SB Ischemia After MB Stenting?

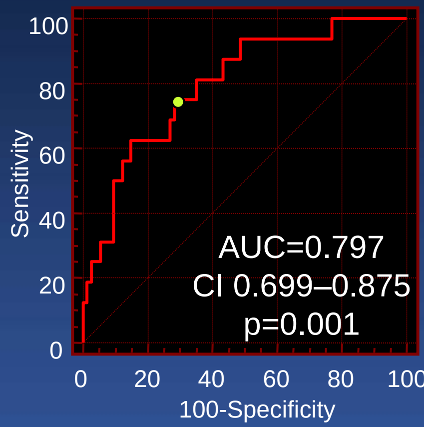
Non-LM bifurcation lesions with SB ostial DS <75%
Prediction of post-stenting SB-FFR<0.80

MLA <2.4mm²



Sensitivity=94%
Specificity=68%
PPV=40%
NPV=98%

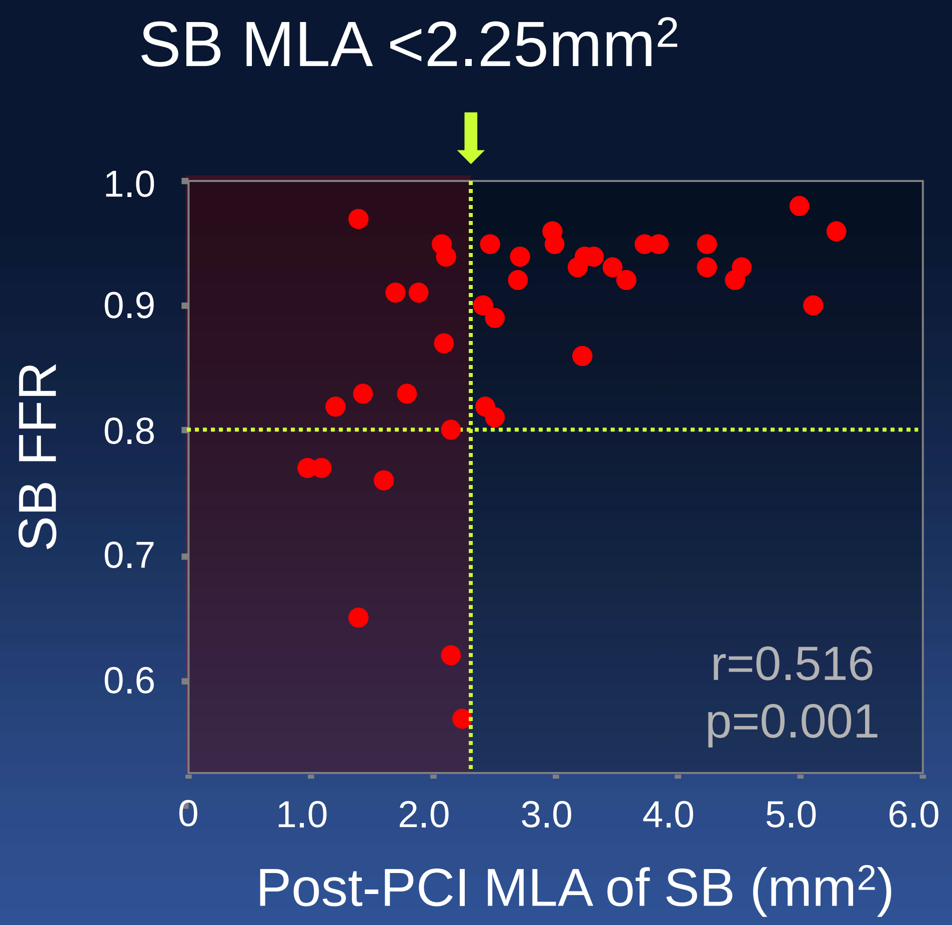
Plaque burden >50%



Sensitivity=75%
Specificity=71%
PPV=36%
NPV=93%

Kang et al. Am J Cardiol 2011;107:1787-93

Post-stenting MLA vs. SB FFR



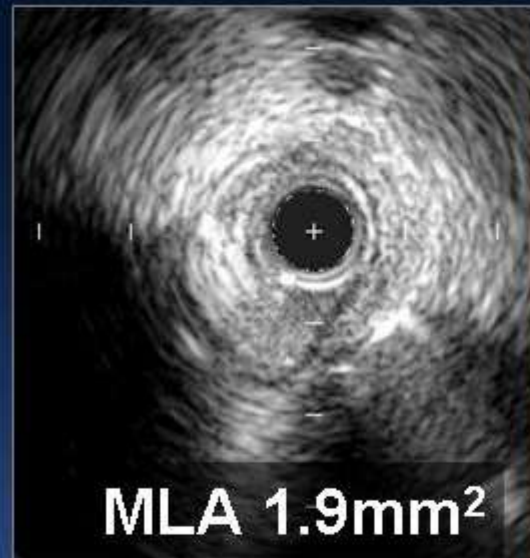
To Predict FFR<0.80

- Sensitivity 100%
- Specificity 71%
- PPV 38%
- NPV 100%

Kang et al. Catheter Cardiovasc Interv 2013;82:1072-82

Why Mismatch?

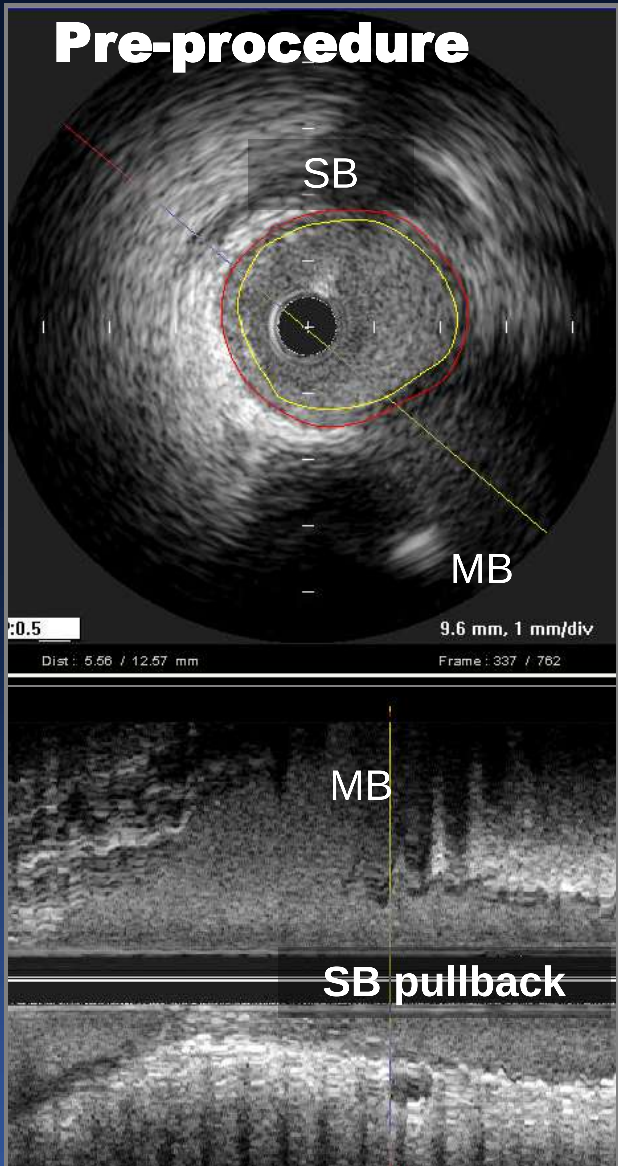
=



≠

FFR 0.83

- Lesion eccentricity of SB
- Negative remodeling of ostium
- Various size of myocardium
- Strut artifacts
- Focal carina shift

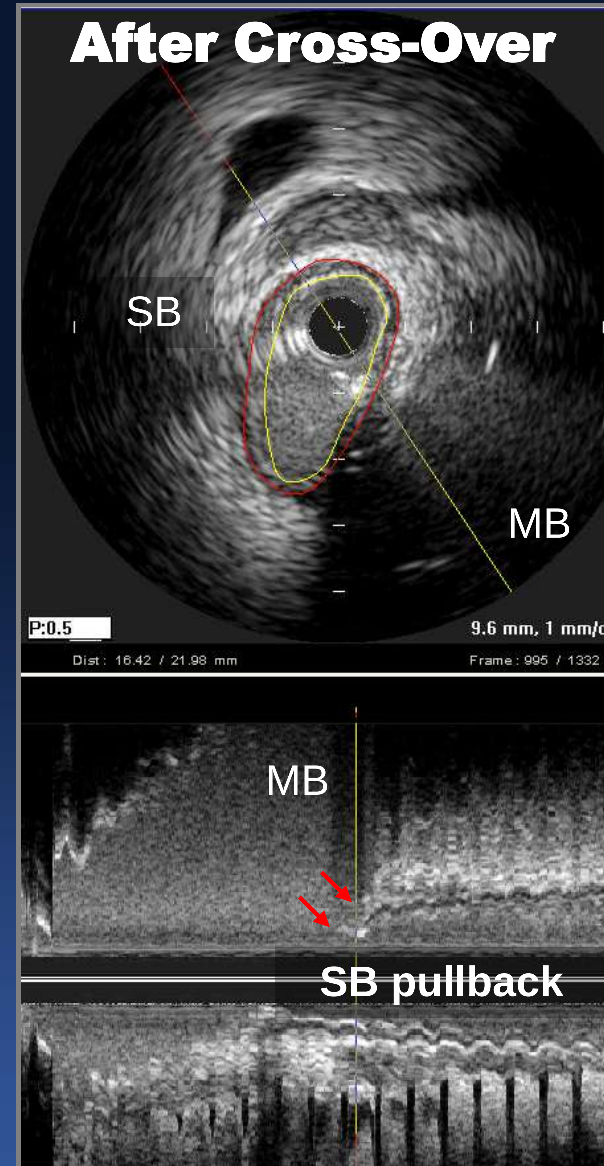


SB MLA 7.2 mm^2
EEM area 9.3 mm^2
P+M area 2.1 mm^2

Carina Shift

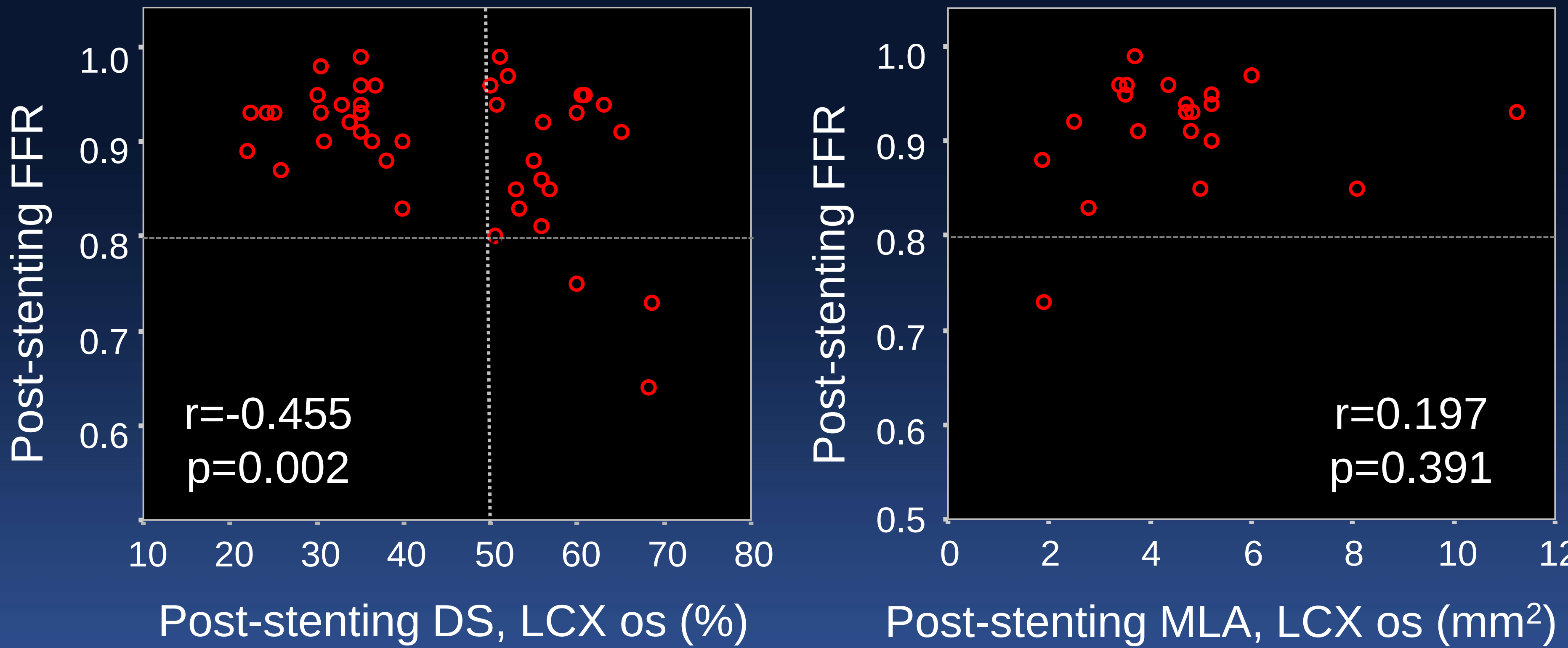
ΔV/ΔL >1
ΔP <0

Area Change	
ΔL	**-3.4 mm^2**
ΔV	**-3.5 mm^2**
ΔP	-0.1 mm^2



SB MLA 3.8 mm^2
EEM area 5.8 mm^2
P+M area 2.0 mm^2

LMCA Bifurcation
Post-stening LCX Stenosis



Small MLA within LCX ostium rarely reflects ischemia

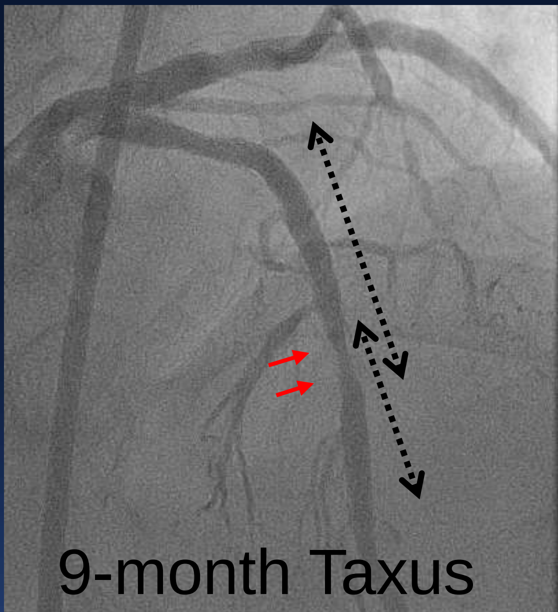
Kang et al. Catheter Cardiovasc Interv 2014;83:542-52

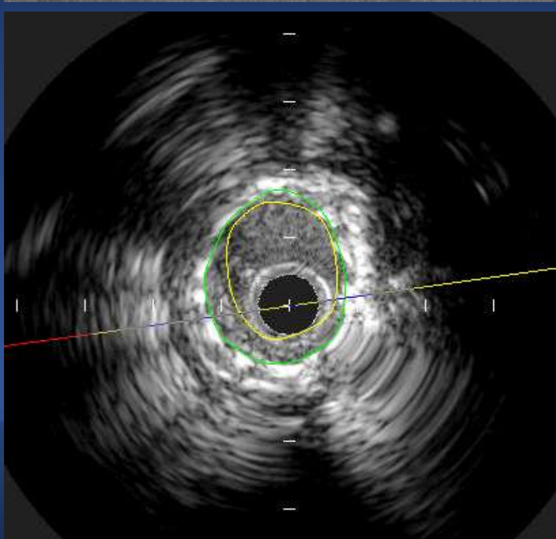
How to Physiologically Interpret IVUS Parameters?

- IVUS MLA
- Plaque Morphology
- Side Branch Stenosis
- In-stent Restenosis

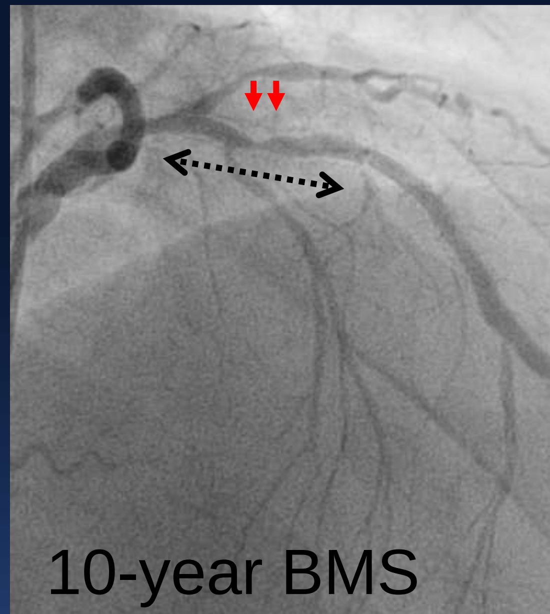
Mechanism of In-stent Restenosis

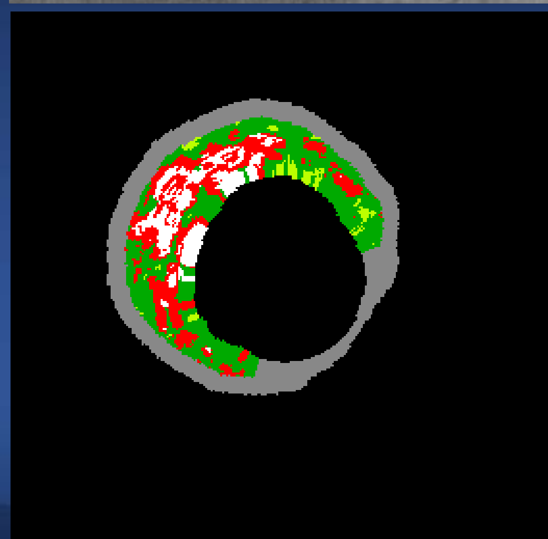
Underexpansion



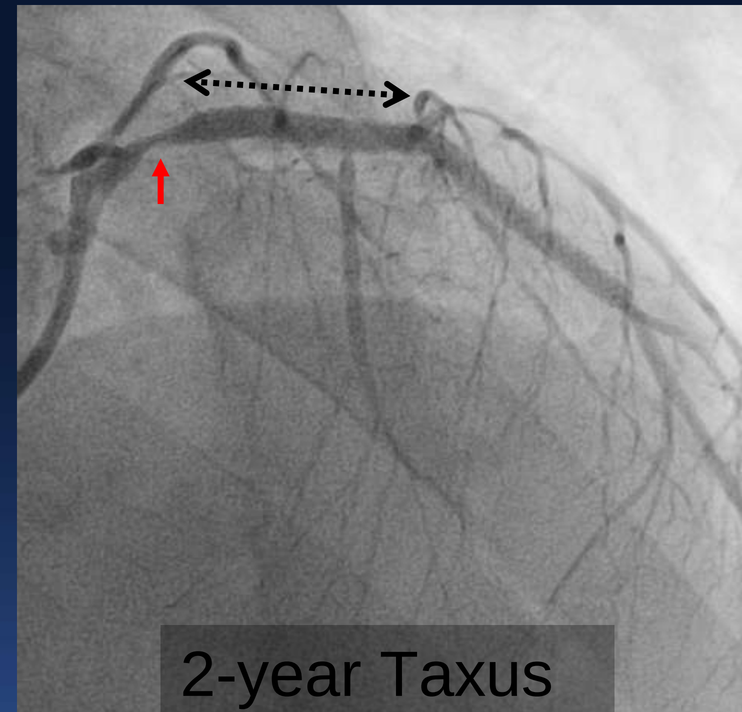


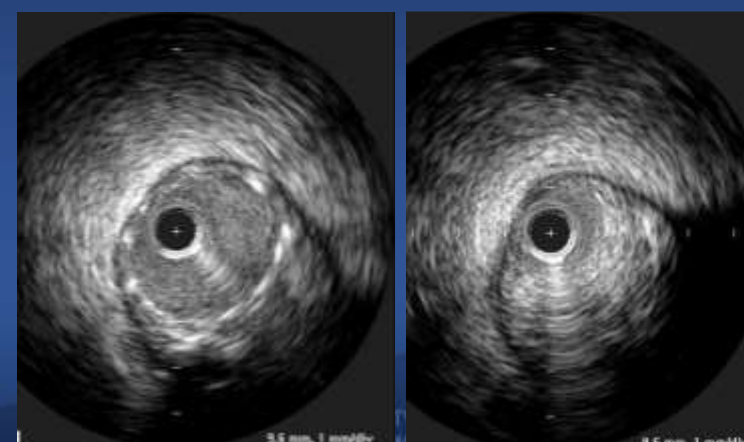
Intimal HP





Edge Restenosis

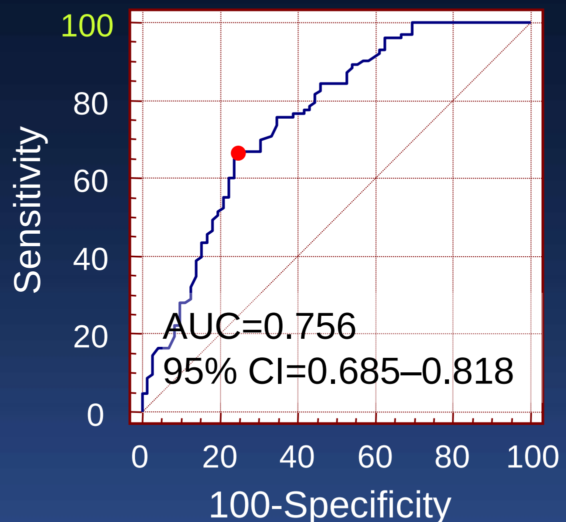




Predictors for Functionally Significant In-stent Restenosis (Positive SPECT)

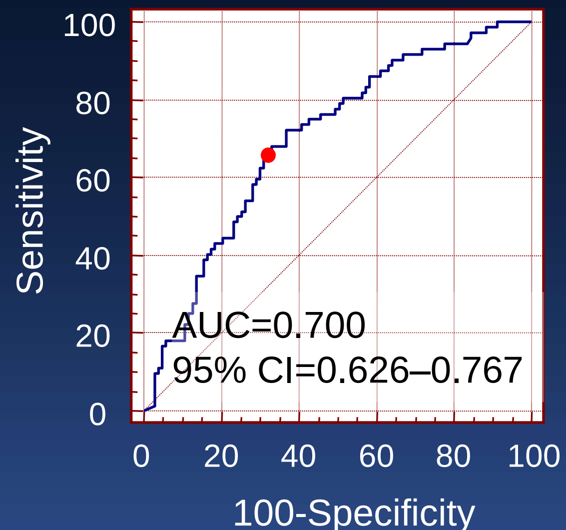
175 patients with ISR of a single coronary artery

In-seg MLA≤1.9mm²



sensitivity 67%
specificity 75%
accuracy 70%

%IH>68%



sensitivity 67%
specificity 69%
accuracy 68%

Kang et al. JACC Cardiovasc Imaging 2013 6:1183-90

Multivariable Analysis for Predicting **Positive SPECT in ISR Lesions**

	OR	95% CI	p
Diabetes	2.41	1.02–5.68	0.046
In-segment angiographic DS	1.06	1.03–1.09	<0.001
In-segment IVUS-MLA	0.30	0.14–0.63	0.001
Underexpansion (MSA<5mm^2)	2.91	1.19–7.07	0.019
Proximal 1/3 location of MLA	4.62	1.75–12.18	0.002
Multi-focal or diffuse ISR	2.50	0.99–6.28	0.050

Kang et al. JACC Cardiovasc Imaging 2013 6:1183-90

Summary

- IVUS-MLA poorly predicts ischemia. But, in pure LMCA, MLA can be alternatively used
- Plaque rupture may contribute to ischemia, while plaque composition rarely affects FFR
- After MB stenting, SB lumen loss is common. But, pre- and post-stenting small SB-MLA does not match with SB ischemia
- Although IVUS provides precise mechanism of ISR, MLA cannot predict functional significance