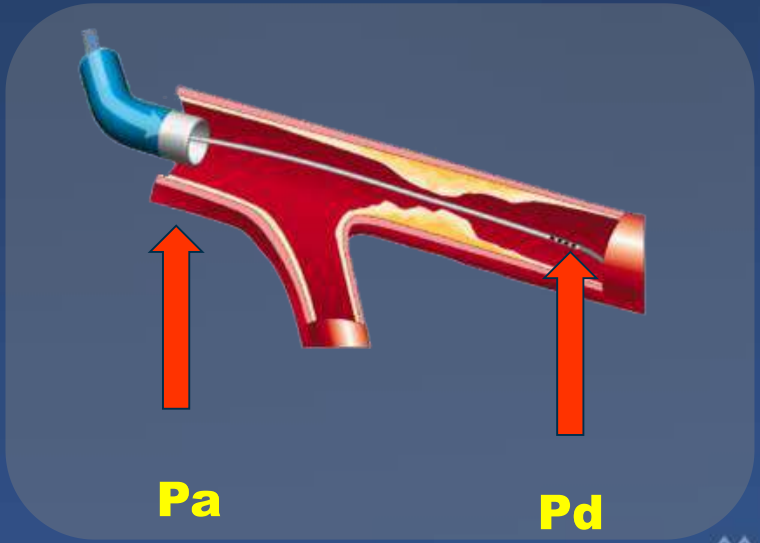
Coronary Imaging

Fractional Flow Reserve

Under the maximal hyperemia

$$FFR = \frac{Qs_{max}}{Qn_{max}} = \frac{(P_d - \cancel{P_v})/\cancel{R}}{(P_a - \cancel{P_v})/\cancel{R}}$$

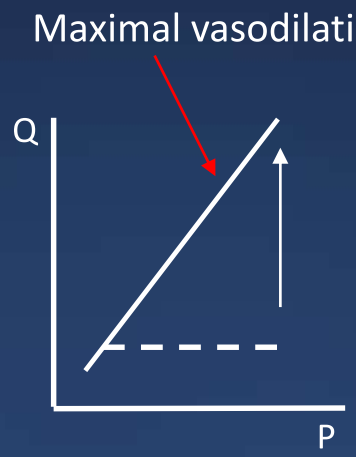
$$= \frac{Pd}{Pa}$$



Importance of Maximum Hyperemia

$$FFR = \frac{Q_S^{max}}{Q_N^{max}}$$

$$= \frac{Pd}{Pa}$$



During maximal vasodilation, the ratio of *stenotic flow* to *normal flow* is proportional to their respective driving pressures.

This is exactly the definition of the FFR: the ratio of *distal coronary pressure* to *aortic pressure*.

Importance of Maximum Hyperemia

Insufficient hyperemia

↓

Underestimation of pressure gradient

↓

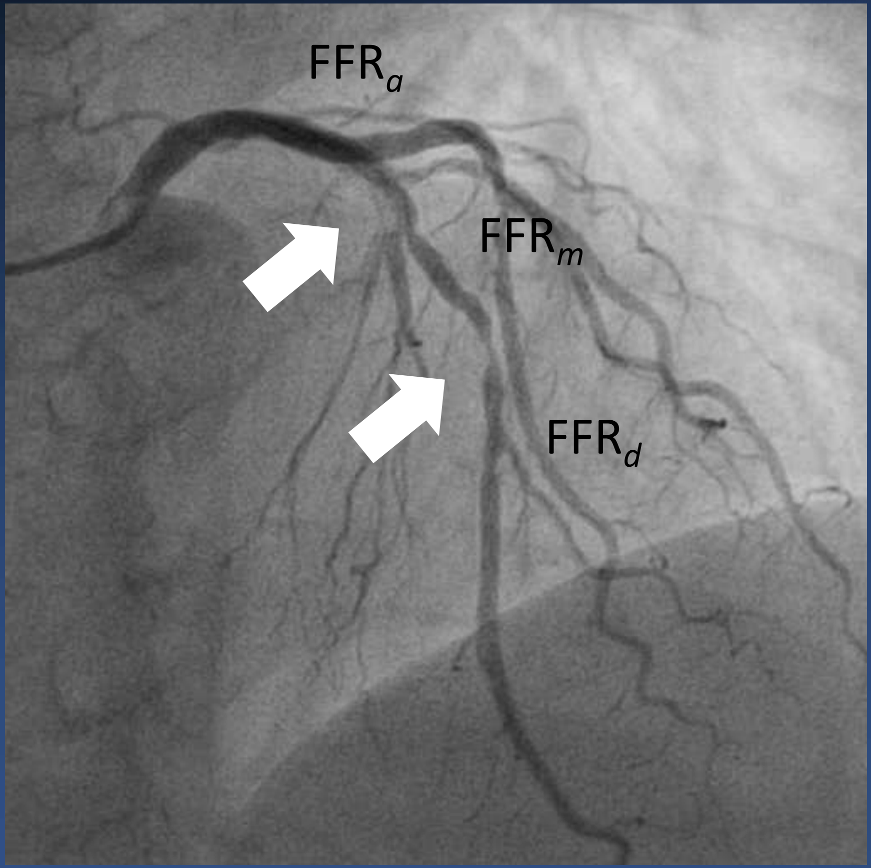
Overestimation of FFR

↓

Underestimation of Stenosis Severity

Coronary Tandem Lesions

Multiple stenoses in series along one coronary artery



Rule of Big Delta

If FFRa-FFRm > FFRm-FFRd

→ Proximal Lesion Tx First

If FFRa-FFRm < FFRm-FFRd

→ Distal Lesion Tx First

Courtesy of SJ PARK

Coronary Tandem Lesions

Multiple stenoses in series along one coronary artery

“a” lesion

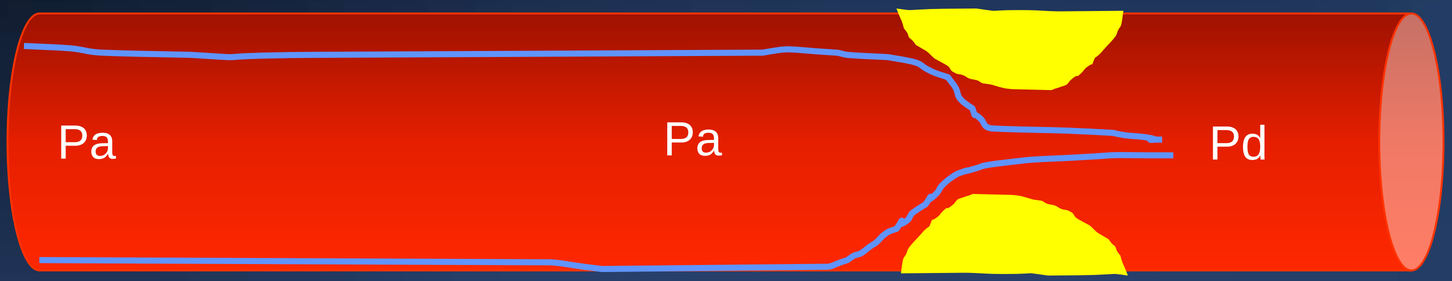
“b” lesion

FFRa = Pa-Pm/Pa

FFRb = Pd-Pm/Pm (at maximal hyperemia)

Coronary Tandem Lesions

Multiple stenoses in series along one coronary artery



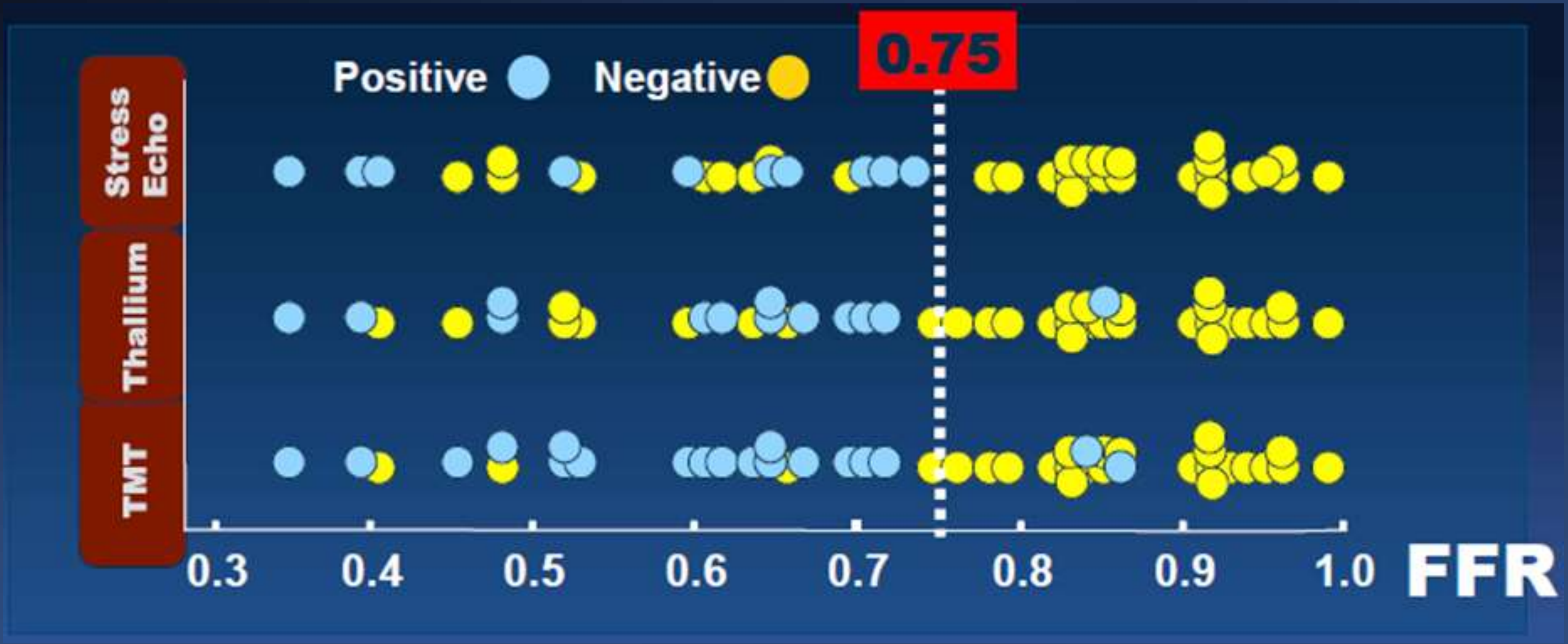
If "a" lesion is removed

FFR of "b" lesion will change

FFRb = Pd-Pa/Pa (At maximal hyperemia)

First Validation of FFR

Comparison with 3 non-invasive functional studies



N = 45 patients

Sensitivity 88%, Specificity 100%, PPV 10%, NPV 88%

N Engl J Med **1996;334:1703-8**

FFR Cut-Off Value

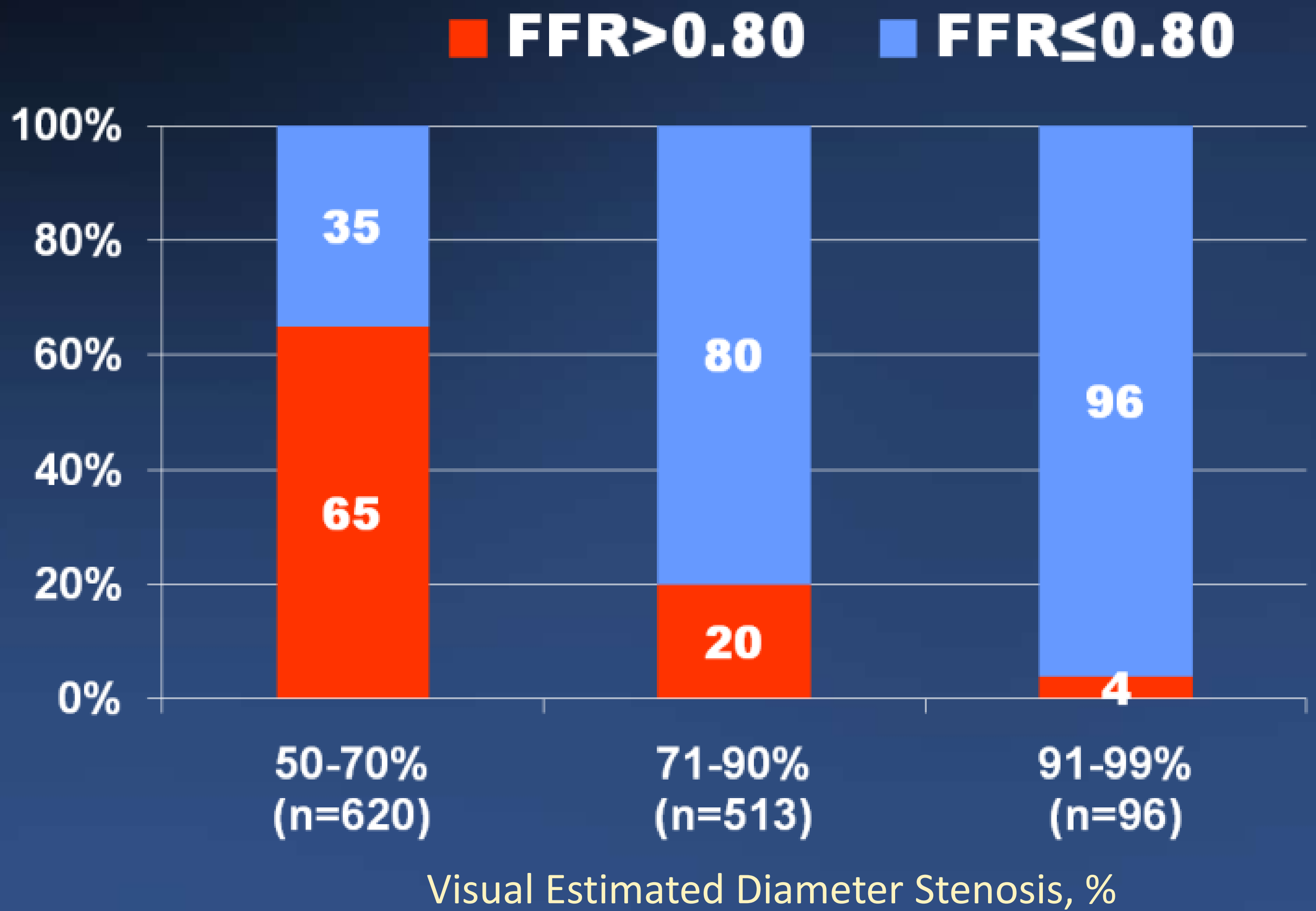
0 ← → 0.75 ↔ 0.80 ← → 1.0

Significant	grey zone	Non-significant

Author	Number	Stress Test	BCV	Accuracy
Pijls et al.	60	X-ECG	0.74	97
DeBruyne et al.	60	X-ECG/SPECT	0.72	85
Pijls et al.	45	X-ECG/SPECT/pacing/DSE	0.75	93
Bartunek et al.	37	DSE	0.68	90
Abe et al.	46	SPECT	0.75	91
Chamuleau et al.	127	SPECT	0.74	77
Caymaz et al.	40	SPECT	0.76	95
Jimenez-Navarro et al.	21	DSE	0.75	90
Usui et al.	167	SPECT	0.75	79
Yanagisawa et al.	167	SPECT	0.75	76
Meuwissen et al.	151	SPECT	0.74	85
DeBruyne et al.	57	MIBI-SPECT post-MI	0.78	85
Samady et al.	48	MIBI-SPECT post-MI	0.78	85

Visual-Functional Mismatch (I)

From FAME Study



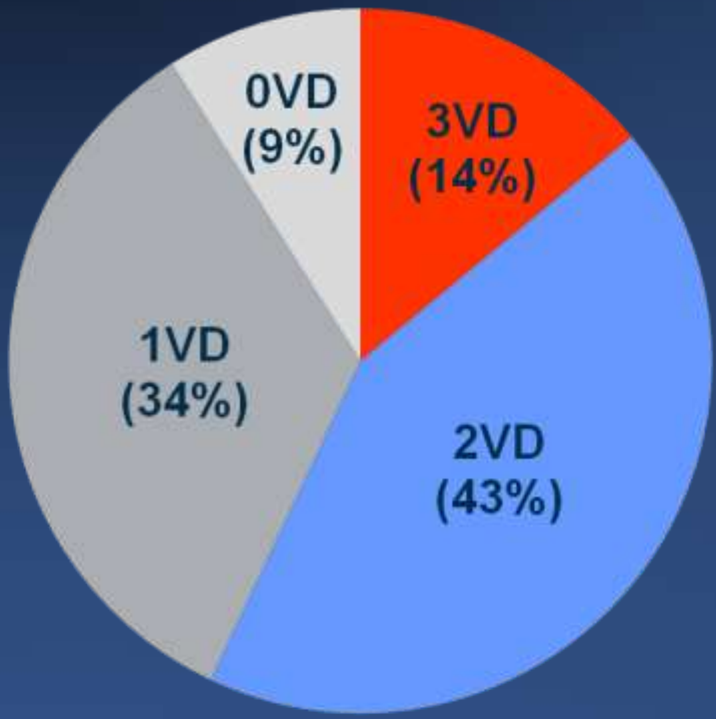
Mismatch
36.3%

J Am Coll Cardiol 2010;55:2816–21

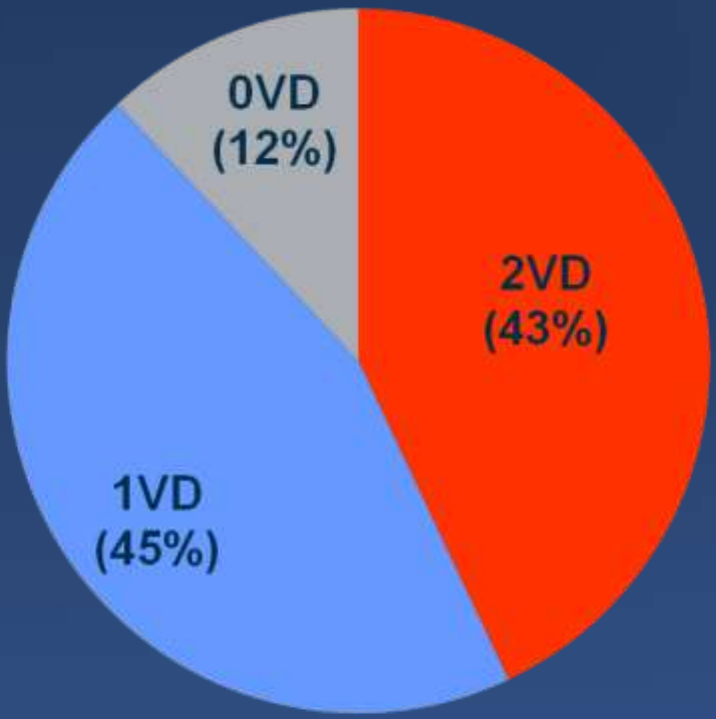
Visual-Functional Mismatch (II)

From FAME Study

Functionally Diseased Coronary Arteries



Angiographic 3VD

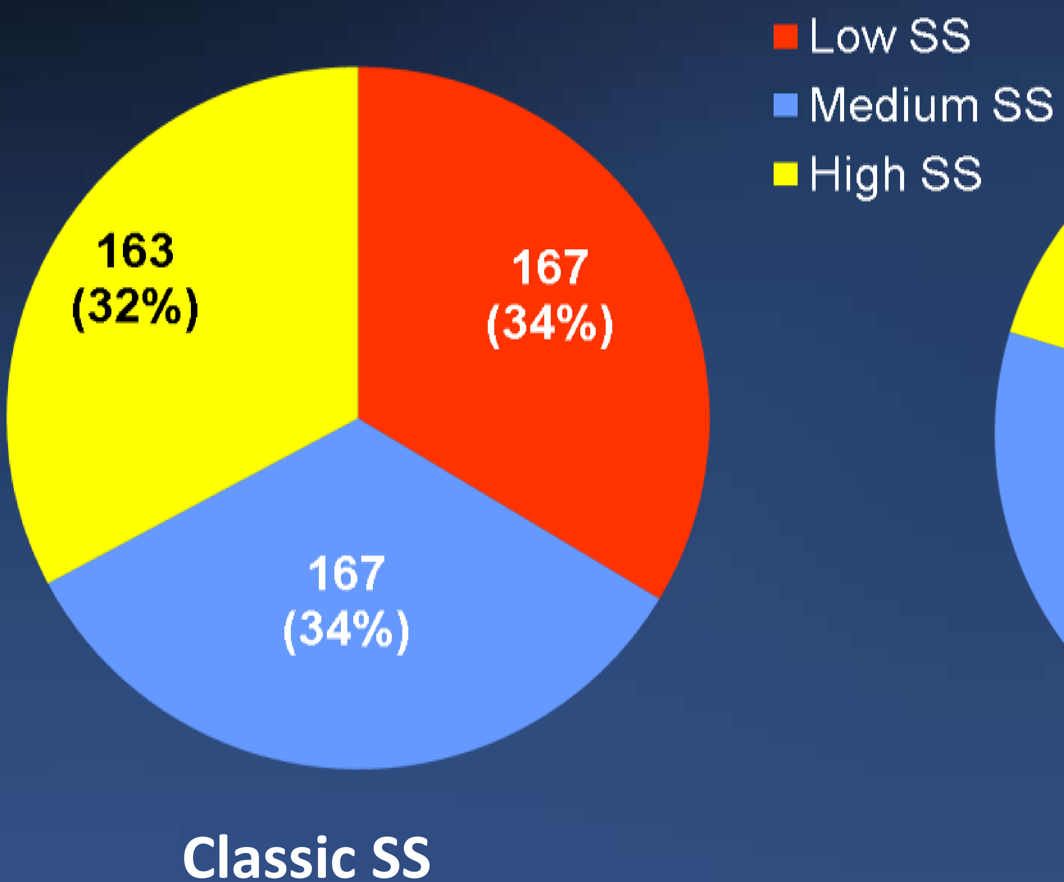


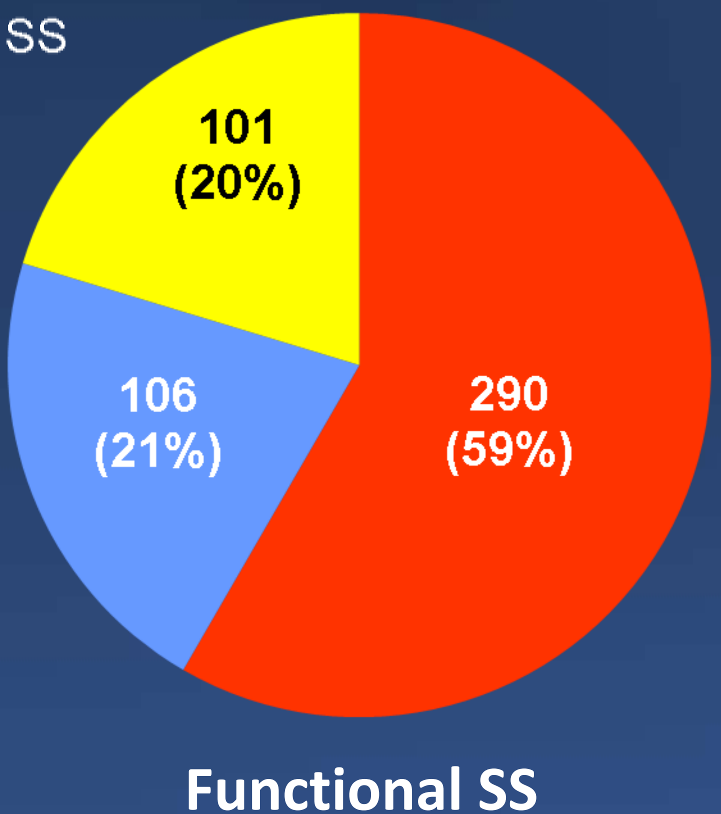
Angiographic 2VD

J Am Coll Cardiol 2010;55:2816–21

Visual-Functional Mismatch (III)

Functional SYNTAX Score in FAME





Nam et al. J Am Coll Cardiol 2011;58:1211–18

FAME @ 2yr FU

A total of 1,005 patients with multivessel CAD were randomly assigned

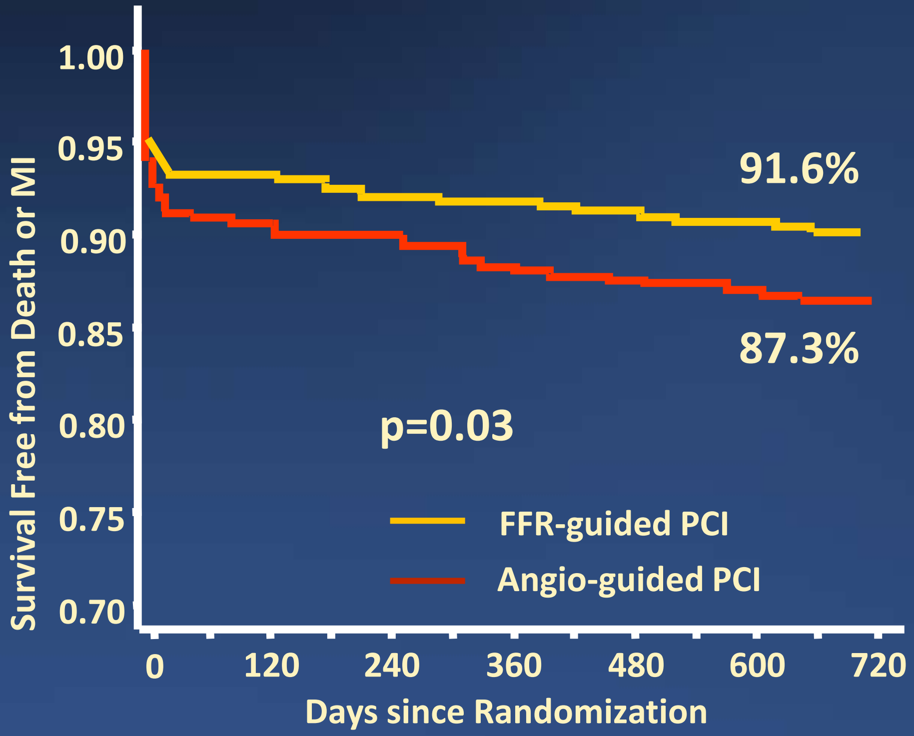
	Angio-Guided N=496	FFR-Guided N=509	p value
Total no. of MACE	139	105	
Individual Endpoints			
Death	19 (3.8)	13 (2.6)	0.25
MI	48 (9.7)	31 (6.1)	**0.03**
CABG or repeat PCI	61 (12.3)	53 (10.4)	0.35
Composite Endpoints			
Death or MI	63 (12.7)	43 (8.4)	**0.03**
Death, MI, CABG, or re-PCI	110 (22.2)	90 (17.7)	0.07
Total no. of MACE	139	105	

J Am Coll Cardiol 2010;56:177-84

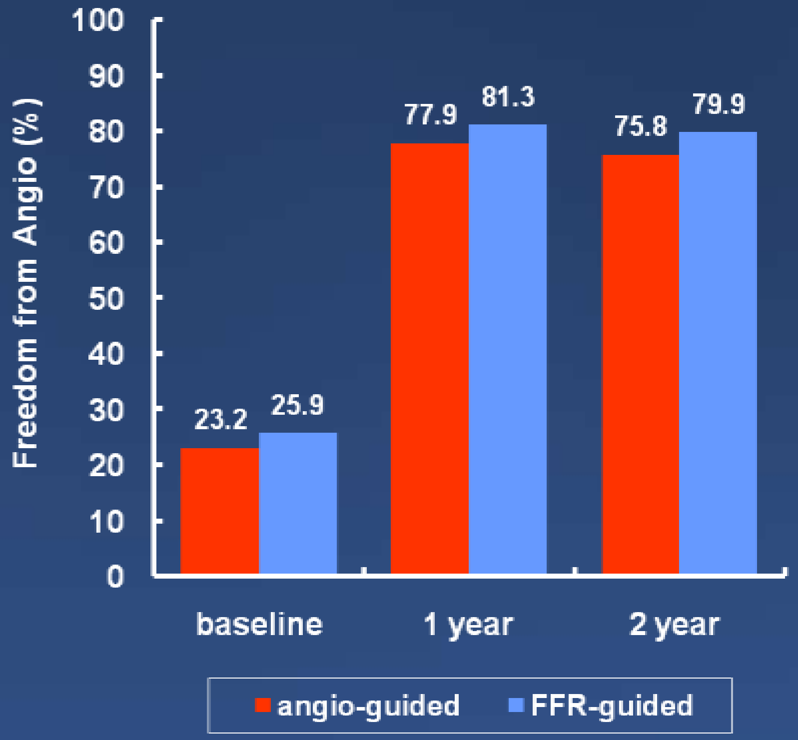
FAME @ 2yr FU

A total of 1,005 patients with multivessel CAD were randomly assigned

Death or MI



Free From Angina



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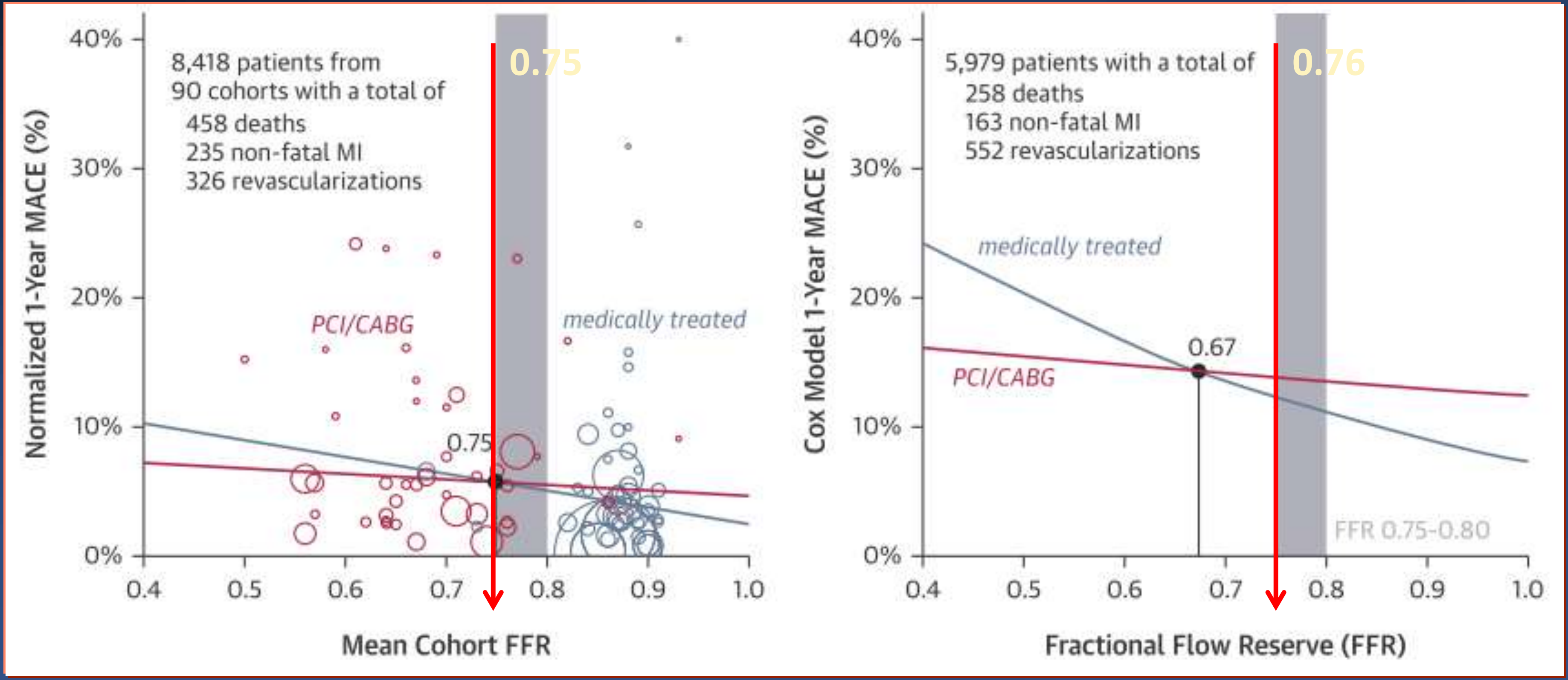
J Am Coll Cardiol 2010;56:177–84

Prognostic Value of FFR on Clinical Outcomes

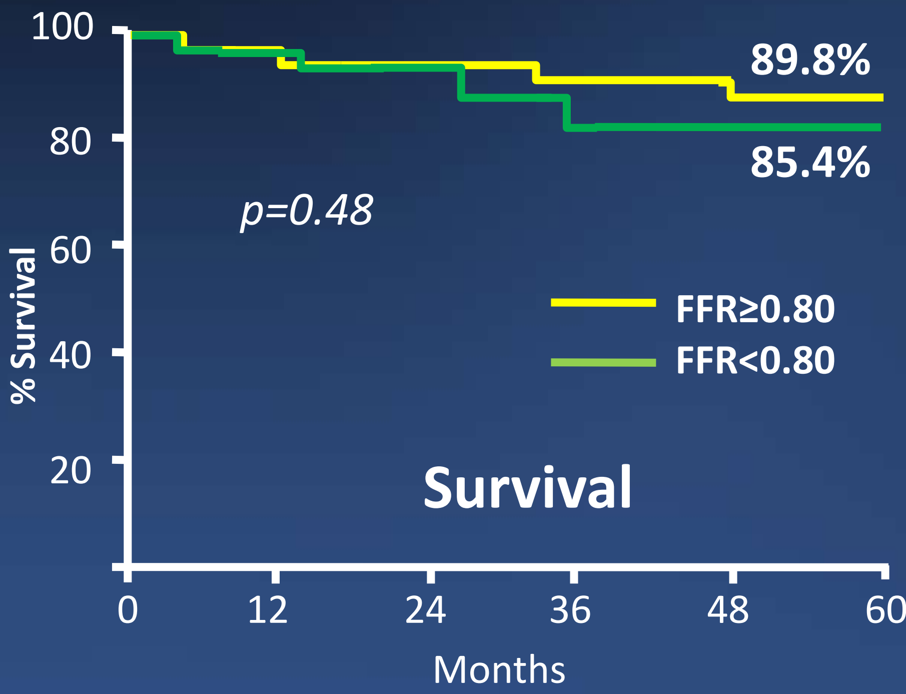
6,961 pts, 9,173 lesions

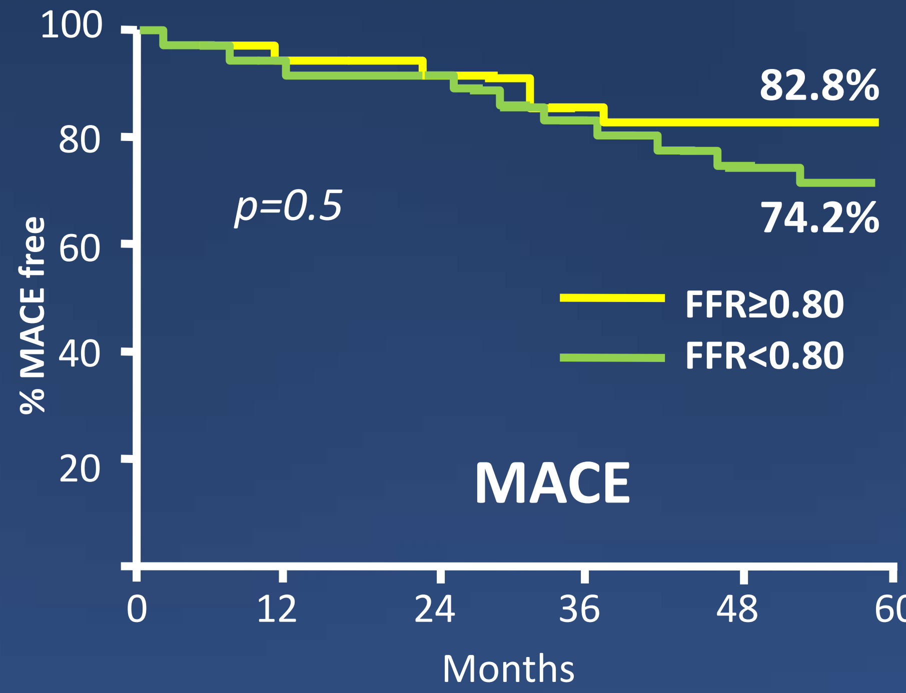


Johnson et al, JACC 2014;64:1641-54

FFR guided PCI in Equivocal LMCA

- In 213 patients with an equivocal LMCA stenosis
- FFR ≥0.80: Medication (n=138) vs. FFR<0.80: CABG (n=75)





An FFR-guided strategy showed the favorable outcome.

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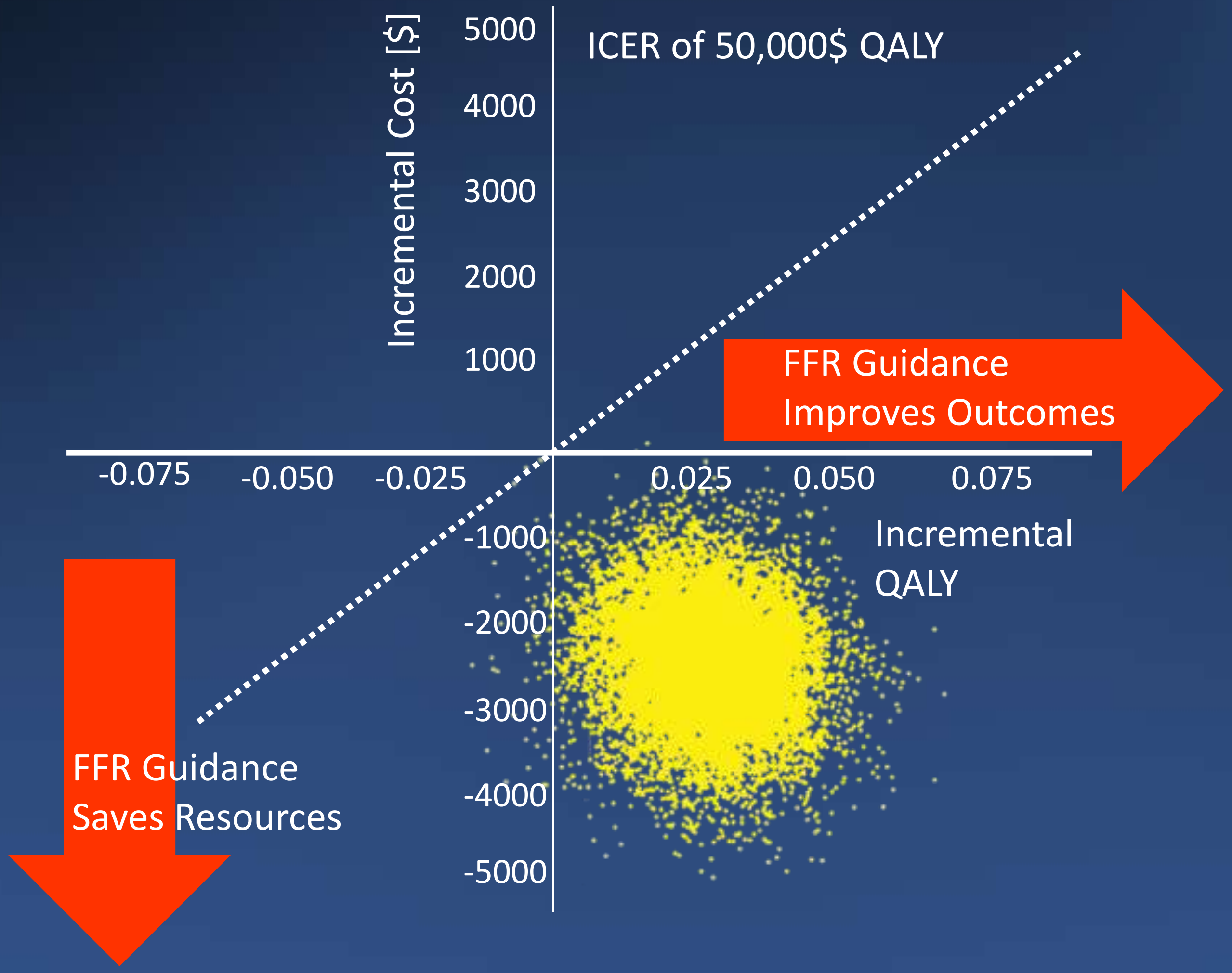
Circulation. 2009;120:1505-1512

CVRF

Saving Costs and Improving Outcomes By FFR guidance



Circulation2010;122:2545-2550

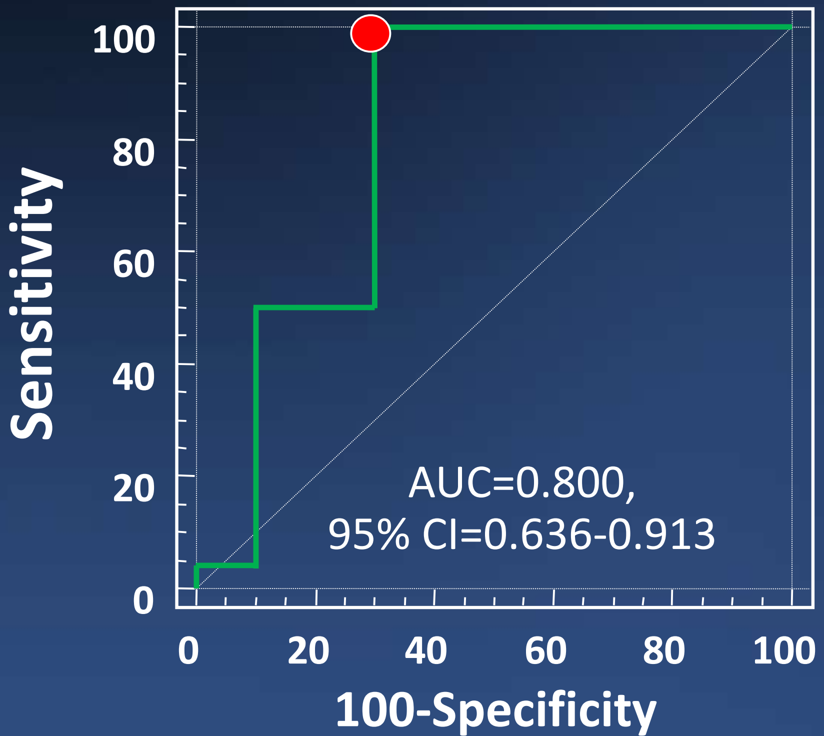
Use of IVUS vs. FFR in SB Assessment

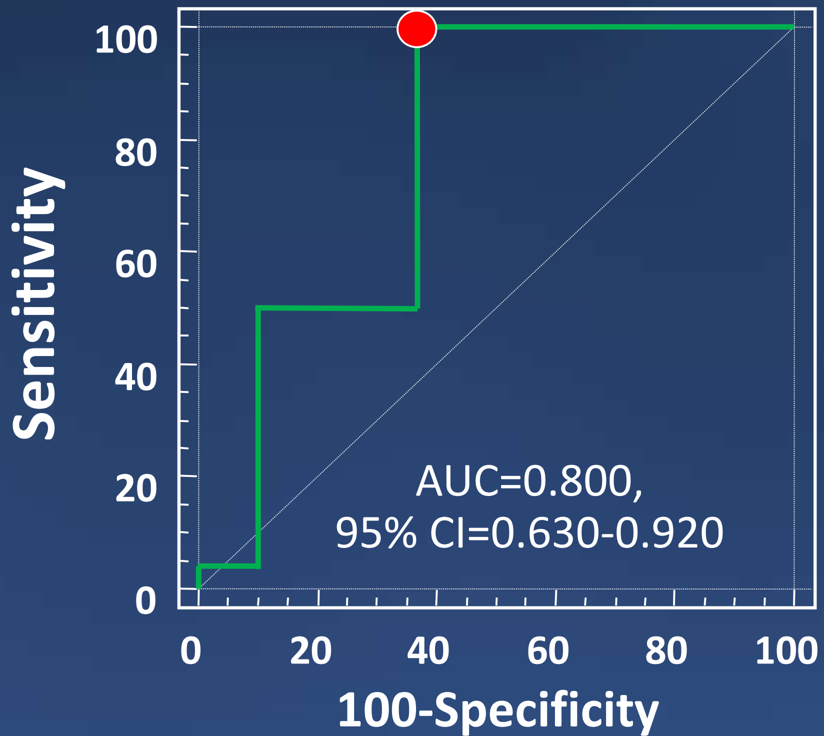
After LM Cross-over

	SB-pullback IVUS	SB FFR
Advantage	▪ Confirm the anatomical compromise and MLA loss ▪ Mechanism of SB jailing	▪ Confirm the functional SB compromise
Pitfalls	▪ MLA-FFR mismatch ▪ No MLA criteria ▪ Low feasibility	▪ Minority - not feasible

Functional Compromise of LCX after LM Cross-Over Stenting

Preporcedural MLA and plaque burden
of poststenting LCX FFR < 0.80





MLA 3.7 mm²

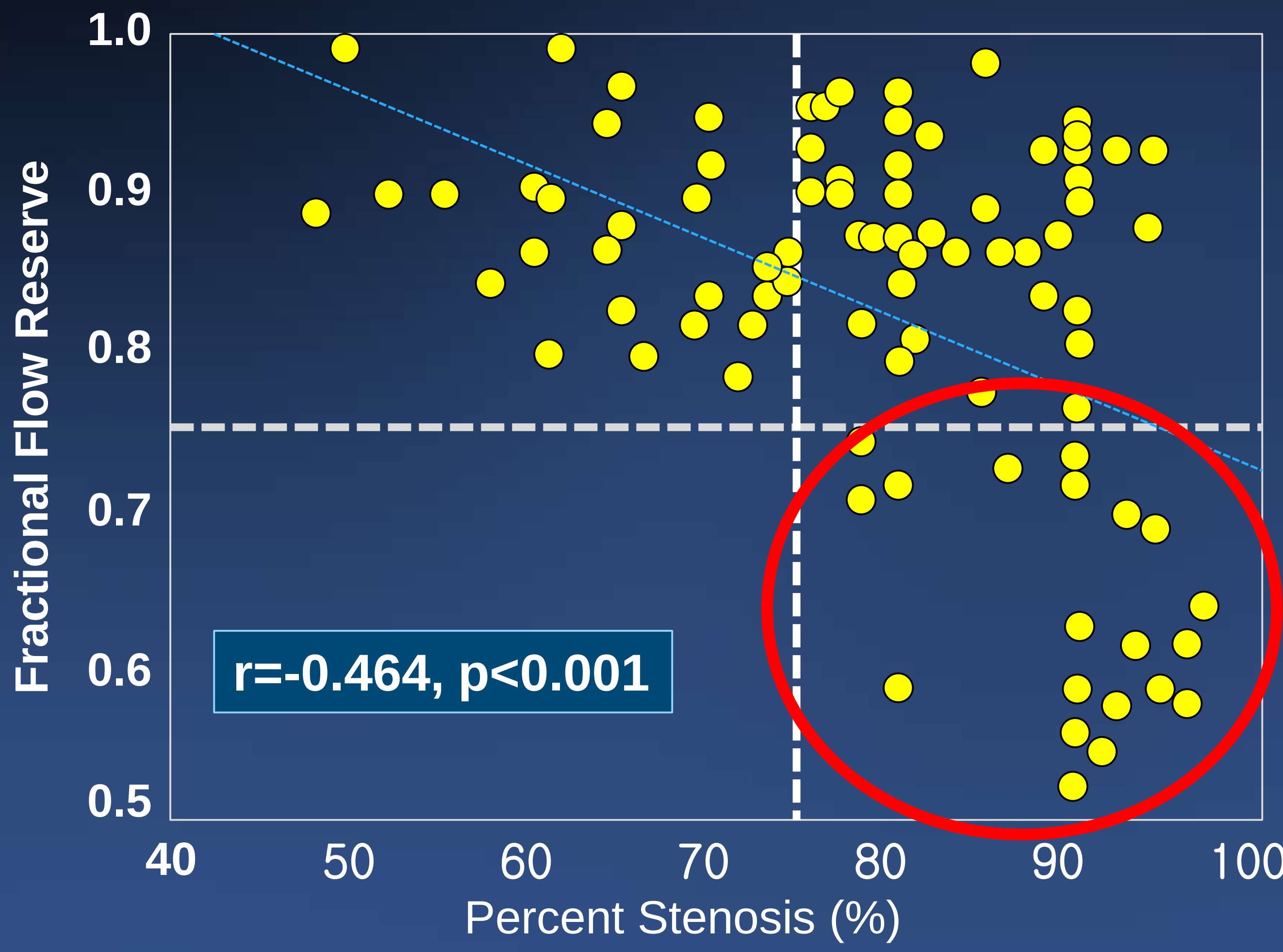
Plaque burden 56%

COMPLEX PCI Make It Simple!

Kang SJ et al. Catheter Cardiovasc Interv. 2014;83:545-552

CVRF

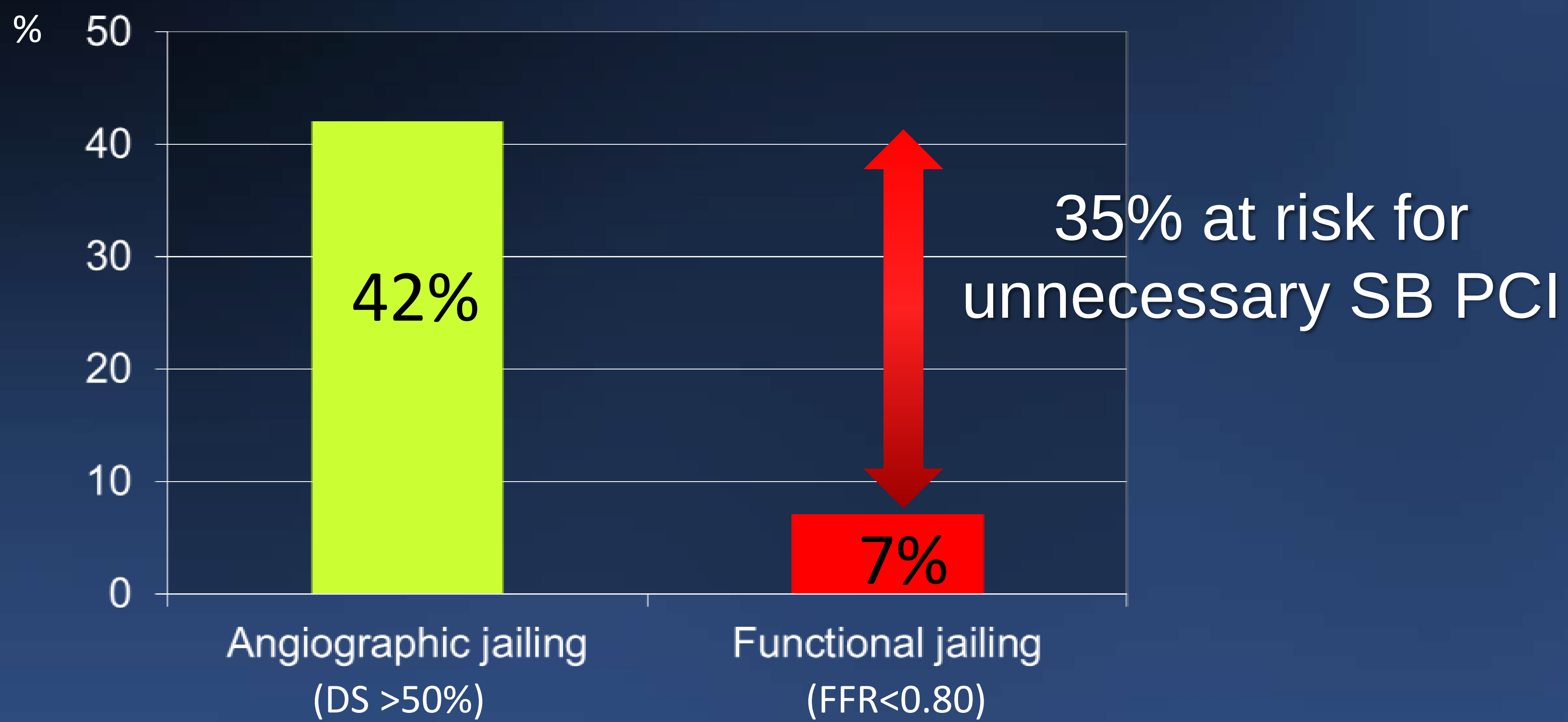
FFR of the Jailed Side Branch



Only 27% among SB with > 75% has FFR < 0.75

Koo BK et al JACC 2005; 46: 633

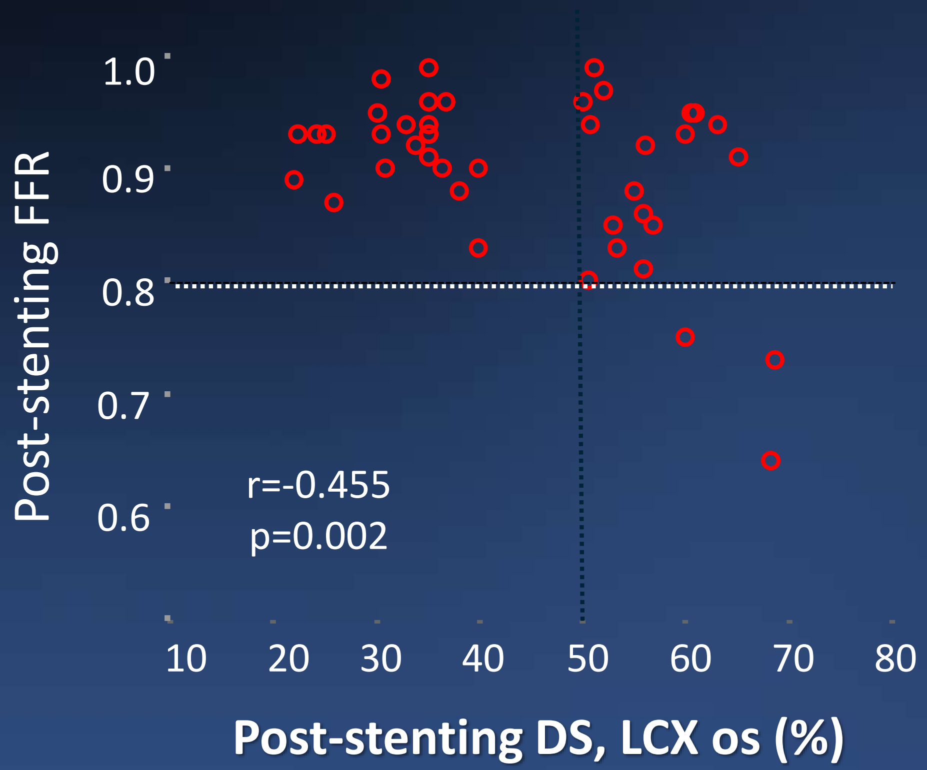
Functional LCX Compromise
In LMCA Bifurcations (LCX ostial DS<50%)

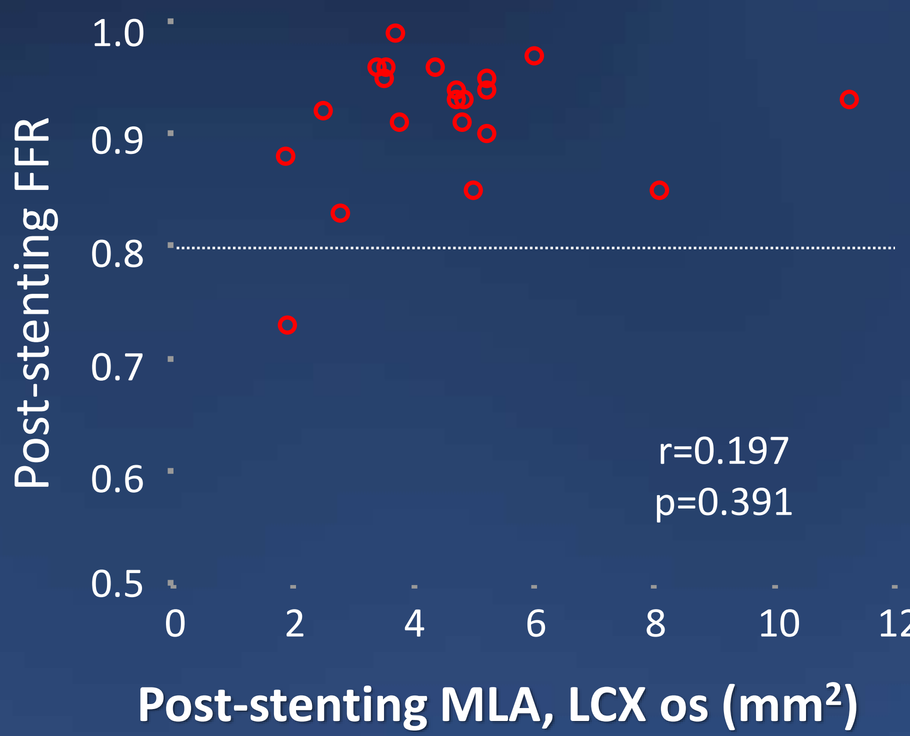


Kang et al. Catheter Cardiovasc Interv 2014;83(4):545-52

When Pre-PCI LCX Ostial DS<50%, Just Do Single Stent!

LMCA Bifurcation
Post-stenting LCX Stenosis

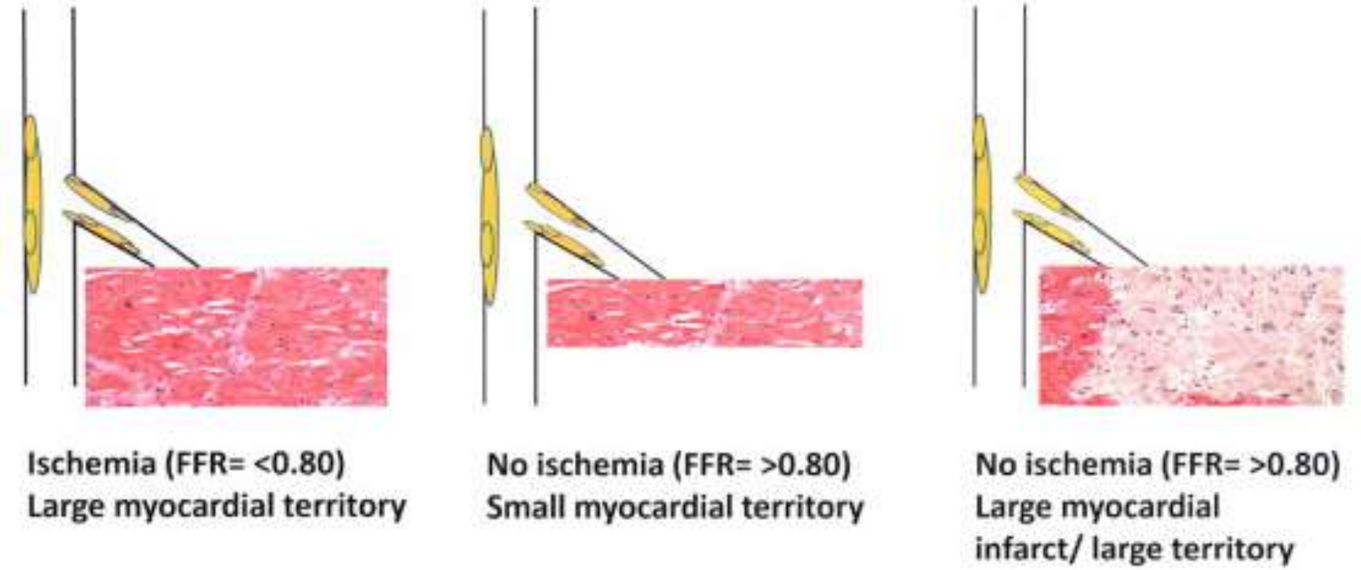




Kang et al. Catheter Cardiovasc Interv 2014;83:542-52

Why Mismatch?

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



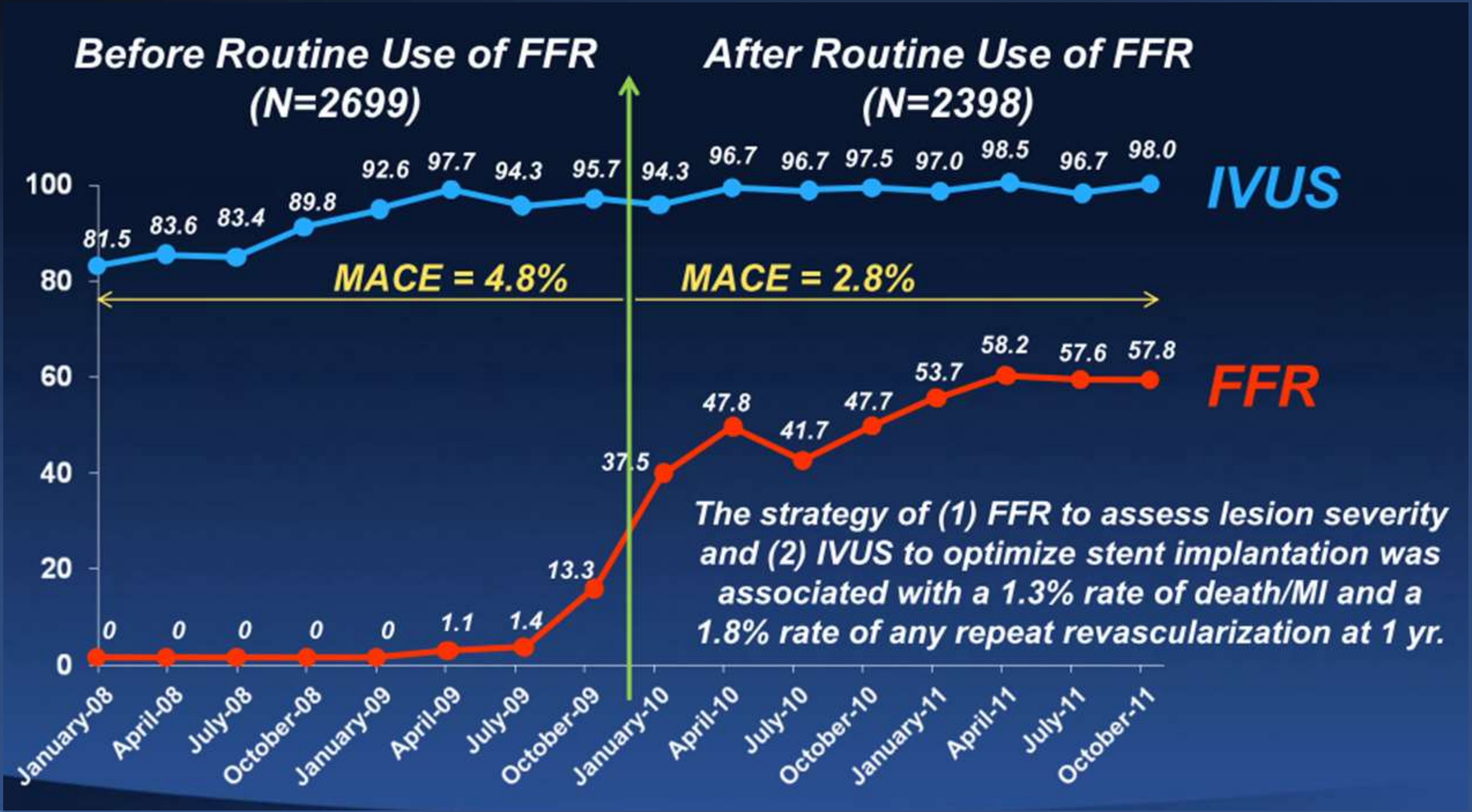
Sachdeva et al. Am J Cardiol 2011;107:1794-5

The Use of FFR

- Single Vessel Stenting
- Multivessel Stenting
- Complex Bifurcation Stenting
- Full Metal Jaket

- Deferral of PCI under OMT
- Single Vessel Stenting
- Simple Bifurcation Stenting
- Selected Stent Implantation

Between Jan 2008 and Dec 2011, 5097 pts underwent PCI at Asan Medical Center, Seoul, Korea and were followed for 1 year



COMPLEX PCI Make It Simple!

SJ Park et al. Eur Heart J 2013;34:3353-61

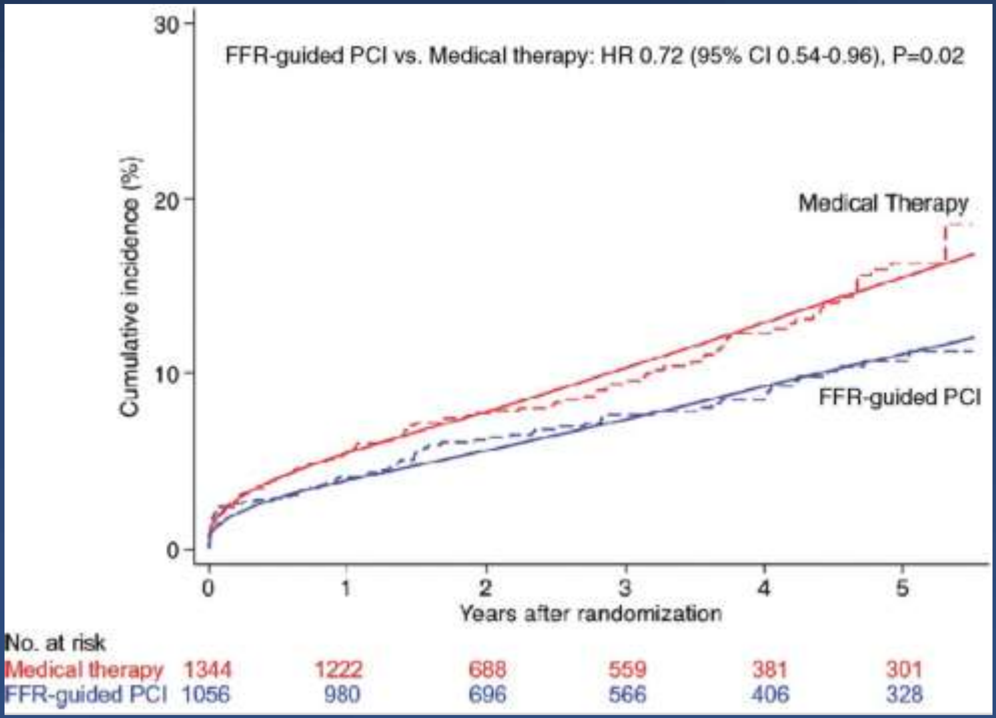
CVRF

FFR–Guided Multivessel Angioplasty in SCAD

- Stable coronary artery disease
- Meta-analysis of 3 randomized control trials
  - FAME 2 study
  - DANAMI-3-PRIMULTI
  - Compare-Acute

- Primary composite end-point : cardiac death or MI

  HR 0.72 (95% CI 0.54-0.96)



FFR–Guided Multivessel Angioplasty in Myocardial Infarction

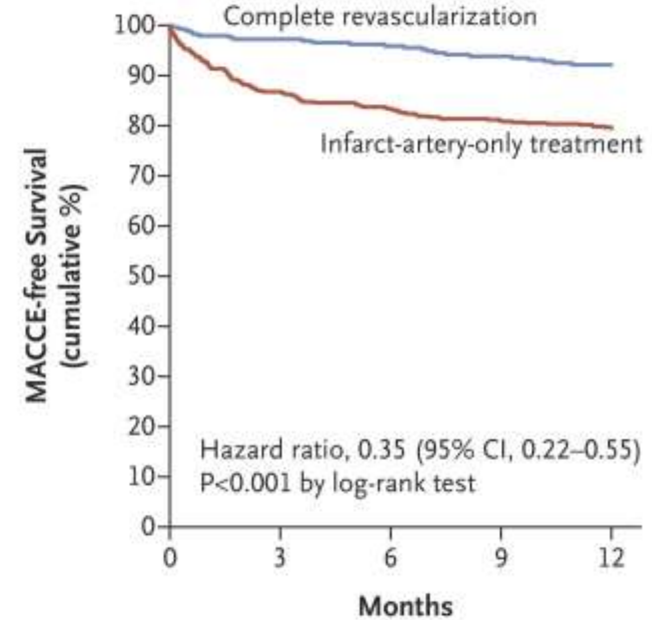
COMPARE-ACUTE trial

- 885 patients with STEMI and multivessel
- underwent primary PCI
- Randomization(1:2)

Complete revascularization of non–infarct-related coronary arteries guided by FFR (295 patients)

VS

No revascularization of non–infarct-related coronary arteries (590 patients)



No. at Risk	0	3	6	9	12
Complete revascularization	295	286	281	264	215
Infarct artery	590	512	492	457	371

Smits PC et al. N Engl J Med 2017;376:1234-1244

FFR–Guided Multivessel Angioplasty in STEMI

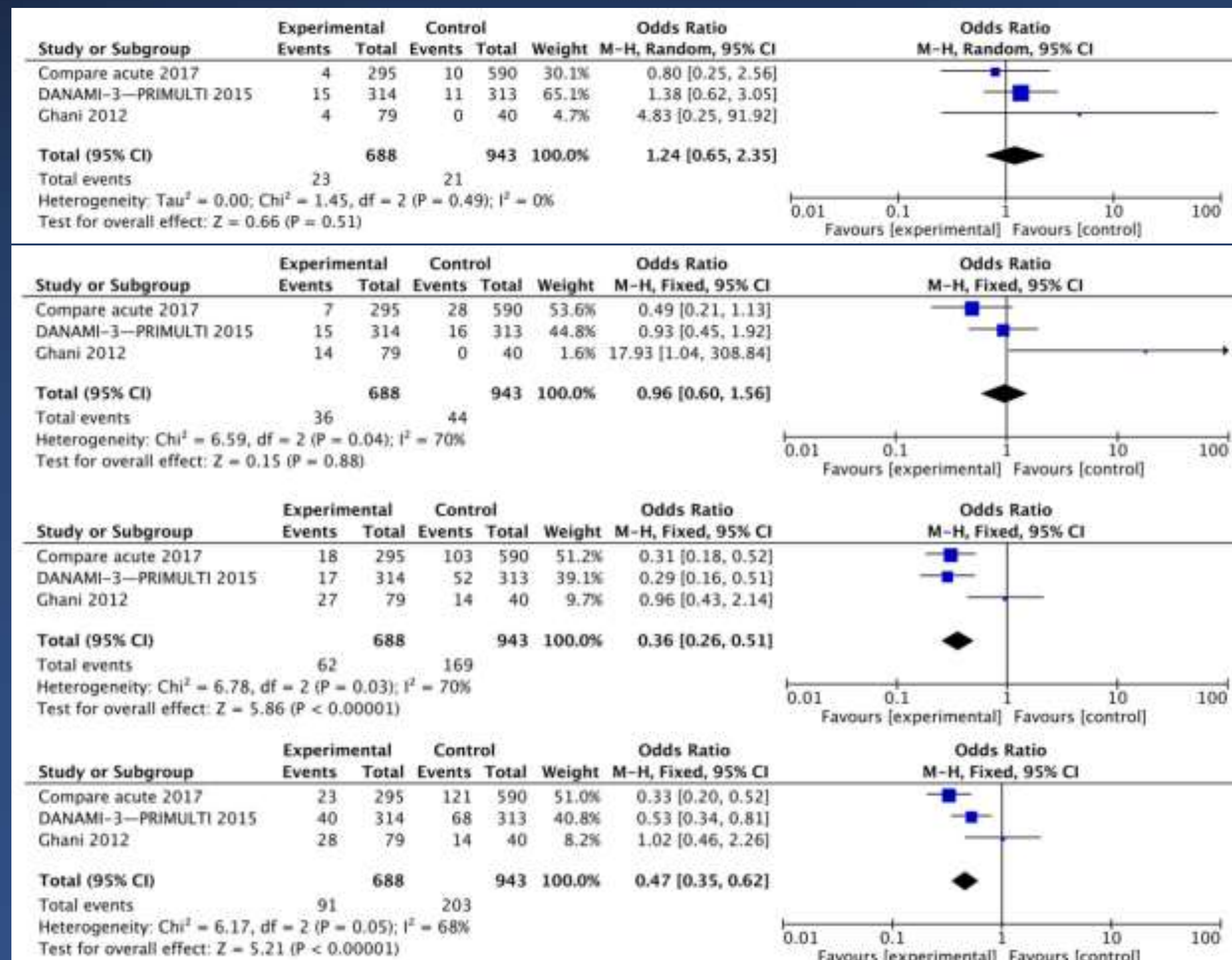
Complete revascularization by FFR vs culprit only revascularization

All cause mortality
HR 1.24 [0.65-2.35]

Non-fatal MI
HR 0.96 [0.60-1.56]

Repeat revascularization
HR 0.36 [0.26-0.51]

MACE
HR 0.47 [0.35-0.62]



Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Random, 95% CI
Compare acute 2017	4	295	10	590	30.1%	0.80 [0.25, 2.56]
DANAMI-3—PRIMULTI 2015	15	314	11	313	65.1%	1.38 [0.62, 3.05]
Ghani 2012	4	79	0	40	4.7%	4.83 [0.25, 91.92]
Total (95% CI)		**688**		**943**	**100.0%**	**1.24 [0.65, 2.35]**
Total events	23		21			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.45$, df = 2 (P = 0.49); $I^2 = 0\%$
Test for overall effect: Z = 0.66 (P = 0.51)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Compare acute 2017	7	295	28	590	53.6%	0.49 [0.21, 1.13]
DANAMI-3—PRIMULTI 2015	15	314	16	313	44.8%	0.93 [0.45, 1.92]
Ghani 2012	14	79	0	40	1.6%	17.93 [1.04, 308.84]
Total (95% CI)		**688**		**943**	**100.0%**	**0.96 [0.60, 1.56]**
Total events	36		44			

Heterogeneity: $Chi^2 = 6.59$, df = 2 (P = 0.04); $I^2 = 70\%$
Test for overall effect: Z = 0.15 (P = 0.88)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Compare acute 2017	18	295	103	590	51.2%	0.31 [0.18, 0.52]
DANAMI-3—PRIMULTI 2015	17	314	52	313	39.1%	0.29 [0.16, 0.51]
Ghani 2012	27	79	14	40	9.7%	0.96 [0.43, 2.14]
Total (95% CI)		**688**		**943**	**100.0%**	**0.36 [0.26, 0.51]**
Total events	62		169			

Heterogeneity: $Chi^2 = 6.78$, df = 2 (P = 0.03); $I^2 = 70\%$
Test for overall effect: Z = 5.86 (P < 0.00001)

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Compare acute 2017	23	295	121	590	51.0%	0.33 [0.20, 0.52]
DANAMI-3—PRIMULTI 2015	40	314	68	313	40.8%	0.53 [0.34, 0.81]
Ghani 2012	28	79	14	40	8.2%	1.02 [0.46, 2.26]
Total (95% CI)		**688**		**943**	**100.0%**	**0.47 [0.35, 0.62]**
Total events	91		203			

Heterogeneity: $Chi^2 = 6.17$, df = 2 (P = 0.05); $I^2 = 68\%$
Test for overall effect: Z = 5.21 (P < 0.00001)

Wang et al. BMC Cardiovascular Disorders (2019) 19:49

Pitfalls with Pressure Measurement

- Introducer needle
- Height of the fluid-filled transducer
- Equalization
- Hyperemia
- Drift
- Guiding catheter wedging
- Side holes
- Whipping
- Accordion effect

Instantaneous wave-Free Ratio (iFR)

$$\Delta P = \Delta Q \times R \longrightarrow \Delta P \approx \Delta Q \times R$$

Changes in pressure across a stenosis
under constant and minimized coronary resistance can
be **a surrogate for blood flow to myocardium**.

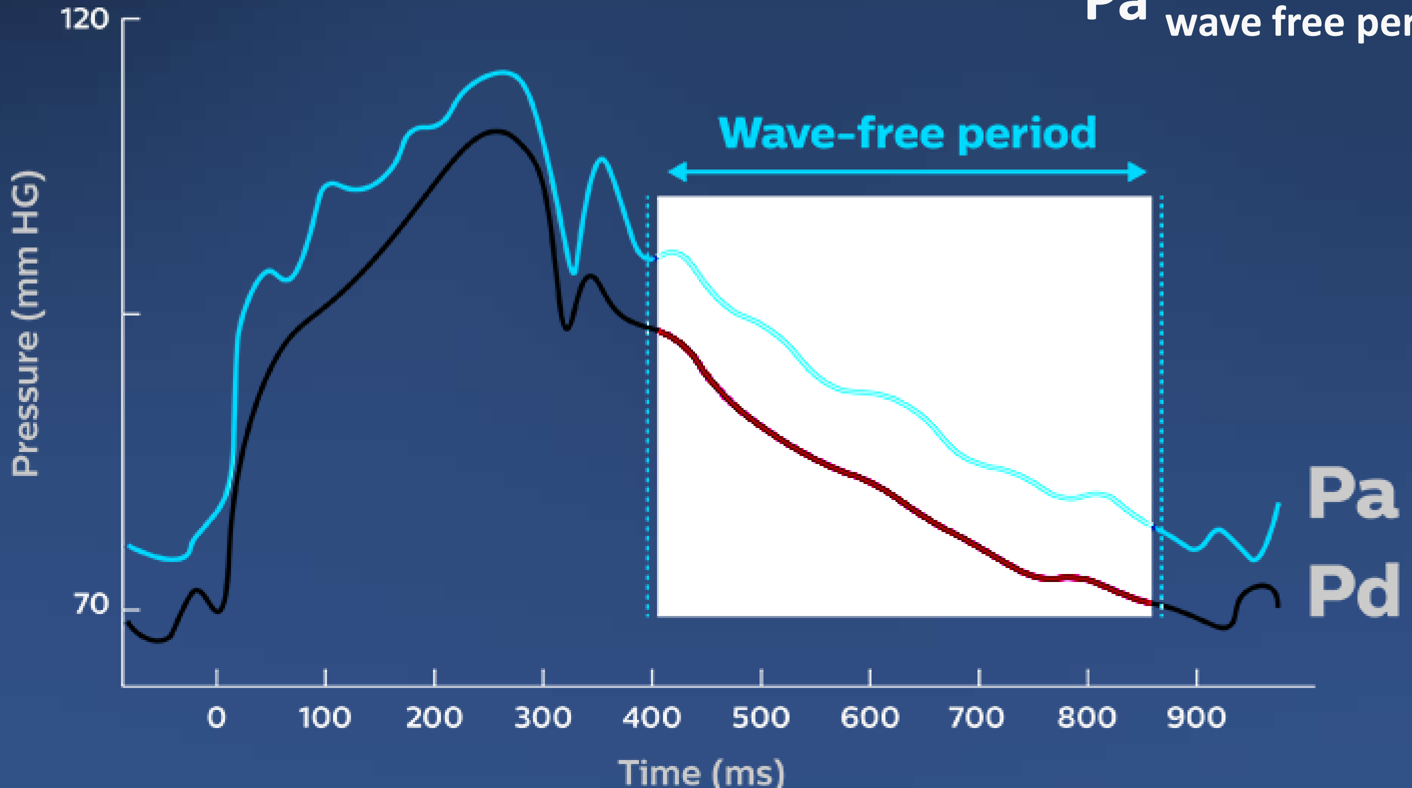
For minimizing intracoronary resistance during measurment

- FFR : adenosine infusion, average over several cycles
- iFR : **wave free period**, instantaneous pressure

Instantaneous wave-Free Ratio (iFR)

- Wave free period ; resistance naturally constant and minimized in the cardiac cycle

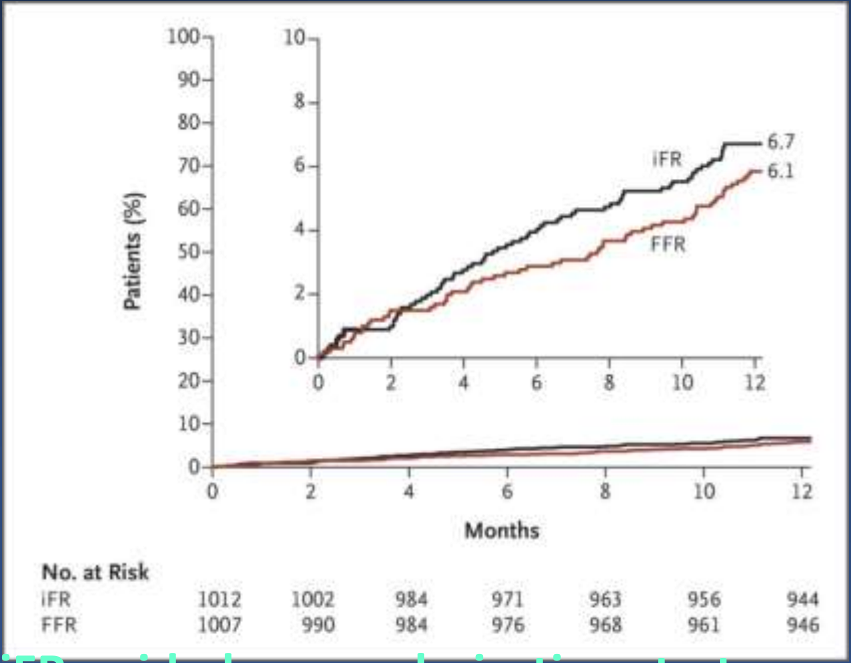
$$iFR = \frac{Pd_{\text{wave free period}}}{Pa_{\text{wave free period}}}$$



iFR vs FFR to Guide PCI

iFR-SWEDEHEART trial

- 2037 participants with stable angina or an acute coronary syndrome
- Underwent coronary revascularization
- Randomization (1:1)
- a multicenter, controlled, open-label clinical trial



iFR-guided
VS
FFR-guided

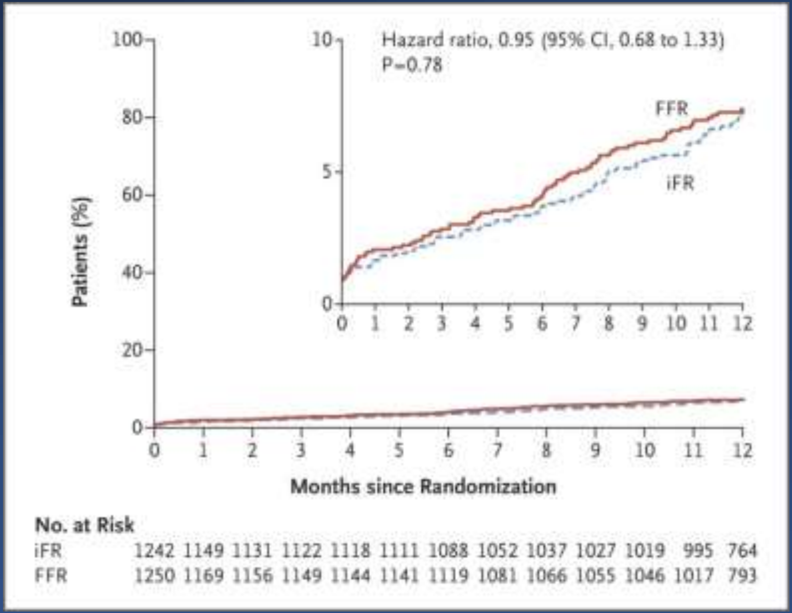
An iFR-guided revascularization strategy was noninferior to an FFR-guided revascularization strategy with respect to the rate of MACE(1yr)

Götberg M et al. N Engl J Med 2017. DOI: 10.1056/NEJMoa1616540

Use of the Instantaneous Wave-free Ratio

DEFINE-FLAIR trial

- 2492 patients with coronary artery disease
- Underwent coronary revascularization
- Randomization (1:1)
- a multicenter, international, blinded trial



iFR-guided
VS
FFR-guided

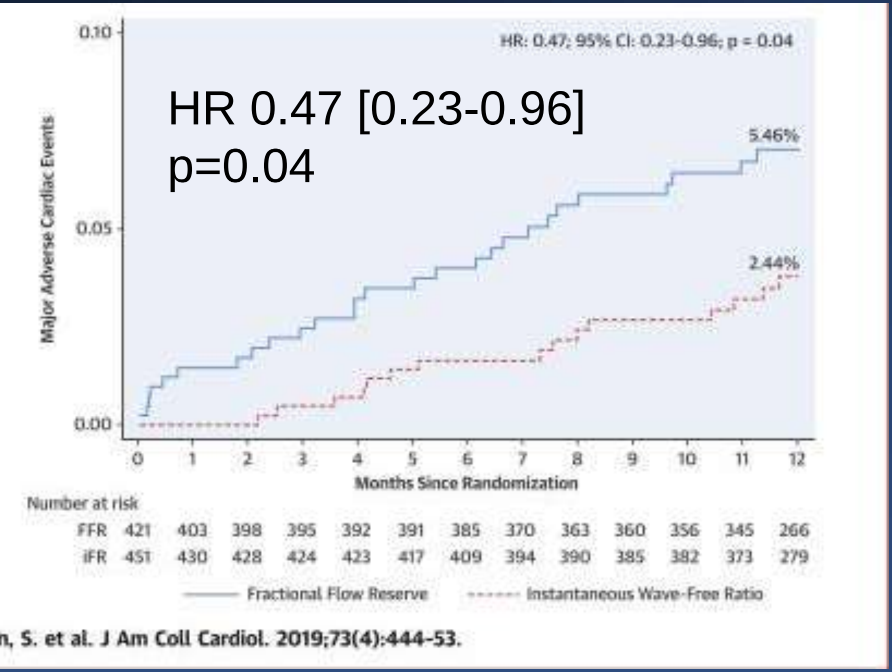
Coronary revascularization guided by iFR was noninferior to revascularization guided by FFR with respect to the risk of MACE(1yr)

Davies JE et al. N Engl J Med 2017. DOI: 10.1056/NEJMoa1700445

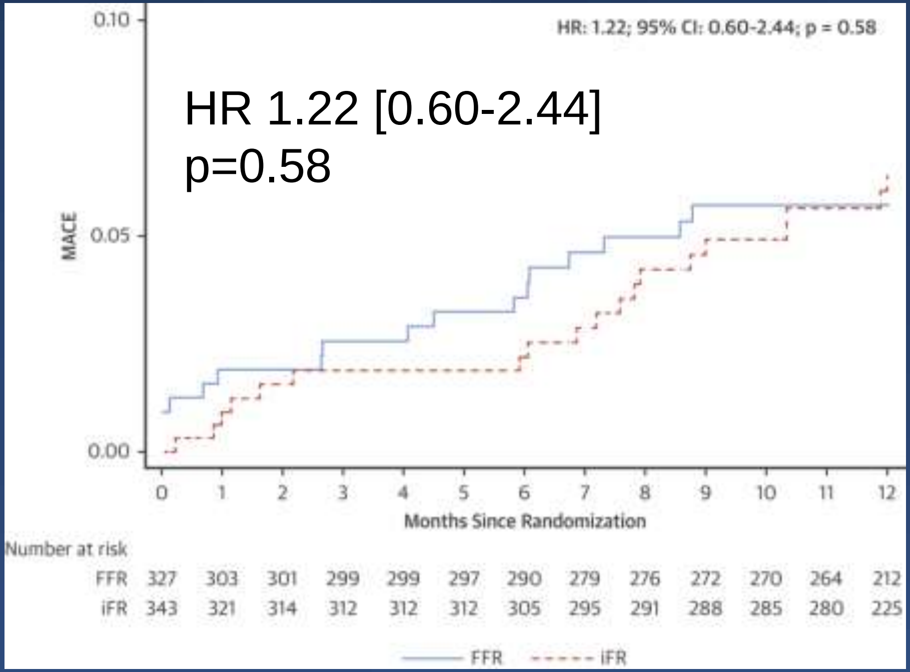
iFR vs FFR in LAD lesions

DEFINE-FLAIR trial sub-study

LAD lesion



Non-LAD lesion



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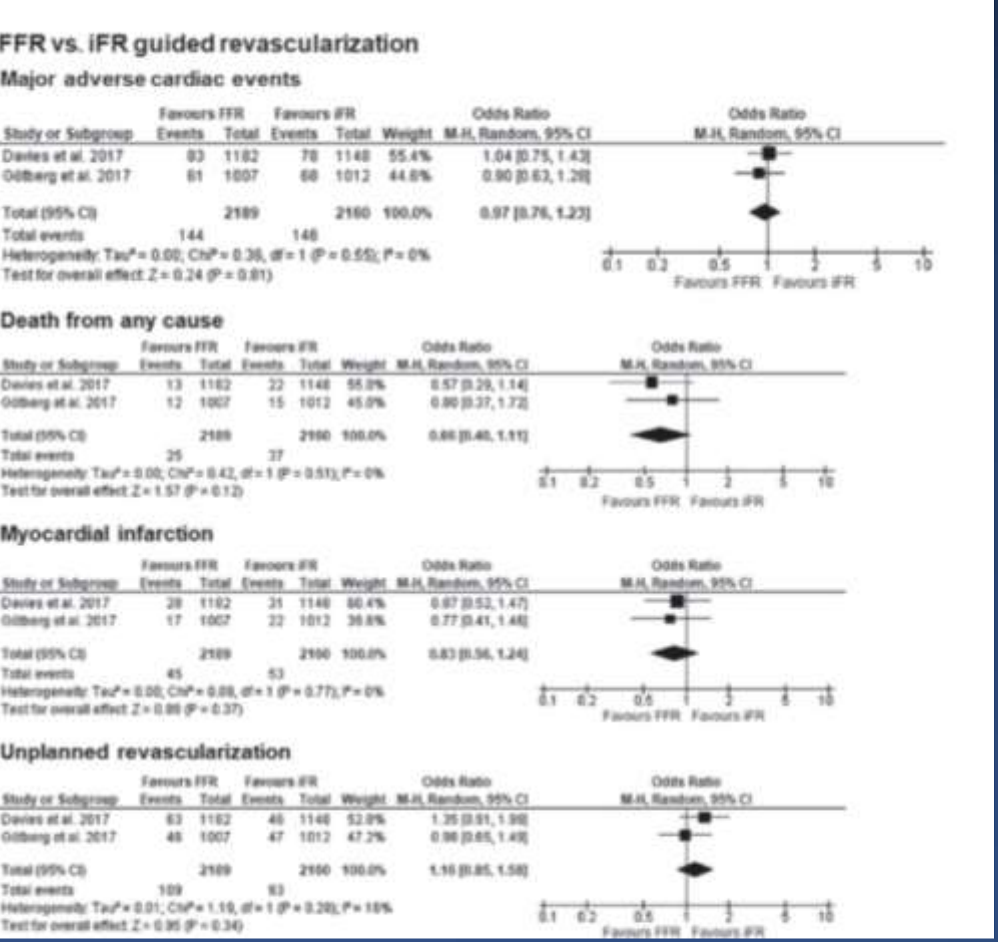
Sayan Sen et al. J Am Coll Cardiol. 2019 Feb 5; 73(4): 444–453.

CVRF

iFR vs FFR to Guide PCI

META-ANALYSIS OF ANGIOGRAPHY, IFR AND FFR GUIDED PCI



iFR-SWEDHEART study
DEFINE-FLAIR study

significant lower numbers in chest discomfort (P<0.001) when using iFR

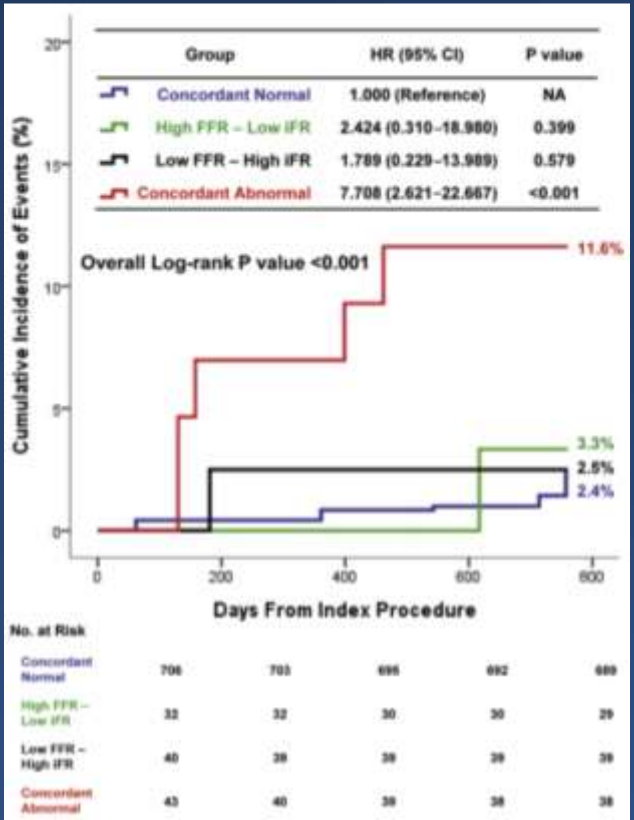
There is no significant superiority of FFR over iFR

Baumann et al. Exp Ther Med. 2019 Mar;17(3):1939-1951. doi: 10.3892/etm.2019.7156. Epub 2019 Jan 7.

iFR vs FFR concordance

3V FFR-FRIENDS substudy

- Comparison of 2-Year Clinical Outcomes of Lesions Classified by FFR and iFR in Deferred Lesions



- 821 deferred lesion (n=374)
- Primary outcome : MACE at 2 years

- Group 1 : FFR > 0.80 and iFR > 0.89
- Group 2 : FFR > 0.80 and iFR ≤ 0.89
- Group 3 : FFR ≤ 0.80 and iFR > 0.89
- Group 4 : FFR ≤ 0.80 and iFR ≤ 0.89

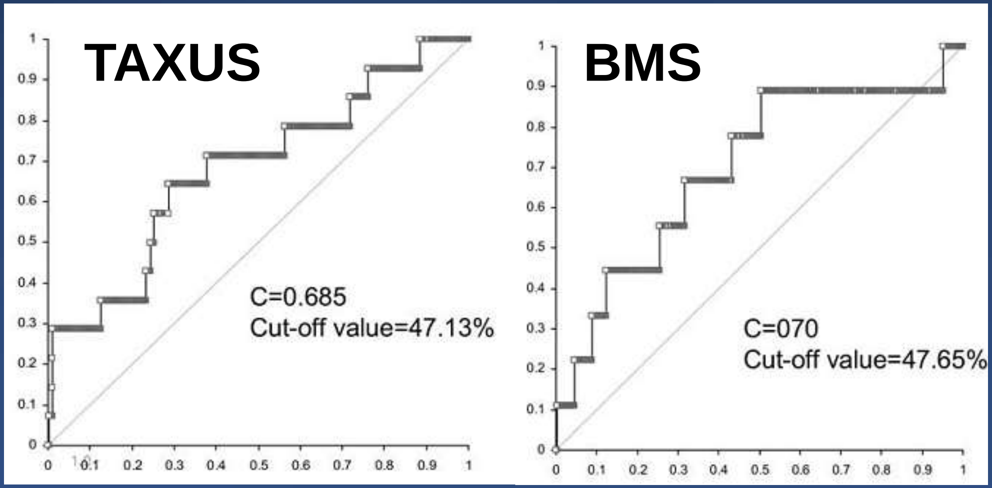
The discordant results between FFR and iFR were not associated with the increased risk of MACE. The risk of MACE was significantly increased only in lesions with abnormal results of both FFR and iFR.

Lee J, Shin E, Nam C et al. JACC Cardiovasc Interv 2017;10(24):2506

IVUS

Residual Plaque Predicts Edge Restenosis

	Population	DES	F/U time	Predictor
SIRIUS[1]	6 edge restenosis vs. 162 controls	SES	8 mo	Ref segment PB 60% vs. 41% (p<0.01)
TAXUS[2]	276 edge stenosis	PES	9 mo	Ref segment PB 47%

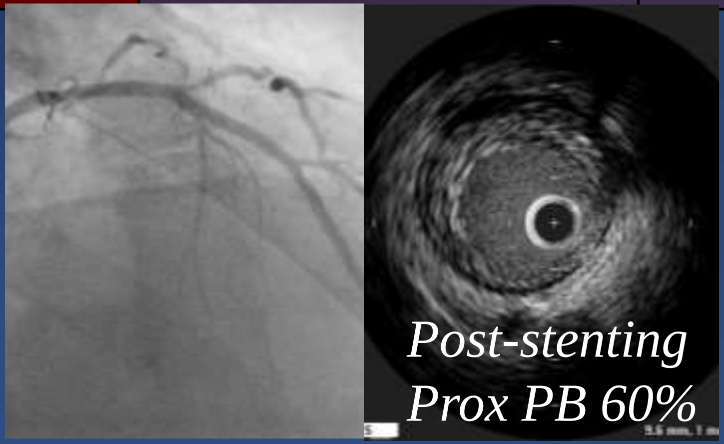


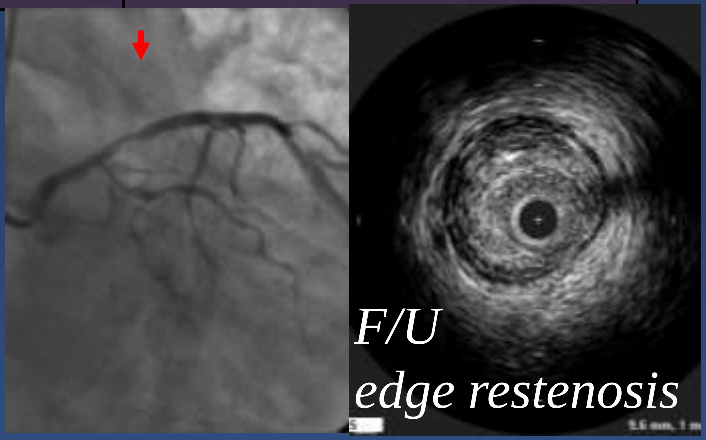
predict 9-mo edge restenosis

[1] *Am J Cardiol 2005;96:1251-3*
[2]*Liu et al. Am J Cardiol 2009;103:501-6*

Residual Plaque Predicts DES Thrombosis

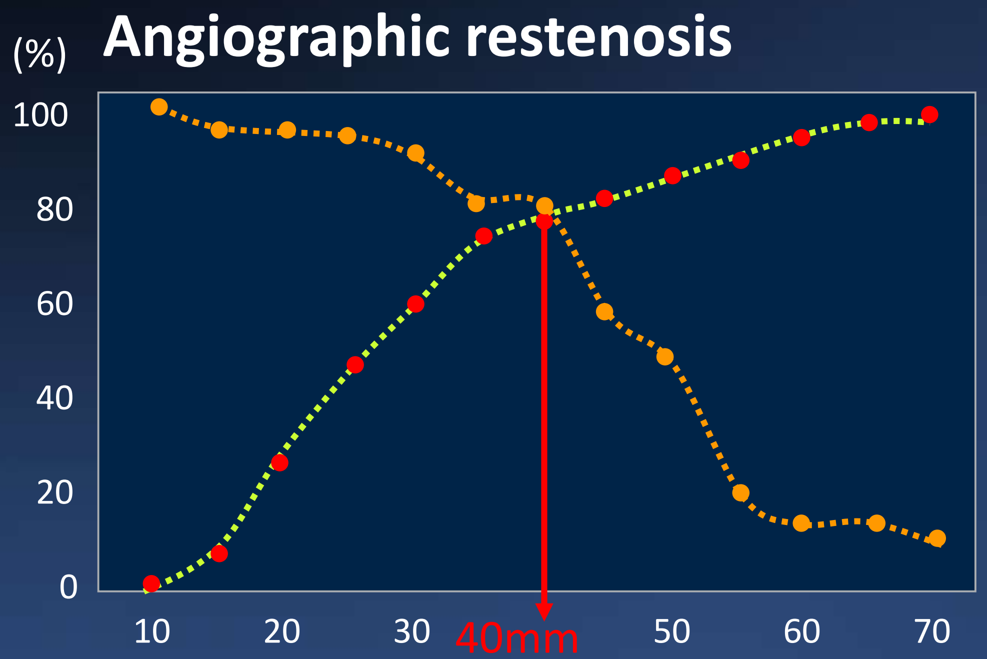
	Population	DES	Endpoint	Predictor
Fujii[1]	15 ST vs. 45 controls	SES	ST <1 mo	**Ref. PB** 62% vs. 46%
Okabe[2]	13 ST vs. 27 controls	DES	ST <1 yr	**Ref. PB** 66% vs. 56%
Liu[3]	20 ST vs. 50 controls	DES	ST <1 yr	**Ref. PB** 57% vs. 38%



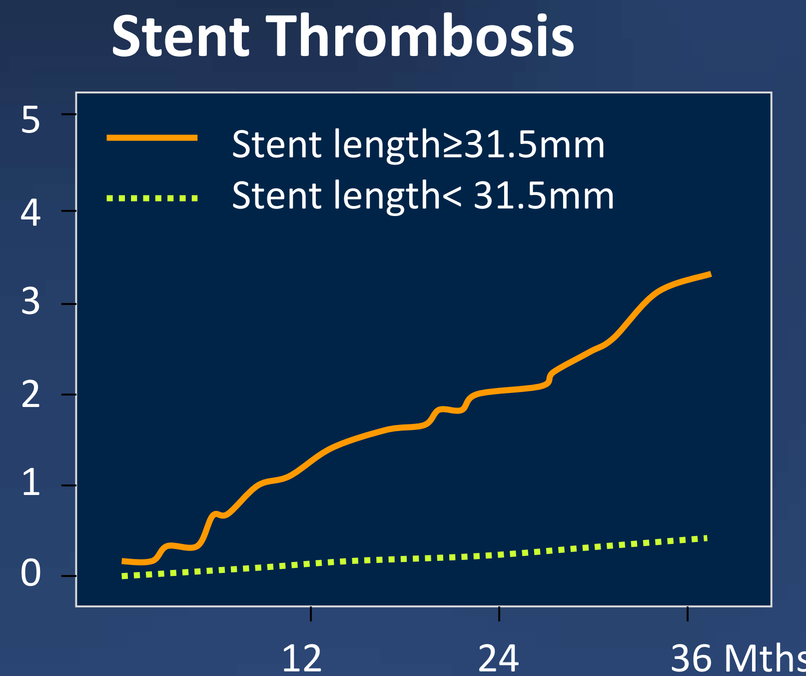


[1] *Fujii et al. J Am Coll Cardiol 2005;45:995-8*
[2] *Okabe et al. Am J Cardiol 2007;100:615-20*
[3] *Liu et al. JACC Cardiovasc Interv. 2009;2:428-34*

Stent Length Predicts DES Failure



Sensitivity 81%, Specificity 78%



HR 7.8 (95% CI 2.5–24.1)

IVUS-guided PCI is necessary to achieve full lesion coverage and to avoid the waste of stent

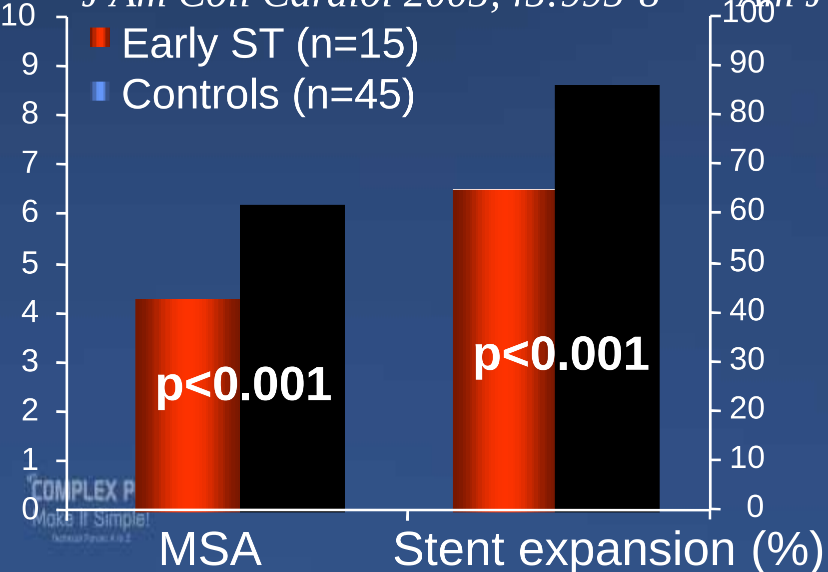
Hong et al. Eur Heart J 2006;27:1305-10

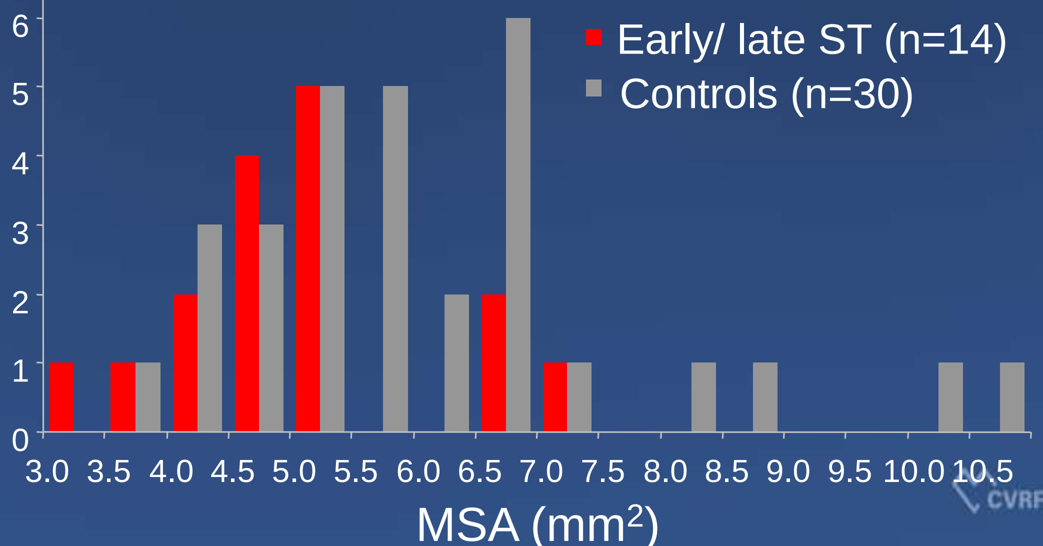
Suh et al. JACC interv 2010;3:383-9

Underexpansion Predicts DES Restenosis

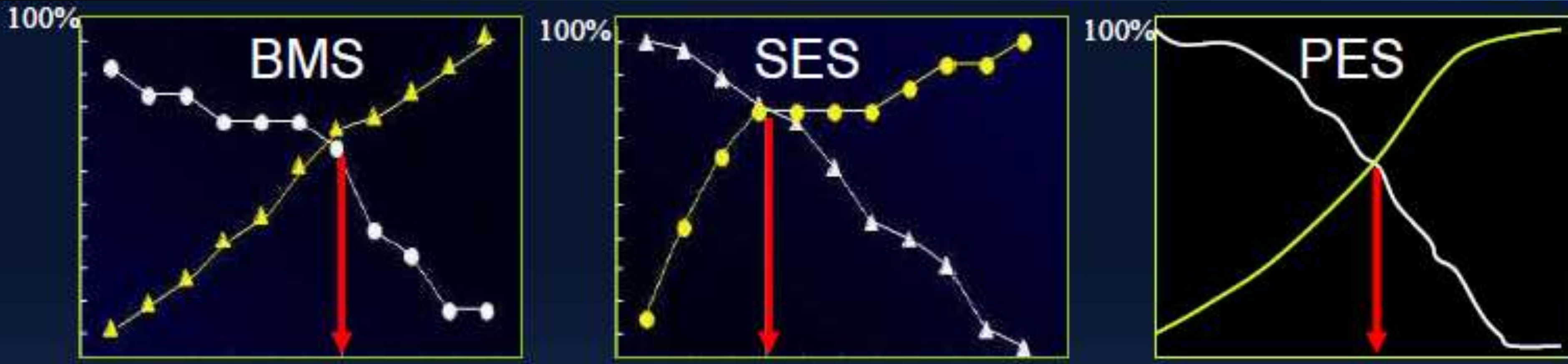
	Population	DES	Endpoint	Rate of Underexpansion
Fujii [1]	15 ST vs. 45 controls	SES	ST <1 month	<5.0mm^2 in **80%** vs. 29%
Okabe [2]	13 ST vs. 27 controls	DES	ST <1 year	<5.0mm^2 in **79%** vs. 40%
Liu [3]	20 ST vs. 50 controls	DES	ST <1 year	<5.0mm^2 in **85%** vs. 26%

[1] J Am Coll Cardiol 2005;45:995-8
[2] Am J Cardiol 2007;100:615-20
[3] JACC interv 2009;2:428-34





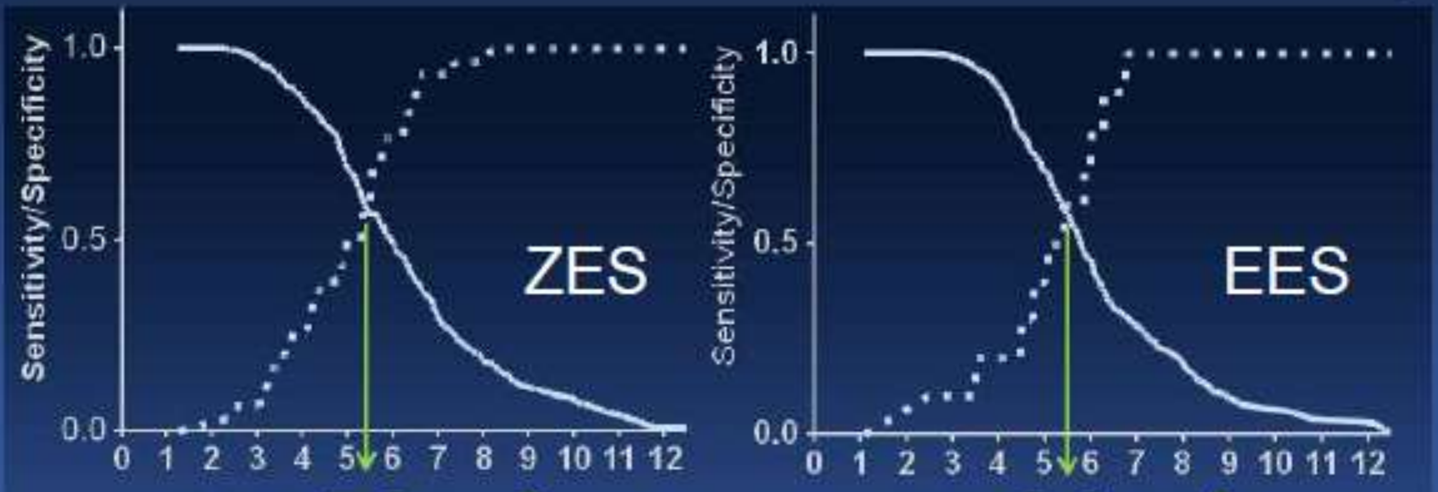
Underexpansion Predicts DES Restenosis



MSA 6.5mm²
Predictive value 56%

MSA 5.0mm²
Predictive value 90%

MSA 5.7mm²
Eur Heart J 2006;27:1305-10
JACC Interv 2009;2:1269-75



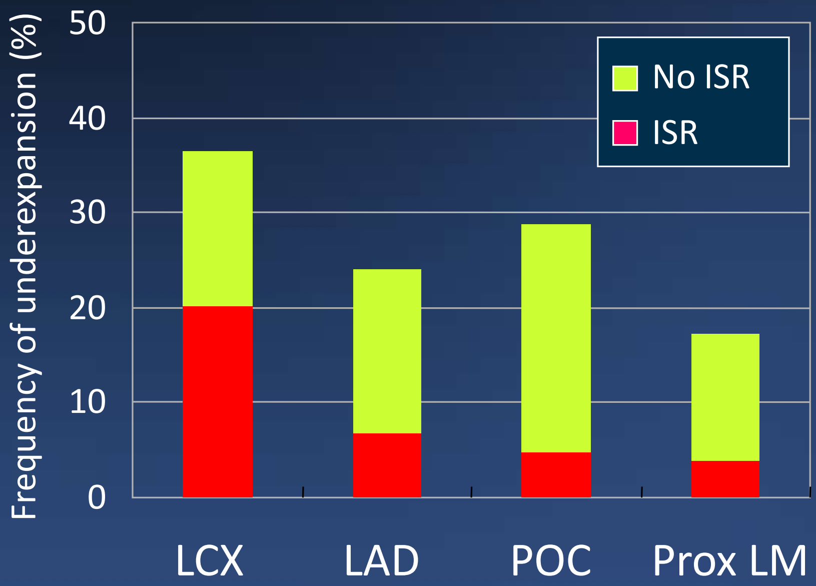
MSA 5.3mm² **MSA 5.4mm²**

Song et al. Catheter Cardiovasc Interv 2012;

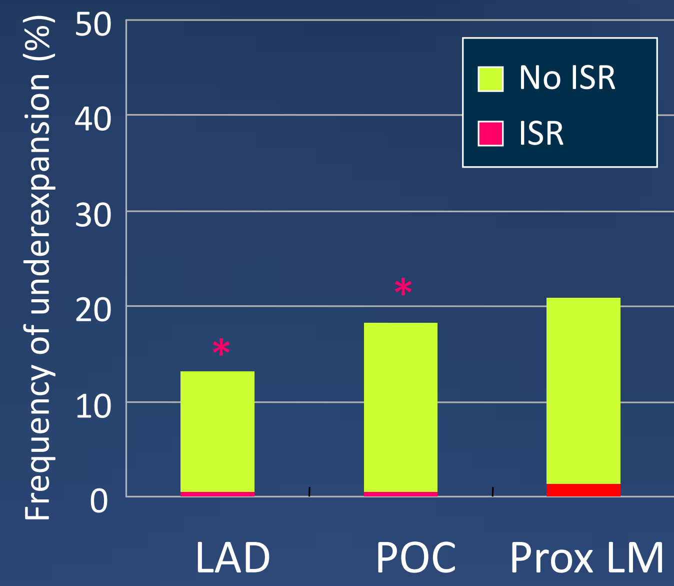
Frequency of Underexpansion and ISR

33.8% *had underexpansion of at least one stented segment*

Two-stent



Single-stent



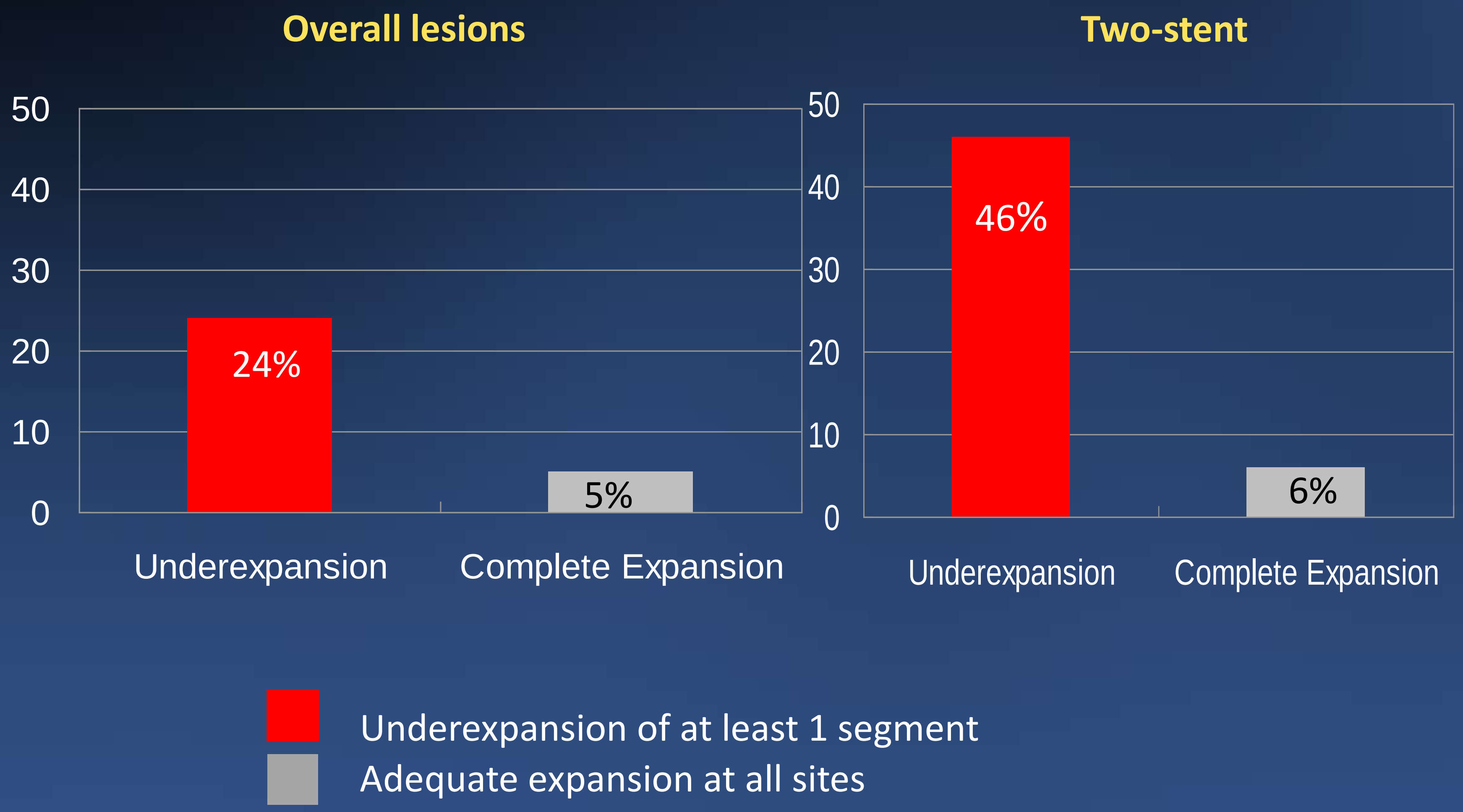
* *single-stent vs. two-stent, p<0.05*

54% had underexpansion in at least one of the 4 stented segments

27% had underexpansion in at least one of the 3 stented segments

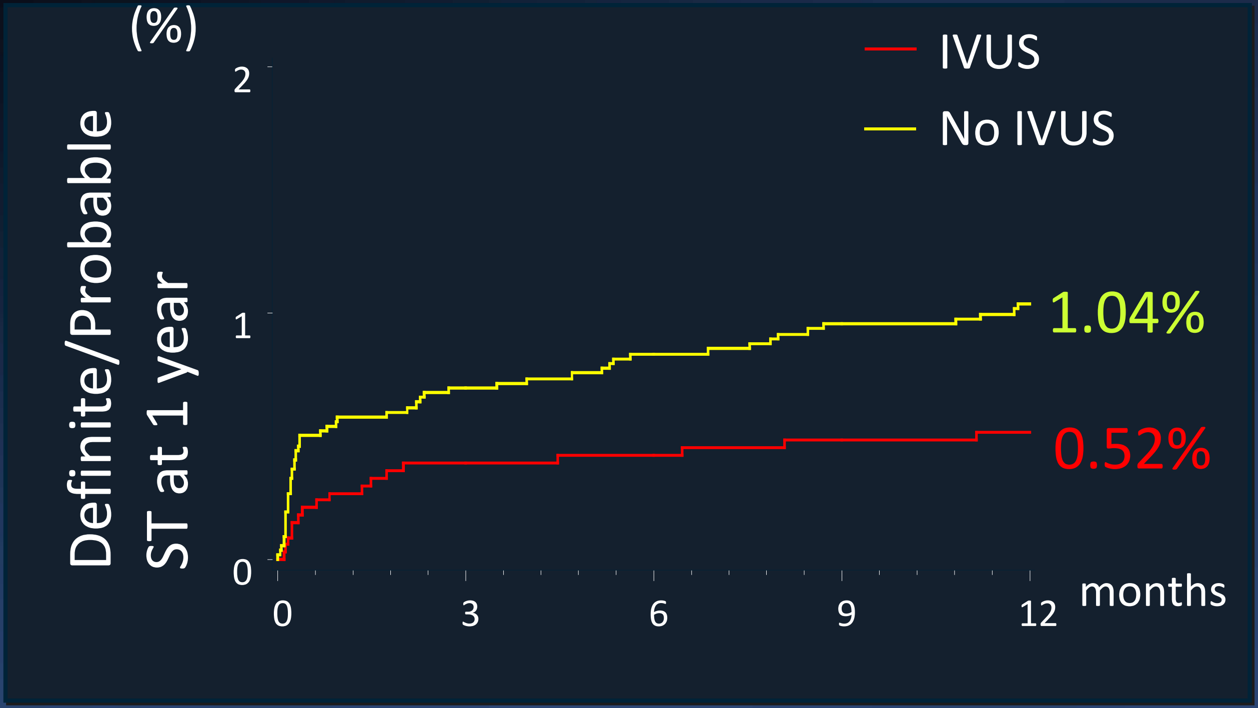
Frequency of ISR in LM Lesions

with vs without Underexpansion



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

ADAPT-DES 1-year Outcomes



p=0.01
HR 0.50
95%CI 0.29-0.86

	IVUS n = 3349	No IVUS n = 5234	p Value
Definite/probable ST	0.52% (17)	1.04% (53)	0.011
All myocardial infarction	2.46% (81)	3.68% (188)	0.0022
Ischemic driven TVR*	2.42% (81)	3.95% (207)	0.0001

Maehara et al. 2013 TCT

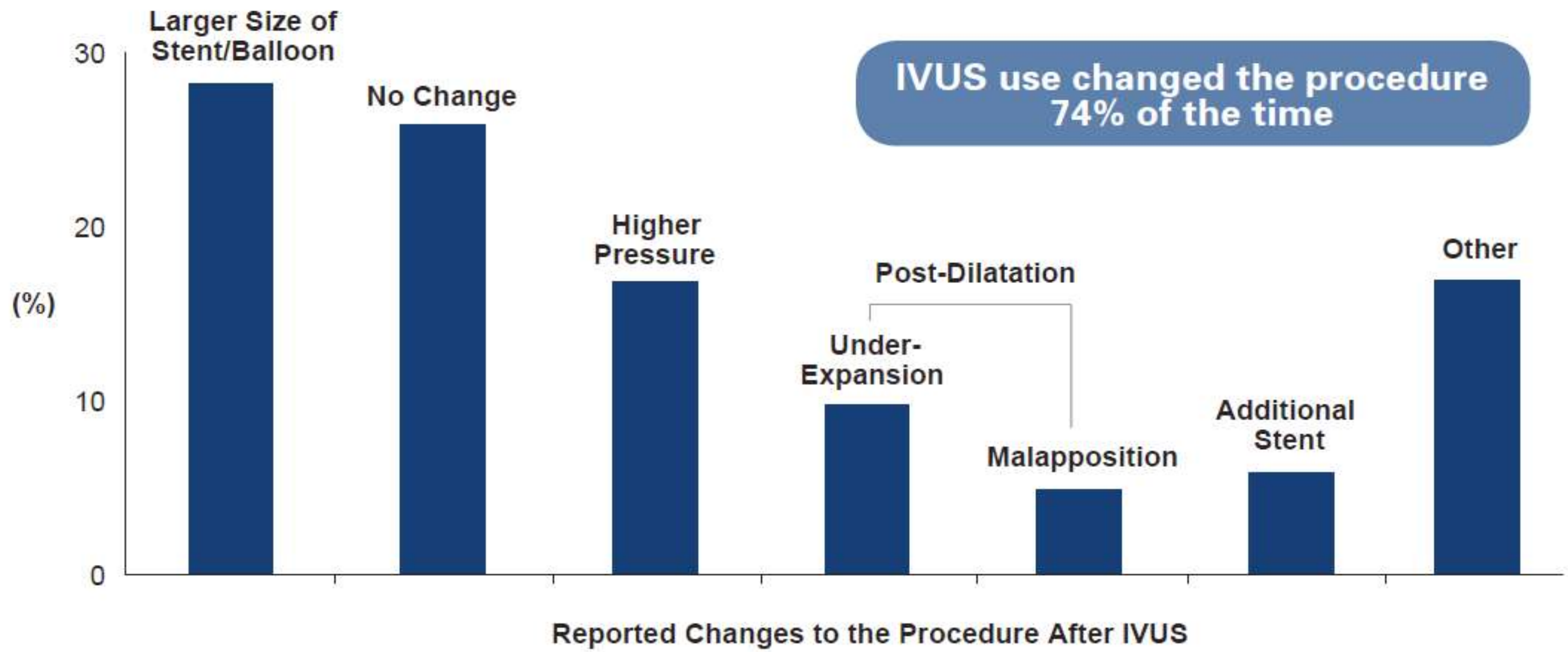
COMPLEX PCI Make It Simple!

CVRF

ADAPT-DES 2-YEAR RESULTS

The largest prospective study of IVUS use to date

IVUS Arm Reported Improved Clinical Outcomes



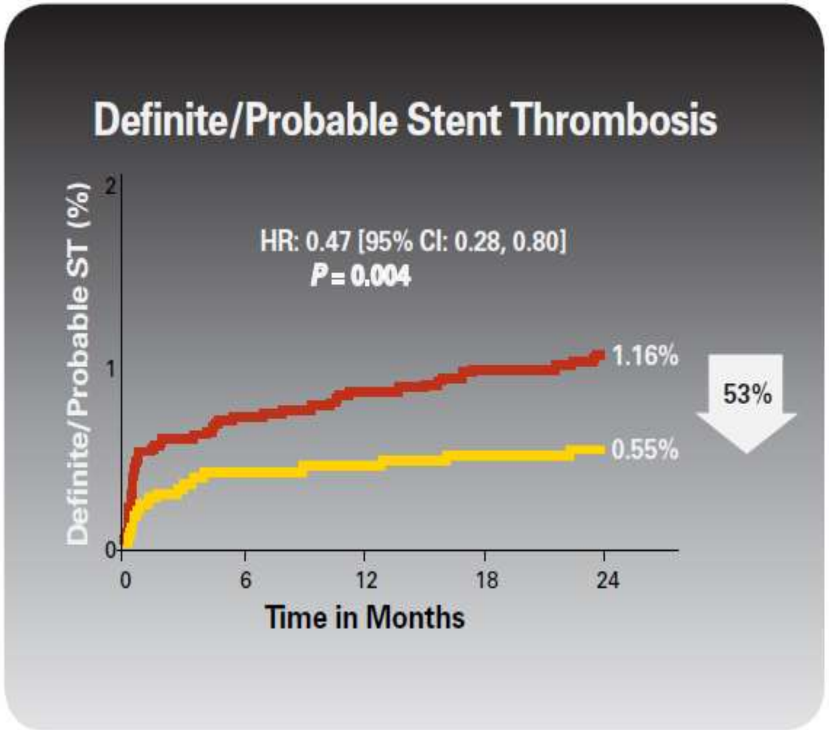
- IVUS use was associated with longer stent length and larger stent size without increasing peri-procedural MI or the number of stents
- IVUS use was associated with reduction of MACE in complex lesions

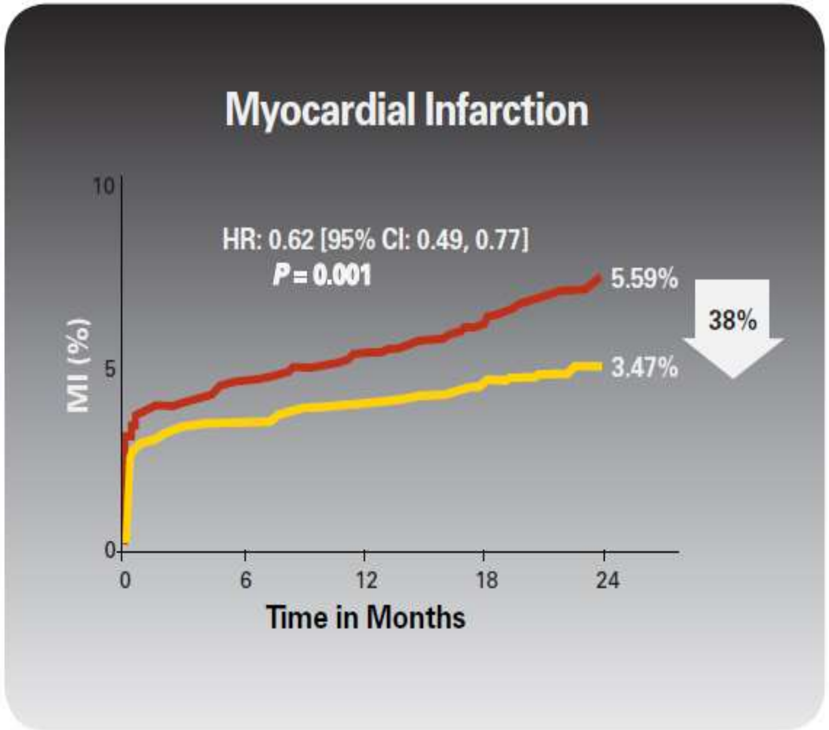
ADAPT-DES 2-YEAR RESULTS

The largest prospective study of IVUS use to date

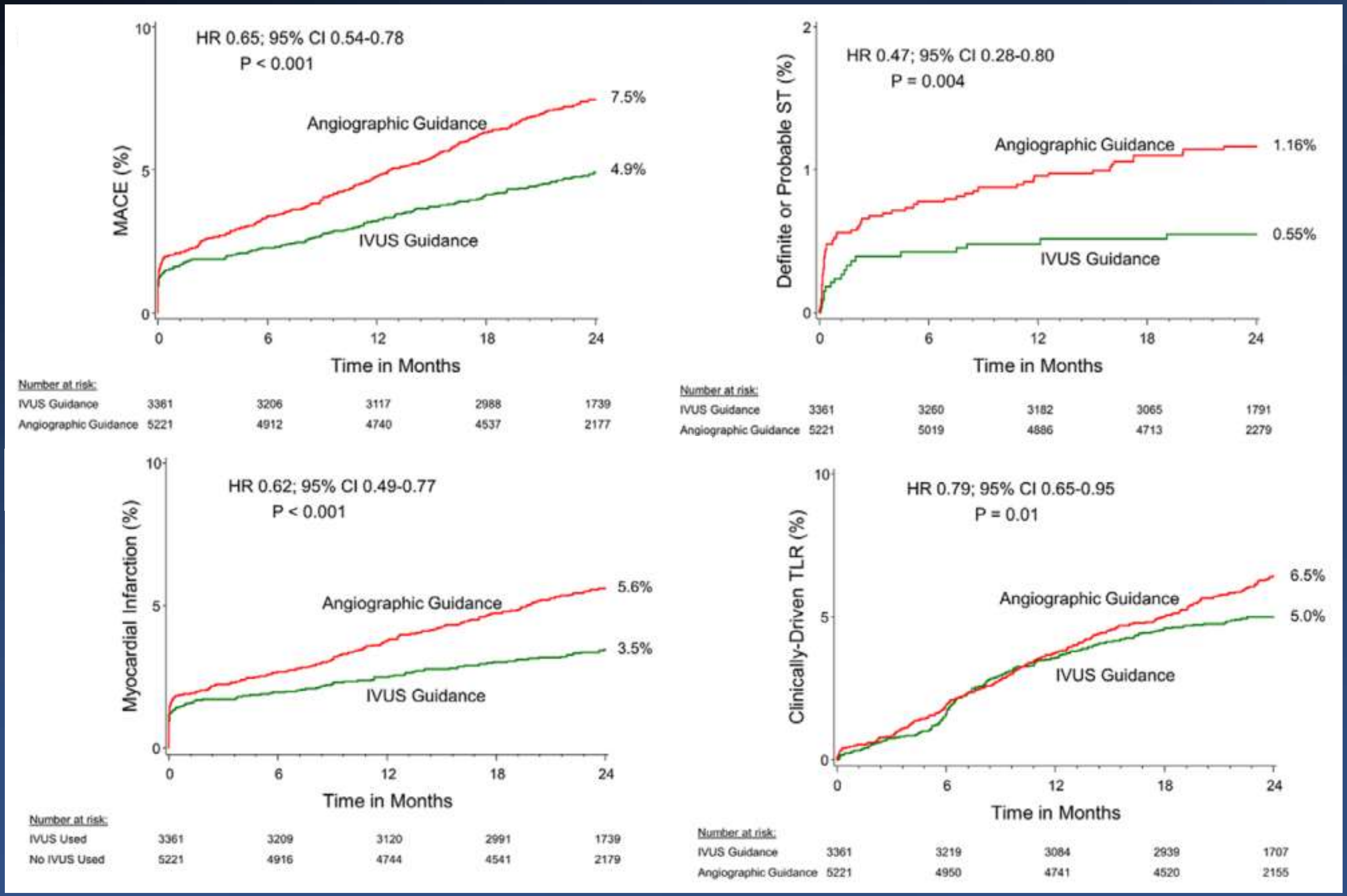
Results From IVUS and No IVUS Study Arms

No IVUS Use   IVUS Use





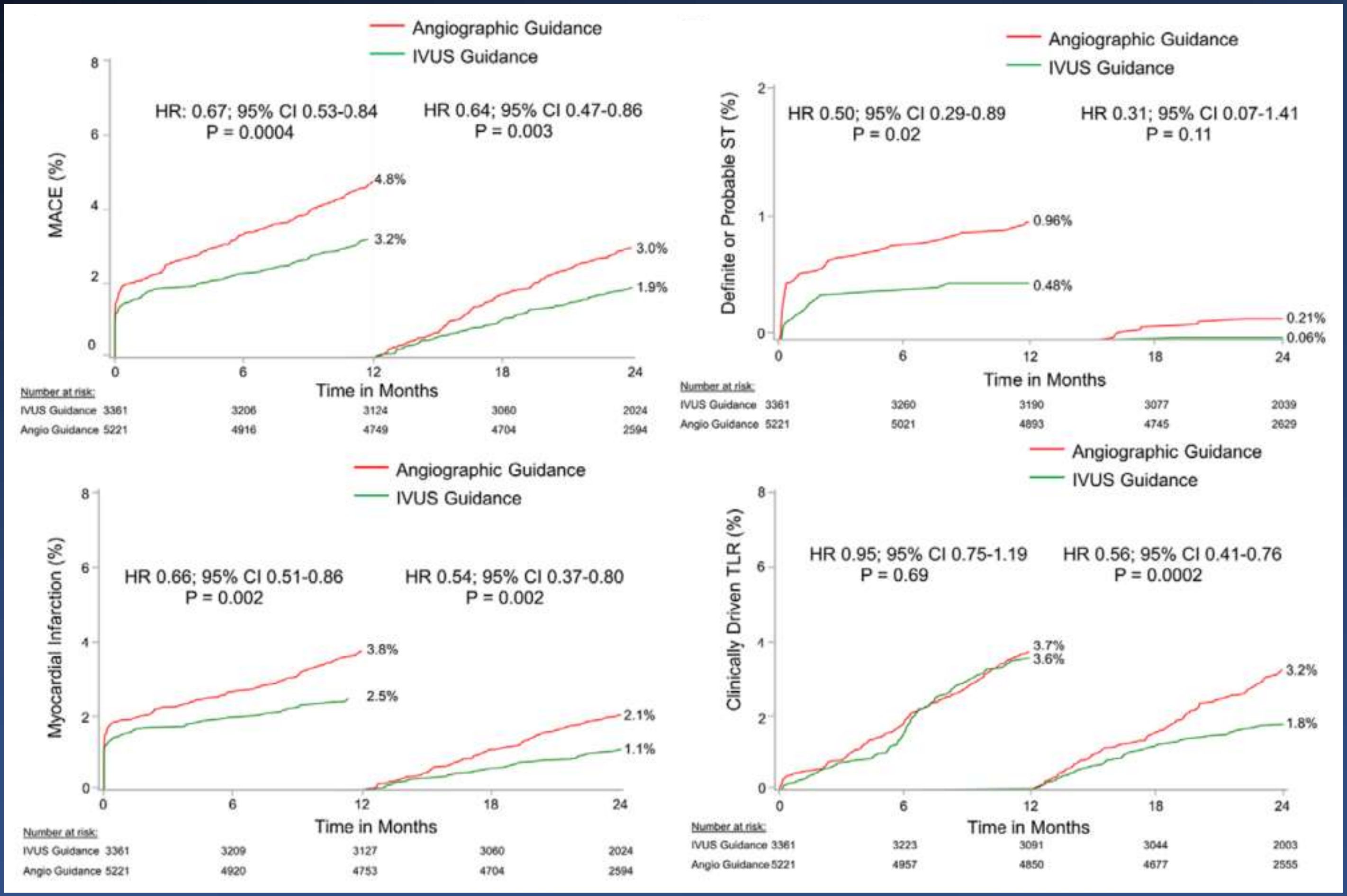
ADAPT-DES 2-years Outcomes



Maehara et al. Circ Cardiovasc Interv. 2018;11:e006243.

ADAPT-DES 2-years Outcomes

Landmark analysis between 1 and 2 year

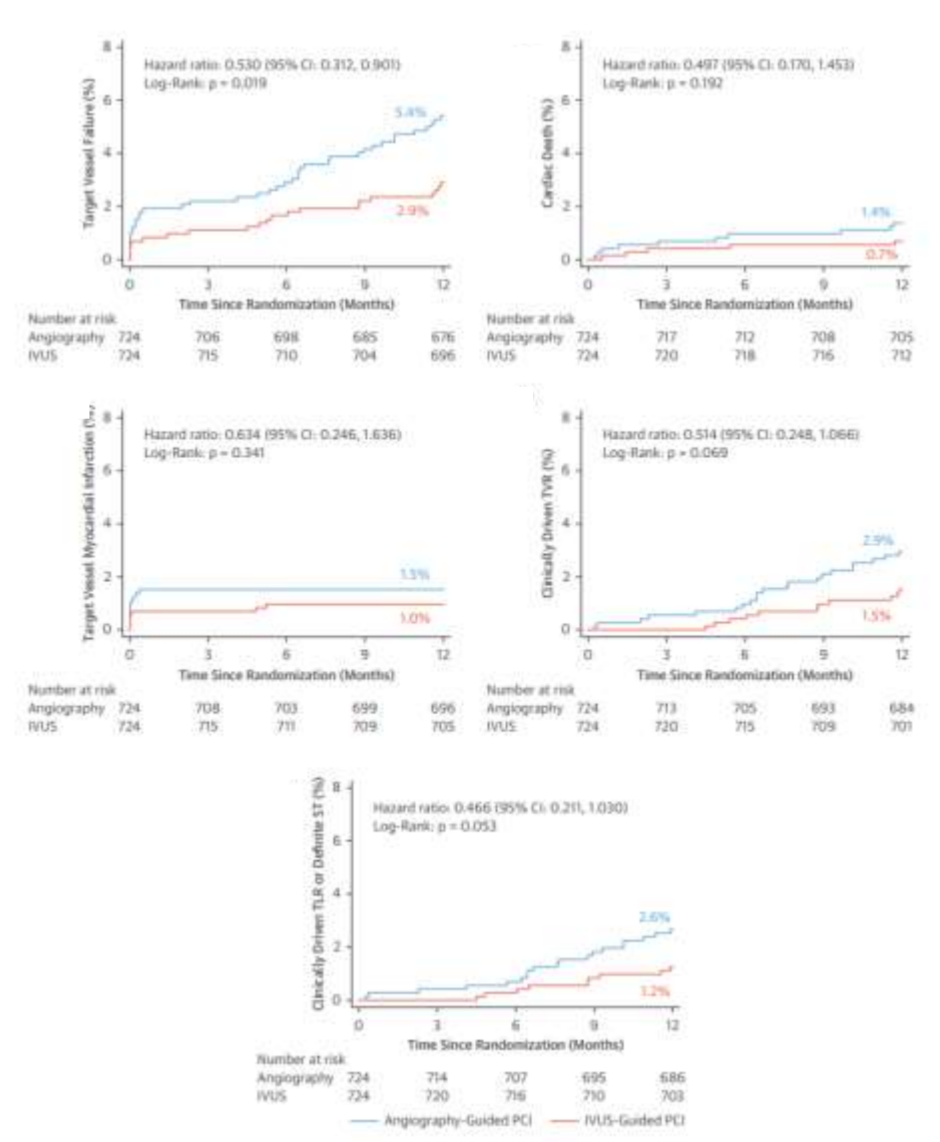


Maehara et al. Circ Cardiovasc Interv. 2018;11:e006243.

IVUS vs angio-guided DES

The ULTIMATE trial

	IVUS guidance	Angiography guidance	p value
number	1.81 ± 0.80	1.76 ± 0.77	0.16
n stent eter	3.14 ± 0.51	2.97 ± 0.48	<0.001
n stent h, mm	49.99 ± 25.10	47.38 ± 22.42	0.02
mum on eter, mm	3.73 ± 0.56	3.51 ± 0.53	<0.001
mum dilation ure, atm	19.7 ± 3.7	19.0 ± 3.7	<0.001



Zhang et al. JACC VOL. 72, NO. 24, 2018

IVUS vs angio-guided DES

Meta-analysis

y/First Author (Ref. #)	Year of Publication	Number of Patients	Study Design	Type of Stent	Follow-Up Duration (Months)
raphy vs. IVUS					
ST (8)	1998	76/79	Randomized	BMS	6
SE (9)	2000	229/270	Randomized	BMS	9
CUS (10)	2001	275/273	Randomized	BMS	12
er et al. (11)	2003	54/54	Randomized	BMS	30
P (12)	2003	76/74	Randomized	BMS	6-12
L (13)	2007	80/83	Randomized	BMS	6
(14)	2009	406/394	Randomized	BMS	12
E DES IVUS (15)	2010	105/105	Randomized	DES	18
et al. (16)	2013	274/269	Randomized	DES	12
(17)	2013	142/142	Randomized	DES	24
IVUS (18)	2015	201/201	Randomized	DES	12
CTO (19)	2015	115/115	Randomized	DES	24
-XPL (20)	2015	700/700	Randomized	DES	12
et al. (21)	2015	62/61	Randomized	DES	24
et al. (22)	2008	884/884	Observational, PSM	DES	12
-COMPARE (23)	2009	201/201	Observational, PSM	BMS/DES	36
RIX (24)	2011	548/548	Observational, PSM	DES	24
et al. (25)	2011	487/487	Observational, PSM	DES	36
et al. (26)	2012	123/123	Observational, PSM	DES	12
bayashi et al. (27)	2012	637/637	Observational, PSM	BMS/DES	12
LLENT (28)	2013	463/463	Observational, PSM	DES	12
Torre Hernandez t al. (29)	2014	505/505	Observational, PSM	DES	36
et al. (30)	2014	291/291	Observational, PSM	DES	12
et al. (31)	2014	201/201	Observational, PSM	DES	24

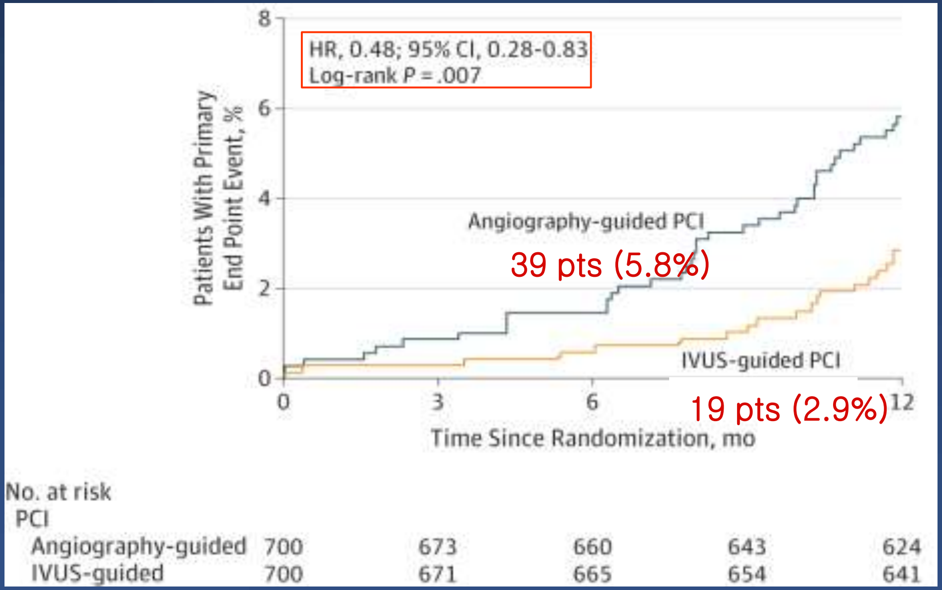
	IVUS vs angiography
Primary endpoints	
All cause mortality	0.75 [0.58-0.98]
Secondary endpoints	
MACE	0.79 [0.67-0.91]
Cardiovascular death	0.47 [0.32-0.66]
MI	0.72 [0.52-0.93]
TLR	0.74 [0.58-0.90]
ST	0.42 [0.20-0.72]

Buccheri et al. ACC Cardiovasc Interv. 2017 Dec 26;10(24):2488-2498

IVUS-XPL Randomized Clinical Trial

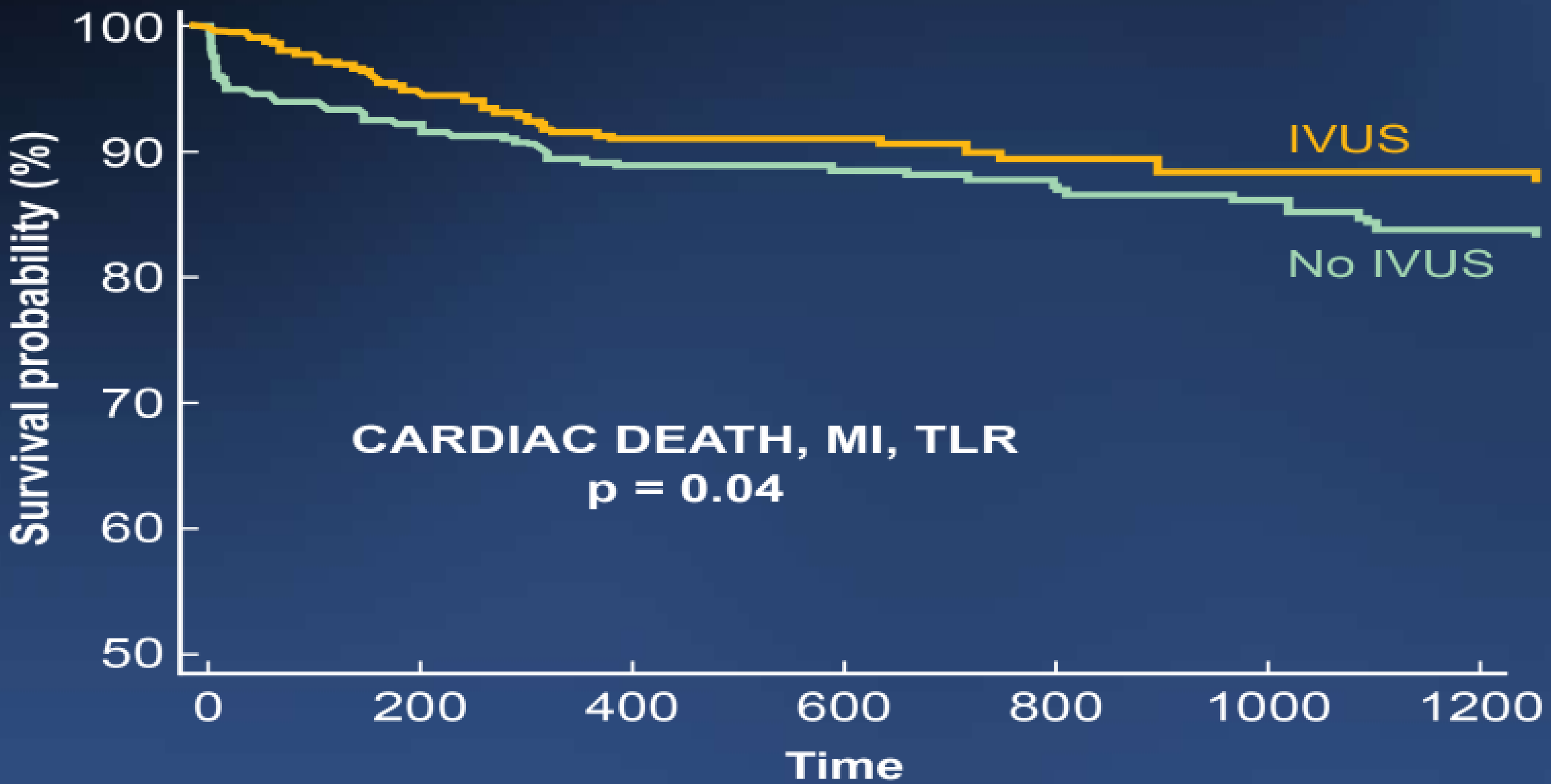
Effect of IVUS–Guided vs Angiography-Guided Everolimus-Eluting Stent Implantation

- Multicenter trial
- 1400 patients with long coronary lesions (implanted stent ≥28 mm in length)
- 1yr follow-up
- Primary end point : MACE



Hong et al. JAMA. 2015;314(20):2155-2163

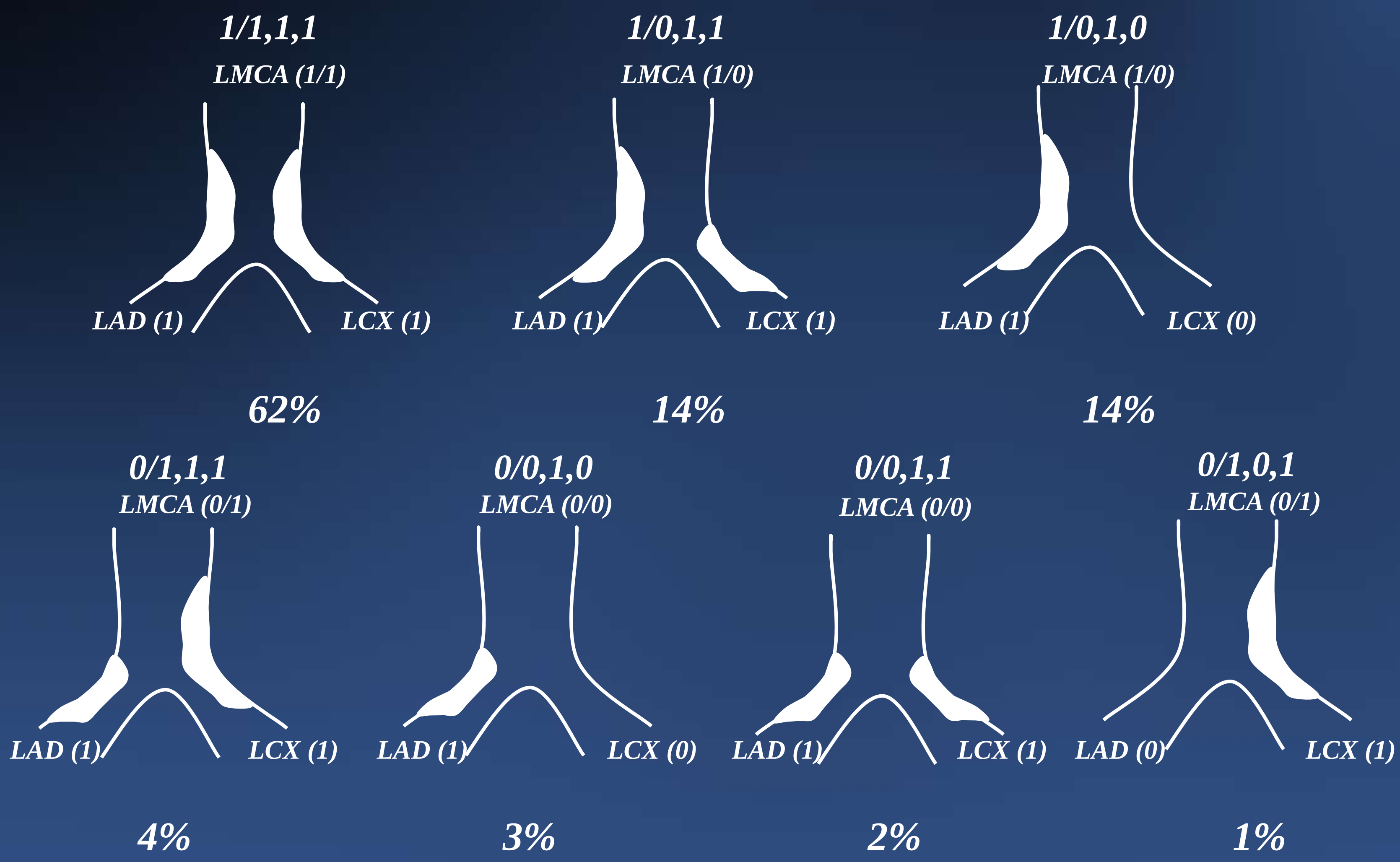
Pooled analysis
:ESTROFA-LM, RENACIMIENTO, Bellvitge, Valdecilla
Effectiveness of IVUS on LM PCI



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

JoseM. de la Torre Hernandez et al. *JACC: cardiovasc interv* 2014;7:244-54

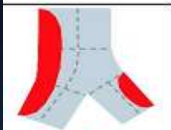
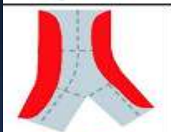
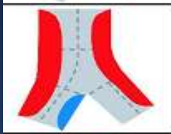
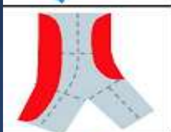
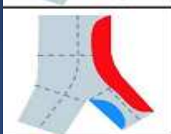
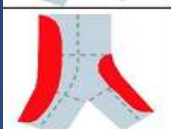
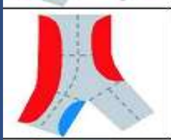
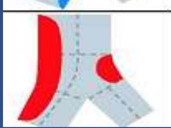
laque Distribution by IVUS (n=140)



In 90% plaque extends from LMCA-LAD

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

Plaque Distribution by IVUS (n=82)

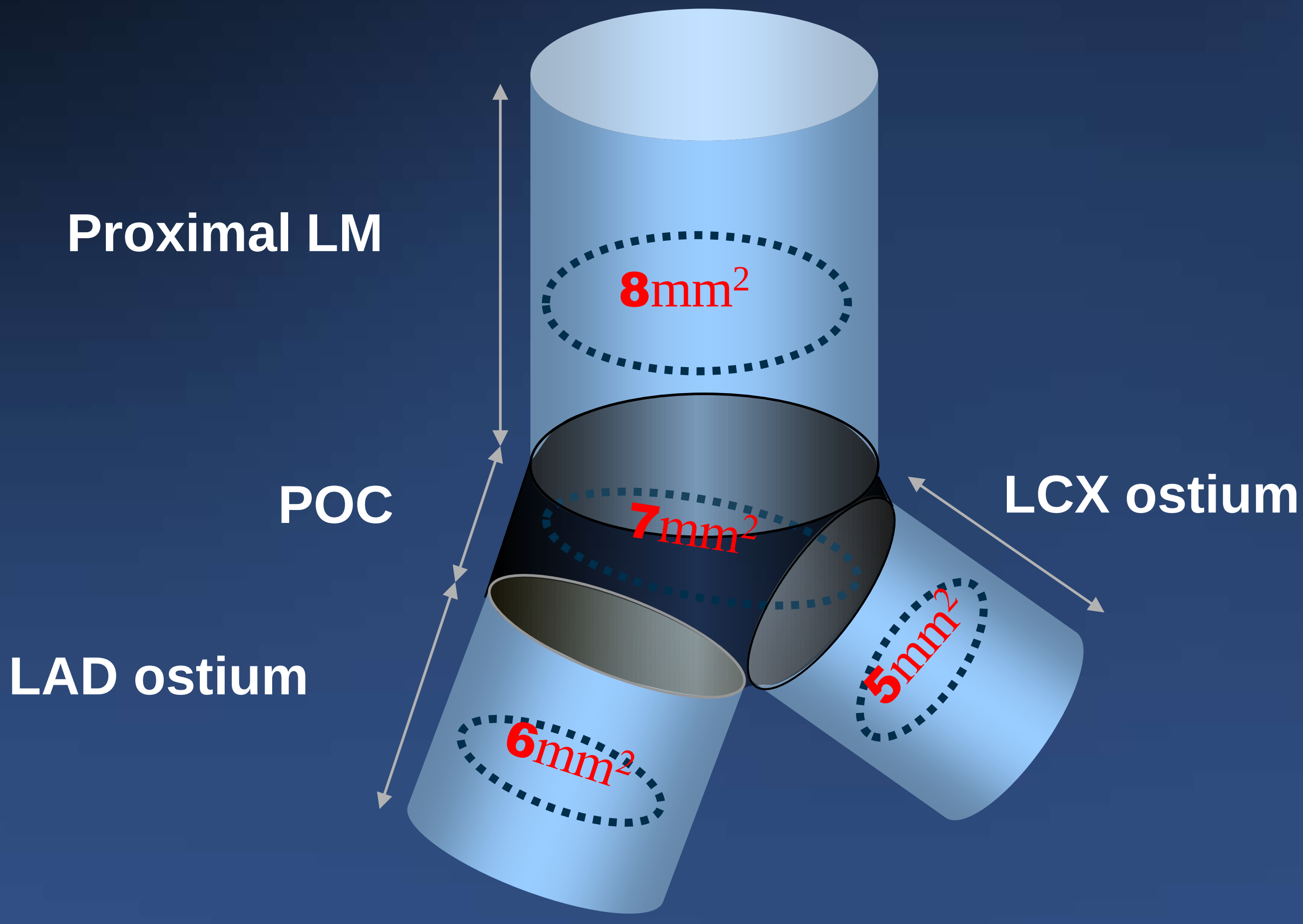
	N. (%)	LAD ostium, MLA (mm^2)	POC, MLA (mm^2)	DLM, MLA (mm^2)	LCX ostium, MLA (mm^2)
	5 (6%)	4.4±2.0	9.6±4.4	8.1±4.7	3.4±1.6
	26 (32%)	4.2±2.8	5.3±2.6	4.6±1.5	3.9±2.1
	12 (15%)	2.6±1.3	4.5±1.6	4.5±2.1	3.3±2.0
	9 (11%)	4.3±2.5	5.6±3.3	5.7±3.8	7.6±3.6
	9 (11%)	3.2±1.4	6.1±2.0	4.8±2.5	3.9±1.4
	4 (5%)	3.4±1.9	5.2±1.9	5.8±4.7	3.9±2.0
	4 (5%)	2.8±0.7	5.1±2.1	5.1±2.2	6.6±1.7
	5 (6%)	3.4±1.9	5.2±2.6	5.1±3.8	4.6±2.1

In all cases, the LM disease extended into LAD and LCX continuously.

Kang et al, Catheterization and Cardiovascular Interventions. 2011 Jul 29.

Optimal MSA

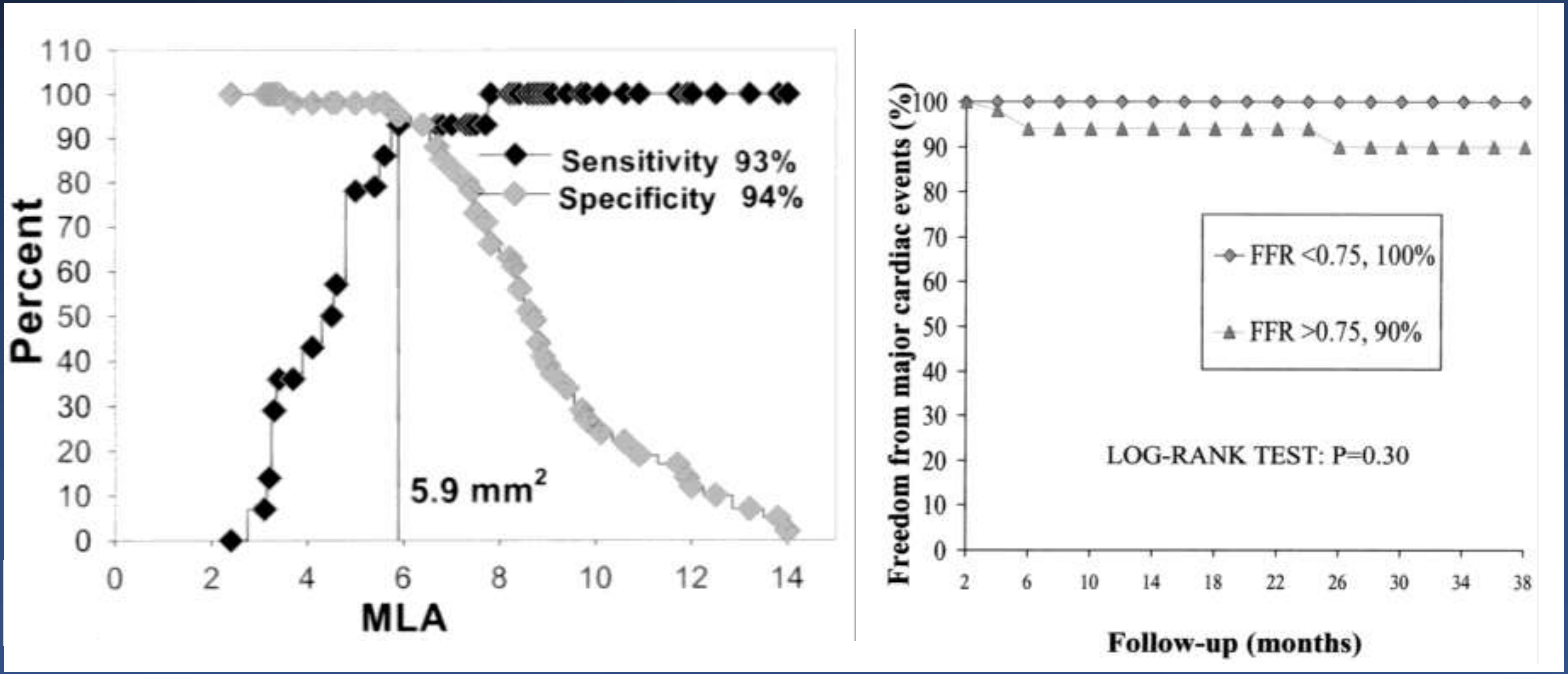
on a segmental basis



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

Cut-off for Predicting LM FFR<0.75
LM MLA 6.0mm^2

- Sum of lumen areas of two daughter vessels (Each of LAD and LCx should be 4.0mm^2) = 150% of the parent LM
- **Murray's Law (*LM* r^3 = *LAD* r^3 + *LCx* r^3)**



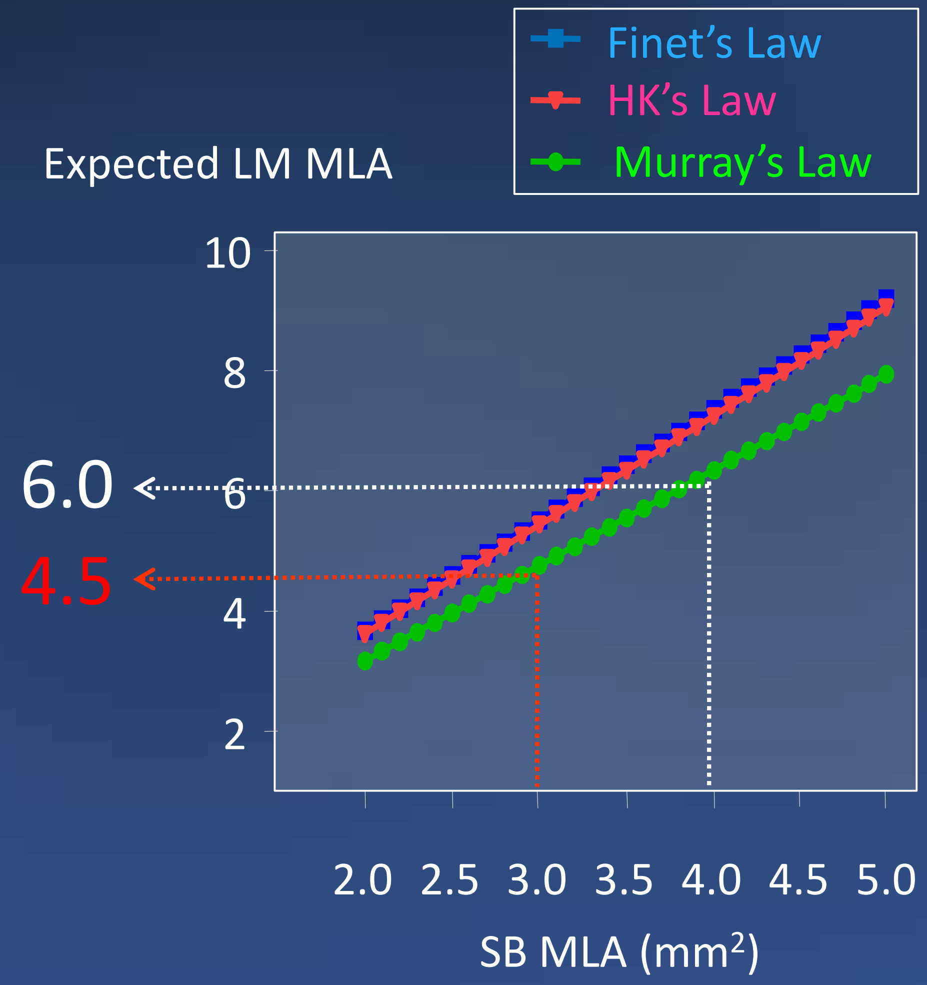
COMPLEX PCI Make It Simple!

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

CVRF

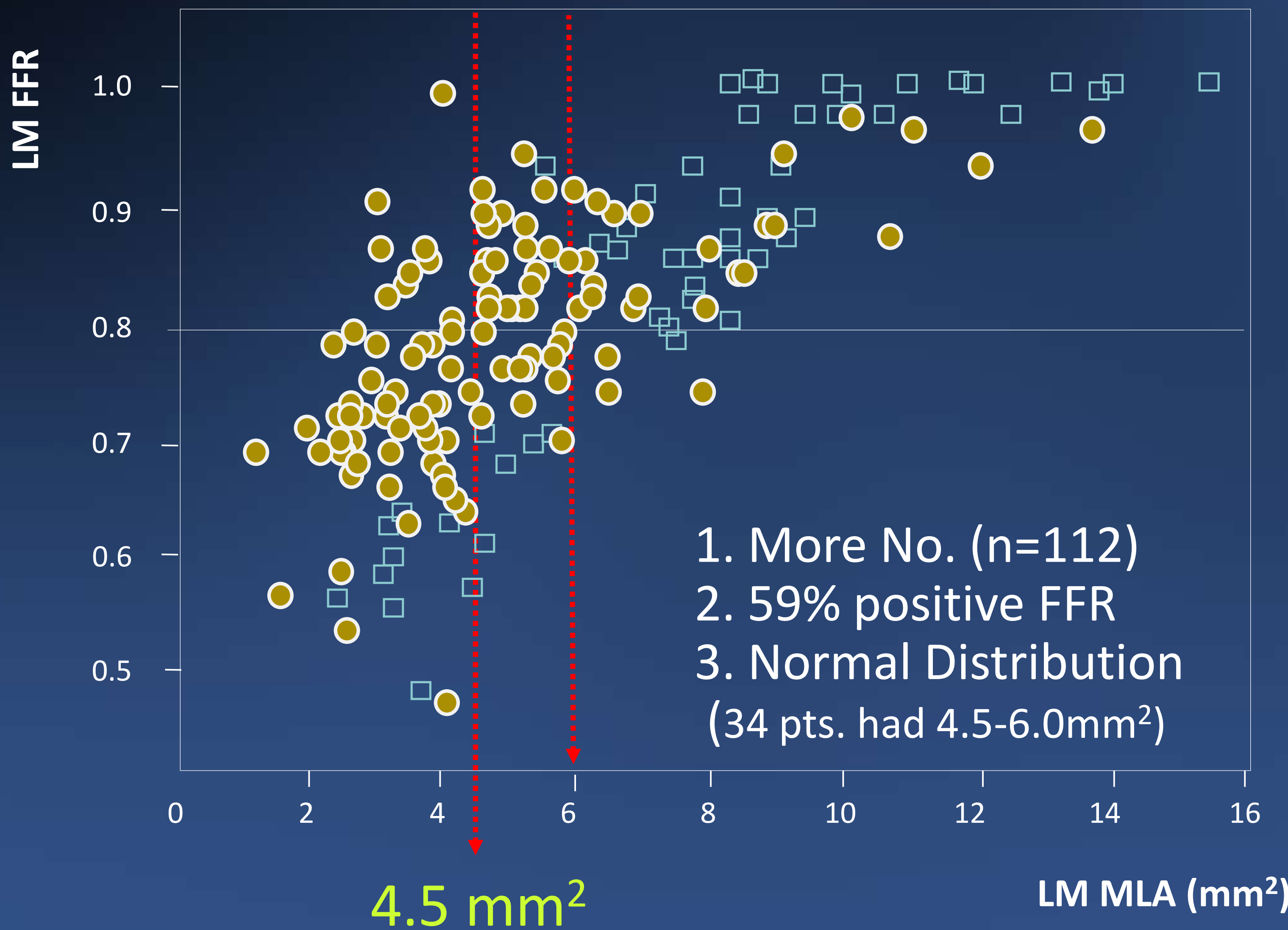
False Assumption…
The used cut-off 4.0mm² is too Big!

LAD	LCX	LM (Murray's)
3.0	3.0	4.76
3.0	2.9	4.68
3.0	2.8	4.60
3.0	**2.7**	**4.53**
3.0	2.6	4.45
3.0	2.5	4.37



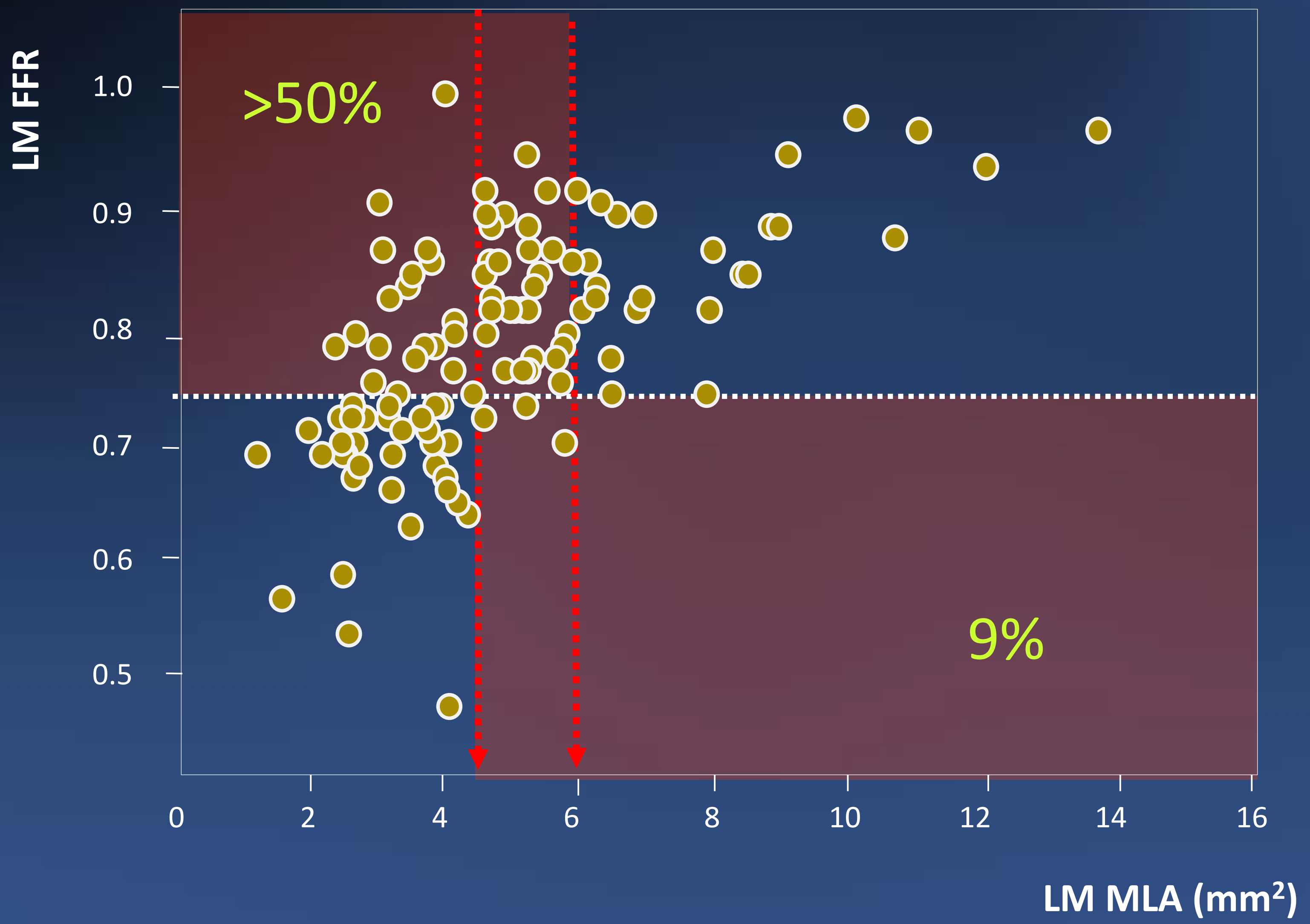
Huo et al. Eurointervention 2012;7:1310-6

AMC New Data (n=112)



Park SJ et al. JACC Interv 2014;7:868–74

AMC New Data (n=112)



Park SJ et al. JACC Interv 2014;7:868–74

- Old data (MLA 6.0mm^2) included downstream SB disease, and 32 of 55 (58%) were distal LM lesions that usually extend to the SB ostia
- Recent data (MLA 4.5mm^2) evaluated only pure LM lesions, which more reliably assessed the impact of LM-MLA on functional significance

TABLE 1. Baseline Clinical, Angiographic, and IVUS Characteristics of Patients (n=55)

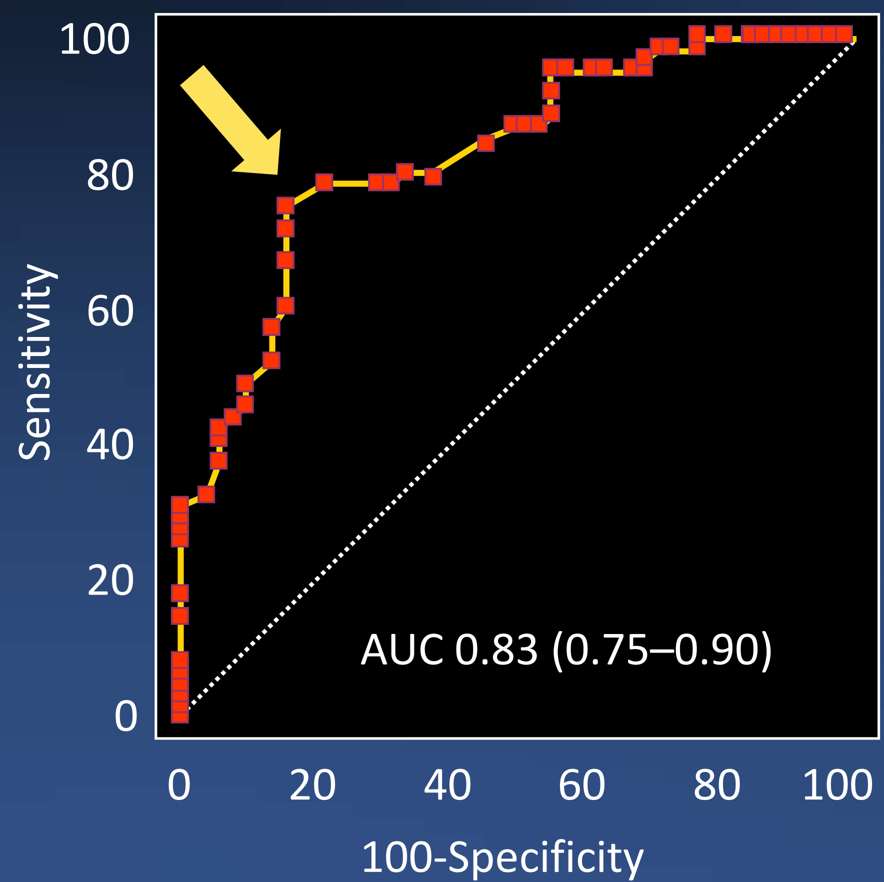
Age, y	62±11
Diabetes mellitus, n	20
Hypertension, n	50
Smoking, n	39
Prior bypass surgery, n	13
Ostial LM stenosis, n	20
Mid-LM stenosis, n	3
Distal LM stenosis, n	32

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

New LM MLA 4.5mm²

Matched with FFR <0.80

Ostial and Shaft LM Disease (N=112)



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

Park SJ et al. JACC Interv 2014;7:868–74

ngio-guided PCI vs. IVUS-guided PCI

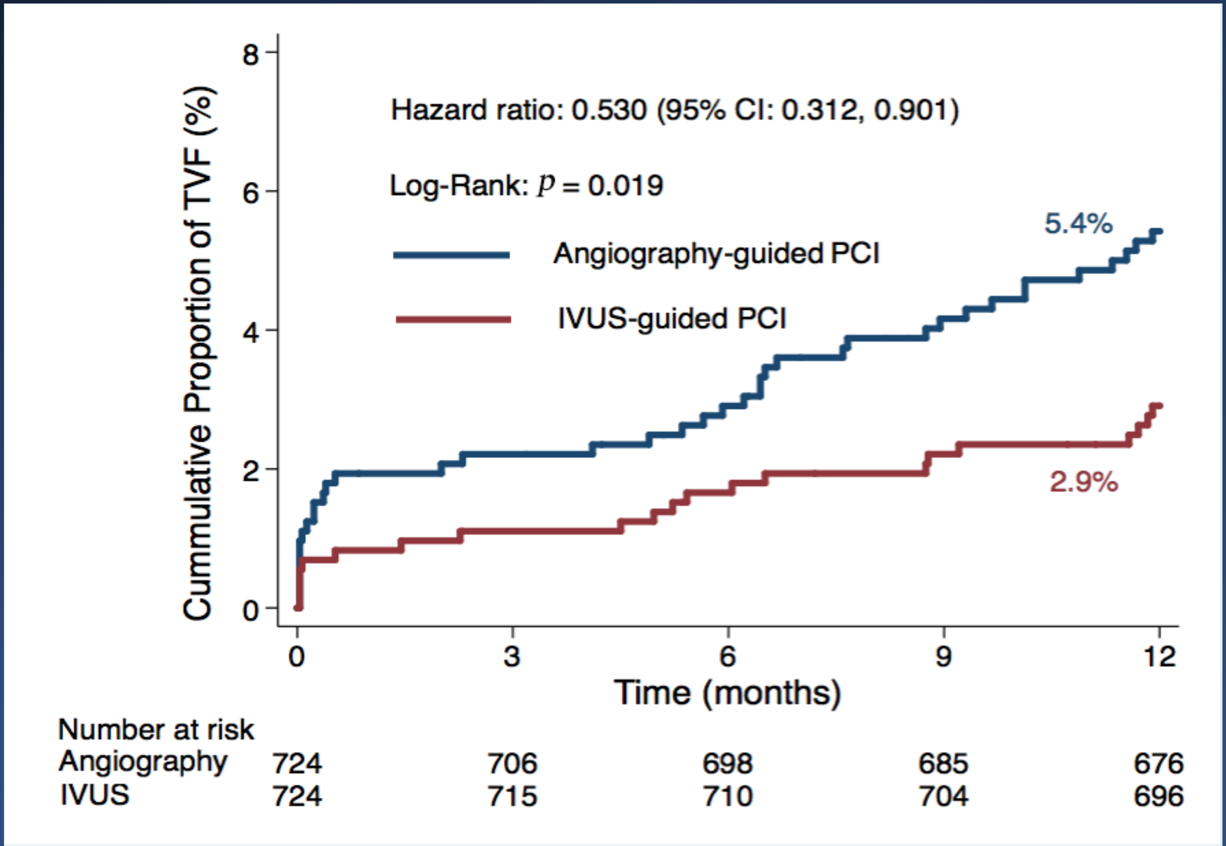
Procedural Data
ULTIMATE trial

	IVUS guidance (n=962)	Angiography guidance (n=1016)	*P*
Per lesion, n (%)			
Stent number	1.81±0.80	1.76±0.77	0.16
Mean stent length, mm	49.99±25.10	47.38±22.42	0.02
Mean stent diameter, mm	3.14±0.51	2.97±0.48	<0.001
Max balloon diameter, mm	3.73±0.56	3.51±0.53	<0.001
Max post-dilation pressure, atm	19.7±3.7	19.0±3.7	<0.001

Jun-Jie Zhang et al. TCT 2018

ngio-guided PCI vs. IVUS-guided PCI

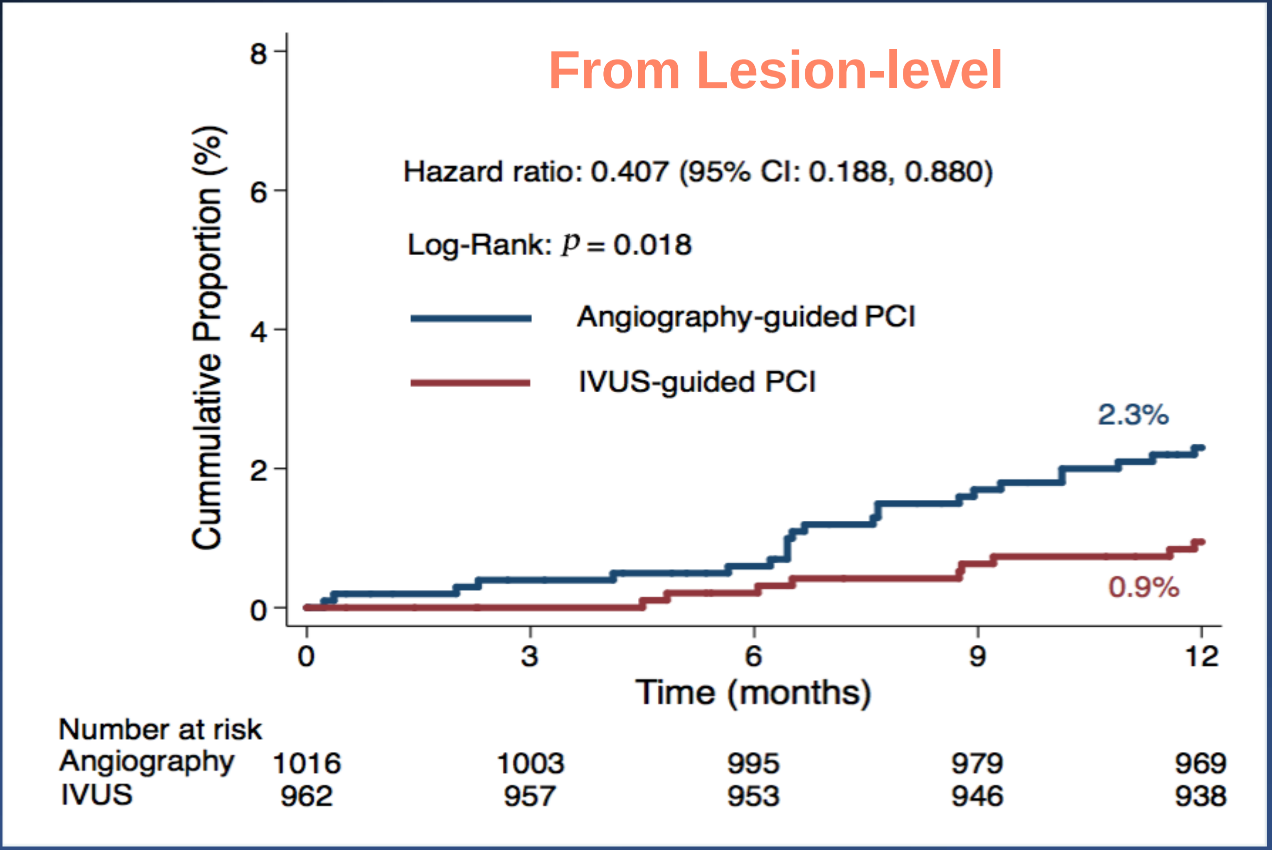
TVF at 12-months
ULTIMATE trial



Jun-Jie Zhang et al. TCT 2018

ngio-guided PCI vs. IVUS-guided PCI

CD-TLR or Definite ST at 12-month
ULTIMATE trial



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On-site Post-procedure IVUS Assessment

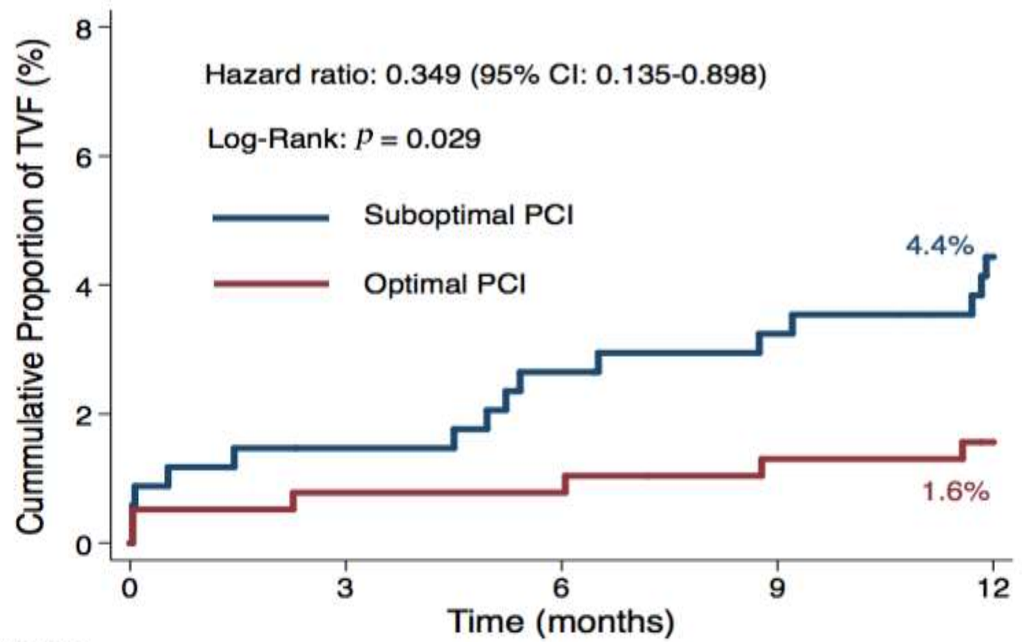
ULTIMATE trial

	Optimal group	Suboptimal group	*P*
Number of patients, n (%)	384 (53.0)	340 (47.0)	
Number of lesions, n (%)	578 (60.1)	384 (39.9)	
MSA, mm^2	6.09	5.45	<0.001
Prox. edge plaque burden	37.2%	51.2%	<0.001
Dist. edge plaque burden	24.2%	35.1%	<0.001

Jun-Jie Zhang et al. TCT 2018

Optimal vs. Suboptimal IVUS-guided PCI

TVF at 12-months
ULTIMATE trial



Number at risk					
Suboptimal	340	334	329	326	320
Optimal	384	381	381	378	376

Jun-Jie Zhang et al. TCT 2018

ngio-guided PCI vs. IVUS-guided PCI

Meta-analysis

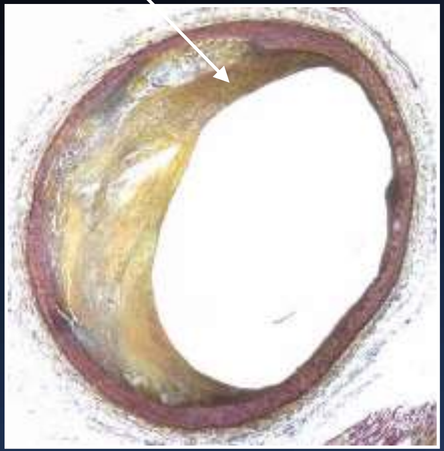
irst Author ef. #)	Year of Publication	Number of Patients	Study Design	Type of Stent	Follow-Up Duration (Months)
hy vs. IVUS					
8)	1998	76/79	Randomized	BMS	6
(9)	2000	229/270	Randomized	BMS	9
S (10)	2001	275/273	Randomized	BMS	12
t al. (11)	2003	54/54	Randomized	BMS	30
2)	2003	76/74	Randomized	BMS	6-12
3)	2007	80/83	Randomized	BMS	6
)	2009	406/394	Randomized	BMS	12
ES IVUS (15)	2010	105/105	Randomized	DES	18
l. (16)	2013	274/269	Randomized	DES	12
)	2013	142/142	Randomized	DES	24
S (18)	2015	201/201	Randomized	DES	12
(19)	2015	115/115	Randomized	DES	24
L (20)	2015	700/700	Randomized	DES	12
l. (21)	2015	62/61	Randomized	DES	24
l. (22)	2008	884/884	Observational, PSM	DES	12
OMPARE (23)	2009	201/201	Observational, PSM	BMS/DES	36
(24)	2011	548/548	Observational, PSM	DES	24
l. (25)	2011	487/487	Observational, PSM	DES	36
al. (26)	2012	123/123	Observational, PSM	DES	12
yashi et al. (27)	2012	637/637	Observational, PSM	BMS/DES	12
ENT (28)	2013	463/463	Observational, PSM	DES	12
rre Hernandez . (29)	2014	505/505	Observational, PSM	DES	36
l. (30)	2014	291/291	Observational, PSM	DES	12
al. (31)	2014	201/201	Observational,	DES	24

	IVUS compared with angiography Odds ratio [95% CI]
Primary outcome	
All cause mortality	0.75 [0.58-0.98]
Secondary outcome	
MACE	0.79 [0.67-0.91]
Cardiovascular death	0.47 [0.32-0.66]
MI	0.72 [0.52-0.93]
TLR	0.74 [0.58-0.90]
ST	0.42 [0.20-0.72]

Buccheri et al. JACC Cardiovasc Interv. 2017 Dec 26;10(24):2488-2498

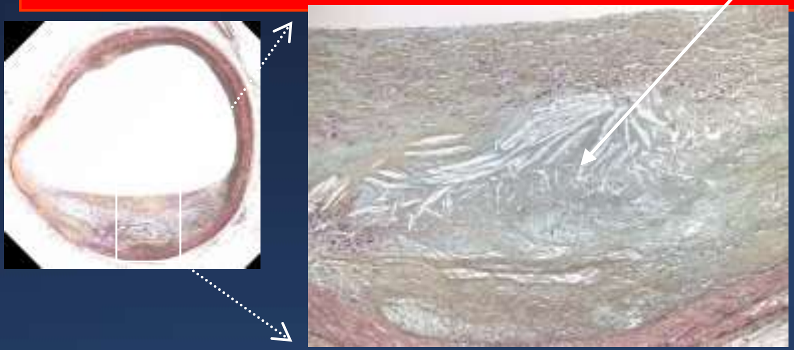
VH-IVUS

Fibrous Tissue



Densely packed collagen fibers with no evidence of lipid accumulation. No evidence of macrophage infiltration.

Necrotic Core

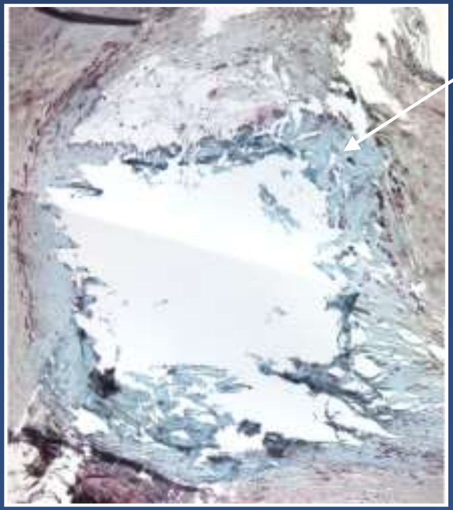


Highly lipidic necrotic region with remnants of foam cells and dead lymphocytes. No collagen fiber, Cholesterol clefts and micro calcifications

Fibro-Fatty

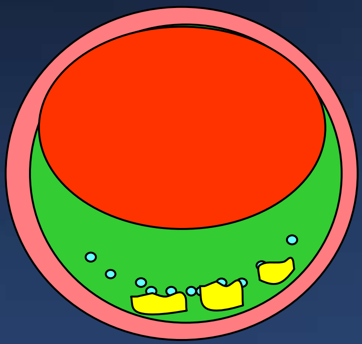
Loosely packed bundles of collagen fibers with regions of lipid deposition present. No cholesterol clefts or necrosis. Increase in extra-cellular matrix

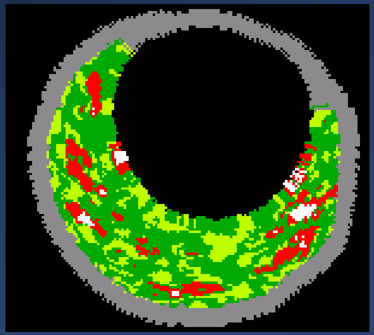
Dense Calcium



Focal dense calcium

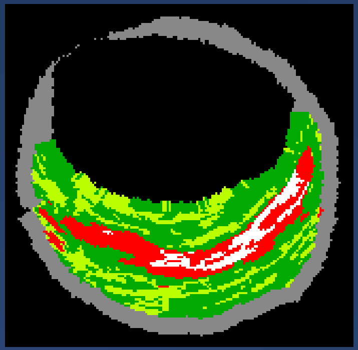
PIT





Plaque thickness > 600um
Fibrofatty >15%

Fibroatheroma

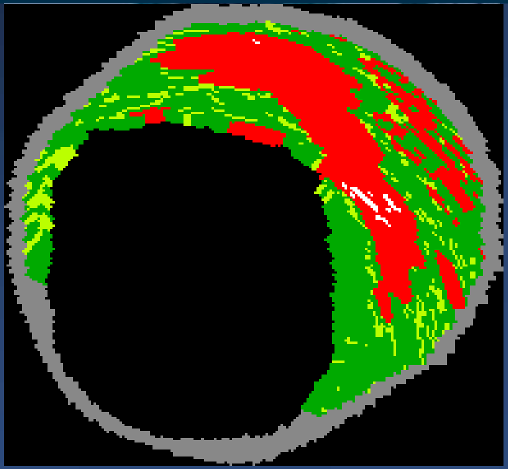


Confluent NC >10%

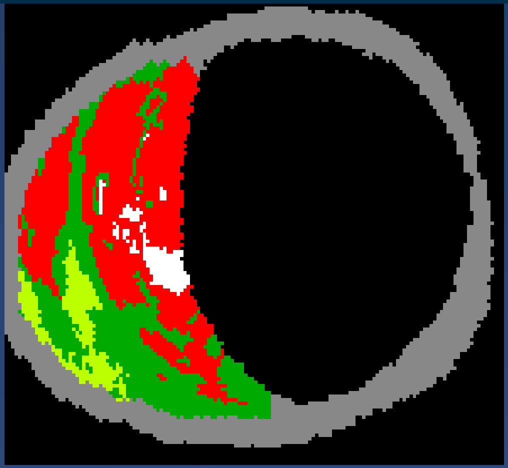
Criteria of TCFA

In at least 3 consecutive frames:

1) Necrotic core ≥ 10%
2) without evident overlying fibrous tissue
3) Percent atheroma area ≥ 40%



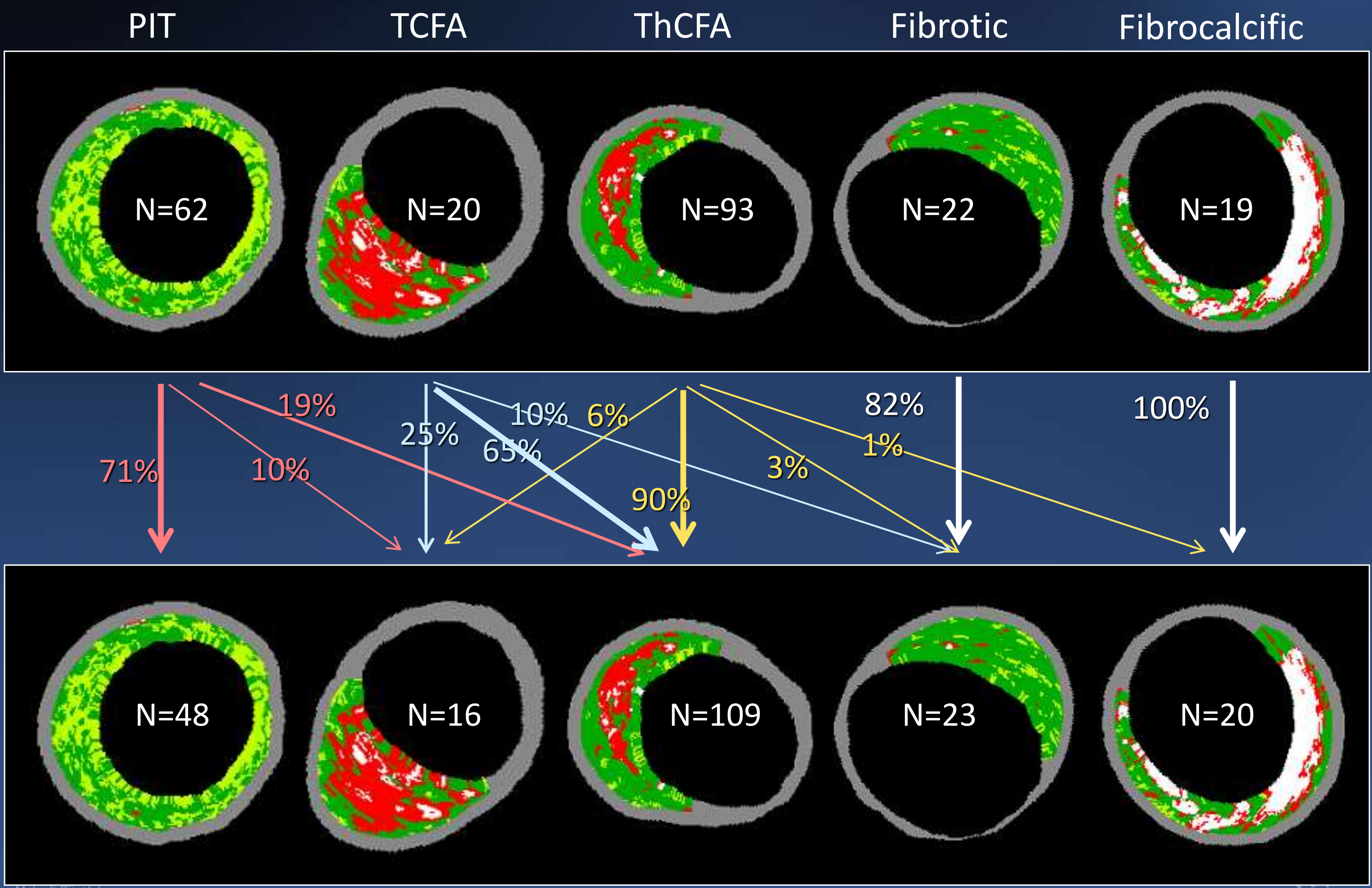
Thick fibrous cap
Low lipid conc
Low macrophage density



Thin fibrous cap
High lipid conc
High macrophage density

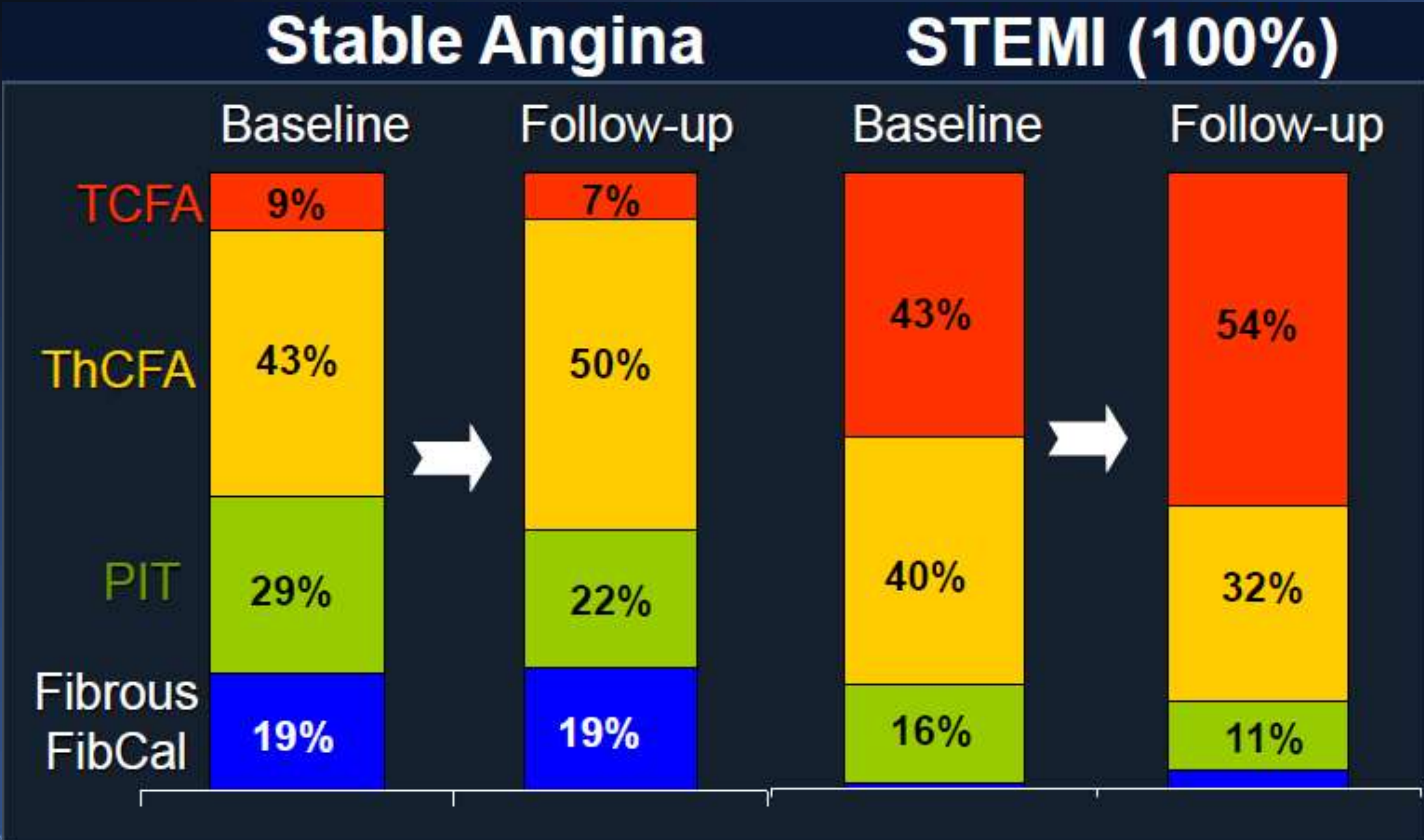
Rodriguez-Granillo et al. J Am Coll Cardiol 2005;46:2038–42

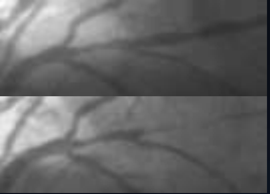
Change of Plaque Type



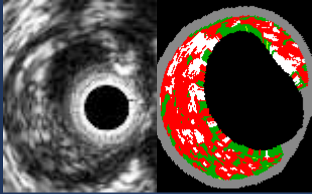
Kubo T, JACC 2010;55:1590

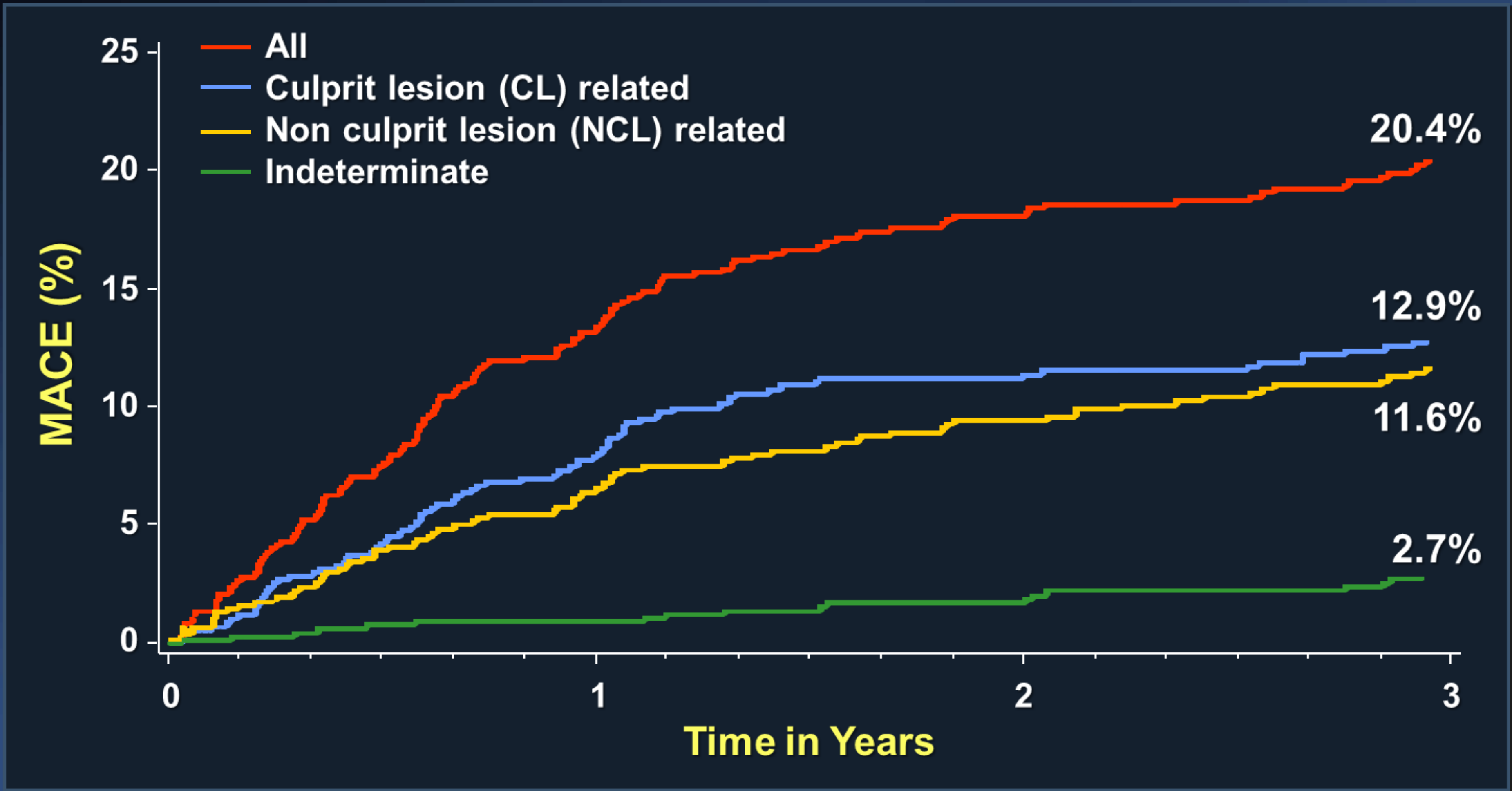
Differences in Temporal Changes of Non-Culprit Lesions





PROSPECT MACE (N=697)





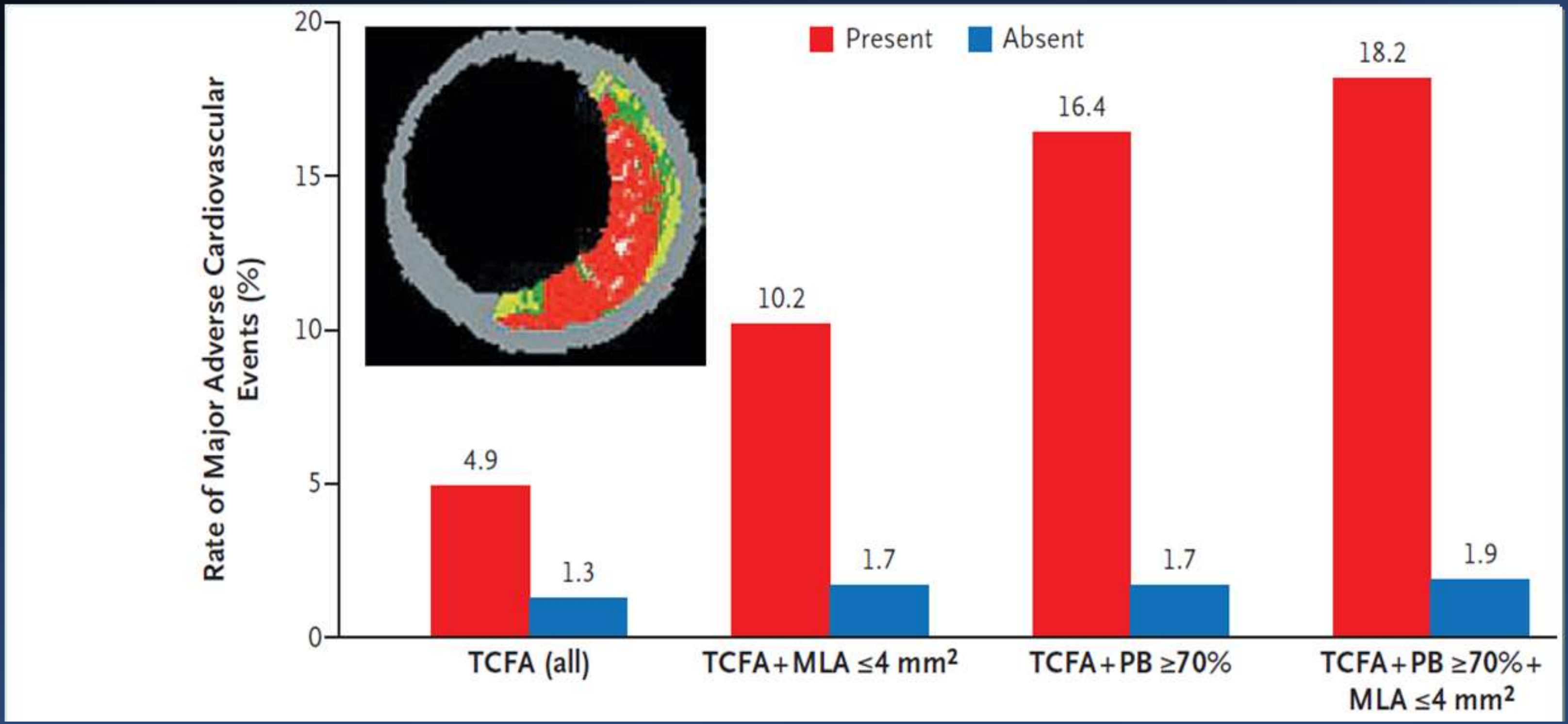
Number at risk

ALL	697	557	506	480
CL related	697	590	543	518
NCL related	697	595	553	521
Indeterminate	697	634	604	583

Stone GW et al. NEJM 2011;364:226-35

PROSPECT 3-year MACE

*MACE = cardiac death, arrest, MI, rehospitalization for unstable/ progressive angina



Predictors	Hazard ratio (95% CI)	p
Plaque burden ≥70%	5.03 (2.51 – 10.11)	<0.001
Thin-cap fibroatheroma	3.35 (1.77 – 6.36)	<0.001
MLA ≤4.0 mm^2	3.21 (1.61 – 6.42)	0.001

Stone G et al. N Engl J med 2011;364:226-35

PROSPECT II Study

PROSPECT II
PROSPECT ABSORB

900 pts with ACS at up to 20 hospitals

in Sweden, Denmark and Norway (SCAAR)

NSTEMI or STEMI >12º

IVUS + NIRS (blinded) performed in culprit vessel(s)

Successful PCI of all intended lesions (by angio ±FFR/iFR)

↓

Formally enrolled

↓

3-vessel imaging post PCI

Culprit artery, followed by non-culprit arteries

Angiography (QCA of entire coronary tree)

IVUS + NIRS (blinded) (prox 6-8 cm of each coronary artery)

↓

PROSPECT II
PROSPECT ABSORB

PROSPECT II Study

PROSPECT ABSORB RCT

900 pts with ACS after successful PCI

3 vessel IVUS + NIRS (blinded)

≥1 IVUS lesion with ≥65% plaque burden present?

Yes (N=300)

R 1:1

ABSORB BVS + GDMT (N~150)

GDMT (N=150)

Routine angio/3V IVUS-NIRS FU at 2 years

No (n=600)

Clinical FU for up to 15 years

The Preventive Implantation of Bioresorbable Vascular Scaffold on Stenosis With Vulnerable Plaque Feature But Functionally Insignificance

PREVENT Trial

Symptomatic or Asymptomatic CAD patients

Any epicardial coronary stenosis
with ***FFR ≥0.80*** and with ***Two*** of the following

- **IVUS MLA ≤4.0mm^2**
- **IVUS Plaque Burden >70%**
- **Lipid-Rich Plaque on NIRS ($_{max}$LCBI$_{4mm}$>400)**

R

BVS+OMT	OMT
N=1000	N=1000

Primary endpoint at 2 years: CV death, MI, Hospitalization d/t unstable angina

OCT sub-study/ NIRS sub-study (300 patients in each arm at 2 years)

OCT

Optical coherence tomography imaging during percutaneous coronary intervention impacts physician decision-making: ILUMIEN I study

William Wijns[1*], Junya Shite[2], Michael R. Jones[3], Stephen W.-L. Lee[4], Matthew J. Price[5], Franco Fabbiocchi[6], Emanuele Barbato[1], Takashi Akasaka[7], Hiram Bezerra[8], and David Holmes[9]

A prospective, non-randomized study to see the impact of OCT on physician decision-making, post-PCI residual ischemia, and clinical outcomes

418 patients with 467 lesions

Mandatory use of FFR and plan PCI strategy

OCT (411 pts, 459 lesions)

Plan changed in 230 (55%) pts, 264 (57%) lesions

Perform PCI

FFR and OCT

Satisfactory result – No optimization in 75% of pts, 73% of lesions

Unsatisfactory result – Optimization in 25% of pts, 27% of lesions

14.5% malapposition
7.6% under-expansion
2.7% edge dissection

Follow-up at discharge and at 30 days (401 pts)

Eur Heart J 2015 in press

ILUMIEN I study

	PCI optimiz, without change	PCI optimiz based on pre-PCI OCT	PCI optimiz, based on post-PCI OCT	PCI optimiz, based on pre- and post-PCI OCT	p
Pre-PCI FFR	0.72±0.14	0.73±0.14	0.72±0.14	0.72±0.14	0.93
Post-PCI FFR	0.89±0.07	0.89±0.07	0.89±0.08	0.86±0.09	0.003
Final FFR			0.90±0.10	0.90±0.10	0.24
In-hos MACE	8.8%	6.7%	12.2%	1.5%	0.118
1-mo MACE	8.8%	8%	12.5%	1.5%	0.127

- Following OCT-guided PCI, the rates of MACEs at 30 days were very low (death 0.25%, MI 7.7%, TLR 1.7%, ST 0.25%)
- Physician decision-making was affected by OCT imaging prior to PCI in 57% and post-PCI in 27% of all cases

Wijins et al. *Eur heart j*, 2015

ILUMIEN II study

Comparison of Stent Expansion Guided by Optical Coherence Tomography Versus Intravascular Ultrasound

The ILUMIEN II Study (Observational Study of Optical Coherence Tomography [OCT] in Patients Undergoing Fractional Flow Reserve [FFR] and Percutaneous Coronary Intervention)

Akiko Maehara, MD,[*†] Ori Ben-Yehuda, MD,[*†] Ziad Ali, MD,[*†] William Wijns, MD, PhD,[‡] Hiram G. Bezerra, MD,[§] Junya Shite, MD,[||] Philippe Généreux, MD,[*†¶] Melissa Nichols, MS,[†] Paul Jenkins, PhD,[†] Bernhard Witzenbichler, MD,[#] Gary S. Mintz, MD,[†] Gregg W. Stone, MD[*†]

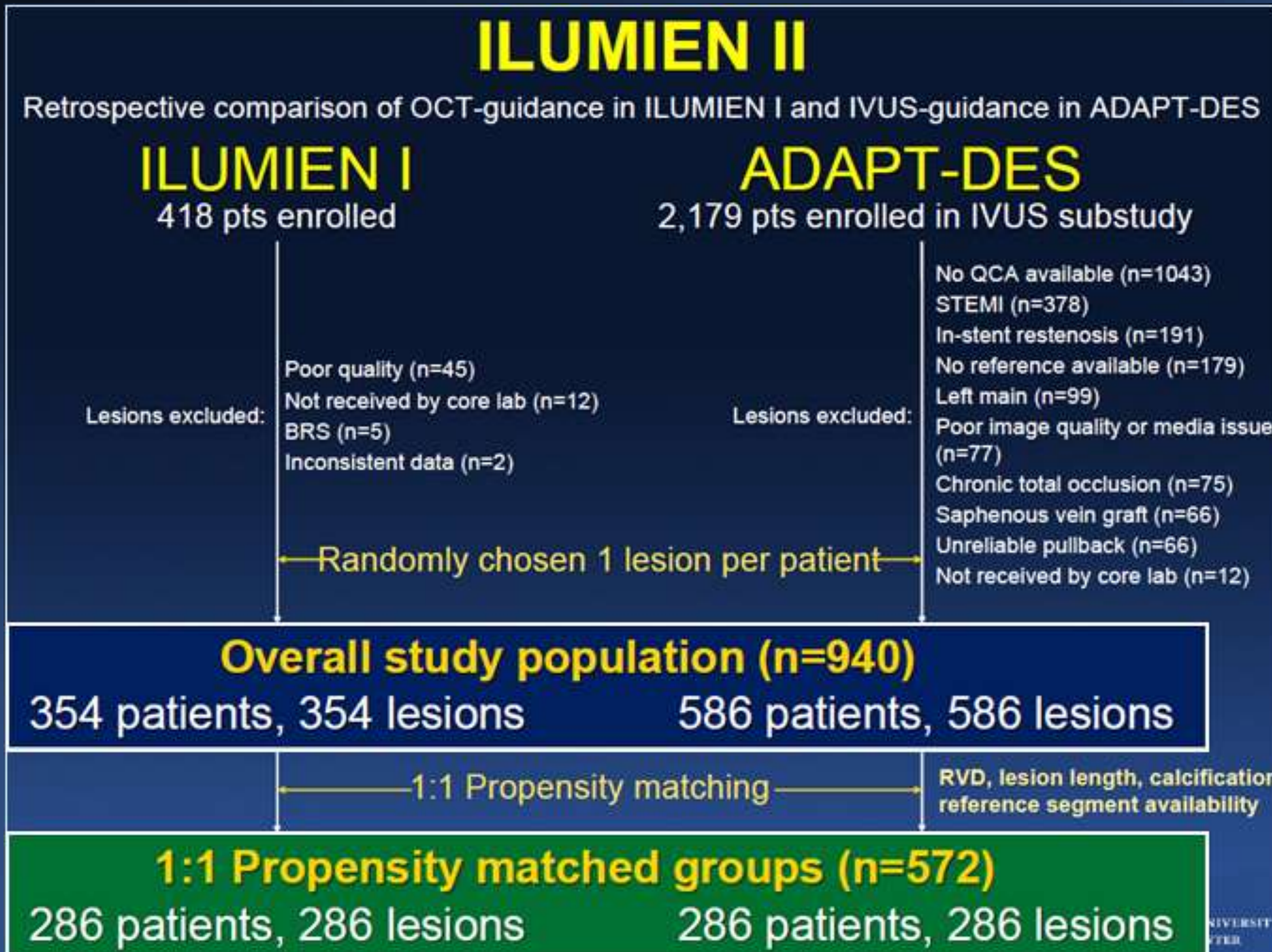
Design: A post-hoc analysis of the outcome of OCT- vs. IVUS-guided PCI from the ILUMIEN I and ADAPT-DES

Aim: To compare a degree of stent expansion achieved by OCT- vs. IVUS-guidance

Primary endpoint: Final post-PCI stent expansion defined as the MSA divided by the mean of the proximal and distal RLA

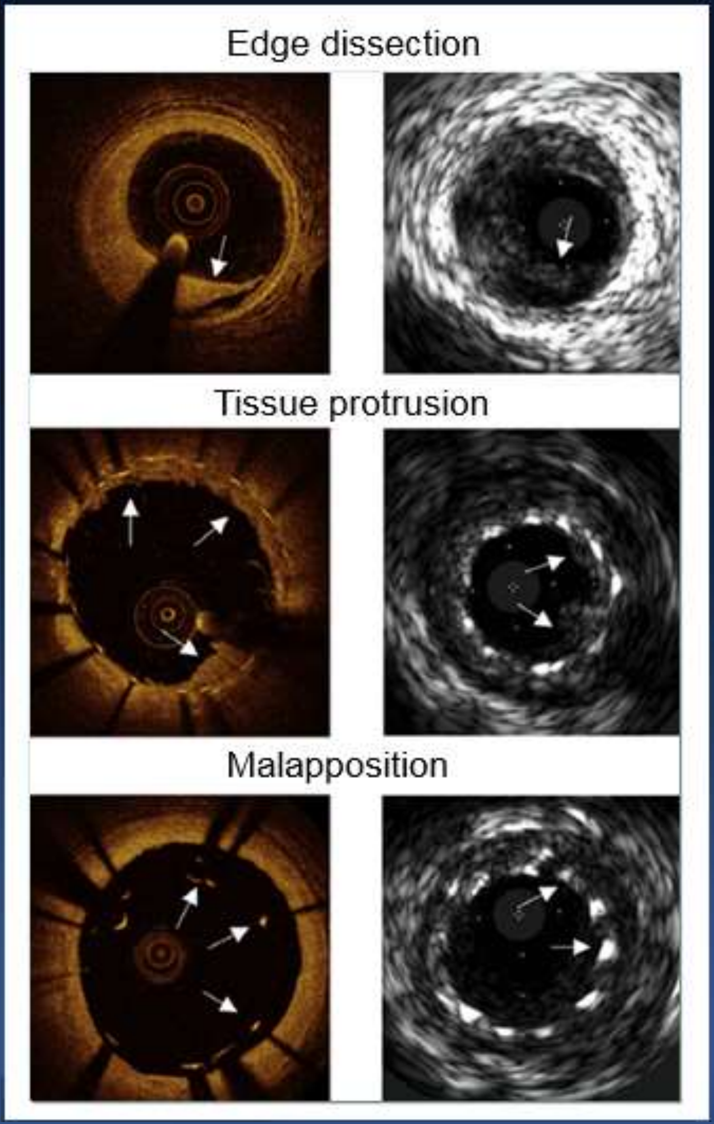
Meahara A. J Am Coll Cardiol Intv 2015;8:1704–14

ILUMIEN II study



Meahara A. J Am Coll Cardiol Intv 2015;8:1704–14

ILUMIEN II study



Qualitative Data in the Propensity-Matched Groups

	OCT	IVUS	p
Any malapposition	27%	14%	0.002
distance/MLD>20%	1%	1%	0.69
Any tissue protrusion	64%	27%	<0.001
protrusion CSA>10%	12%	8%	0.17
Any edge dissection	23%	5%	<0.001
dissec length ≥3mm	2%	1%	0.29

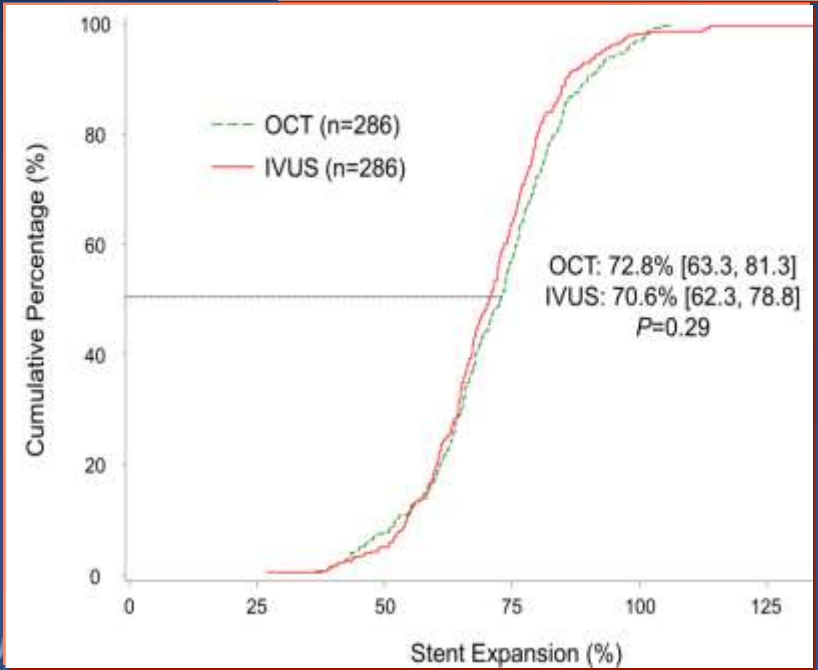
Meahara A. J Am Coll Cardiol Intv 2015;8:1704–14

Meahara A. J Am Coll Cardiol Intv 2015;8:1704–14

ILUMIEN II study

TABLE 5 Multivariable Analysis in the Entire Study Population (N = 940)

	Endpoints			
	Stent Expansion, %	Mean Stent Expansion, %	Diameter Stenosis In-Stent, %	Diameter Stenosis In-Segment, %
Measurement by OCT (N = 354)	72.6 (63.5, 81.4)	89.6 (79.2, 98.5)	6.4 (2.7, 9.9)	13.3 (8.9, 20.2)
Measurement by IVUS (n = 586)	70.5 (62.1, 79.5)	86.8 (77.1, 96.8)	6.4 (3.0, 10.7)	11.2 (7.6, 17.2)
	Adjusted p Values			
OCT vs. IVUS	0.84	0.30	0.19	0.009



Conclusion

OCT-guidance was related to comparable stent expansion, and similar rates of major edge dissection, stent malapposition, and tissue protrusion as compared to IVUS-guidance

Meahara A. J Am Coll Cardiol Intv 2015;8:1704–14

LUMIEN III : OPTIMIZE PCI

OCT-Guided vs IVUS-Guided vs Angio-Guided PCI

- Randomly allocated 450 patients (1:1:1)
  - OCT guidance ; 158 [35%]
  - IVUS guidance ; 146 [32%]
  - Angiography guidance ; 146 [32%]

- All patients underwent final OCT imaging

- Primary efficacy endpoint ; post-PCI minimum stent area
- Primary safety endpoint ; procedural MACE

Ali ZA et al. The Lancet 2016, Vol 388; 2618-28

ILUMIEN III : OPTIMIZE PCI

OCT-Guided vs IVUS-Guided vs Angio-Guided PCI

Efficacy Endpoints

	OCT (n=140)	IVUS (n=135)	Angio (n=140)	P (OCT vs IVUS)	P (OCT vs Angio)
Minimal stent area(mm^2)	5.79 [4.54-7.34]	5.89 [4.67-7.80]	5.49 [4.39-6.59]	0.42	0.12
Minimum stent expansion(%)	88±17	87±16	83±13	0.77	0.02
Mean stent expansion(%)	106 [98-120]	106 [97-117]	101 [92-110]	0.63	0.001

OCT guidance was non-inferior to IVUS guidance (one-sided 97.5% lower CI –0.70 mm2; p=0.001), but not superior (p=0.42).
OCT guidance was also not superior to angiography guidance (p=0.12).

Ali ZA et al. The Lancet 2016, Vol 388; 2618-28

ILUMIEN III : OPTIMIZE PCI

OCT-Guided vs IVUS-Guided vs Angio-Guided PCI

Primary Safety Endpoints

	OCT (n=158)	IVUS (n=146)	Angio (n=146)	P (OCT vs IVUS)	P (OCT vs Angio)
Procedural MACE(%)	2.5	0.7	0.7	0.37	0.37
Complication					
Dissection(%)	1.3	0.0	0.7	0.50	1.00
Perforation	0.0	0.7	0.0	0.48	-
Thrombus	1.3	0.0	0.0	0.50	0.50
Acute closure	0.6	0.0	0.0	1.00	1.00

Procedural MACE was infrequent and not significantly different between the three groups.

Ali ZA et al. The Lancet 2016, Vol 388; 2618-28

ILUMIEN III : OPTIMIZE PCI

OCT-Guided vs IVUS-Guided vs Angio-Guided PCI

Postprocedure OCT measure

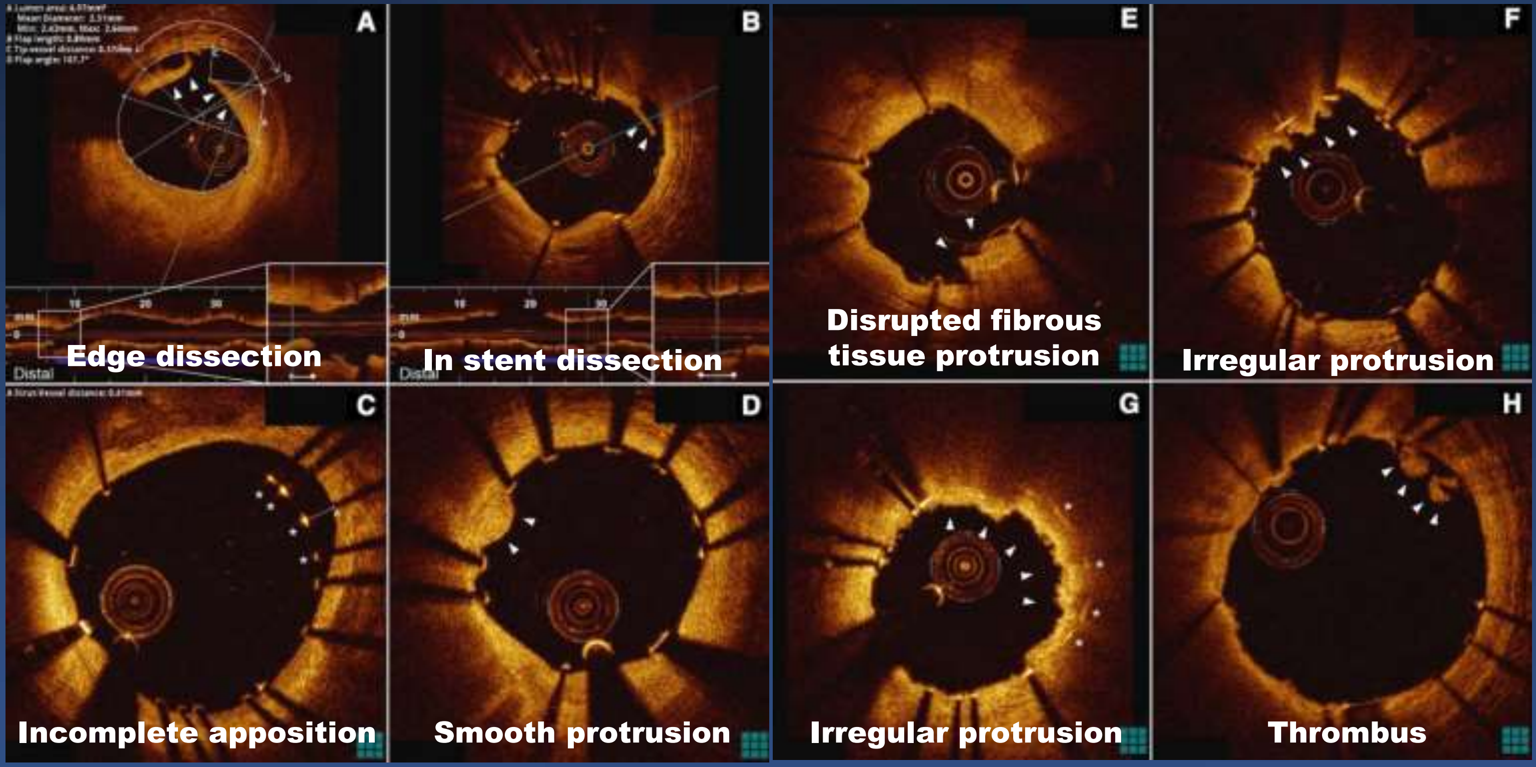
	OCT (n=140)	IVUS (n=135)	Angio (n=140)	P (OCT vs IVUS)	P (OCT vs Angio)
Any dissection(%)	39(28)	53(40)	64(44)	0.04	0.006
Major(%)	19(14)	35(26)	26(19)	**0.009**	0.25
Minor(%)	20(14)	18(13)	35(25)	0.84	0.02
Any malposition(%)	58(41)	52(39)	83(59)	0.62	0.003
Major(%)	15(11)	28(21)	44(31)	0.02	<0.001
Minor(%)	43(31)	24(18)	39(28)	0.01	0.60

OCT-guided PCI resulted in the fewest untreated major dissection and areas of major stent malapposition.

Ali ZA et al. The Lancet 2016, Vol 388; 2618-28

Post-stent OCT Findings

From MGH OCT registry, 900 lesions in 786 patients with post-stenting OCT were analyzed to identify the OCT predictors for device-oriented clinical end points (cardiac death, target vessel-related MI, TLR and stent thrombosis)



Soeda T, Jang IK et al. Circulation 2015;132:1020-9

Post-stent OCT Findings

Incidence of Post-stent Qualitative and Quantitative OCT Findings (Lesion-Level)

	No MACE	MACE	p
N	795	39	
Edge dissection	29%	31%	0.78
Malapposition	38%	36%	0.76
Tissue protrusion	97%	100%	0.63
Irregular protrusion	52%	74%	0.003
Thrombus	38%	51%	0.13
Small MSA*	40%	59%	0.039

*Small MSA : <5.0 mm^2 for DES and <5.6 mm^2 for BMS

Soeda T, Jang IK et al. Circulation 2015;132:1020-9

Post-stent OCT Findings

Multivariable Predictors of
Device-oriented MACE and TLR

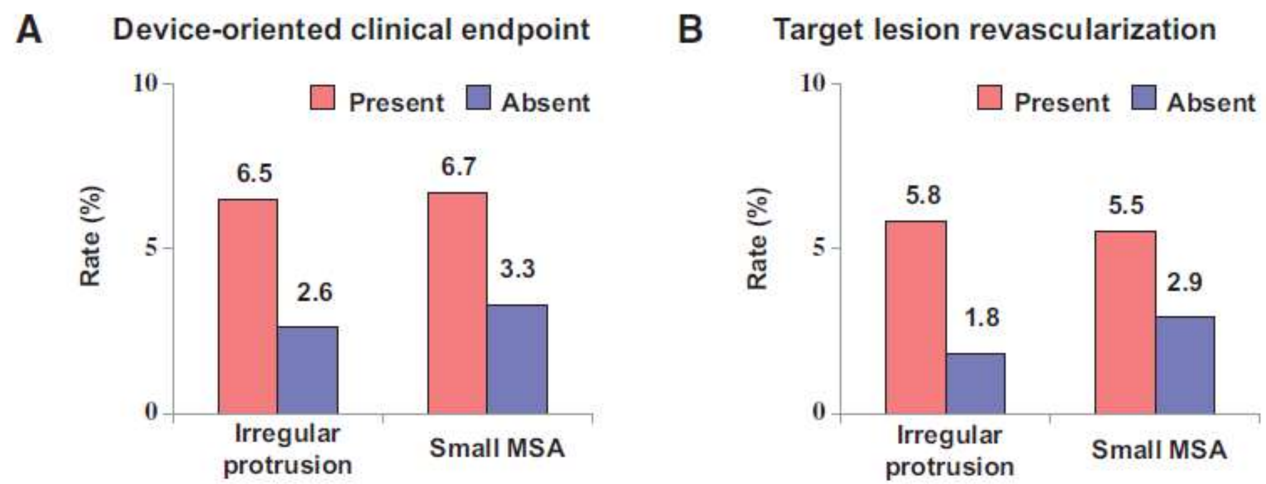
	MACE		TLR	
	OR (95% CI)	p	OR (95% CI)	p
Age, year	NA		0.98 (0.95-1.02)	
Male	3.13 (0.92-10.69)	0.068	NA	
BMS	1.75 (1.19-2.58)	0.005	1.80 (1.23-2.63)	0.002
Irregular protrusion	2.64 (1.40-5.01)	0.003	2.66 (1.40-5.05)	0.003
Small MSA*	2.54 (1.23-5.25)	0.012	2.54 (1.24-5.21)	0.011

*Small MSA : <5.0 mm^2 for DES and <5.6 mm^2 for BMS
Patient-level analysis

Soeda T, Jang IK et al. Circulation 2015;132:1020-9

Post-stent OCT Findings

Rates of Device-oriented MACE and TLR
from multivariable models



	A: Irregular protrusion	A: Small MSA	B: Irregular protrusion	B: Small MSA
Odds ratio (95%CI)	2.64 (1.40 – 5.01)	2.54 (1.23 – 5.25)	2.66 (1.40 – 5.05)	2.57 (1.24 – 5.24)
P-value	0.003	0.012	0.003	0.011
Sensitivity, %	74.4	59.0	78.8	57.6
Specificity, %	47.7	59.6	47.7	59.4
PPV, %	6.5	6.7	5.8	5.5
NPV, %	97.4	96.7	98.2	97.1

Irregular protrusion and small MSA were the independent OCT predictors of MACE, which were primarily driven by TLR

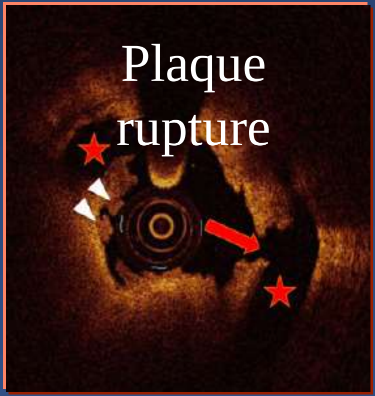
Soeda T, Jang IK et al. Circulation 2015;132:1020-9

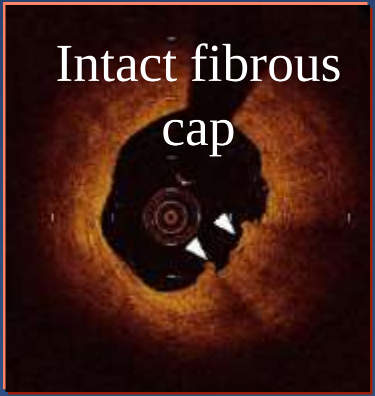
Plaque rupture and prognosis in ACS

Plaque rupture and intact fibrous cap assessed by optical coherence tomography portend different outcomes in patients with acute coronary syndrome

Giampaolo Niccoli[1*], Rocco A. Montone[1], Luca Di Vito[2,3], Mario Gramegna[1], Hesham Refaat[1,4], Giancarla Scalone[1], Antonio M. Leone[1], Carlo Trani[1], Francesco Burzotta[1], Italo Porto[1], Cristina Aurigemma[1], Francesco Prati[2,3], and Filippo Crea[1]

- To evaluate the prognostic value of plaque rupture vs. intact fibrous cap in 139 ACS patients undergoing PCI
- No differences in clinical, angiographic, or procedural data



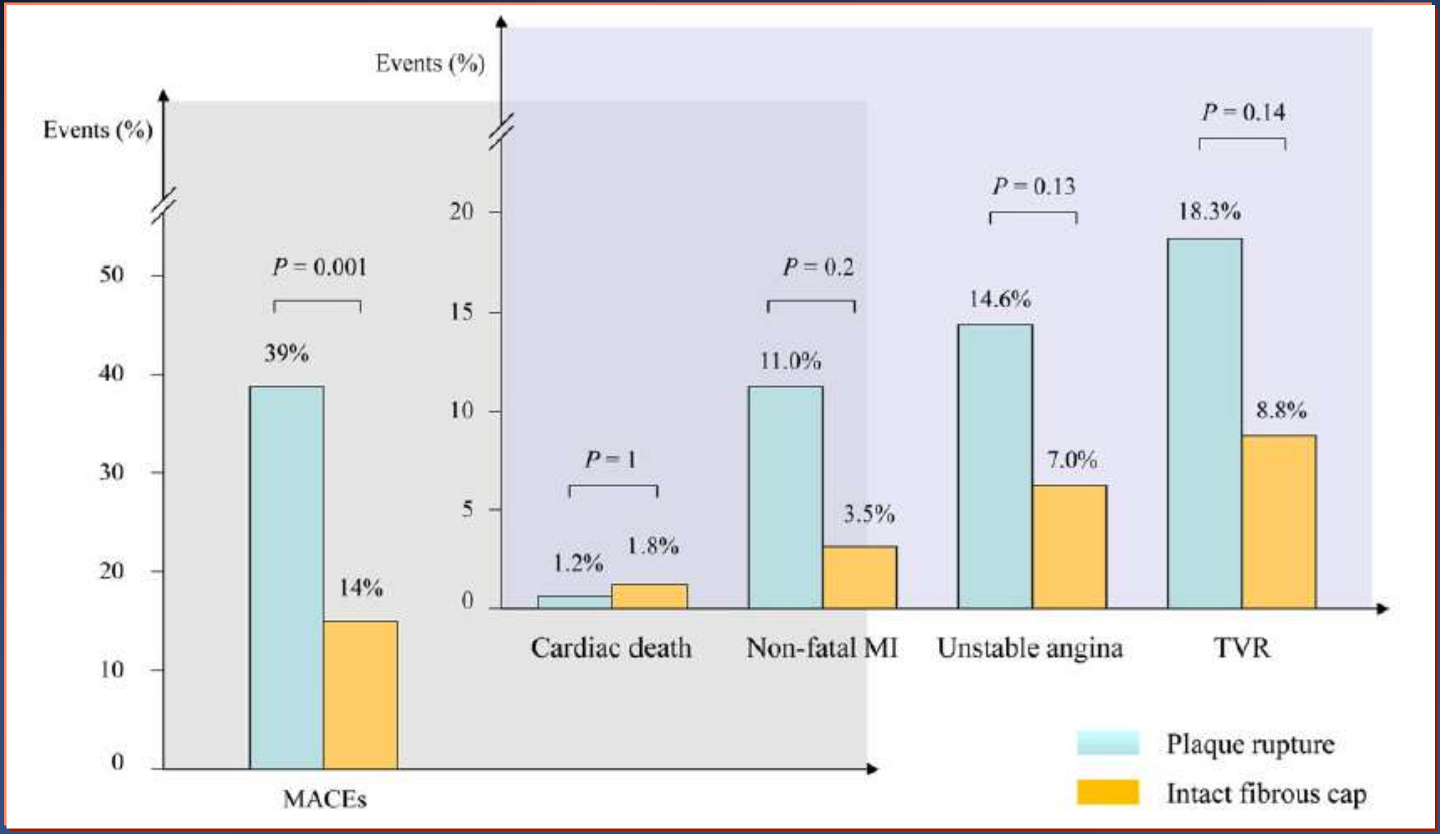


Niccoli et al. Eur Heart J 2015;36:1377-84

Plaque rupture and prognosis in ACS

MACE rates

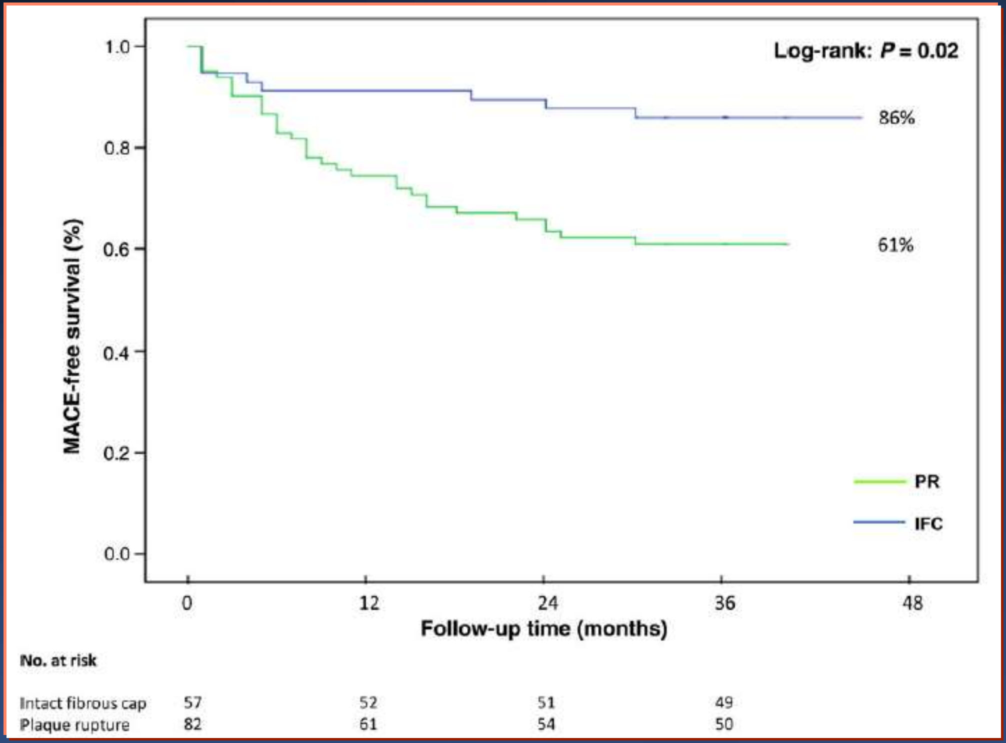
Patients with plaque rupture vs. with intact fibrous cap



Niccoli et al. Eur Heart J 2015;36:1377-84

Plaque rupture and prognosis in ACS

Kaplan–Meier Analysis



Conclusion

Patients with plaque rupture had a worse MACE-free survival (61% vs. 86%) compared with those having an intact fibrous cap

Niccoli et al. Eur Heart J 2015;36:1377-84

Plaque rupture and prognosis in ACS

Predictors of 3-year MACEs
Multivariable Cox regression analysis

	HR	95% CI	p
Obesity (BMI >35)	1.688	0.822-3.845	0.15
Plaque rupture	3.735	1.358-9.735	0.010
Previous PCI	1.449	0.610-4.146	0.34
Stent length	1.028	0.980-1.081	0.26
Age	1.005	0.977-1.034	0.73
Male	1.36	0.335-1.591	0.76

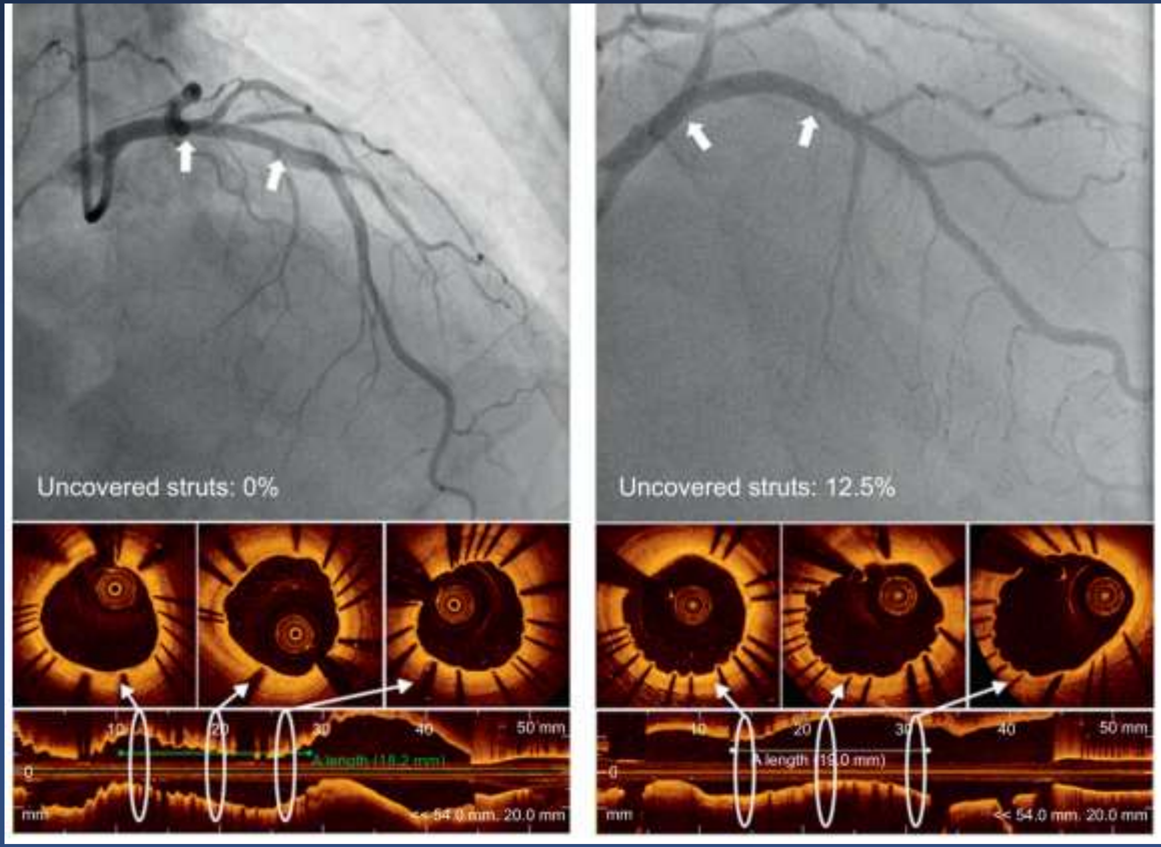
Conclusion

ACS patients with plaque rupture in culprit lesion have a worse prognosis compared to those with IFC, which should be taken into account in risk stratification and management of ACS

Niccoli et al. Eur Heart J 2015;36:1377-84

Stent coverage following OCT vs angio-guided PCI

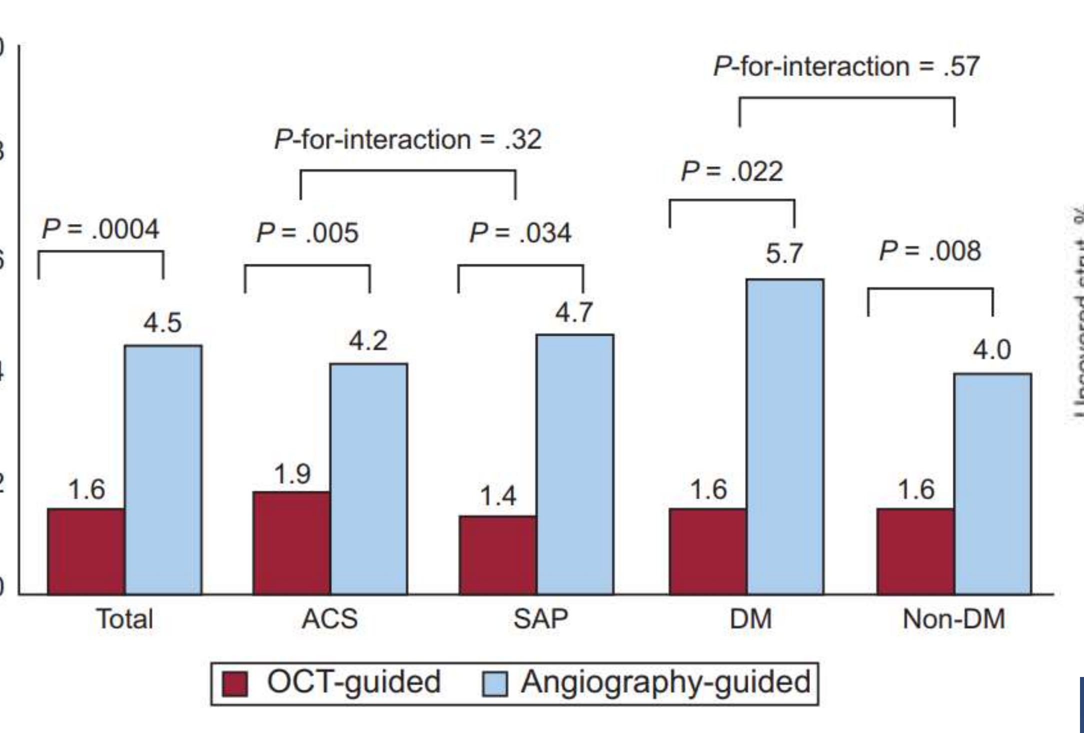
- RCT
- 101 patients (105 lesions)
- OCT guided PCI (n=51) vs angio-guided PCI (n=54)
- 6 months follow-up OCT
- Primary endpoint : incidence of uncovered struts

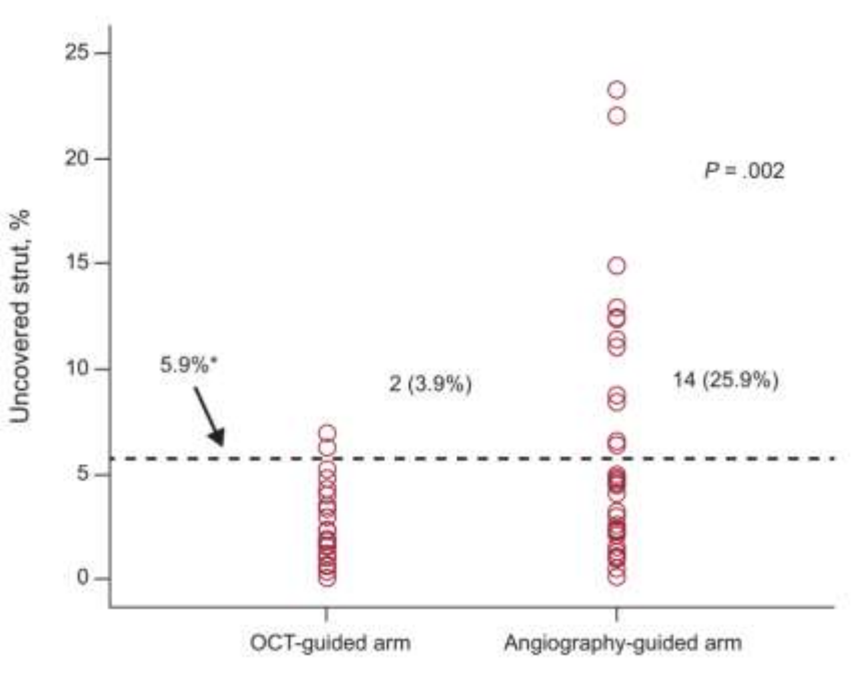


OCT−guided Angio−guided

Hong et al. Rev Esp Cardiol (Engl Ed). 2015 Mar;68(3):190-7

Stent coverage following OCT vs angio





Hong et al. Rev Esp Cardiol (Engl Ed). 2015 Mar;68(3):190-7

OCT guidance vs angiographic guidance
CLI-OPCI study

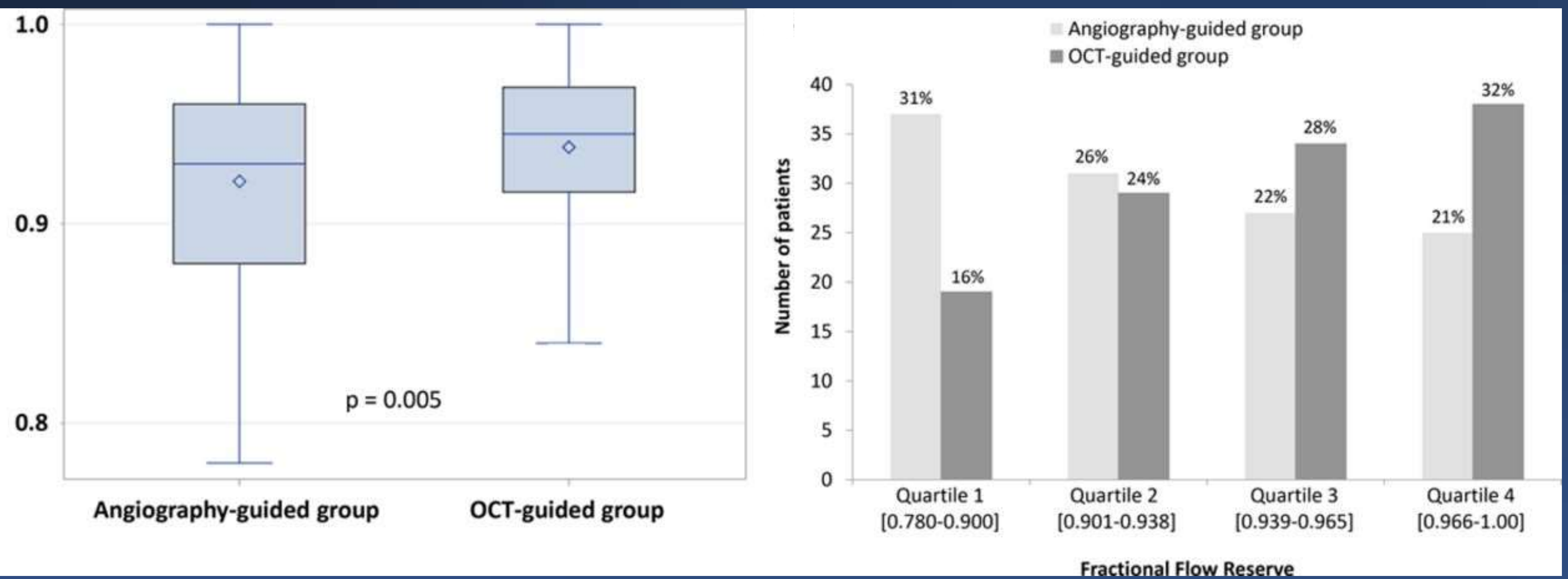
One year outcome	OCT (n=335)	CAG (n=335)	P
Death	3.3%	6.9%	0.035
Cardiac death	1.2%	4.5%	0.010
MI	5.4%	8.7%	0.096
TLR	3.3%	3.3%	1
Definite ST	0.3%	0.6%	0.6
Cardiac death/MI	6.6%	13.0%	0.006
Cardiac death/MI or repeat revascularization*	9.6%	15.1%	0.034

***Even after accounting for baseline and procedural differences (OR=0.49, p=0.037)**

Prati et al. Eurointervention 2012;8:823-9

OCT guidance vs angiographic guidance
DOCTORS study

N=240 (120 vs 120)
Multicenter, prospective, randomized trial



FFR after PCI in the angio vs OCT guided group

Meneveau et al. Circulation. 2016;134:906–917

OCT guidance vs angiographic guidance
DOCTORS study

Variable	Pre-stenting	Immediately poststenting	Post-OCT optimization	p-value
Reference diameter, mm	2.92±0.53	3.10±0.45	3.11±0.48	0.27
MLD, mm	1.21±0.33	2.79±0.46	2.84±0.43	0.001
Diameter stenosis, %	58.4±10.9	9.5±6.1	8.4±3.9	<0.0001
Reference area, mm	7.0±2.23	7.62±2.42	7.72±2.43	0.10
MLA, mm2	1.28±0.71	5.99±2.11	6.41±1.99	<0.0001
Area stenosis, %	81.1±9.82	21.1±12.4	15.9±7.3	<0.0001

Meneveau et al. Circulation. 2016;134:906–917

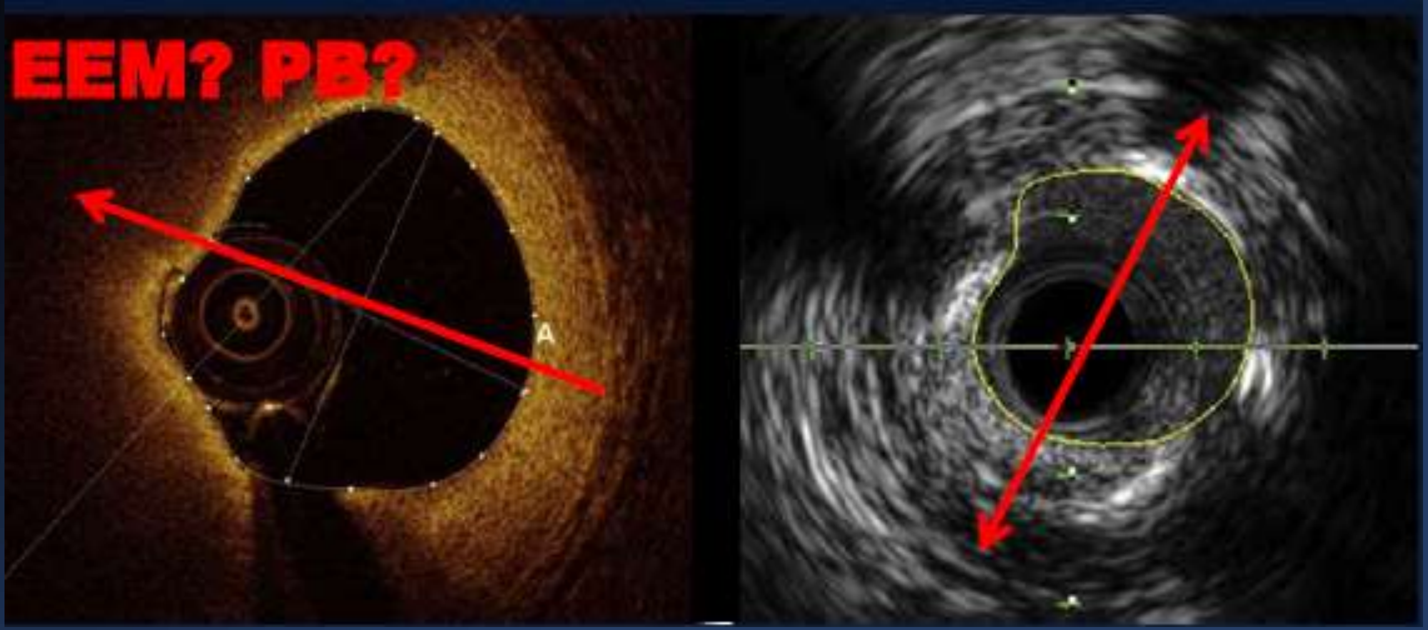
OCT guided PCI

Stent underexpansion
PLUS…
(Minor) findings not seen on IVUS
- Malapposition
- Tissue protrusion
- Edge dissection

Stent underexpansion
PLUS…
Geographical miss
(major edge dissections,
Plaque burden >50%)

Characteristics of devices

	IVUS	OCT
Energy source	US	NIR laser
Resolution	100-200 um	10-20 um
Frame rate	30 fps	160 fps
Pullback velocity	0.5-2.0 mm/sec	0.5-40 mm/sec
Catheter type	RX 2.4 Fr	RX 2.4 Fr
Penetration depth	5 mm	1-2 mm
Scan diameter	20 mm	10 mm
Blood evacuation	-	Lactate Ringer and/or Contrast medium flush



Ability to Detect Suboptimal Findings (OPUS-CLASS)

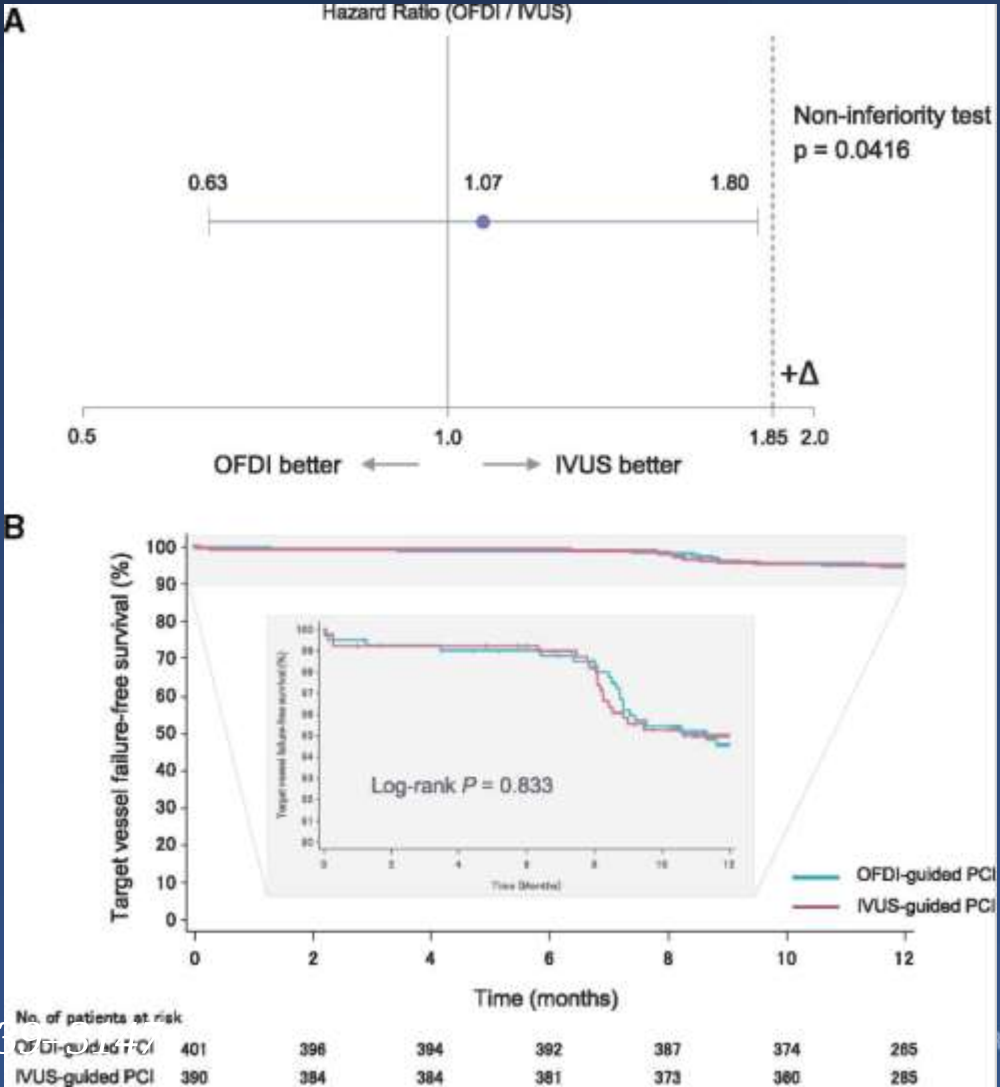
Post-PCI	IVUS	OCT	P
Malapposition	14%	39%	< 0.001
Tissue protrusion	18%	95%	< 0.001
Dissection	0%	13%	0.013
Thrombus	0%	13%	0.013

Kubo et al. JACC imaging 2013;6:1095-104

IVUS vs OCT guided PCI

OPINION Trial

- ulticenter, Prospective, Randomized ial
- ptical frequency domain imaging OFDI) vs IVUS
- rimary endpoint
  - target vessel failure within 12 months



o T et al. Eur Heart J. 2017 Nov 7; 38(42): 313

IVUS vs OCT guided PCI

OPINION Trial

	OFDI-guided PCI (n = 412)	IVUS-guided PCI (n = 405)	P-value
Stent diameter (mm)	2.92 ± 0.39	2.99 ± 0.39	0.005
Total stent length (mm)	25.9 ± 13.2	24.8 ± 13.2	0.06
Multiple stenting	68 (16.5)	59 (14.6)	0.50
Pre-dilatation	316 (76.7)	316 (78.0)	0.67
Post-dilatation	316 (76.7)	304 (75.1)	0.62
Balloon dilatation of side -branch	39 (9.5%)	41 (10.1%)	0.81
Maximum balloon diame ter (mm)	3.1 ± 0.8	3.3 ± 1.2	0.06
Maximum inflation press ure, atmosphere	16.0 ± 4.2	16.0 ± 4.2	0.70
No. of OFDI/IVUS proc edure	3.0 ± 1.1	3.0 ± 1.1	0.14
Total amount of contrast	164 ± 66	138 ± 56	<0.001

Kubo T et al. Eur Heart J. 2017 Nov 7; 38(42): 3139–3147.

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Intravascular Ultrasound Versus Optical Coherence Tomography Guidance

Ron Waksman, MD, Hironori Kitabata, MD, Francesco Prati, MD, Mario Albertucci, MD, Gary S. Mintz, MD

IVUS remains the more trusted modality for stent sizing and optimization until OCT own criteria are validated with clinical outcomes

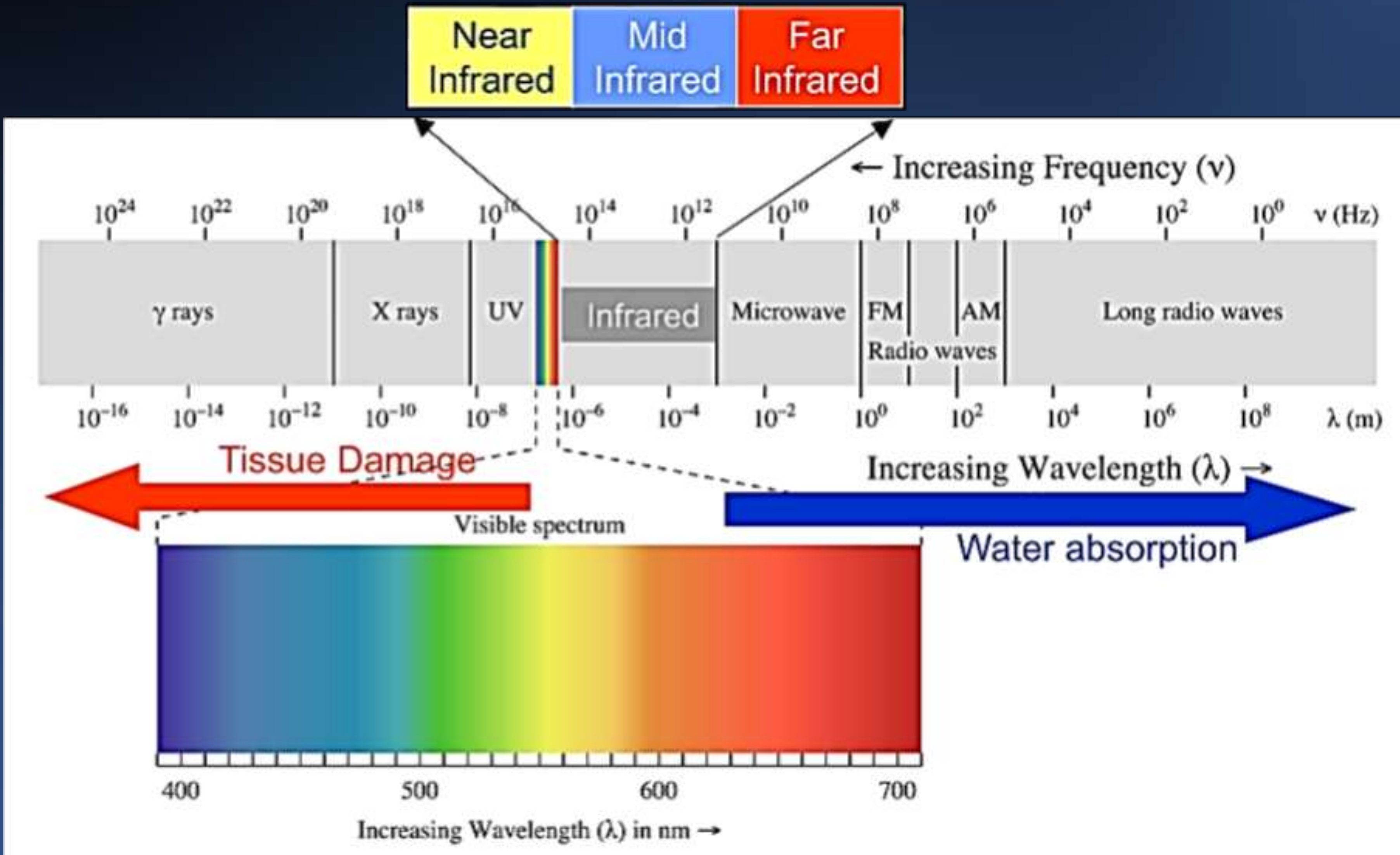
COMPLEX PCI Make It Simple!

CVRF

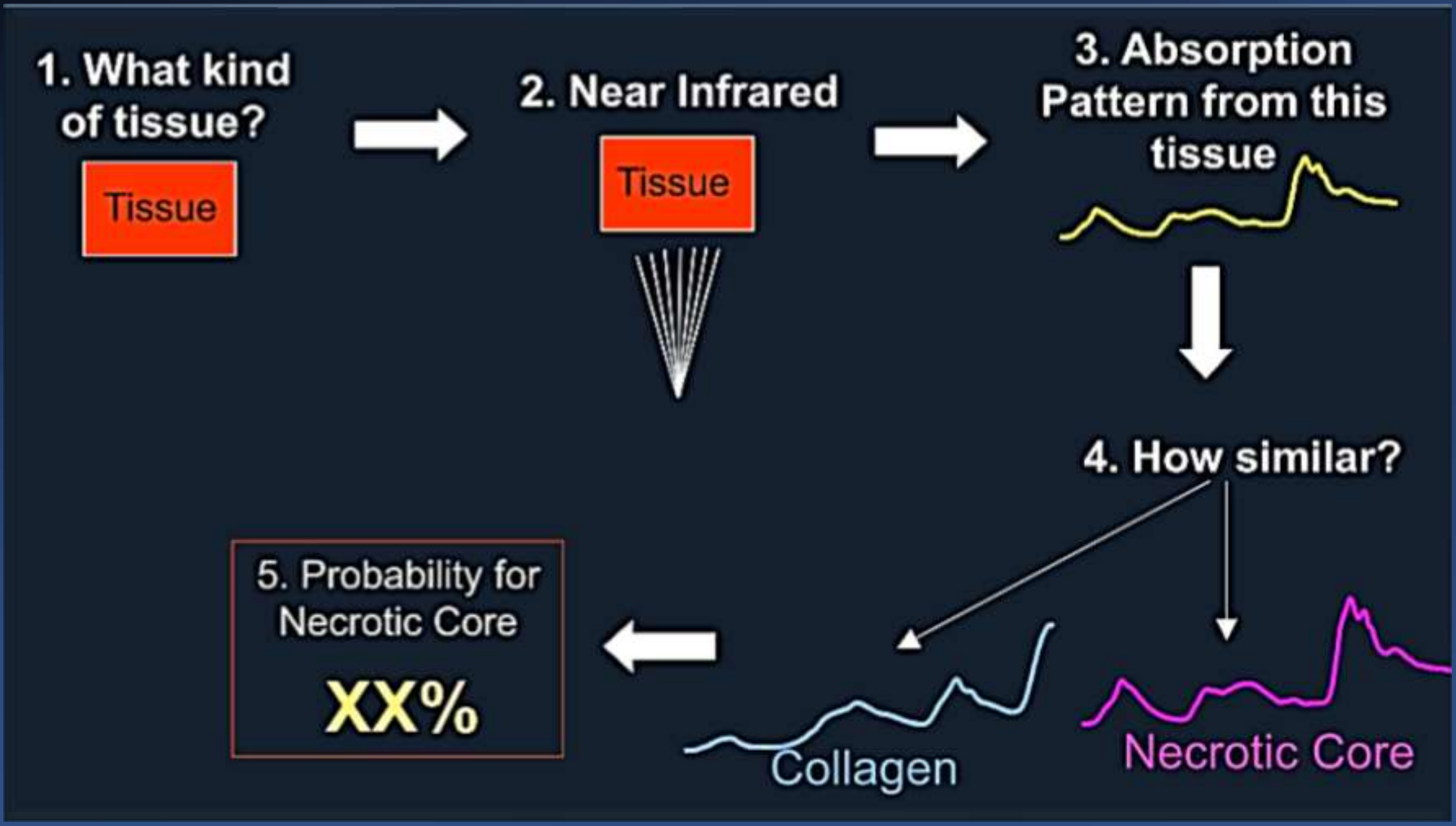
NIRS

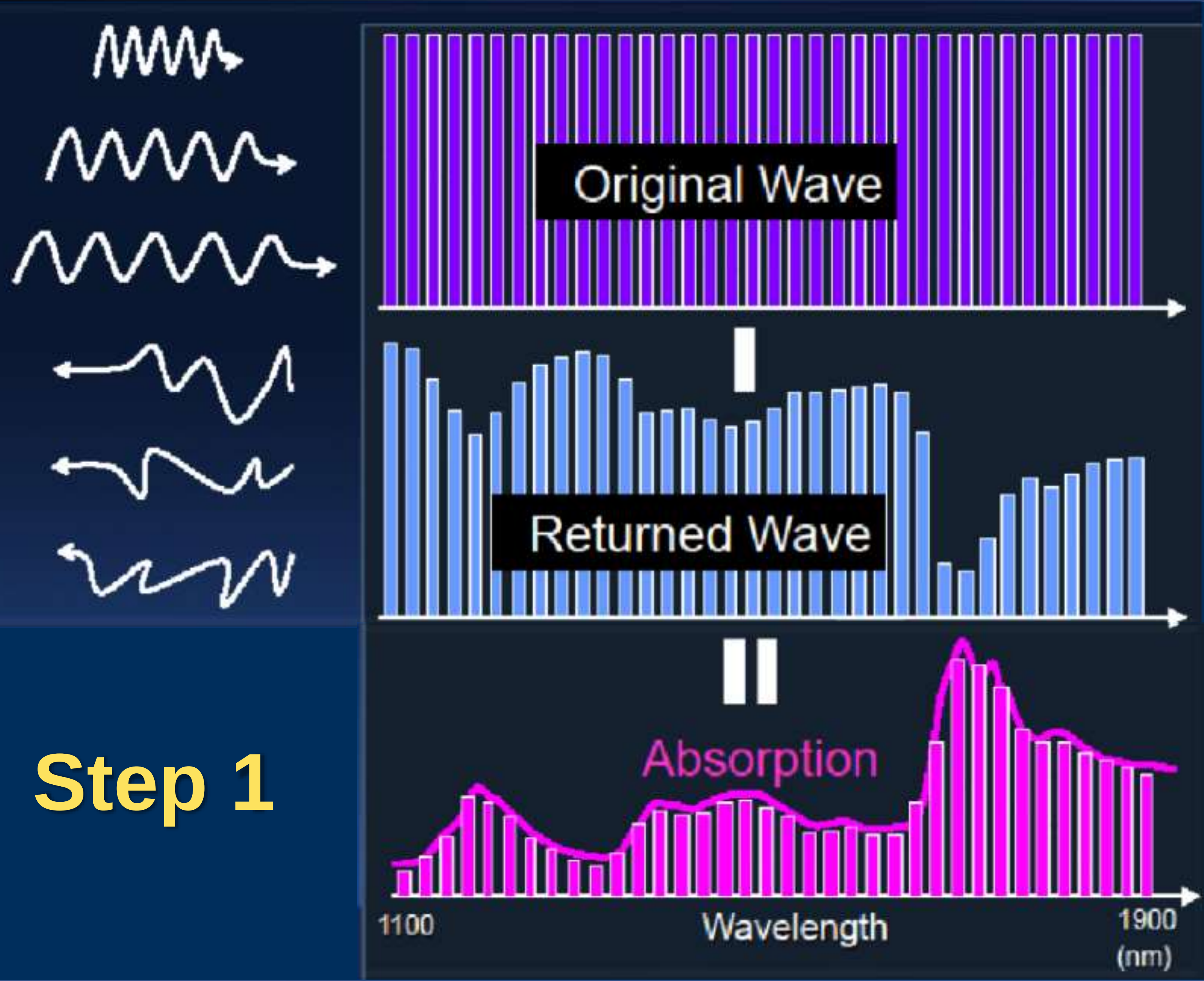
Near-infrared Spectroscopy

Near-infrared Spectroscopy



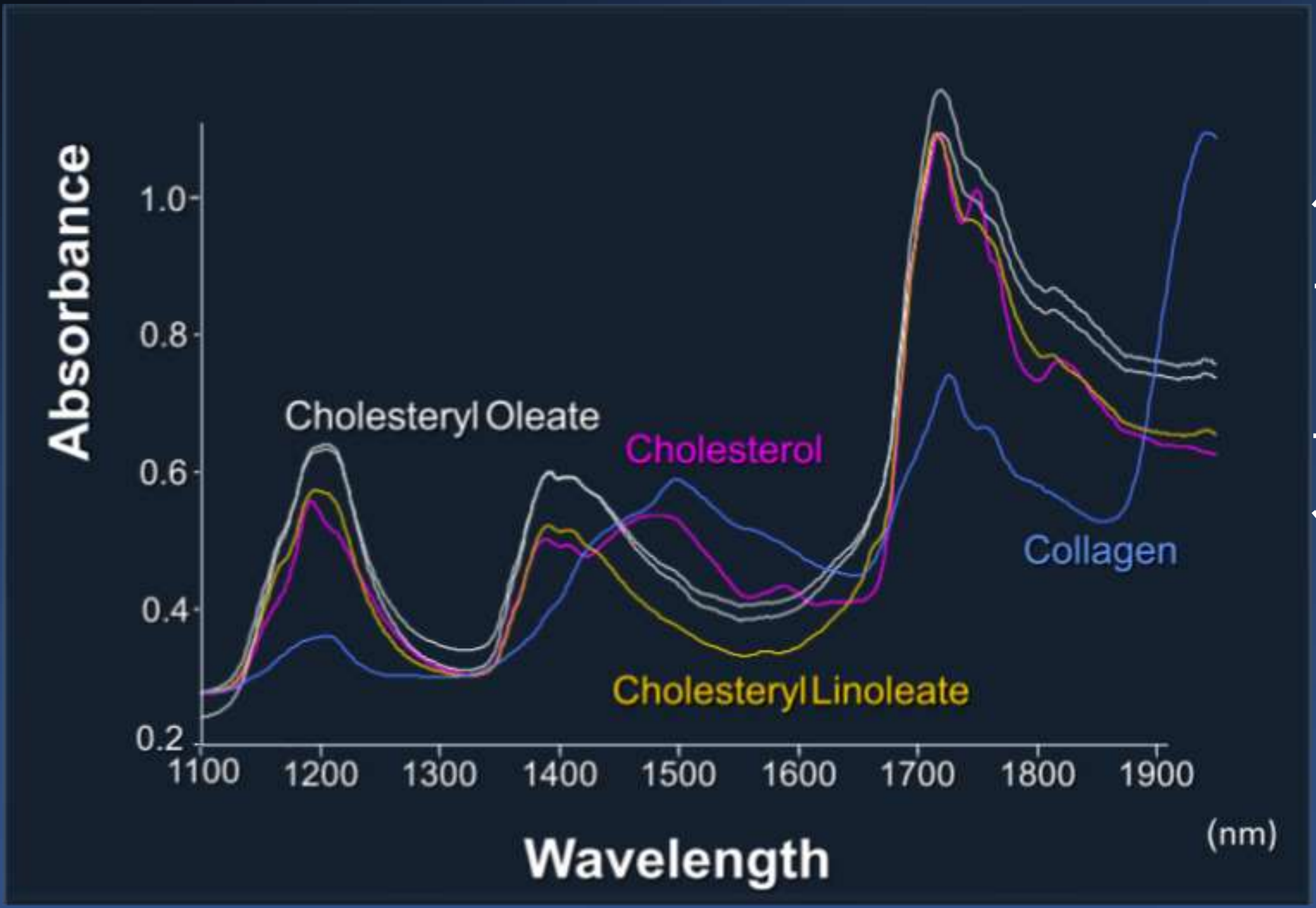
Process of NIR Spectroscopy



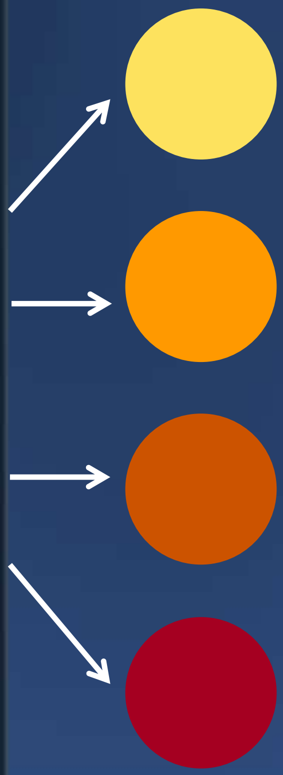

Original Wave
Returned Wave
Absorption
1100
Wavelength
1900
(nm)

Step 1

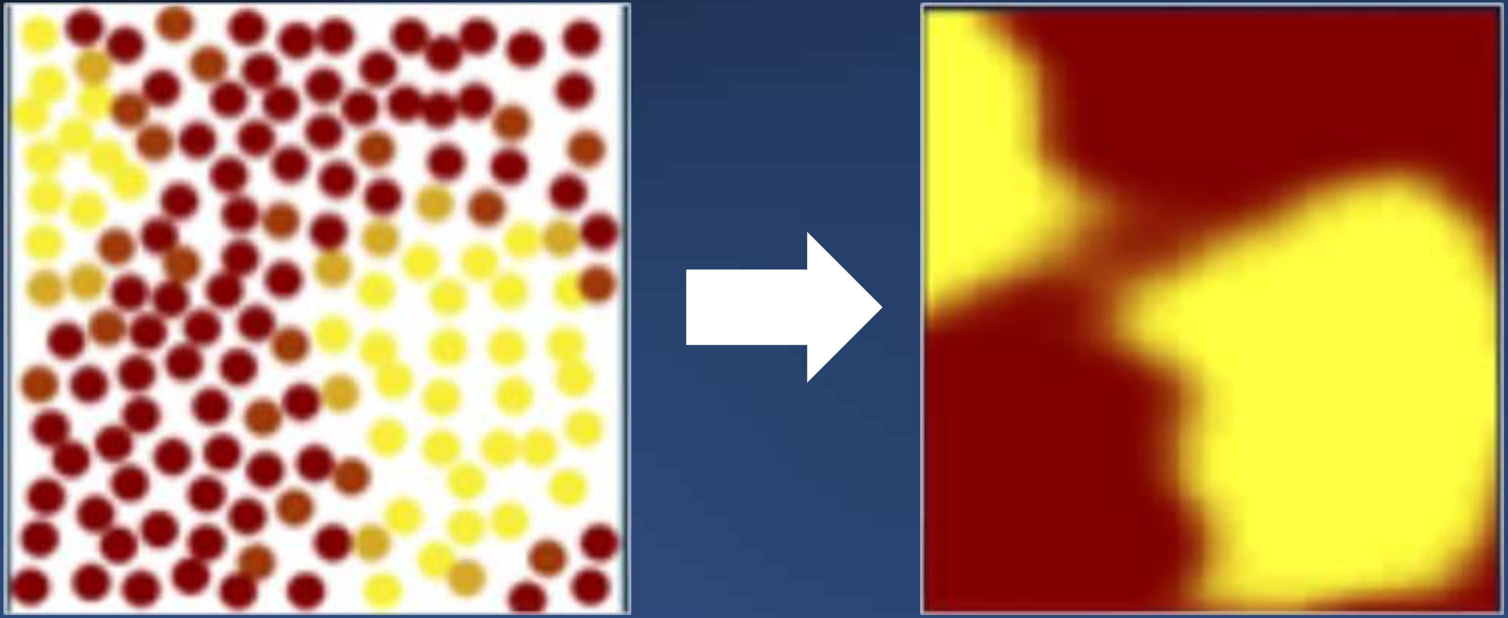
Step 2



Absorbance
1.0
0.8
0.6
0.4
0.2
Cholesteryl Oleate
Cholesterol
Collagen
Cholesteryl Linoleate
1100
1200
1300
1400
1500
1600
1700
1800
1900
(nm)
Wavelength



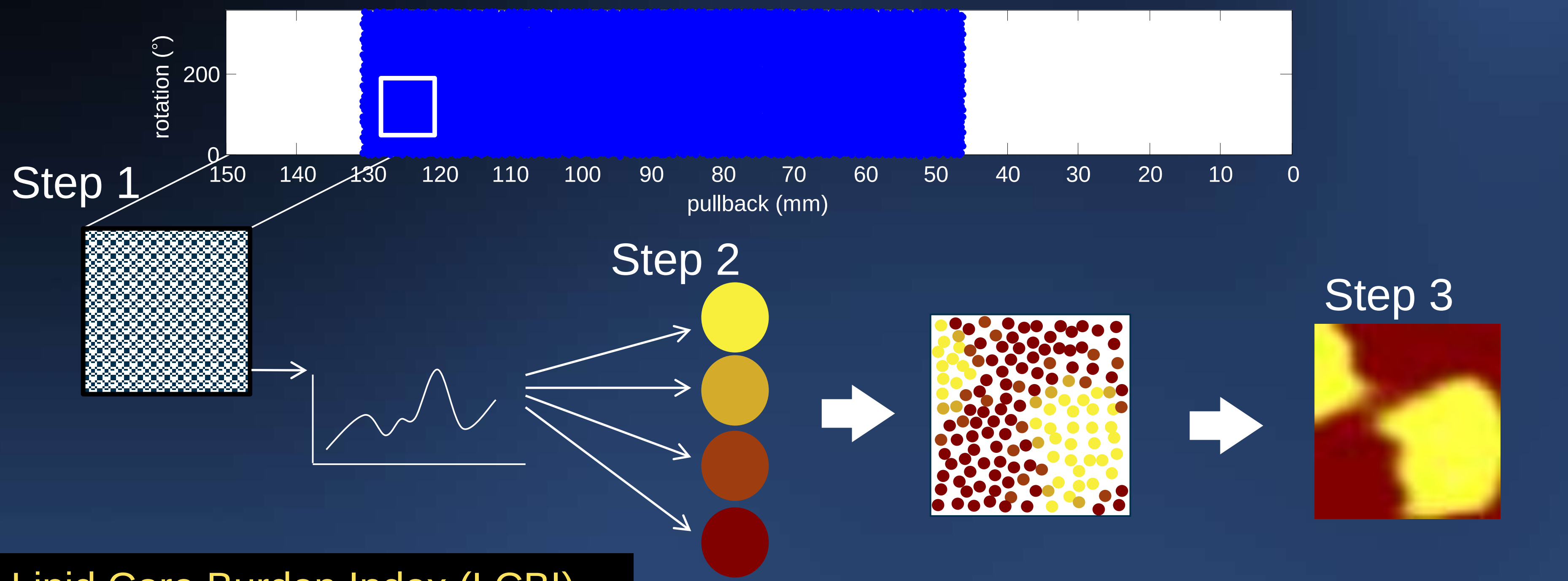
Step 3



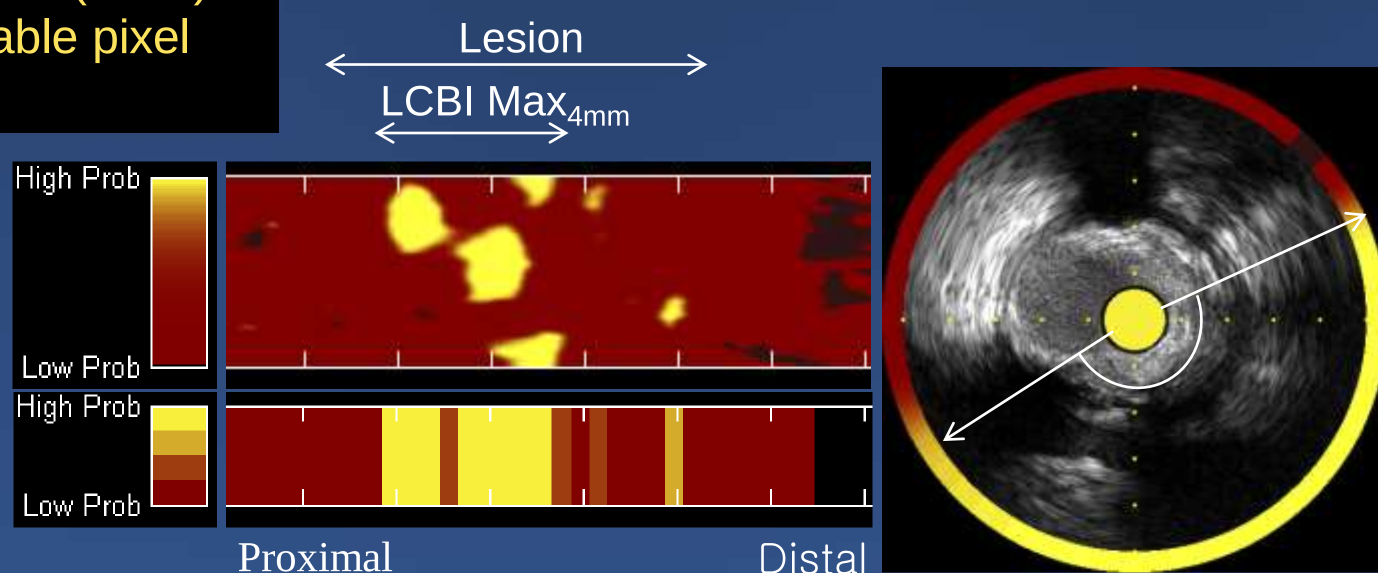
Lipid Core Burden Index (LCBI)

= Yellow pixel / All variable pixel x 1000

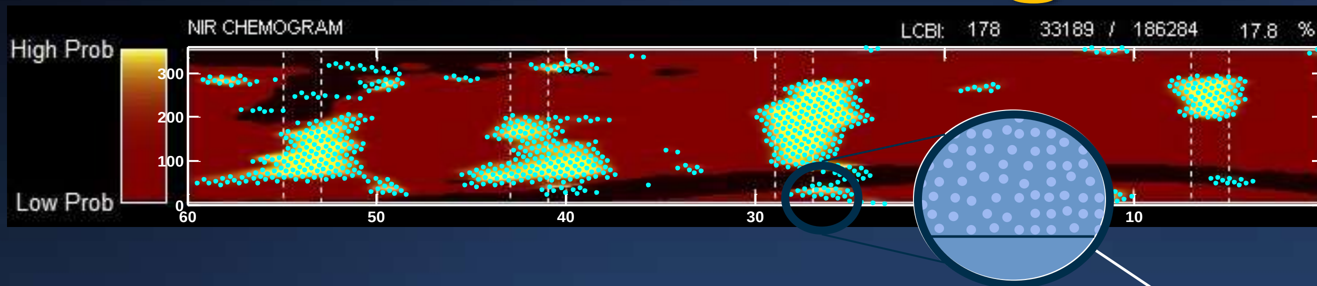
Near Infrared Spectroscopy



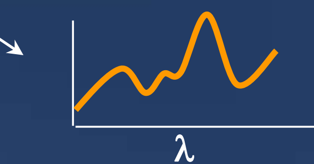
Lipid Core Burden Index (LCBI)
=Yellow pixel /All variable pixel
×1000



Formation of the Cap Thickness Prediction Image

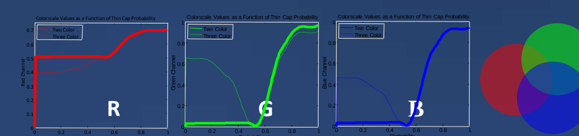


Spectra acquired at discrete pullback and rotation positions

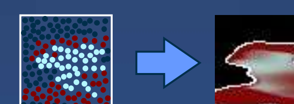


LCP Spectra transformed into posterior probability of thin cap presence

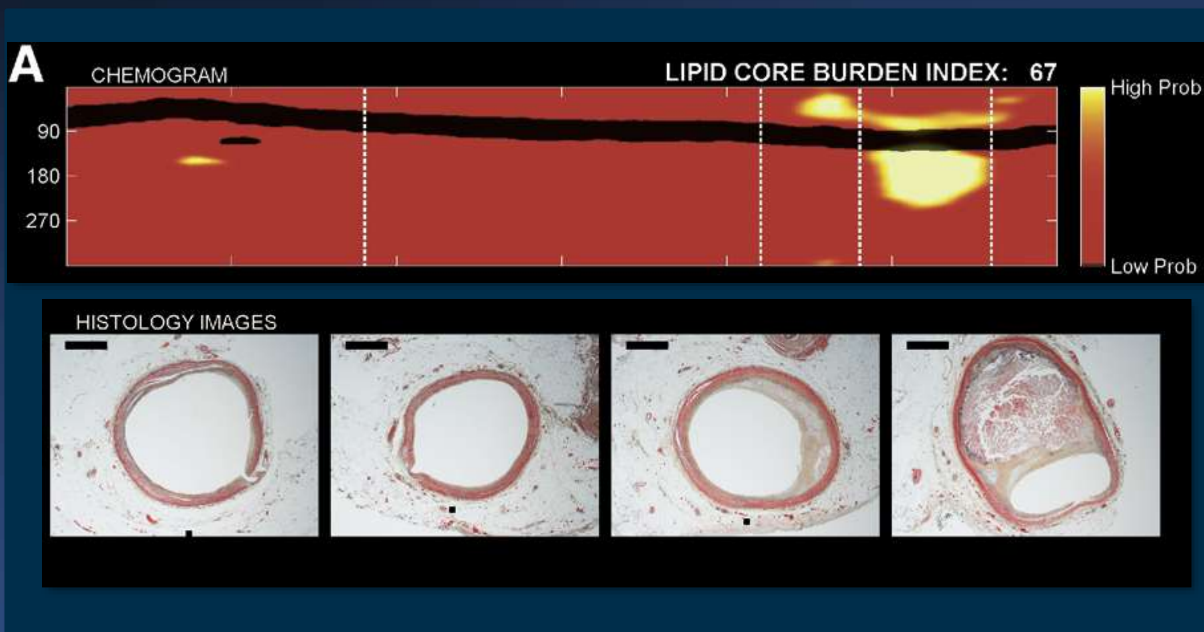
Probability mapped to a color



Pixels formed into an image



Quantification with Lipid Core Burden Index



LCBI = Lipid Core Burden Index (% yellow pixels of ROI x 10)

maxLCBI = the 4 mm segment with highest lipid content

Chemogram Color	Indication
Red	Low probability of LCP
Yellow	High probability of LCP
Black overlay	Indeterminate

Possible causes:
- Guide wire
- Thrombus
- Flow disturbance

Combination NIRS-IVUS Instrument

TVC Imaging System™

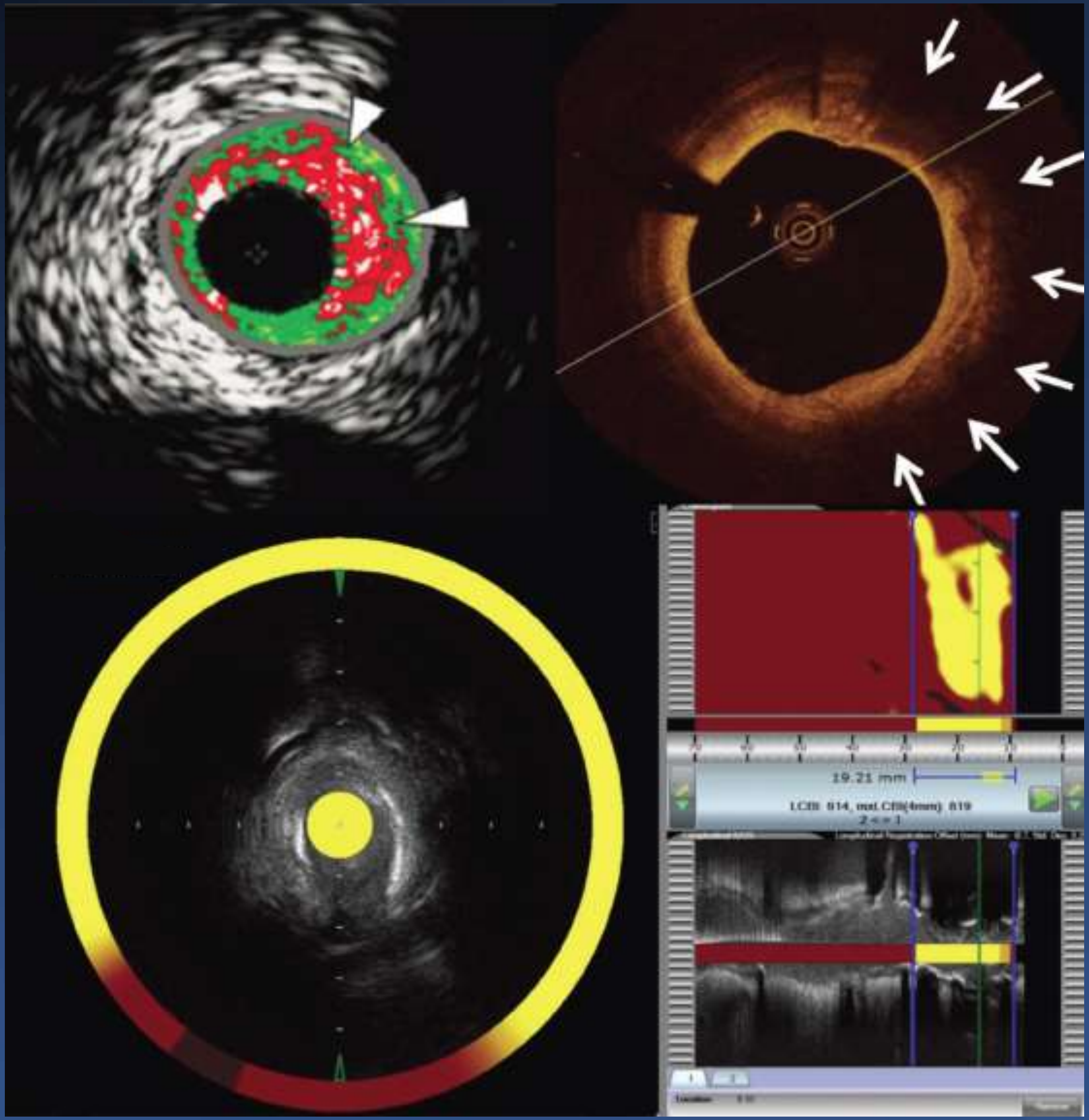
- Laser
- Dual monitors, touchscreen interfac
- Pull-back and rotation device

TVC Insight™ Catheter

- Single use, 3.2 Fr
- Dual modality
  - Spectroscopy detects lipid core plaqu
  - IVUS detects vessel structure

Lipid Core Plaque Imaging

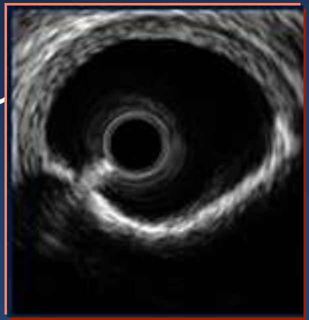
VH-IVUS vs. OCT vs. NIRS-IVUS



Fuh et al JIC Supplement 2013

Different type of Calcified Plaque

Necrotic core
Behind Calciu

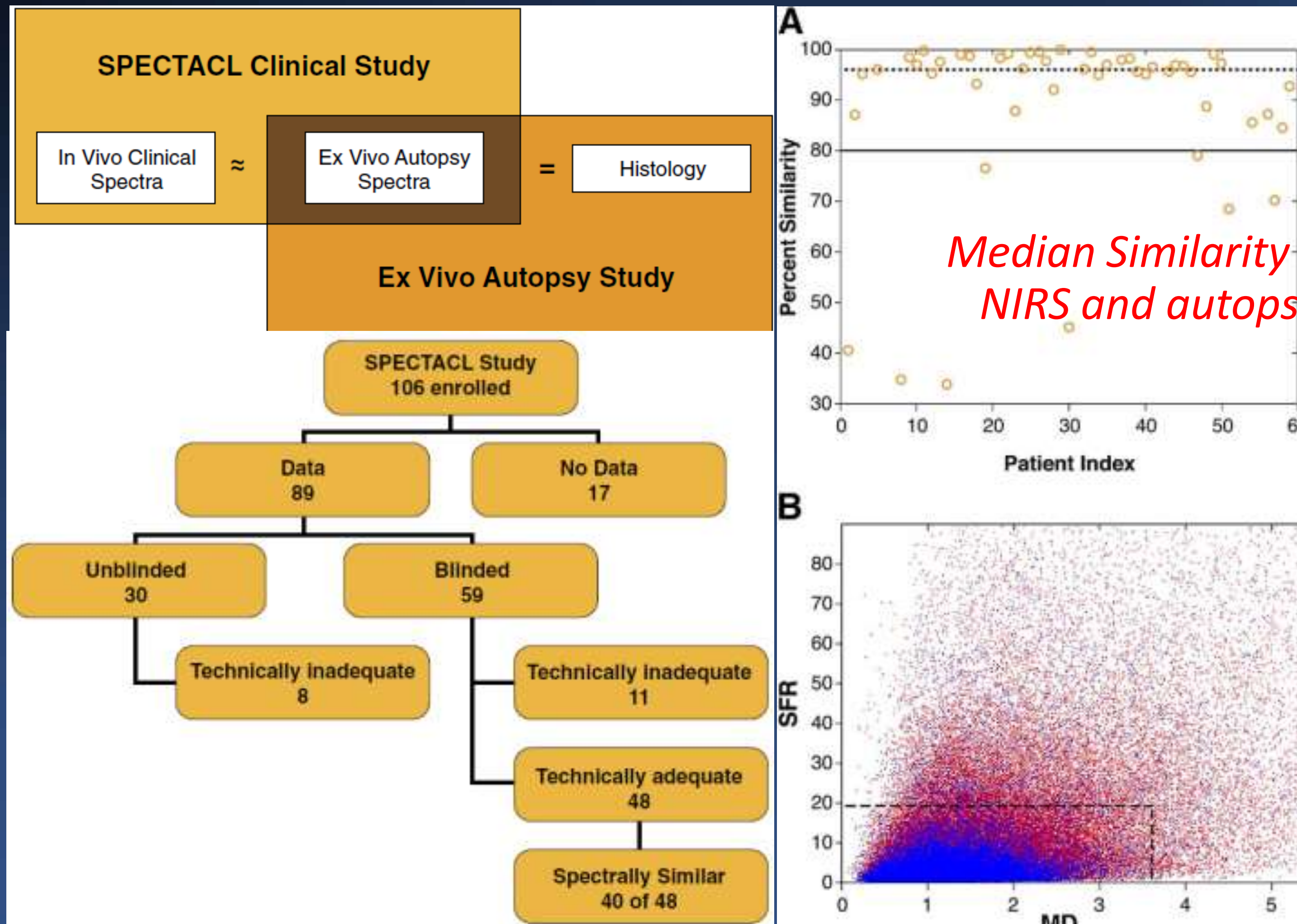


Calcium only



SPECTACL Study

In vivo Validation of NIRS for Detection of Lipid Core Coronary Plaques



Median Similarity between NIRS and autopsy : 96%

Sergio et al. *J Am Coll Cardiol Img,* 2009

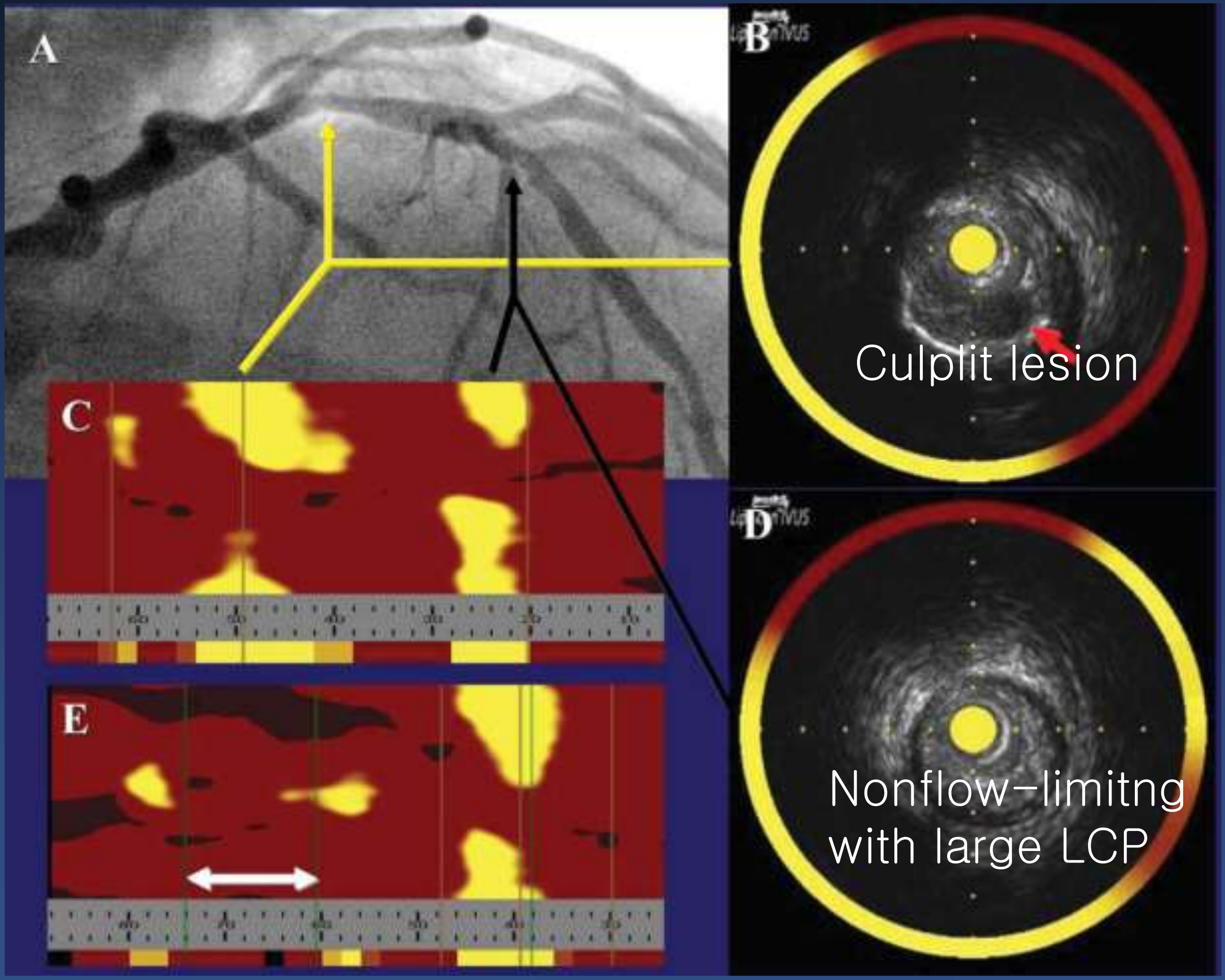
The Applications of NIRS-IVUS

- Identifying lesions possessing both architectural features and compositional data characteristic of vulnerable plaques
- Identifying large volume lipid-core plaque (LCP), which may be at greater risk for distal embolization during PCI
- Using IVUS to determine the length of vessel having significant plaque burden and delineating by NIRS the extent of the plaque burden occupied by LCP, data which may influence stent length selection
- Localizing nonculprit lesions with morphologic and compositional characteristics of "vulnerable plaque"
- Analyzing plaque composition in heavily calcified segments, a setting in which other imaging modalities have limited utility

RD Madder et al. Catheterization and Cardiovascular Interventions, 2013

The Applications of NIRS-IVUS

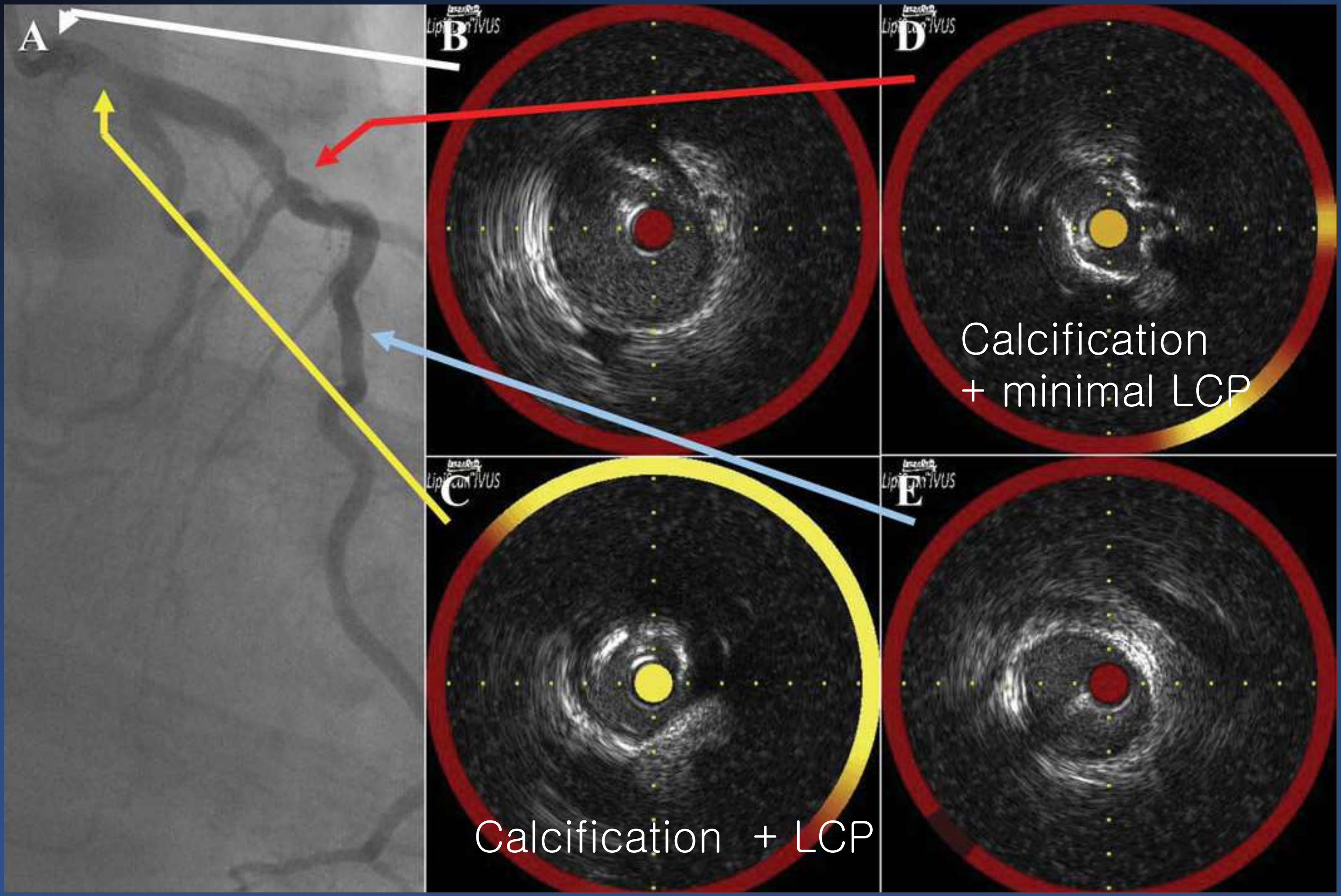
Detection of Potentially Vulnerable Nonflow-Limiting Plaque



RD Madder et al. Catheterization and Cardiovascular Interventions, 2013

The Applications of NIRS-IVUS

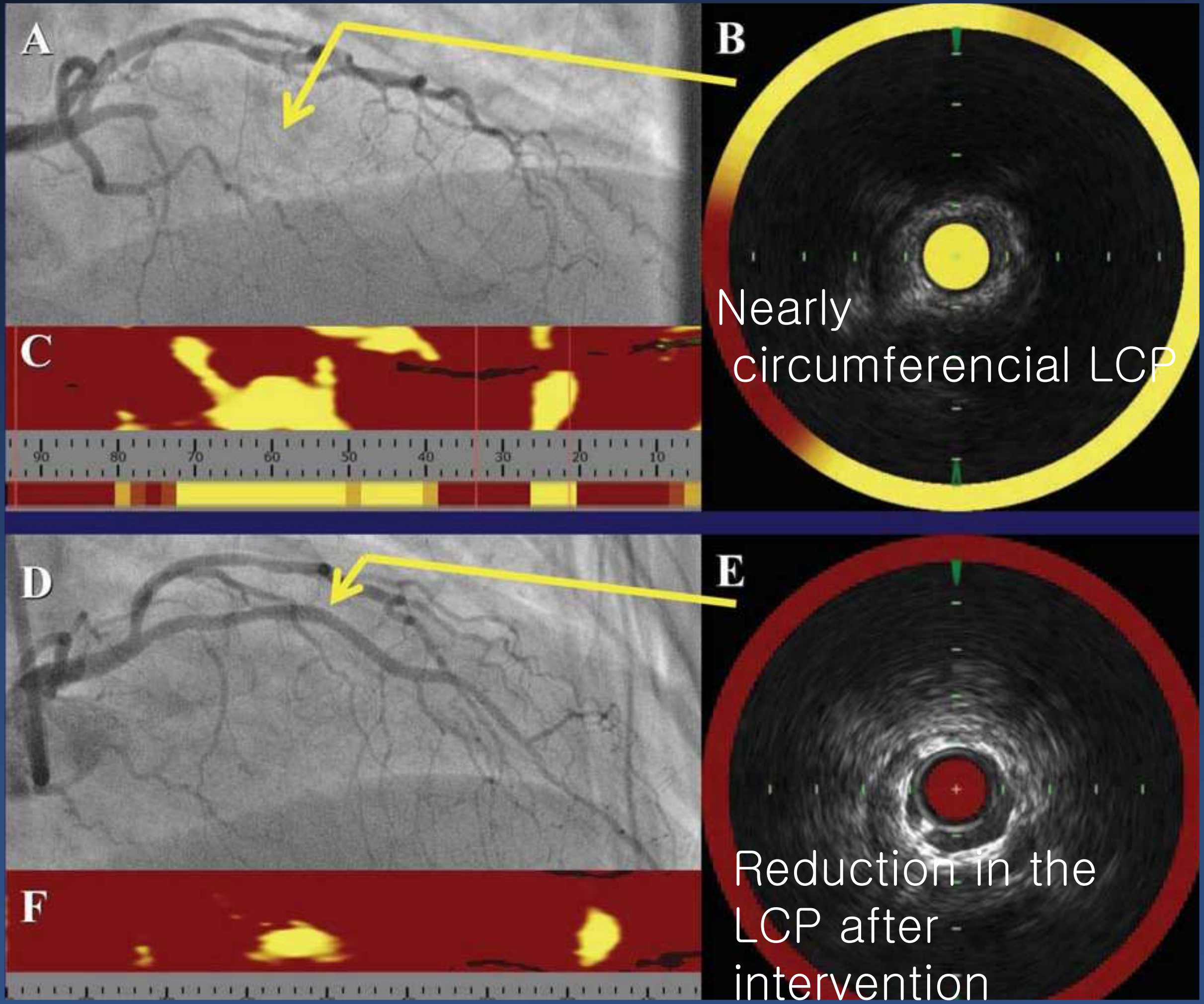
Detection of LCP despite Extensive Calcification



RD Madder et al. Catheterization and Cardiovascular Interventions, 2013

The Applications of NIRS-IVUS

Characterization of a Lesion Causing Chronic Total Occlusion

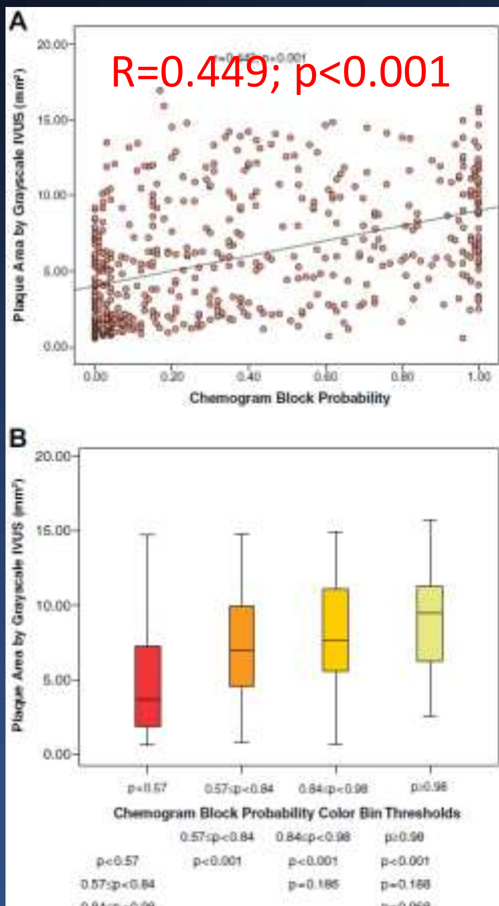


RD Madder et al. Catheterization and Cardiovascular Interventions, 2013

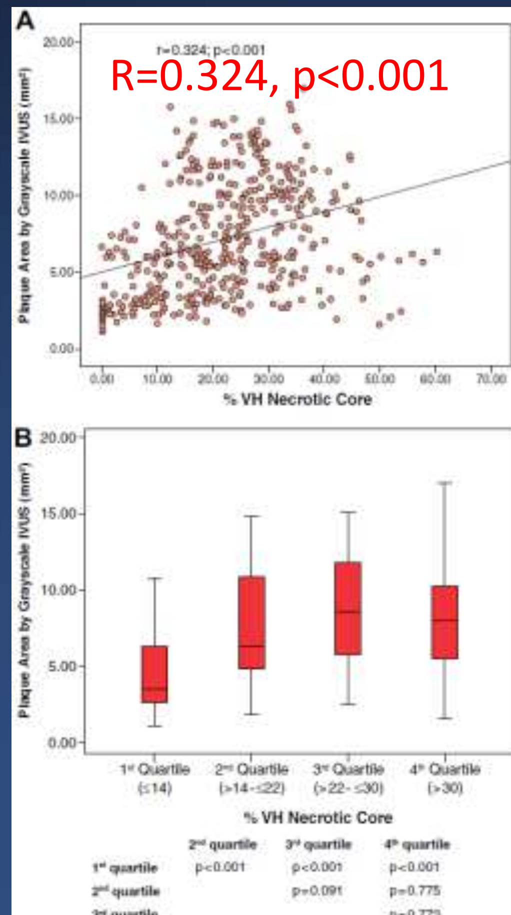
Characterization of Atherosclerosis

correlation among IVUS,NIRS and VH-NC

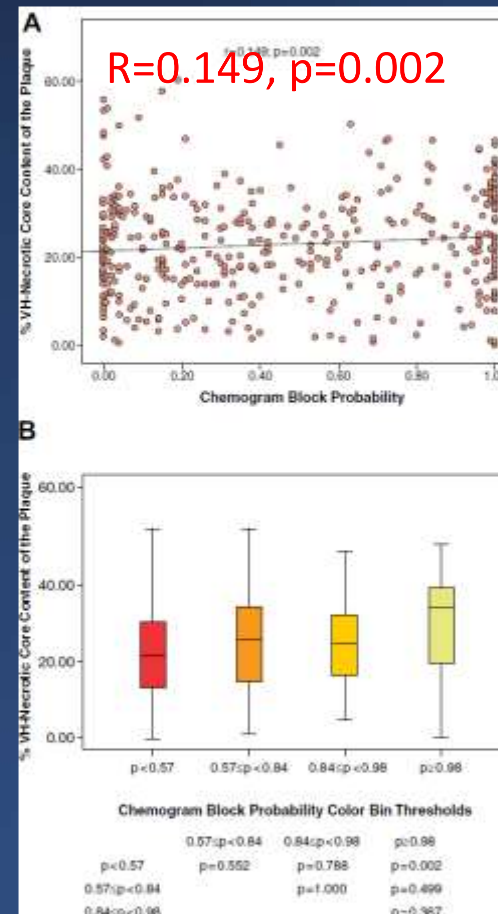
IVUS and NIRS



IVUS and VH-NC



NIRS and VH-NC



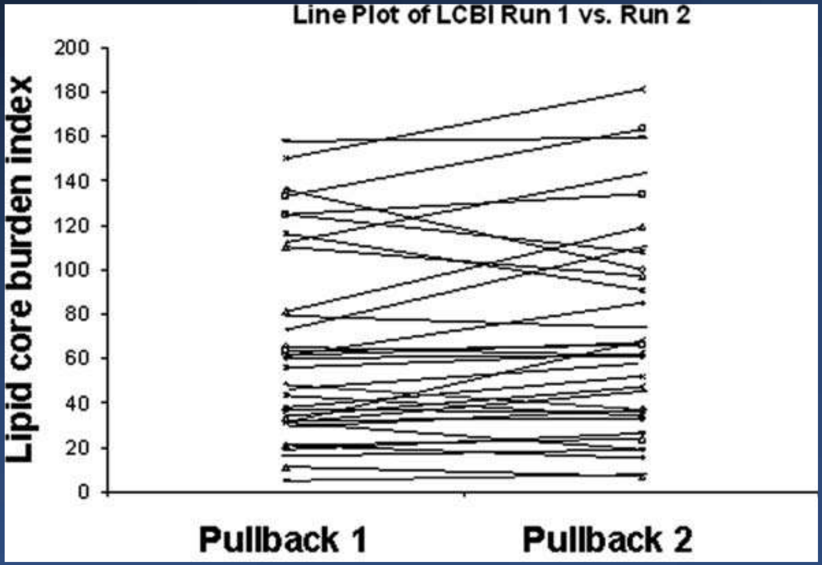
**31 patients with a common region of interest between 2 side branches*

**IVUS : graysclae plaque area *NIRS : chemogram block *VH-NC : necrotic core percentage*

Brugaletta et al. JACC: Cardiovascular Imaging, 2011

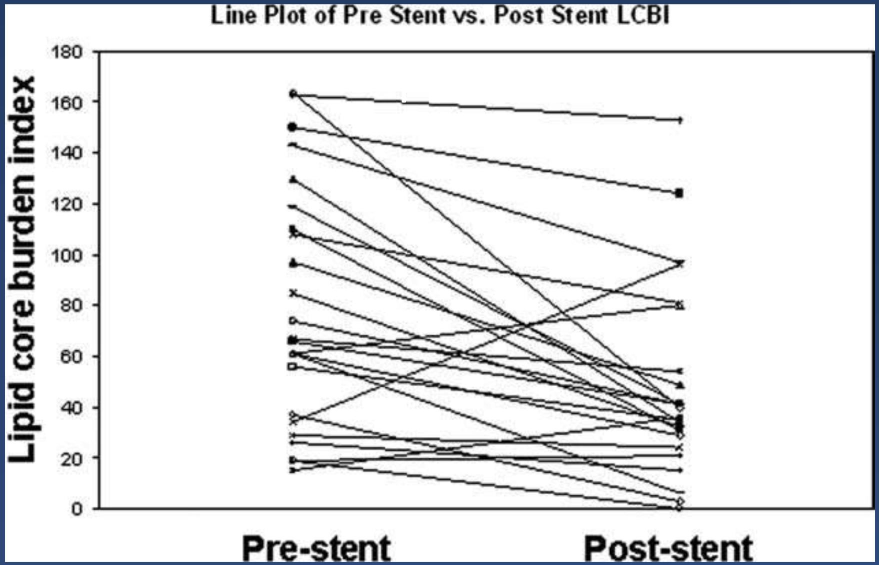
Reproducibility of NIRS

Automated pullback catheter performed in duplicate in 36 vessels in 31 patients



Excellent correlation

The changes in LCBI after stenting in 25 vessels in 22 patients

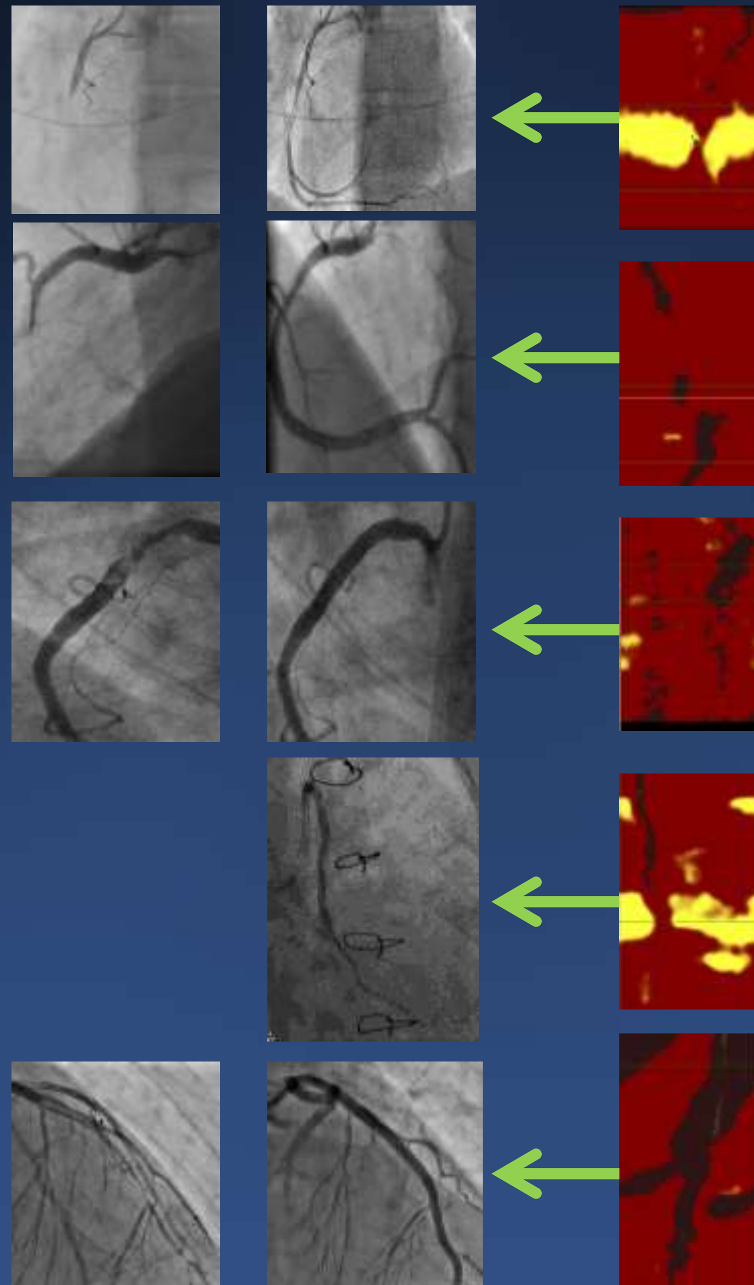


The mean LCBI decreased by 40%

BA Garcia et al. Catheterization and Cardiovascular Interventions, 2010

Five Different STEMIs

NIRS-IVUS Reveals Five Different Causes



Lipid Core Plaque

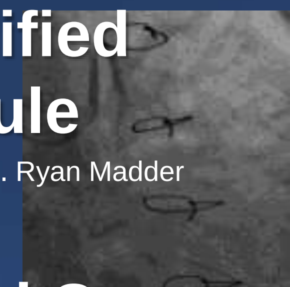
Courtesy Dr. Ryan Madder

Stent Thrombosis

Courtesy Dr. David Erlinge

Calcified Nodule

Courtesy Dr. Ryan Madder



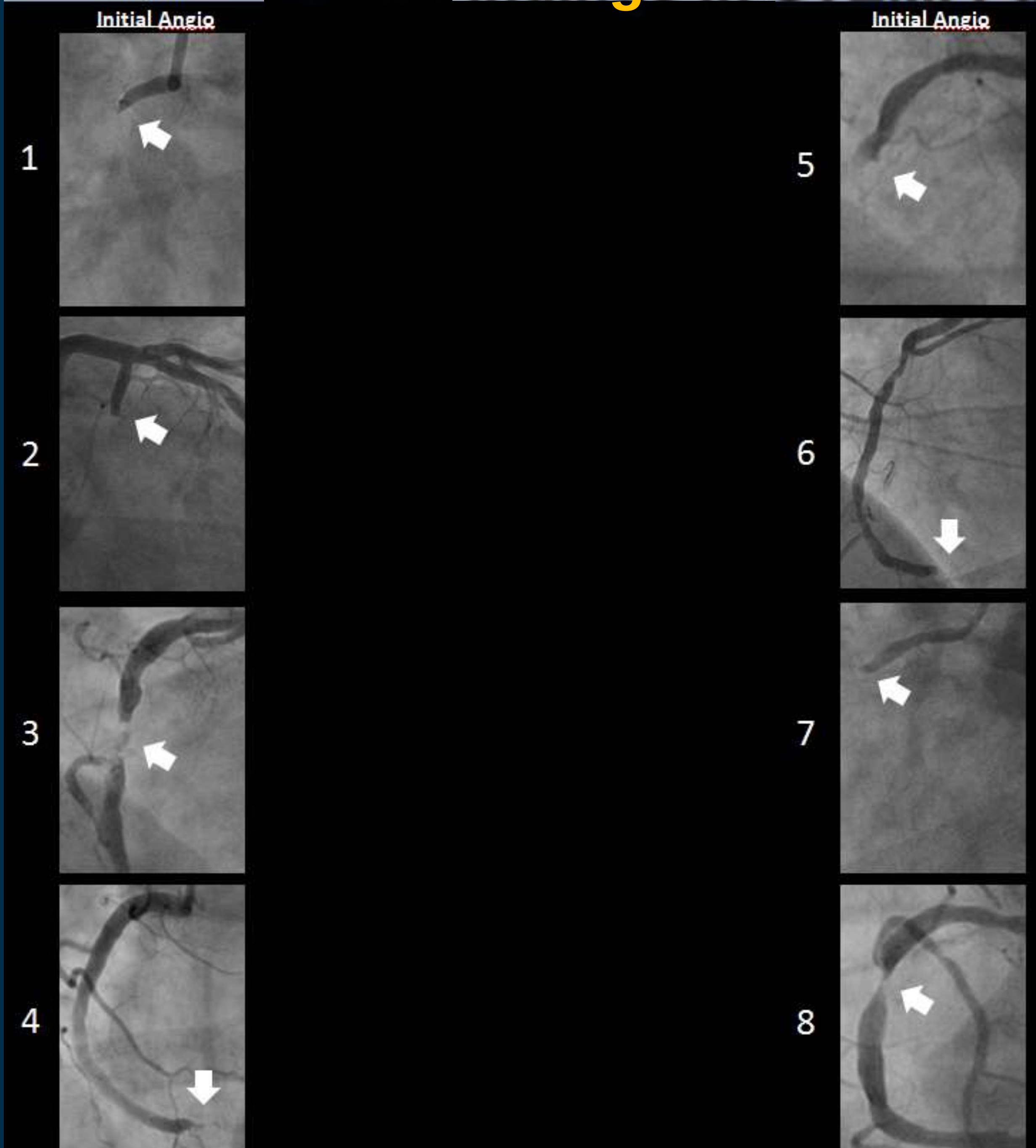
Lipid Core In SVG

Courtesy Dr. David Erlinge

Dissection

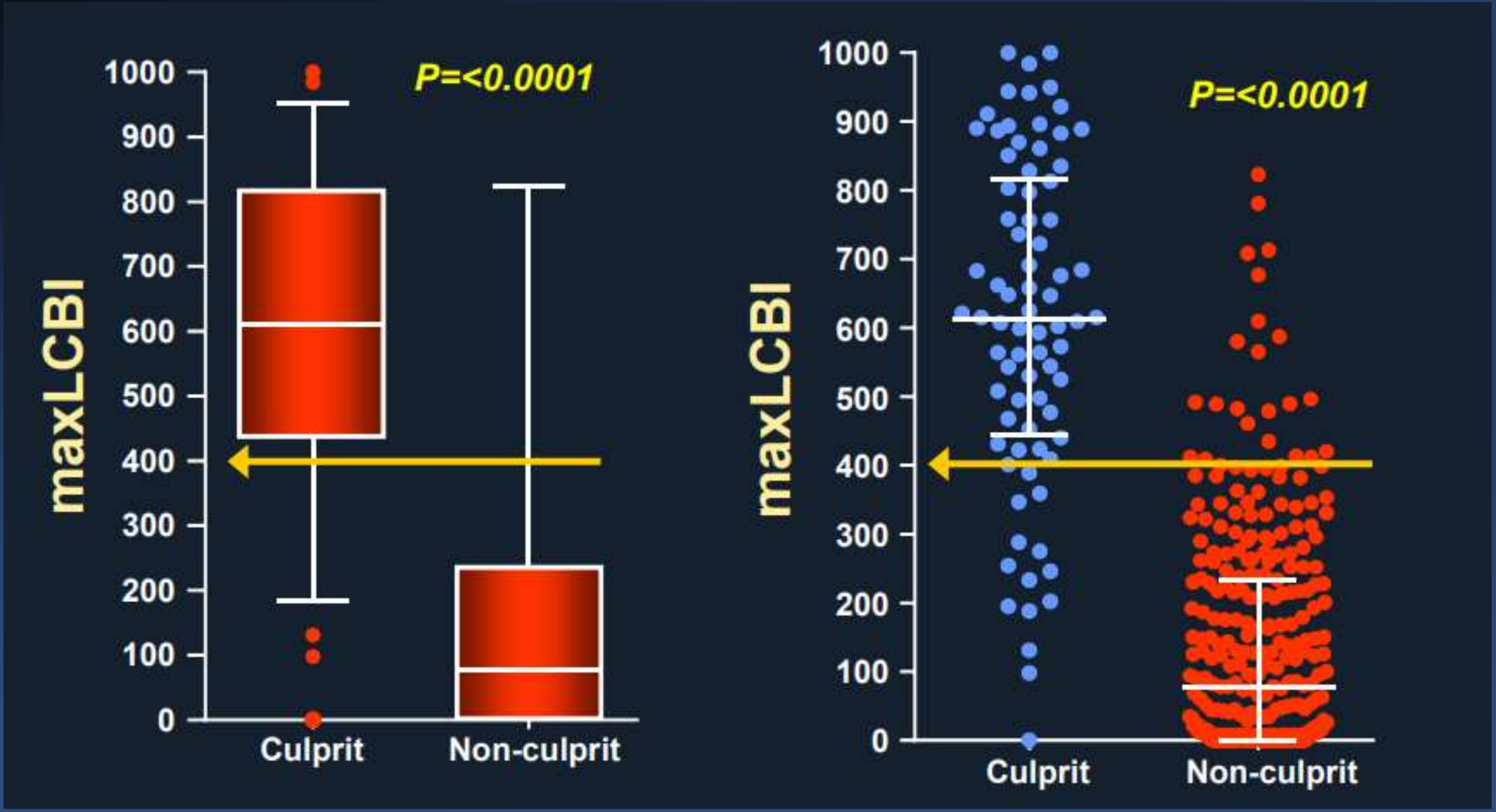
Courtesy Dr. David Erlinge

NIRS Findings in STEMI Patients



Culprit vs. non-culprit in STEMI

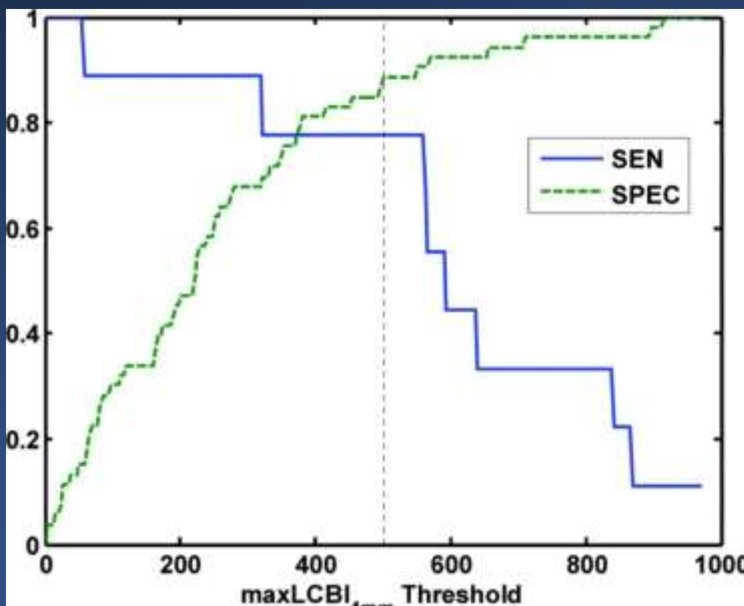
The characteristic of NIRS

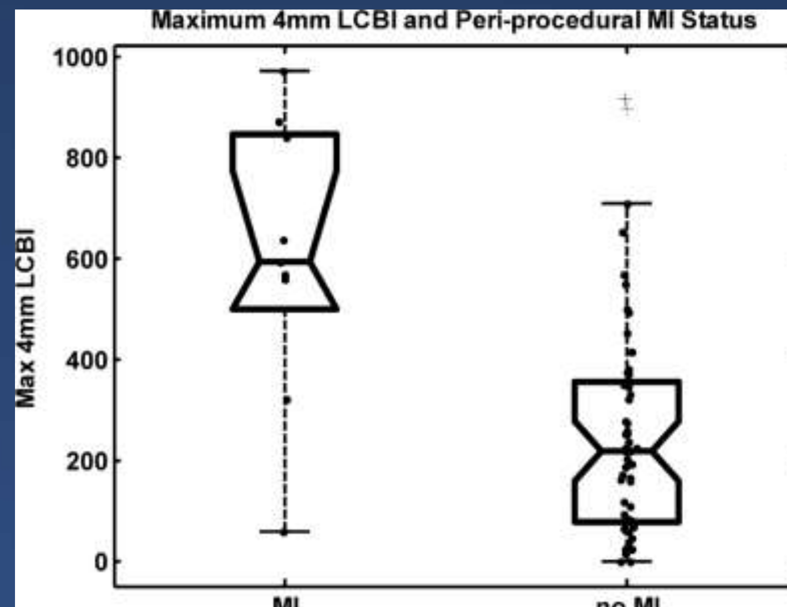


Erlinge D et al. ICI 2013

Lipidic Plaque detected by NIRS and Periprocedural MI

Parameter*	Threshold†	Relative risk of peri-procedural MI (95% CI)	p‡
		0 10 20 30 40 50	
$maxLCBI_{4mm}$	≥500	12 (3.3 to 48)	0.0002
LDL – mg/dL	>100	5.4 (1.4 to 23)	0.03§
Complex Plaque	Y	3.5 (0.91 to 14)	0.15
Degree Stenosis – %	>75	3.1 (0.92 to 11)	0.14**





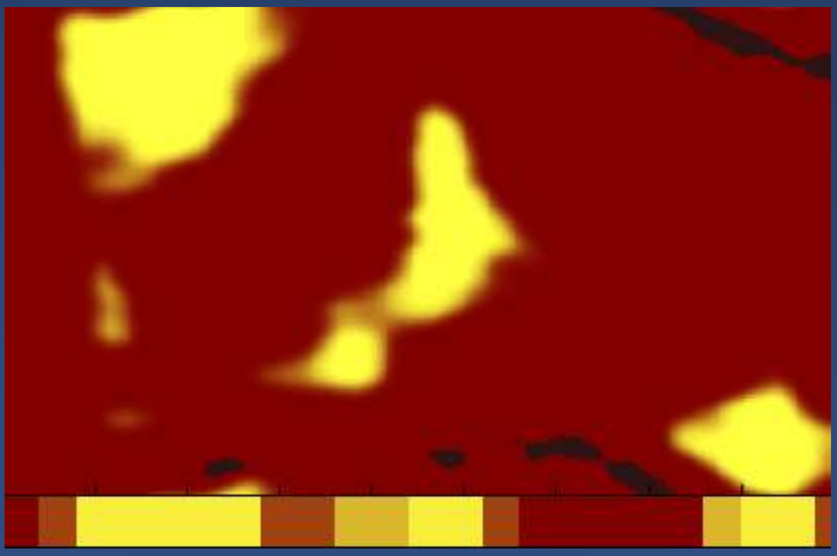
LCBI > 500 associated with 50% risk of periprocedural MI (95% CI, 28–62)

Goldstein, JA, et al. Circulation: Cardiovascular Interventions. 2011; 4: 429-437

Relationship between Lipidic Plaque detected by NIRS and Outcomes

- Prospective Single Center Study, 206 patients (ACS 47%)
- Primary Endpoint: Composite of all-cause mortality, non-fatal ACS, stroke and unplanned PCI during one-year FU
- >40mm non culprit segment of NIRS

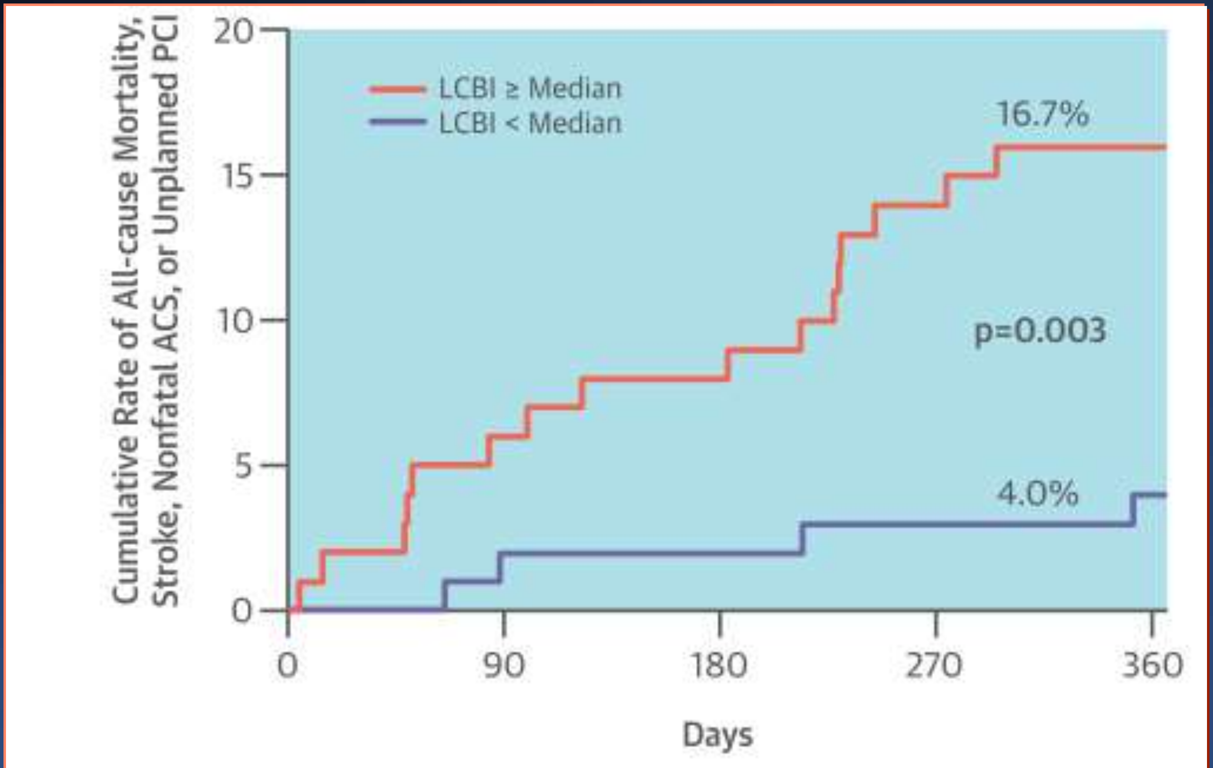
Lipid Core Burden Index (LCBI)=188



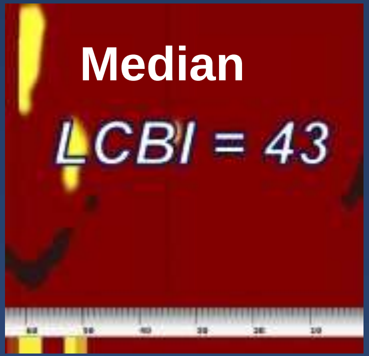
45mm

Oemrawsingh RM et al, ESC2003

Relationship between Lipidic Plaque detected by NIRS and Outcomes



No. at Risk					
LCBI < Median	101	99	99	97	91
LCBI ≥ Median	102	94	92	86	83

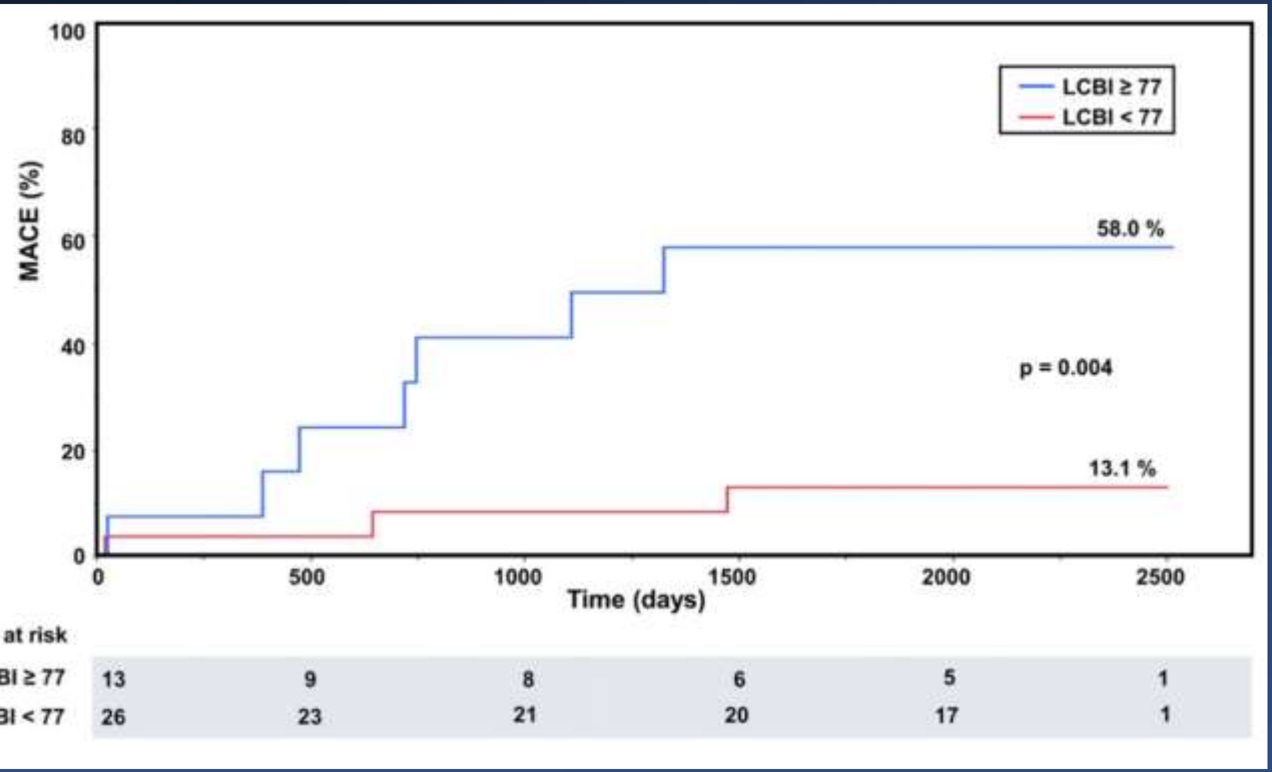


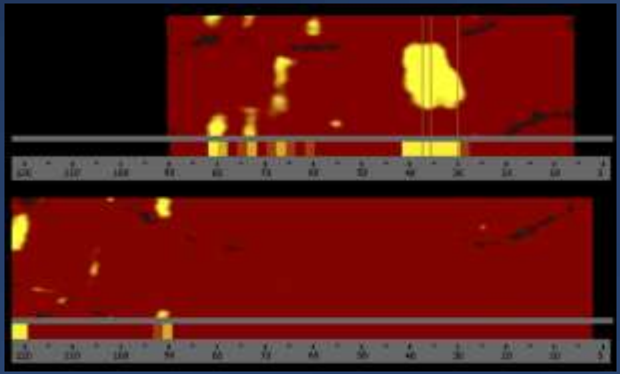
Adjusted HR 4.04 95% CI:1.3-12.3 p=0.01

Oemrawsingh RM et al, JACC 2014;64:2510-8

Relationship between Lipidic Plaque detected by NIRS and Outcomes

ORACLE-NIRS registry





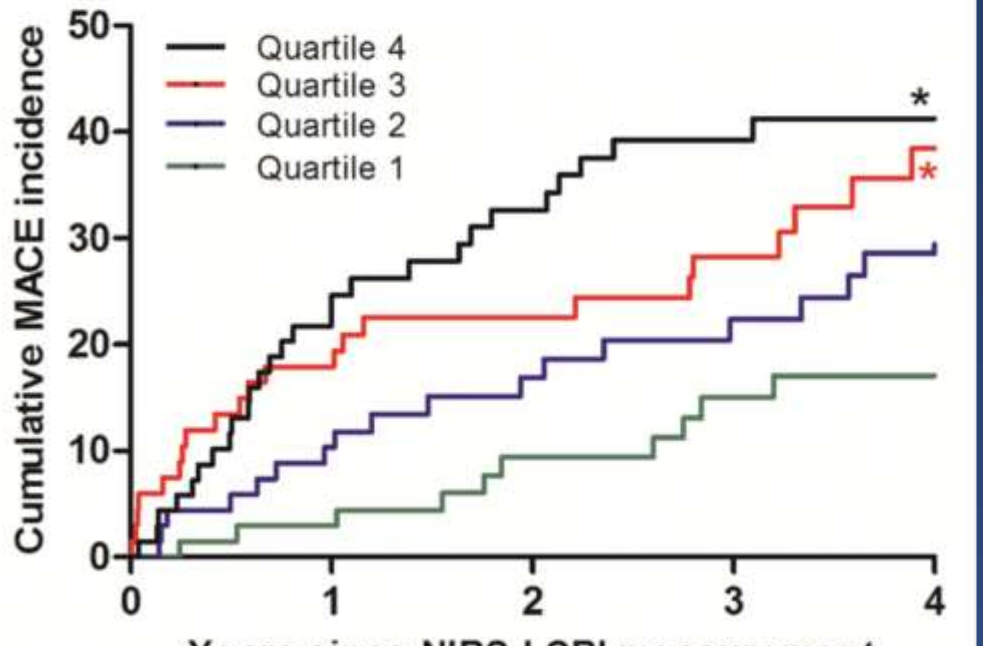
Danek BA et al. Cardiovasc Revasc Med. 2017 Apr - May;18(3):177-181

Relationship between Lipidic Plaque detected by NIRS and Outcomes

ATHEROREMO-NIRS and IBIS-3-NIRS substudy

ATHEROREMO-NIRS
n= 203 (Apr 2009 – Jan 2011)
IBIS-3-NIRS
n= 131 (Jan 2010 – Jun 2013)

Diagnostic CAG or PCI for ACS and SAP
Median follow-up : 4.1 yrs



No. at risk	0	1	2	3	4
LCBI Q1(<83.0)	68	66	52	43	29
LCBI Q2 (≥83.0-227.0)	68	61	47	40	31
LCBI Q3 (≥227.0-360.0)	67	55	42	35	22
LCBI Q4 (≥360.0)	70	53	41	30	25

*p<0.01 as compared to first quartile (reference).

Schumann et al Eur Heart J. 2018 Jan 21;39(4):295-302.

Capabilities of Coronary Imaging Techniques

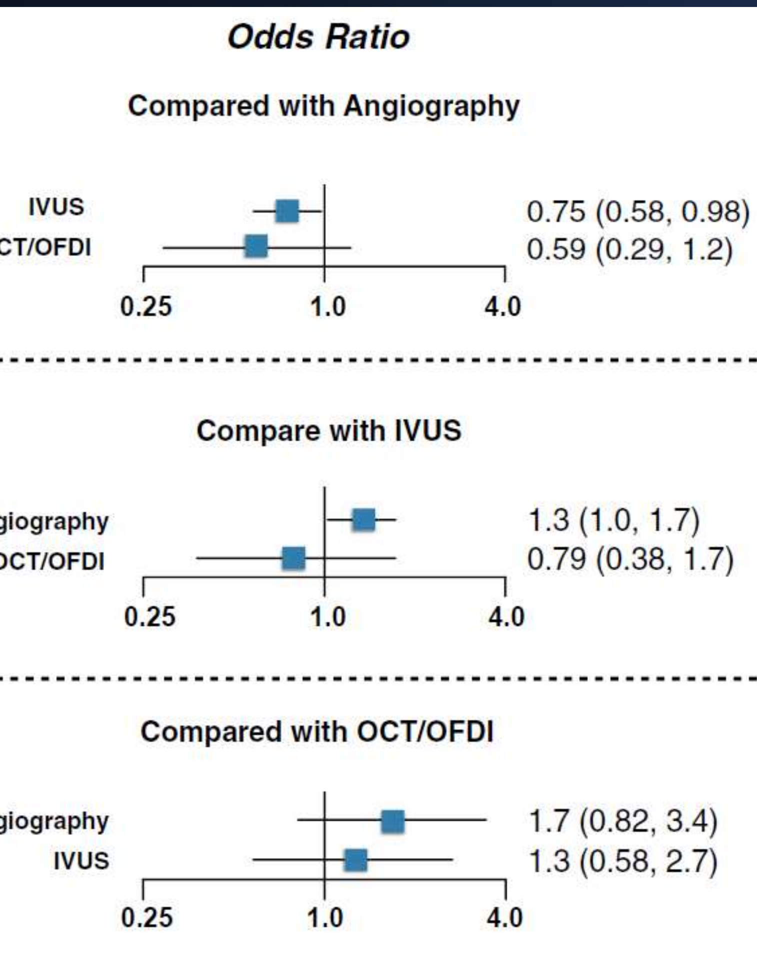
	CAG	Angioscopy*	OCT*	IVUS	NIRS
Lipid Core		○	○	○	●
Expansive Remodeling				●	
Plaque Burden				●	
Calcification	○		○	●	
Lumen Dimension	○		●	●	
Stent Apposition/Expansion	○		●	●	
Thin Cap		○	●	○	○
Thrombus	○	●	●	○	○

● Direct, robust, and/or validated
○ Indirect, inferred from signal dropout, debated and/or unvalidated

** Require blood-free field of view*

Angio vs. IVUS vs. OCT/OFDI
Meta analysis

All cause mortality



	Angiography	IVUS	OCT/OFDI
MACE			
Angiography	-	0.79 (0.67-0.91)	0.68 (0.49-0.97)
IVUS	1.30 (1.10-1.50)	-	0.87 (0.61-1.30)
OCT/OFDI	1.50 (1.00-2.00)	1.10 (0.78-1.60)	-
Cardiovascular death			
Angiography	-	0.47 (0.32-0.66)	0.31 (0.13-0.66)
IVUS	2.10 (1.50-3.10)	-	0.66 (0.27-1.50)
OCT/OFDI	3.20 (1.50-7.60)	1.50 (0.66-3.70)	-
MI			
Angiography	-	0.74 (0.58-0.90)	0.66 (0.35-1.20)
IVUS	1.40 (1.10-1.90)	-	1.10 (0.60-2.10)
OCT/OFDI	1.30 (0.72-2.30)	0.90 (0.47-1.70)	-
TLR			
Angiography	-	0.74 (0.58-0.90)	0.66 (0.35-1.20)
IVUS	1.40 (1.10-1.70)	-	0.88 (0.47-1.60)
OCT/OFDI	1.50 (0.83-2.90)	1.10 (0.61-2.10)	-
Stent thrombosis			
Angiography	-	0.42 (0.20-0.72)	0.39 (0.10-1.20)
IVUS	2.40 (1.40-5.10)	-	0.93 (0.24-3.40)
OCT/OFDI	2.60 (0.80-10.0)	1.10 (0.29-4.20)	

ccheri et al.JACC: cardiovascular interventions vo