New Findings from COLOR Registry

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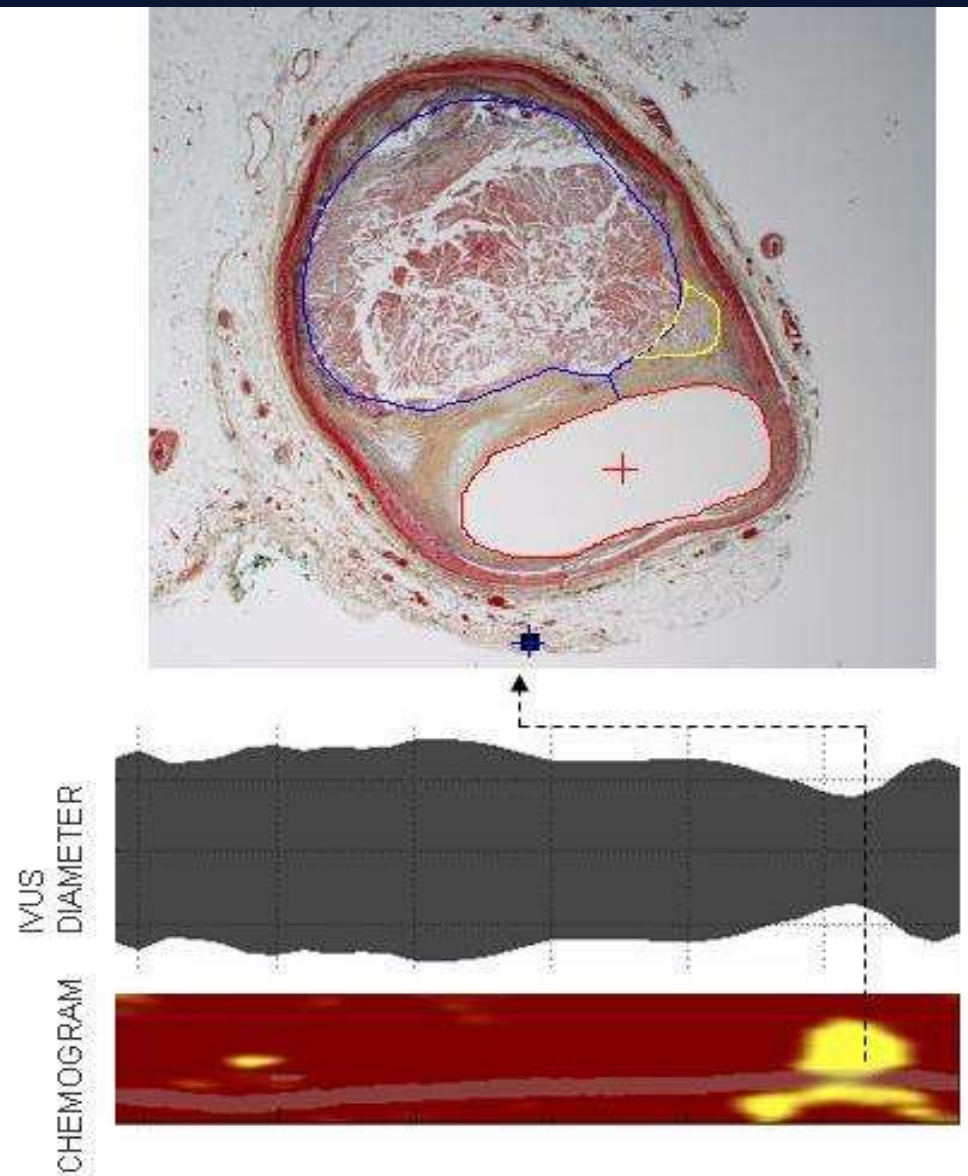
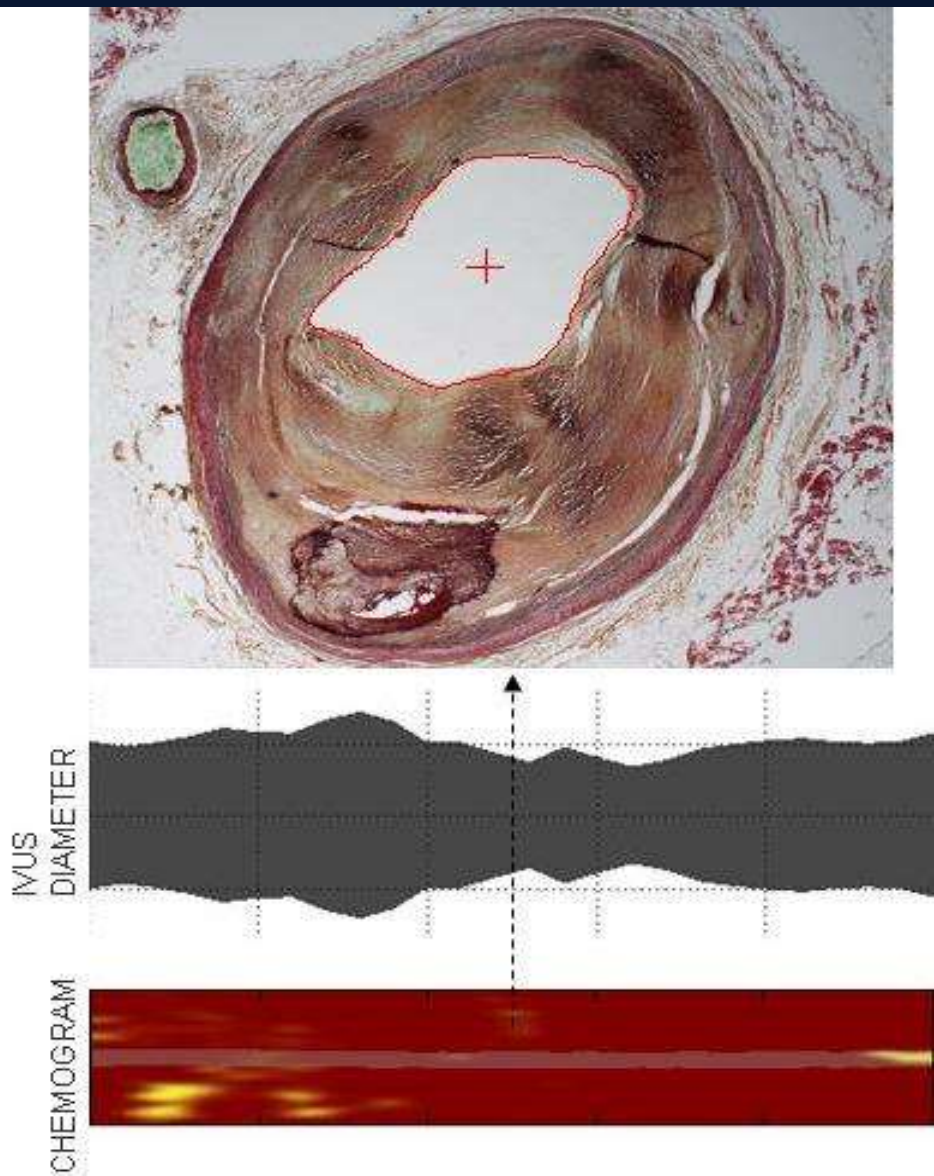
Conflict of Interest Disclosure

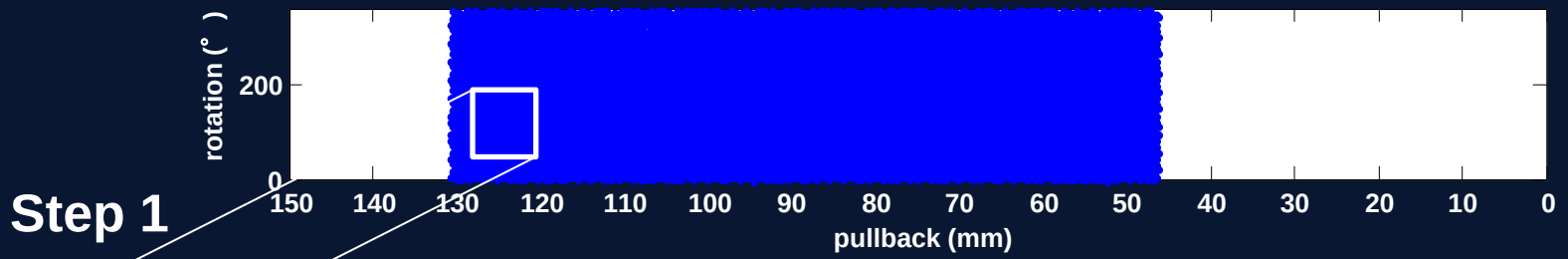
- Akiko Maehara
  - Personal: Consultant for Boston Scientific Corporation, Speaker fee: St Jude Medical
  - Cardiovascular Research Foundation: Boston Scientific Corporation

NIR can Distinguish Lipid-rich from Fibrotic Plaques

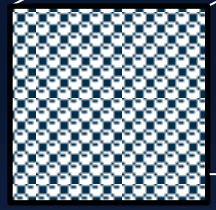




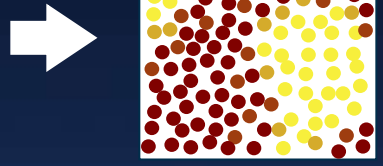
Near Infrared Spectroscopy



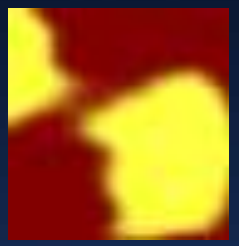
Step 1



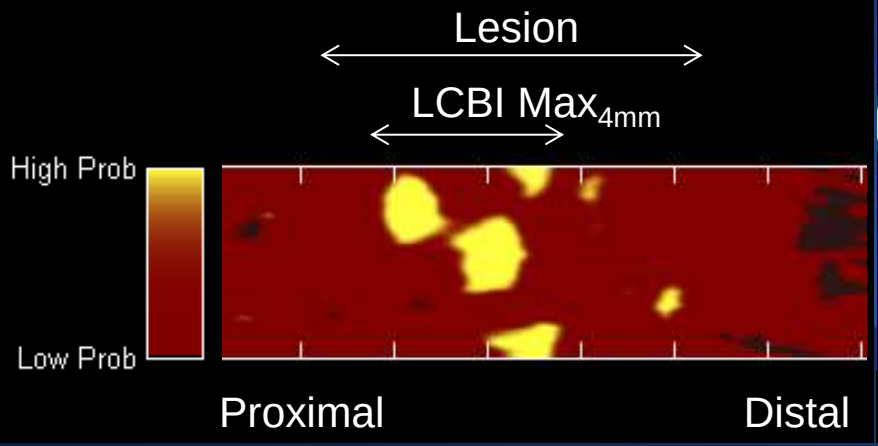
Step 2

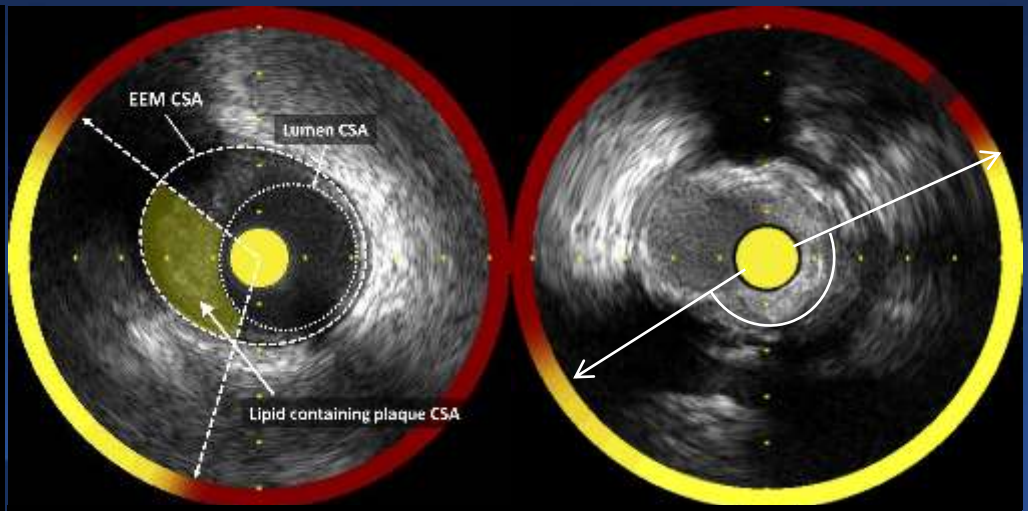


Step 3



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





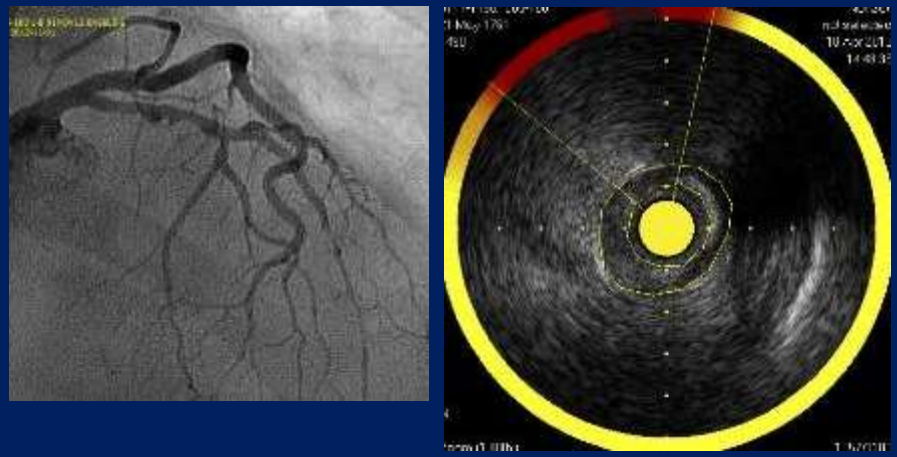
Lipid Rich Plaque (LRP) burden (%)

COLOR Enrollment

infraredx
Sound Insight Into Vascular Disease

Relationship between the extent of lipid-rich plaque and clinical presentation (n=800)

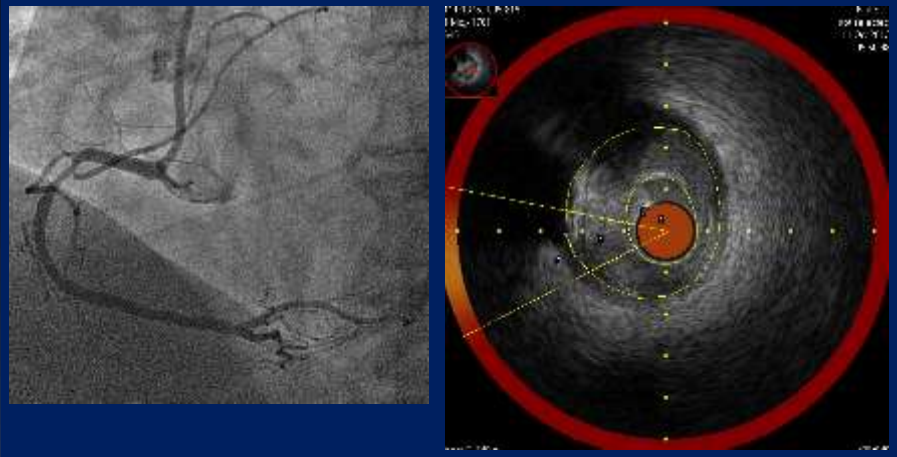
NSTEMI



Max $LCBI_{4mm}$ = 802

PB=72%, LRP burden = 60%

Stable IHD



Max $LCBI_{4mm}$ = 166

PB=76%, LRP burden = 17%

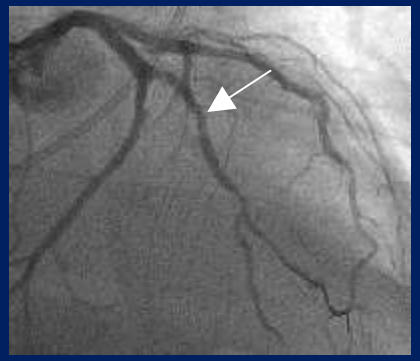
Relationship between the extent of lipid-rich plaque and clinical presentation (n=800)

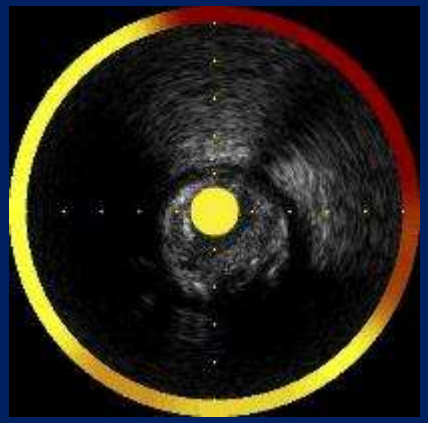
	MI (N=130)	Unstable AP (N=339)	Stable CAD (N=331)	P-value
Age, years	60 (54, 67)	65 (58, 73)	65(59, 71)	< 0.001
Male	78.9%	73.9%	82.2%	0.046
Hypertension	81.5%	91.0%	91.6%	0.01
Diabetes	30.6%	37.0%	39.3%	0.28
Dyslipidemia	80.2%	92.9%	94.3%	< 0.001
Prior PCI	33.9%	55.0%	43.0%	< 0.001
Lesion length, mm	24 (18, 30)	24 (18, 31)	24 (18, 34)	0.66
Plaque burden at MLA site, %	78.9 (72.5, 84.2)	75.4 (68.7, 82.0)	75.3 (67.0, 81.8)	0.18
LRP burden at MLA, %	35.0 (14.7, 49.1)	18.1 (0.0, 38.5)	26.0 (0.0, 47.9)	0.06
LCBI in lesion	141 (65, 247)	93 (29, 171)	98 (41, 185)	< 0.001
$MaxLCBI_{4mm}$	392 (205, 661)	288 (96, 478)	305 (138, 495)	0.001

Lee C. ACC 2016

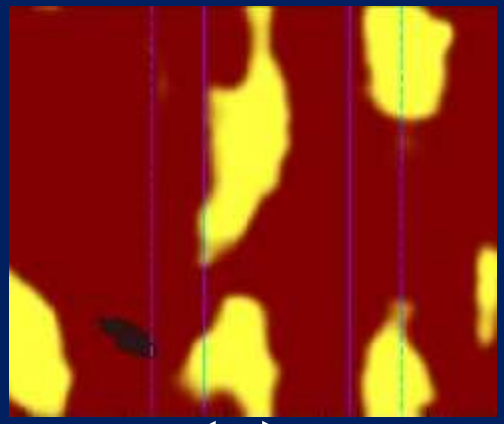
Relationship between the extent of lipid-rich plaque and peri-procedural MI (n=243)

Pre-Intervention



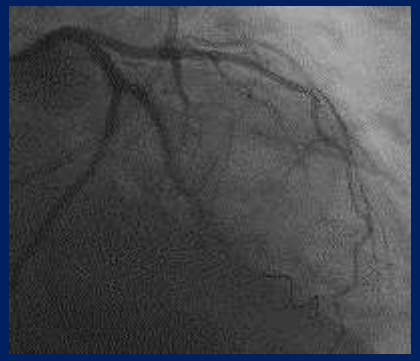


LRP with superficial attenuated plaque
LRP burden=73.4%

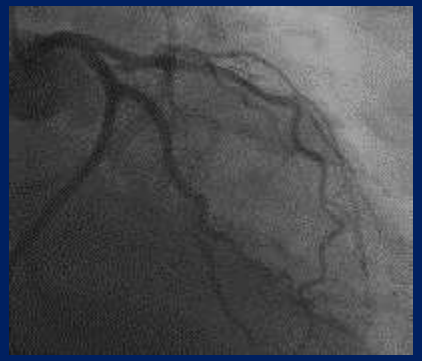


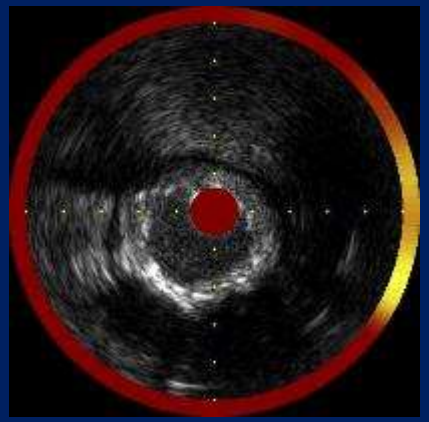
$maxLCBI_{4mm}$ = 746

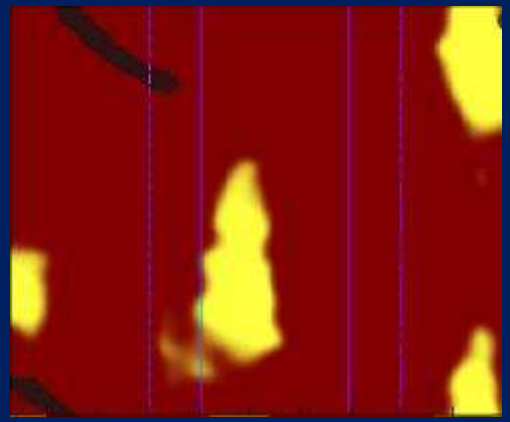
Slow flow



Final

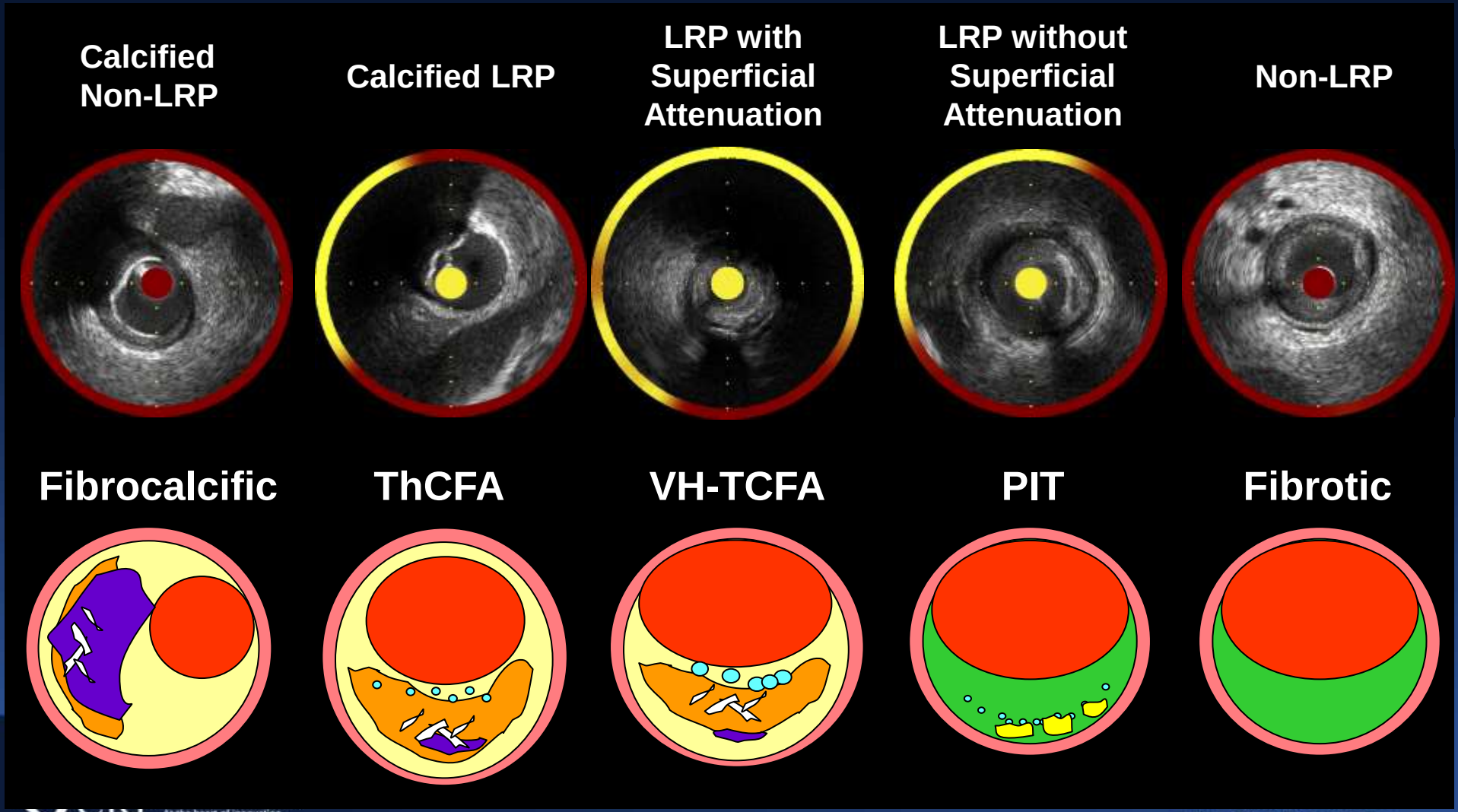




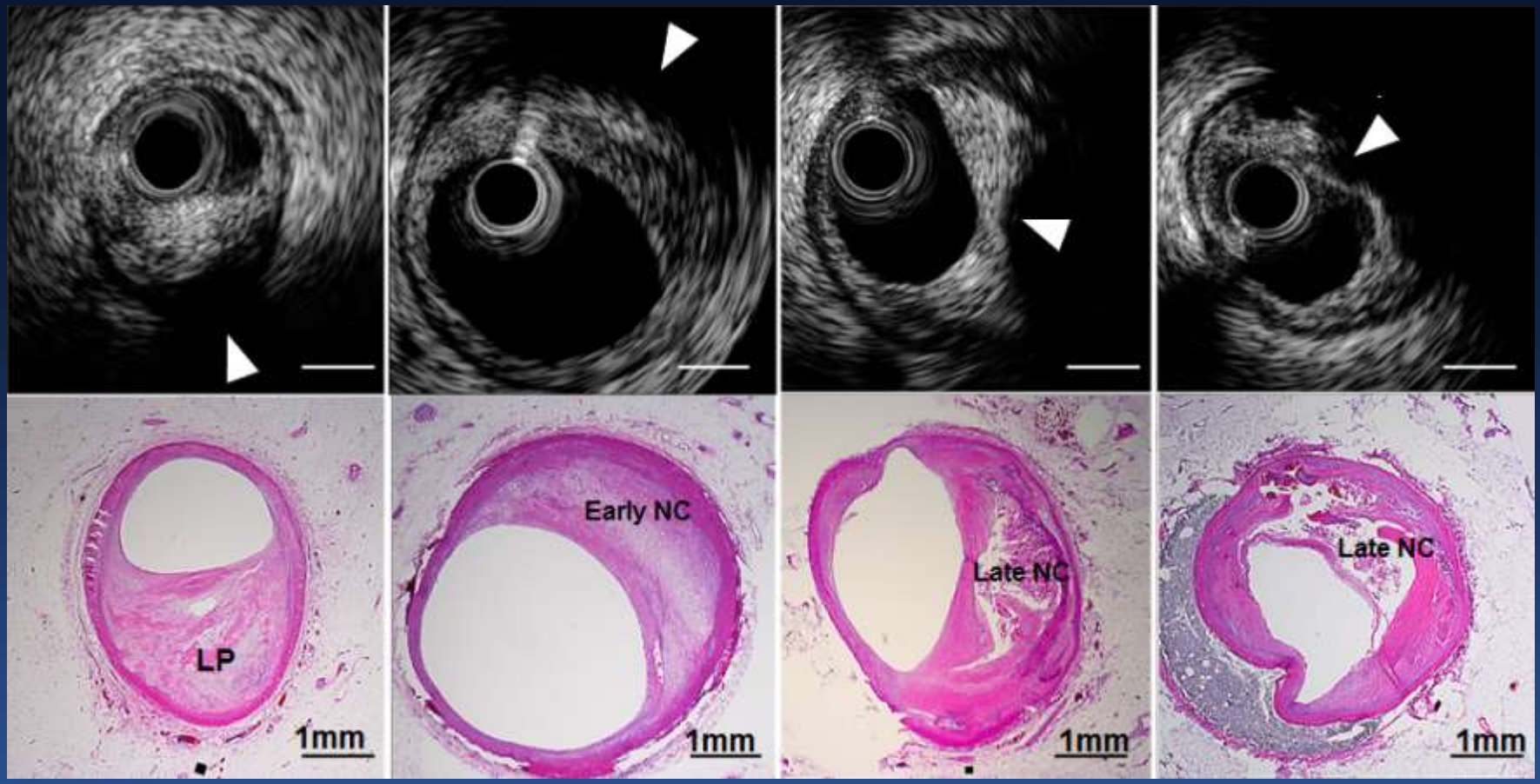


$maxLCBI_{4mm}$ = 484

NIRS/IVUS Plaque Phenotype



Superficial Attenuated Plaque



Pu J, et al. JACC 2014;63:2220-33.

Relationship between the extent of lipid-rich plaque and peri-procedural MI (n=243)

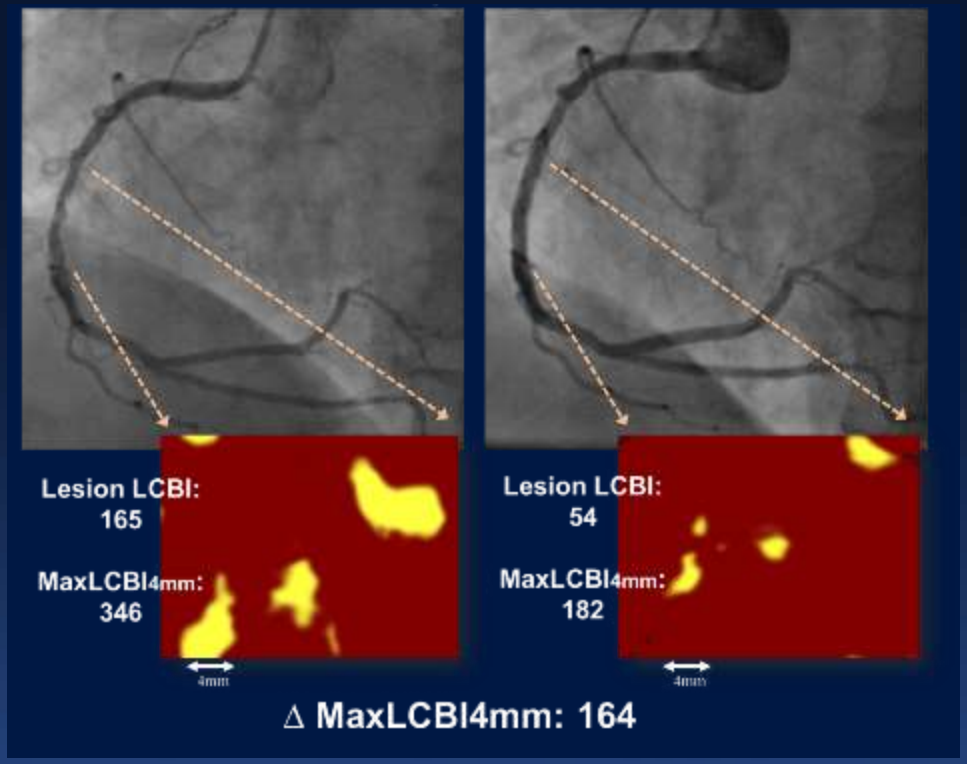
Cut off of $MaxLCBI_{4mm}$ to predict peri-procedural MI=383, AUC=0.94, p=0.006

	Peri-MI n=45	Non–Peri-MI n=198	p Value
Age, years	64.0 (57.0, 69.0)	65.0 (58.0, 72.0)	0.46
Female	15.6%	19.7%	0.52
Body mass index	29.1 (26.9, 33.8)	28.7 (25.9, 32.4)	0.30
Diabetes mellitus	53.3%	38.9%	0.08
Tobacco use	66.7%	64.8%	0.82
Hypertension	93.3%	93.4%	1.00
Hyperlipidemia	90.9%	94.9%	0.29
Family history of CAD	46.7%	53.5%	0.41
Plaque burden, %	72.5 (67.7, 79.2)	78.3 (69.4, 84.2)	0.21
LRP burden, %	40.5 (12.4, 50.5)	15.5 (0.0, 37.9)	0.03
LRP with superficial AP	50%	20%	0.005
$MaxLCBI_{4mm}$ in Lesion	401 (162, 678)	276 [84, 464)	0.008
Lesion LCBI	127 (50, 222)	97 (28, 176)	0.08

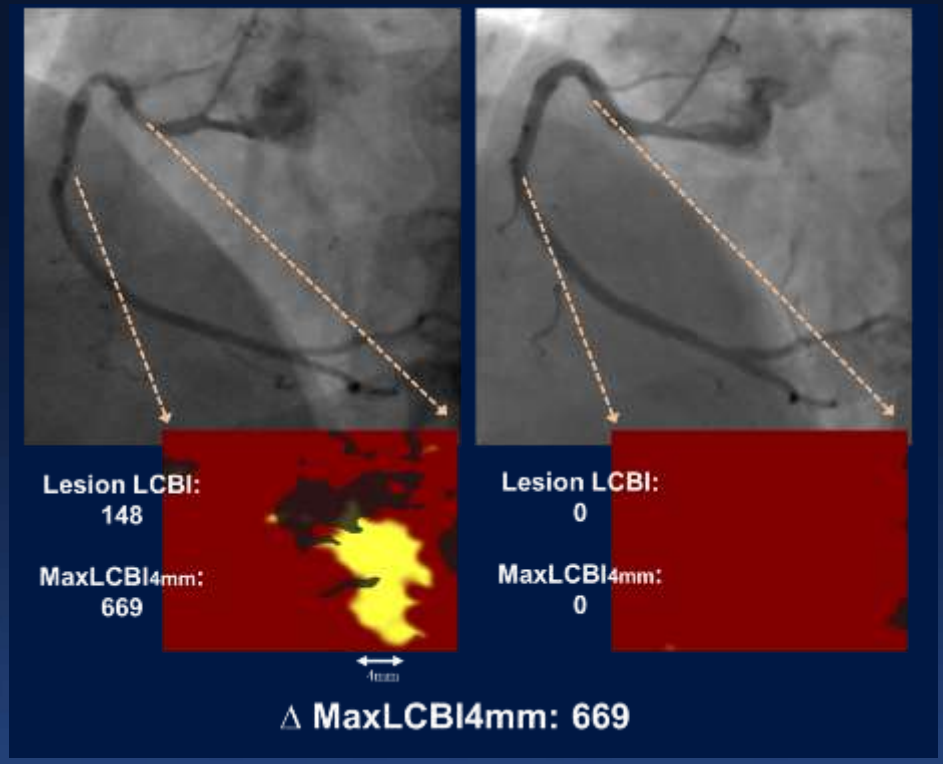
Zhang W. ACC 2016

Representative Cases

Statin Use (+)



Statin Use (-)



Independent predictors for ΔMaxLCBI4mm: Pre LCBImax4mm (p<0.001), Pre-admission statin use (0.04) in multivariate linear regression model

Dohi T. ACC 2014

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Factors associated with a reduction of lipid core plaque in 154 patients undergoing PCI

	Δ maxLCBI$_{4mm}$ <median (n=77)	Δ maxLCBI$_{4mm}$ >median (n=77)	p-value
Baseline characteristics			
Age, years	64 ± 10	62 ± 10	0.27
Male	86%	92%	0.22
Hypertension	90%	93%	0.42
Diabetes mellitus	27%	39%	0.11
Dyslipidemia	90%	93%	0.42
ACS	53%	56%	0.75
Culprit LAD	51%	53%	0.58
Statin use at admission	84%	75%	0.16
NIRS findings			
Lesion length, mm	24 (18, 33)	28 (21, 45)	0.012
Pre Max$_{4mm}$ LCBI	217 (110, 431)	586 (412, 704)	<0.001
Post Max$_{4mm}$ LCBI	178 (36, 380)	133 (20, 284)	0.22
Δ Lesion LCBI	-31 (-68, -2)	-146 (-206, -101)	<0.001
Δ Max$_{4mm}$ LCBI	-72 (-126, 10)	-350 (-538, -256)	<0.001

Relationship between the statin usage and extent of lipid-rich plaque (n=728)

	Statin at admission n=548	No statin at admission n=180	p Value
Dyslipidemia	97.8%	72.3%	<0.001
LDL cholesterol, mg/dL	72 (56, 96)	105 (84, 134)	<0.0001
Age, years	64 (57, 72)	64 (57, 73)	0.92
Male	78.8%	76.1%	0.45
Body mass index	29.2 (26.0, 33.1)	29.0 (26.0, 33.9)	0.85
Diabetes mellitus	39.5%	29.1%	0.01
Hypertension	93.0%	80.0%	<0.001
Lesion length, mm	24 (18, 32)	24 (18, 31)	0.52
Minimum lumen area, mm^2	2.6 (1.9, 3.5)	2.4 (1.9, 3.2)	0.15
Plaque burden at MLA, %	75.3 (67.3, 81.8)	77.2 (70.3, 84.5)	0.06
Maximum LRP burden, %	32.1 (20.0, 47.9)	37.3 (26.2, 55.8)	0.01
$MaxLCBI_{4mm}$ in Lesion	292 (116, 475)	369 (181, 594)	0.0005
Lesion LCBI	94 (32, 173)	128 (58, 222)	0.0003

Relationship between the extent of lipid-rich plaque and LDL level (n=554)

LDL Level at admission	<67mg/dL (N=197)	67-95mg/dL (N=169)	>95 mg/dL (N=188)	P-value
LDL cholesterol, mg/dL	54 (47, 60)	78 (74, 87)	119 (105, 145)	<0.0001
Statin at admission	91.3%	78.4%	56.5%	<0.001
Dyslipidemia	94.9%	91.7%	85.6%	0.001
Age, years	65 (59, 72)	63 (57, 70)	63 (55, 72)	0.19
Male	85.8%	79.3%	72.3%	0.006
Diabetes	48.7%	29.6%	26.2%	<0.0001
Hypertension	93.4%	91.7%	85.6%	0.03
Prior MI	34.5%	25.2%	20.7%	0.009
Lesion length, mm	25 (18, 36)	24 (18, 31)	23 (18, 29)	0.23
Plaque burden at MLA site, %	76.5 (67.6, 83.3)	76.9 (69.9, 81.4)	76.4 (68.7, 82.9)	0.99
LRP burden at MLA, %	29.9 (21.3, 44.4)	35.1 (21.3, 49.1)	37.8 (22.7, 52.4)	0.37
LCBI in lesion	93 (34, 176)	106 (45, 162)	108 (40, 190)	0.46
$MaxLCBI_{4mm}$	299 (140, 463)	298 (161, 486)	323 (97, 506)	0.70

Two/Three Vessel CAD (n= 87)

After stenting the target vessel
The non-target lesion underwent FFR

FFR≤0.8 ➔IVUS, NIRS

Randomized

Standard	Aggressive
n = 43	n = 44
Continue statin the patient was taking	Rosuvastatin 40 mg daily
Dual antiplatelet therapy for 1 year	Dual antiplatelet therapy for 1 year

Follow up Cath (6-8 weeks)
FFR, IVUS and NIRS repeated.
If FFR ≤0.8, lesion stented and imaging repeated.
If FFR > 0.8 the patient was treated medically.

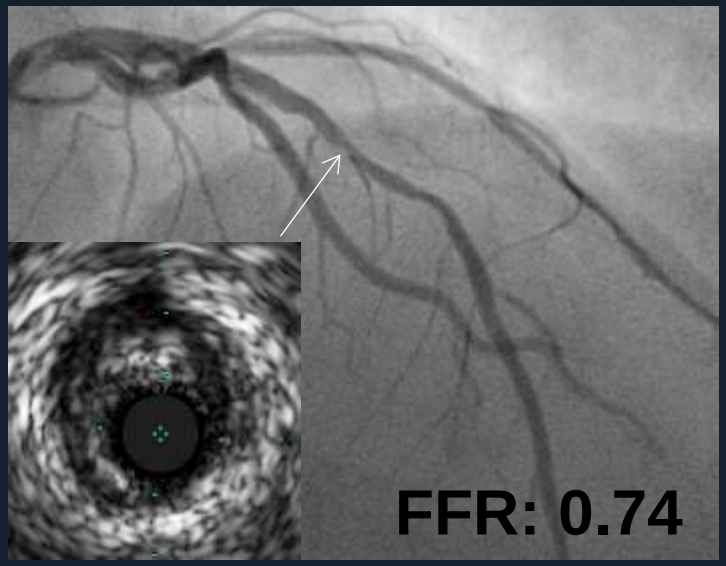
Imaging data analyzed by CRF Core Lab
Data analysis for primary outcome analyzed by MSH independent Core Lab

*Optimal medical therapy for all patients

Kini A et al. *JACC* 2013; 62: 21-9.

Case Example

Baseline

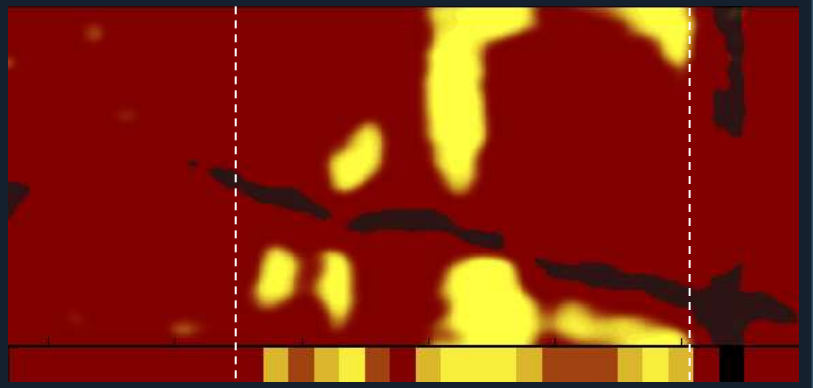


Plaque Area
5.6mm^2

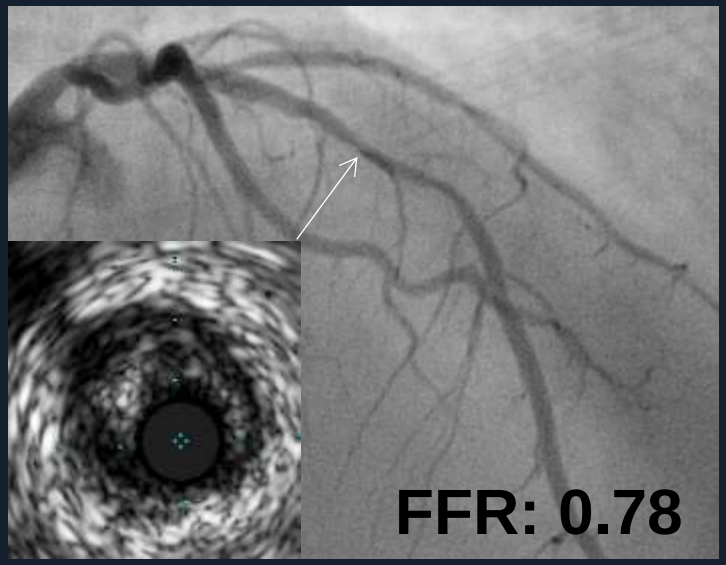
Lesion LCBI: 259

Max10mm LCBI: 511

Max4mm LCBI: 802



Follow-up

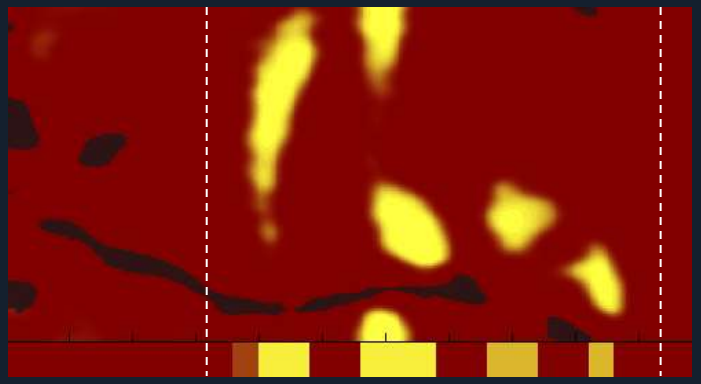


Plaque Area
5.5mm^2

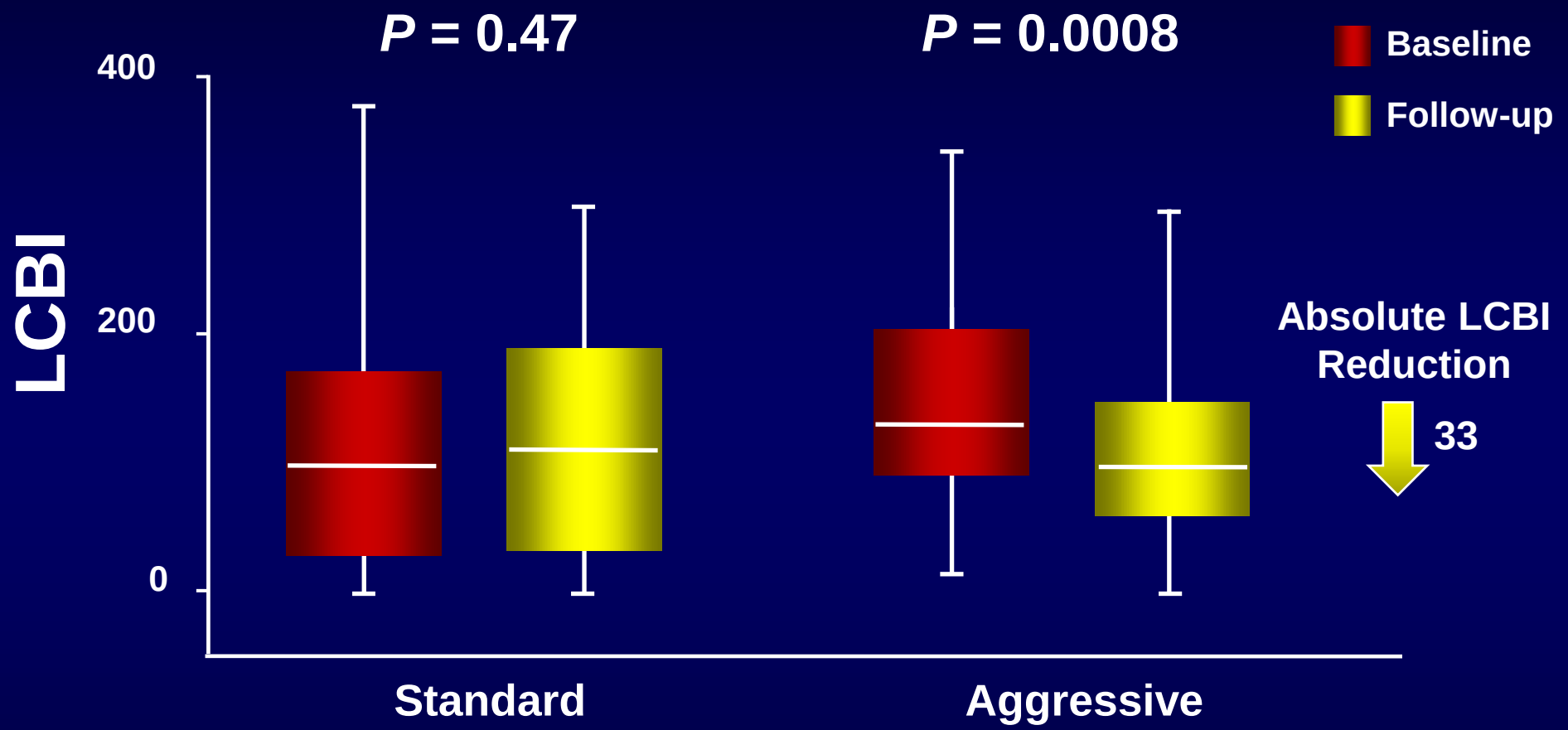
Lesion LCBI: 177

Max10mm LCBI: 289

Max4mm LCBI: 474



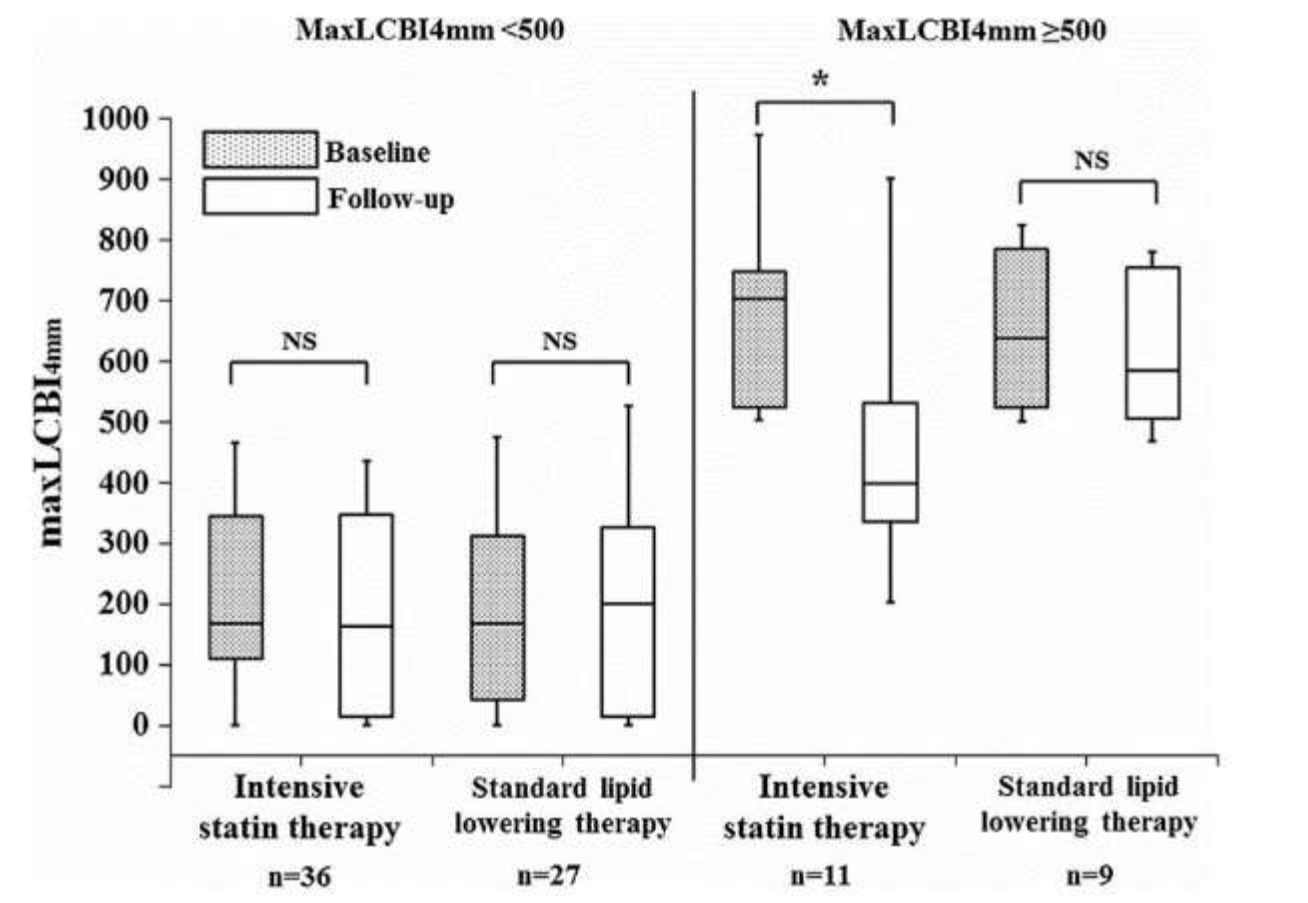
Paired Analysis – Lesion LCBI



Variable	Standard (n = 43)	Aggressive (n = 44)	*P*
Percent atheroma volume	0.26%	0.24%	0.98

Kini A et al. *JACC* 2013; 62: 21-9.

Relationship between Lipid Regression and maxLCBI$_{4mm}$

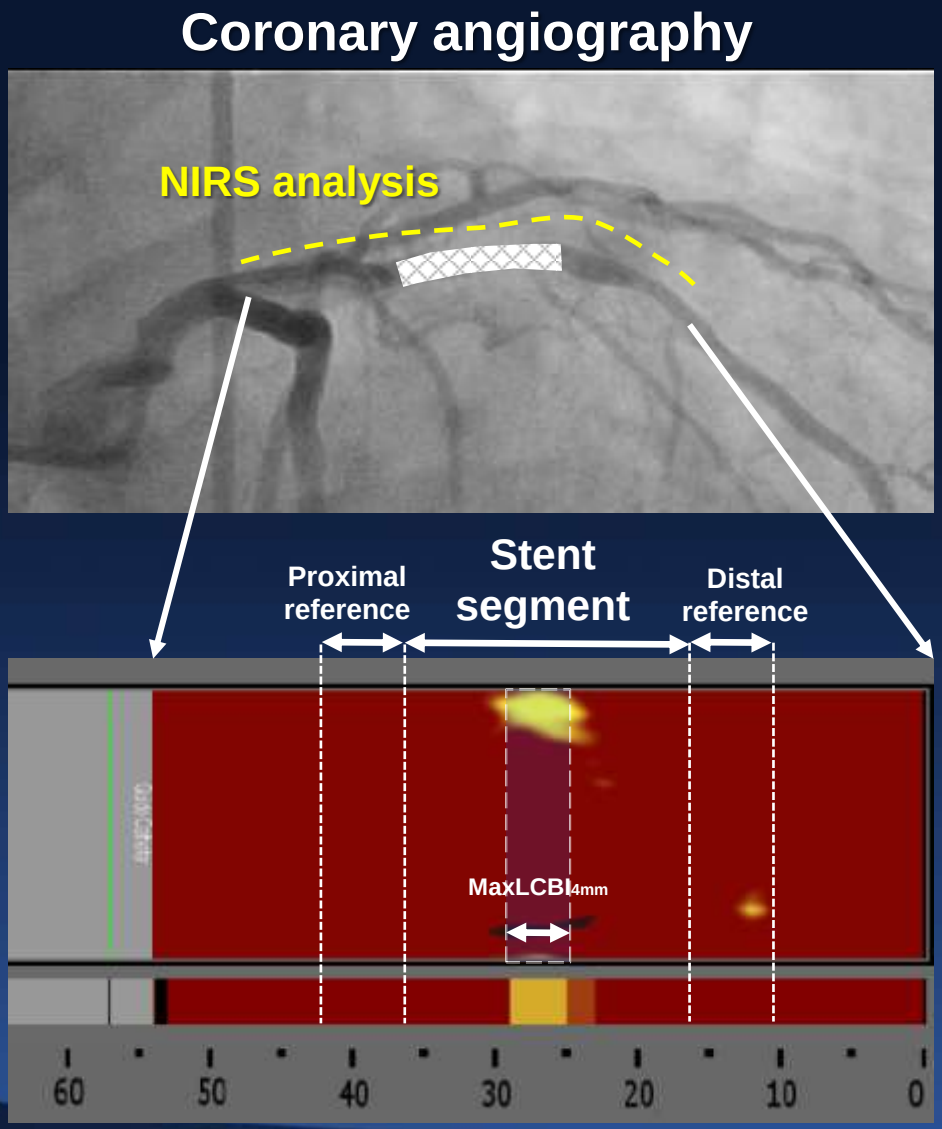


Dohi T et al. *Eur Heart J Imaging* 2014

Extent of lipid rich plaque by NIRS may predict DES restenosis

- From a total of 478 patients with complete data between February 2009 and November 2011, we identified 14 patients with stent failure.
- Of 14 patients with restenosis, ISR was found in 13 patients (9 focal, 3 diffuse, 1 total occlusion), and proximal edge restenosis was found in 1 patient.
- All implanted stents were DES, and the median follow-up time was 392 days (IQR: 300 to 418) after index PCI.
- Thirty case-matched controls were identified.

Co-registration of NIRS with Angiogram



- The stent segment was defined as the length of vessel in which any stent implantation was performed.
- The corresponding stenting zone on the chemogram was identified by colocalized registration marks placed on the chemogram by the treating physician.

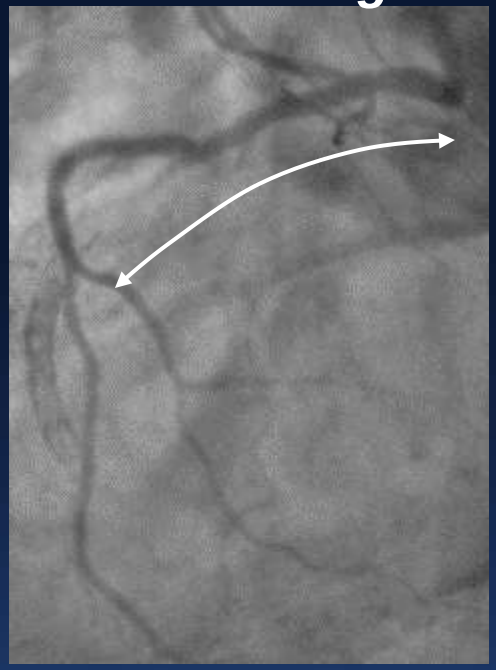
Clinical Characteristics and QCA Results

	Restenosis (N=14)	No-restenosis (N=30)	p value
Baseline characteristics			
Age, years	62±7	61±7	0.69
Male	93%	100%	0.32
Diabetes mellitus	50%	53%	0.84
Acute coronary syndrome	43%	47%	0.81
Final QCA results at index procedure			
Total stent length, mm	30 (14, 51)	25 (17, 49)	0.95
Minimal lumen diameter, mm	2.0 (1.9, 2.2)	2.2 (2.0, 2.5)	0.13
Reference vessel diameter, mm	2.5 (2.2, 3.1)	2.8 (2.6, 3.2)	0.26
Percent diameter stenosis, %	19.7 (12.8, 29.3)	16.3 (11.3, 24.9)	0.70

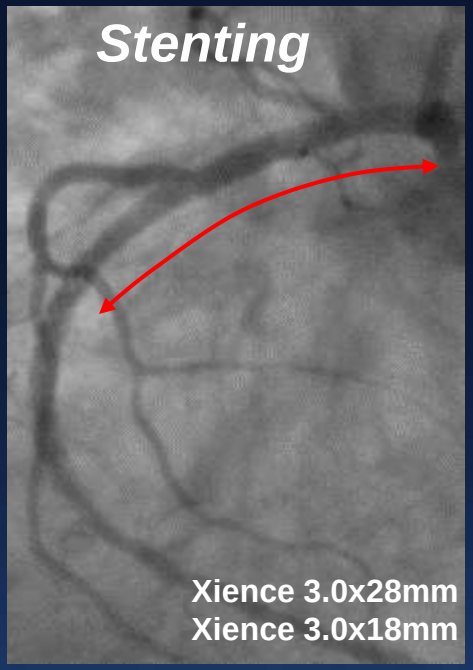
Case 1- Restenosis in Mid RCA-

Index PCI

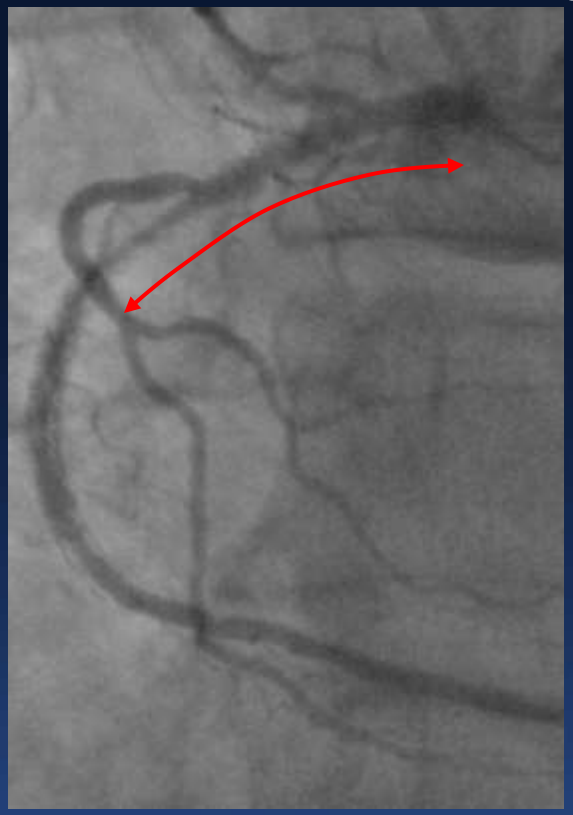
Pre Stenting



Post Stenting



In-stent Restenosis after 1 year



Stent segment

Pre PCI NIRS findings

LCBI in stent segment: **196**

MaxLCBI4mm in stent segment: **940**

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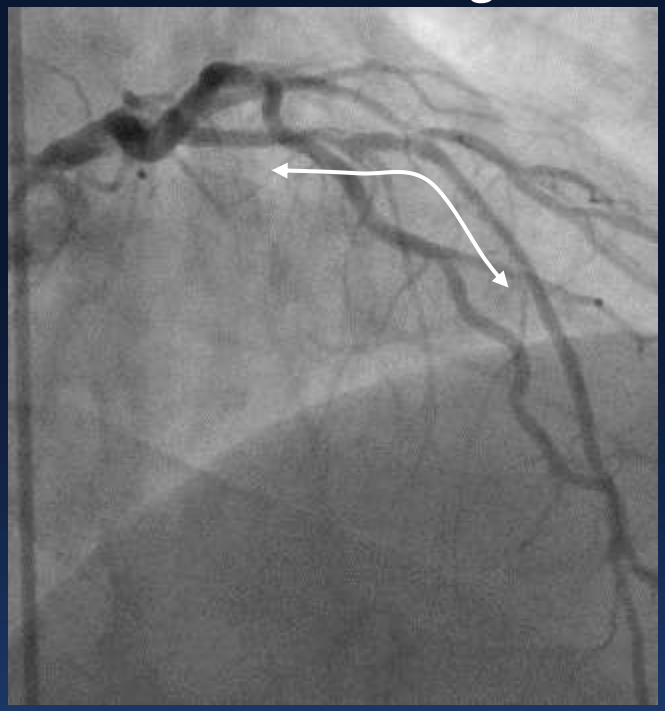
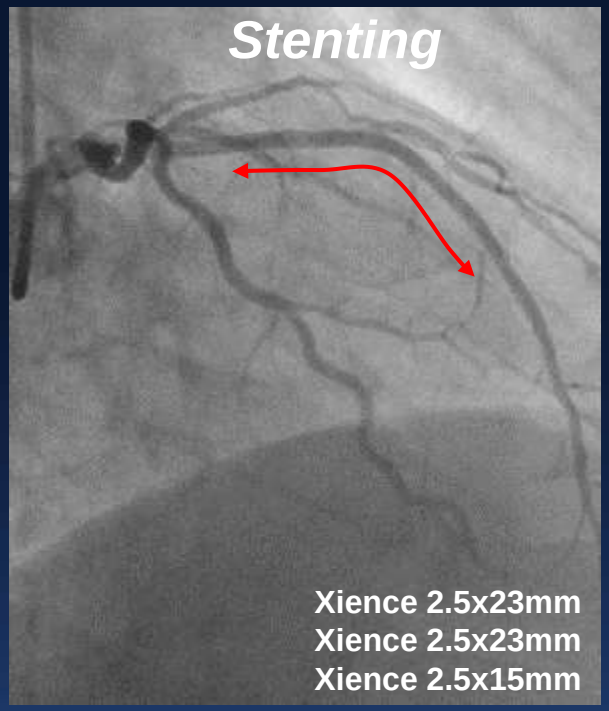
Case 2 - Control case in Middle LAD-

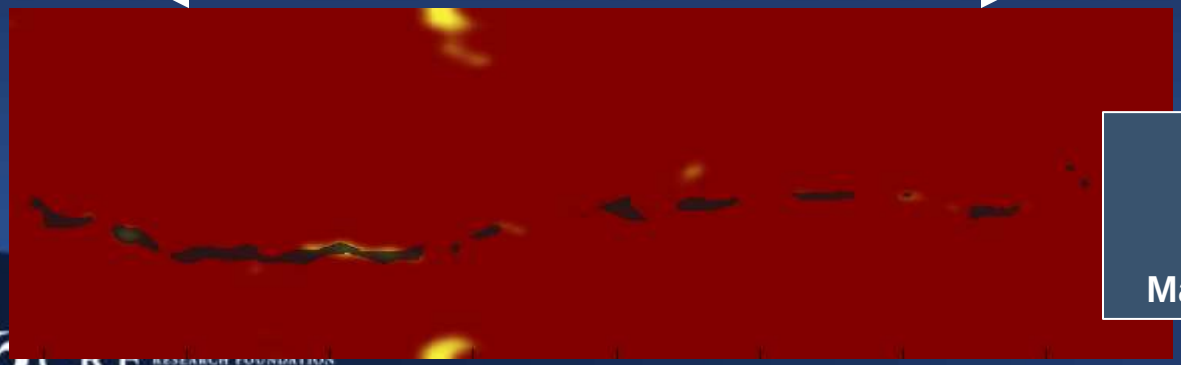
Pre Stenting



Post Stenting



Stent segment



Pre PCI NIRS findings

LCBI in stent segment: **14**

MaxLCBI4mm in stent segment: **157**

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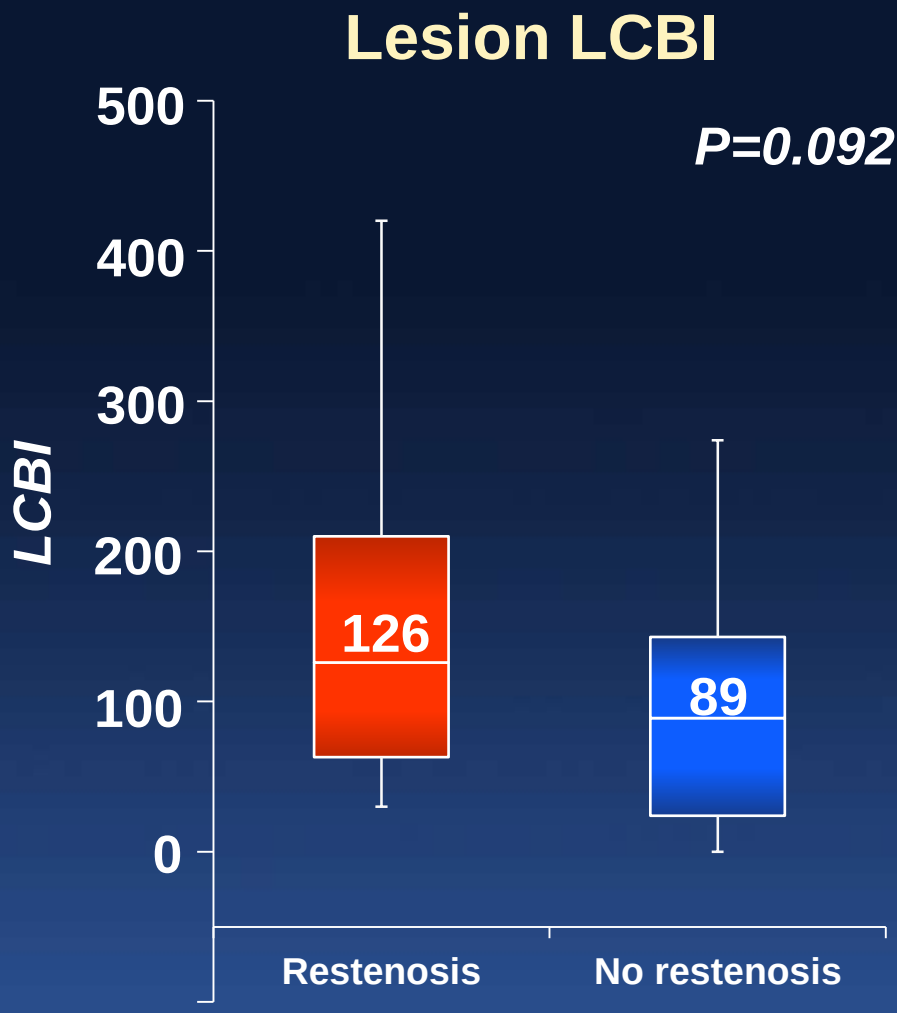
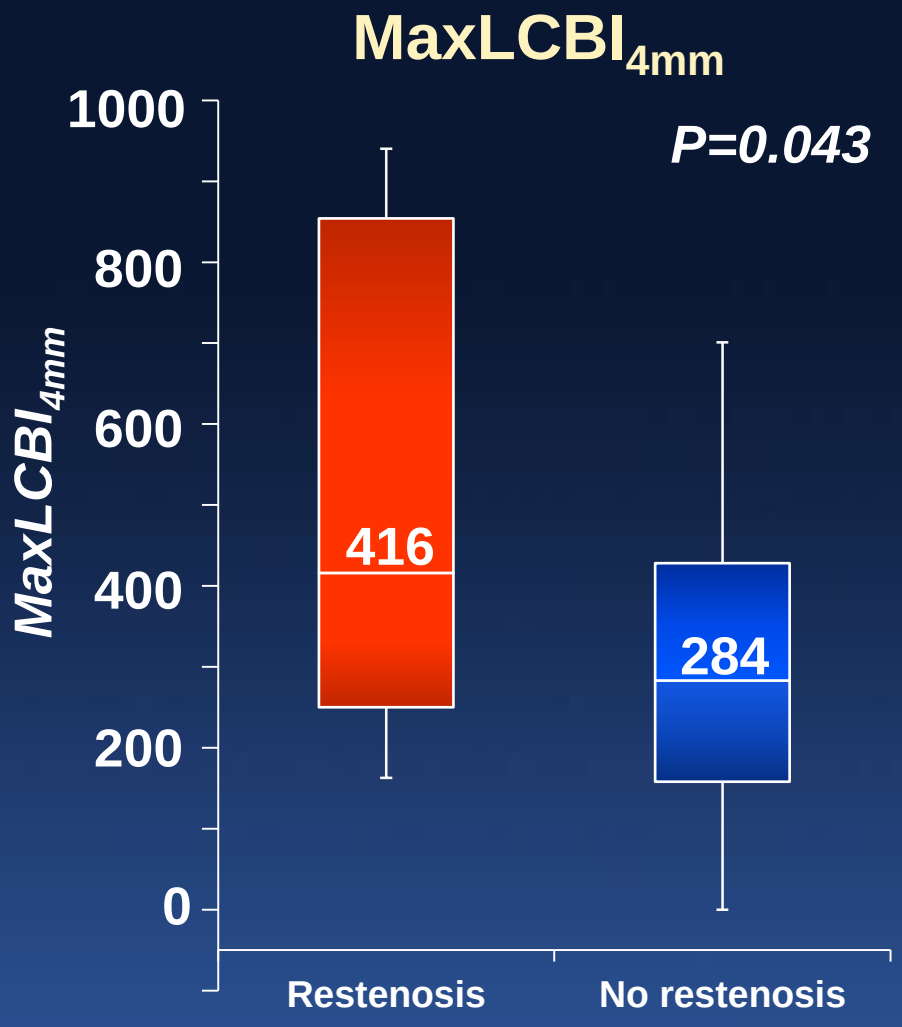
Comparison of LCBI and maxLCBI$_{4mm}$
in the Stented Segment Grouped by Occurrence of Restenosis





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NIRS findings with and without restenosis

	Restenosis (N=14)	No-restenosis (N=30)	p value
LCBI in the stented segment	126 (63, 210)	89 (24, 143)	0.092
$MaxLCBI_{4mm}$	416 (250, 854)	284 (158, 428)	0.043
LCBI in the proximal reference	31 (1, 105)	19 (0, 90)	0.65
LCBI in the distal reference	3 (0, 91)	0 (0, 8)	0.71
$MaxLCBI_{4mm}$ <200	7%	37%	0.047
$MaxLCBI_{4mm}$ <100	0%	0%	0.092

Data are expressed as median (interquartile range).

* $MaxLCBI_{4mm}$ = maximum LCBI in any 4 mm-long segment

Accuracy evaluation using ROC curve analysis

- The best cut-off of maxLCBI4mm for detecting stent failure was 525 (AUC=0.693) with a specificity of 85% and a sensitivity of 50%.
- A cut-off of 200 maxLCBI4mm had a 93% sensitivity and 92% negative predictive value.

Summary

1. NIRS can detect the lipid rich plaque (LRP) in the coronary artery.
2. There are associations between LRP and 1) clinical presentation, 2) statin usage, 3) peri-procedural MI, and 4) in-stent restenosis.
3. No existence of LRP ($maxLCBI_{4mm}$<200) shows high negative predictive value for absence of in-stent restenosis (92%).