Combined IVUS-NIR Spectroscopy: How to Predict Vulnerable Plaque and PCI Outcome

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Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship	Company
• Grant/Research Support	• Boston Scientific Corporation
• Consulting Fees/Honoraria	• Boston Scientific Corporation, ACIST
• Speaker Fee	• Volcano Corporation, St Jude Medical

Unstable Plaque=Causing Thrombosis

Plaque Rupture

Plaque Erosion

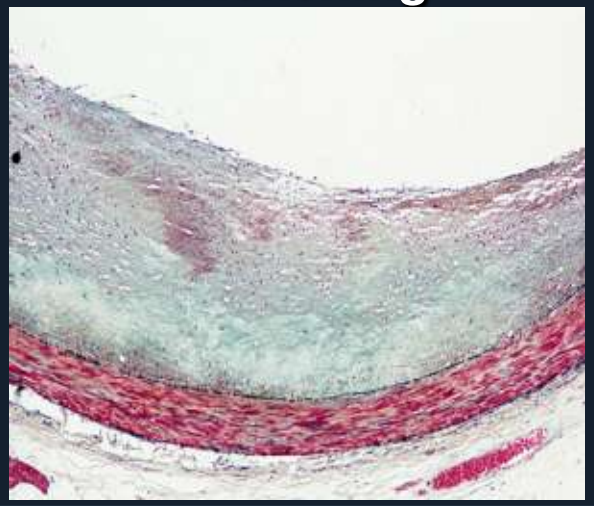
Calcified Nodule

Stable Plaque=Not Causing Thrombosis

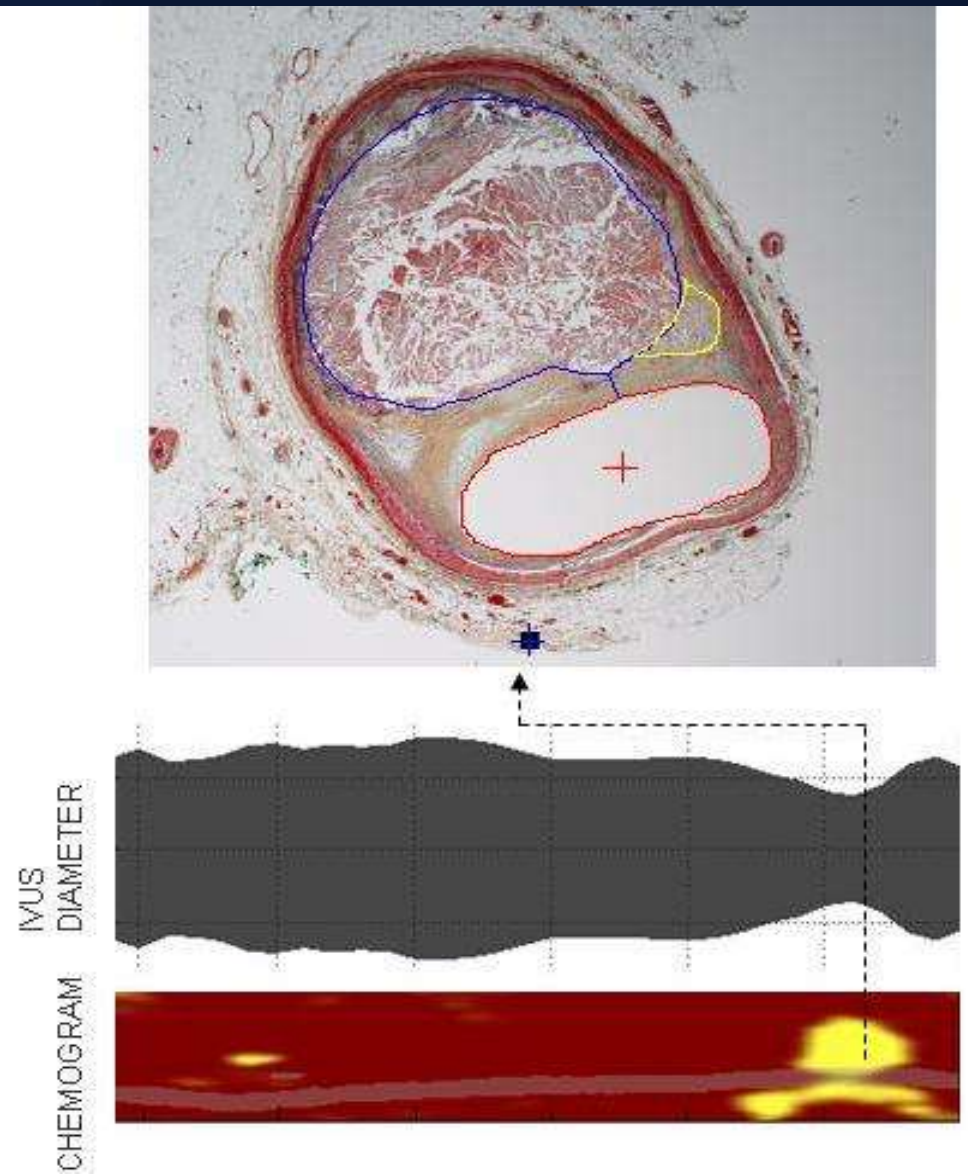
Fibrocalcific Plaque

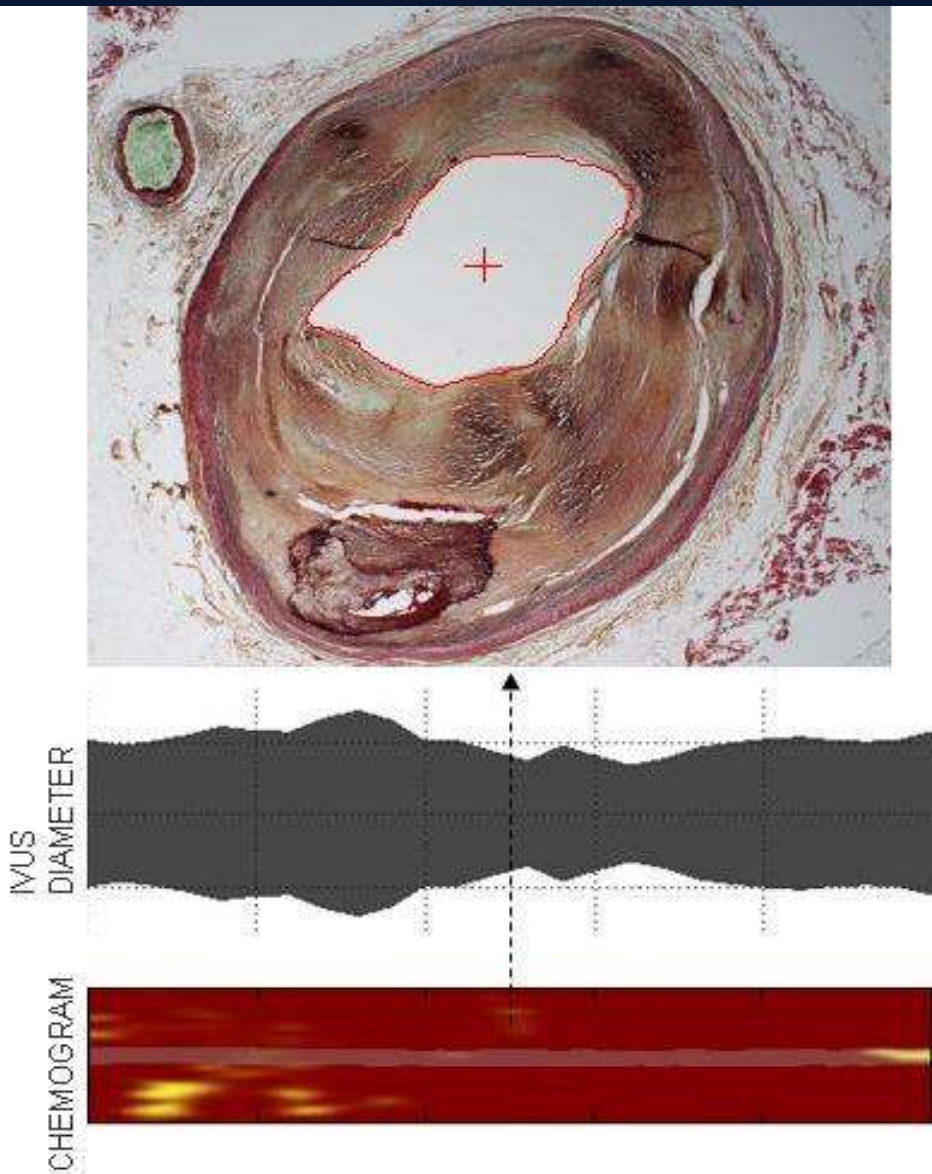
Healed Rupture

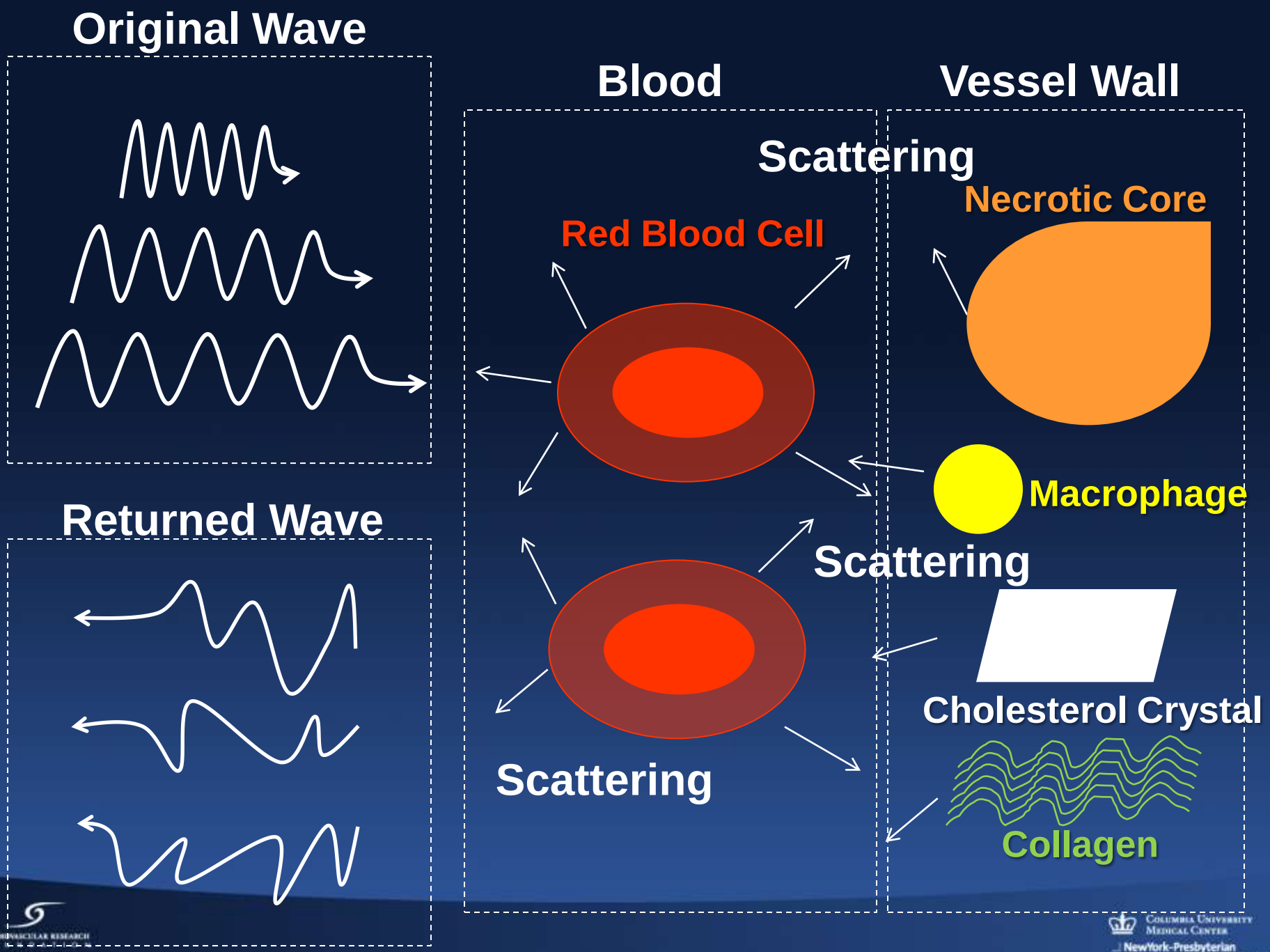
Pathological Intimal Thickening

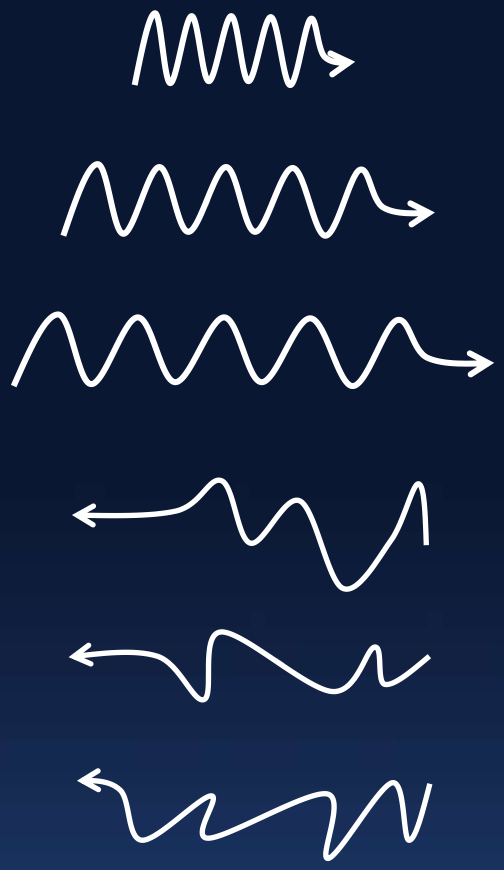


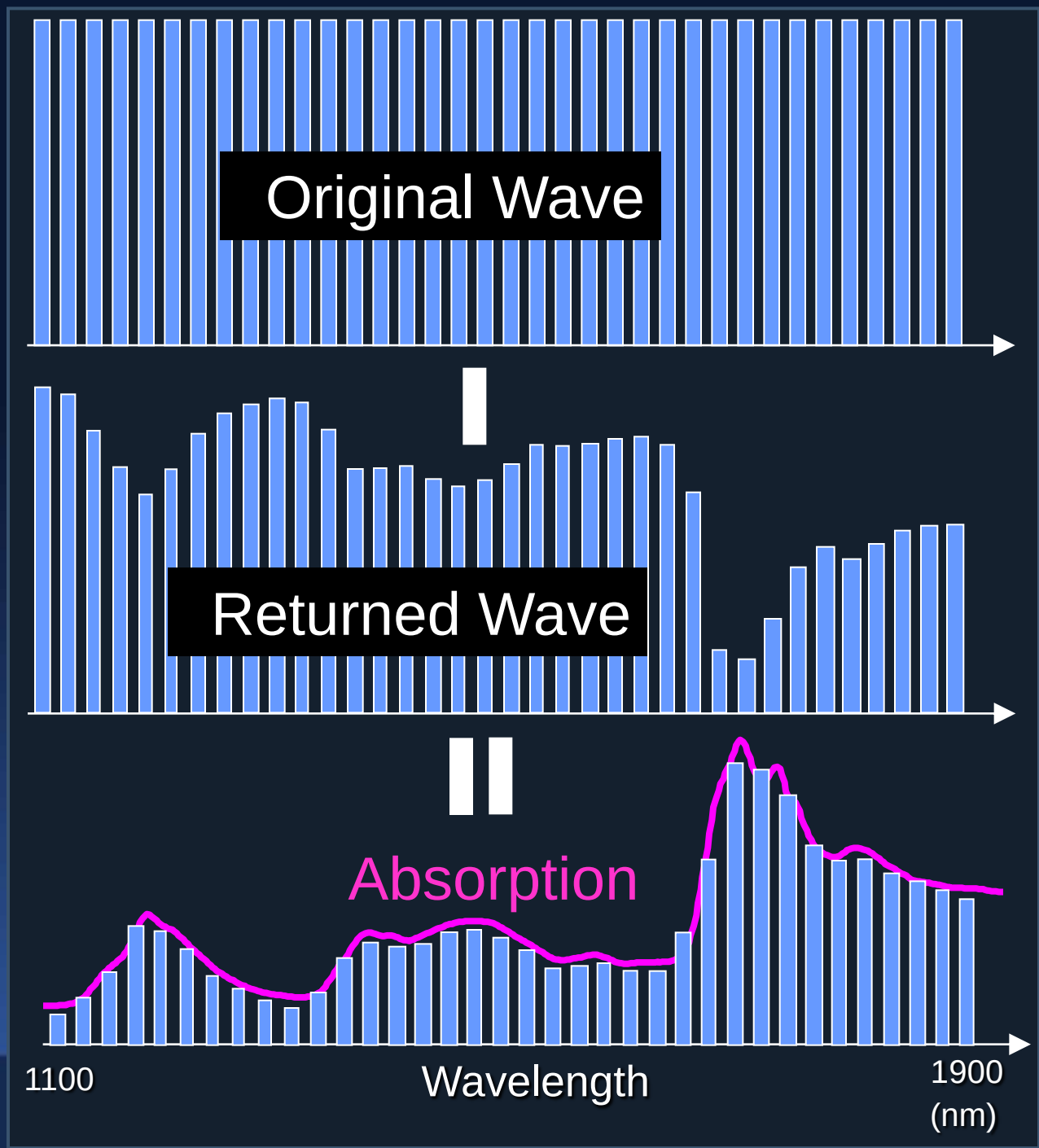
NIR can Distinguish Lipid-rich from Fibrotic Plaques






Original Wave
Blood
Vessel Wall
Scattering
Necrotic Core
Red Blood Cell
Macrophage
Returned Wave
Scattering
Cholesterol Crystal
Scattering
Collagen





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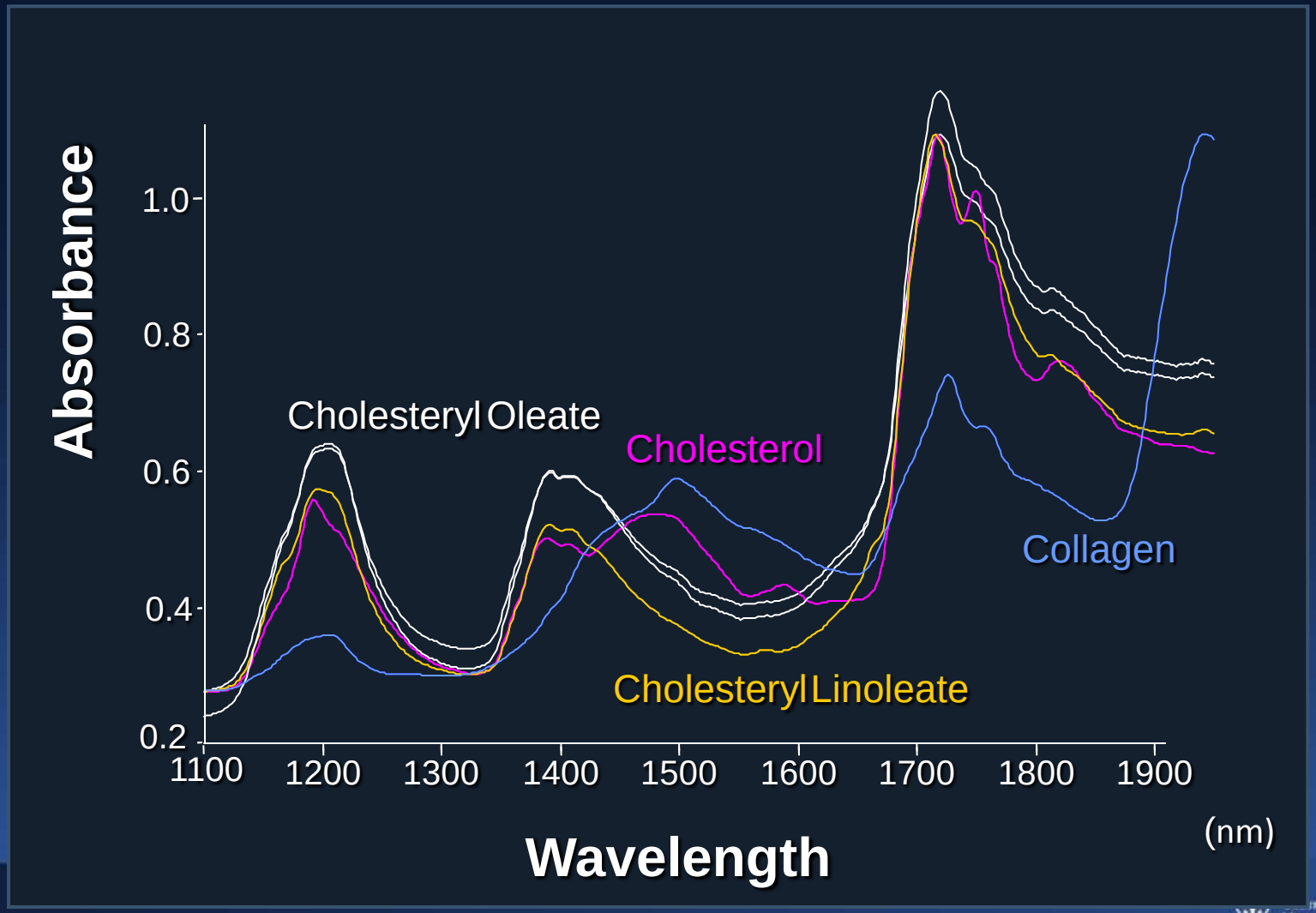
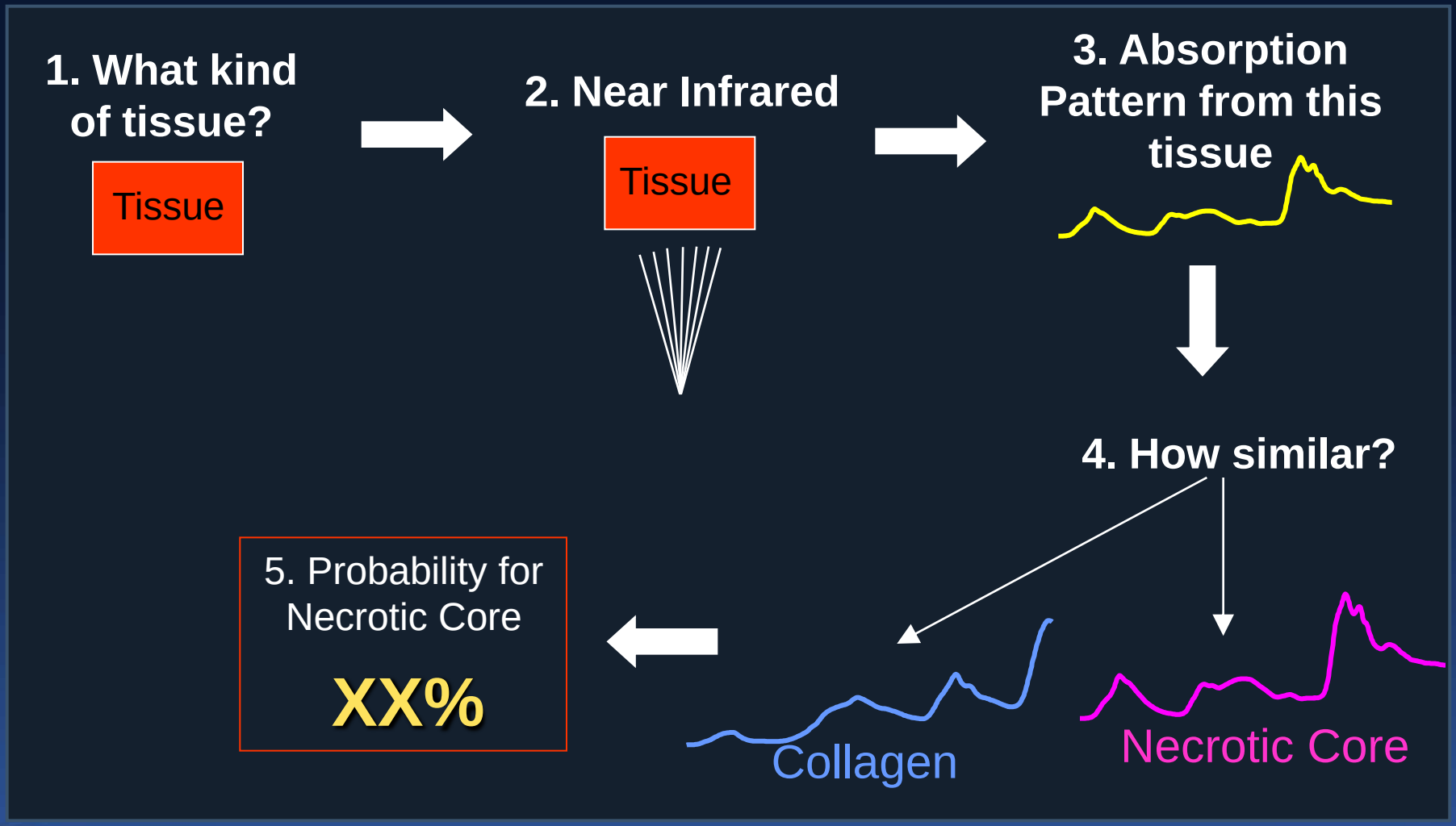
NIR Spectroscopy

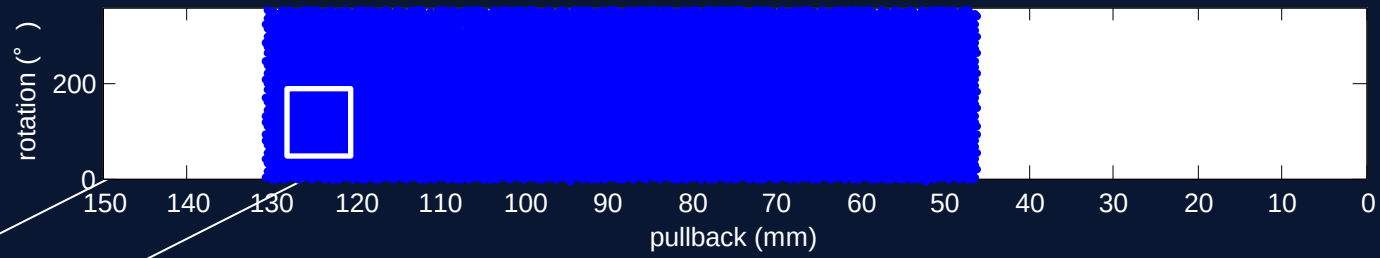
- Necrotic Core>0.2mm thick, >60°, Cap<0.45mm



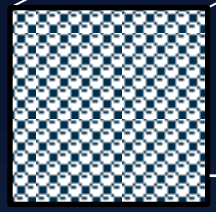
Process of NIR Spectroscopy



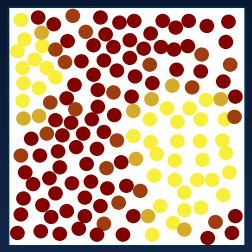
Near Infrared Spectroscopy



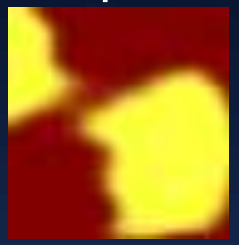
Step 1



Step 2



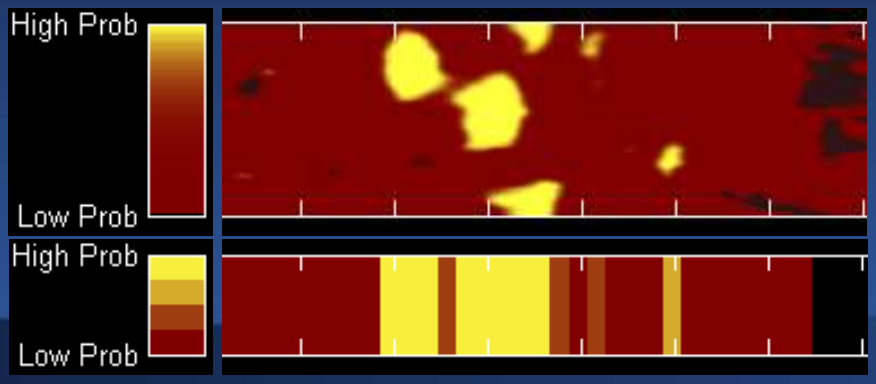
Step 3

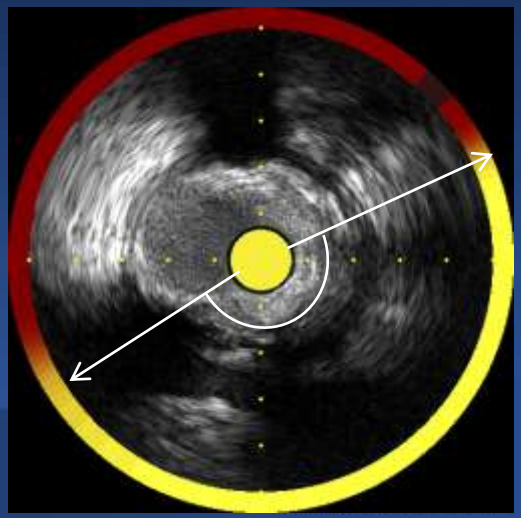


Lipid Core Burden Index (LCBI)
=Yellow pixel /All variable pixel
× 1000

Lesion

LCBI Max_{4mm}





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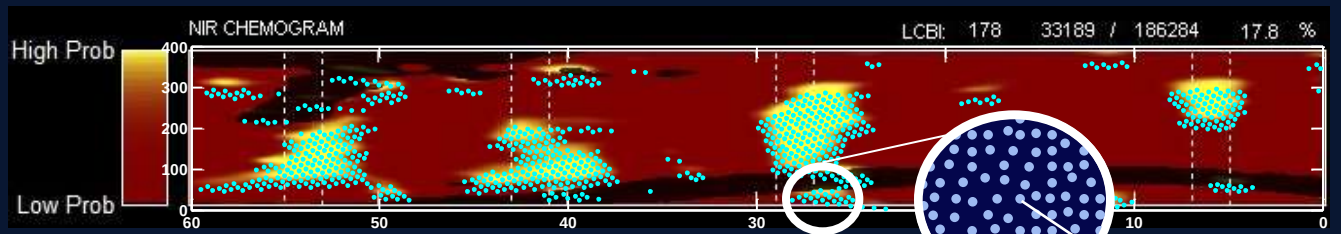
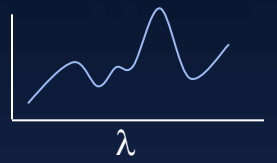
Formation of the Cap Thickness Prediction Image



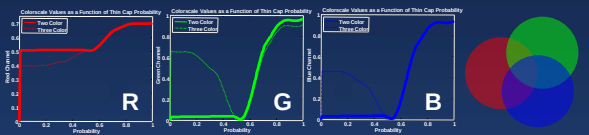


Spectra acquired at discrete pullback and rotation positions

LCP Spectra transformed into posterior probability of thin cap presence

0→1

Probability mapped to a color



Pixels formed into an image

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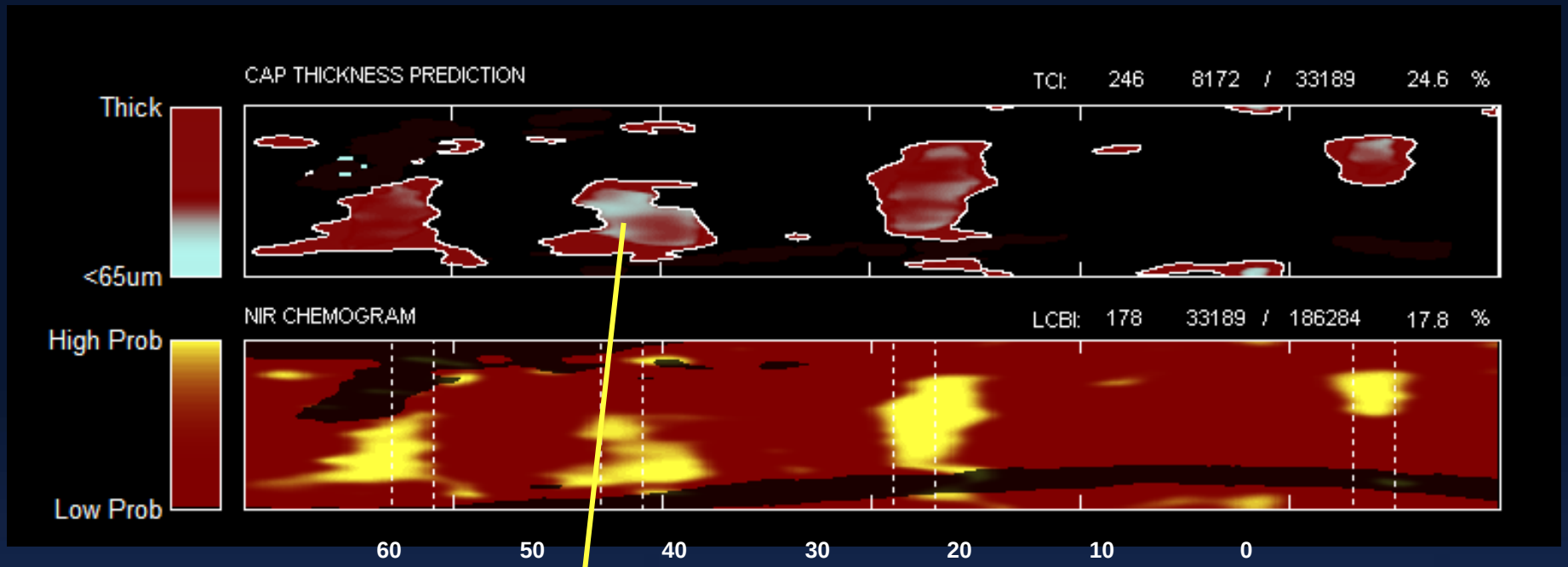
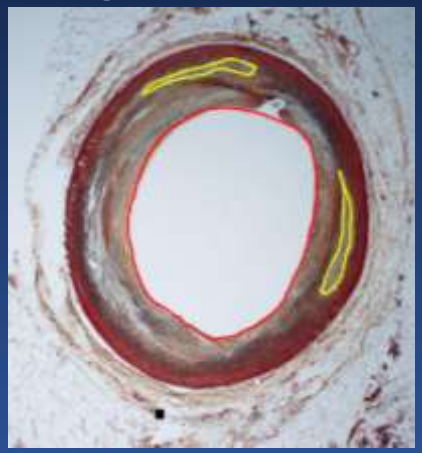
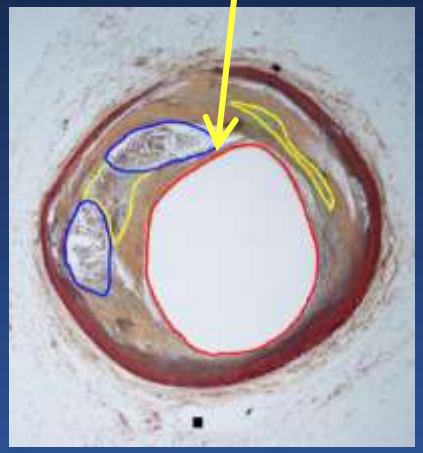


52mm



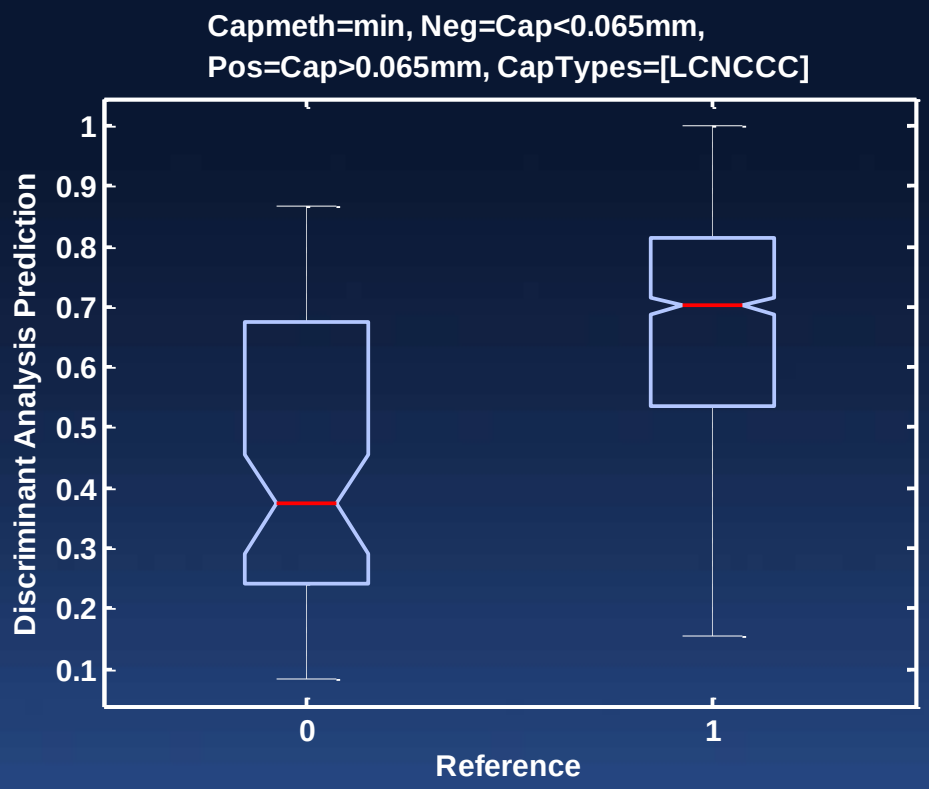
42mm

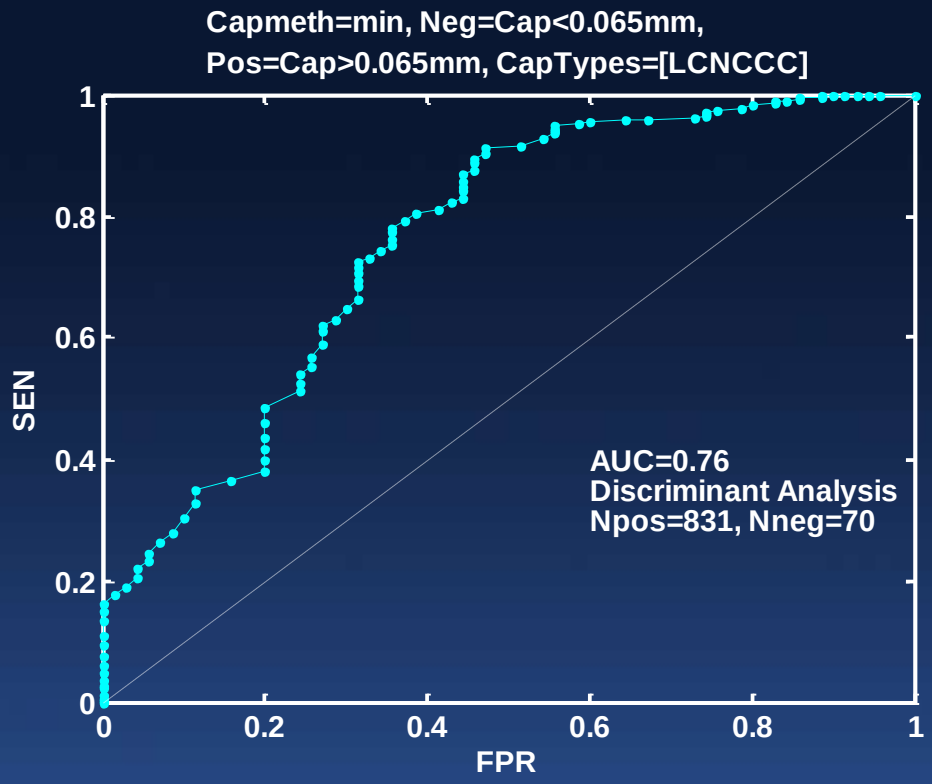


28mm

6mm

Ability to Predict Thin Cap (<0.065mm)



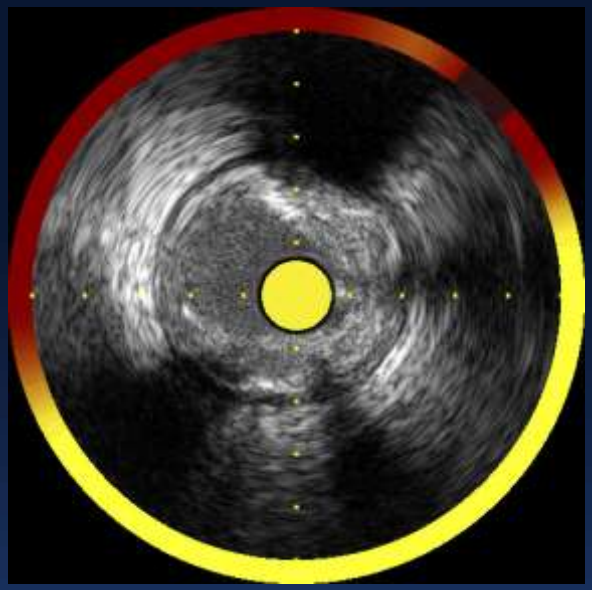


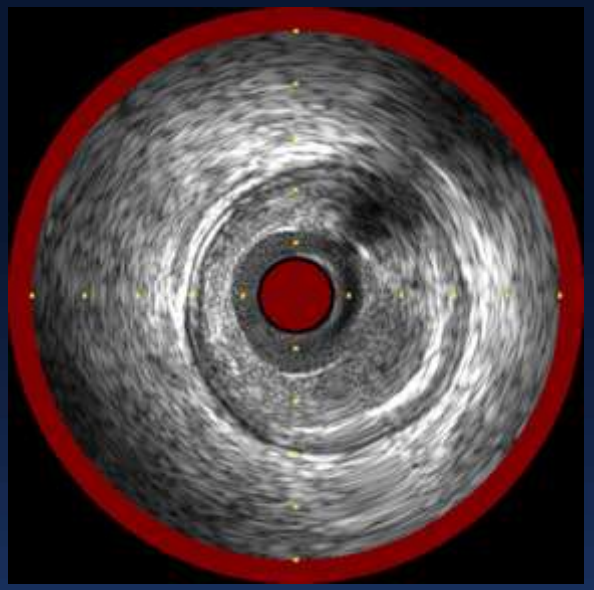
Detection of Necrotic Core

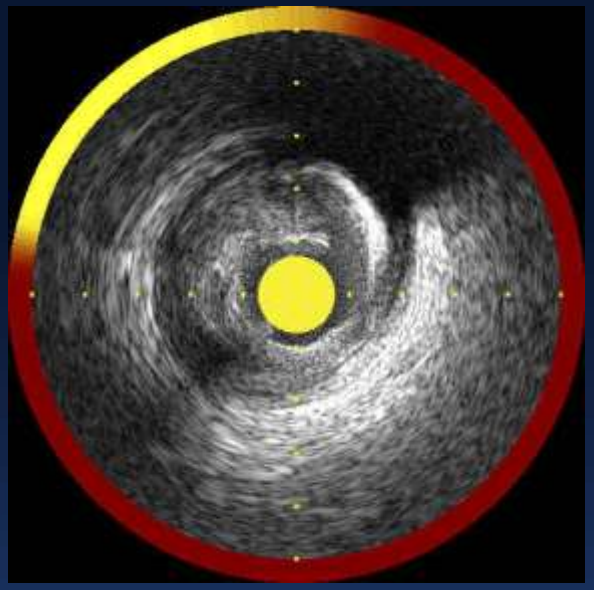
TCFA

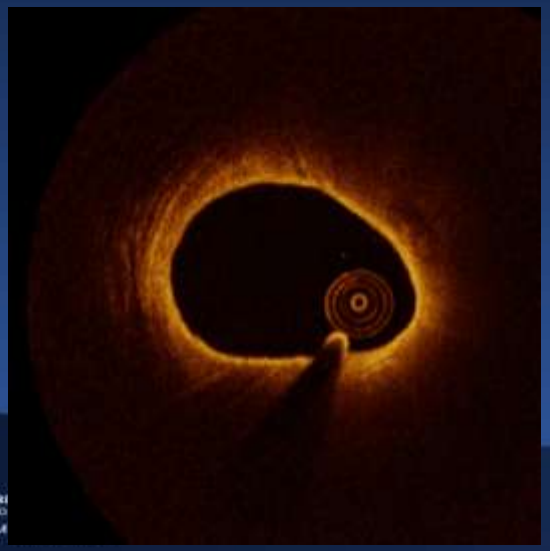
Ruptured plaque

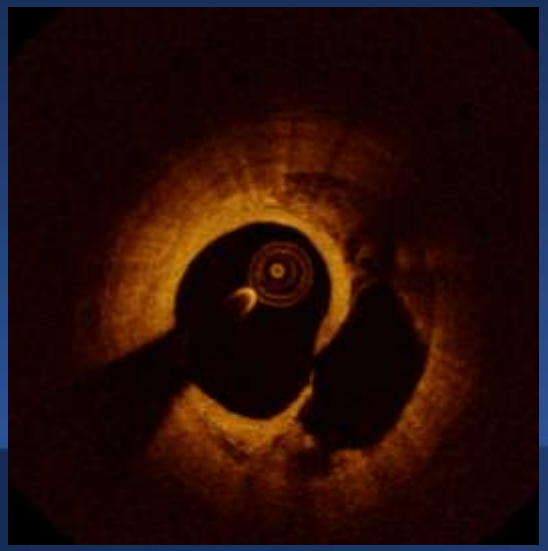
Ruptured plaque with thrombus

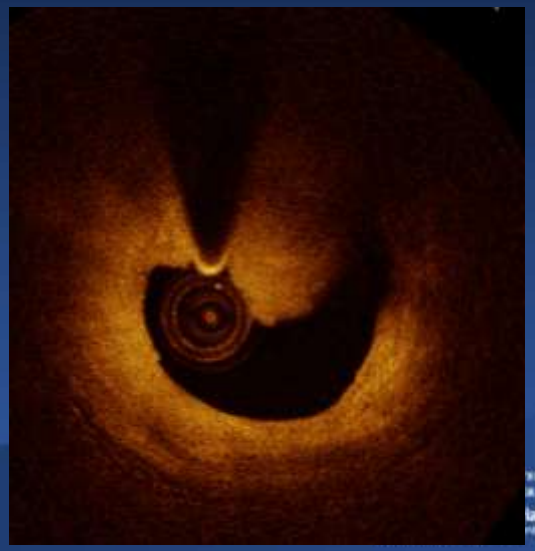






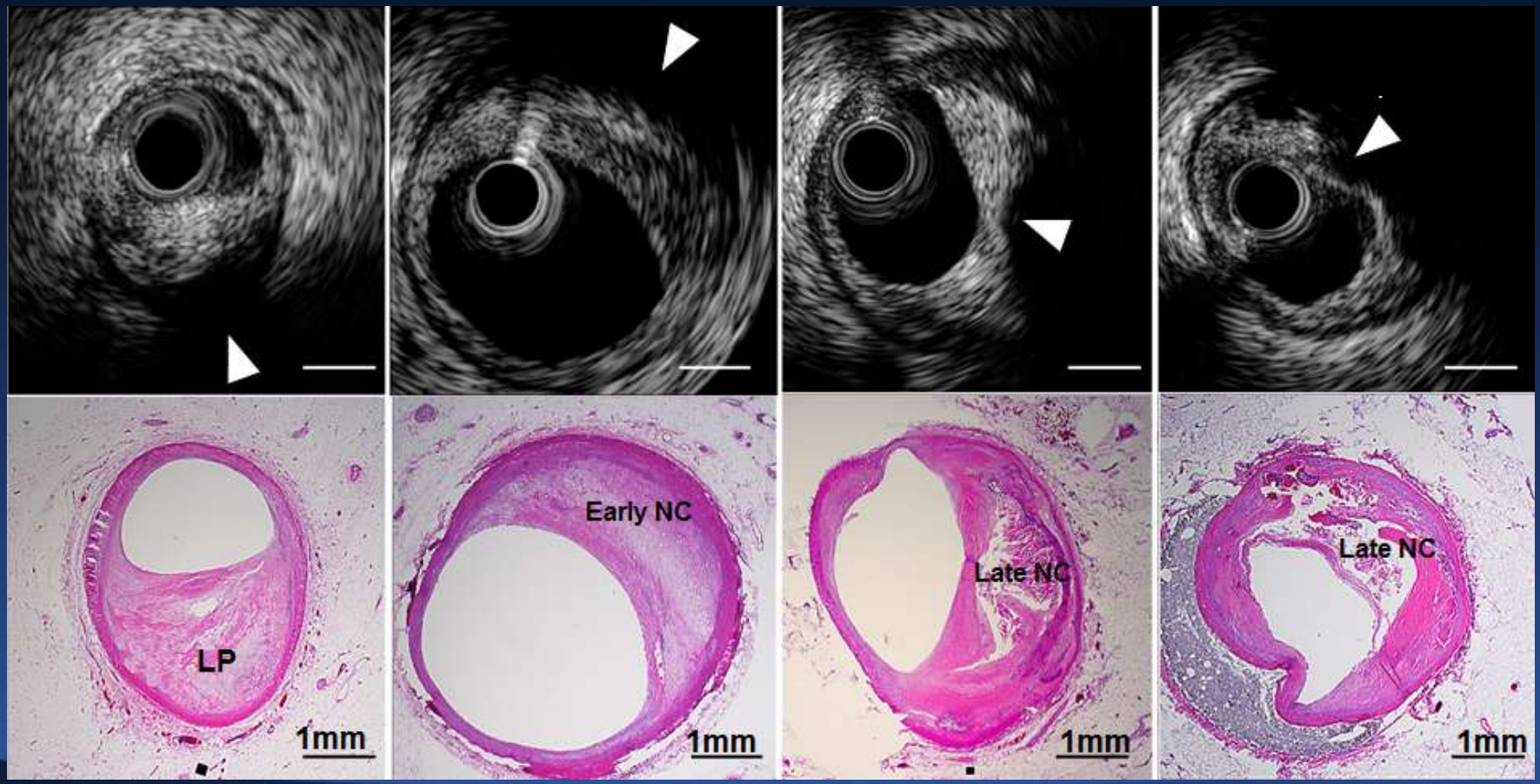






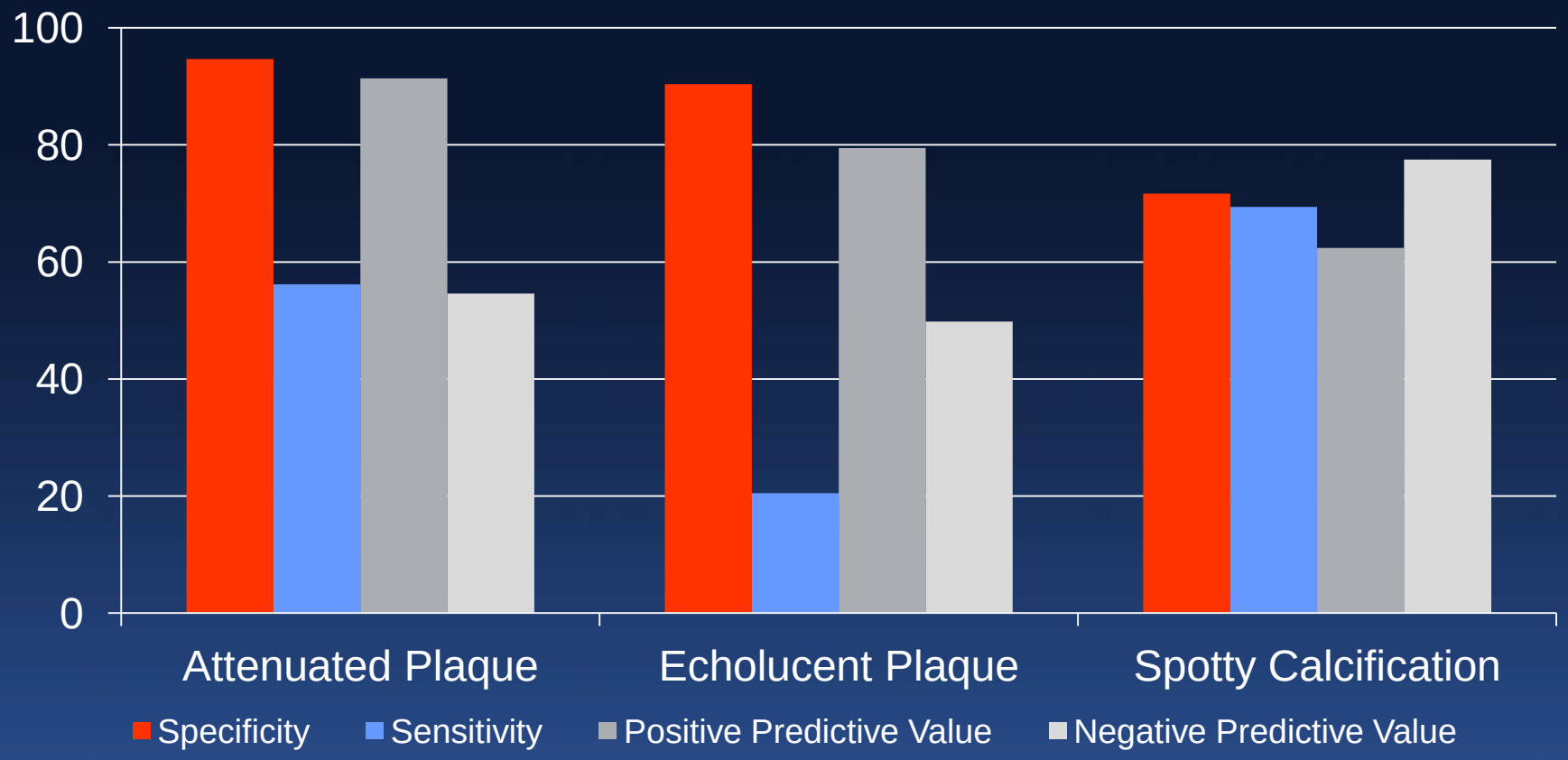
Attenuated Plaque (Superficial, Deep)

- 2,292 2-mm long segments from 151 coronary specimens in 62 autopsy hearts.
- Data obtained in the CDEV3 Study, Gardner et al, JACC Imaging, 2008, sponsored by InfraReDx, Inc.



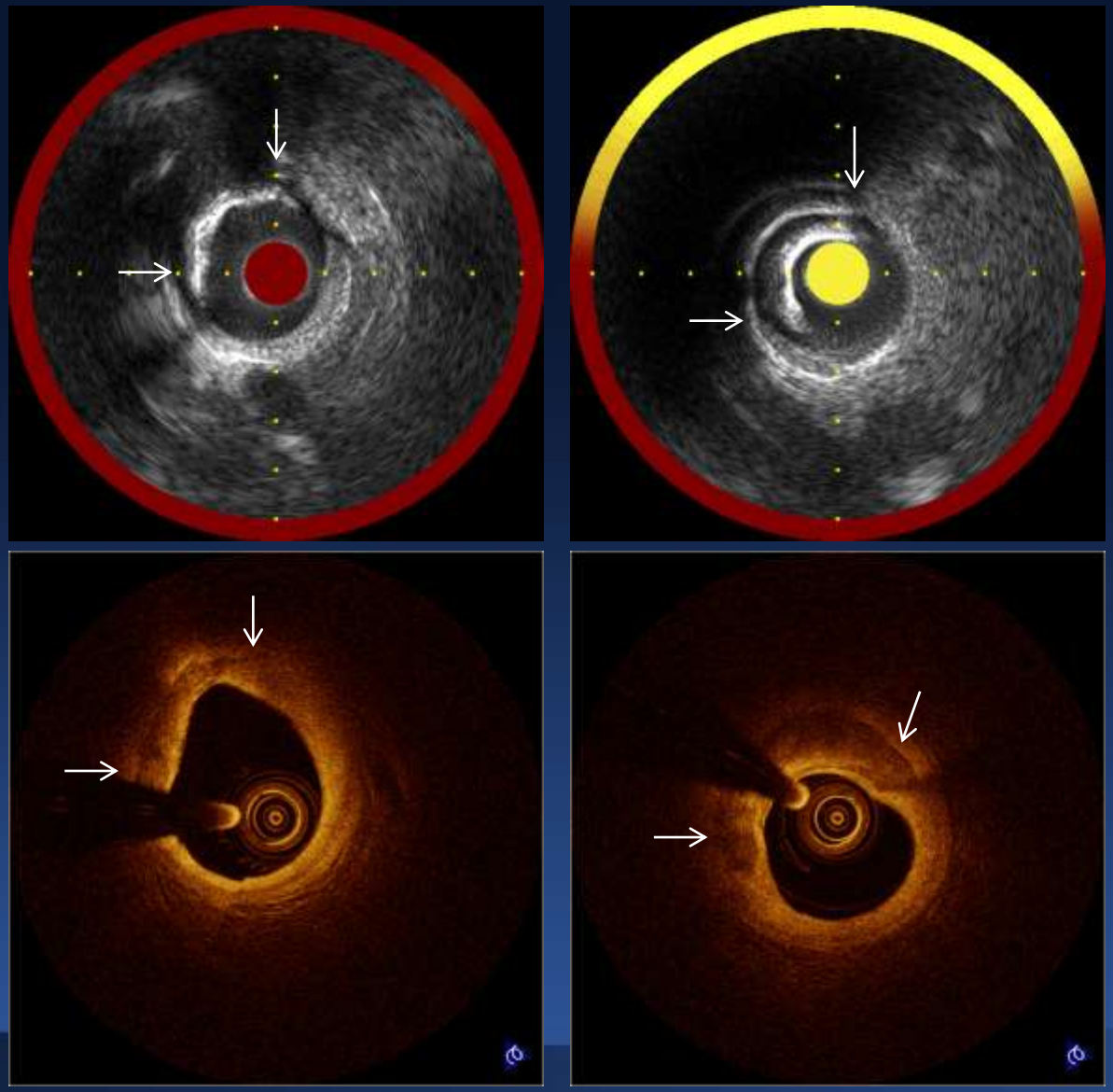
Pu J, et al. JACC *in press*

Diagnostic Summary



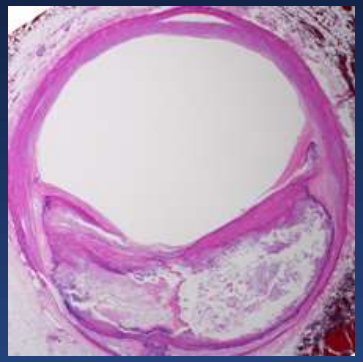
Pu J, et al. JACC *in press*

Different type of Calcified Plaque

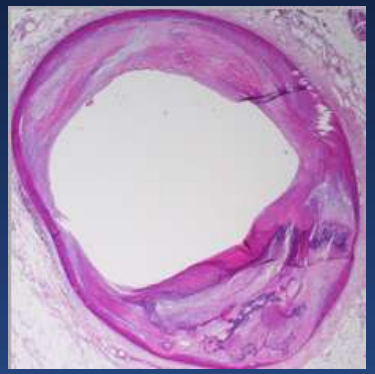


Different type of Calcified Plaque

Necrotic core behind calcium



Calcium Only



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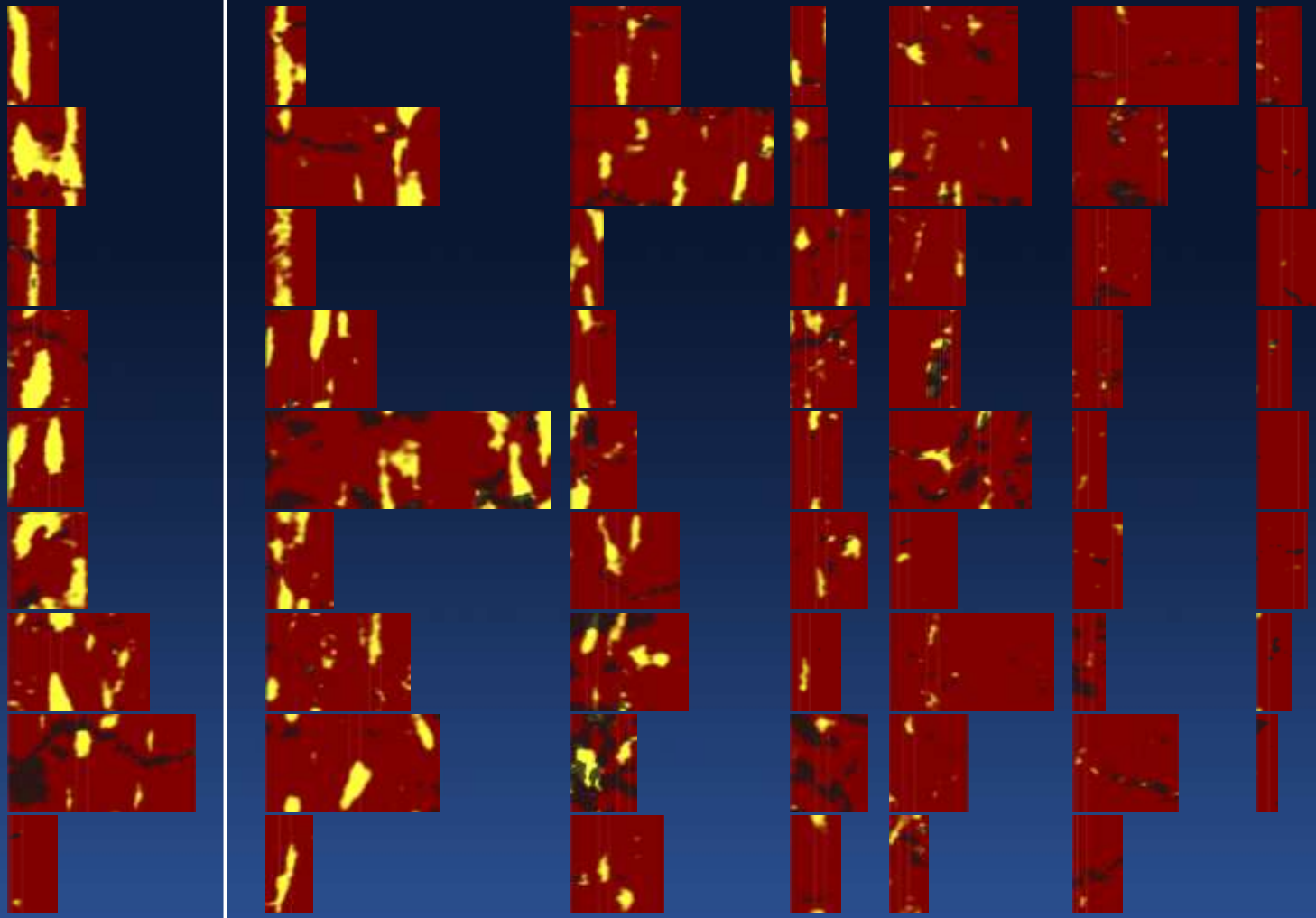
The University Hospital of Columbia and Cornell

NIRS and post-PCI MI



MI

No MI

Goldstein et al. Circ Intv 2011

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Near-Infrared Spectroscopy and Inadequate Flow

STEMI NSTEMI/UAP Stable AP

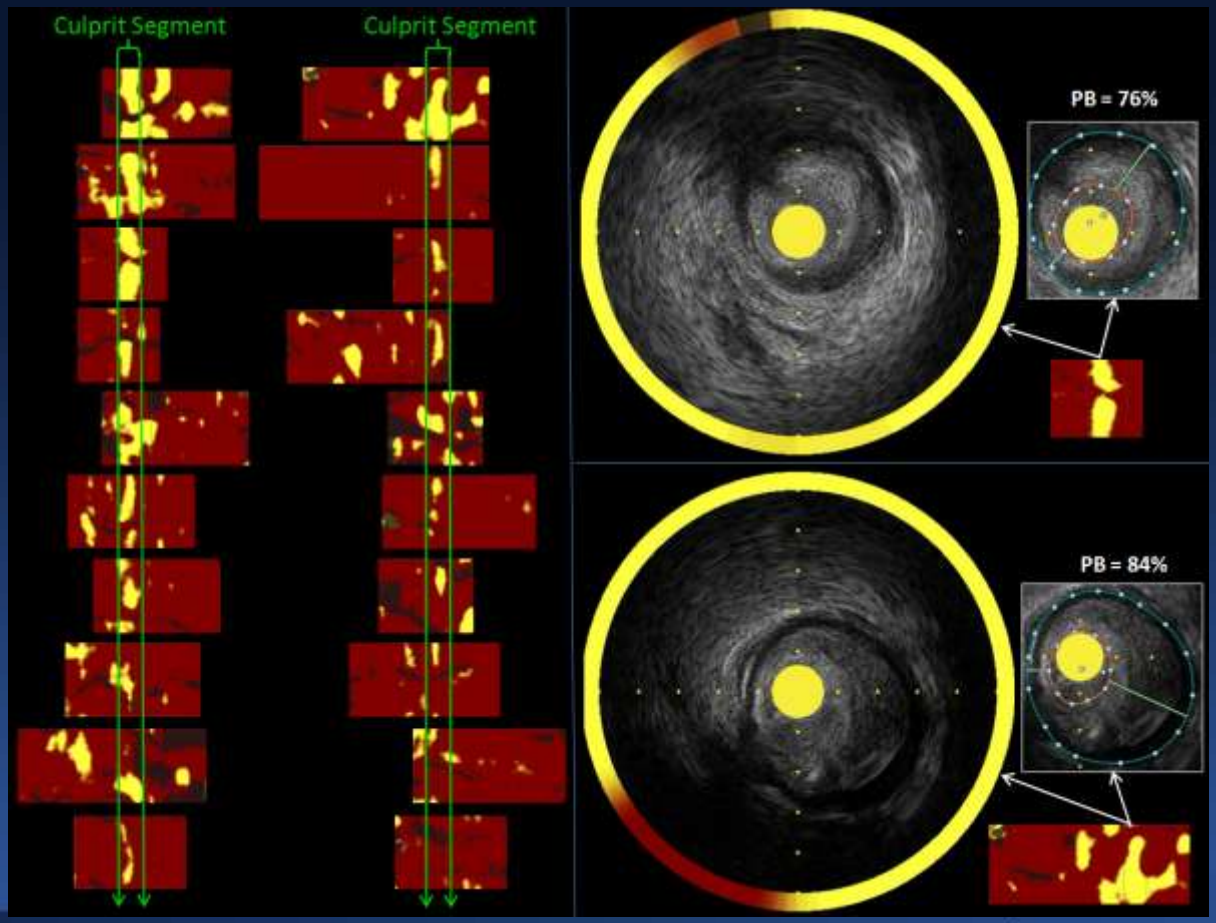
Author	# of pt	Symptom	Morphological Predictor	Endpoint
Goldstein	**62**		LCB I max4mm≥500	Trop or CK-MB>3UNL
Raghunathan	**30**		Lesion LCBI 145 vs 110	CK-MB>UNL

Goldstein et al Circ Cardiovasc Interv 2011;4:429-37, Ragunathan D et al. AJC 2011;107:1613-8

Is there a characteristic signal of lesions that cause STEMI?

Near infrared spectroscopy (InfraReDx) was performed immediately after infarct artery recanalization in 20 pts with STEMI

The NIRS chemograms of all 20 STEMI pts. The culprit segments contain LCP in 19 cases (95%), all with large plaque burden.



Madder RD. JACC Interv 2013

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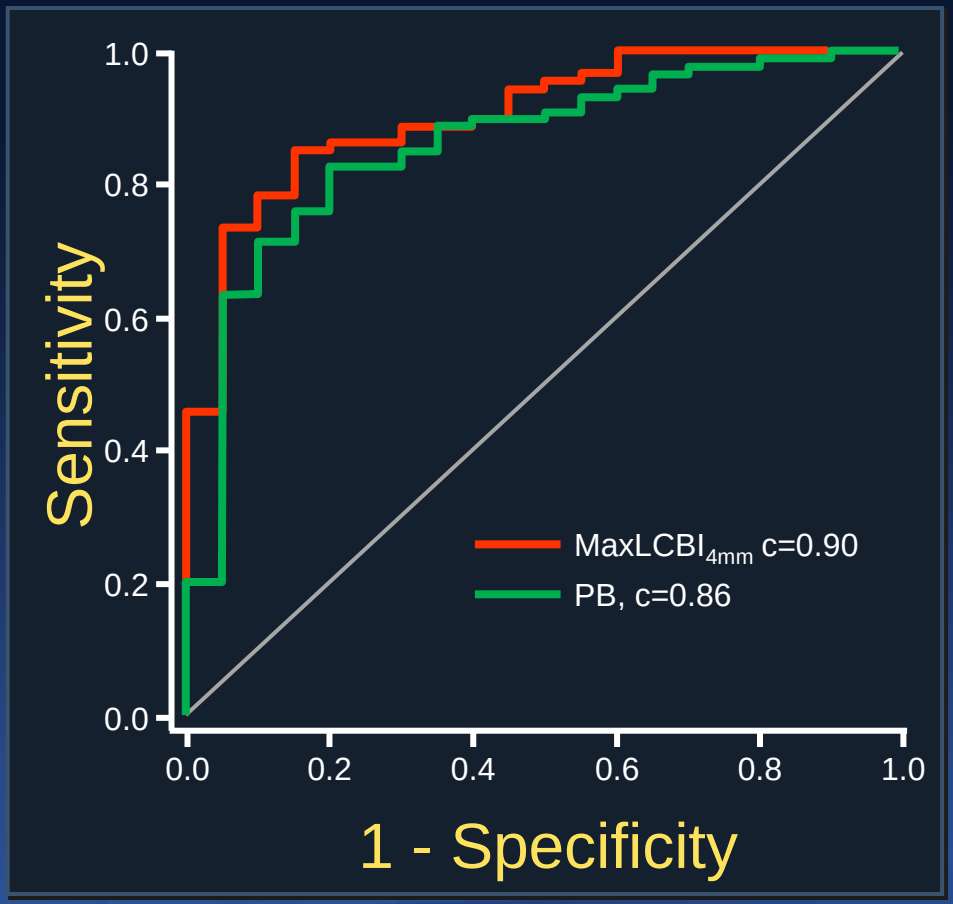
Is there a characteristic signal of lesions that cause STEMI?

Near infrared spectroscopy (InfraReDx) was performed immediately after infarct artery recanalization in 20 pts with STEMI

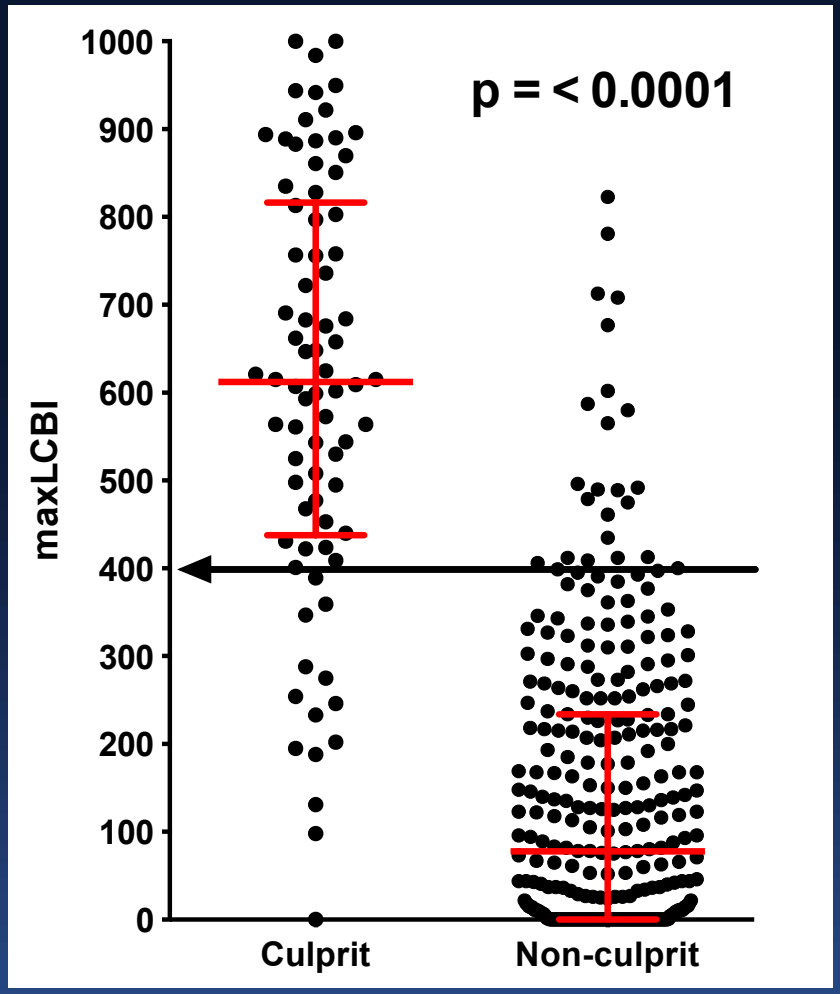
Ability of NIRS ($maxLCBI_{4mm}$) and IVUS (plaque burden and calcification) to distinguish the culprit segment from non-culprit segments of the STEMI culprit vessel:

- AUC for $maxLCBI_{4mm}$ = 0.90
- AUC for plaque burden = 0.86



Madder RD. JACC Interv 2013

STEMI culprit vs. non-culprit segments



Mann-Whitney U test
Median ± interquartile range

STEMI culprit lesions:
$maxLCBI_{4mm}$ = 612 (438-817)

Non-culprit lesions:
$maxLCBI_{4mm}$ = 78 (0-234)

$MaxLCBI_{4mm}$ >400 was present at the STEMI culprit site in 63 of the 78 cases

$MaxLCBI_{4mm}$ >400 was present at the non-culprit site in 22 of the 304 segments

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.

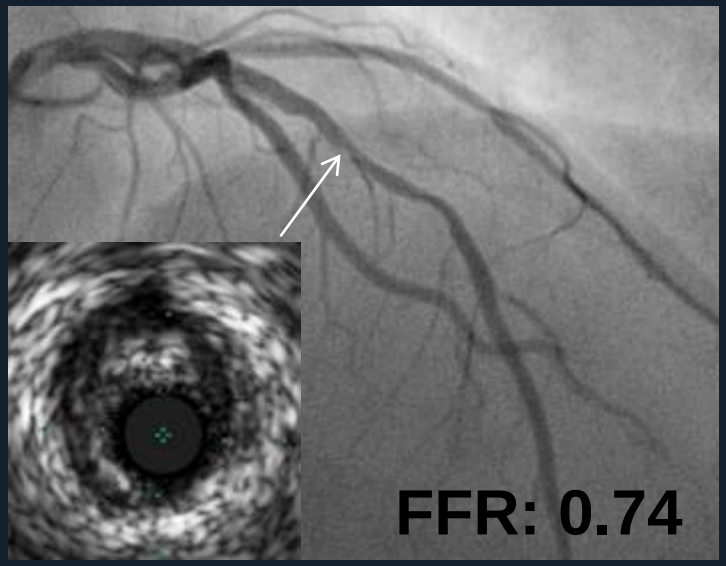
Imaging data analyzed by CRF Core Lab
Data analysis for primary outcome analyzed by MSH independent Core Lab

*Optimal medical therapy for all patients

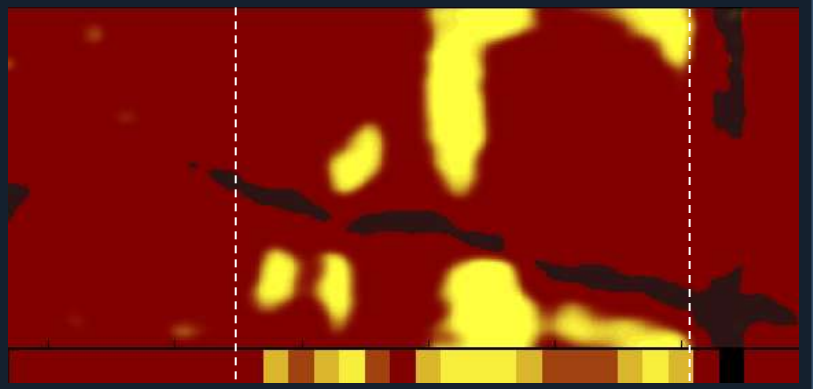
Kini A et al. *JACC* 2013; 62: 21-9.

Case Example

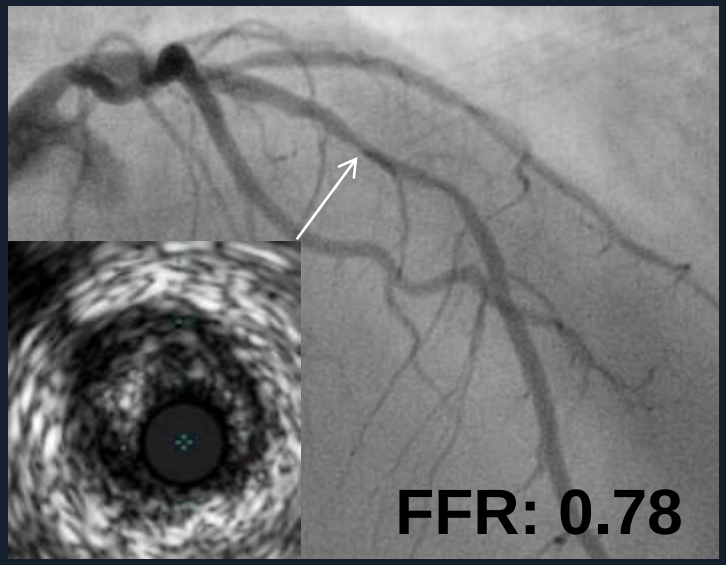
Baseline



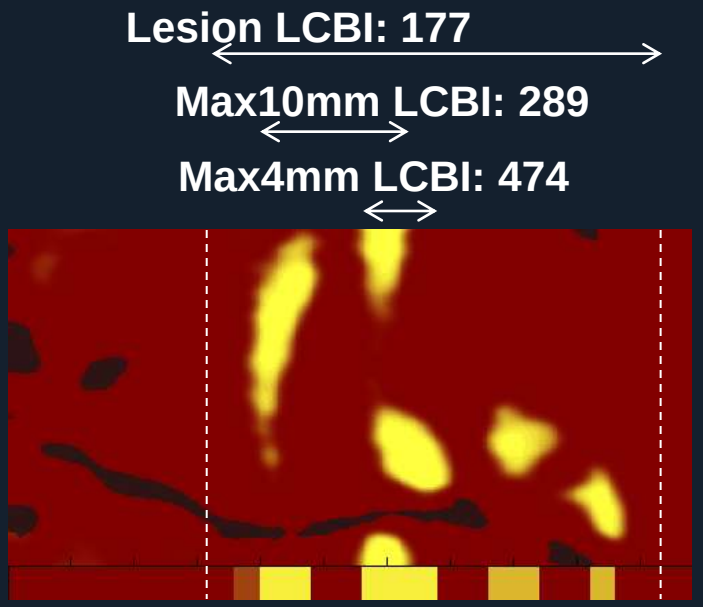
Plaque Area
5.6mm^2



Follow-up

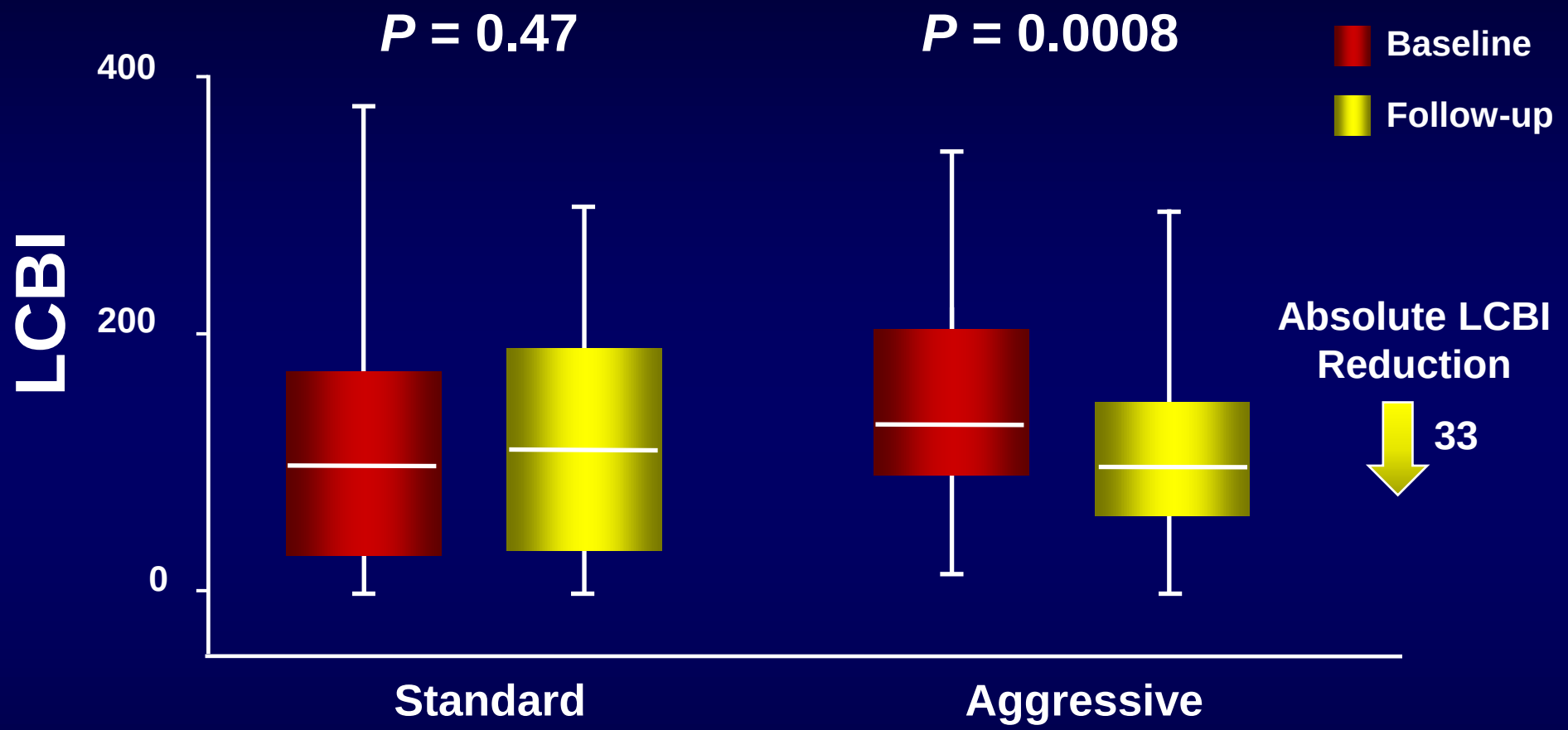


Plaque Area
5.5mm^2



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

Paired Analysis – Lesion LCBI



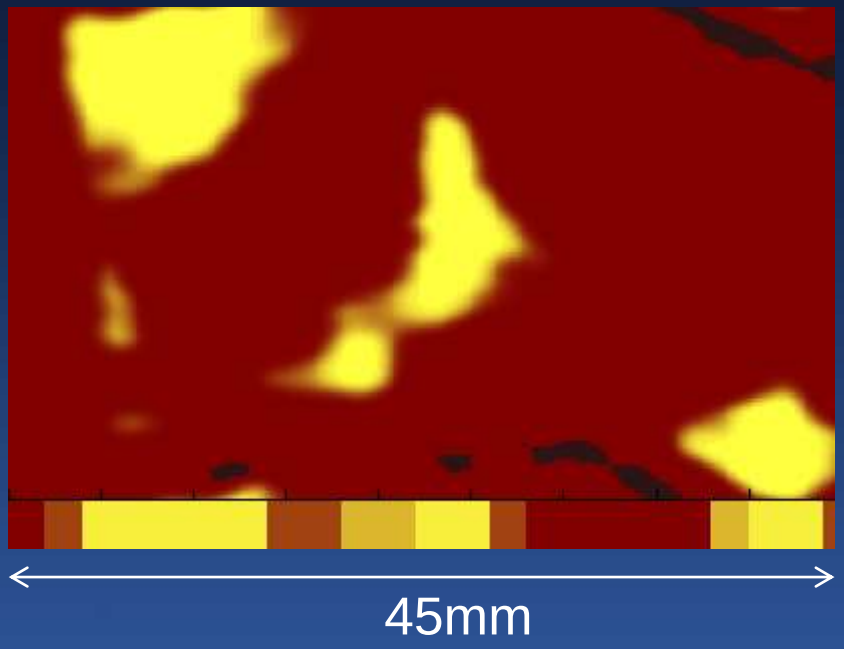
Variable	Standard (n = 43)	Aggressive (n = 44)	*P*
Percent atheroma volume	0.26%	0.24%	0.98

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

Relationship between Lipid Rich Plaque detected by NIRS and Outcomes

- Prospective Single Center Study, 206 patients (ACS47%)
- 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

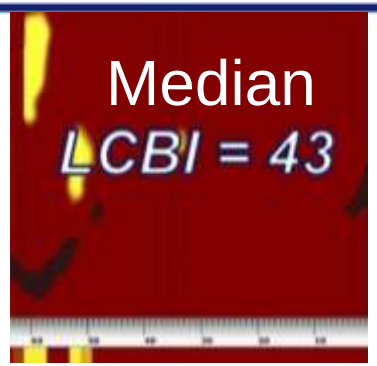


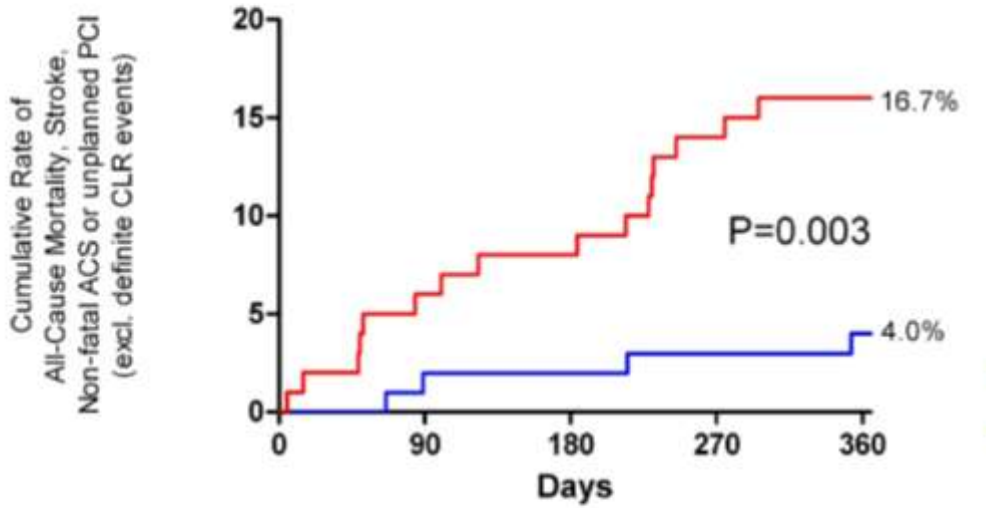
Oemrawsingh RM et al, *ESC2003*

Relationship between Lipidic Plaque detected by NIRS and Outcomes

Primary endpoint

Erasmus MC



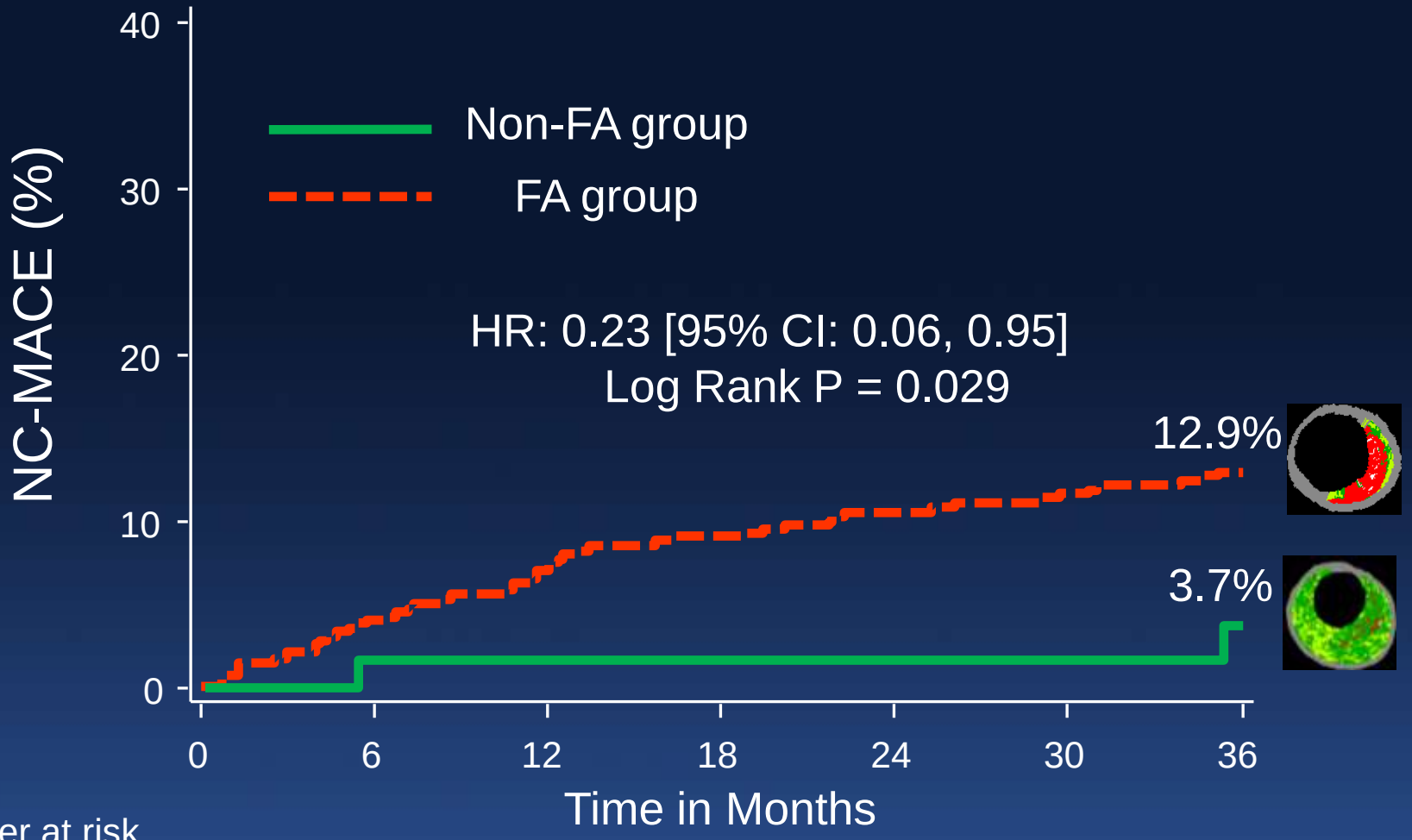


No. at Risk					
LCBI < Median	101	99	99	97	91
LCBI ≥ Median	102	94	92	86	83

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

Oemrawsingh RM et al, *ESC2003*

PROSPECT: Non-FA Lesions

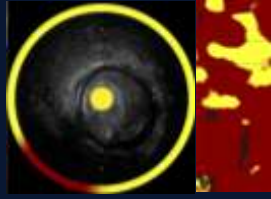


Number at risk

Non-FA group	67	62	61	61	60	57	29
FA group	542	485	463	443	424	406	248

Dohi et al, *JACC Img* 2013; 6: 908-16.

PROSPECT II Study



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

↓

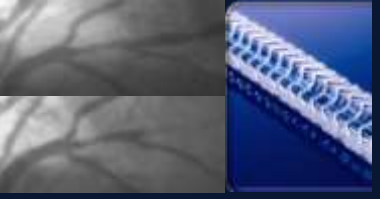
3-vessel imaging post PCI

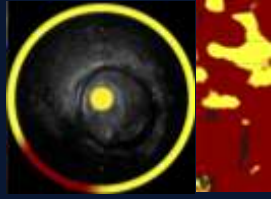
Culprit artery, followed by non-culprit arteries

Angiography (QCA of entire coronary tree)

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

↓





PROSPECT II Study
PROSPECT ABSORB RCT

900 pts with ACS after successful PCI

3 vessel IVUS + NIRS (blinded)

≥1 IVUS lesion with ≥70% plaque burden present?

Yes
(N=300)

No
(n=600)

R
1:1

ABSORB BVS + GDMT (N~150)

GDMT
(N=150)

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

Clinical FU for ≥3 years

CARDIOVASCULAR RESEARCH FOUNDATION
A Passion for Innovation

COLUMBIA UNIVERSITY MEDICAL CENTER
NewYork-Presbyterian

PI: Dr.Ron Waksman

"To evaluate the relationship between non-obstructive lipid-rich plaque and a new coronary events"

Index
N=9000

Suspected Index Culprit Lesion **-or-** Index Culprit Lesion

BLINDED

Index Non Culprit Artery (IVUS is un-blinded)

Send to Core Lab

Core Lab will Un-blind NIRS data

BLINDED

N= 3000
Large LRP
(MaxLCBI4mm ≥ 250)

2yr Follow-Up

BLINDED

N= 6000
Small/No LRP
(MaxLCBI4mm < 250)

N= 3000

2yr Follow-Up

N= 3000

Terminate upon Discharge

LRP CLINICAL STUDY

Summary

1. NIRS uses scattering and identify the absorption pattern in relation to the wave length which is unique for each plaque type.
2. NIRS shows good reproducibility for evaluation of regression lipid rich plaque (LRP) in short time period (8 weeks).
3. Large prospective studies are on-going to evaluate the natural history of LRP and feasibility of aggressive therapy for these lesions.