NIRS: Fundamentals and Clinical Applications

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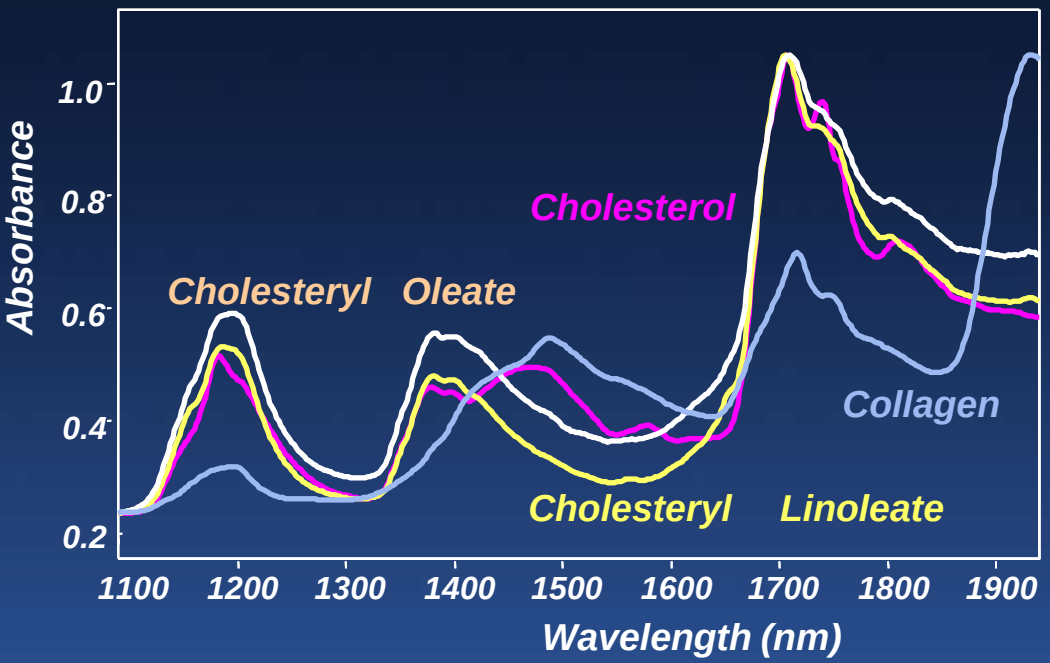
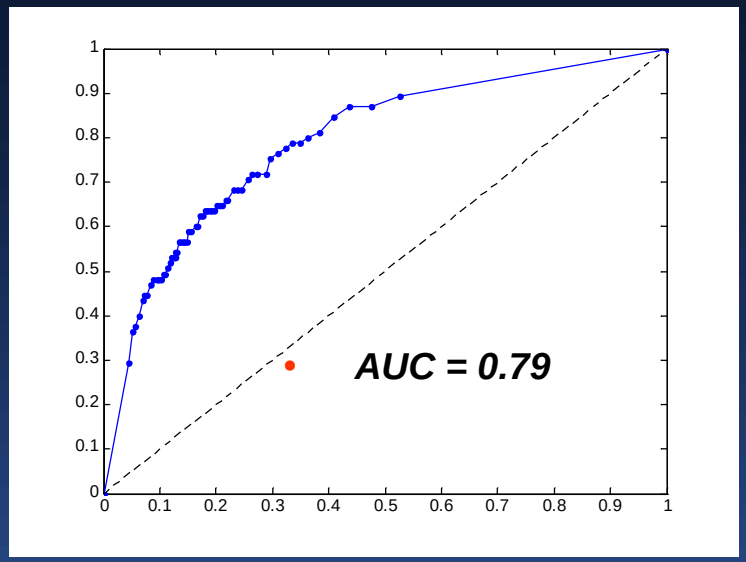
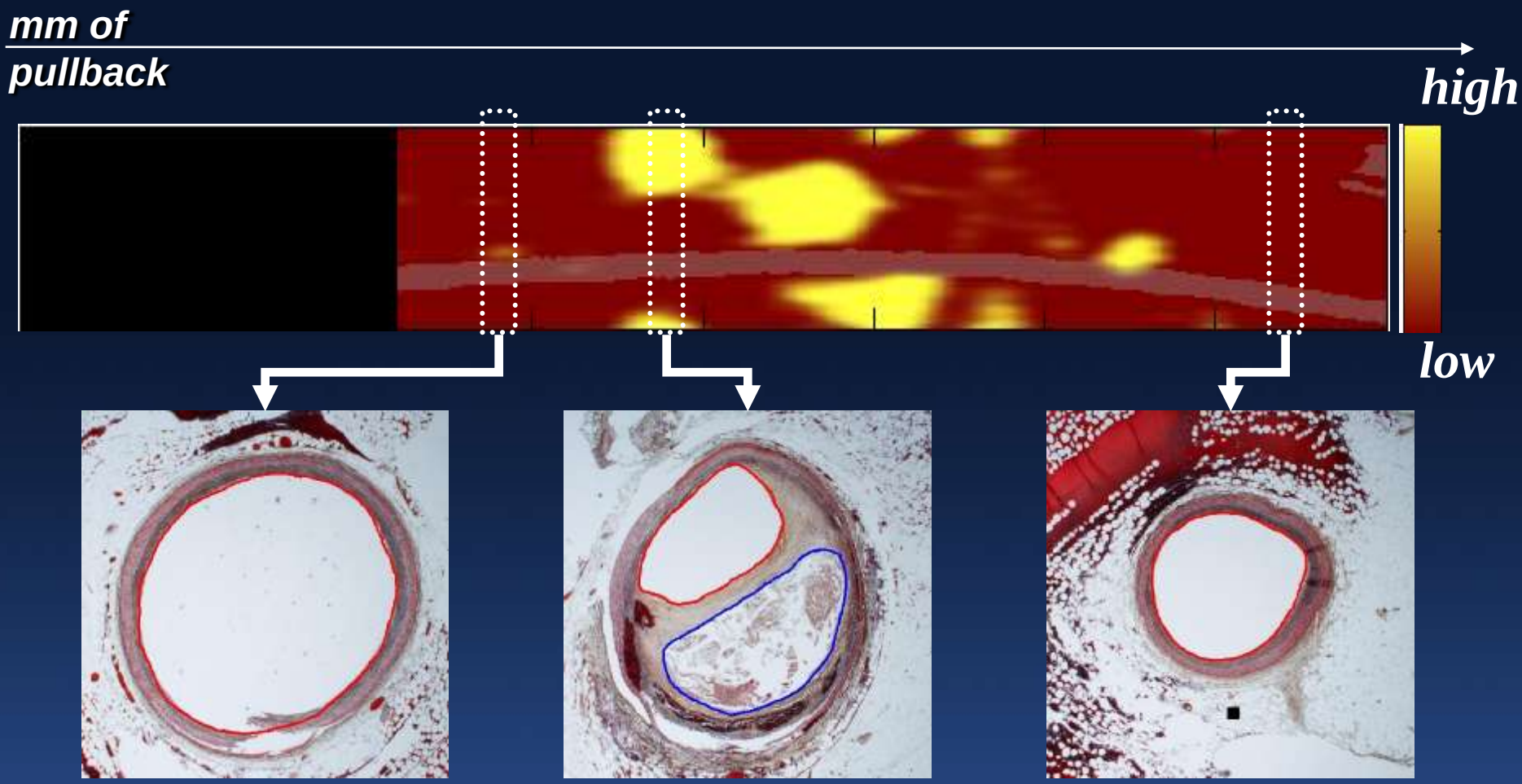
Identification lipid core plaque (LCP) is based on distinction of cholesterol spectral features. ROC Analysis of validation of NIR spectroscopy in 51 autopsy hearts for detection of confluent [>0.2mm thick and >60° in circumference] and relatively superficial necrotic core [overlying fibrous cap thickness <0.45mm])






mm of
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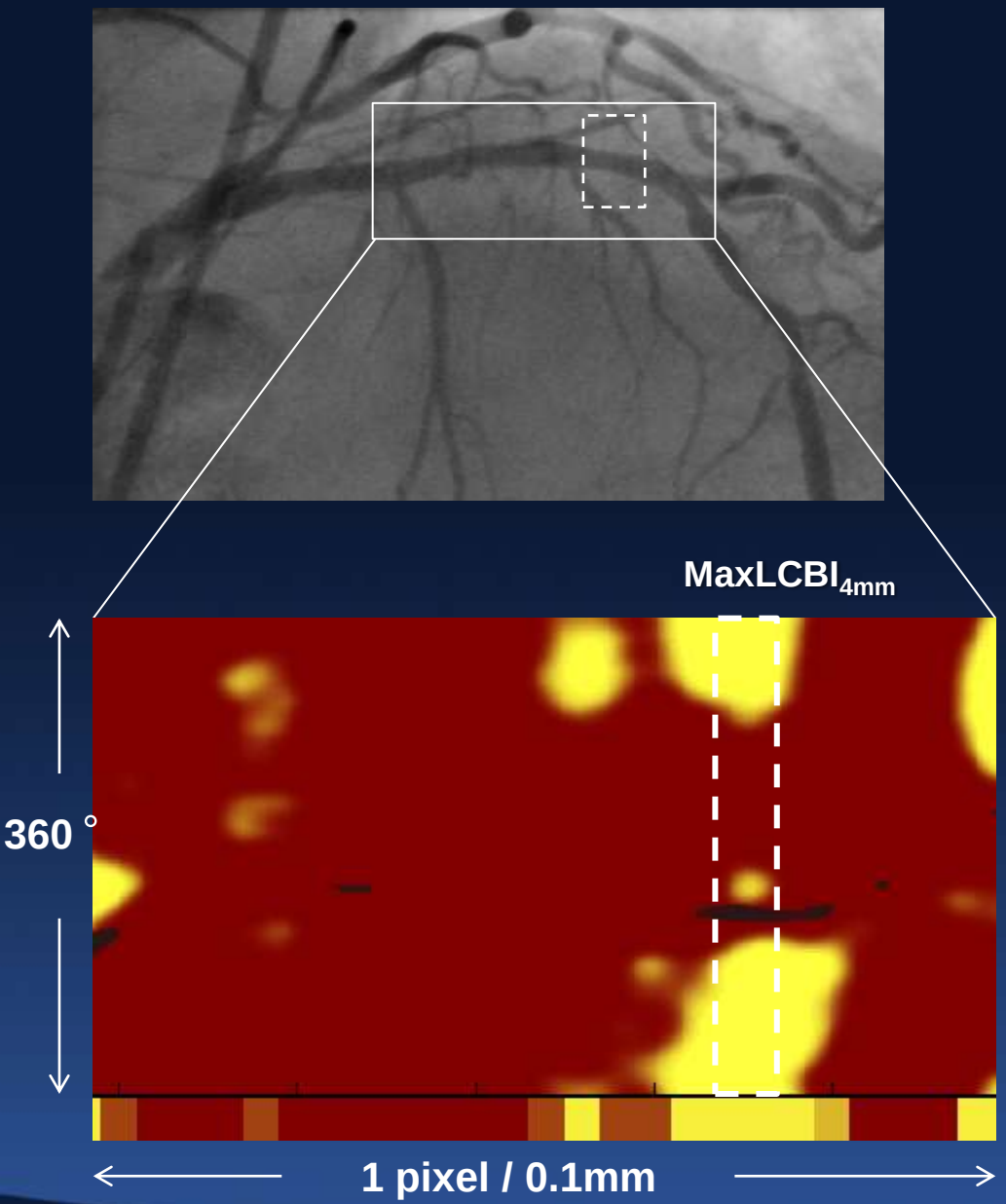
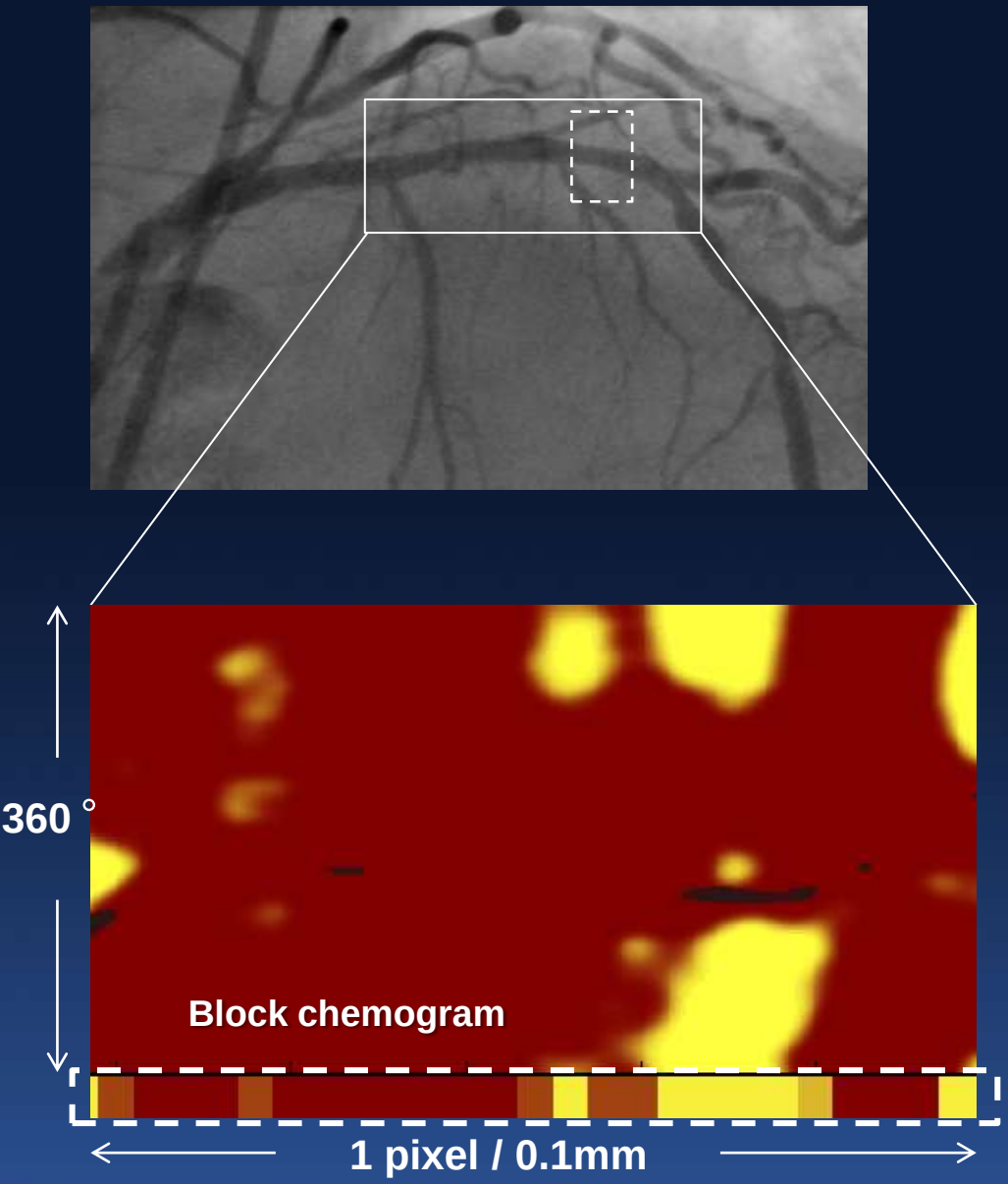


Chemogram

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

***MaxLCBI$_{4mm}$** = LCBI in 4 mm segment with highest lipid content*

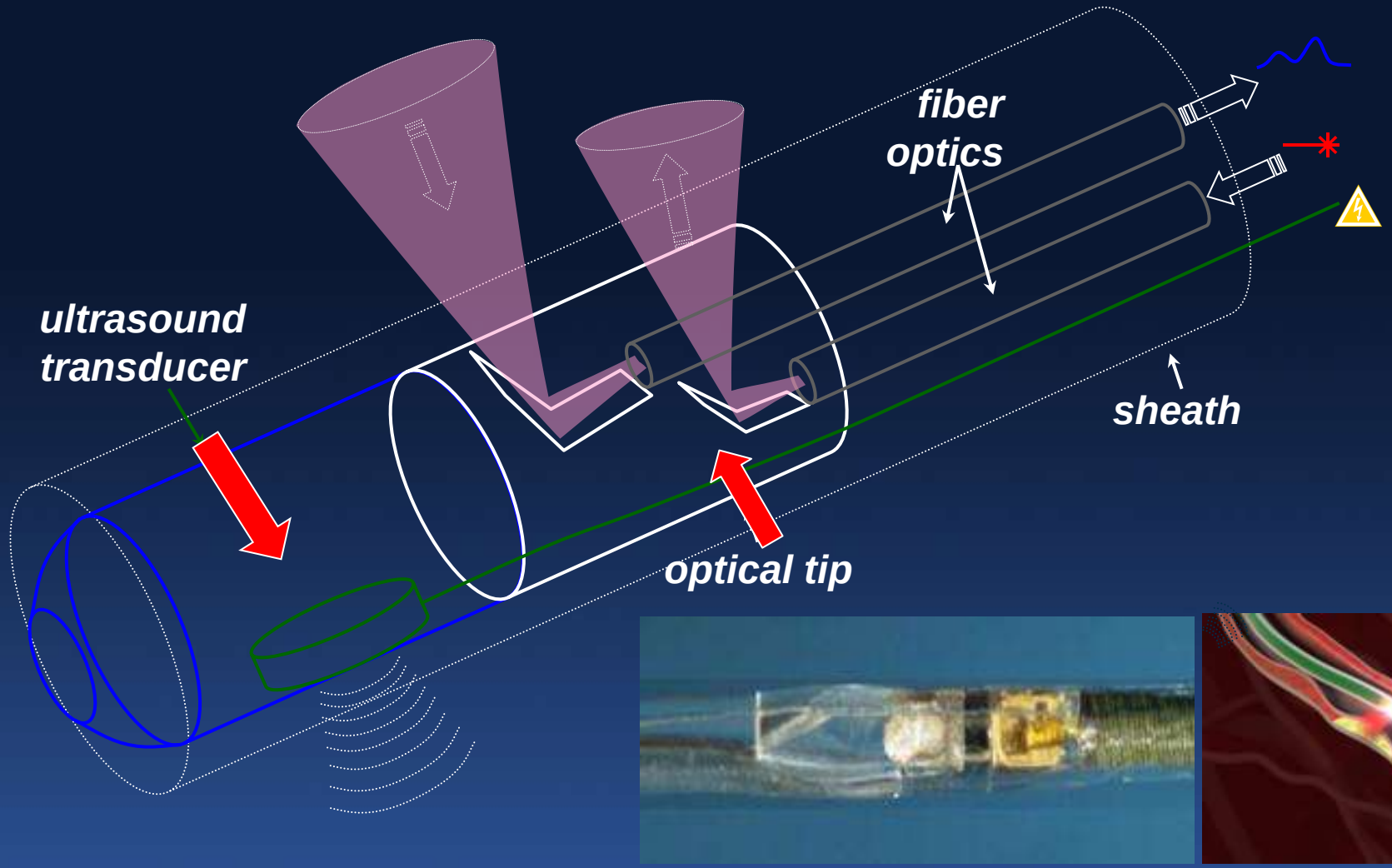
Block Chemogram

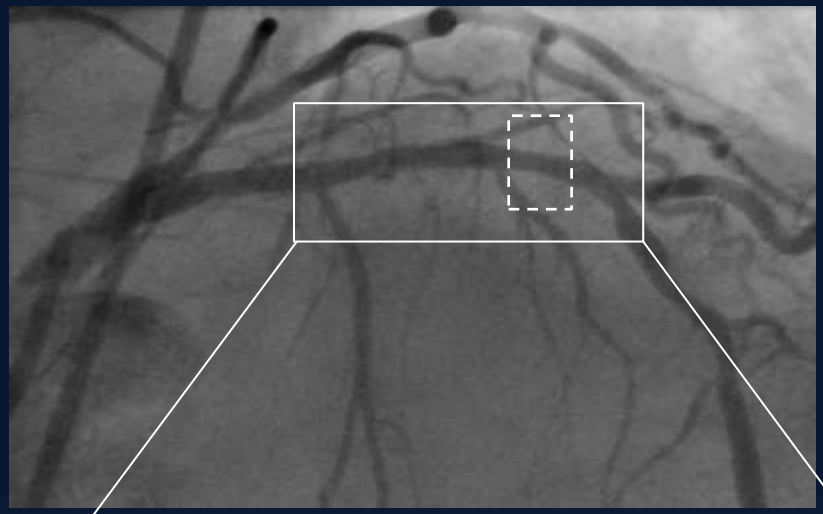


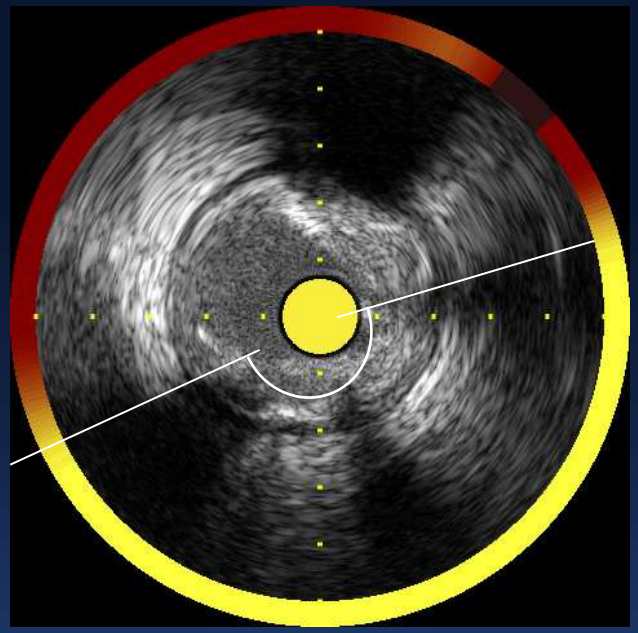
Summary metric of the probability that lipid rich plaque is present for all measurements using the top 10th percentile pixel information (i.e. the 90th percentile value) of the corresponding 2-mm "chemogram" segment.

- ***Red:*** **probability *<0.57***
- ***Orange:*** ***probability 0.56-0.84***
- ***Tan:*** ***probability 0.84-0.98***
- ***Yellow:*** ***probability >0.98***

Combined NIRS-IVUS Catheter





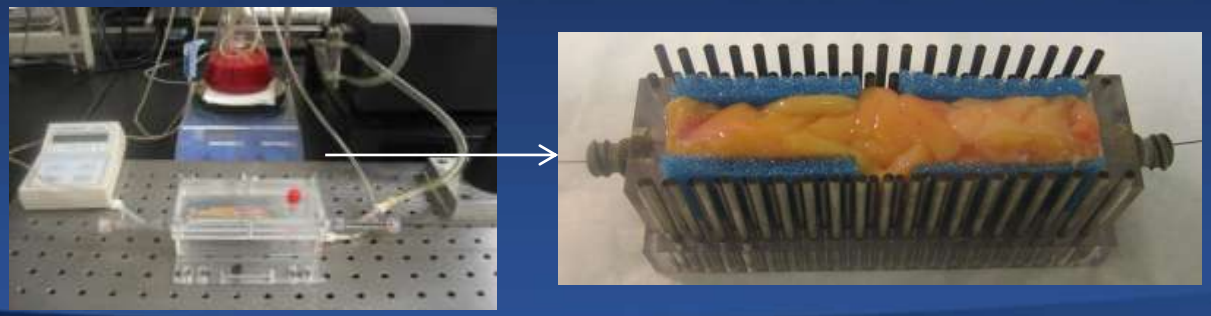


360 °

1 pixel / 0.1mm

IVUS vs Histopathology (*1,943 2-mm long segments from 103 coronary arteries from 56 autopsied hearts)*

- Human coronary specimens were obtained over a 2-year period from autopsied pts.
- Hearts were received within 48 hrs after death, maintained on ice at 4° C, and imaged within 96 hrs after death.
- The major coronary arteries were harvested following in situ angioscopic screening to exclude occluded segments impassable by the IVUS catheter. Sidebranches were ligated; adventitial fat surrounding the arterial segments was kept intact.
- Each artery was mounted in a unique custom fixture with vertical guideposts at 2-mm intervals to be used as reference points when comparing imaging versus histopathology. Both ends of the artery were attached to luer connectors that allowed fluid flow and catheter entry. A varistaltic pump supplied pulsatile flow at 60 cycles/min and a flow rate of approximately 130 mL/min with pressure inside the artery maintained at physiologic levels (80-120 mmHg) at 37.0° C.

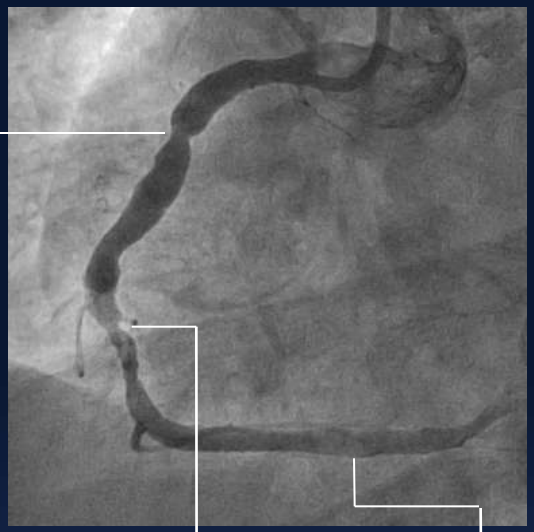


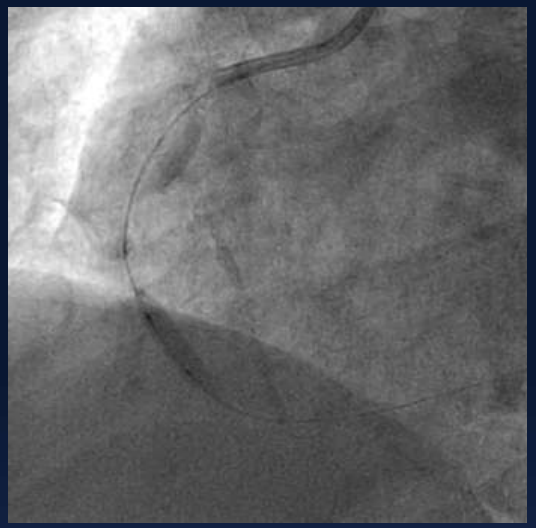
Gardner et al, JACC Cardiovasc Imaging 2008;1:638-48

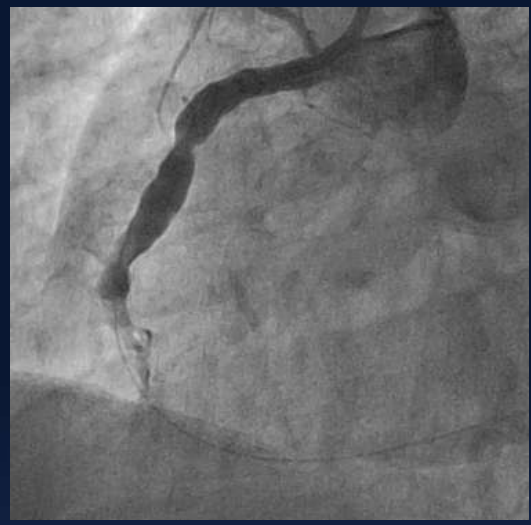
Factors affecting detection of a fibroatheroma (FA) by IVUS or NIRS

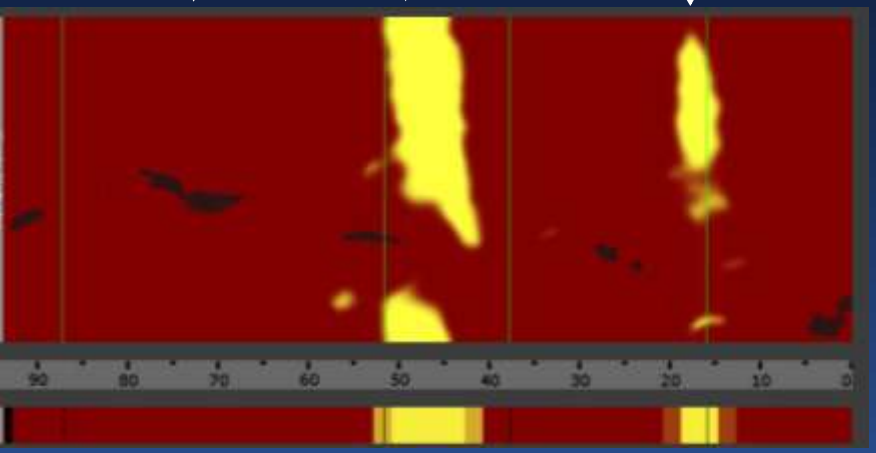
IVUS Attenuation		NIRS-Lipid Rich Plaque	
False Positive (Non-FA with attenuation)	False negative (FA without attenuation)	False Positive (Non-FA with lipid rich plaque)	False negative (FA without lipid rich plaque)
Large lipid pool	Calcification	PIT	Focal FA (≤2mm
	Focal FA (≤2mm)	Fibrocalcific plaque	Smaller plaque burden
	Large lumen	Larger lipid pool	Less necrotic core
	Smaller plaque burden	Larger plaque burden	
	Less necrotic core		
	Early stage FA		

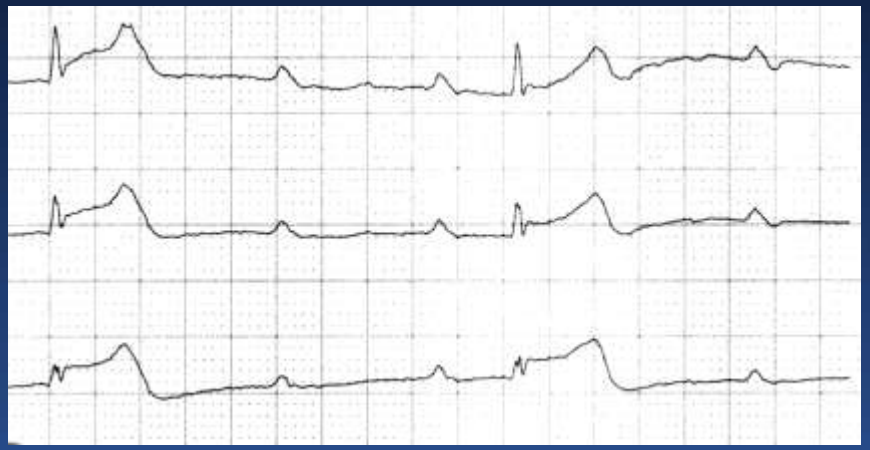
Kang. Unpublished



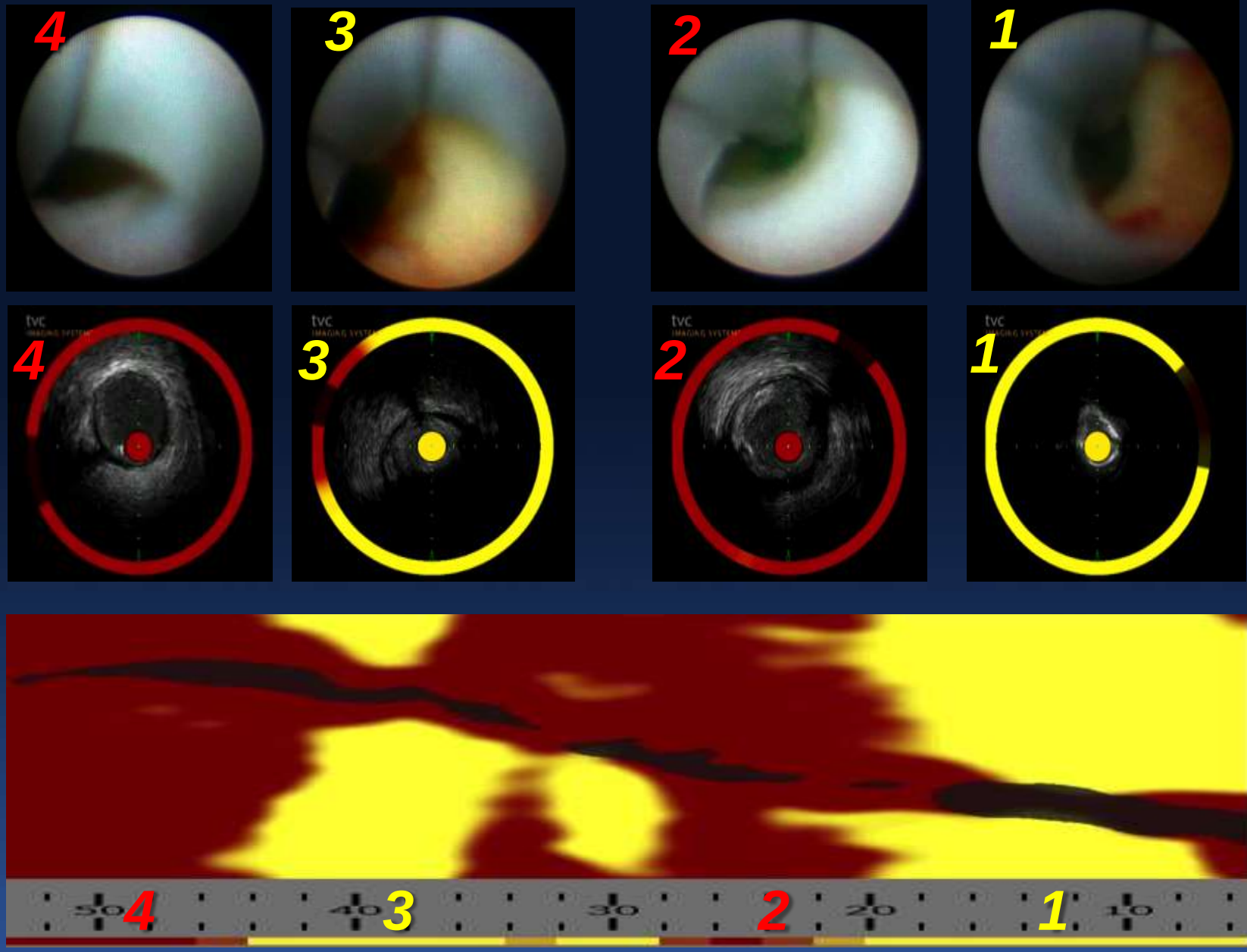








Goldstein et al. JACC Cardiovasc Imaging. 2009;2:1420-4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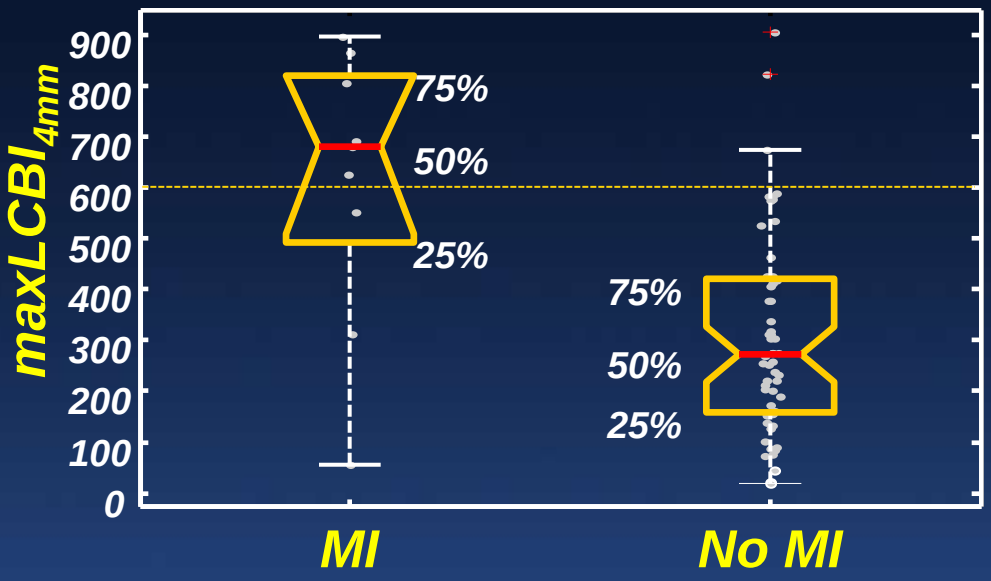
COLOR Registry - I

62 pts were studied pre-PCI using NIRS. Peri-procedure MI (cTnI >3x normal) occurred in 9 pts.

Predictors	RR	p
maxLCBI$_{4mm}$ >500	12.0	0.0002
LDL >100mg/dL	5.4	0.03
Angiographic complex plaque	3.5	0.15
Angiographic DS >75%	3.1	0.14

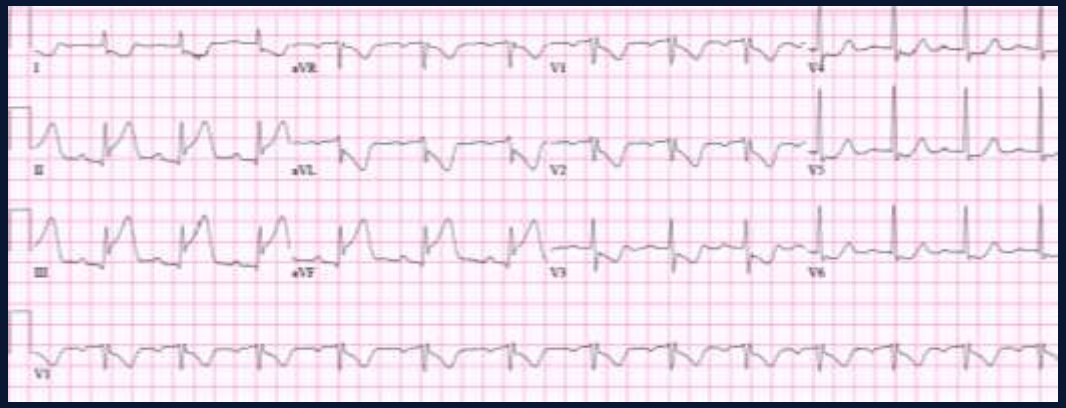


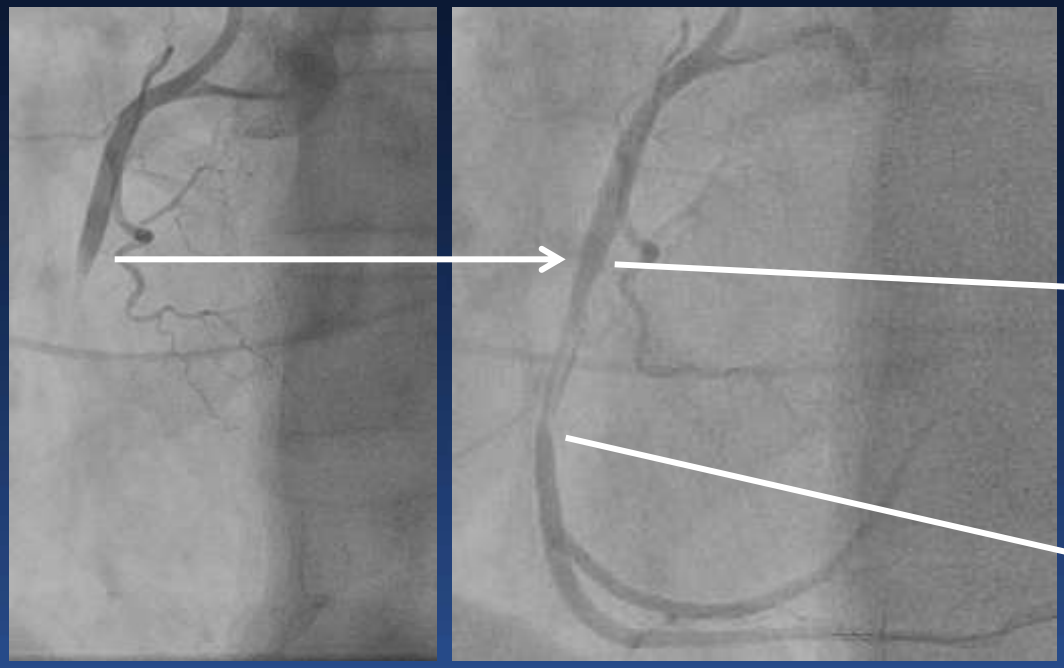
Goldstein et al. Circ Cardiovasc Interv 2011;4:429-37

COLOR Registry - II

Peri-procedural MI - defined as an elevation >5 ✕ the ULN for either CPK-MB or Troponin I occurred in 21.6% of 88 pts with normal baseline biomarkers

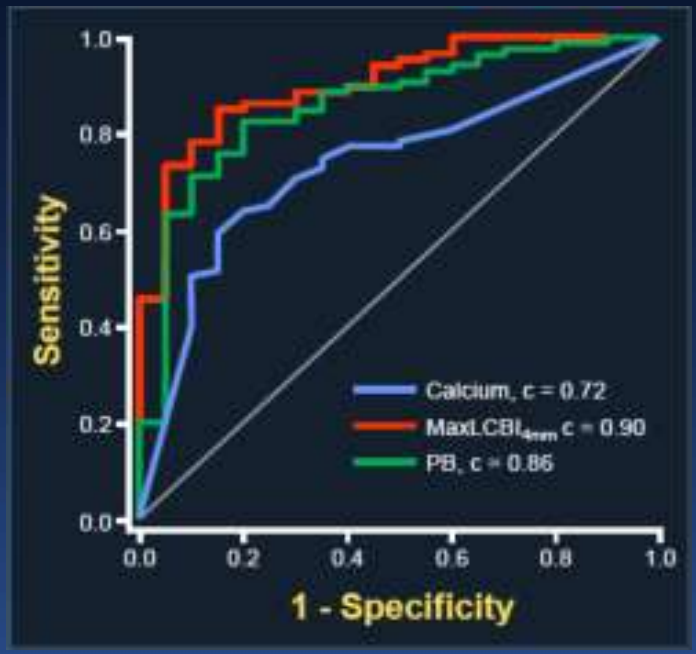
- *No differences in clinical or angiographic variables*
- *The best cut-off of $maxLCBI_{4mm}$ for detecting peri-procedural MI was 524 (AUC=0.672) with a specificity of 63% and a sensitivity of 78%.*
- *Peri-procedural MI occurred in 17 of 69 pts (24.6%) with $maxLCBI_{4mm}$ <500 compared with 12 of 19 pts (63.2%) with $maxLCBI_{4mm}$ ≥500 (p=0.002). The relative risk of peri-procedural MI for pts with $maxLCBI_{4mm}$ ≥500 was 5.2 (95% CI 1.8 to 16.2, p=0.002).*





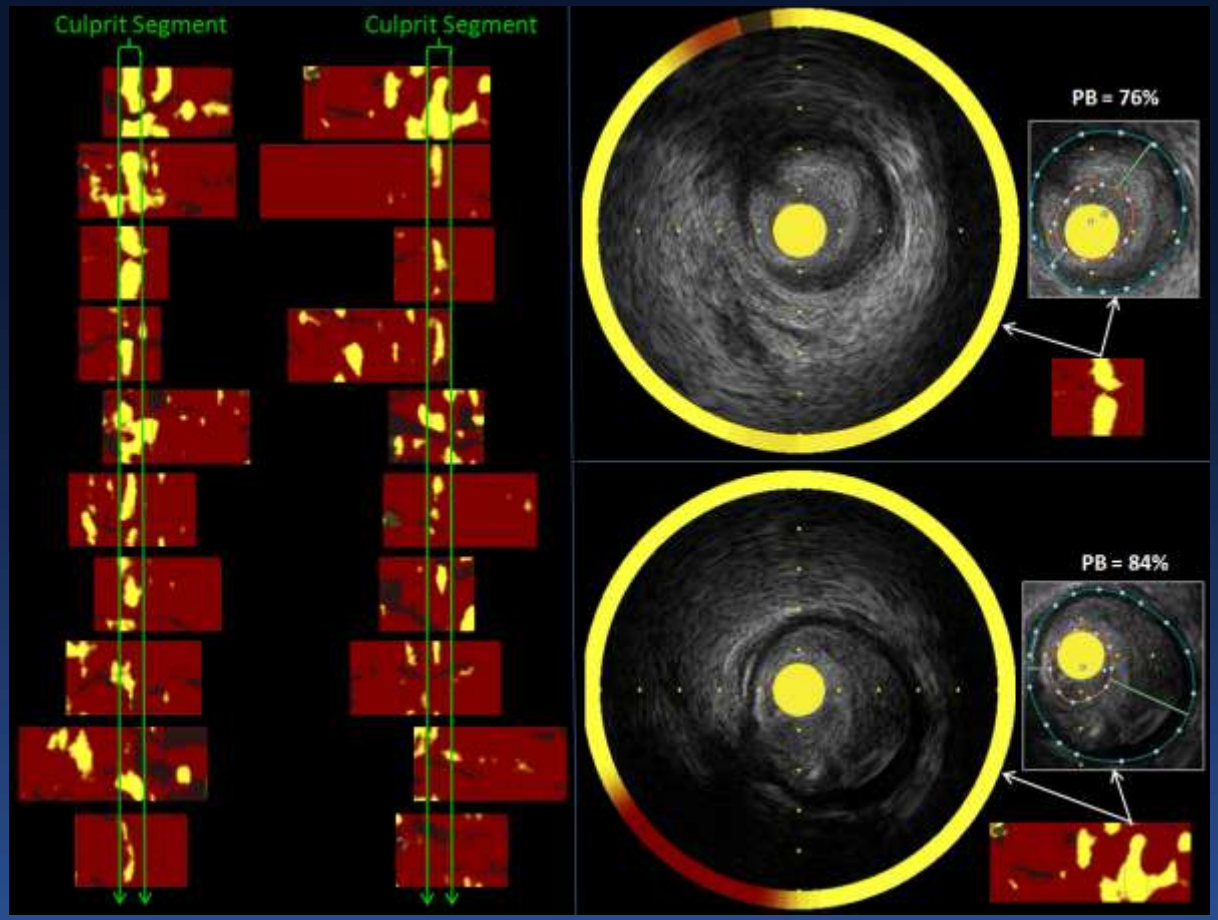
IVUS and NIRS were performed pre-PCI in 20 STEMI pts. Culprit lesions were compared to nonculprit segments in the same artery and to autopsy control segments.

	STEMI Culprit	STEMI Non-culprit	Histology
#	20	87	279
MaxLCBI$_{4mm}$	524 (445, 821)	90 (6, 265)	6 (0, 88)
Plaque burden (%)	64±14	44±15	44±14
Calcification (%)	89	38	0



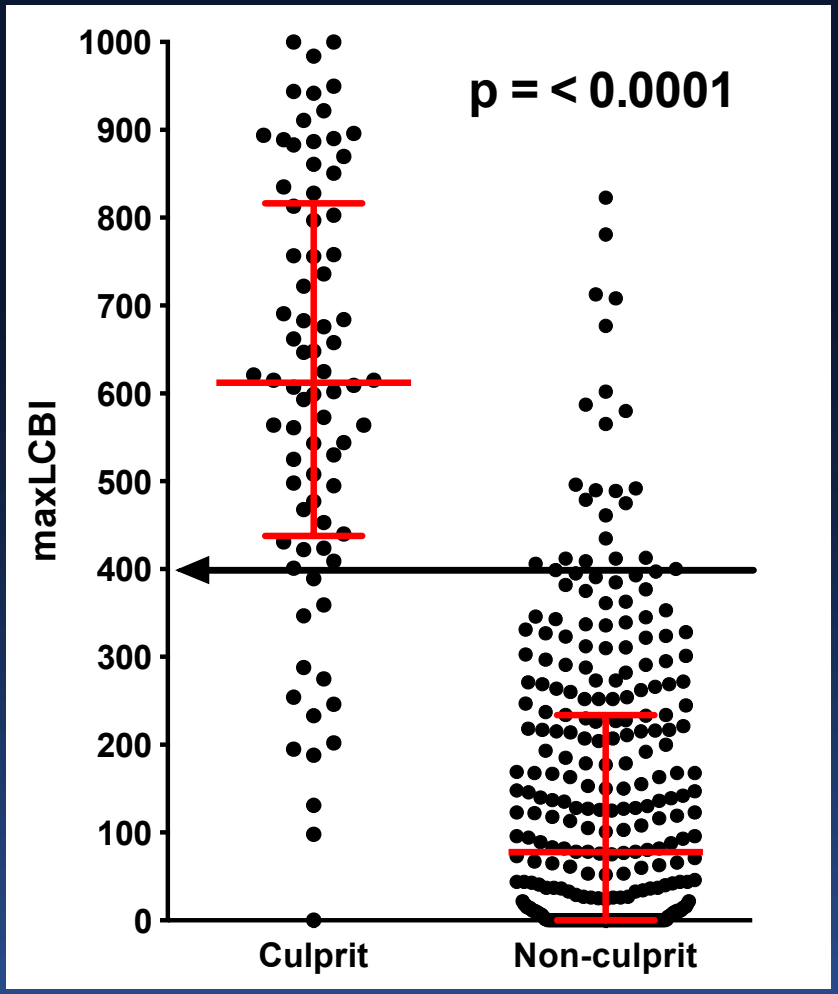
Madder et al, JACC Cardiovasc Interv 2013;6:838-46

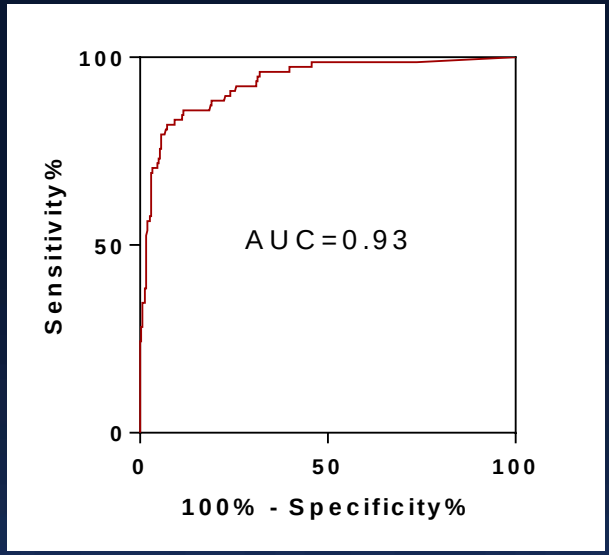
The culprit segments contain lipid rich plaque in 19 of 20 STEMI cases (95%), all with a large plaque burden.



Madder et al, JACC Cardiovasc Interv 2013;6:838-46

NIRSTEMI-II: STEMI culprit vs. non-culprit segments (n=78)

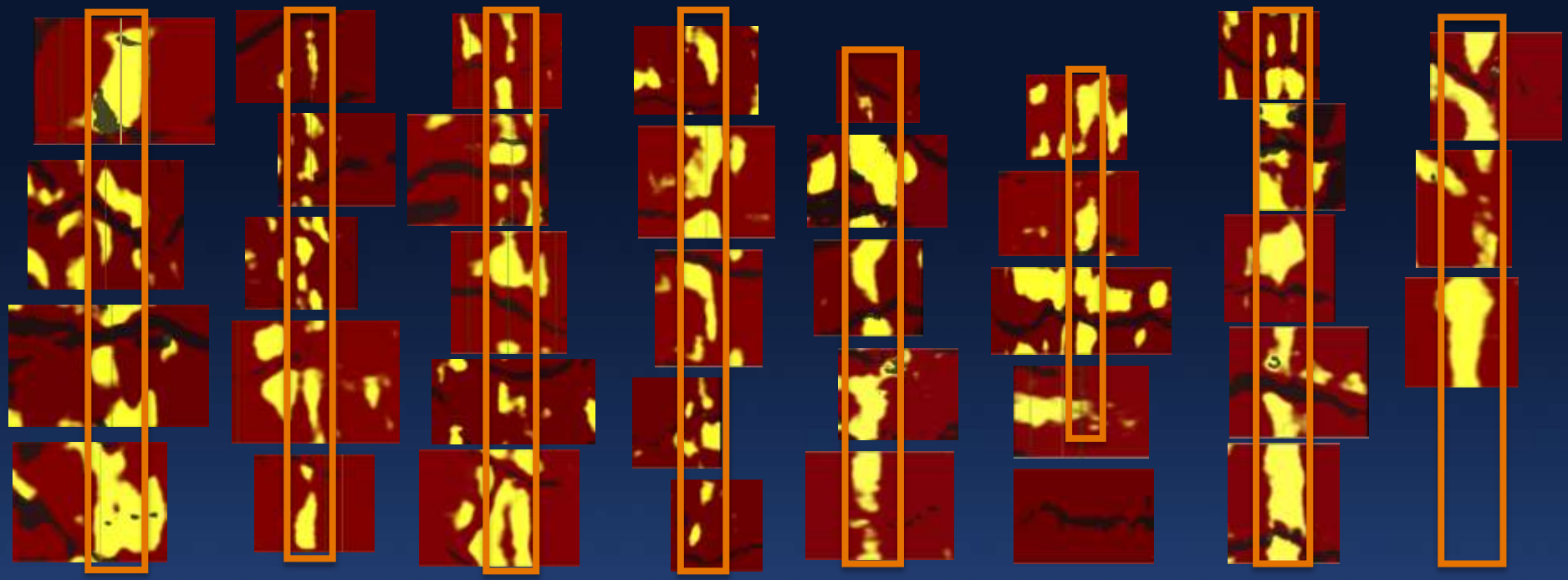




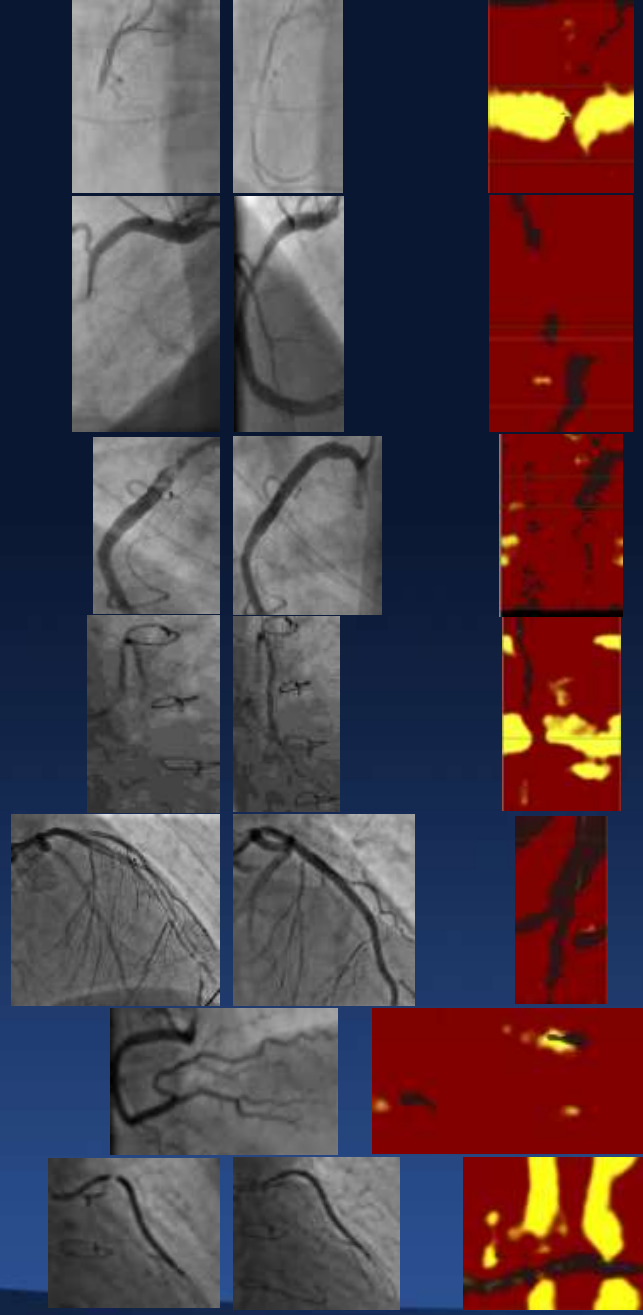
Cut-off: MaxLCBI$_{4mm}$ >400:
Sensitivity = 82%
Specificity = 93%

Madder et al. J Am Coll Cardiol 2013;62:B201

NIRSTEMI-II: Culprit segments (N=37)



Madder et al. J Am Coll Cardiol 2013;62:B201



Lipid Rich Plaque

Stent Thrombosis

Calcified Nodule

Lipid Core In SVG

SCAD

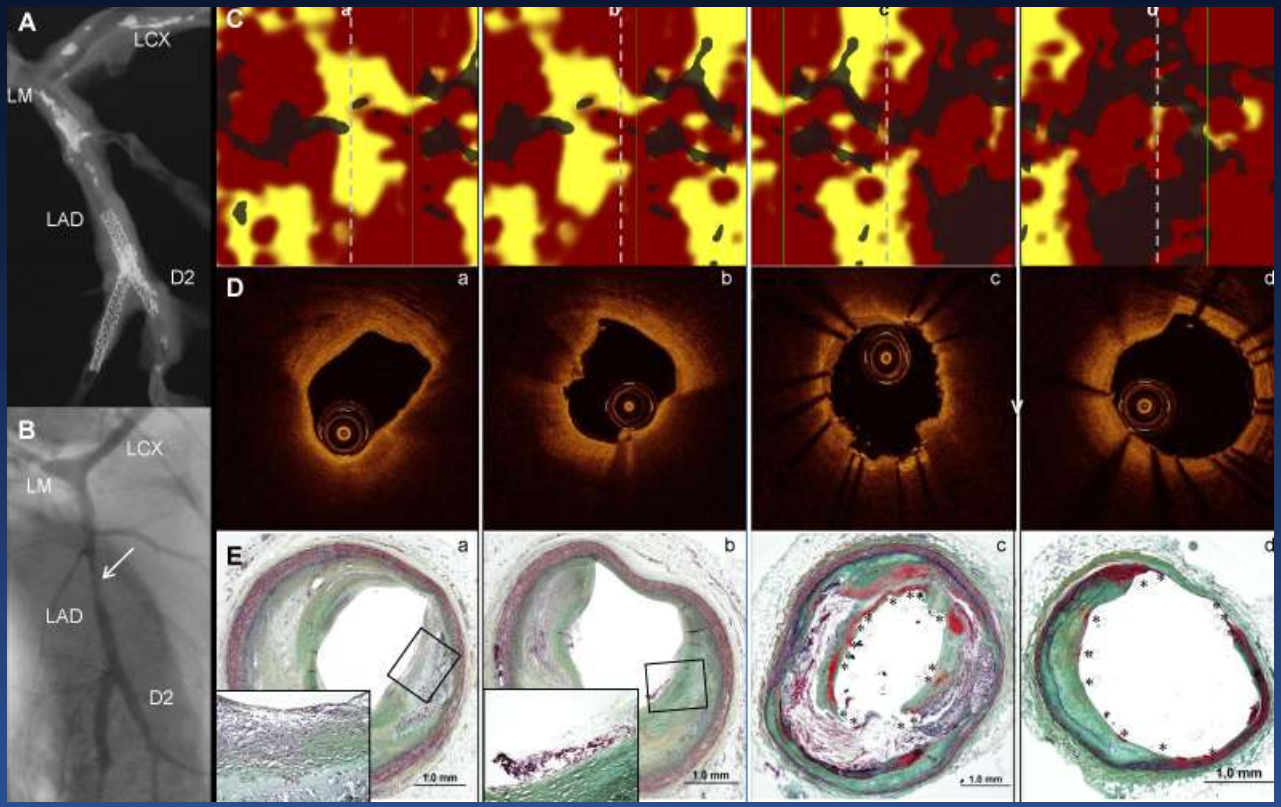
Takotsubo

Neoatherosclerosis

Erlinge. TCT2013

NIRS and Neoatherosclerosis

Using NIRS, lipid was detected within stented vessels in 58 of 65 patients. LCBI/4mm measured 173±191. NIRS identified lipid that was not detected by OCT in 18 (28%) stented vessels of which 3 (18%) had evidence of thin-cap neointima.



Ali et al. Circ Cardiovasc Interv 2013;6:506-17

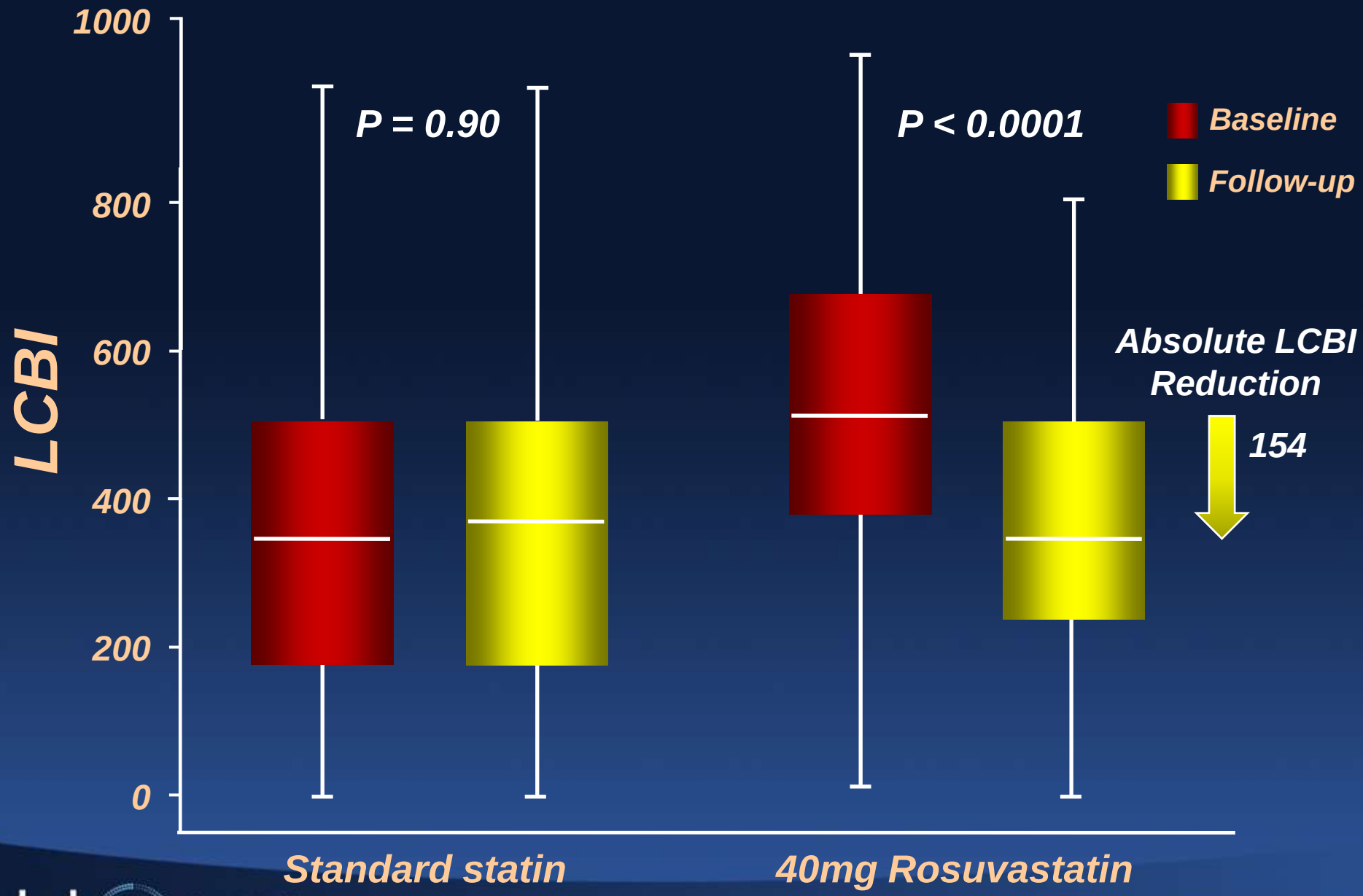
YELLOW

- *87 pts with multivessel disease who had undergone stenting of the target vessel and were scheduled for staged PCI of a second, obstructive lesion were randomized to rosuvastatin 40mg/day vs standard statin*
- *All lesions were characterized with IVUS, FFR, and NIRS at baseline and after 6 to 8 weeks*

	40mg Rosuvastatin	Standard statin therapy	P
#	44	43	
Δtotal cholesterol, mg/dl	-20.0±4.8	5.2±5.4	0.001
ΔLDL-C, mg/dl	*-19.0±4.0*	*-0.2±4.7*	*0.003*
ΔHDL-C, mg/dl	*0.6±1.2*	*1.5±0.9*	*0.58*
Δ%atheroma volume	*0.24%*	*0.26%*	*1.0*
FFR >0.80	9.0%	4.6%	0.47

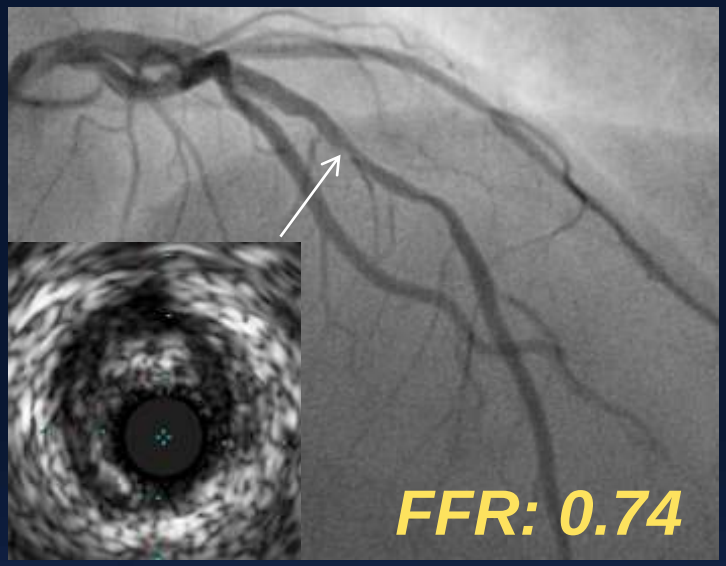
Kini et al. J Am Coll Cardiol 2013;62:21-9

Paired Analysis – 4mm maximum LCBI

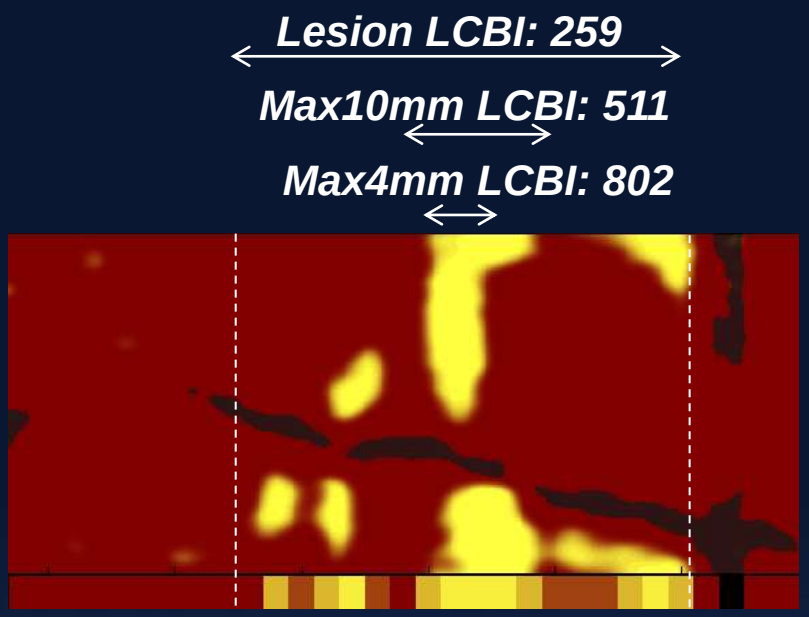


Kini et al. J Am Coll Cardiol 2013;62:21-9

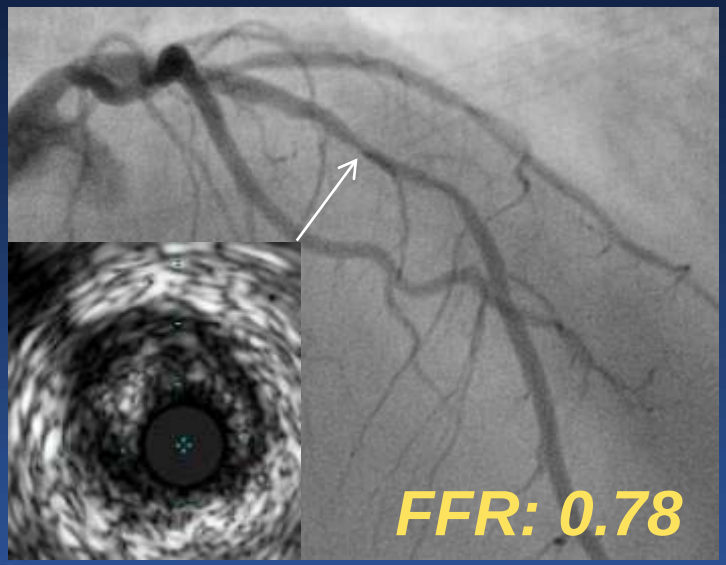
Baseline



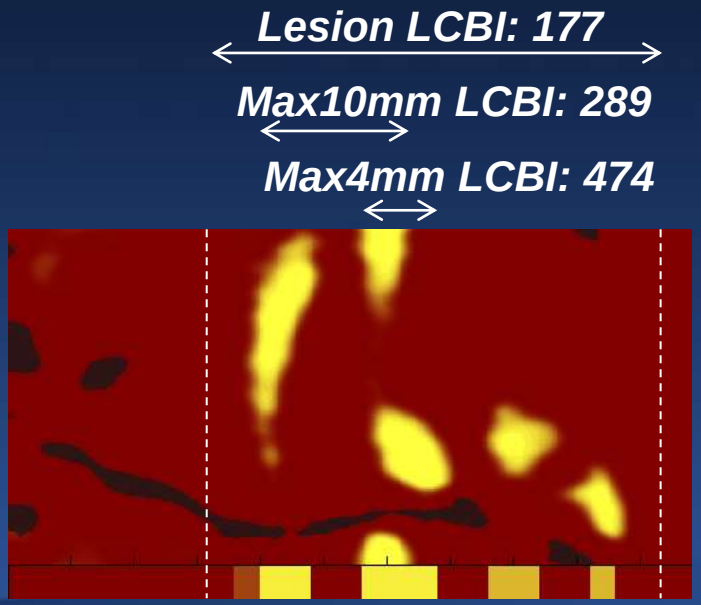
Plaque Area
5.6mm²



Follow-up



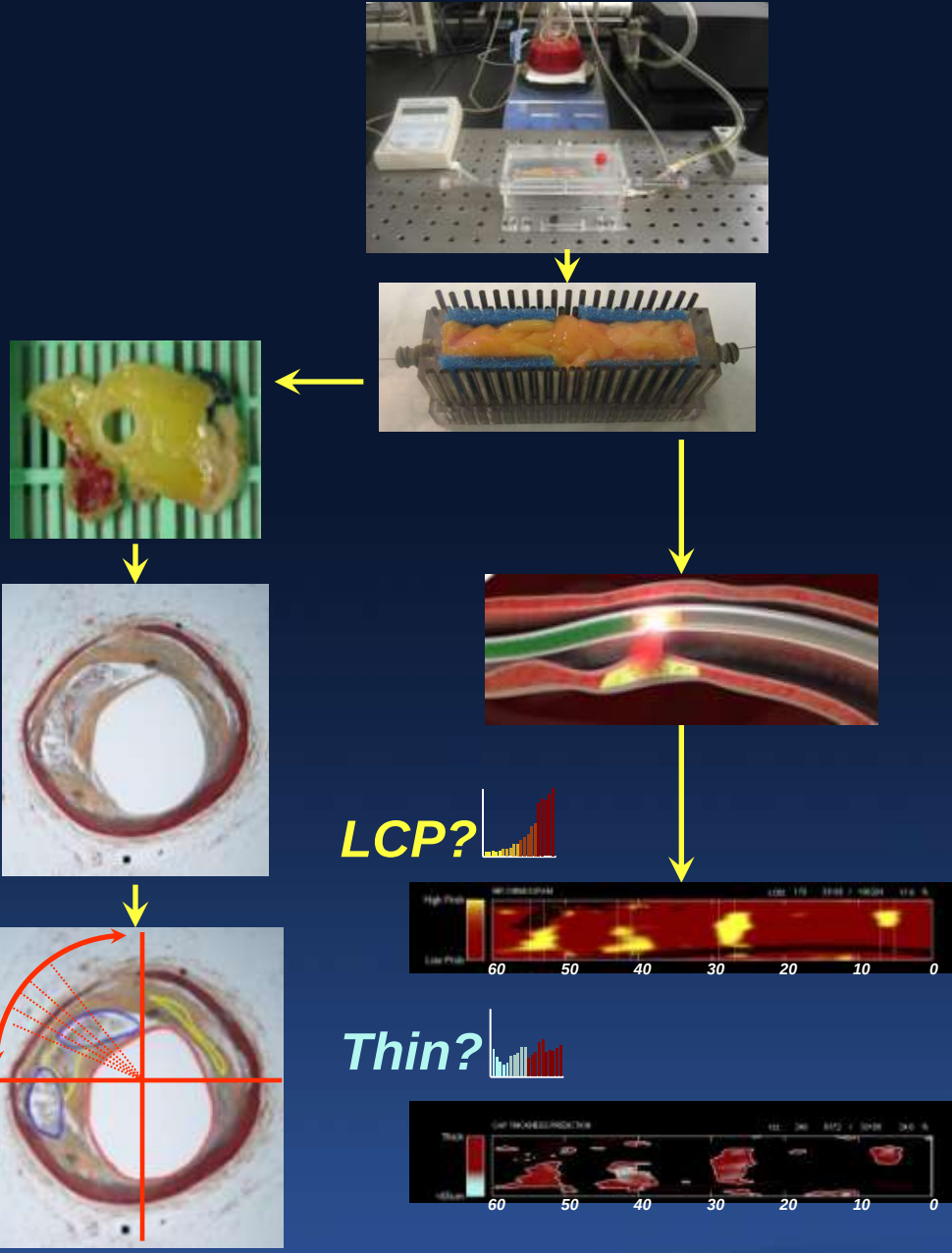
Plaque Area
5.5mm²



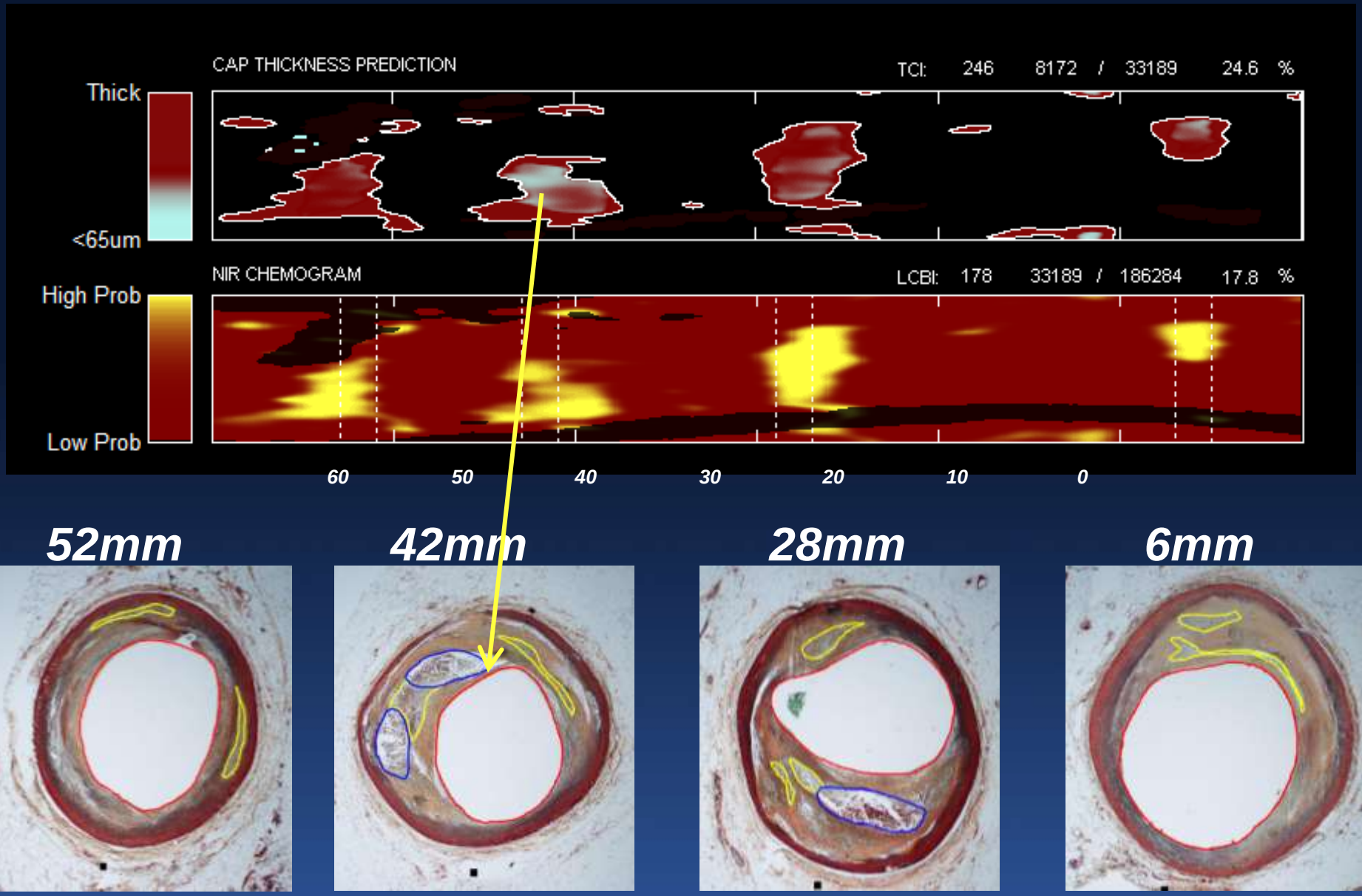
Kini et al. J Am Coll Cardiol 2013;62:21-9

Spectral differences can be used to distinguish LRP with thin fibrous cap (less collagen) from LCP with thicker fibrous cap (more collagen)

- NIRS performed through flowing pulsatile blood at physiologic temperature in 212 coronary arteries from 84 autopsy hearts
- One spectrum and one histologic section for every 2 mm of artery
- Histologic cross-sections digitized
- Cap thickness evaluated at areas of lipid pool, necrotic core, and calcified necrotic core
- Thin fibrous cap defined as minimum cap thickness <0.065μ



Madden et al. J Am Coll Cardiol 2012;59:E308



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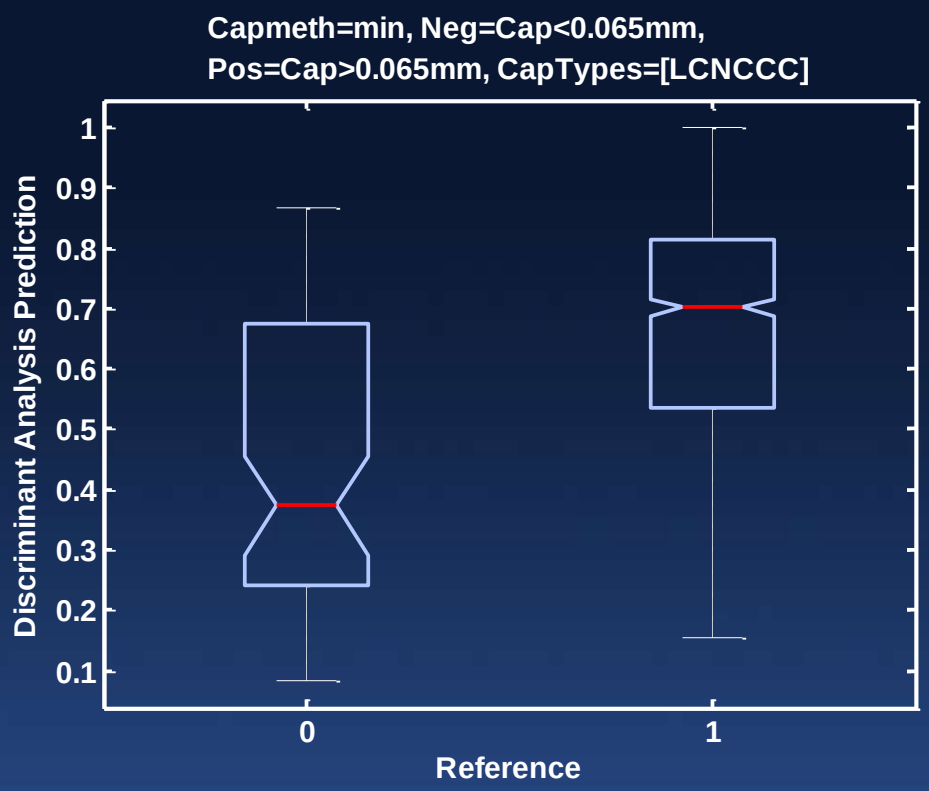
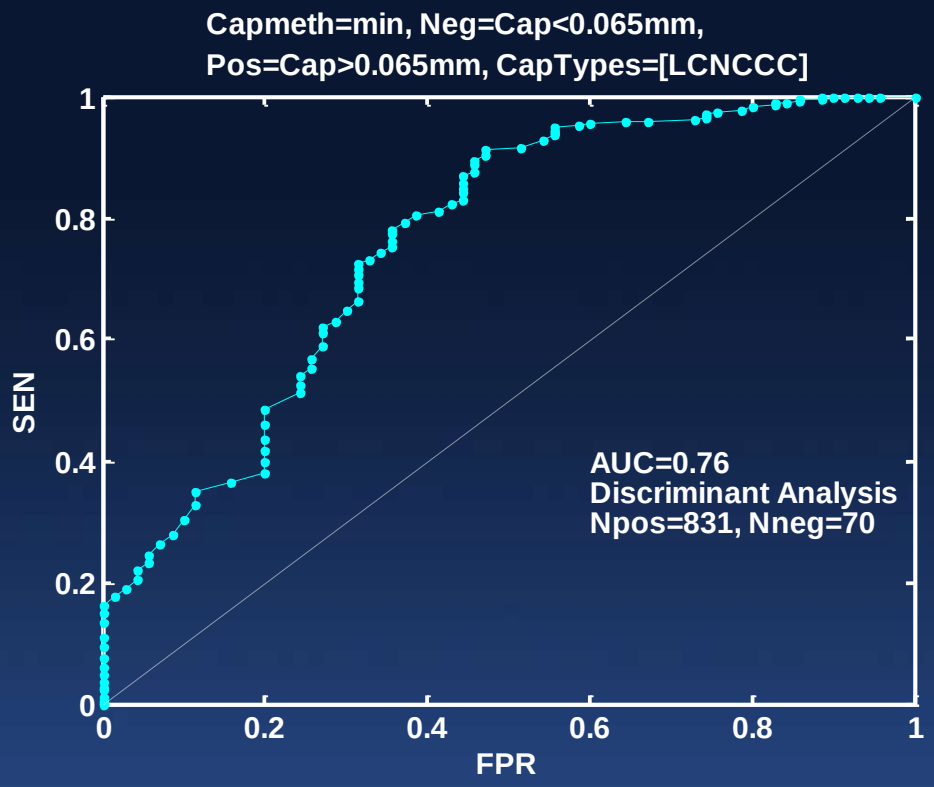
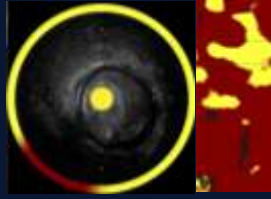




Madden et al. J Am Coll Cardiol 2012;59:E308

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

↓

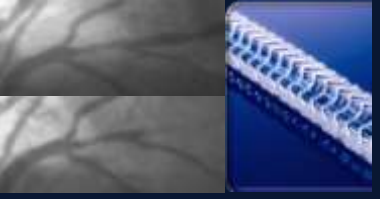
3-vessel imaging post PCI

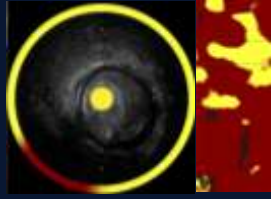
Culprit artery, followed by non-culprit arteries

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

Conclusions

- NIRS has been extensively validated to detect lipid rich plaque
- NIRS has been combined with IVUS in the first clinically available combination imaging device
- Clinical data indicates that NIRS is useful
  - In predicting peri-procedural MI
  - Identifying the culprit lesion in MI patients
  - Identifying lipid rich neointima in patients with neoatherosclerosis
- NIRS may also be useful in studies of progression, regression, and lesion stability