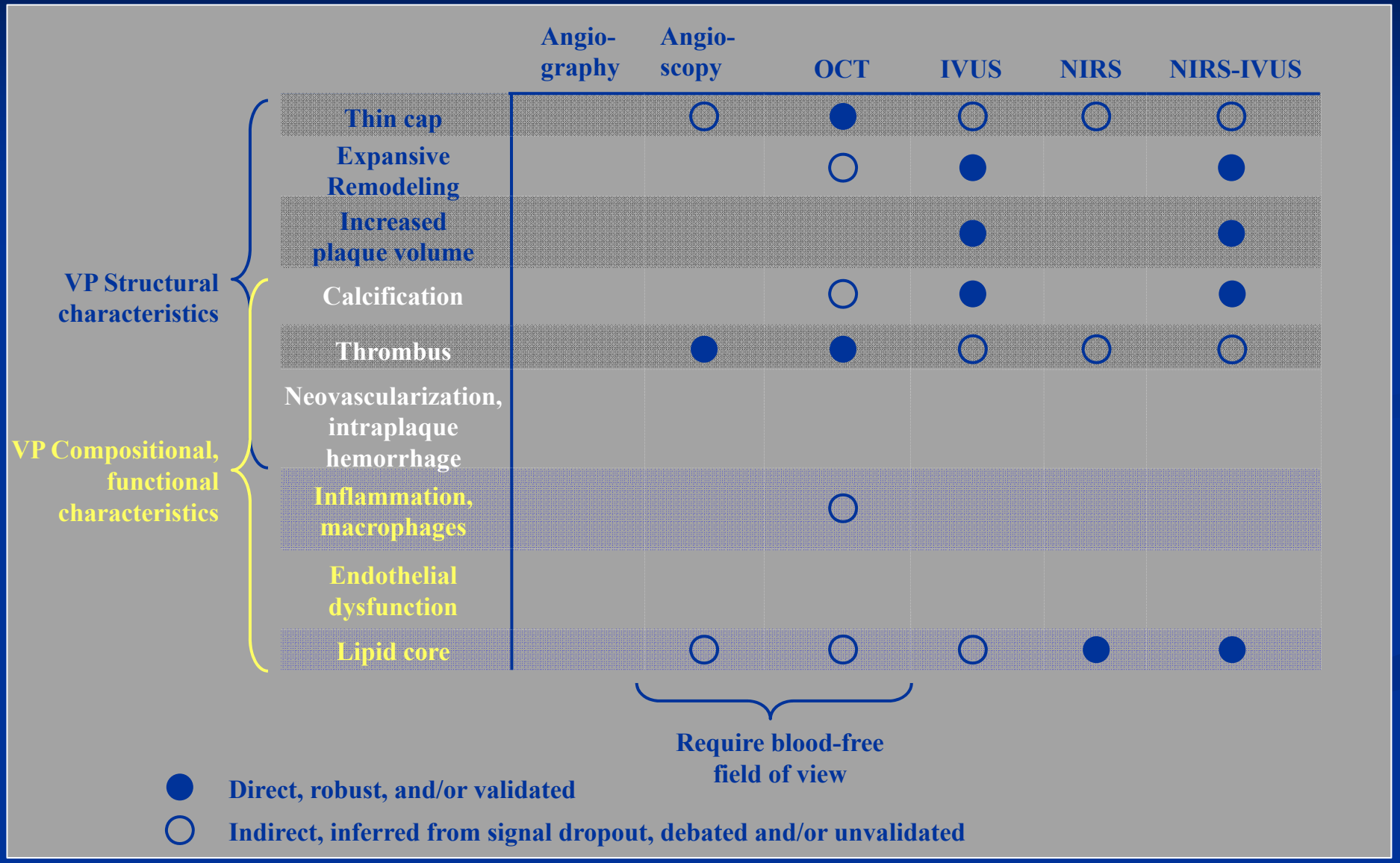
The Science Behind TVC Imaging Using NIR Spectroscopy

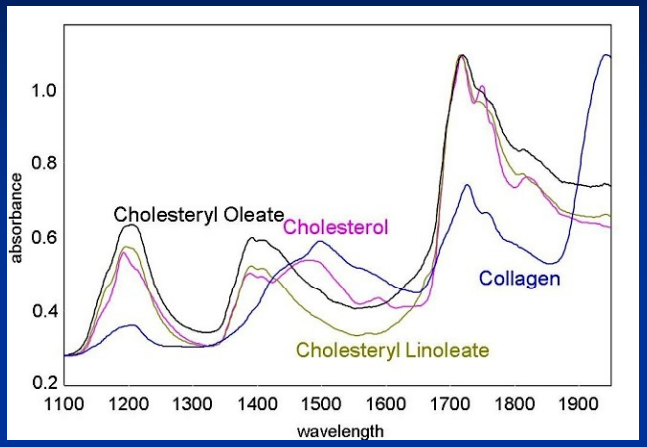
John McB. Hodgson, M.D.

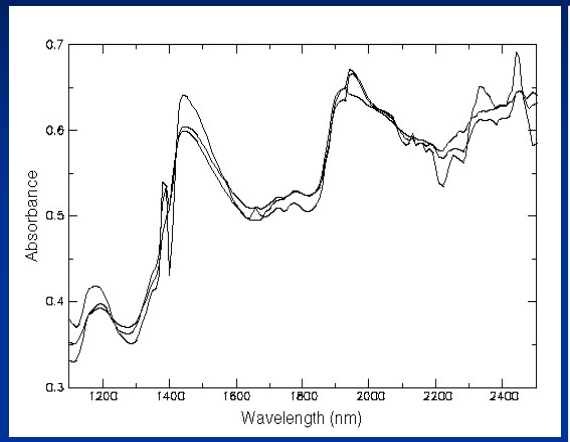
ANGIOPLASTY SUMMIT
TCTAP 2012

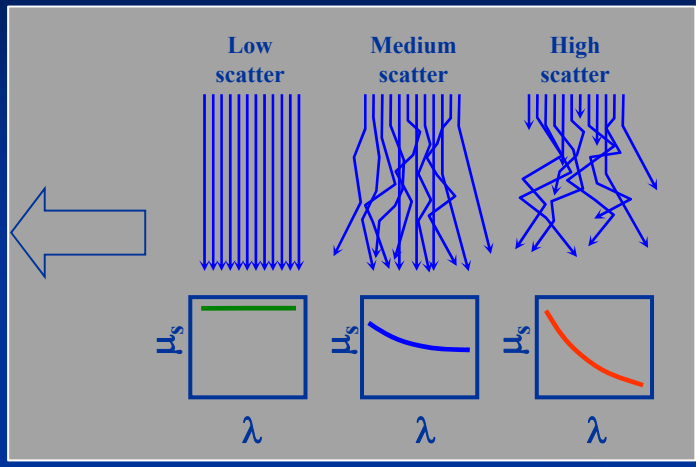
Intravascular Detection of Plaque Suspected to be Vulnerable Plaque



NIRS Principle of Operation







Multiple components

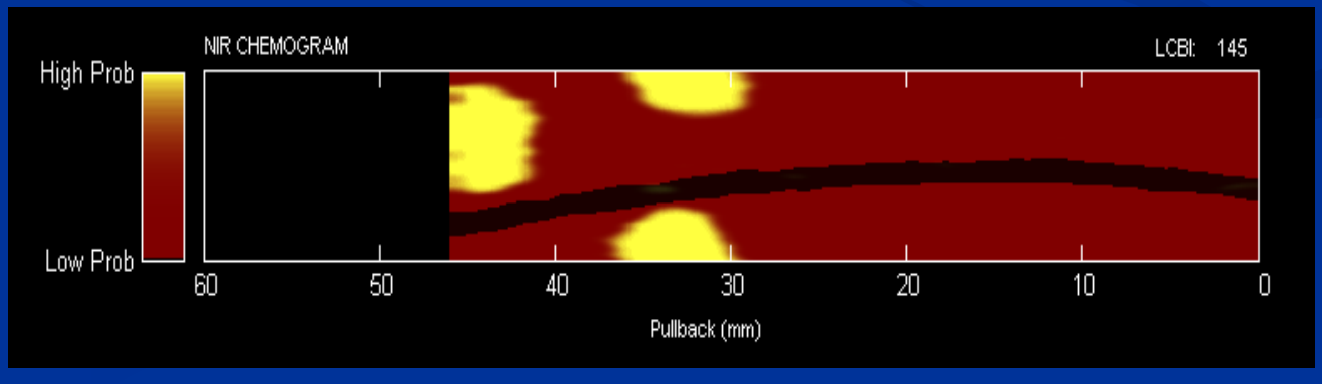
Complex mixture spectra

Variable scattering properties

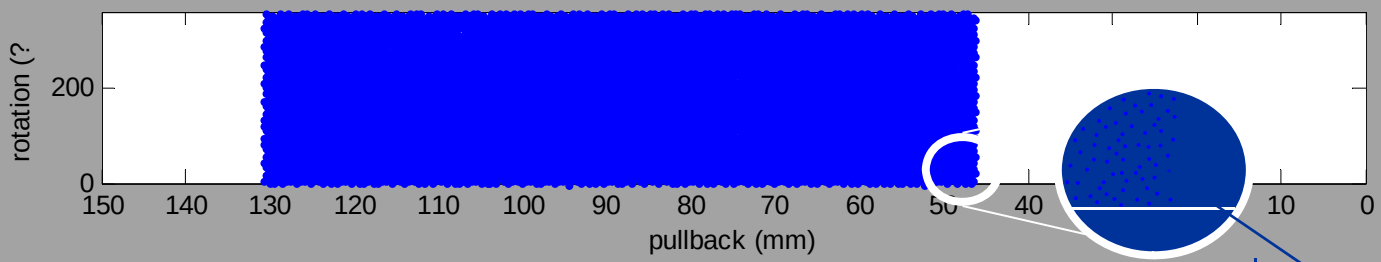
$\Sigma \lambda$
$\pi \mu$
$x \sqrt{} \div$

Chemometric Algorithms

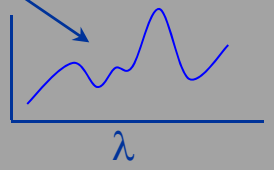
Algorithms extract the relevant portions of the mixture signal and create a probability map of lipid core plaque



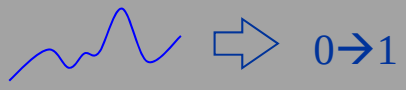
Formation of the Chemogram



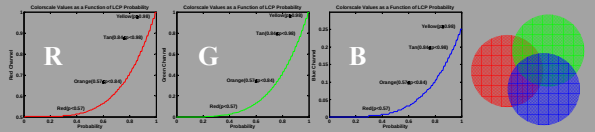
Spectra acquired at discrete pullback and rotation positions



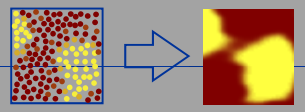
Spectra transformed into posterior probability of LCP presence

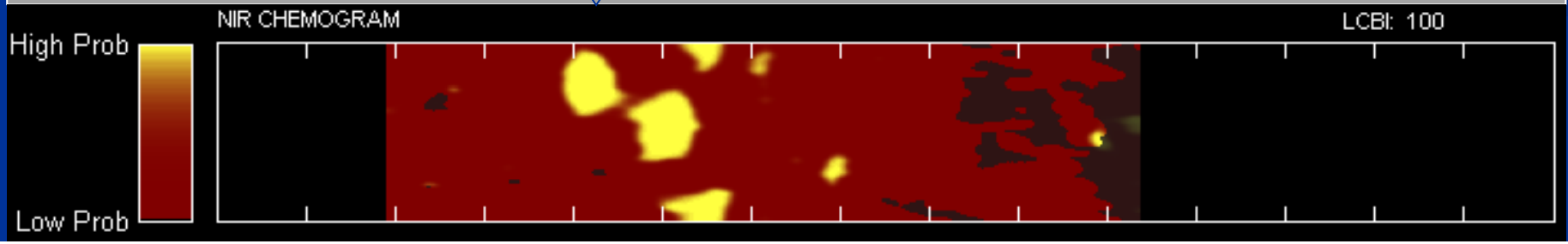


Probability mapped to a color



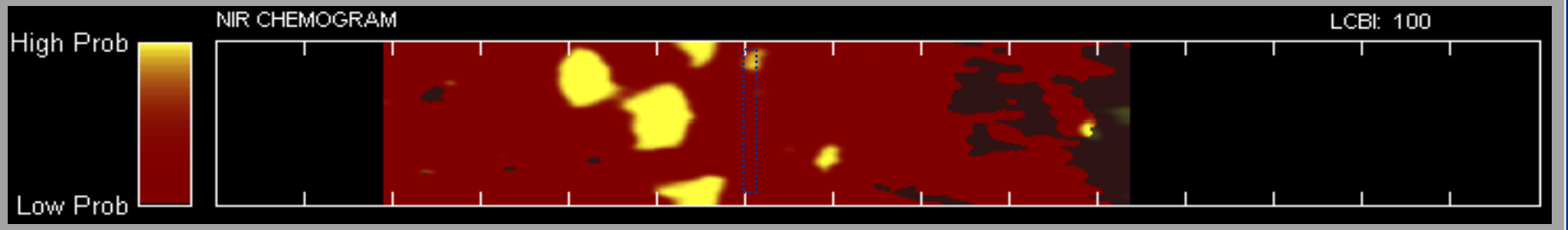
Pixels formed into an image



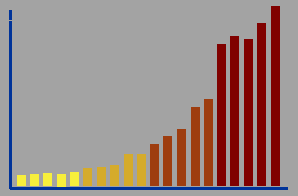


Formation of the Block Chemogram from the Chemogram

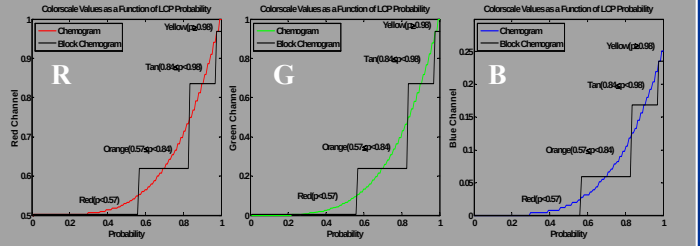
Block Chemogram is a vertical summary of the Chemogram at 2mm pullback intervals

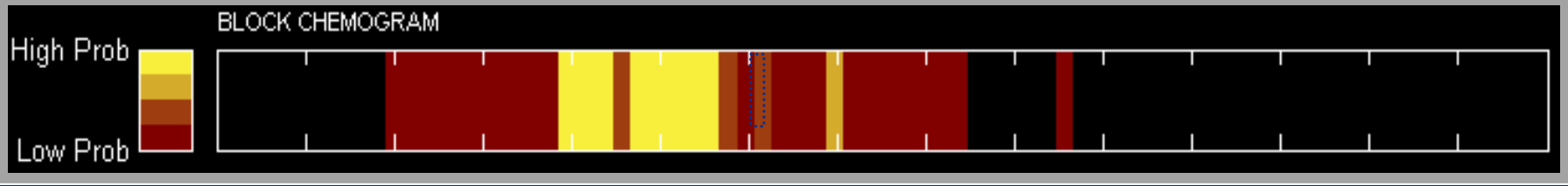


Determine a single value for each 2mm slice (90th percentile)



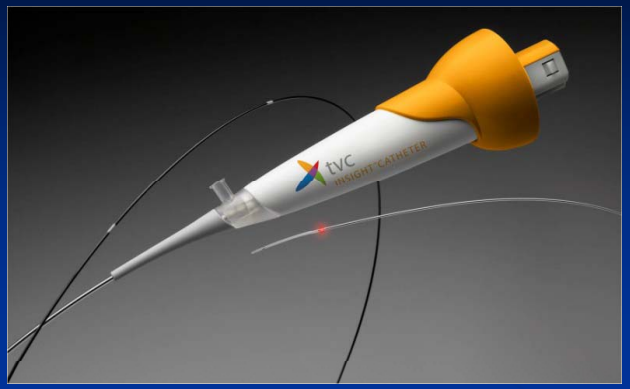
Map to same color scheme as Chemogram, binned to four discrete colors



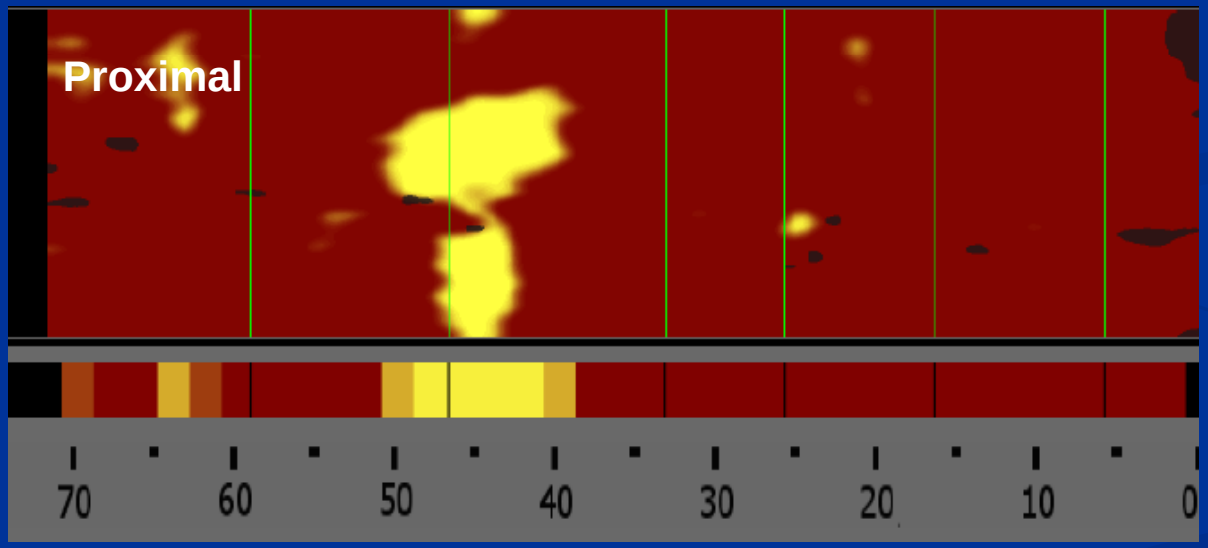


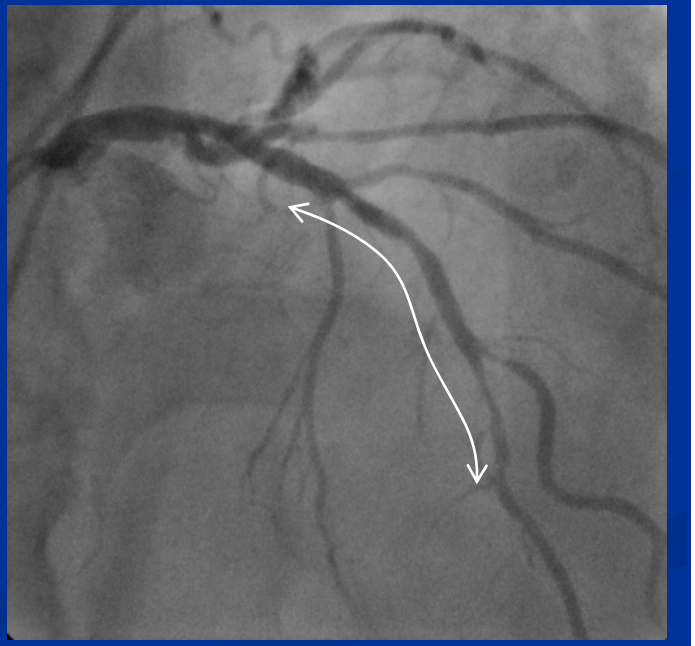
Near Infrared Spectroscopy Catheter

NIR provides lipid content probability based on the spectra obtained.
Displayed as a chemogram and a block chemogram



Chemogram

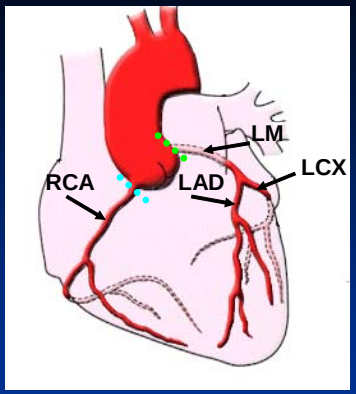


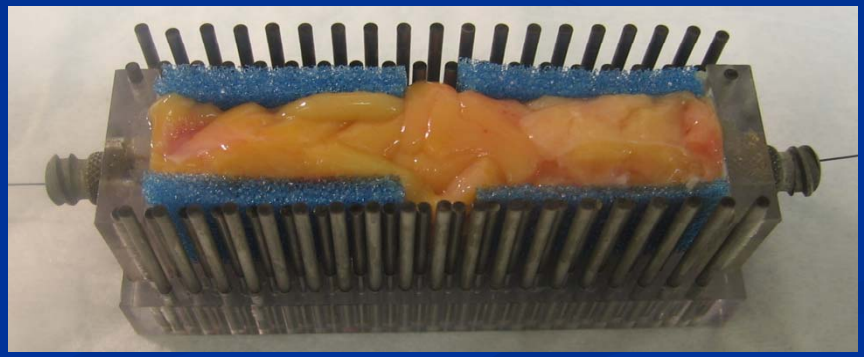


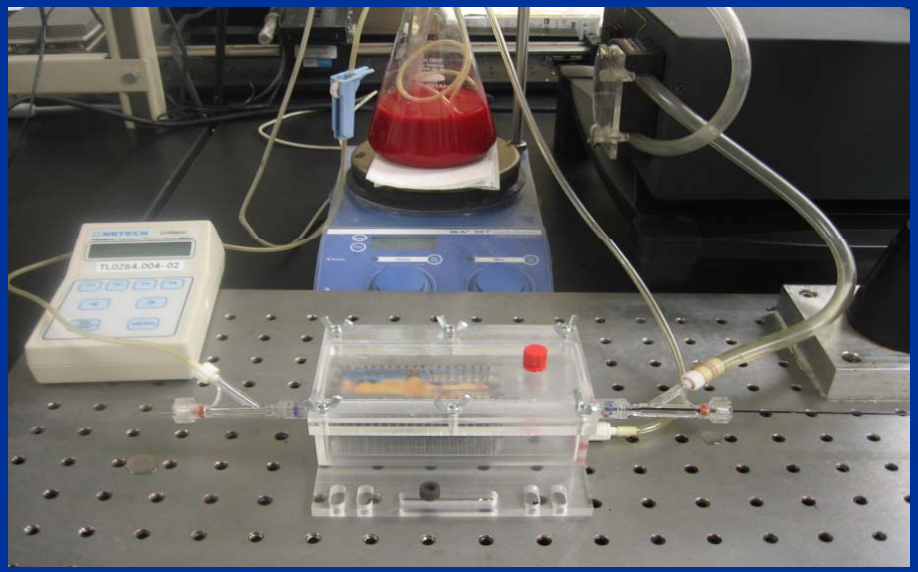
Block Chemogram

Validation: human coronary autopsy specimens

- Artery segments mounted in registration chamber
- Artery perfused with pulsatile human blood at 80–120 mm Hg
- NIR scan performed
- Artery prepared for histology

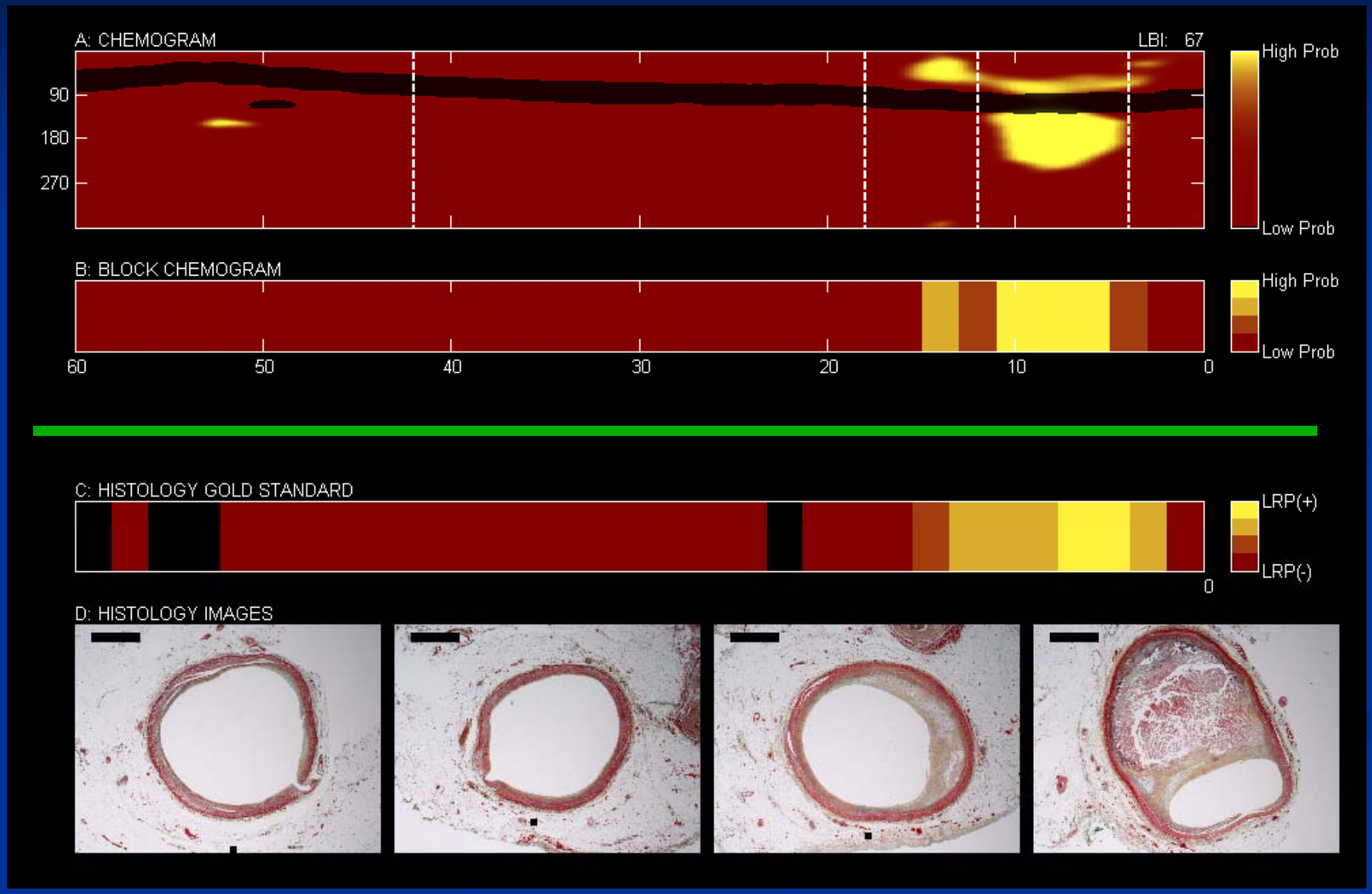




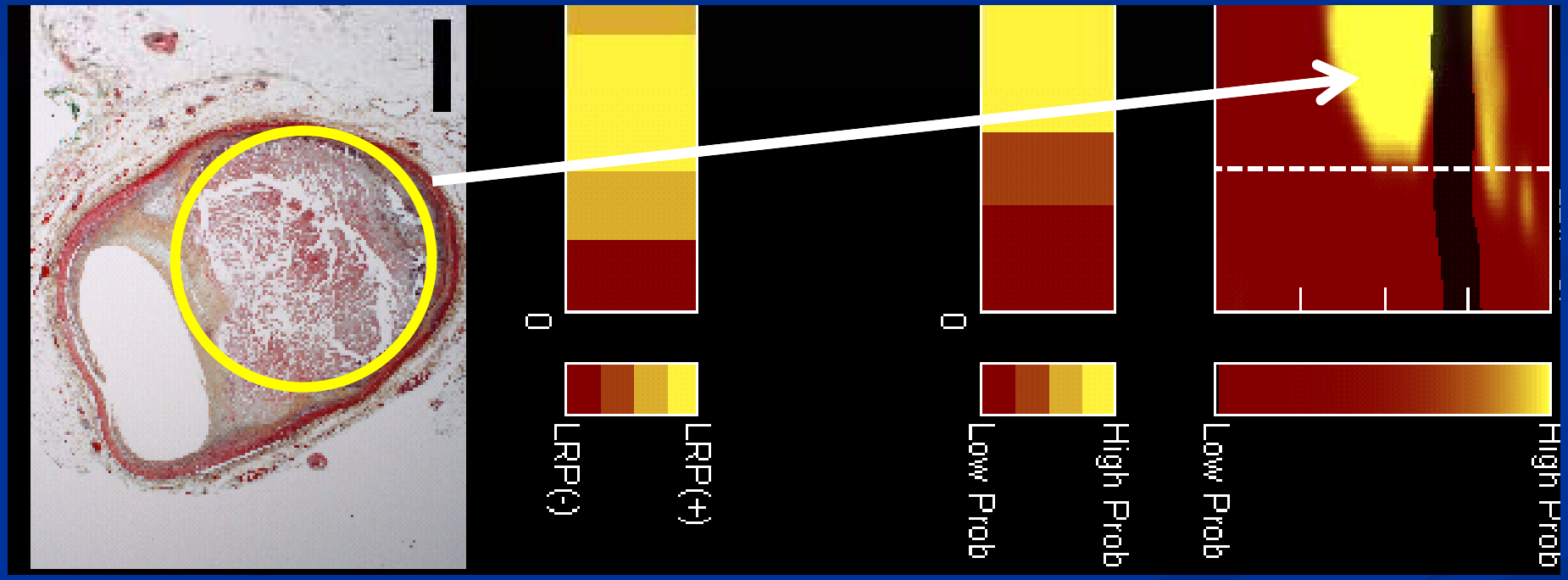


Over 2,000,000 spectra acquired in over 550 NIR pullbacks of 51 validation hearts

Validation with histology



Detected lipid core plaque displayed as yellow

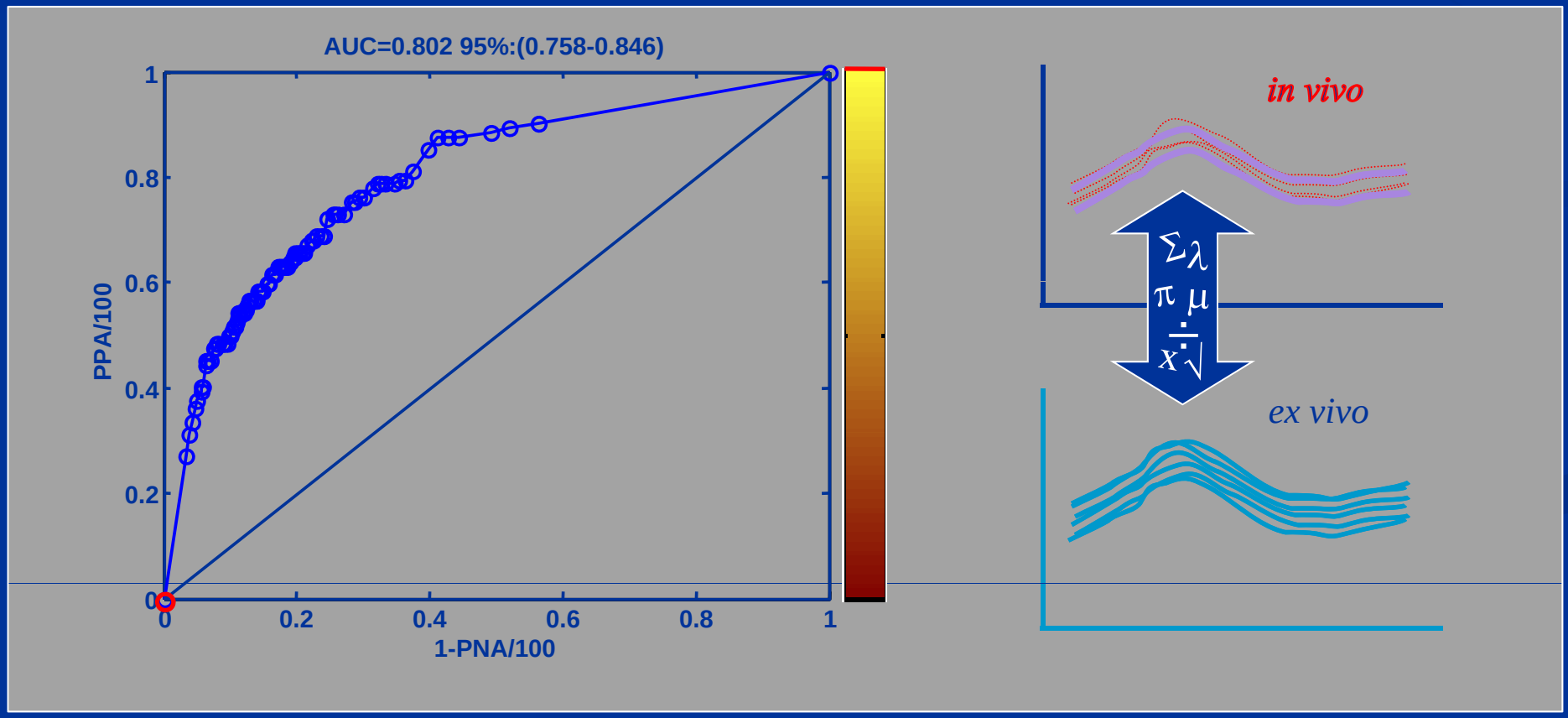


Histology score

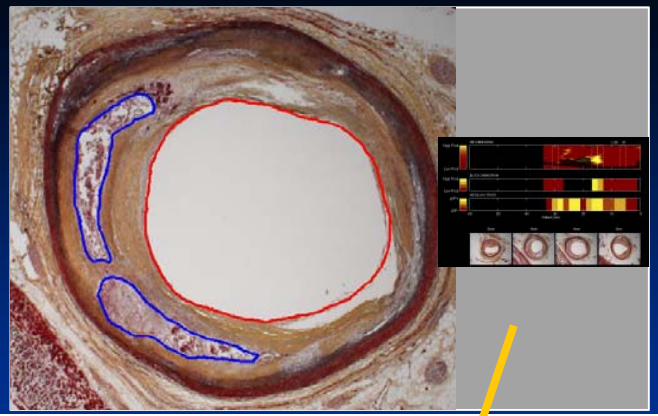
NIRS probability

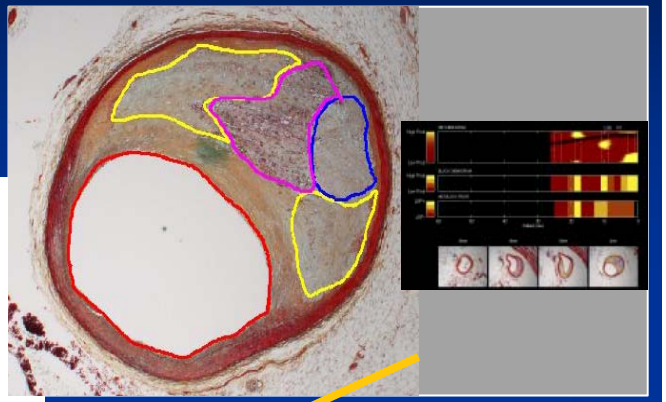
NIRS Validation Performance

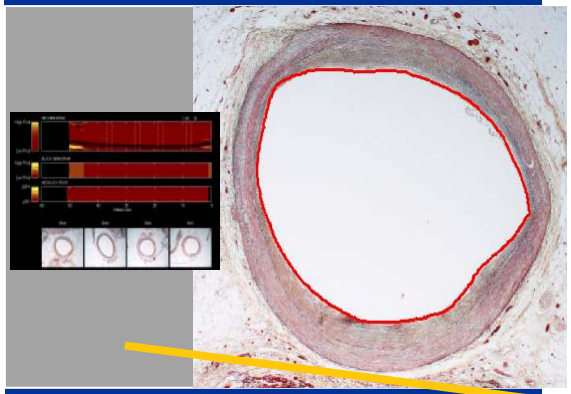
- Accuracy versus histology in autopsy specimens. AUC = 0.80 (95% confidence interval: 0.76–0.84)
- Spectral similarity of in vivo data versus autopsy data demonstrated

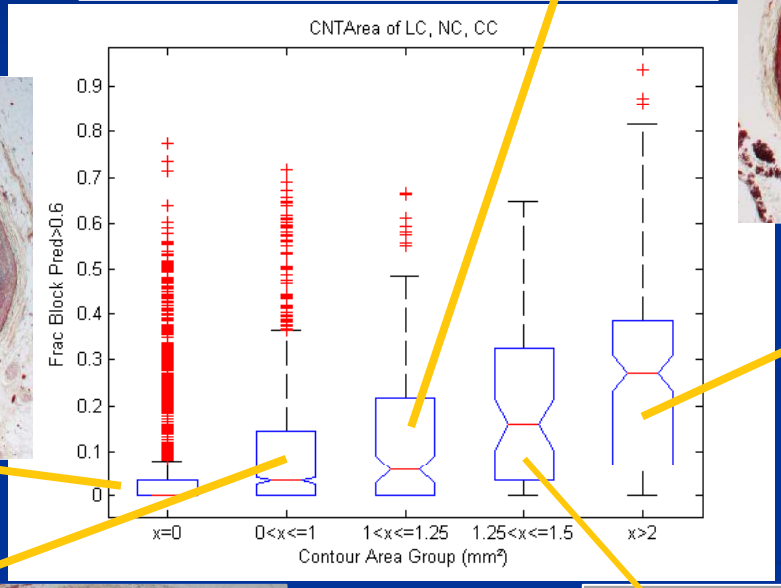


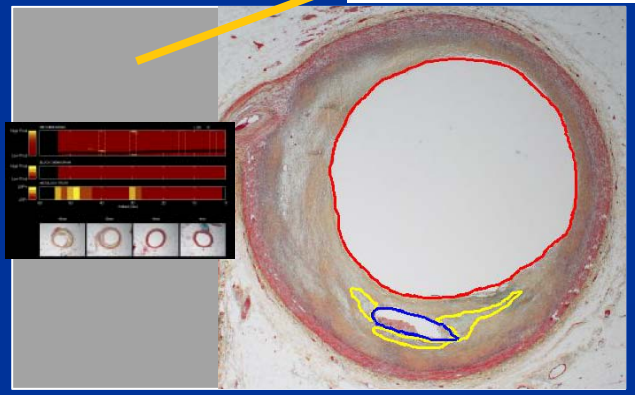
Larger lipid core cross sectional area gives greater proportion of yellow pixels





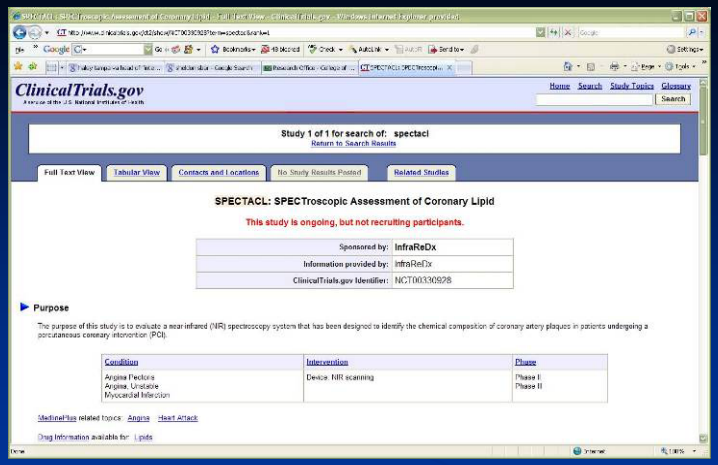






Validation

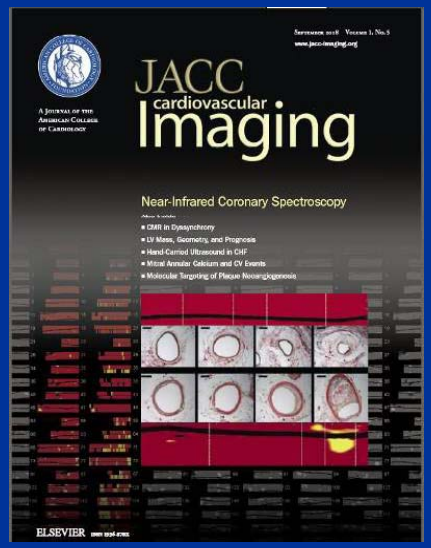
- In-Vivo
  - Study of 100+ patients in 6 hospitals
  - Endpoint requirement was spectral similarity between patient scans and Ex-Vivo scans



SPECTACL Clinical Study

In Vivo Clinical Spectra ≈ Ex Vivo Autopsy Spectra ≈ Histology

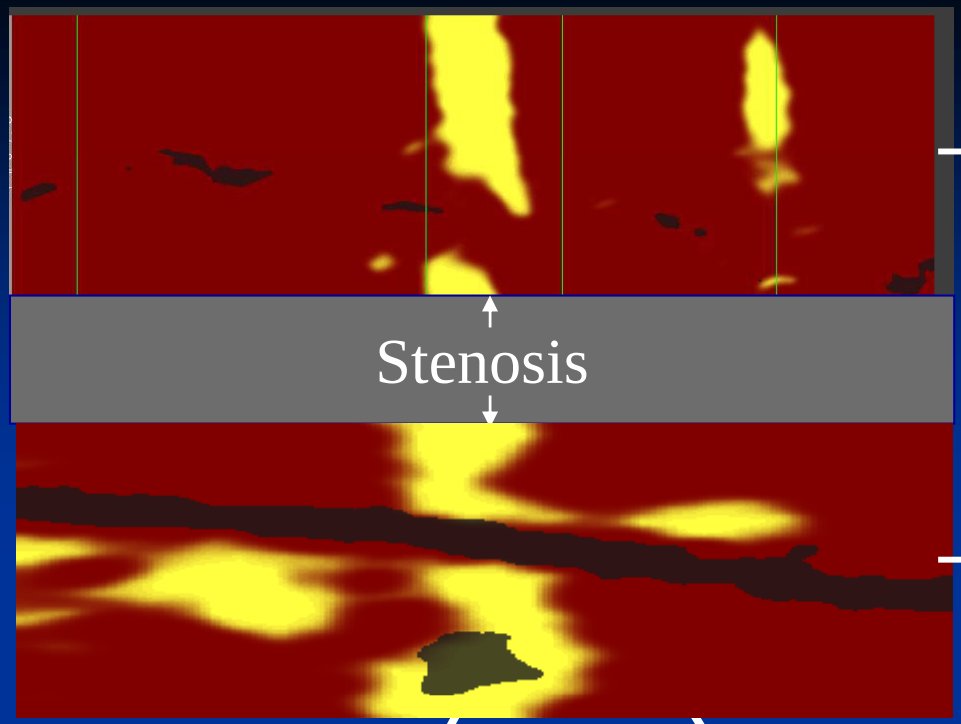
Ex Vivo Autopsy Study



- Ex-Vivo
  - Scanning NIR Spectroscopy through blood in 212 coronary segments from 84 autopsy hearts
  - One histologic segment for every 2 mm of artery
  - 33 hearts used to develop algorithm
  - 51 hearts used in double-blind manner to evaluate accuracy of method

Gardner, et al, *JACC Imaging*, 2008

RCA with ring LCP at stenosis in 62 yo male

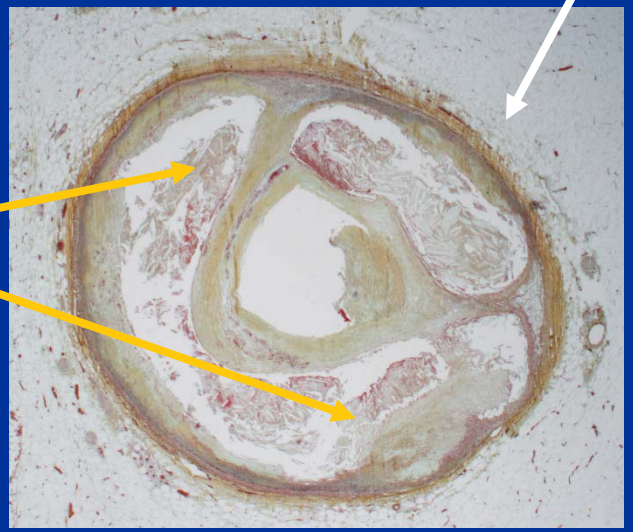


Distal embolization following PCI leading to MI and CPR

Similar finding with ring LCP from autopsy of 48 yo male

Sudden Cardiac Death

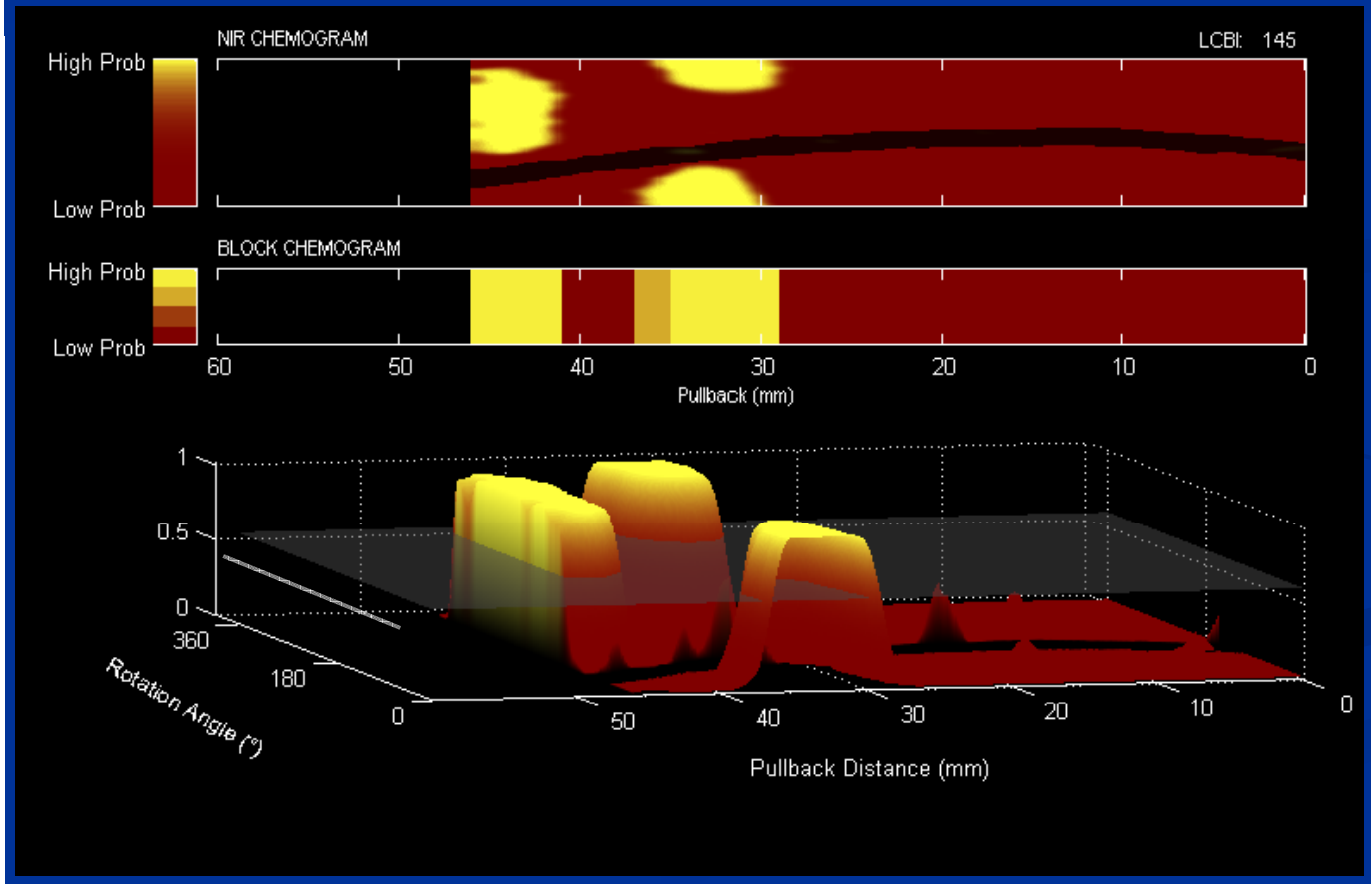
Massive LCP



Thrombus remnant

“Lipid Core Burden Index” – LCBI

- Quantitative summary metric of LCP content in Chemogram
  - Potentially useful as measure of risk or of therapeutic efficacy
- Fraction of Chemogram image pixels above probability of 0.6
  - Scaled from 0 to 1000



LCBI Calculation

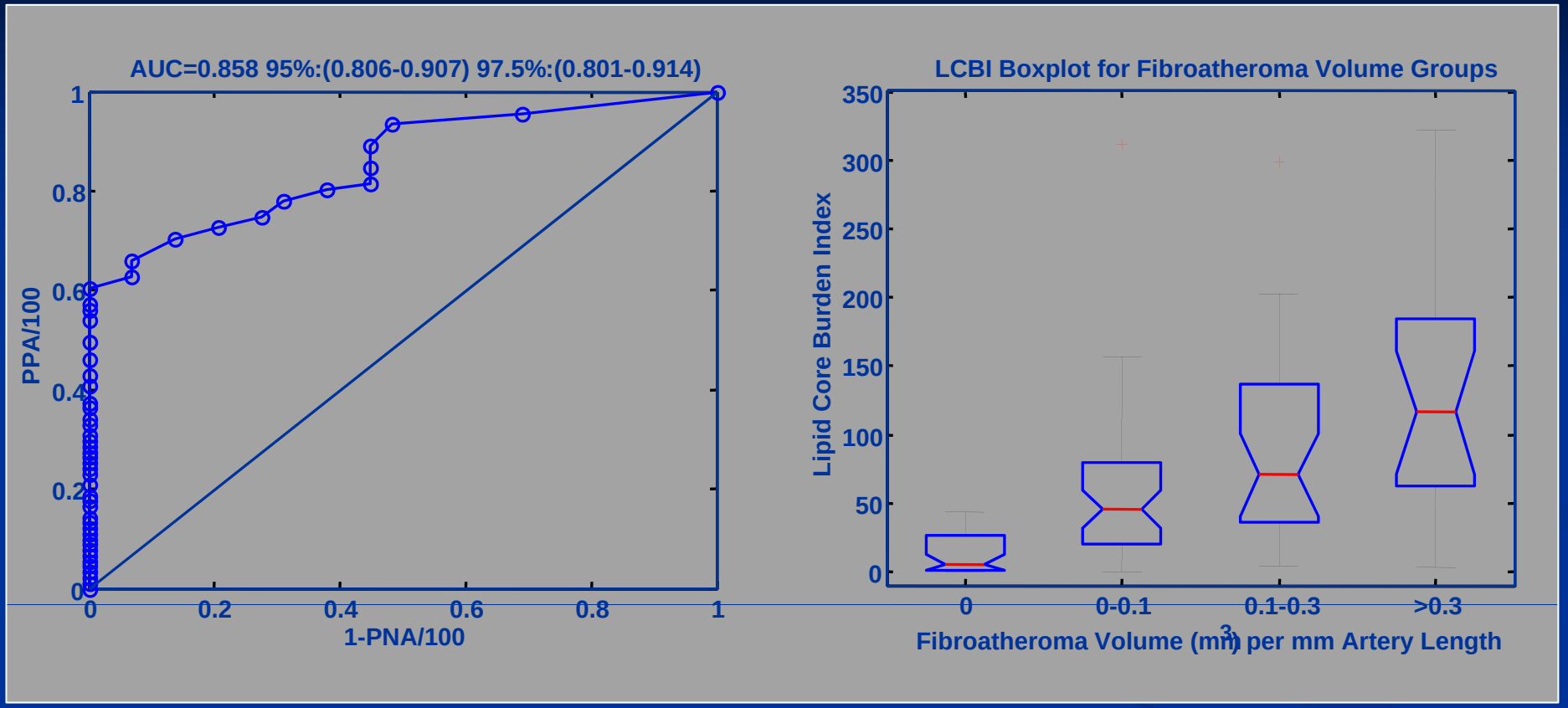
Image pixels > 0.6: 21239

Image pixels: 145974

$$\frac{21239}{145974} \times 1000 = 145$$

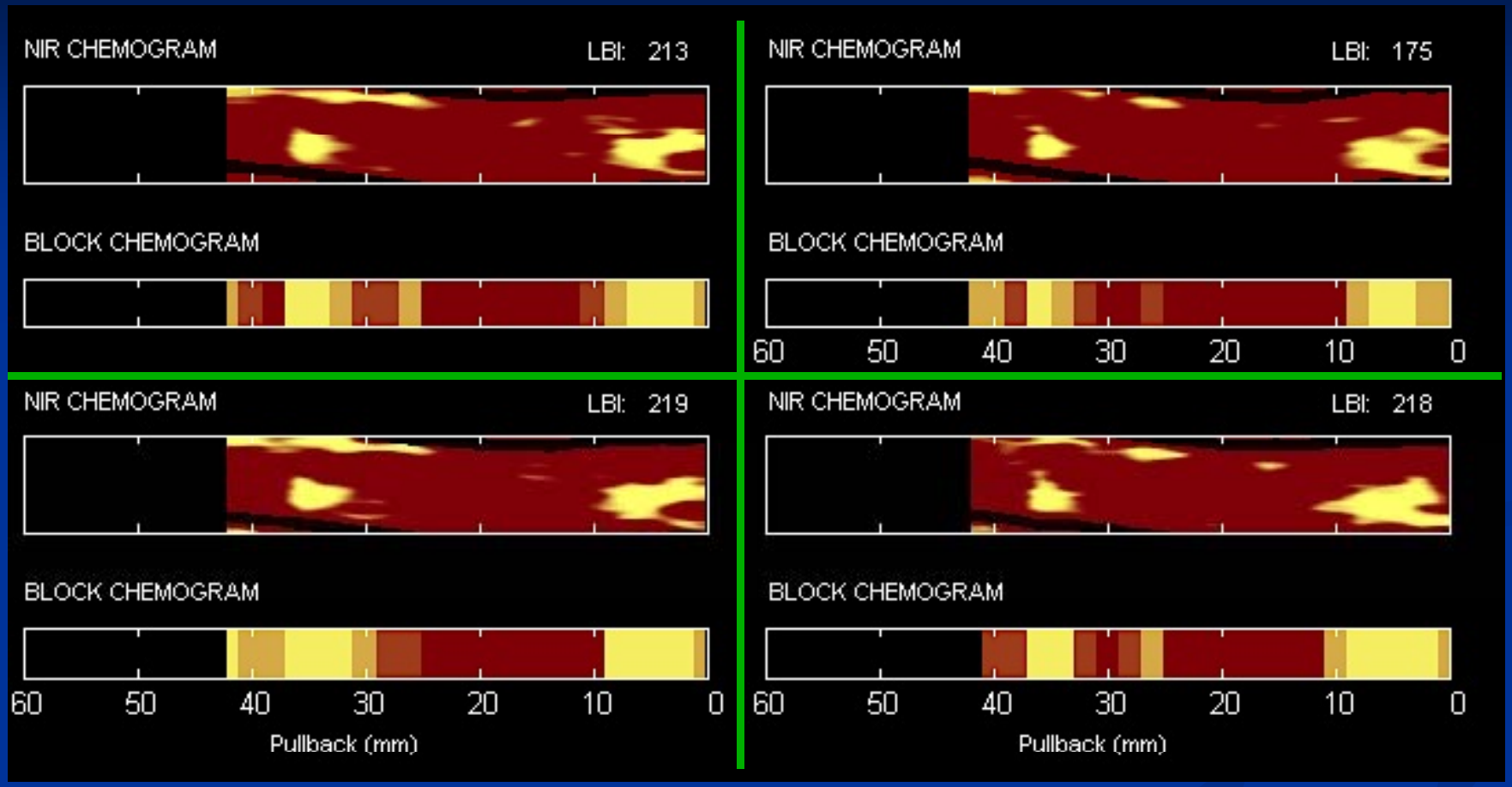
(outliers and guidewire excluded)

LCBI – Validation



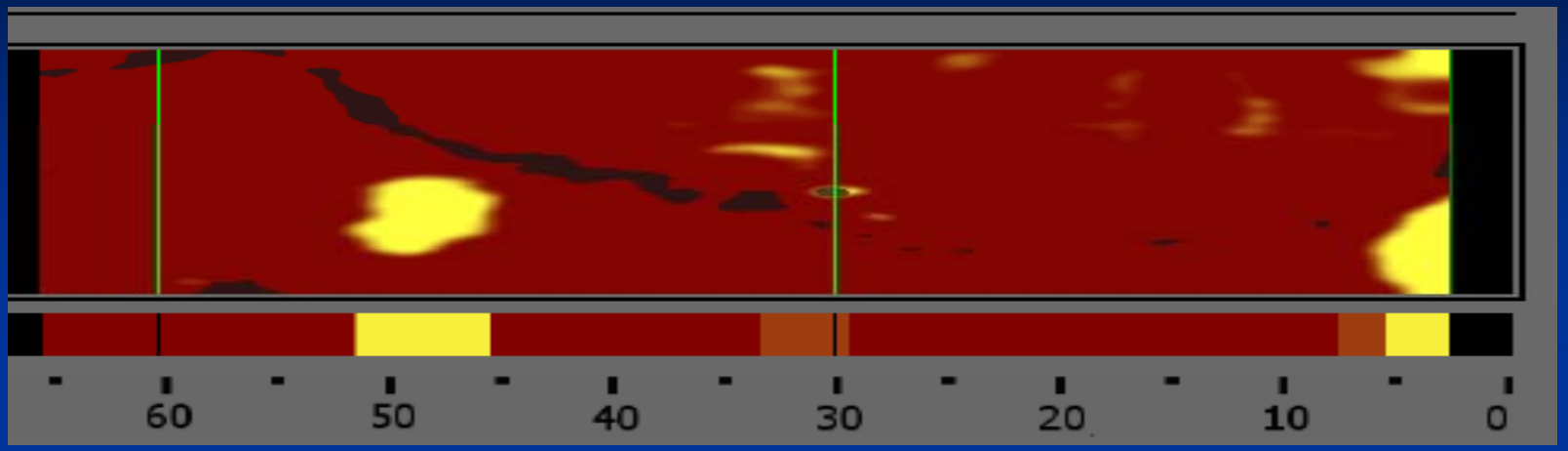
- LCBI predicts presence of fibroatheroma in the scanned segment accurately
  - AUC>0.85 (95%: 0.81 – 0.91)
- LCBI correlated with fibroatheroma volume per mm of artery length
  - $R = 0.53$, $p < 10^{-9}$

Ex Vivo Reproducibility

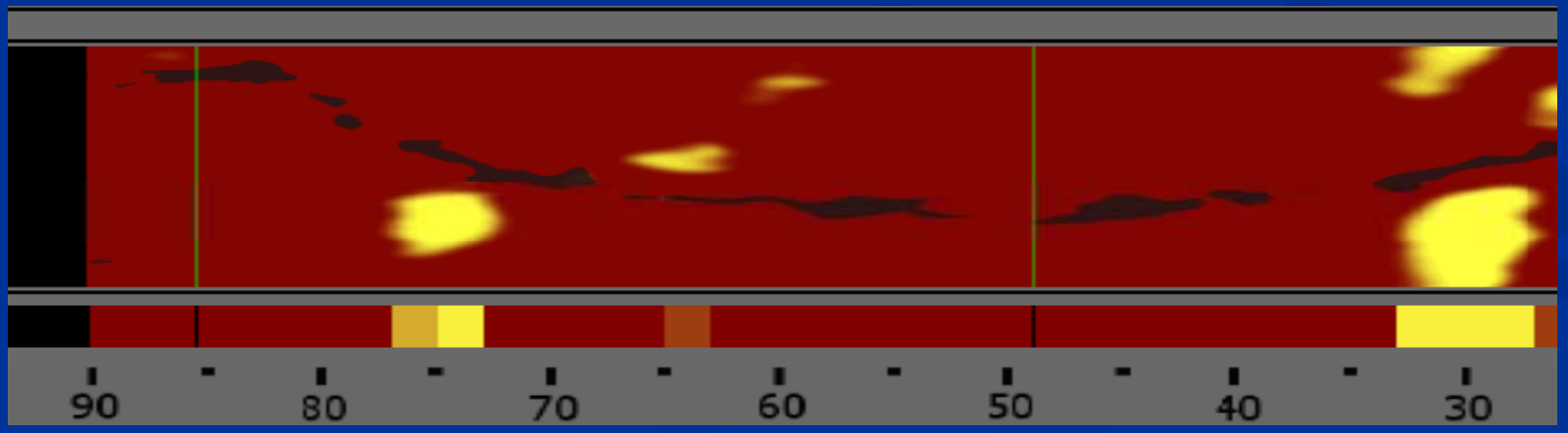


Four repeated acquisitions with visual agreement between Chemogram, block Chemogram, and LCBI

Clinical reproducibility

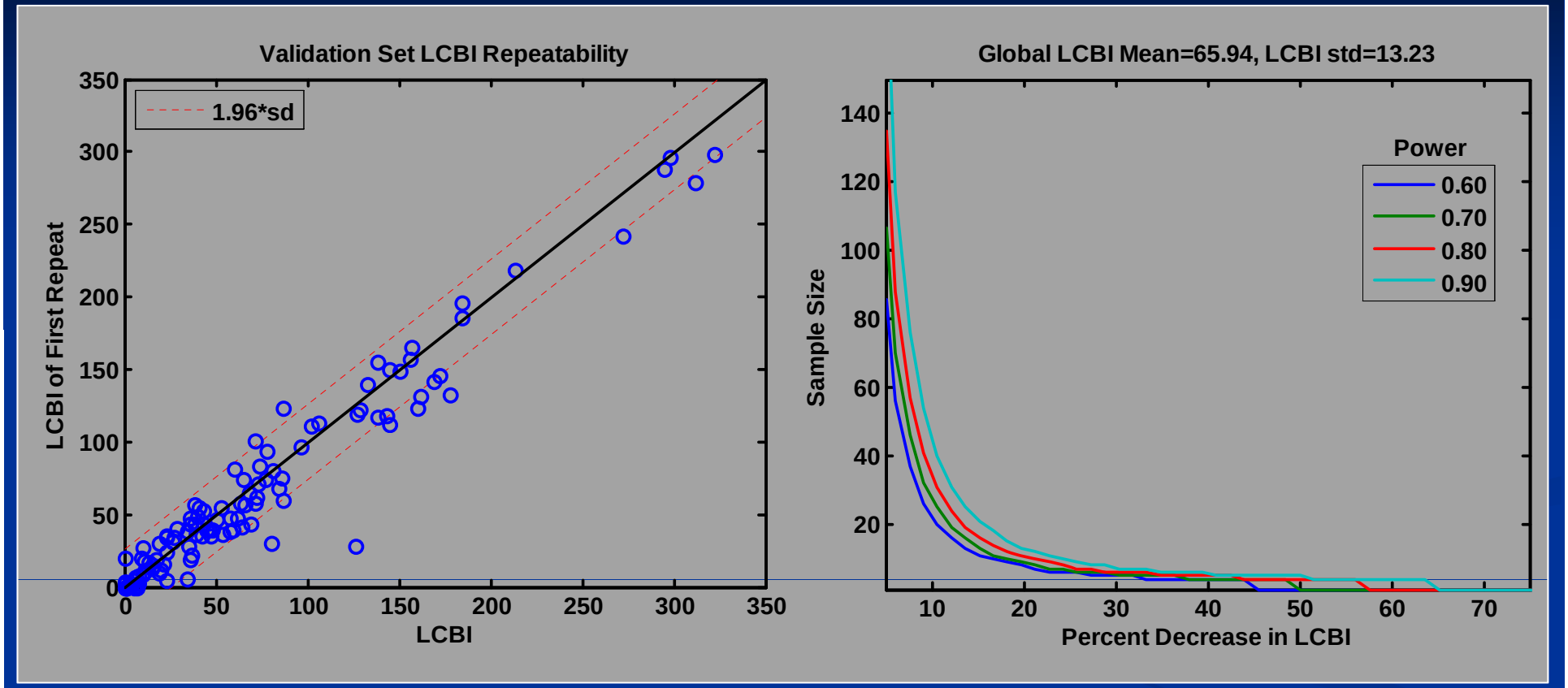


Blinded chemograms one year apart: IBIS 3 Study



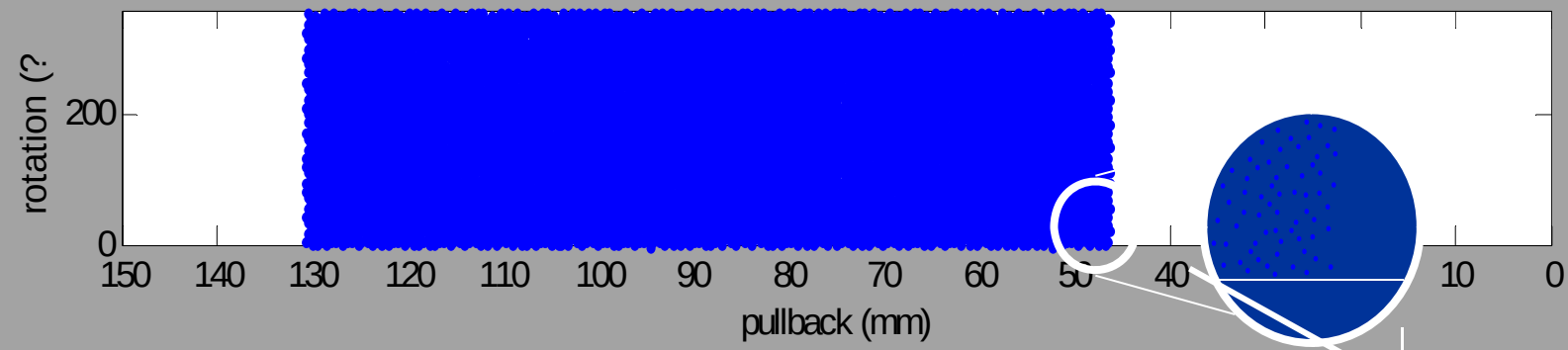
Courtesy Dr. Patrick Serruys

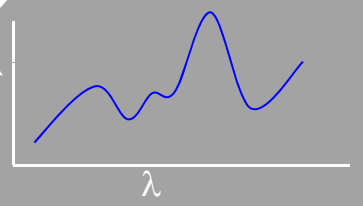
LCBI Reproducibility



- Serial change in LCBI has been large in preclinical studies
- LCBI in-vitro reproducibility excellent
  - Sample size needed for adequate power to detect change in lipid is <100

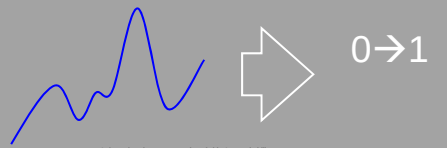
Use of NIRS to Identify Cap Thickness



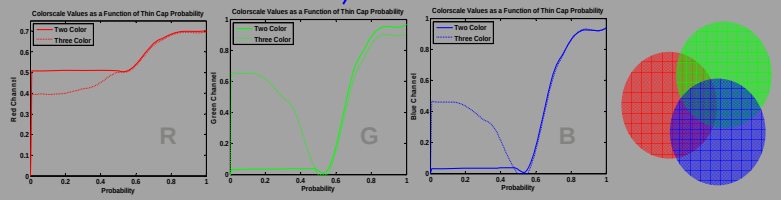


Spectra acquired at discrete pullback and rotation positions

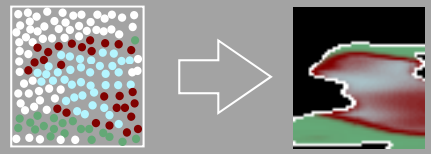
Spectra transformed into posterior probability of thin cap presence

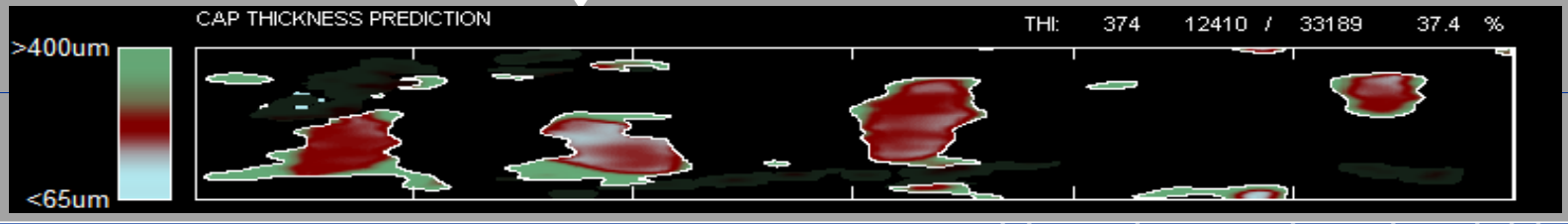


Probability mapped to a color



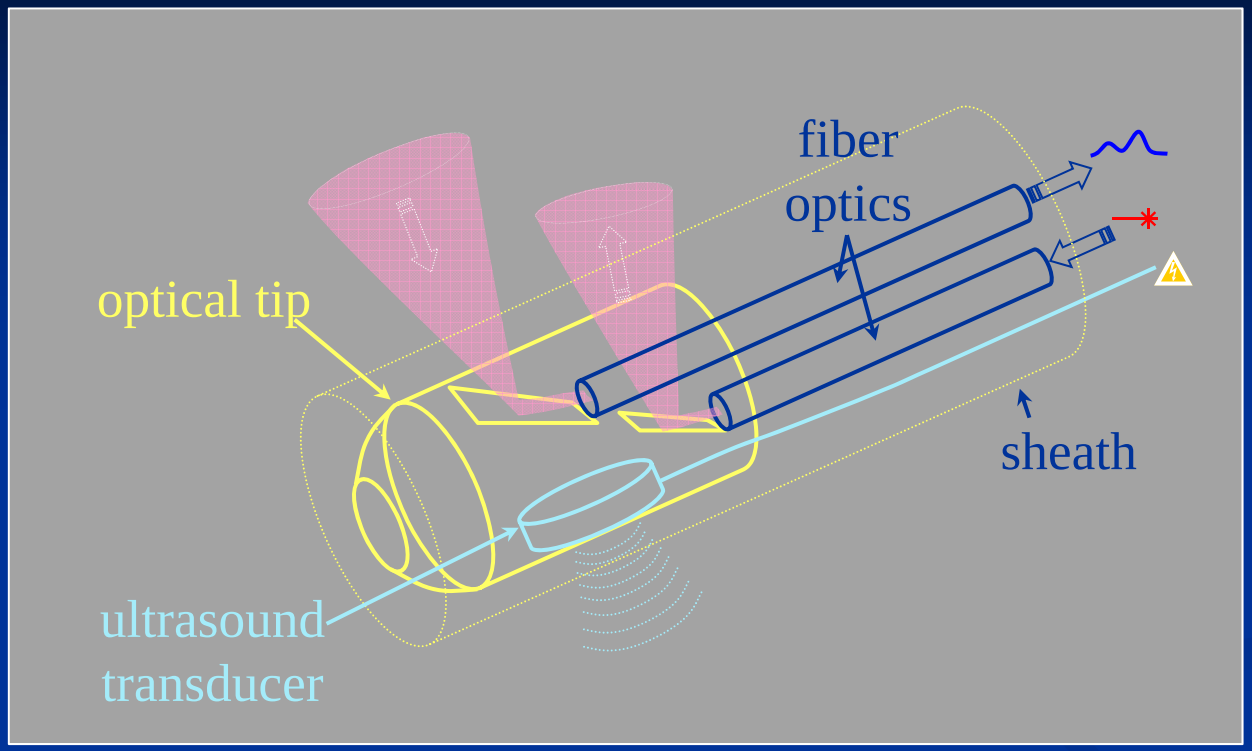
Pixels formed into an image

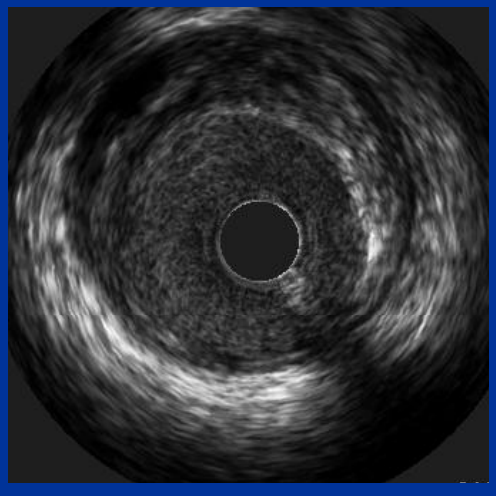


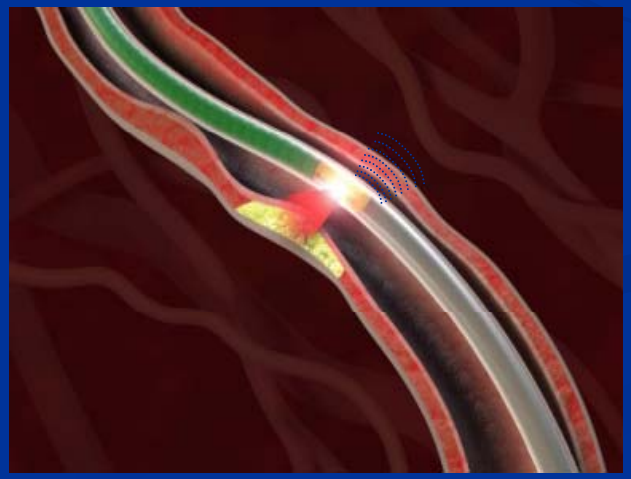


Sean Madden Ph.D and Joel Raichlen, MD

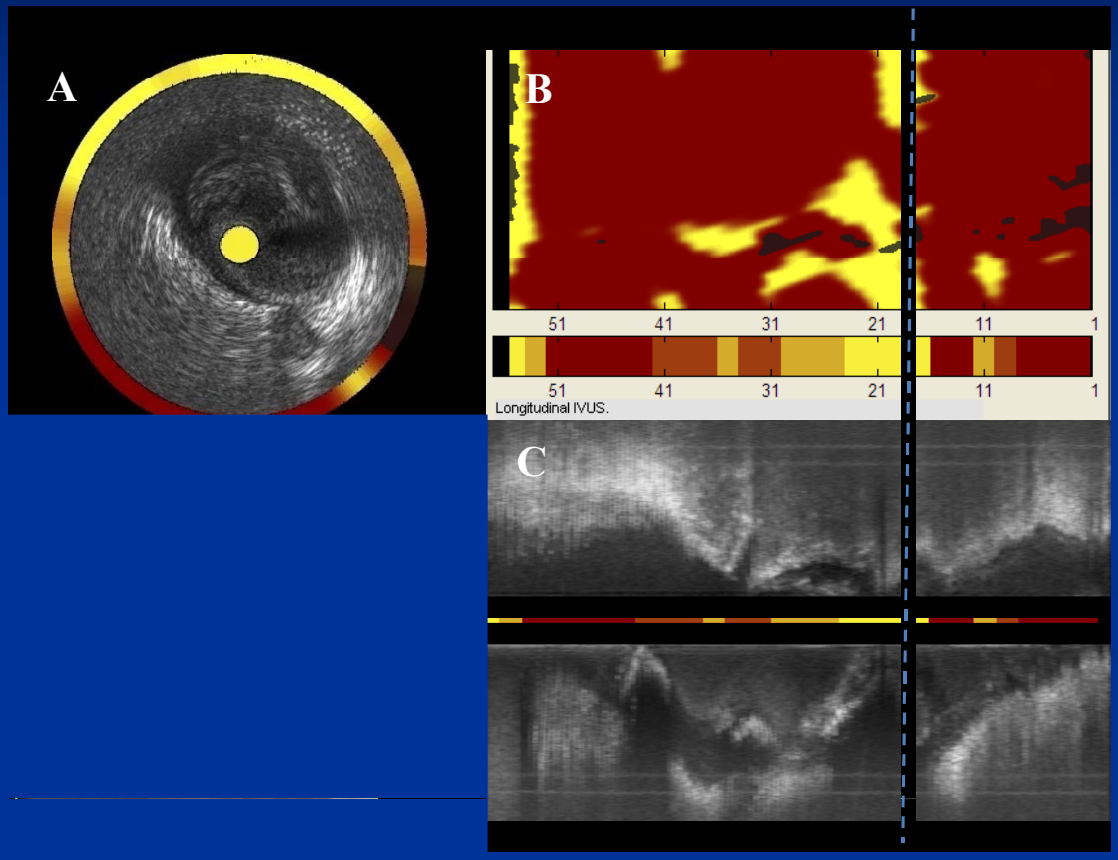
LipiScan IVUS: single catheter

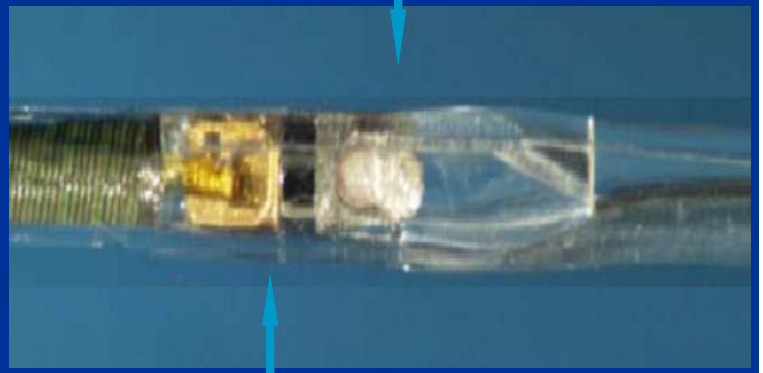






Combination catheter: proof of concept

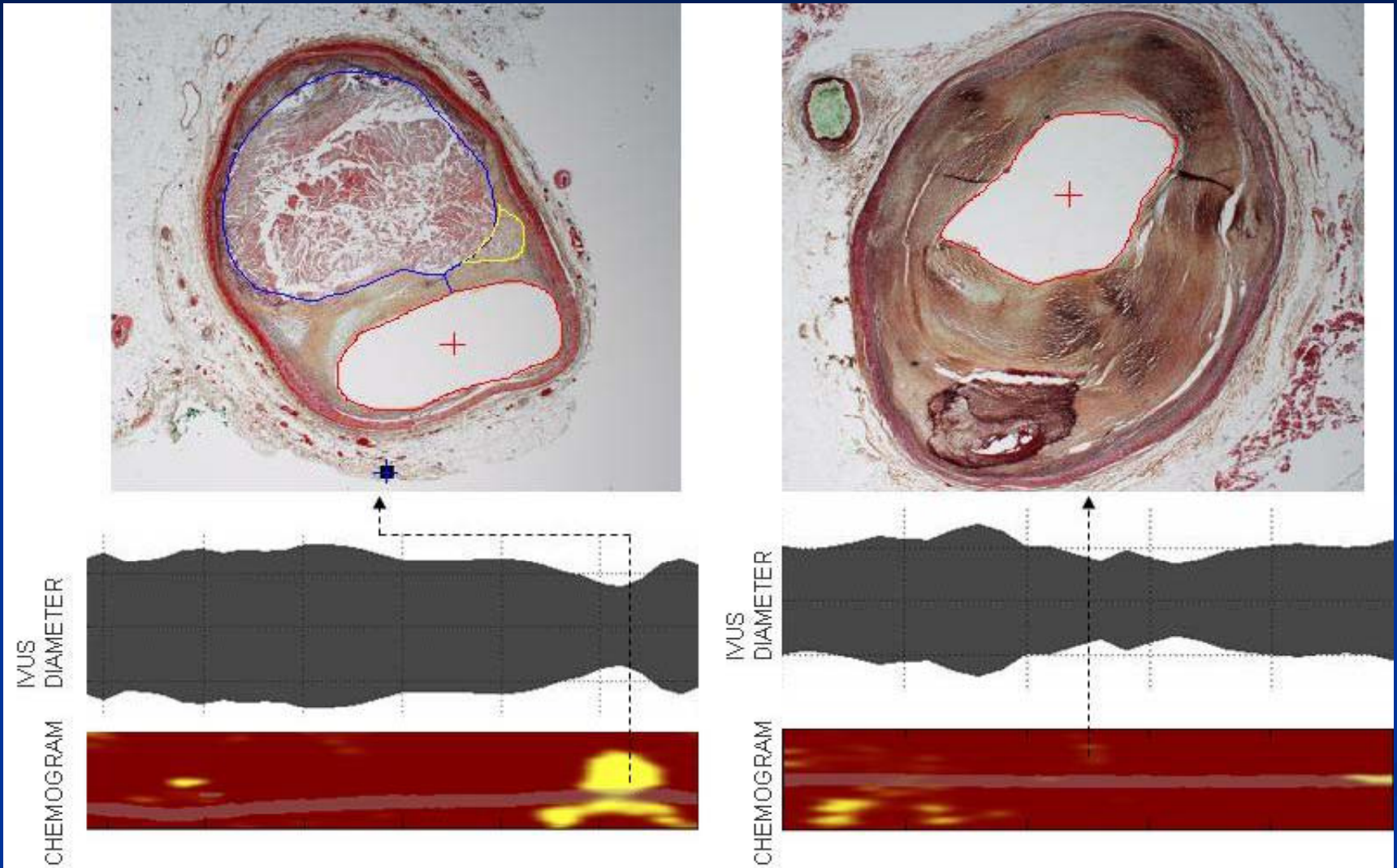




NIR – Lipid Core
IVUS – Structural Image

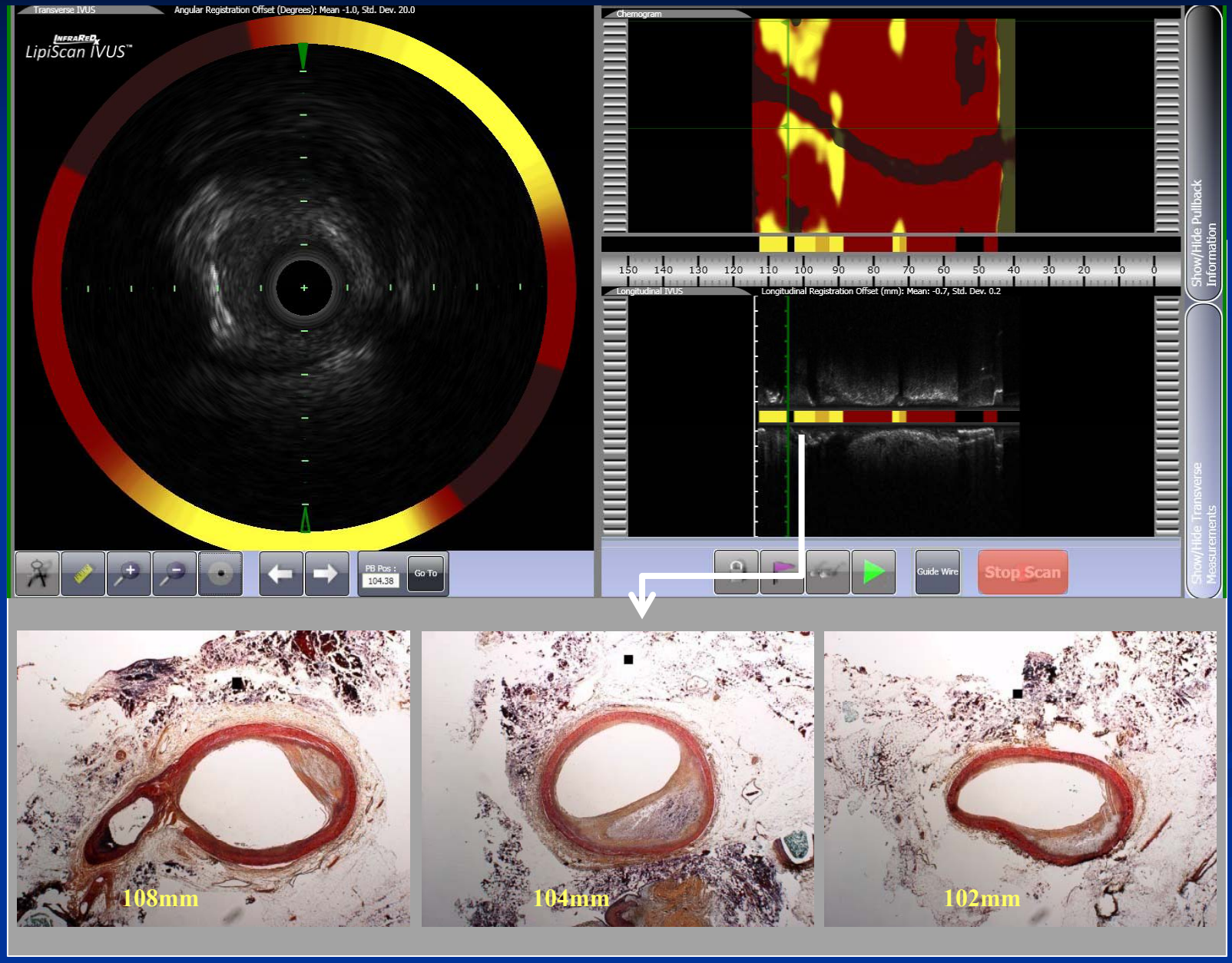
Schulz et al. JACC 2009

Structure and composition

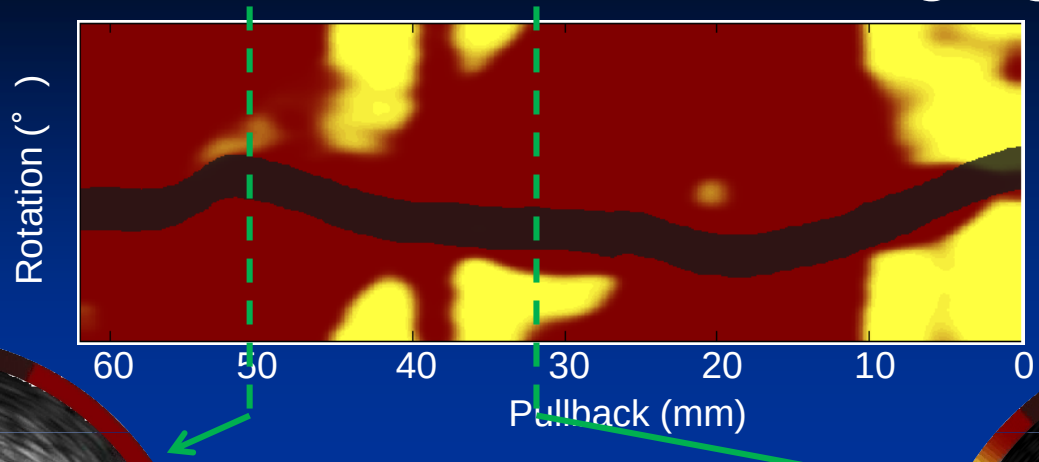


Two areas with same stenosis, but different composition

LipiScan IVUS with histology

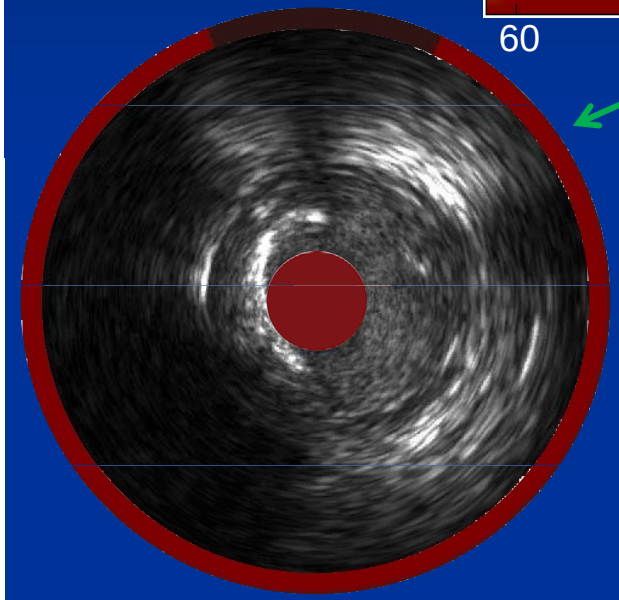


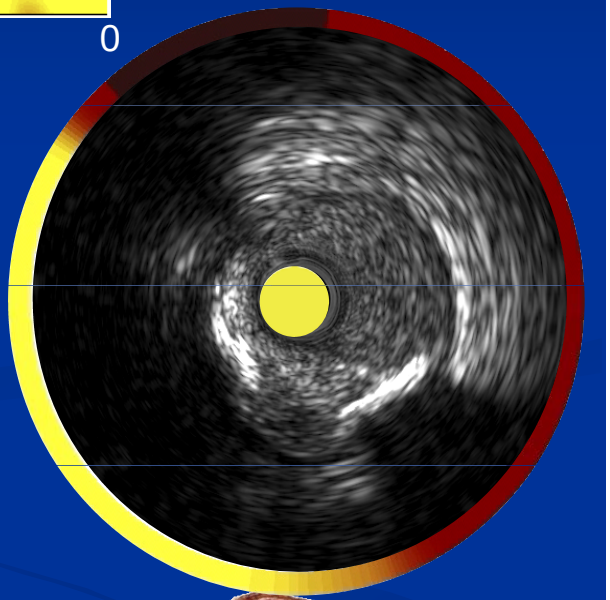
Simultaneous IVUS and NIR Imaging: Autopsy



A

B





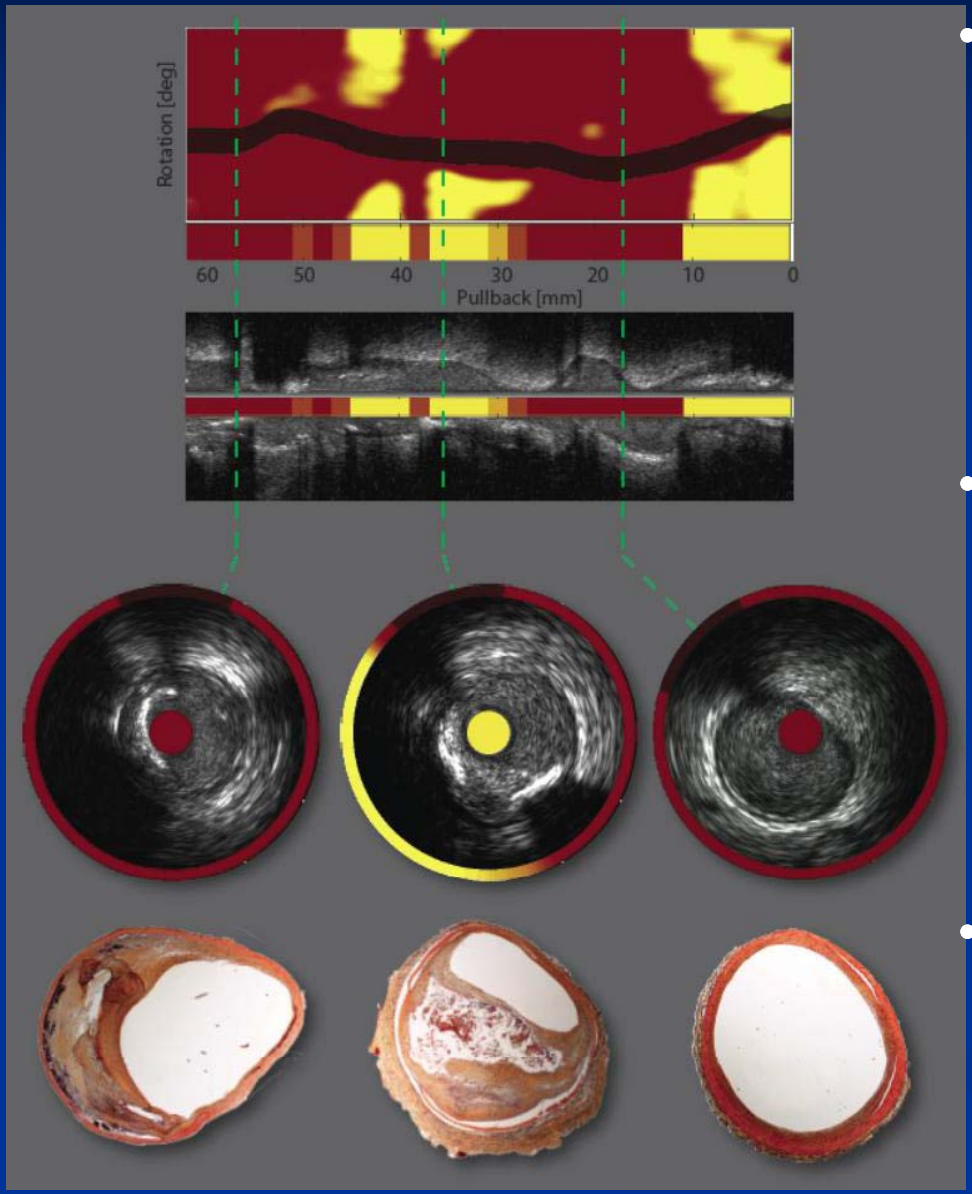
NIR indicates fibrous plaque at A lipid core plaque at B

IVUS images show calcification and suggest attenuated plaque

Histology confirms calcified fibrous plaque at A

Lipid core plaque at B

LipiScan IVUS with Histology



- *Left*
  - **High plaque burden, calcium shadowing and signal dropout on IVUS, but no lipid core plaque by NIRS**
  - **Histology confirms calcified fibrous plaque**
- *Center*
  - **High plaque burden, calcium shadowing and signal dropout on IVUS, and substantial lipid core plaque by NIRS**
  - **Histology confirms large lipid core plaque**
- *Right*
  - **No plaque burden on IVUS and no lipid core plaque by NIRS**
  - **Histology confirms normal vessel**

Summary

- Near infra red light can detect the presence of lipid in vessel walls
- This can be displayed with high spatial resolution, either alone, or in combination with co-registered IVUS images
- Well validated in perfused human coronary arteries
- Performance characteristics should allow the study of lipid content over time, or in response to treatment