Invasive Coronary Imaging Modalities for Vulnerable Plaque Detection

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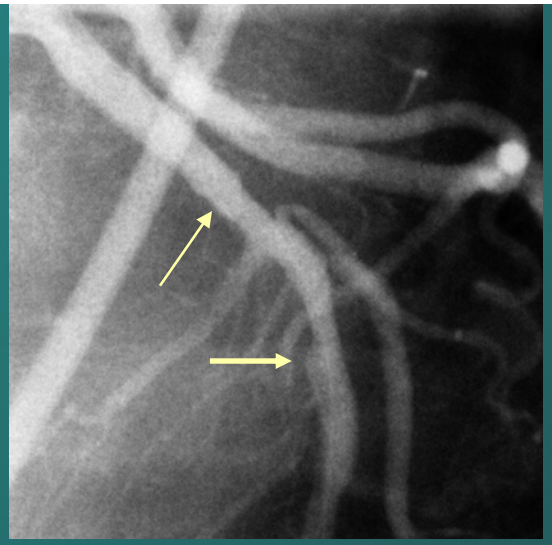
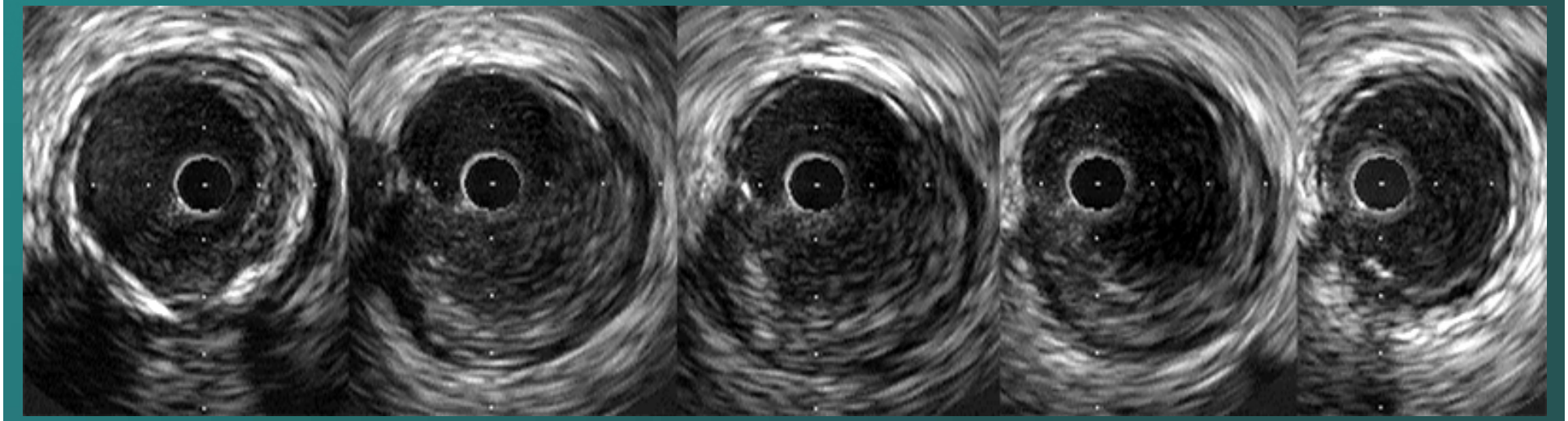
Greyscale IVUS studies have shown

- Plaque ruptures do not occur randomly or at minimally diseased sites.
- Rather, plaque ruptures (and, therefore, rupture-prone plaques) predictably occur in large, proximal coronary arteries with significant plaque accumulation and positive remodeling. It is only the degree of lumen compromise that is variable and often insignificant.
- Nevertheless, greyscale IVUS cannot predict or even detect a vulnerable plaque.



Proximal 0 → 3mm → 12mm



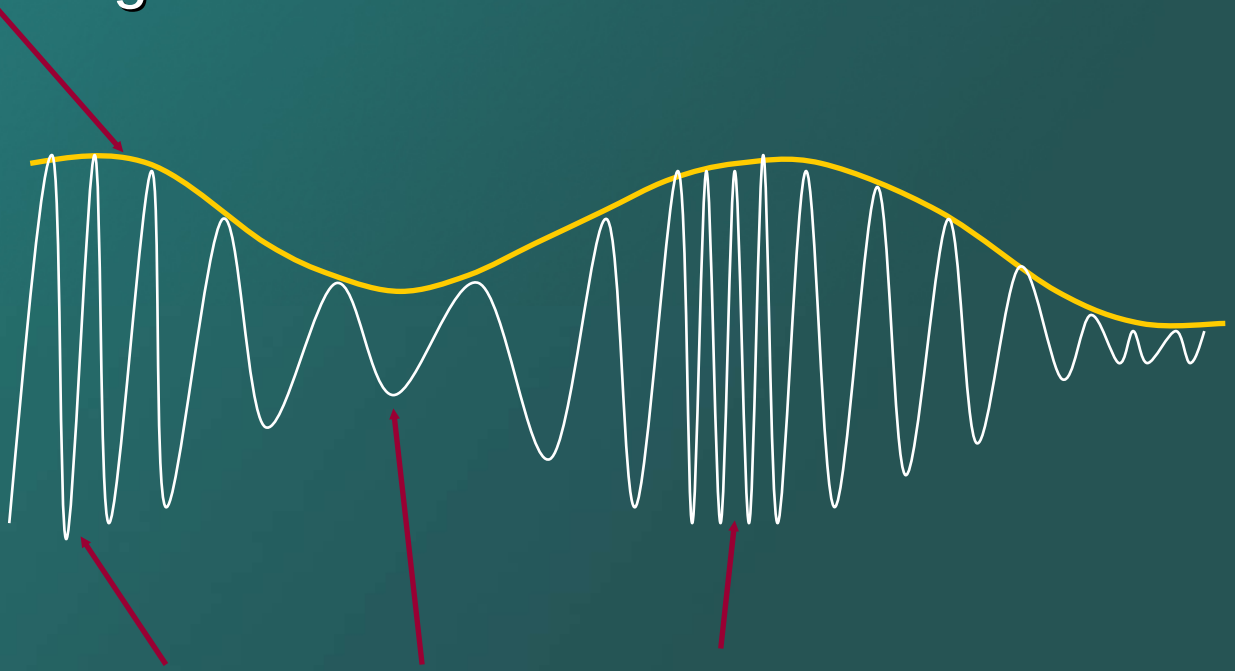
EEM CSA = 21.0mm^2
Lumen CSA = 9.5mm^2
P+M CSA = 11.5mm^2

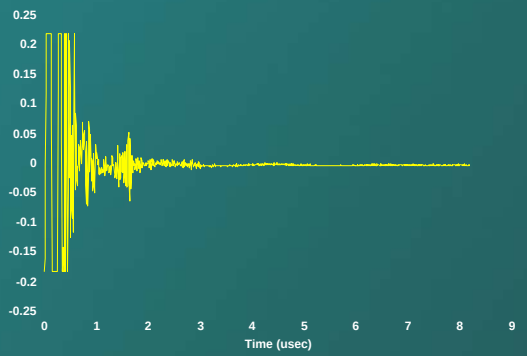
EEM CSA = 23.5mm^2
Lumen CSA = 5.5mm^2
P+M CSA = 18.0mm^2
Max P+M Thickness=3.0mm
Plaque burden=0.79
Remodeling index=1.3

EEM CSA = 13.7mm^2
Lumen CSA = 9.3mm^2
P+M CSA = 4.4mm^2

Virtual Histology (VH) - IVUS

Only the envelope amplitude (echo intensity) is used to form the **gray-scale IVUS** image

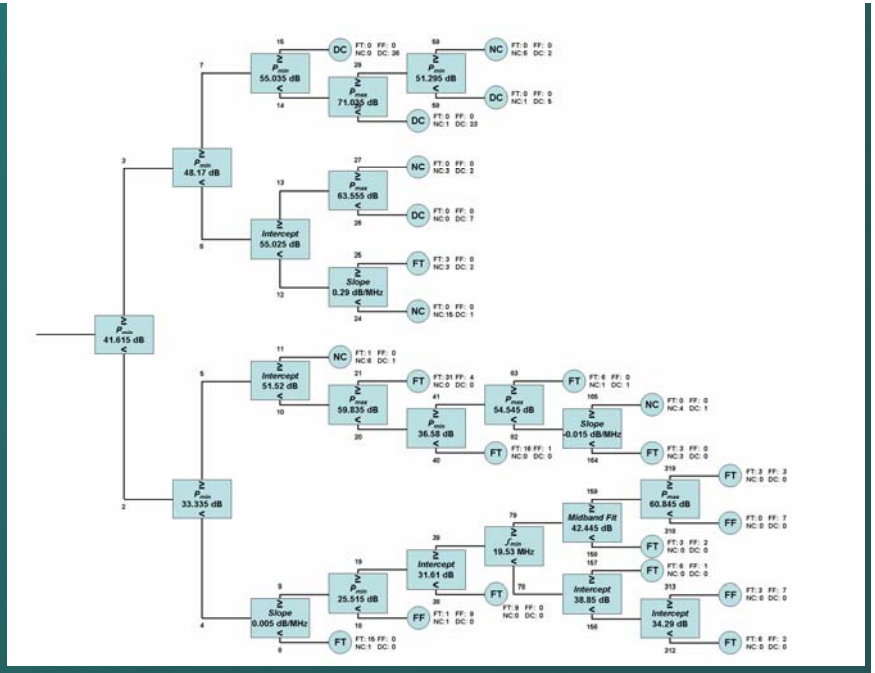


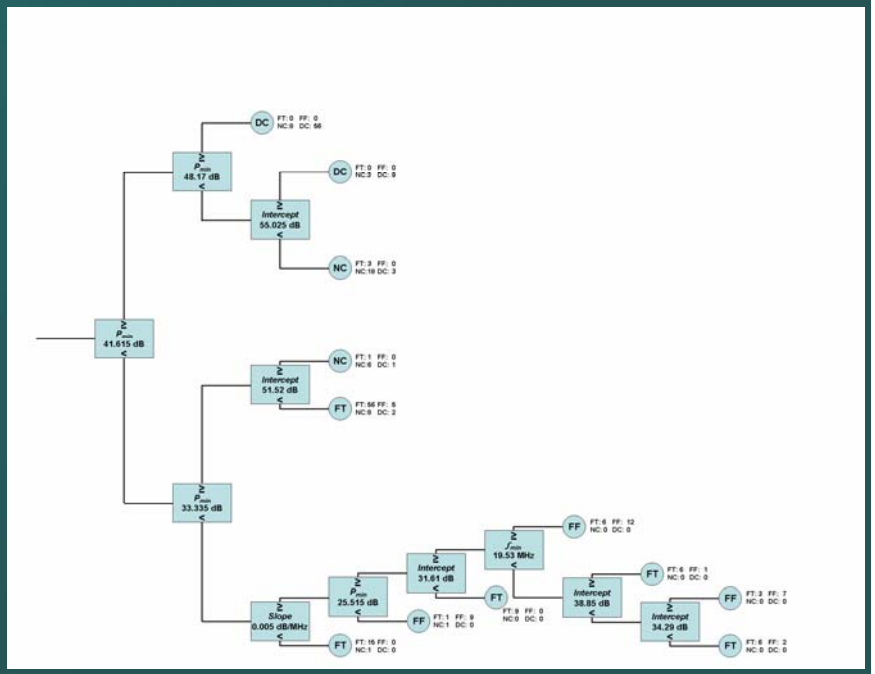


Among reflected ultrasound signals of the same intensity, frequency can also vary depending on the tissue

Two examples of plaque composition classification trees based on these 8 parameters

- maximum power
- corresponding frequency
- minimum power
- corresponding frequency
- Slope
- *y*-intercept
- mid-band fit
- integrated backscatter





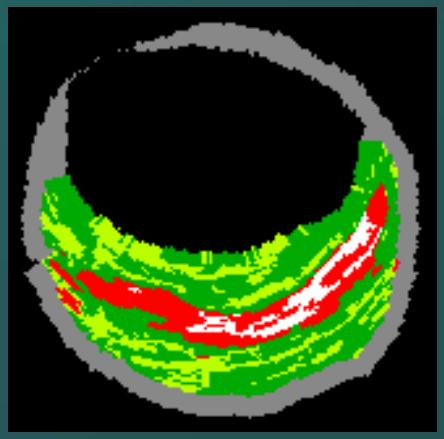
Eagle Eye (20MHz Electronic Array Transducer)

VH IVUS vs histopathology from fresh 51 fresh, post mortem LADs (115 sections and 407 regions of interest)

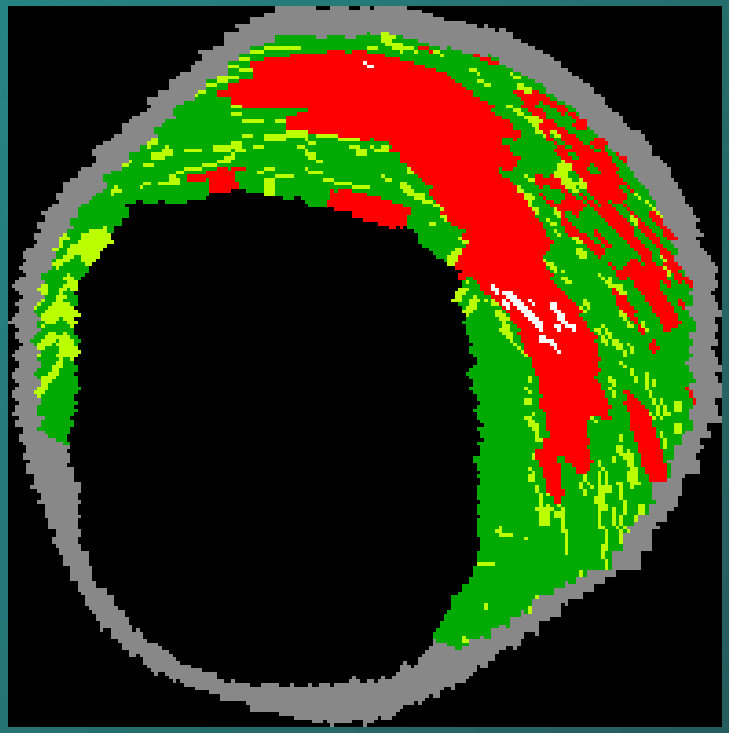
	Sensitivity	Specificity	Predictive Accuracy
Fibrous tissue (n=162)	84.0%	98.8%	92.8%
Fibrofatty (n=84)	86.9%	95.1%	93.4%
Necrotic core (n=69)	97.1%	93.8%	94.4%
Dense calcium (n=92)	97.8%	99.7%	99.3%

Fibroatheroma

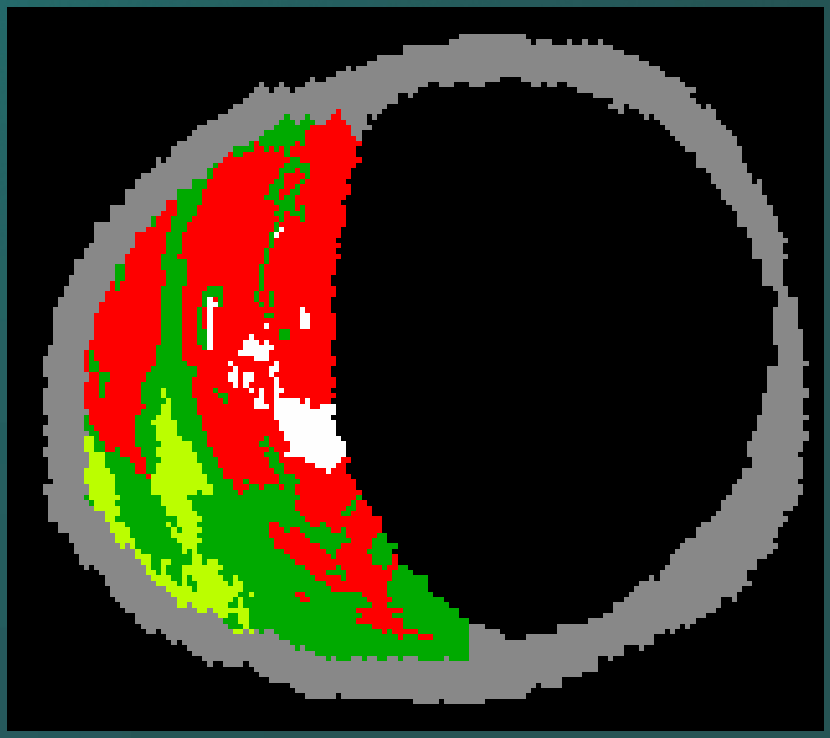
Fibrotic cap and significant necrotic core
(confluent NC >5% of total plaque volume)
within fibrotic or fibrofatty tissue



Fibroatheroma with evidence of thick fibrous cap

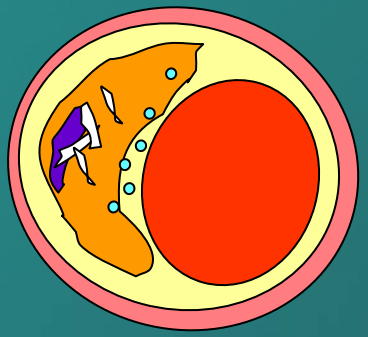


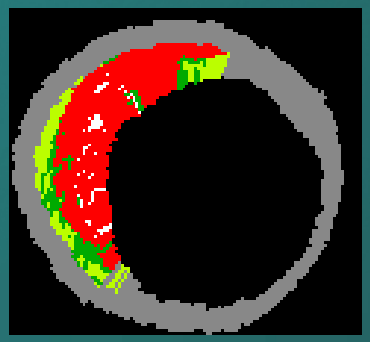
Fibroatheroma without evidence of thick fibrous cap

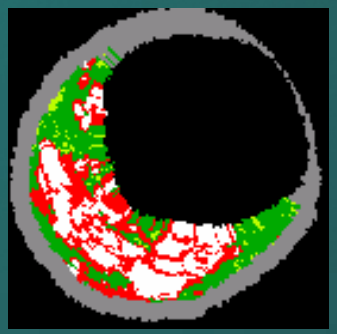


Thin Cap Fibroatheroma (TCFA)

"Thin Cap Fibro-Atheroma (TCFA)" or "Vulnerable Plaque" -- Necrotic Core >10% of total plaque and located at or near the lumen in 3 consecutive frames. Based on the presence or absence of Ca, the length of the NC, or signs of previous ruptures, TCFA can be further sub-classified for the purpose of risk assessment



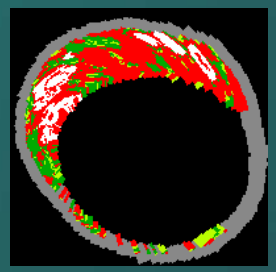


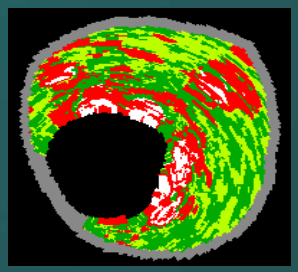


<5% calcium **>5% calcium** **multiple layers**

Still further sub-classification can be based on presence of luminal narrowing.

"TICFA without significant narrowing" - plaque burden <50% on IVUS and/or less than 25% narrowing on angiogram. (Pathologic data suggests that TCFA without significant plaque burden are less "vulnerable")



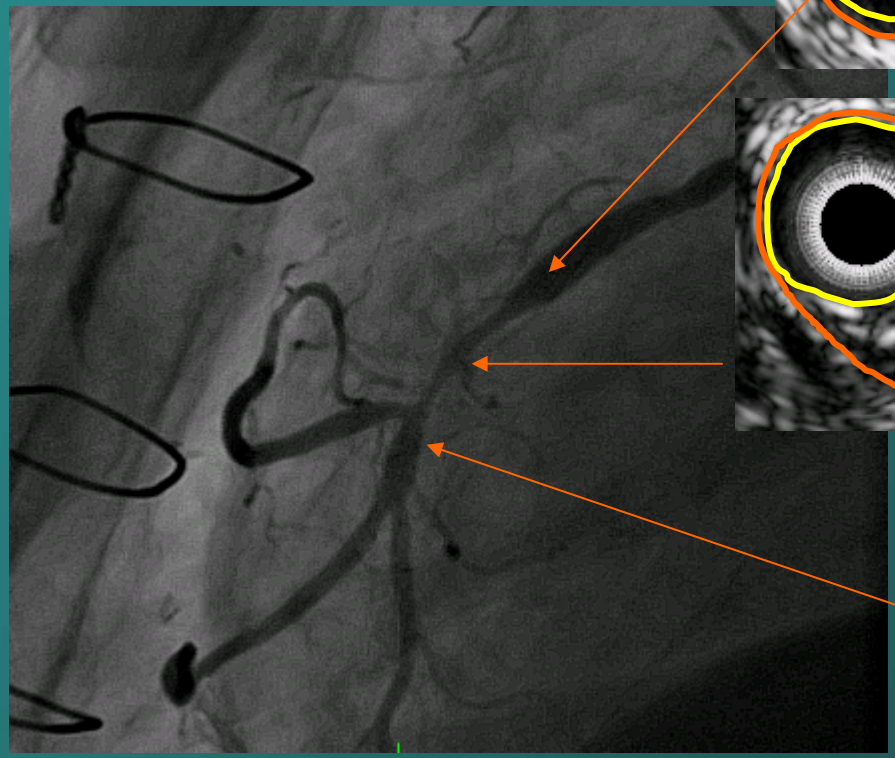


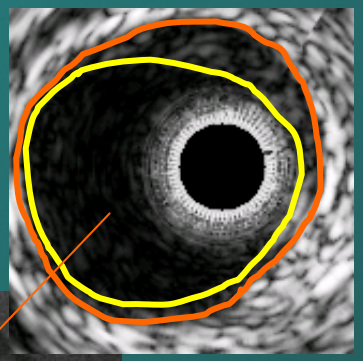
"Highest Risk TCFA"

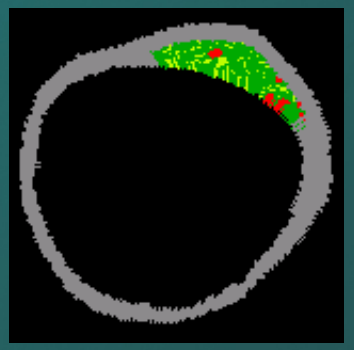
a. **Confluent NC>20%**
b. **No evidence of fibrotic cap**
c. **Calcium >5%**
d. **Remodeling index >1.05**
e. **>50% plaque burden by IVUS**

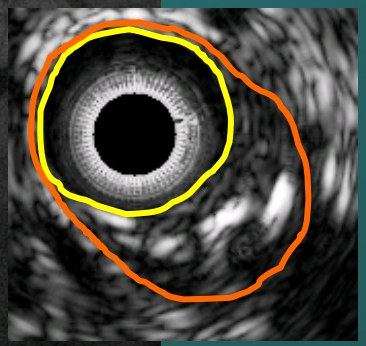
(Pathologic data suggests that TCFA with significant plaque burden are the most vulnerable)

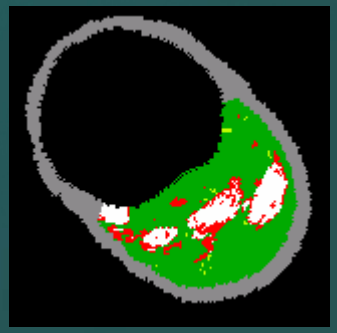
Multiple small calcific deposits by greyscale IVUS, multiple necrotic cores by VH-IVUS

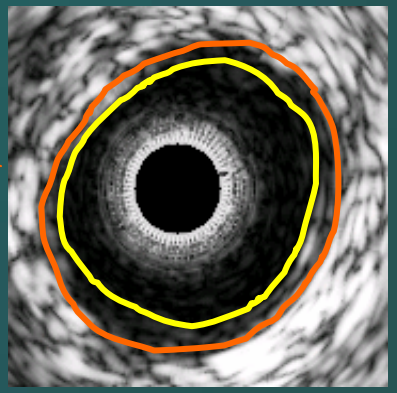


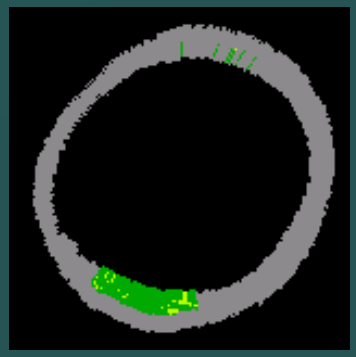










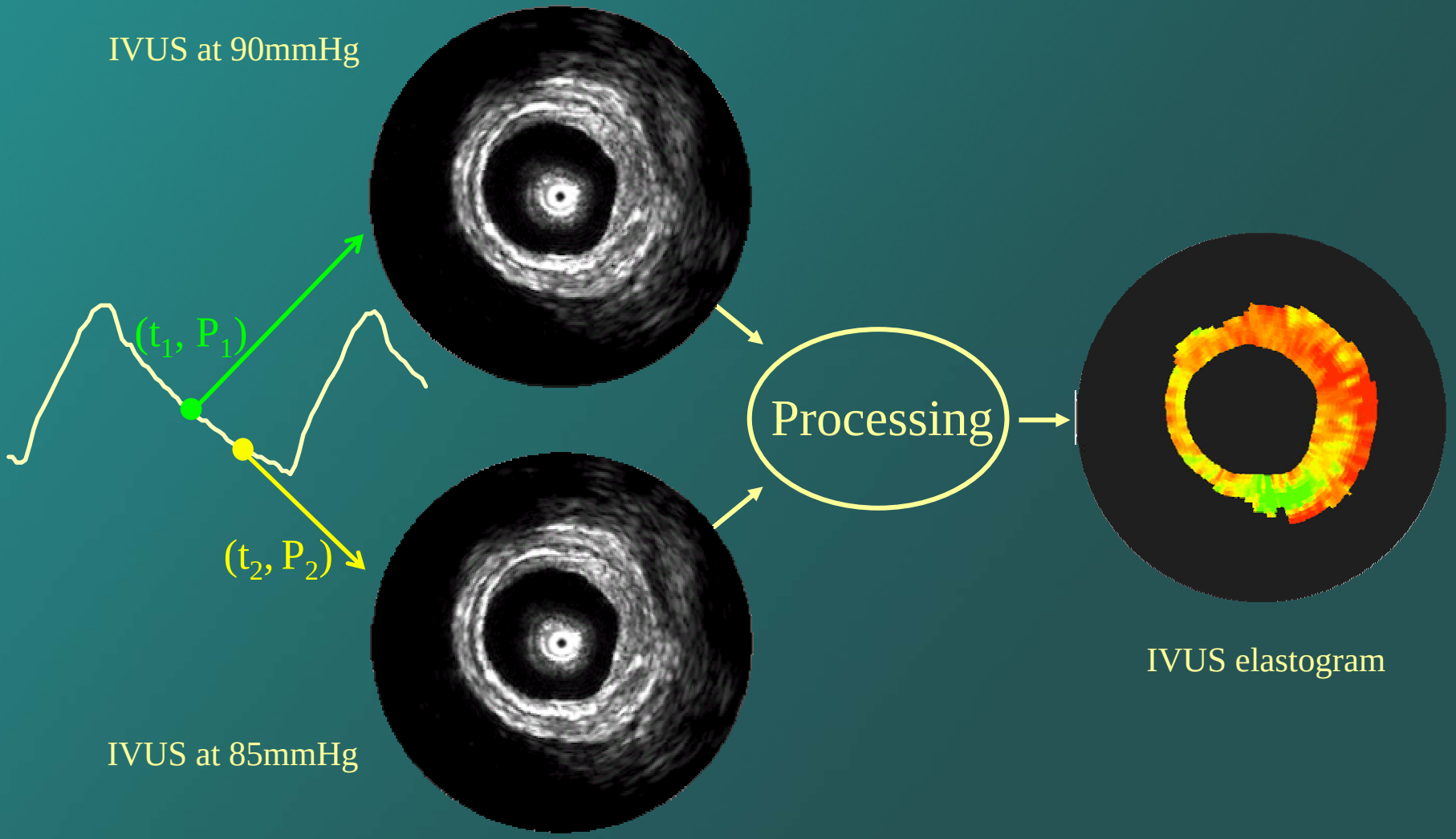


Healed ruptures are common in patients with acute events

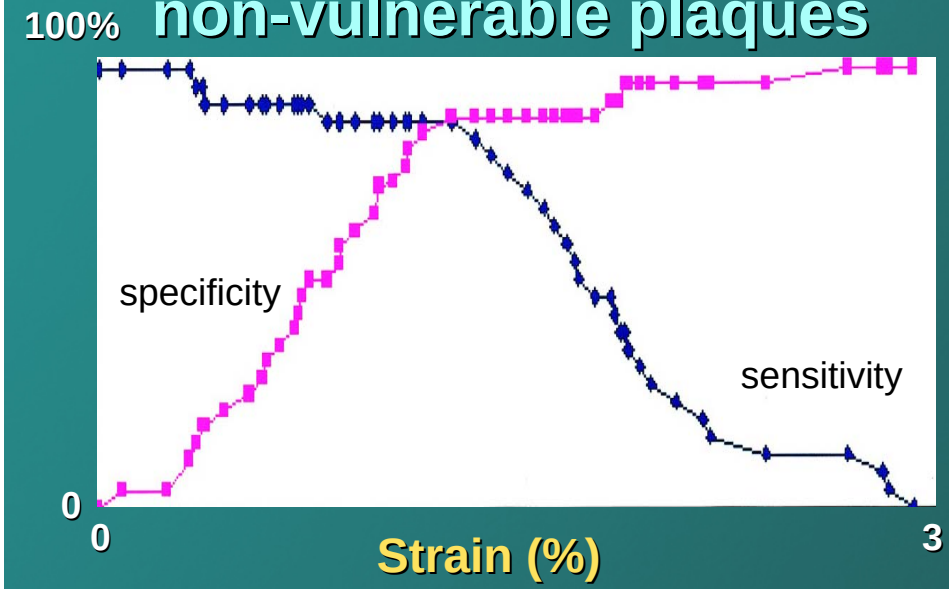
- In 142 men with sudden cardiac death, the mechanism of death was presumed to be acute plaque rupture with acute thrombus in 44, acute plaque erosion with acute thrombus in 23, stable plaque with healed MI in 41, and stable plaque without MI in 34
- There were 189 healed rupture sites. Healed ruptures were present in 75% of hearts with acute plaque rupture and 80% of hearts with stable plaque and healed MI
- Of the 44 acute rupture sites, 9 showed 1 healed previous rupture site, 9 showed 2 healed previous rupture sites, 9 showed 3 healed previous rupture sites, and 6 showed 4 healed previous rupture sites.
- Acute ruptures at sites of ≥3 healed previous ruptures demonstrated greater underlying plaque burden (94±4%) than those without healed previous rupture (74±12%).

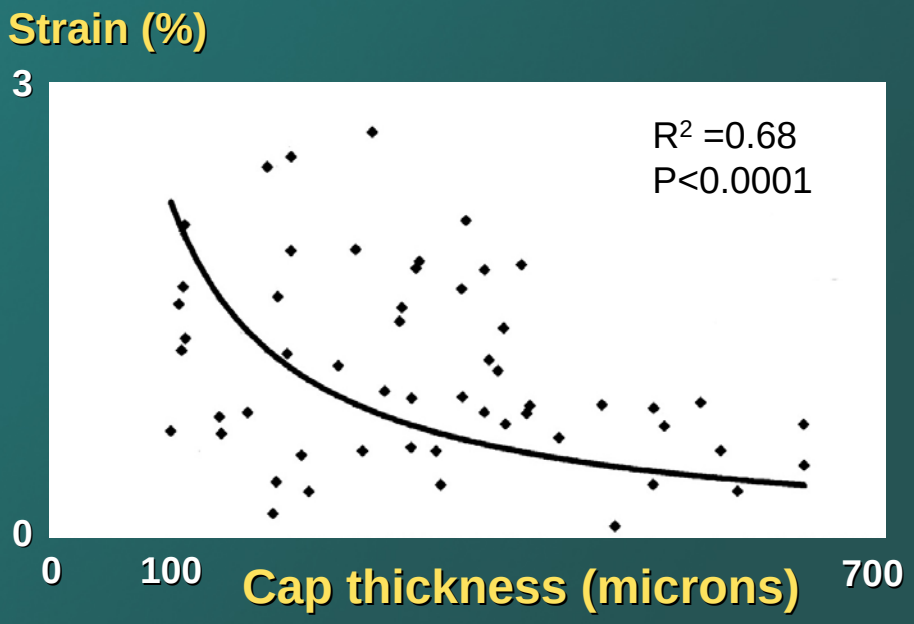
(Burke et al. Circulation 2001;103;934-40)

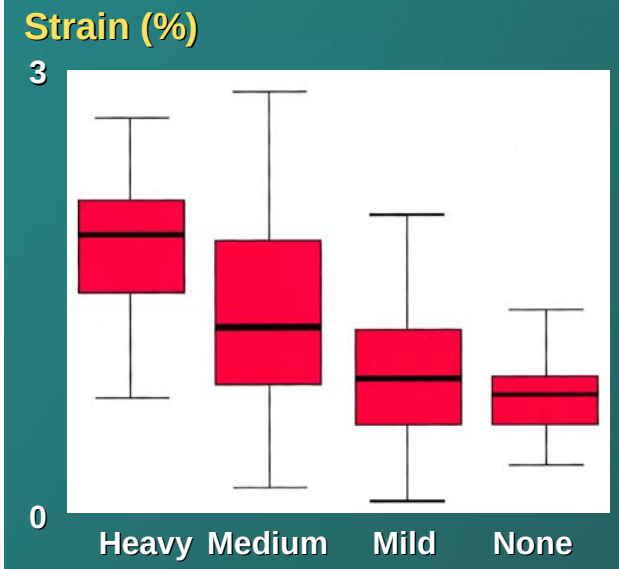
Palpography

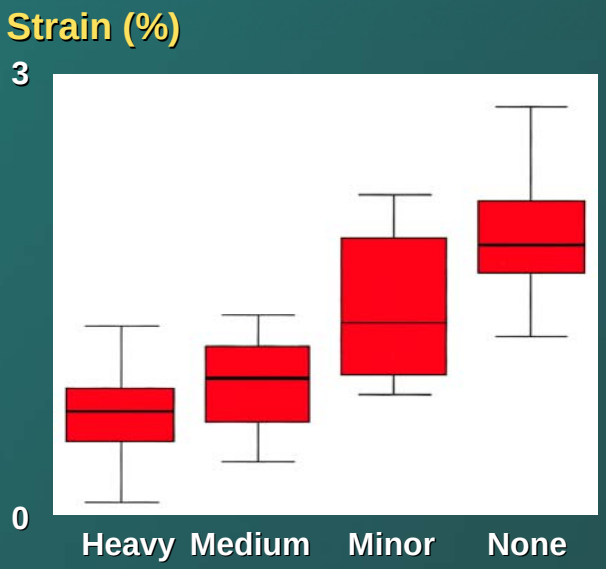


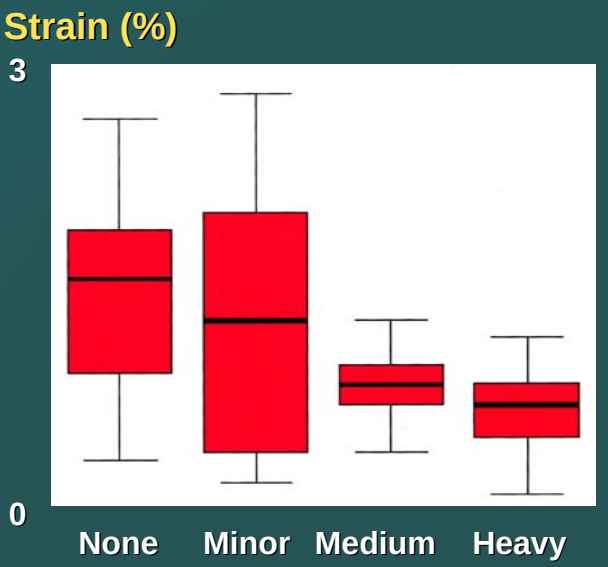
26 vulnerable vs 28 non-vulnerable plaques



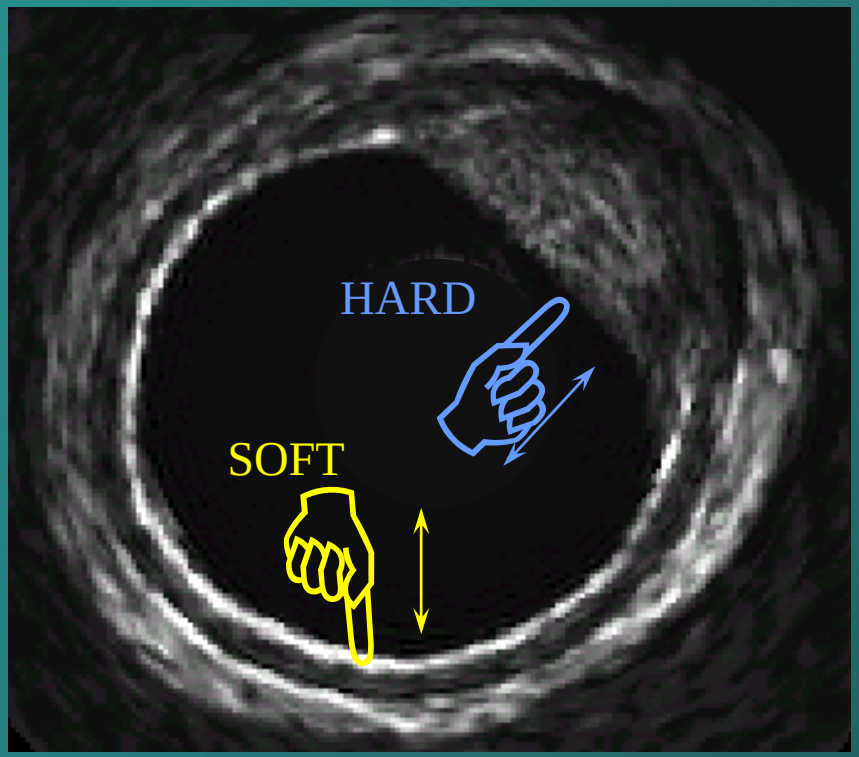


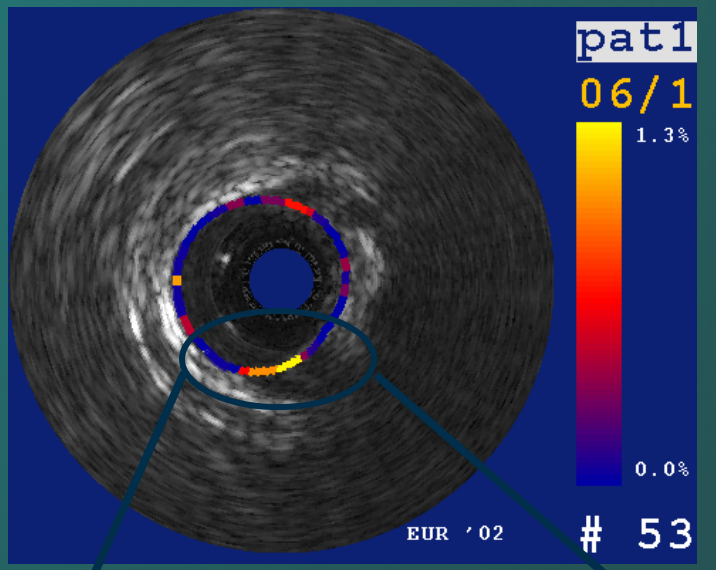


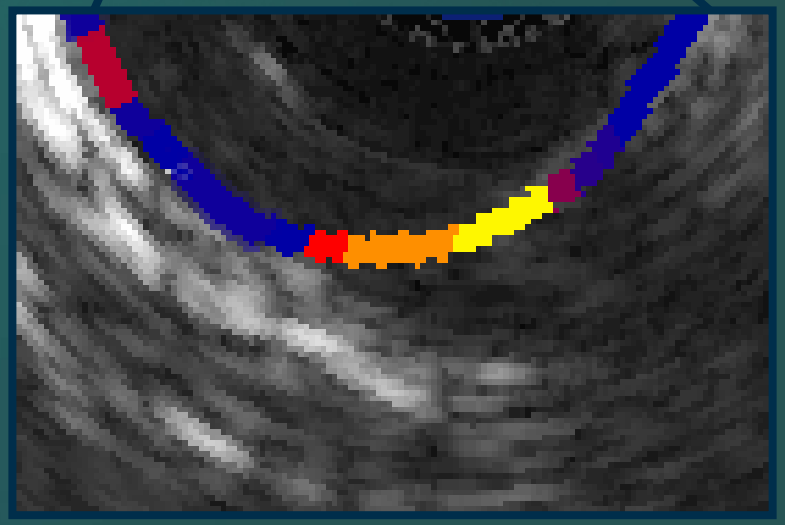




(Schaar et al. Circulation 2003;108:2636-41)







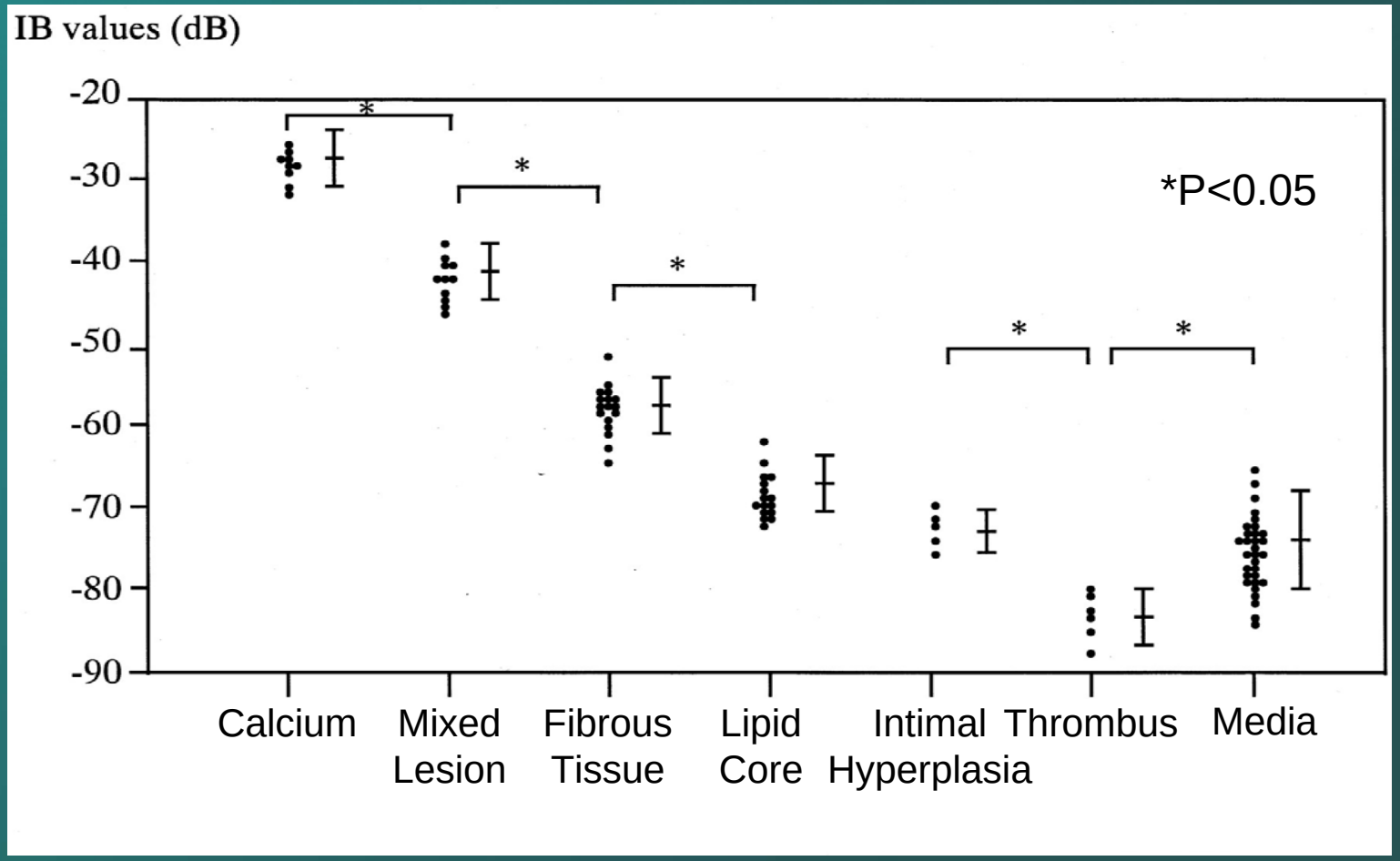
Independent predictors of strain were macrophages (p=0.006) and smooth muscle cells (p=0.0001)

VH-IVUS vs Palpography (N=27 patients, 60 high strain spots, and 63 low strain spots)

- Weak inverse correlation between %dense calcium and strain level (r=-0.20, p=0.03)
- No significant correlation between %necrotic core (r=0.11, p=0.25) or fibrotic or fibrofatty plaque vs strain level
- Strain was higher when necrotic core was in contact with the lumen (1.03±0.5% vs 0.86±0.4%, p=0.06)
- Necrotic core in contact with the lumen was the only independent predictor of high strain (OR=5.0, p=0.003)
- Sensitivity of VH-IVUS 75% and specificity 44% to detect high strain.

(Rodriguez-Granillo et al. Am Heart J 2006;151:e1-e6)

Integrated Backscatter (IB) IVUS



(Kawasaki, M. et al. Circulation 2002;105:2487-2492)

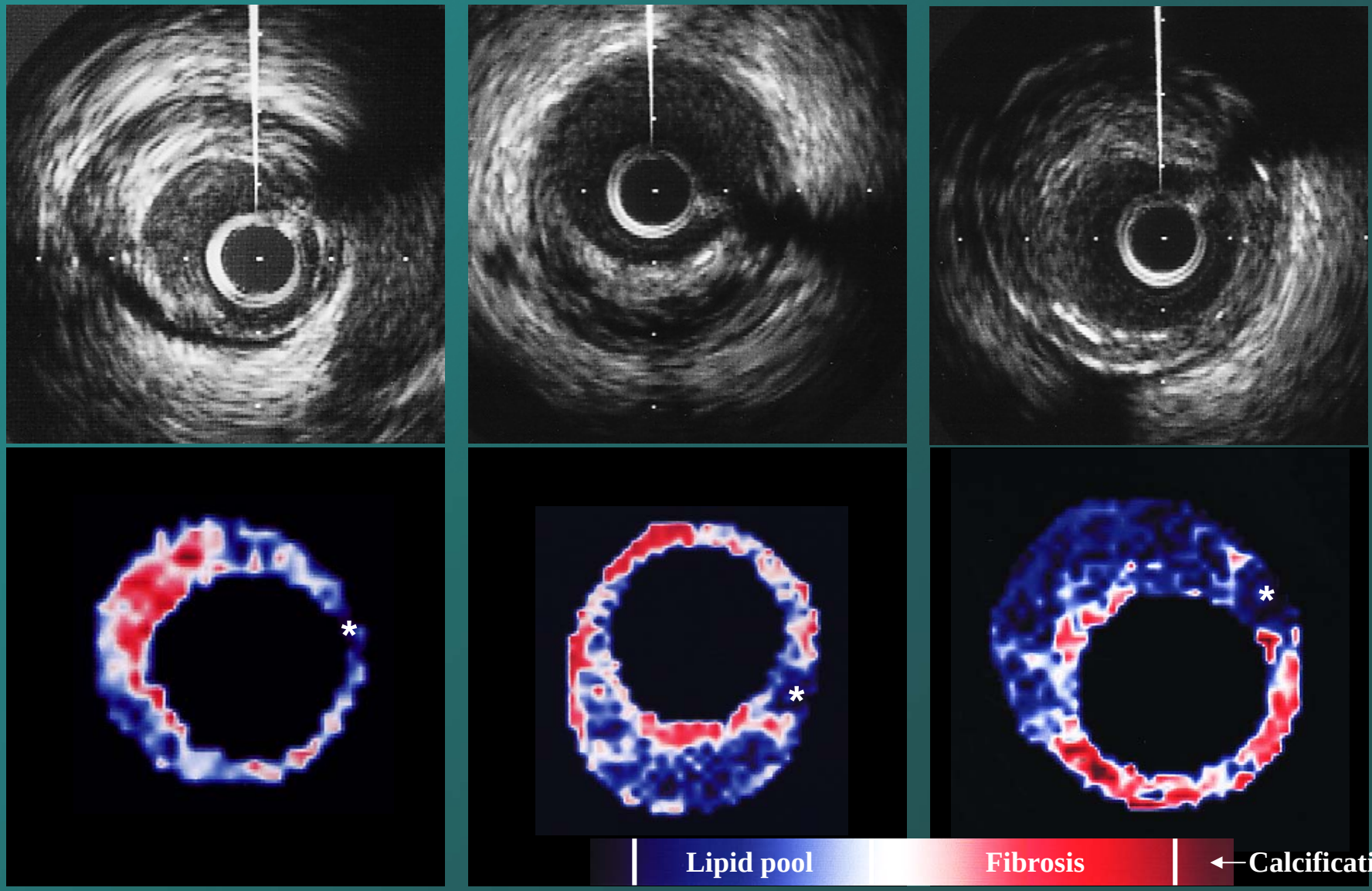
Diagnostic accuracy of real-time IB (Integrated Backscatter)-IVUS

	Sensitivity	Specificity	PPV	NPV
Calcification (n=144)	95%	99%	93%	99%
Fibrosis (n=335)	94%	93%	93%	94%
Lipid pool (n=205)	90%	92%	85%	90%

(Kawasaki et al. Circulation2002;105:2487-92)

Stable Plaque

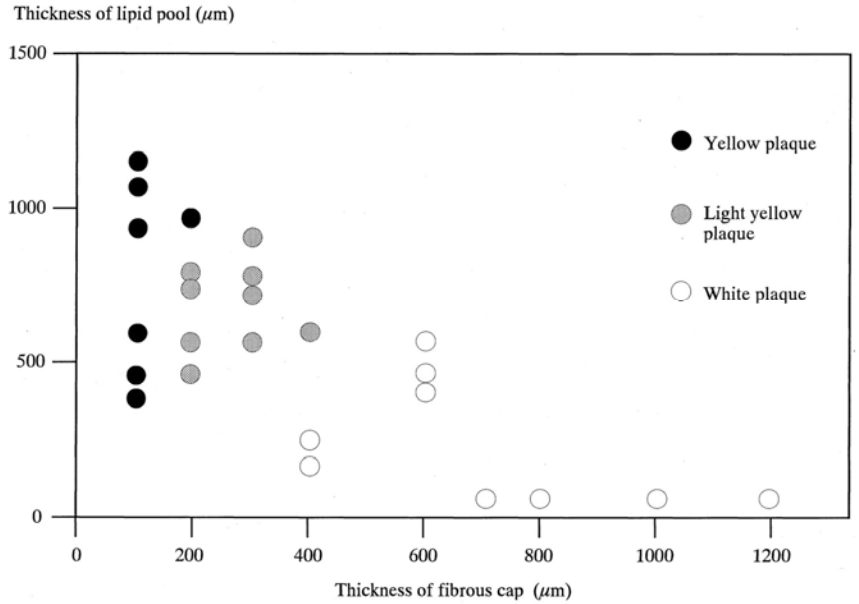
Vulnerable Plaque Causing ACS

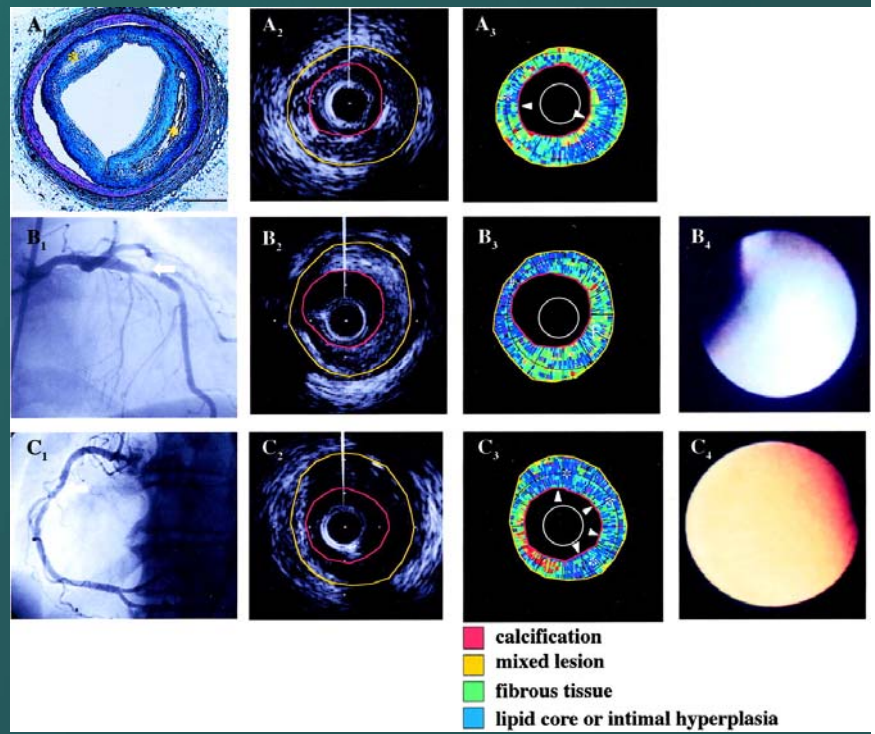


* guidewire artifact

(Sano et al. J Am Coll Cardiol 2006;47:734-41)

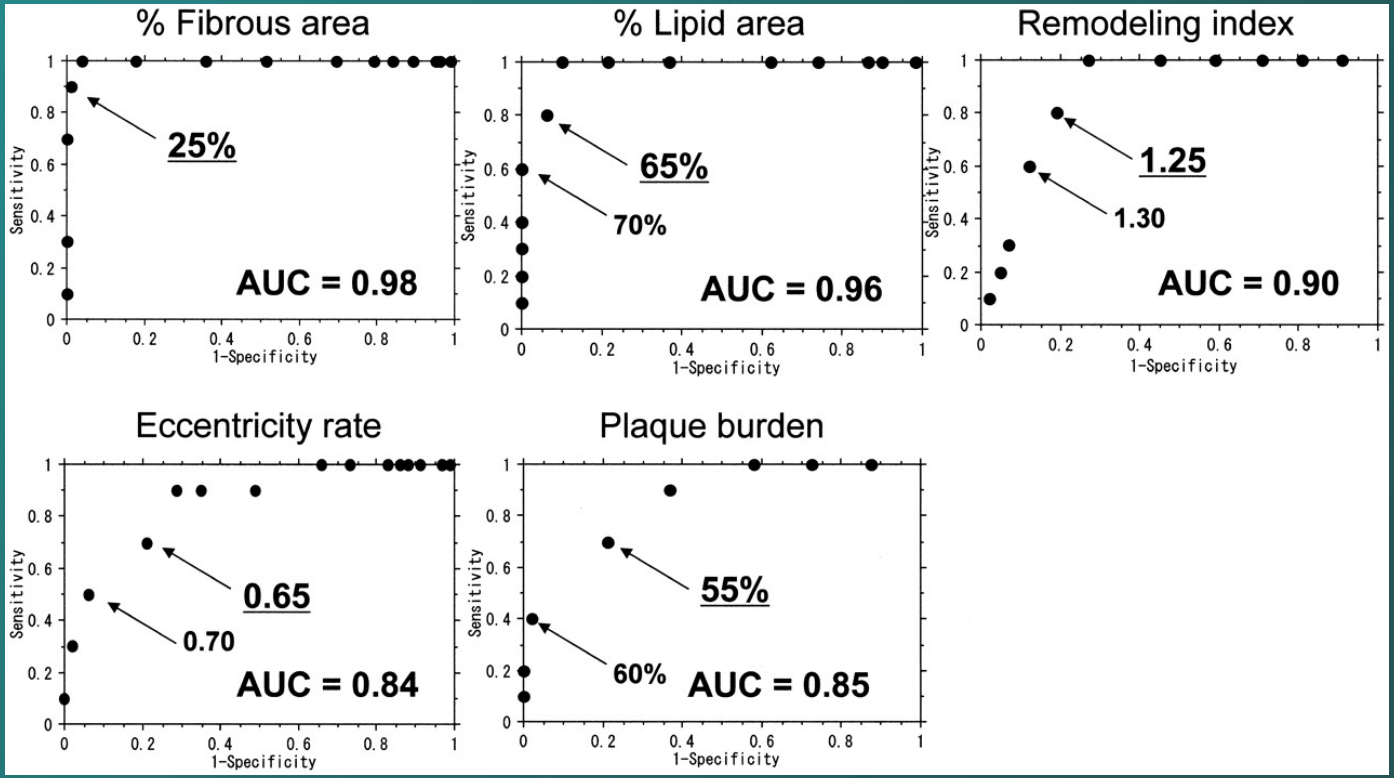
Relation between IB-IVUS thickness of fibrous cap, thickness of lipid core, and angioscopic appearance: Angioscopic plaque color reflects thickness of fibrous cap rather than size of lipid core





(Kawasaki, M. et al. Circulation 2002;105:2487-2492)

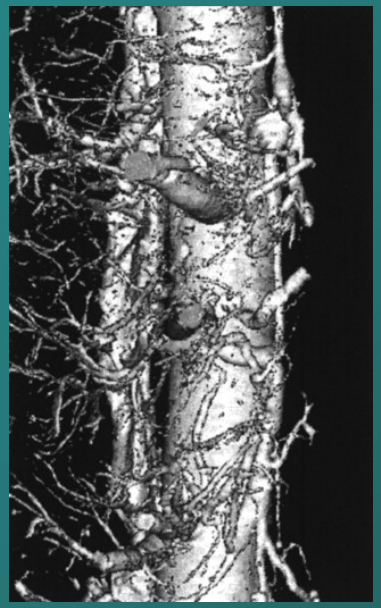
IB-IVUS predictors of vulnerable plaques



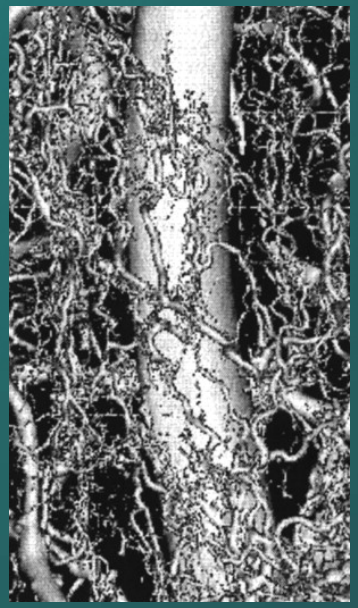
	Sens	Spec	PPV	NPV	Accuracy
%fibrous area (<25%)	90%	96%	69%	99%	95%
%lipid area (>65%)	80%	90%	42%	98%	89%

(Sano, K. et al. J Am Coll Cardiol 2006;47:734-741)

Vasovasorum Imaging



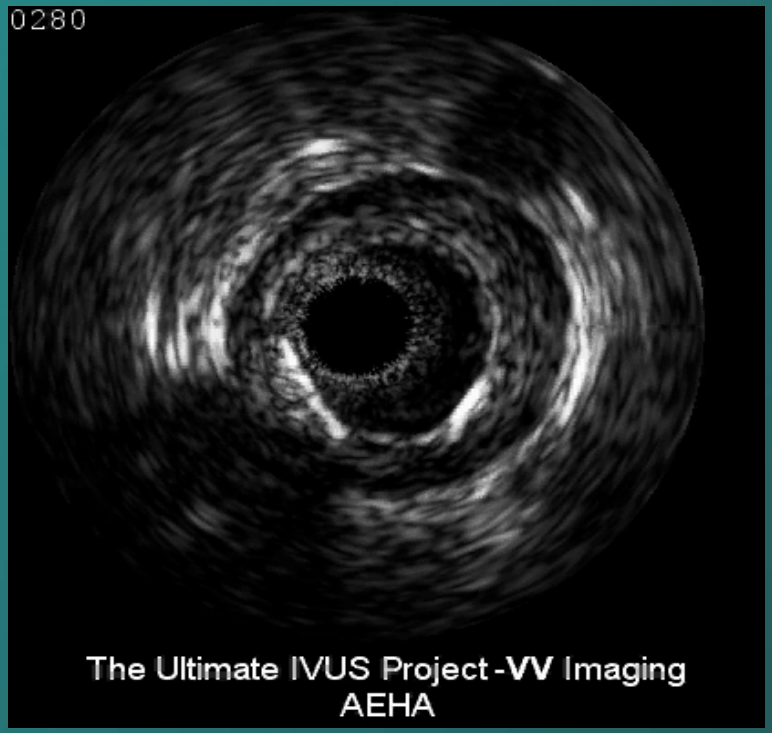
Normal

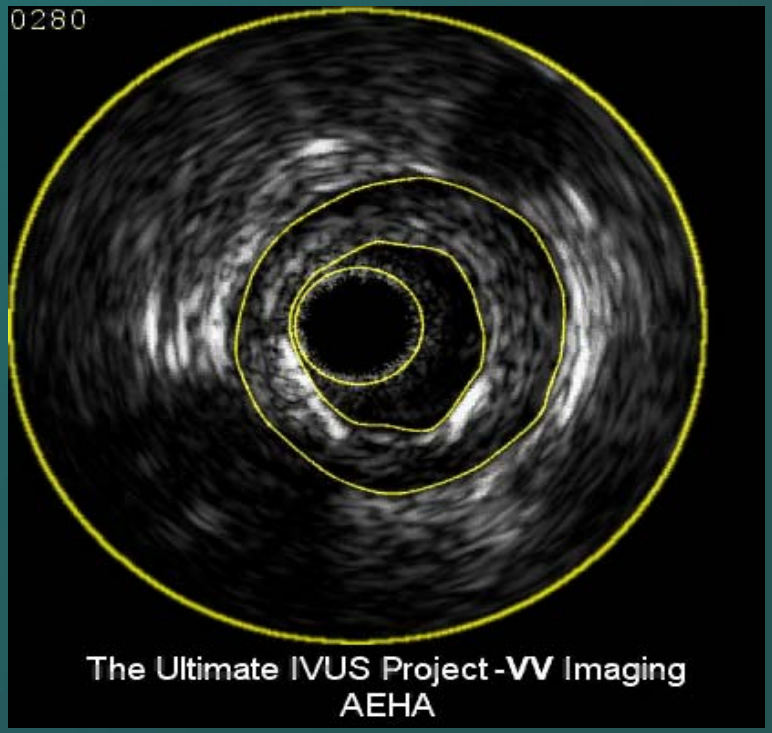


Hypercholesterolemia

Hypercholesterolemia + Statin

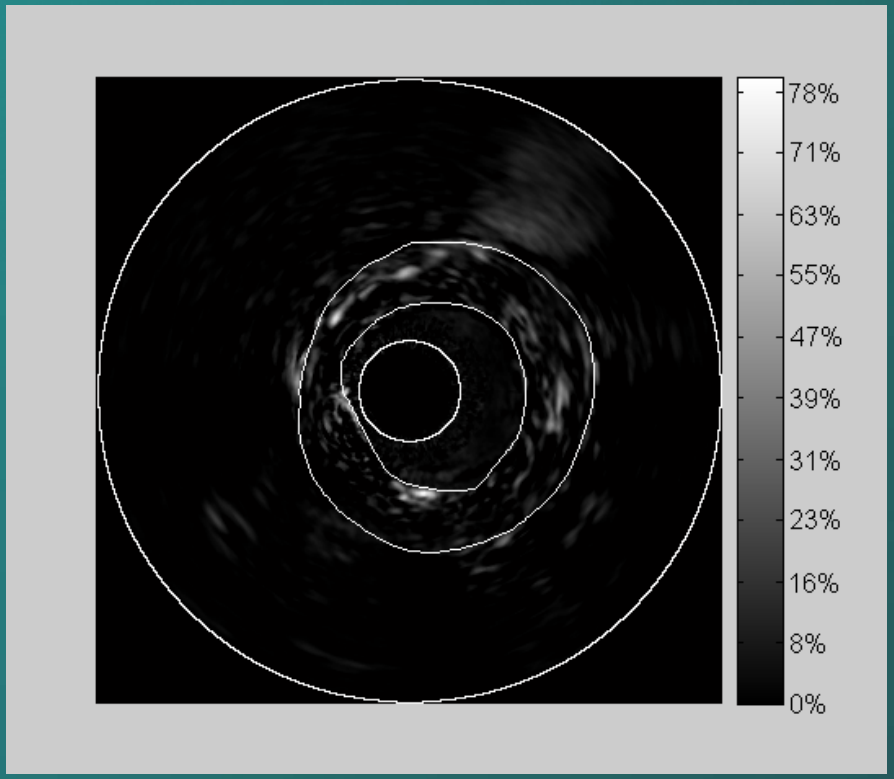
Baseline images are acquired for 20 seconds, and regions of interest are assigned

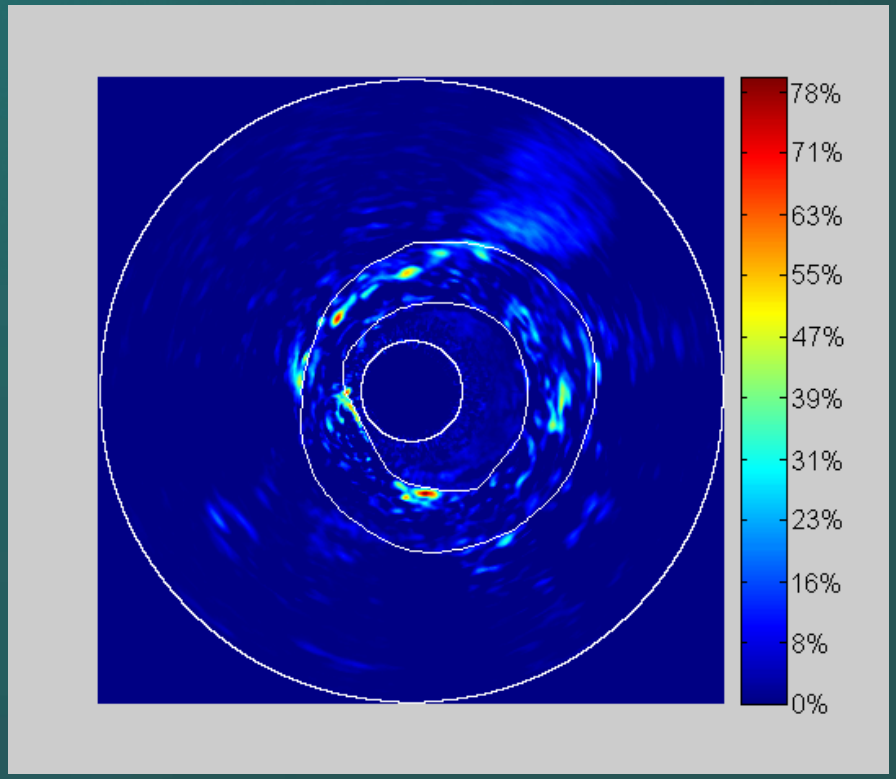


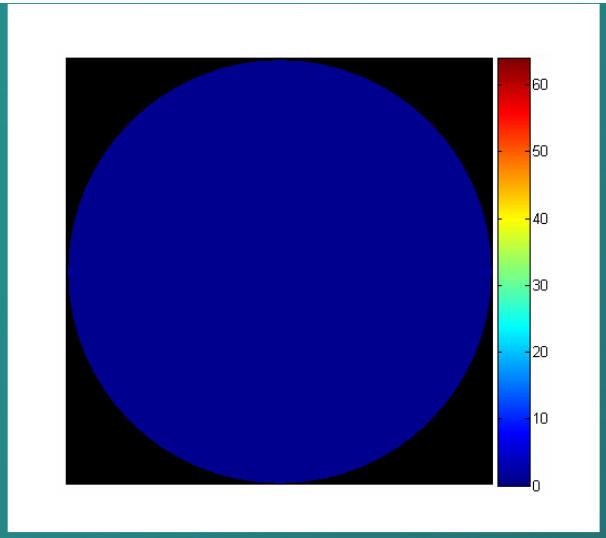


Contrast is injected, images are acquired for 120 seconds post-injection, and baseline images are subtracted

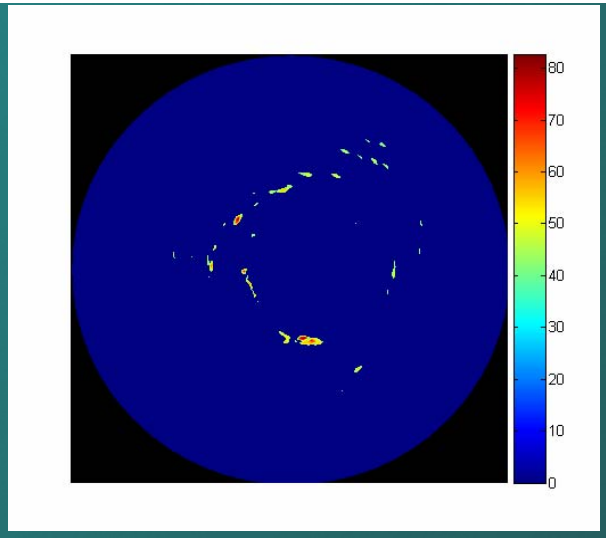
Range of enhancement



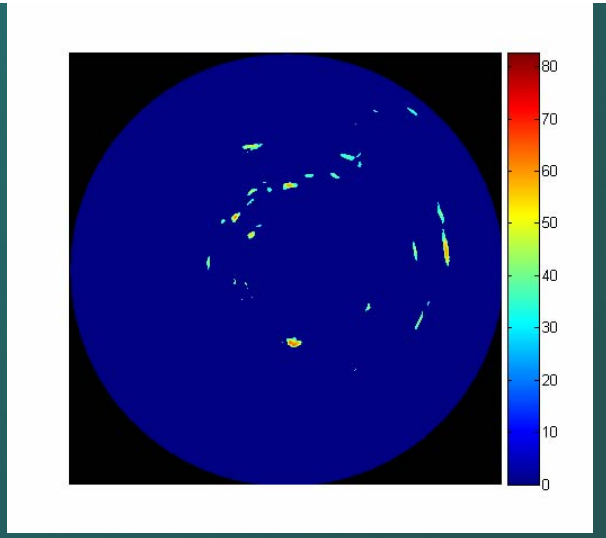




Pre-injection
(Frame #200)

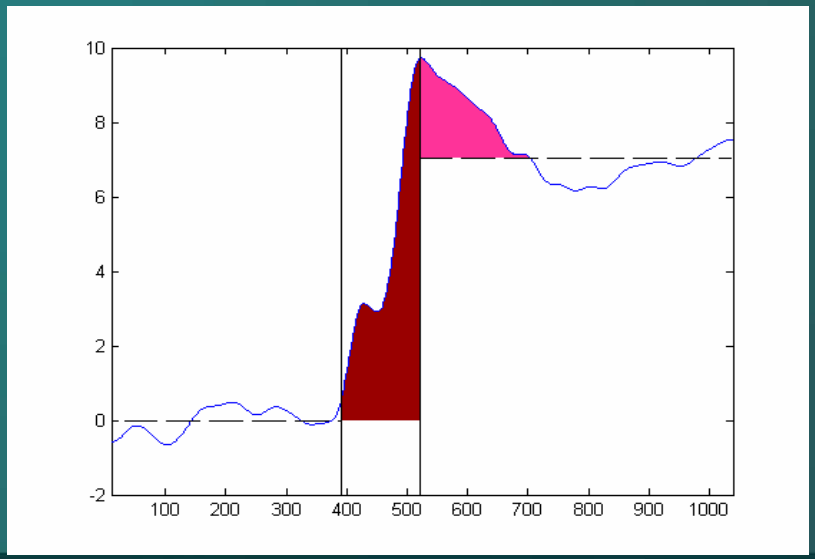


Peak Injection
(Frame #600)

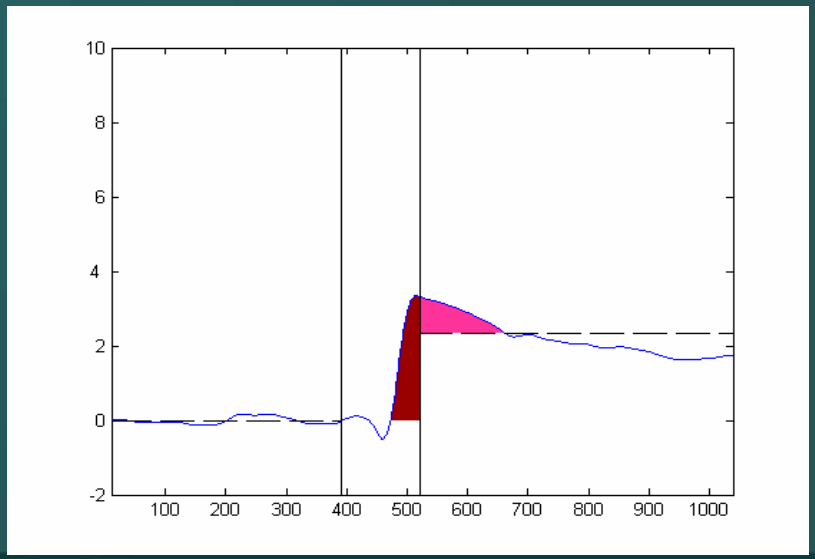


Post-injection
(Frame #800)

Intima-Medial and Plaque Area

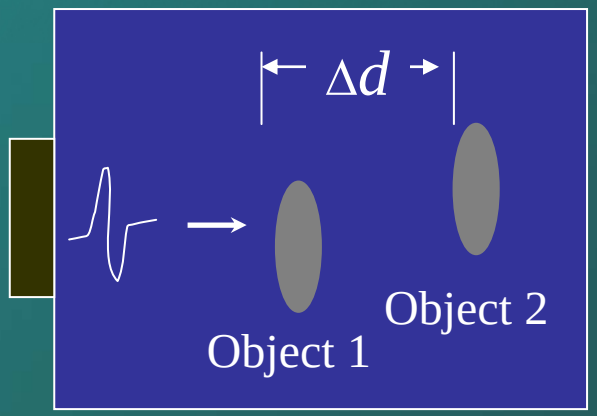


Adventitia Area



Optical Coherence Tomography (OCT)

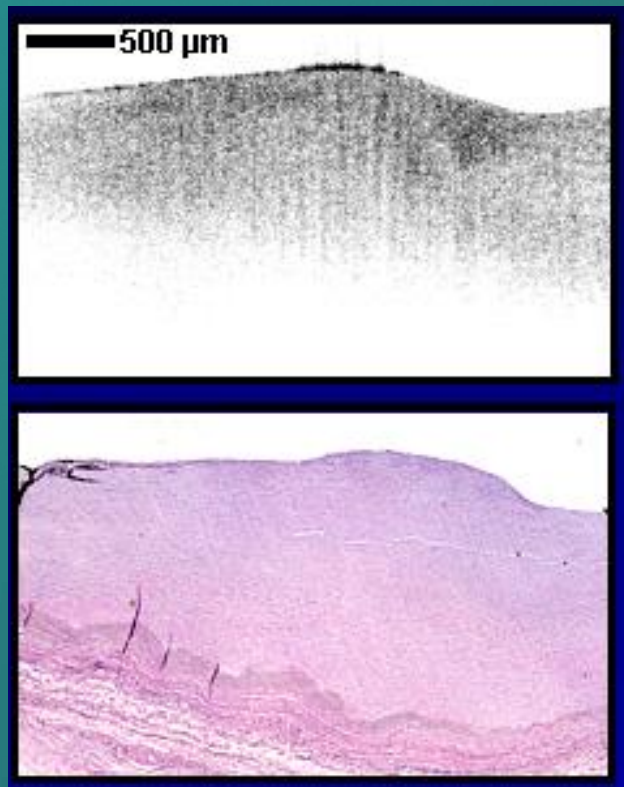
The optical analog of IVUS, OCT measures optical reflections.



	IVUS	OCT	OFDI
Resolution *(axial)*	100 - 150 μm	10 μm	10 μm
(lateral)	150 - 300 μm	25 - 40 μm	25 - 40 μm
Size of imaging core	0.8 mm	0.4 mm	0.4 mm
Dynamic range	40 - 60 dB	90 - 100 dB	90 - 100 dB
Frame rate	30 frames/s	15 frames/s	400 frames/s
Scan area			
Max. penetration	4 - 8 mm	1 – 1.5 mm	1 – 1.5 mm
Blood clearing	Not required	Required	Required
Balloon Occlusion		Required	Not required
Flushing		Required	Required
Pullback	0.5mm/s (no limit)	1mm/s (35mm)	30mm/s (90mm)

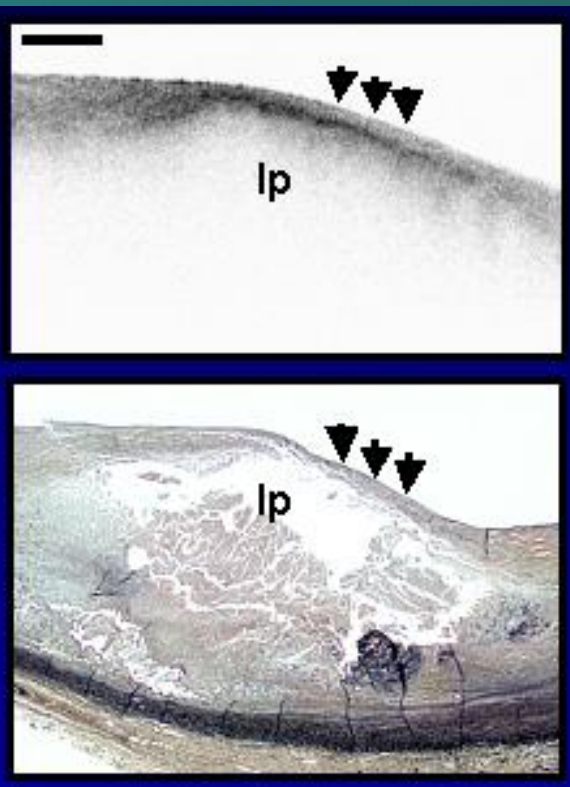
Plaque characteristics

Fibrous



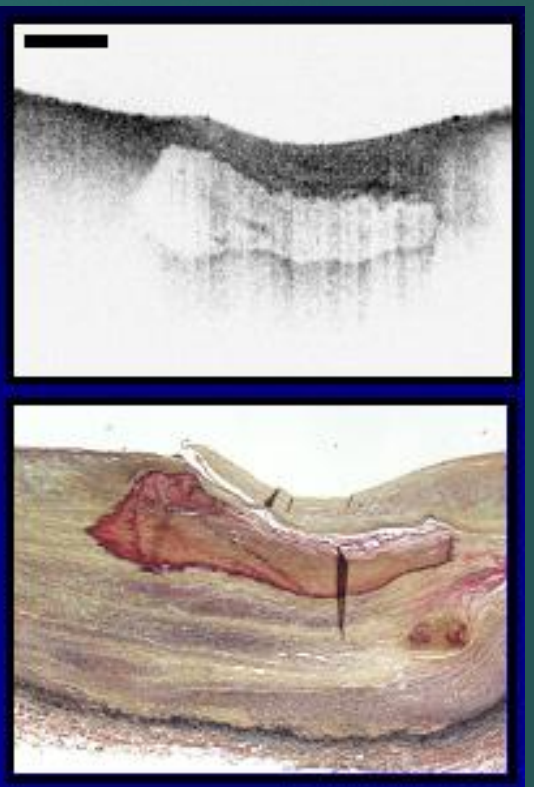
- High reflectivity
- Homogenous
- Finely textured

Lipid-rich



- Low reflectivity
- Homogenous
- Diffuse margins

Calcific



- Low reflectivity
- Inhomogenous
- Sharp margins

(or isolated, strong reflections in dark background)

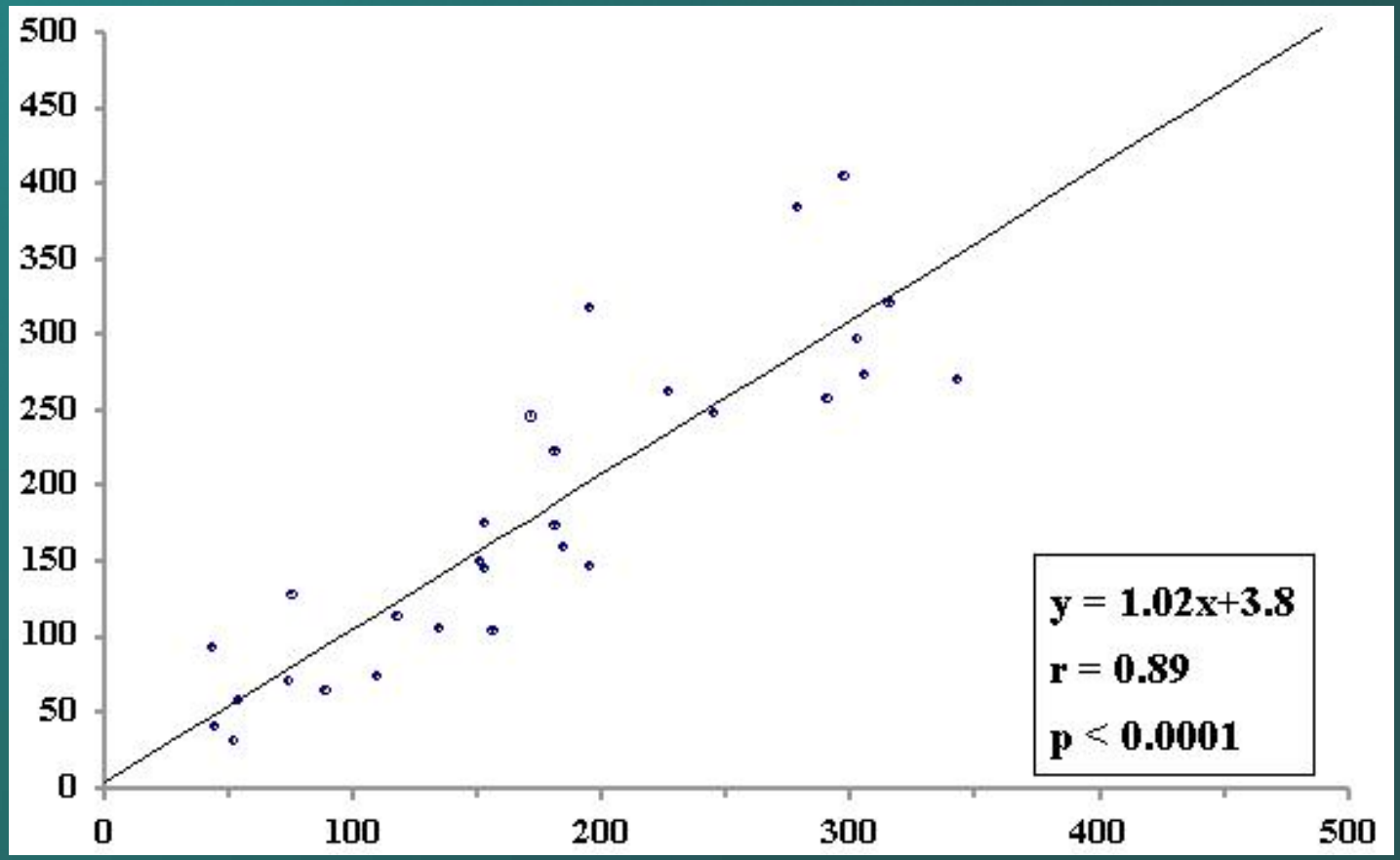
In vitro Validation

	Sensitivity	Specificity	+ Predictive Value	- Predictive Value
Fibrous	**.87**	**.97**	**.88**	**.96**
Calcific	**.95**	**1.0**	**1.0**	**.95**
Lipid Pool	**.92**	**.94**	**.81**	**.97**

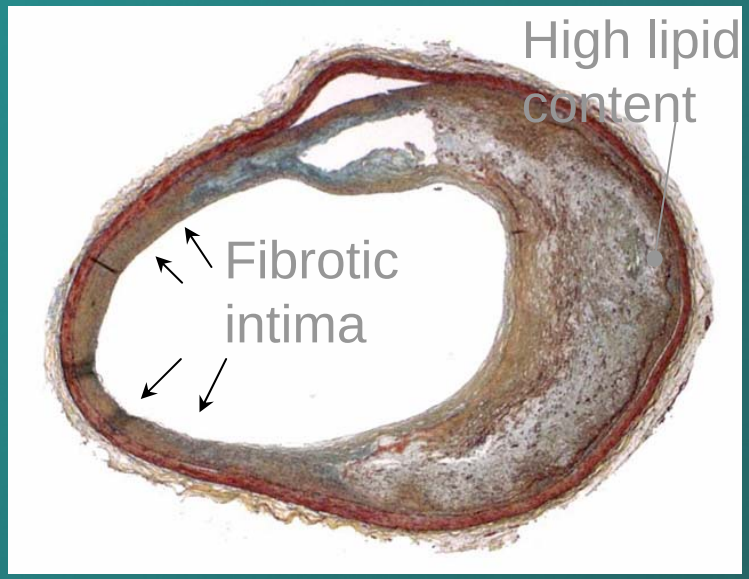
Interobserver k = 0.88; Intraobserver k = 0.91

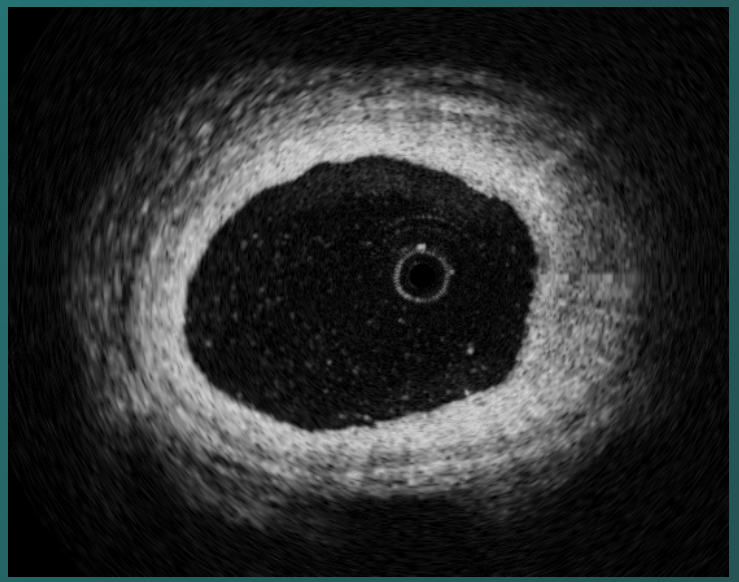
(Yabushita et al. Circulation 2002;106:1640-5)

Correlation between OCT and Histology Measures of Fibrous Cap Thickness

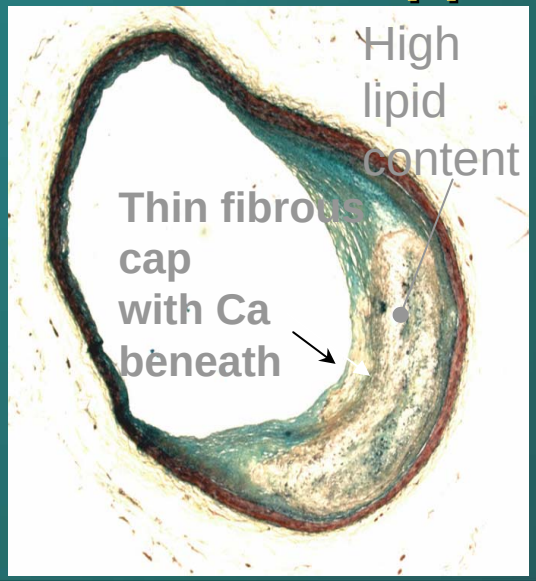


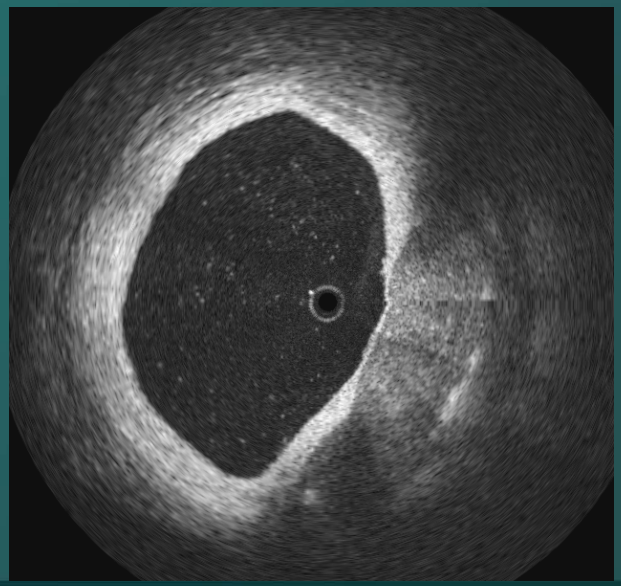
Thick-capped fibroatheroma





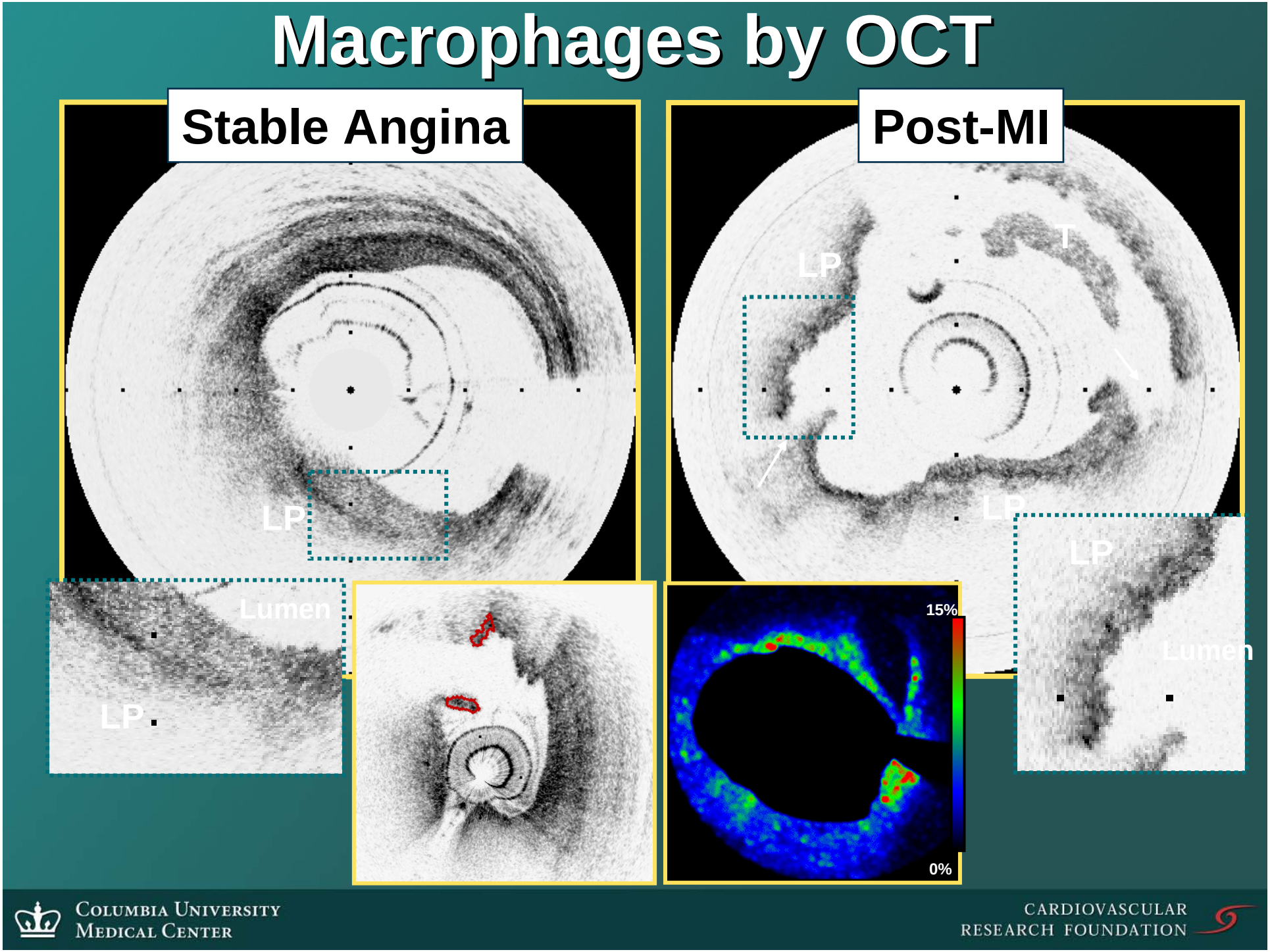
Thin-capped fibroatheroma



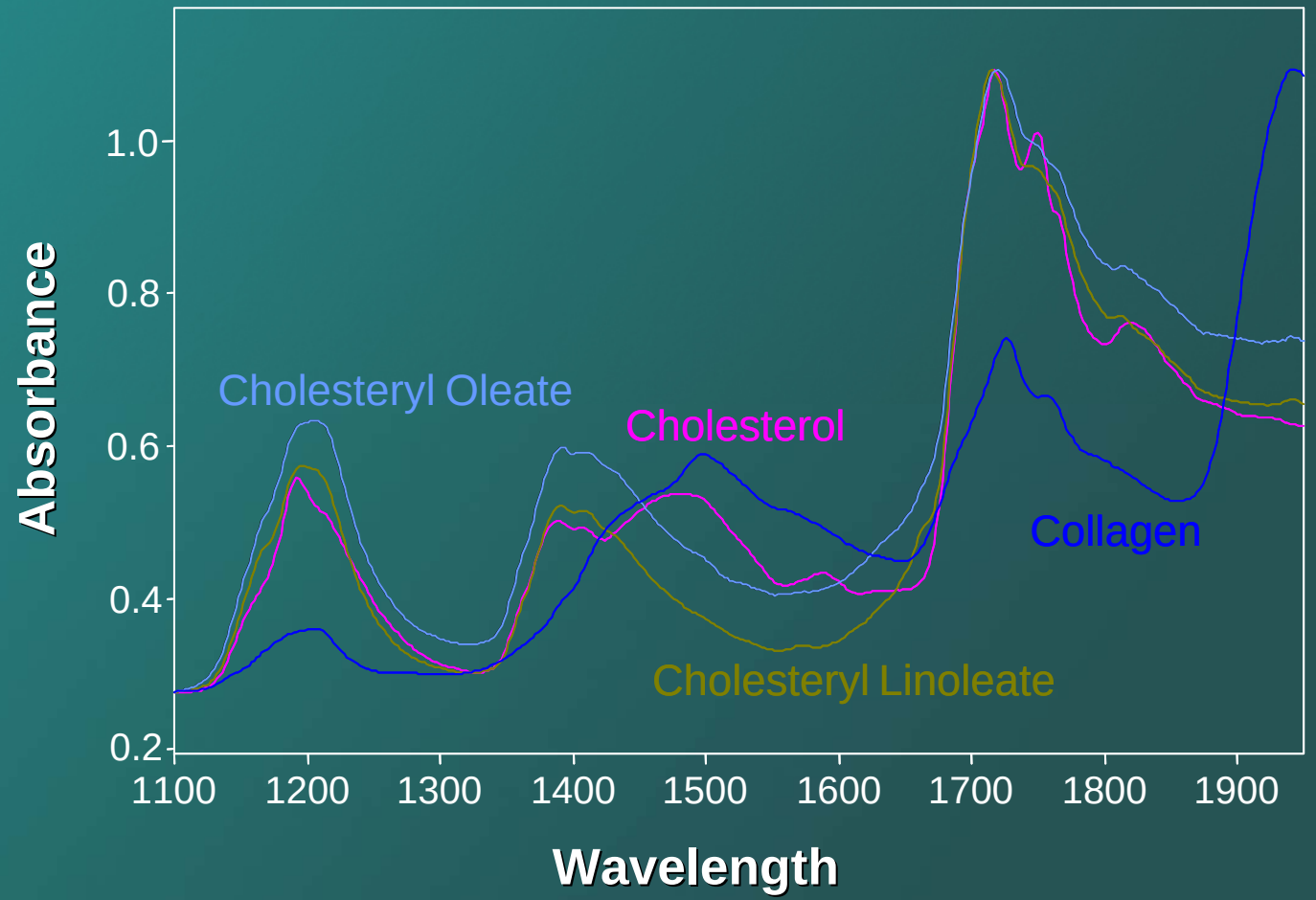


Histology courtesy of E. Mont and R. Virmani, Armed Forces Instiute of Pathology, Washington, DC

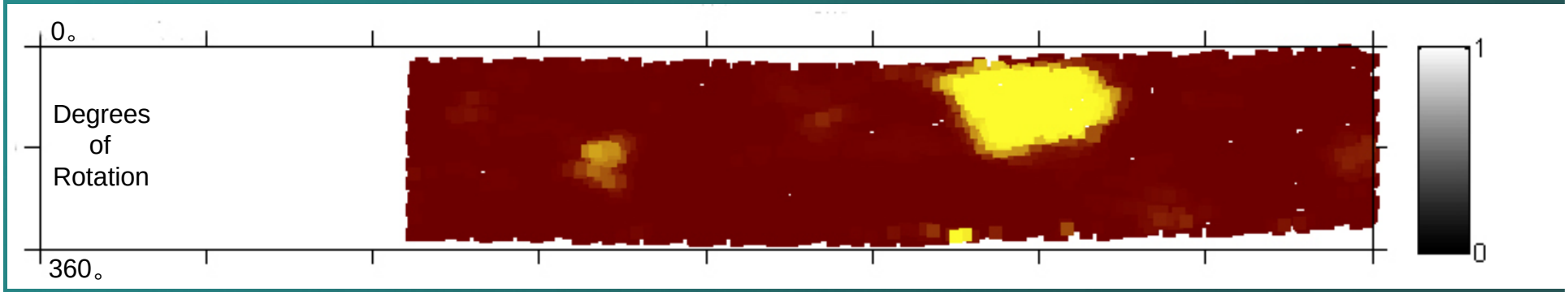
Macrophages by OCT



NIR Spectroscopy can identify the chemical composition of unknown substances and distinguish cholesterol from collagen



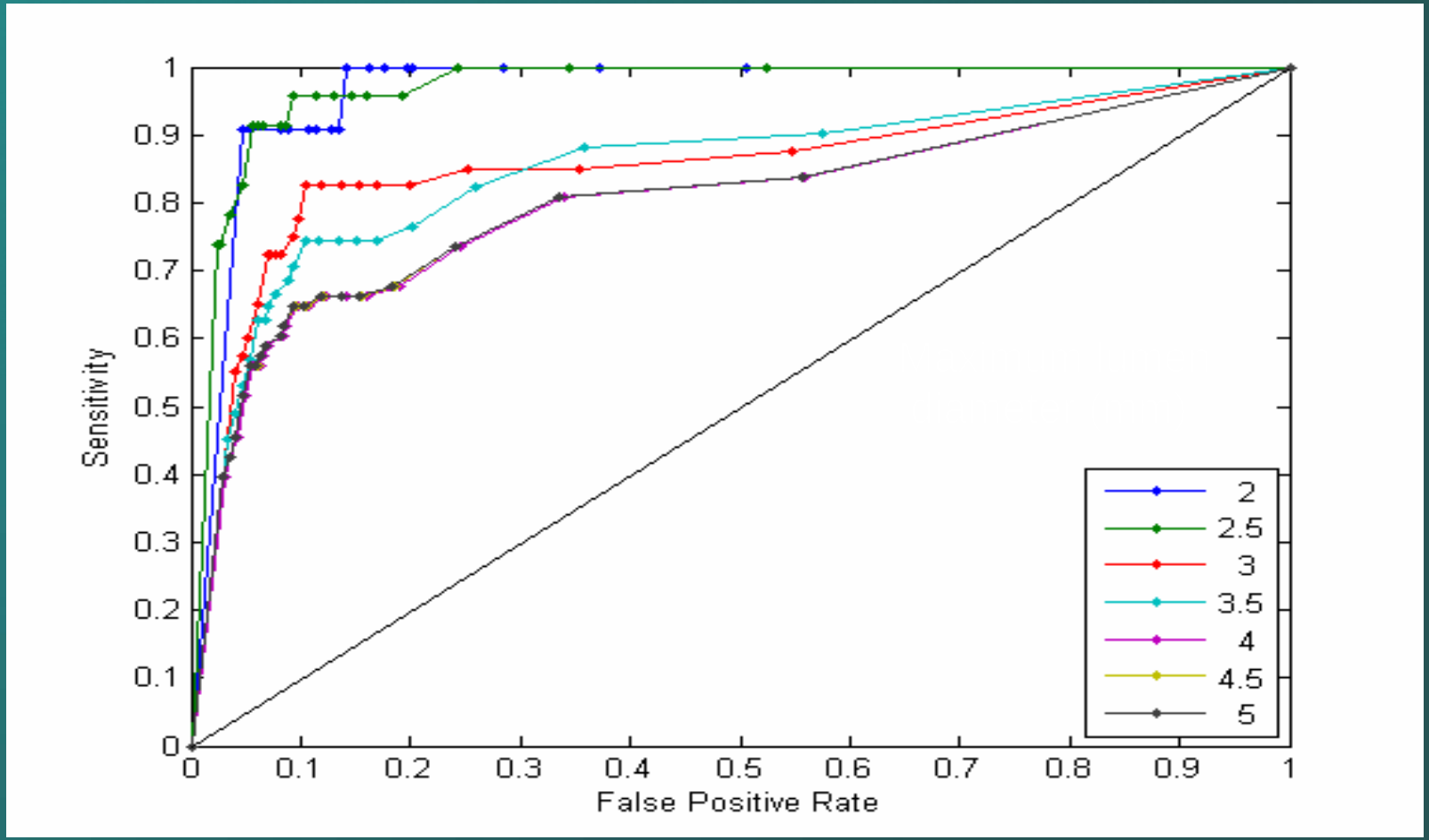
Chemogram Showing NIR Detection of Lipid-rich Plaque



mm of pullback

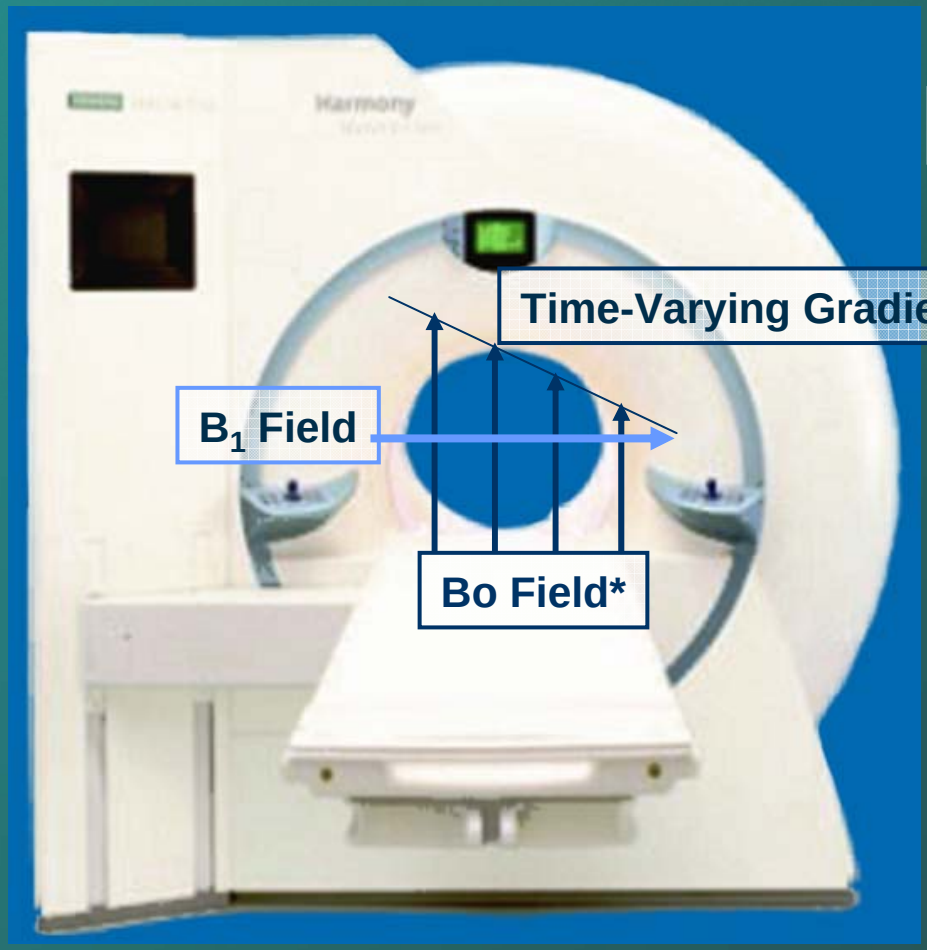
Coding Based on Histology (LRP=Lipid-rich Plaque)

Identification of lipid-rich plaque by NIR in 9 test hearts

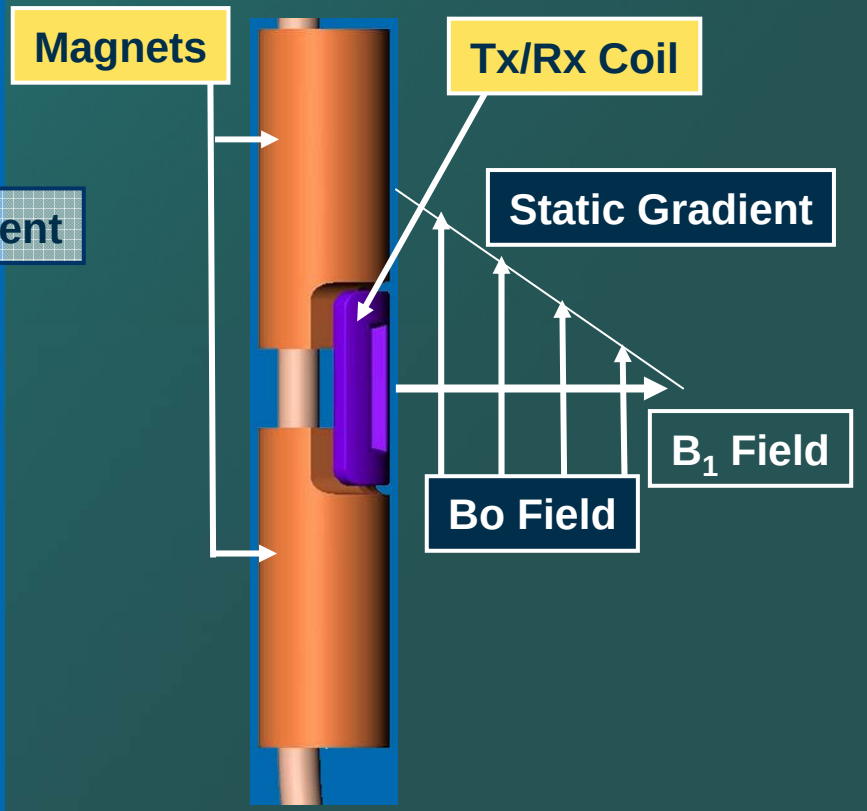


Intravascular MRI

Conventional MRI Scanner

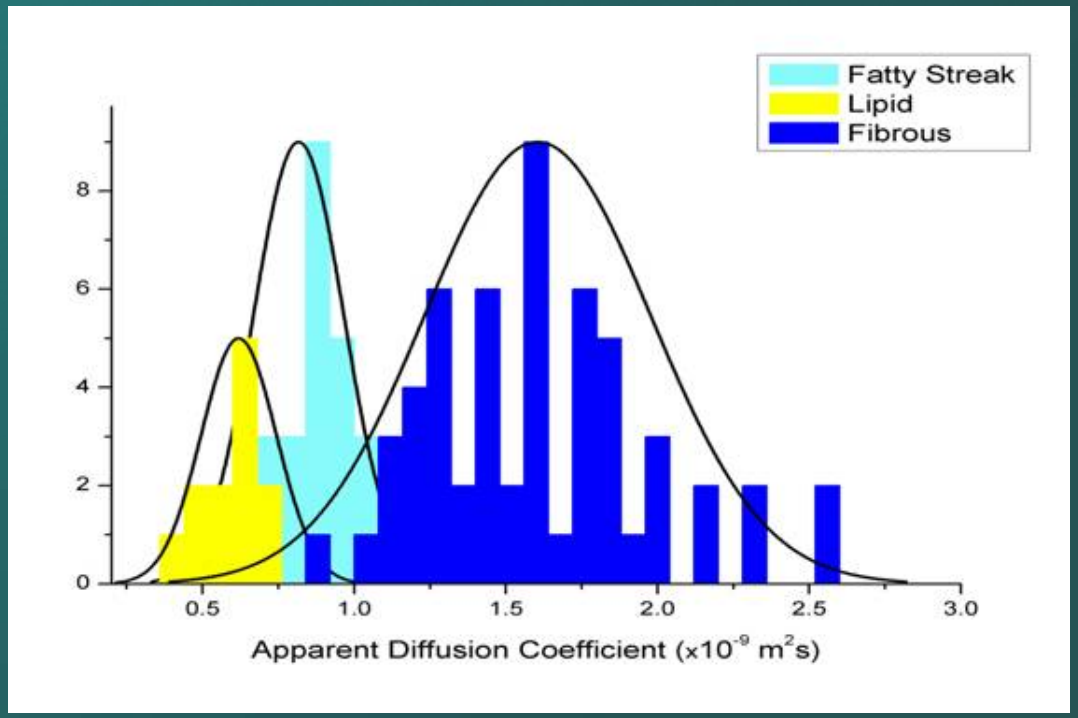


Intravascular MRI Probe

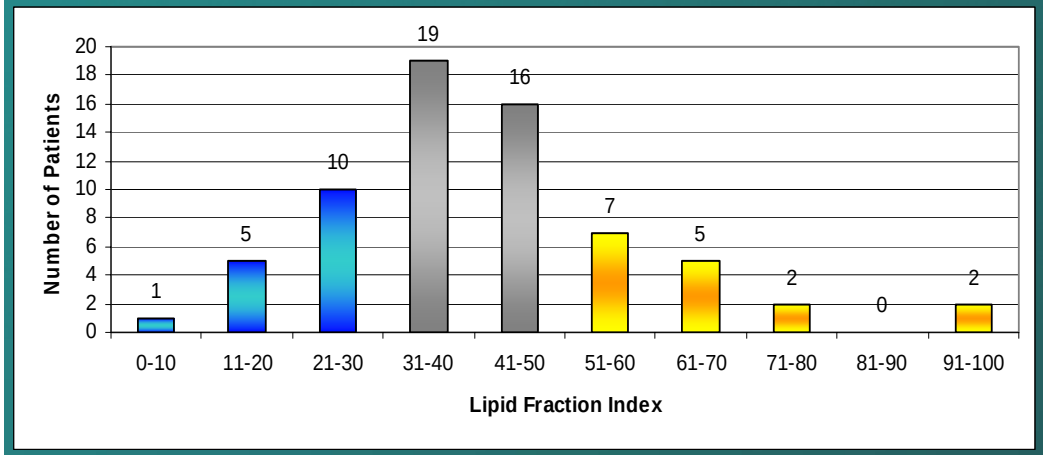


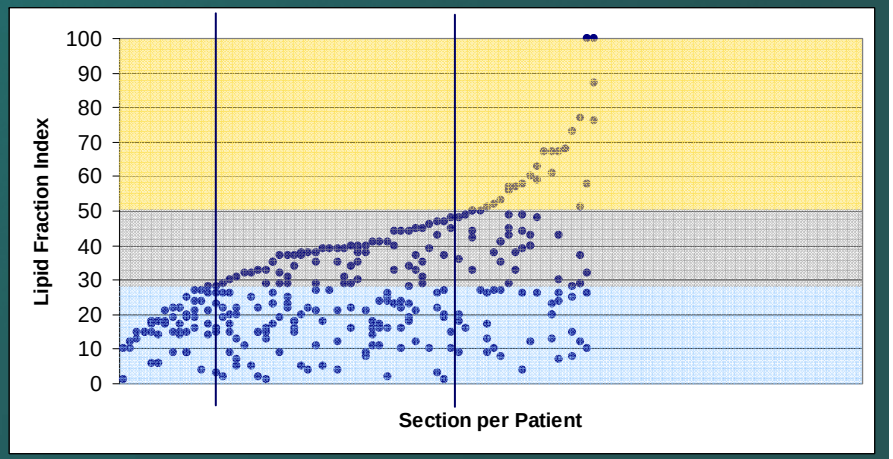
Blank et al, Magnetic Resonance in Medicine, June 2005

ADC vs. Histology in Human Aortas



Lipid fraction index (LFI) per patient and per lesion. LFI does not correlate with angiographic diameter stenosis

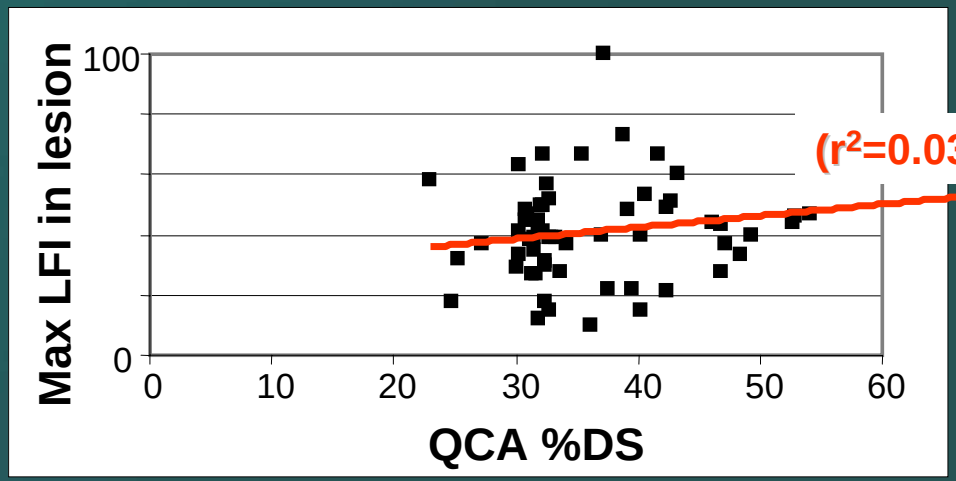




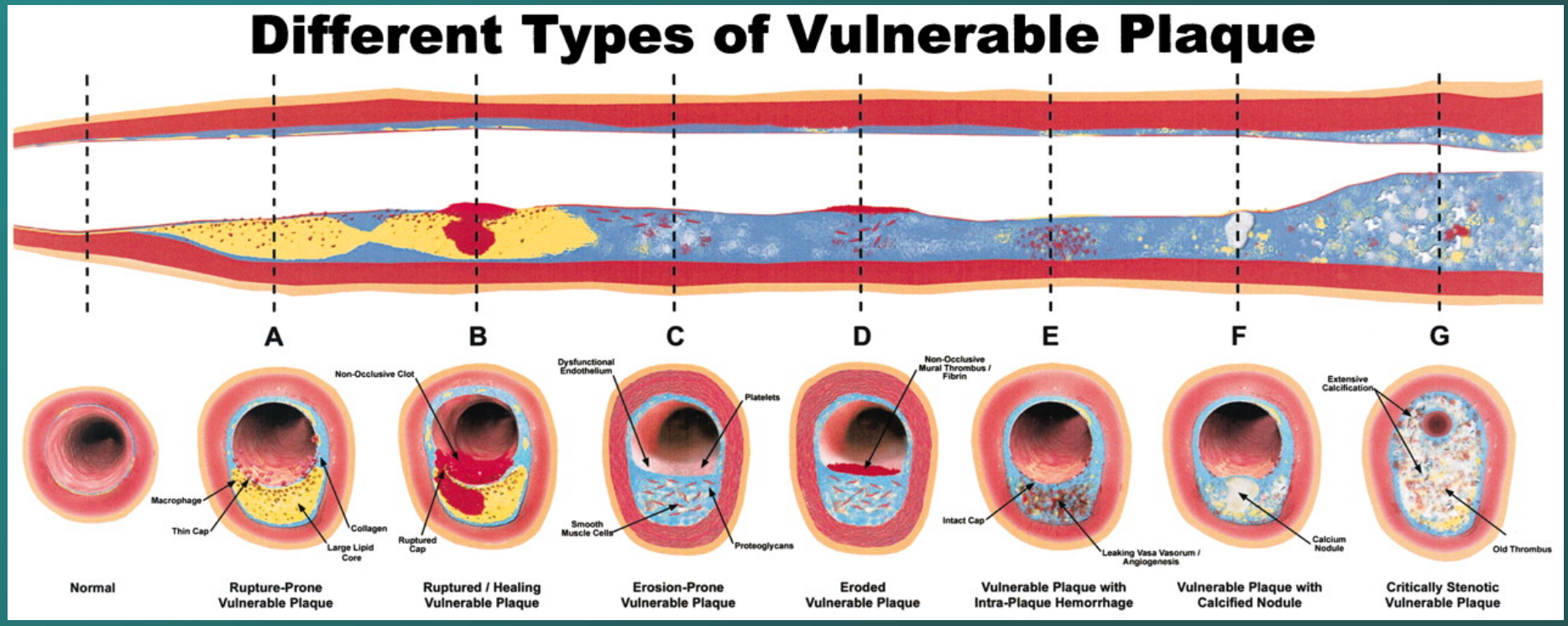
Low Lipid

Moderate Lipid

High Lipid



No study has shown the predictive value of any of the previously mentioned technologies. In addition, thin-capped fibroatheromas (TCFAs) represent only an estimated 70% of vulnerable plaques



TCFAs

(Naghavi et al. Circulation 2003;108:1664-72)