Pathogenesis, Detection, and Treatment of Vulnerable Plaque: IVUS, VH, and other IVUS-based Imaging Diagnostics

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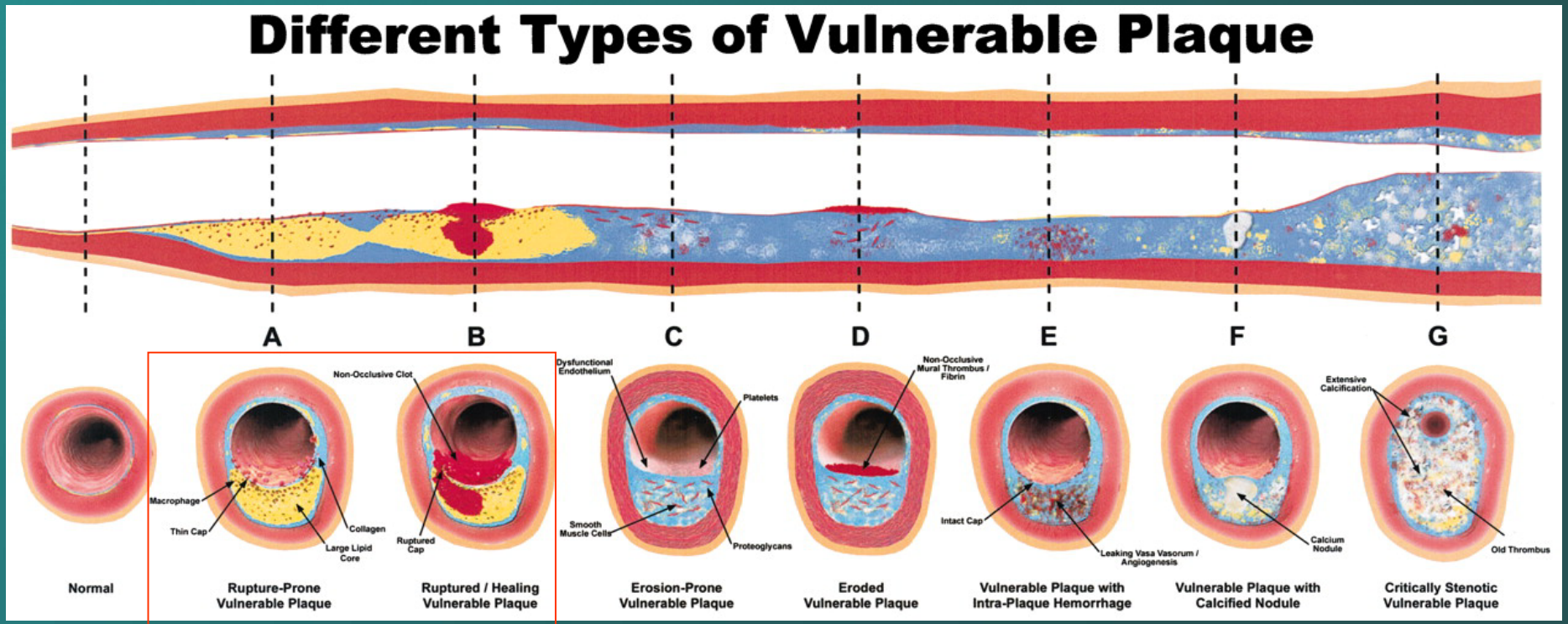
Disclosures

- Boston Scientific
- Volcano
- Light Lab
- Terumo

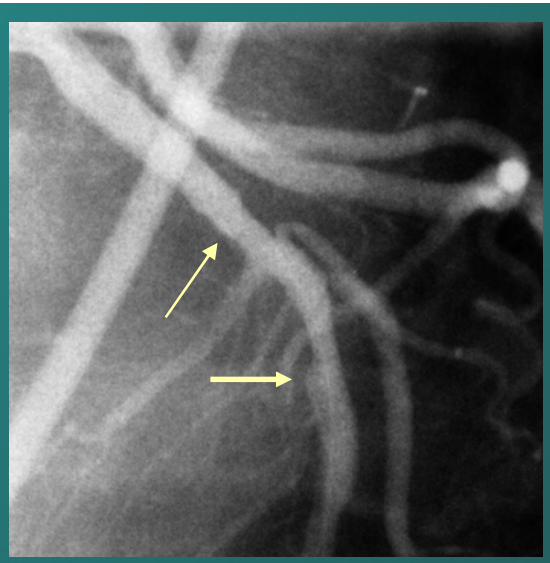
"Vulnerable Plaque" = thrombosis-prone plaque and plaque with a high probability of undergoing rapid progression



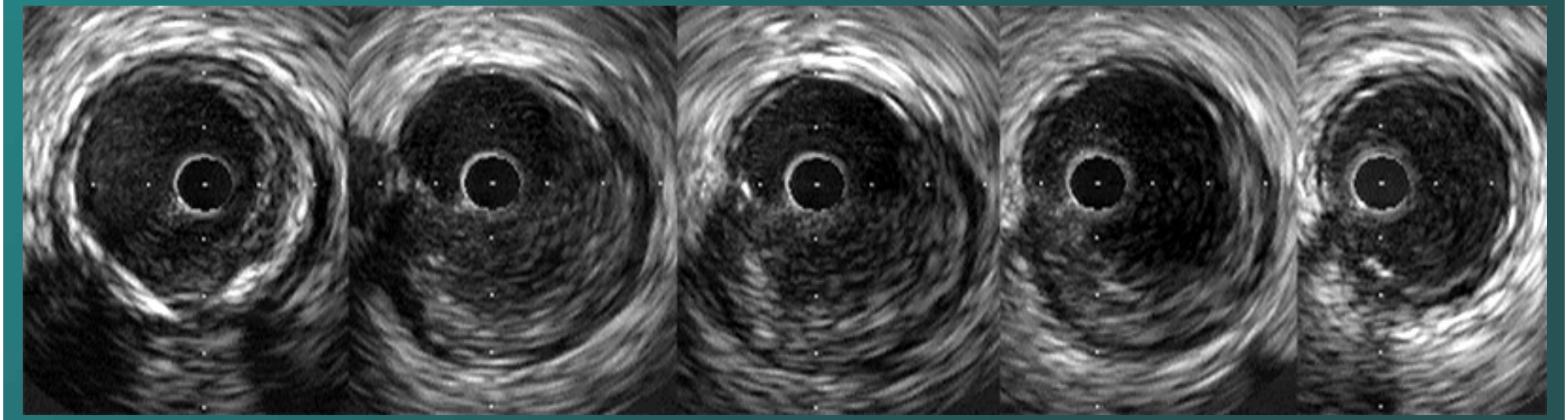
70% of ACS culprit lesions

30% of ACS culprit lesions

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

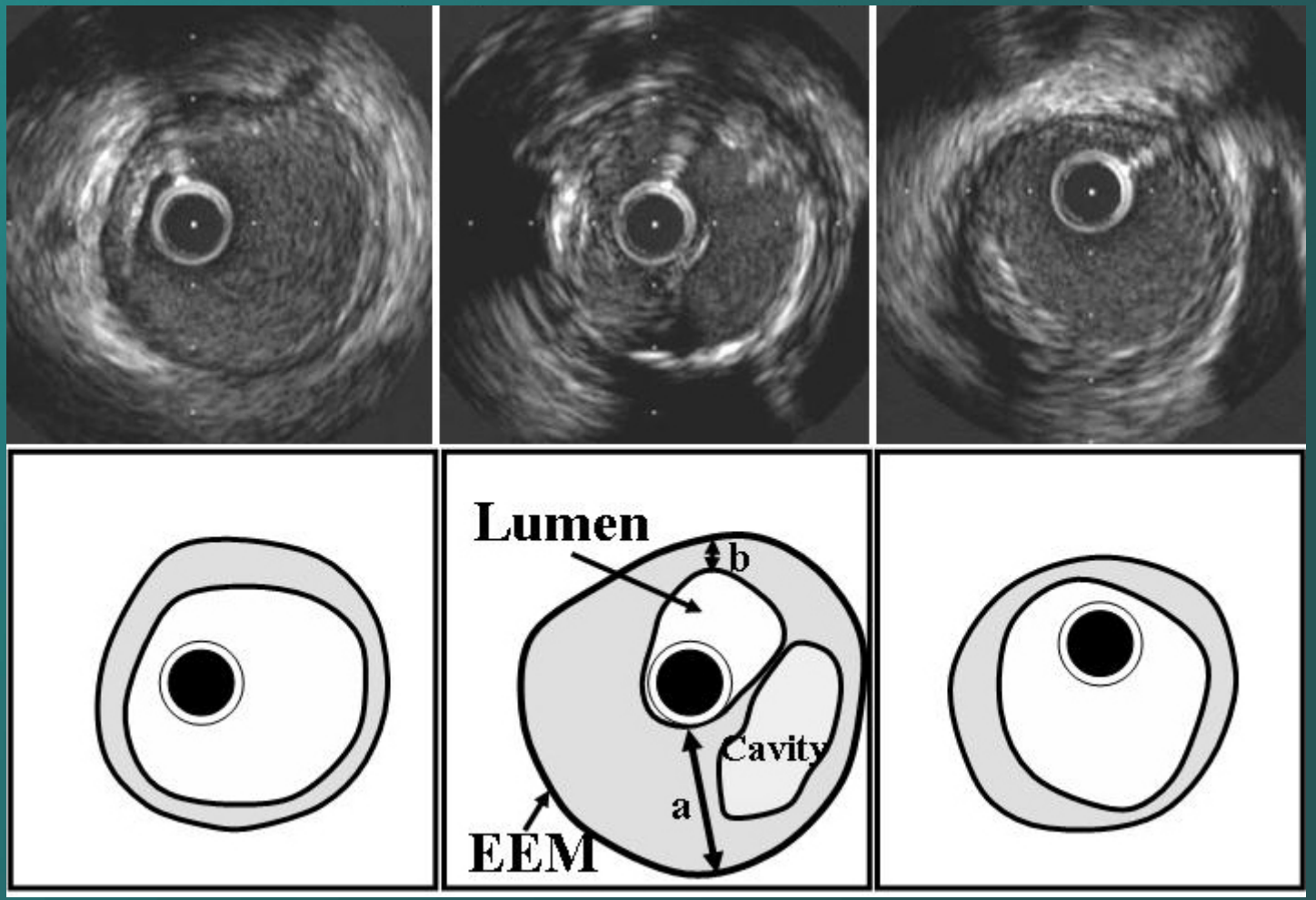


Proximal 0 → 3mm → 12mm



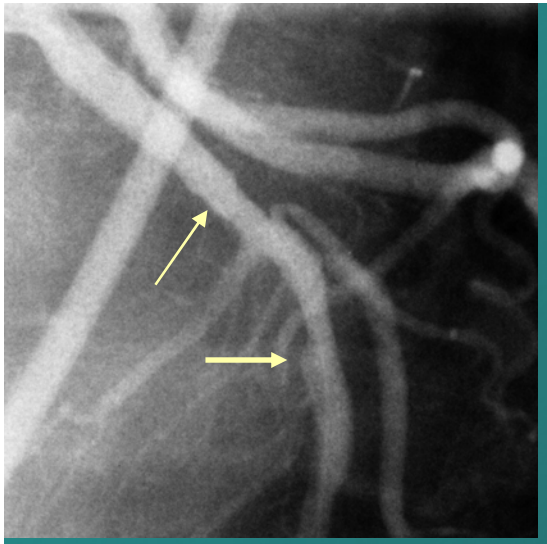
EEM CSA = 21.0mm^2 EEM CSA = 23.5mm^2 EEM CSA = 13.7mm^2

IVUS profile of ruptured plaques: Insights into pre-rupture morphology



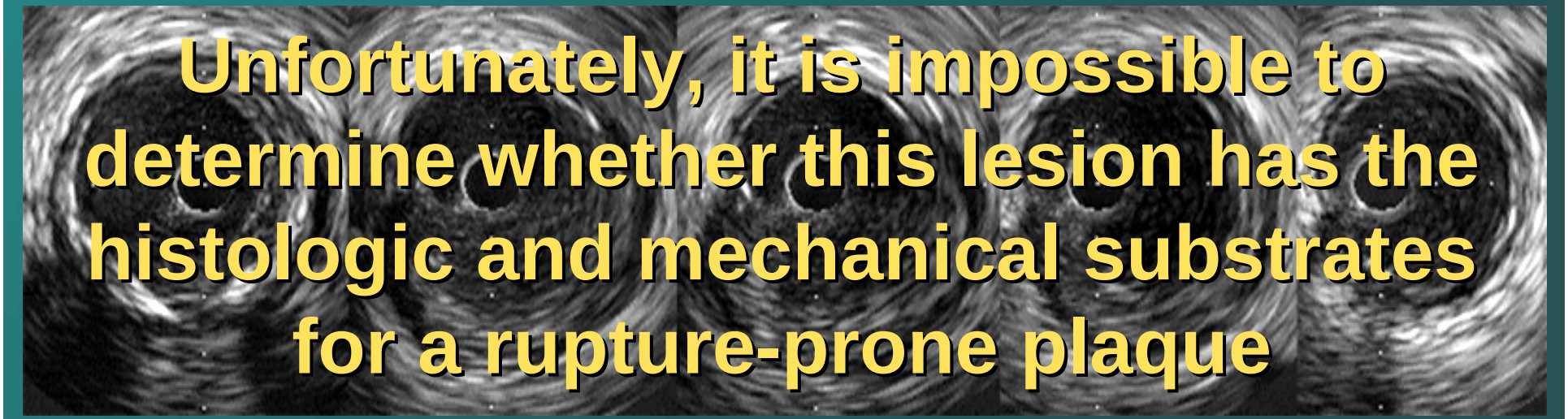
	Mean±1SD	CoV	10th Percentile	90th Percentile
Reference				
Lumen CSA	11.7±3.5	0.29	8.1	15.3
EEM CSA	20.2±5.6	0.27	14.2	26.7
P&M CSA	8.5±3.0	0.35	4.9	12.4
Plaque Burden	0.42±0.75	0.18	0.31	0.49
Lesion				
Lumen CSA	4.9±2.7	0.55	2.1	8.6
EEM CSA	20.8±6.0	0.29	14.3	28.5
P&M CSA	15.9±4.9	0.31	9.8	22.4
Min P&M Th	0.5±0.3	0.58	0.2	1.0
Max P&M Th	2.3±0.6	0.25	1.6	3.0
Eccentricity	0.32±0.23	0.71	0.09	0.66
Plaque Burden	0.76±0.10	0.12	0.63	0.88
AS	0.57±0.19	0.34	0.28	0.80
RI	1.10±0.20	0.18	0.87	1.38
Arc of Ca^{++}	46.9±51.2	1.09	0	106.7

99% of ruptured plaques fit 4 of these 5 parameters



- The 10th or 90th percentile parameters of the 5 variables with the narrowest coefficient of variance were
  - Reference lumen area >8.1mm^2
  - Lesion EEM area >14.3mm^2
  - Lesion max plaque thickness >1.6mm
  - Lesion plaque burden >0.63
  - Remodeling index >0.87

Proximal 0 → 3mm → 12mm



Unfortunately, it is impossible to determine whether this lesion has the histologic and mechanical substrates for a rupture-prone plaque

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

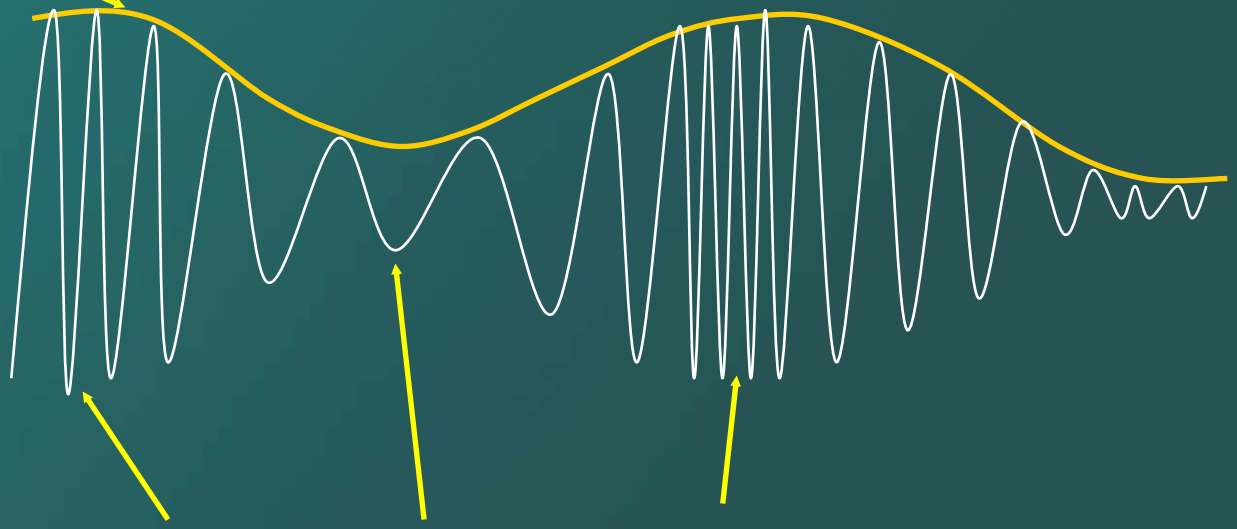
EEM CSA = 23.5mm^2
Lumen CSA = 5.5mm^2
P+M CSA = 18.0mm^2
Max P+M Thickness=3.0mm
Plaque burden=0.79
Remodeling index=1.3

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

Virtual Histology™ IVUS

Only the envelope amplitude (echo intensity) is used in formation of the gray-scale IVUS image

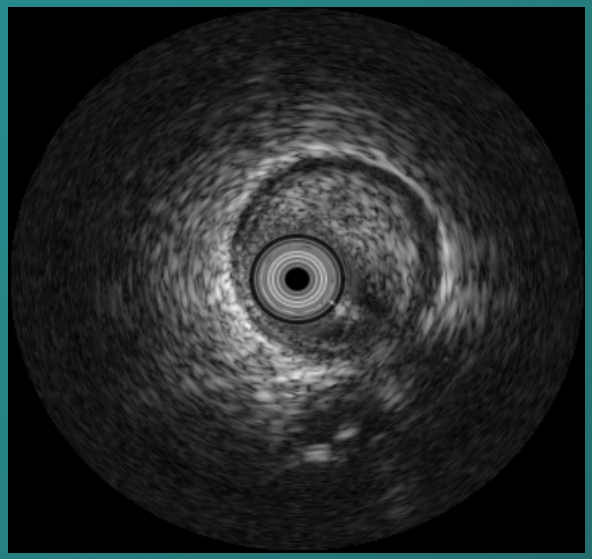
Eight amplitude *and* frequency parameters are used in Virtual Histology



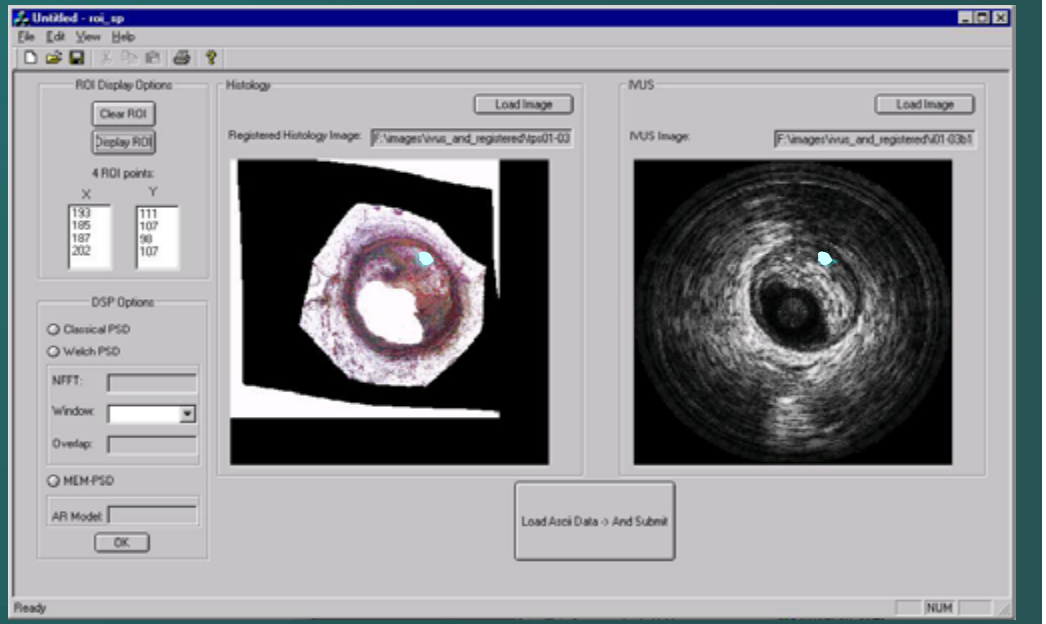
Frequency of echo signal can also vary, depending on the tissue

Thin plate spline morphing after which the computer was taught to recognize four basic tissue types

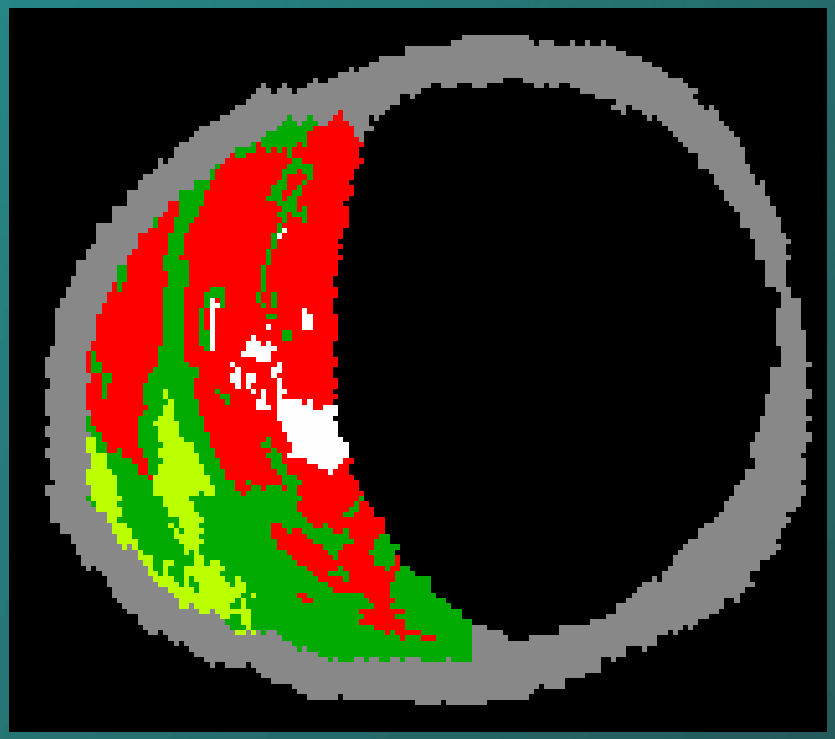
IVUS B scan



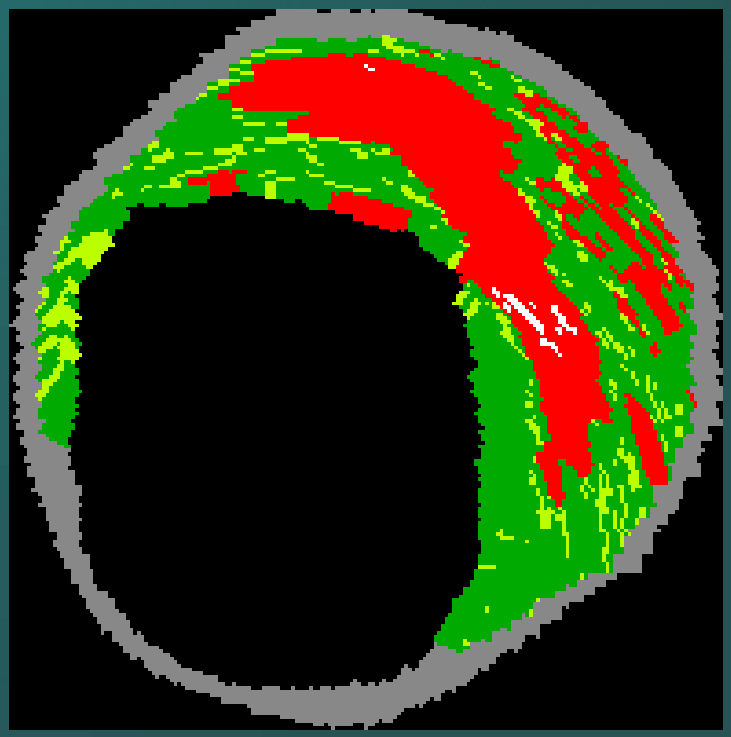
Movat pentachrome stain



Fibroatheroma without evidence of thick fibrous cap

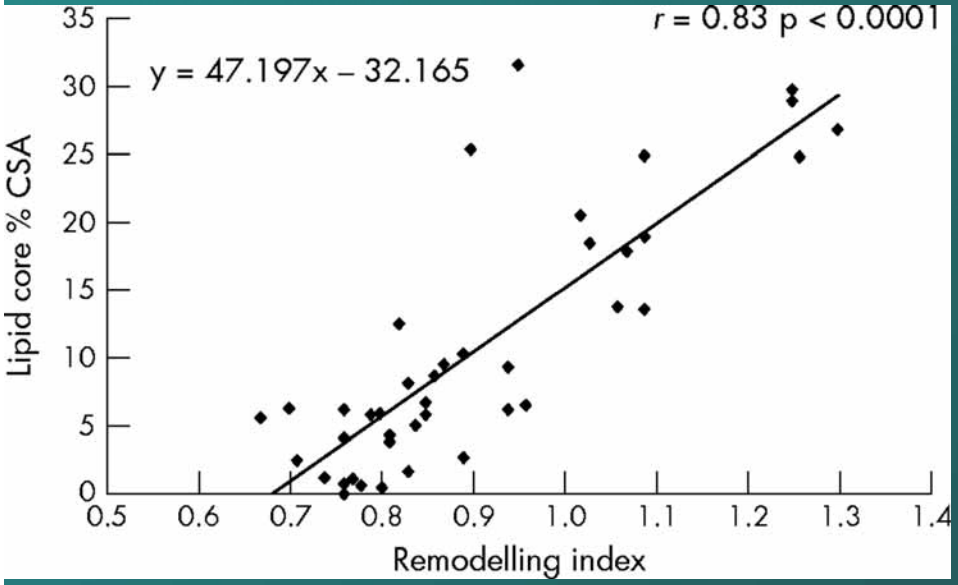


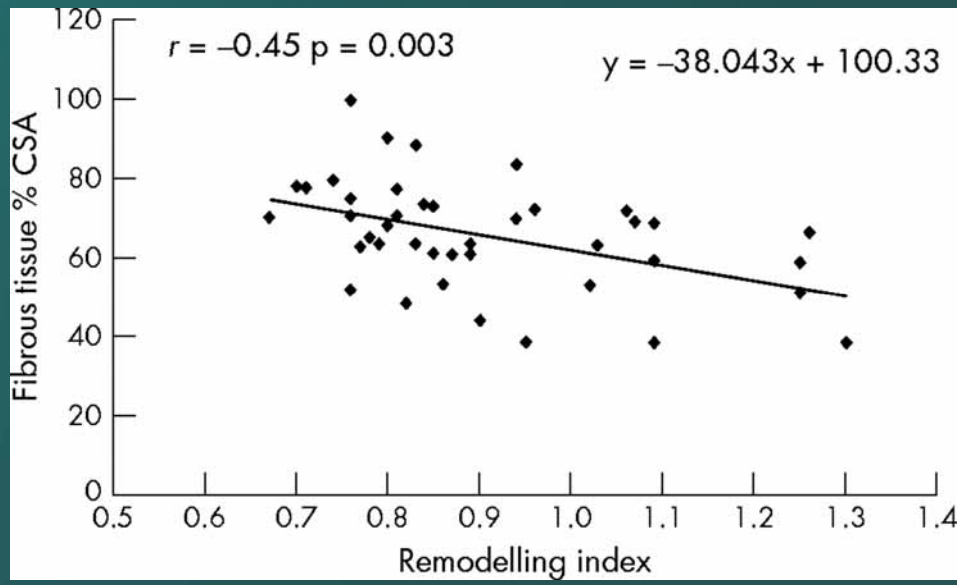
Fibroatheroma with evidence of thick fibrous cap



P Margolis, Volcano Corp.

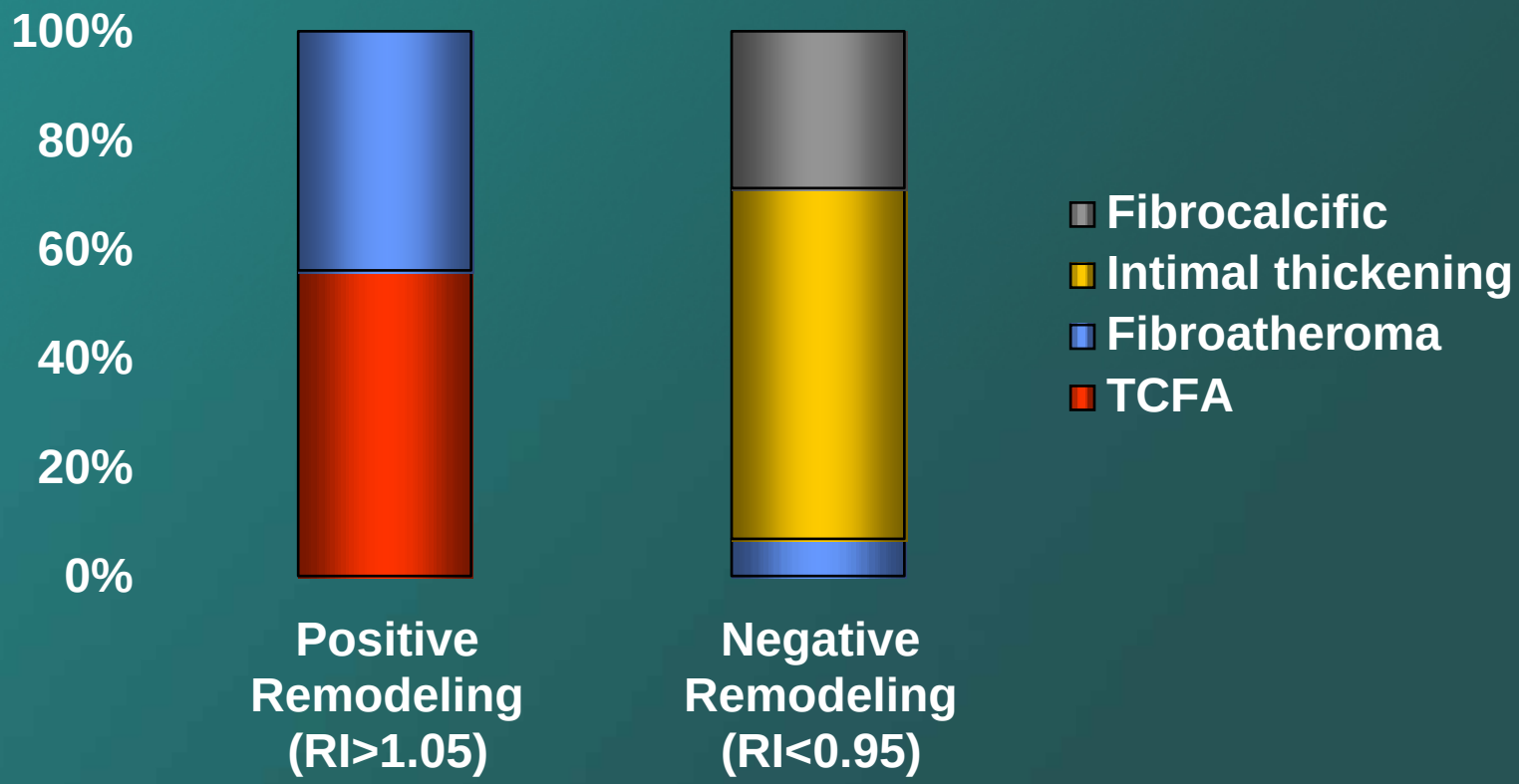
Positive correlation between lipid core and remodeling - negative correlation between fibrous tissue and remodeling





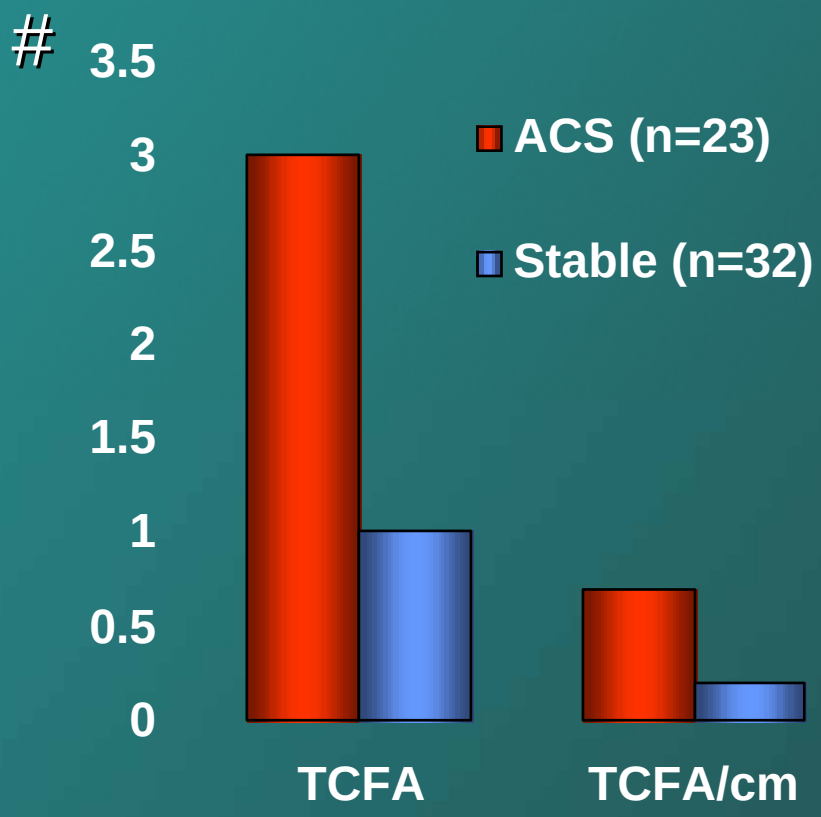
Rodriguez-Granillo, et al. Heart 2006;92:388-391

Lesion types and remodeling



Rodriguez-Granillo, et al. Heart 2006;92:388-391

Frequency of TCFA in secondary non-obstructive lesions (<50%DS, n=55)

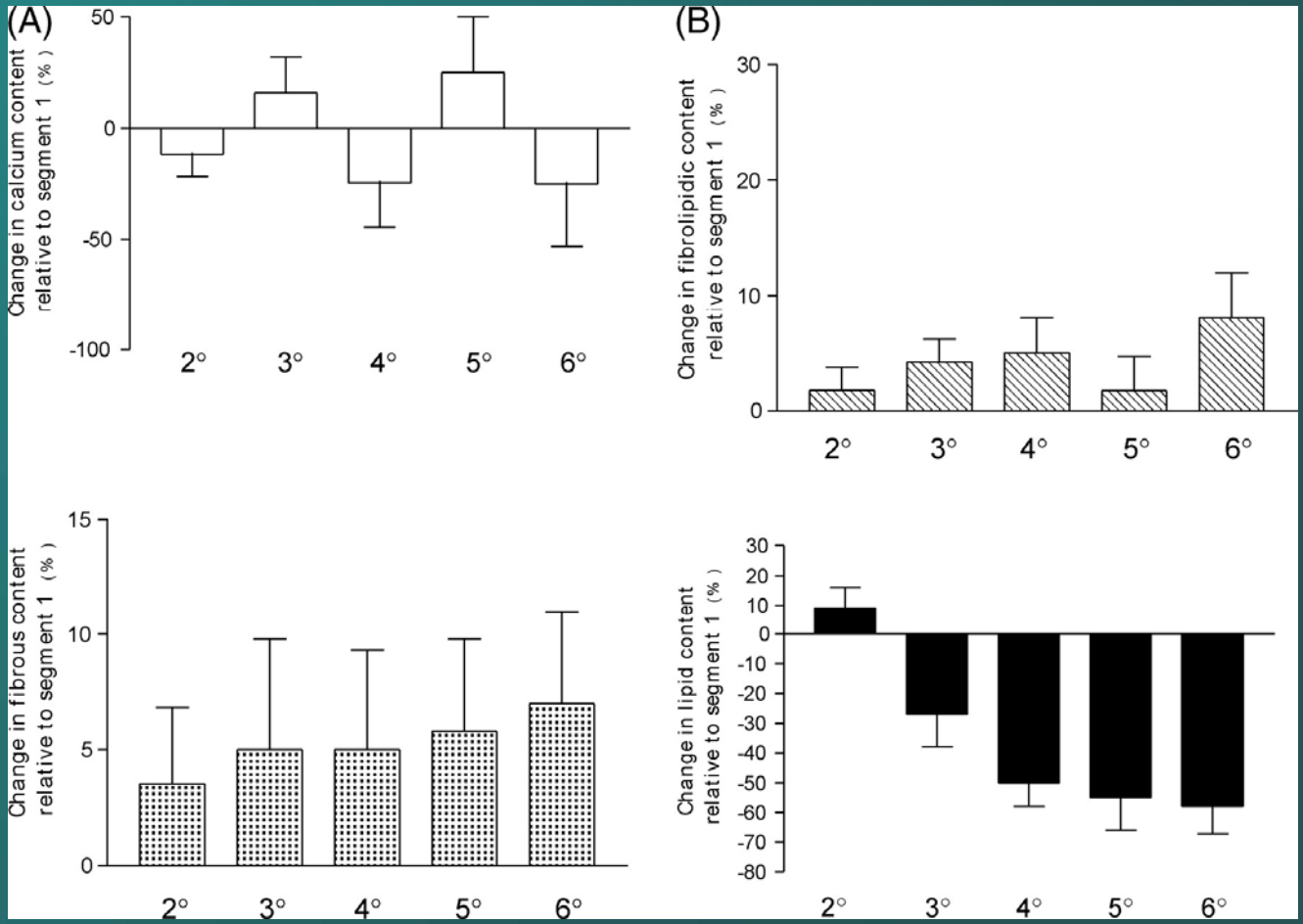


- 99 TCFA identified
- No relationship between TCFA and gender, diabetes, smoking, hypercholesterolemia, hypertension, family history
- Located within
  - 1st 10mm in 35%
  - 10-20mm in 31%
  - 20-30mm in 19%
  - 30-40mm in 14%

On average the proximal 35mm of the artery was imaged

(Rodriguez-Granillo et al. J Am Coll Cardiol 2005;46:2038-42)

Changes in Plaque Content at Distances from the Ostium of the Coronary artery



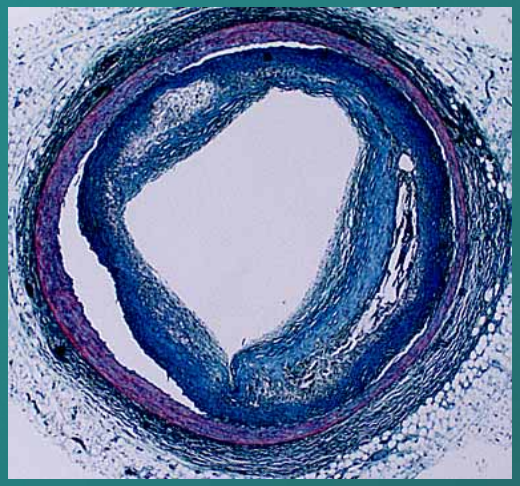
Valgimigli et al. Eur Heart J 2006 27:655-663

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

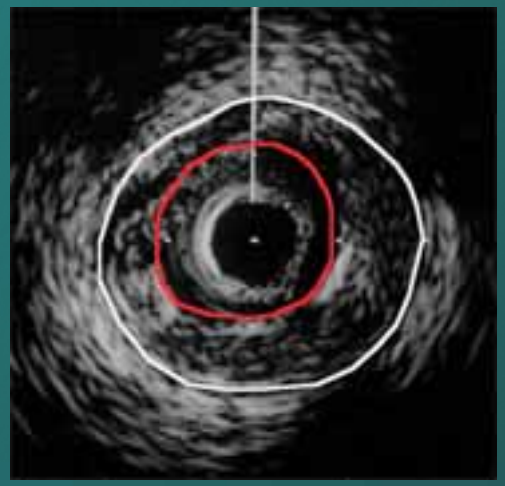
	Sensitivity	Specificity	PPV	NPV
Calcification (n=144)	95%	99%	93%	99%
Fibrosis (n=335)	94%	93%	93%	94%
Lipid pool (n=205)	90%	92%	85%	90%

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

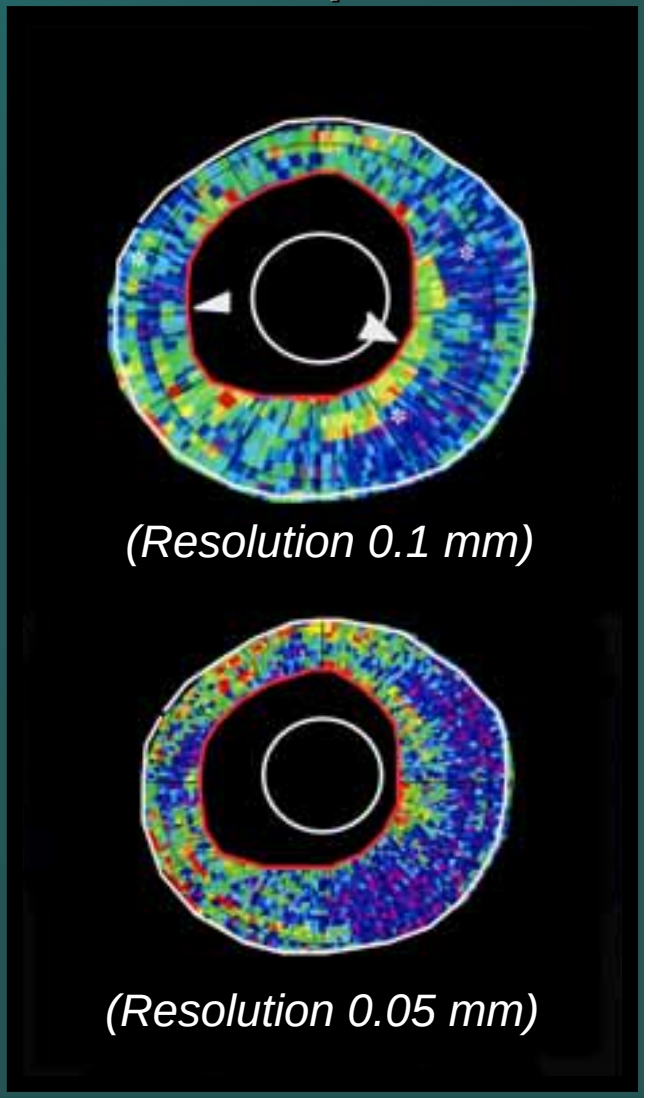
Masson Trichrome Staining



Conventional IVUS



Integrated Backscatter Intravascular Ultrasound (IB-IVUS) Color-coded Map



(Resolution 0.1 mm)

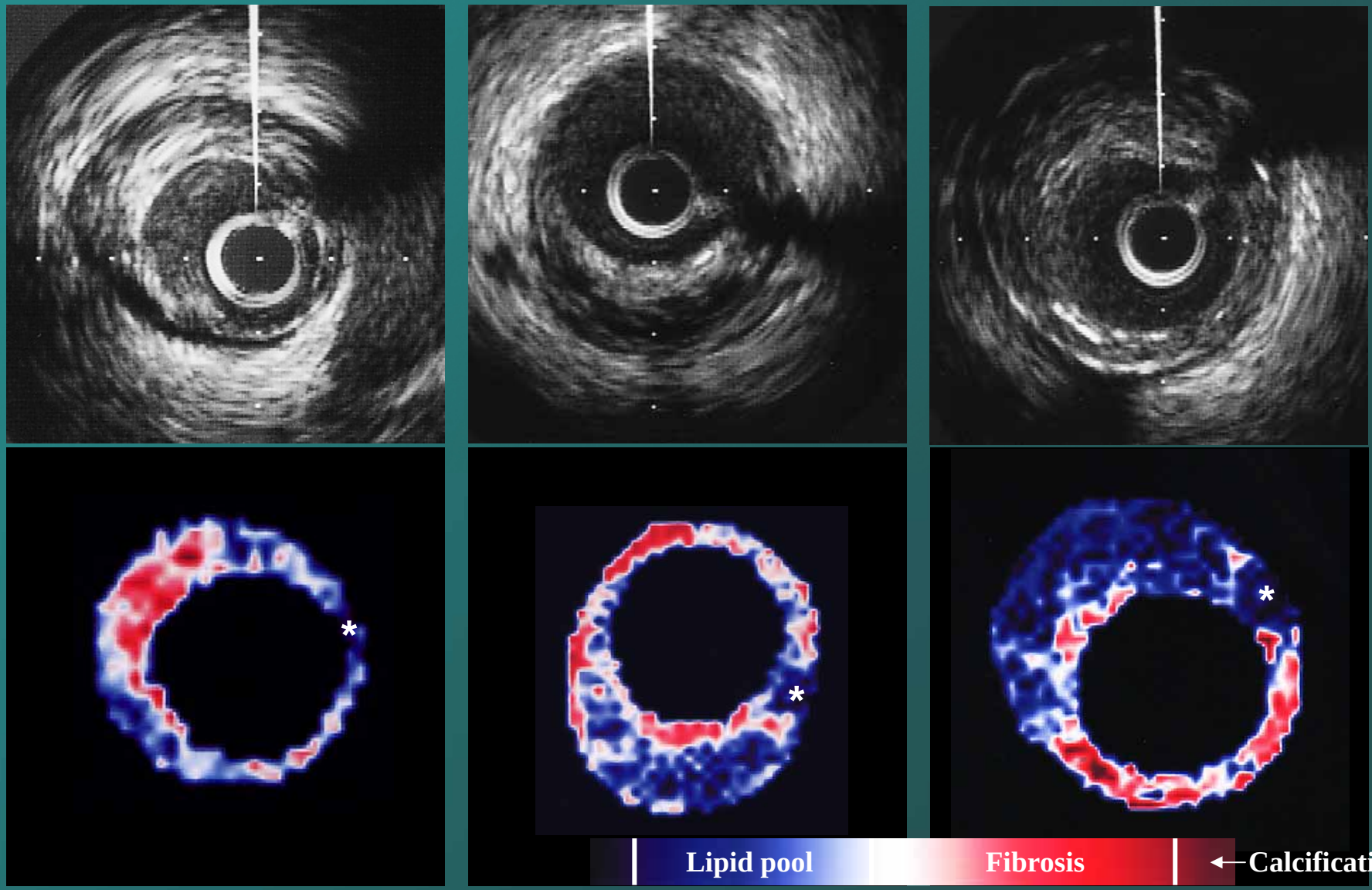
(Resolution 0.05 mm)

- *Calcification*
- *Dense fibrosis*
- *Fibrosis*
- *Lipid pool or Intimal Hyperplasia*

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

Stable Plaque

Vulnerable Plaque Causing ACS



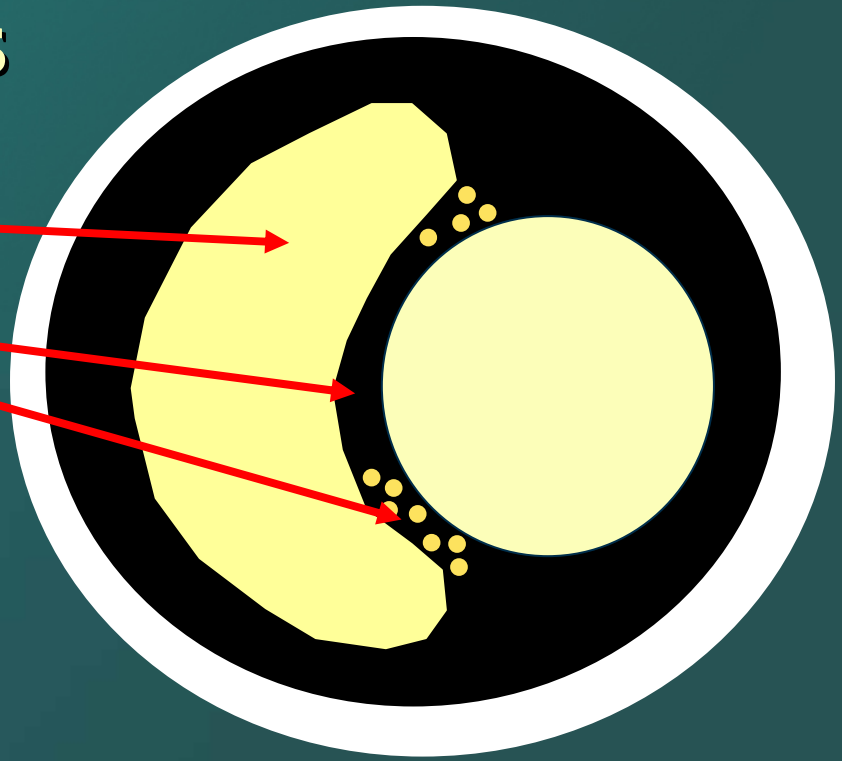
* guidewire artifact

(Sano et al. J Am Coll Cardiol in press)

Plaque Vulnerability

Compositional properties

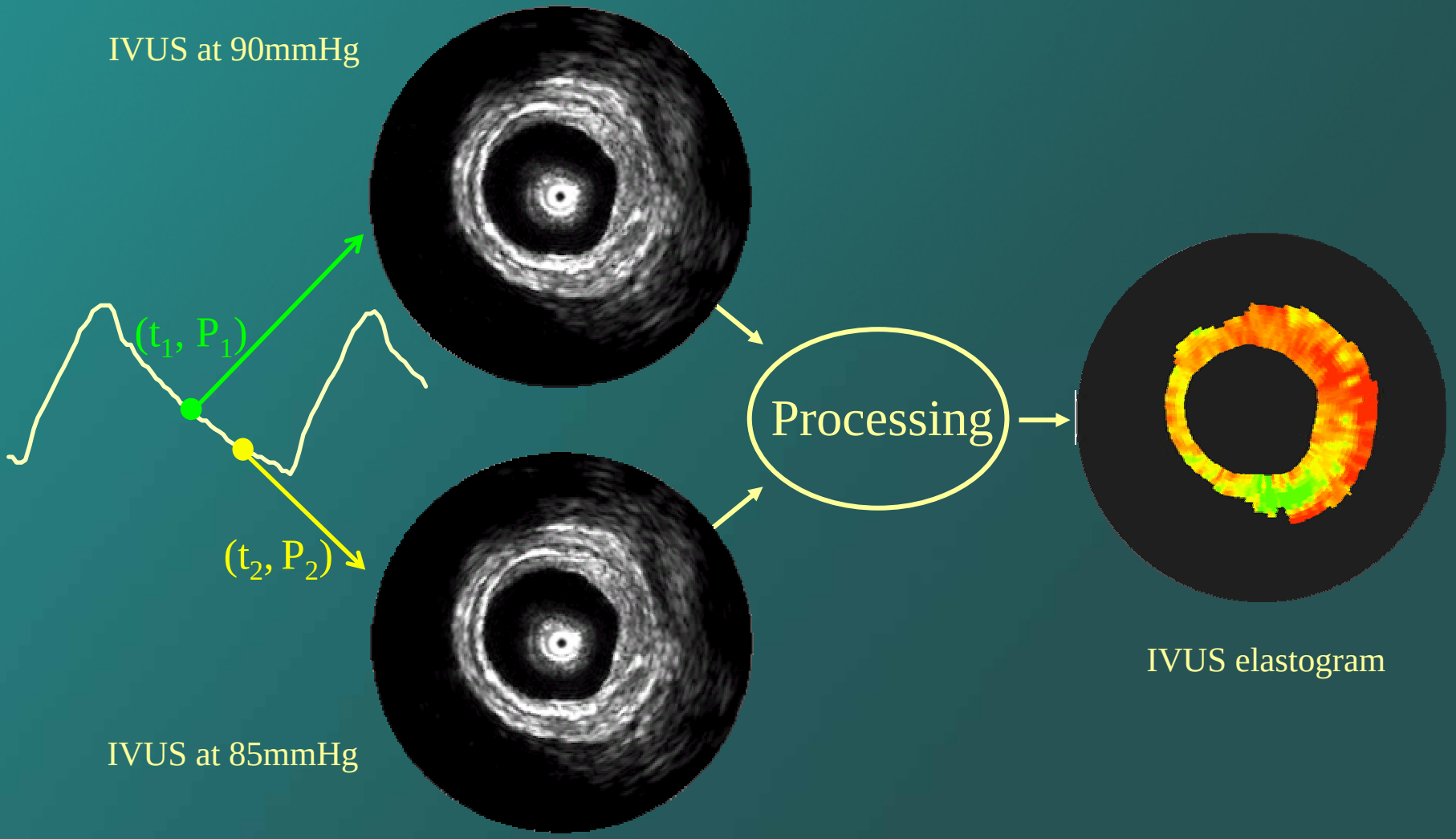
- Large lipid pool
- Thin fibrous cap
- Presence of macrophages



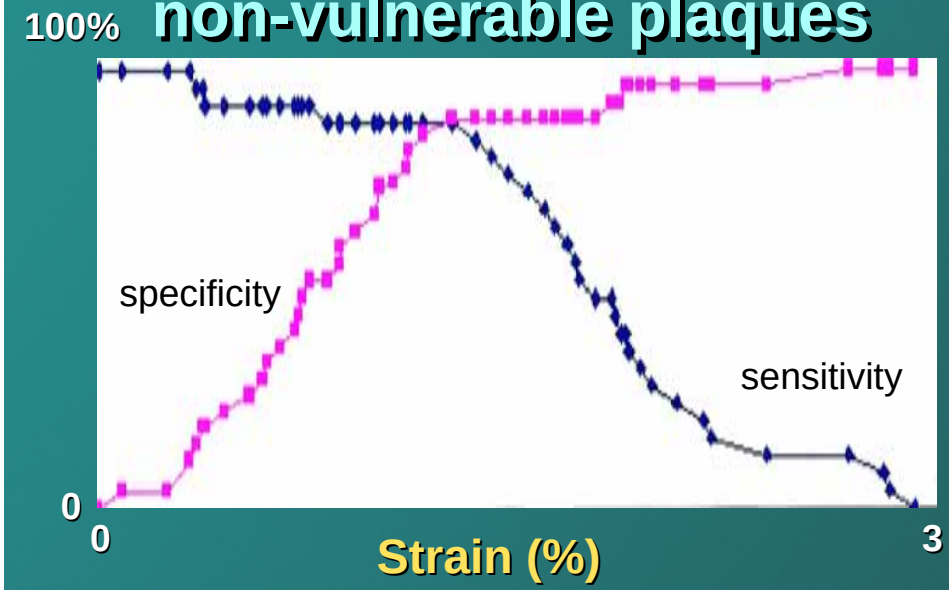
Mechanical properties

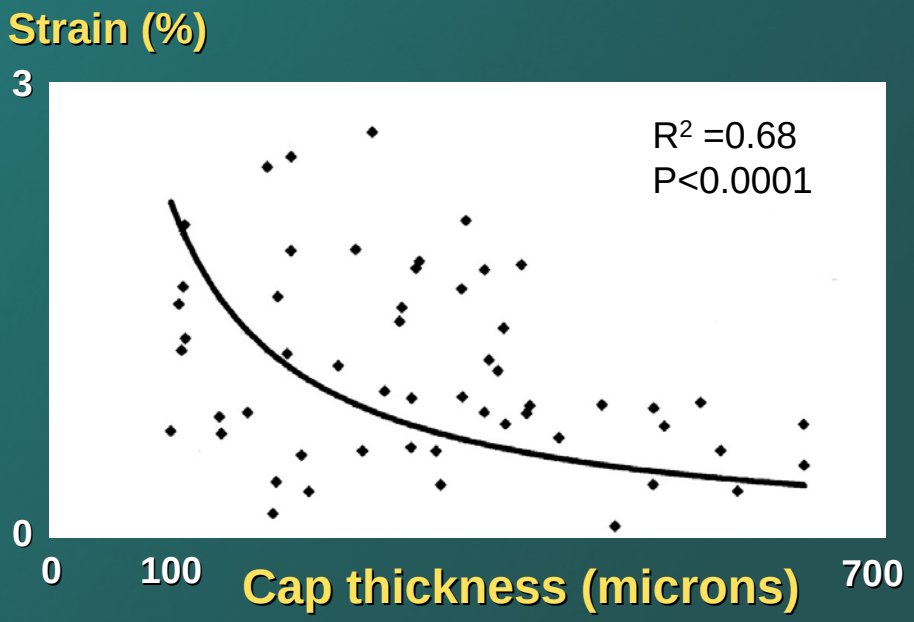
- High strain region

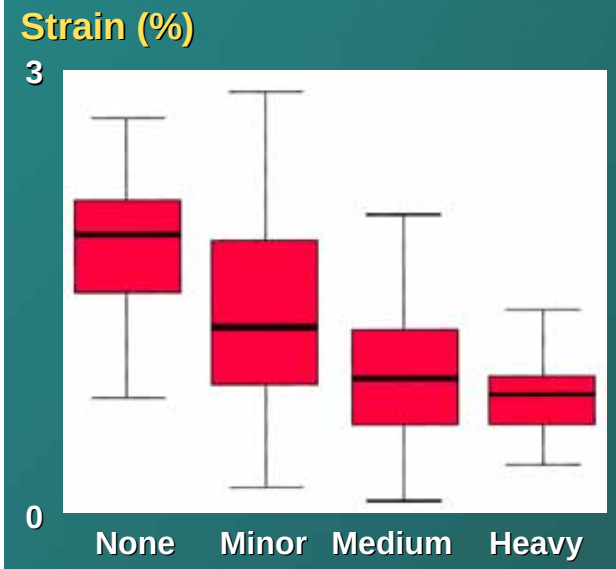
Principles of Palpography

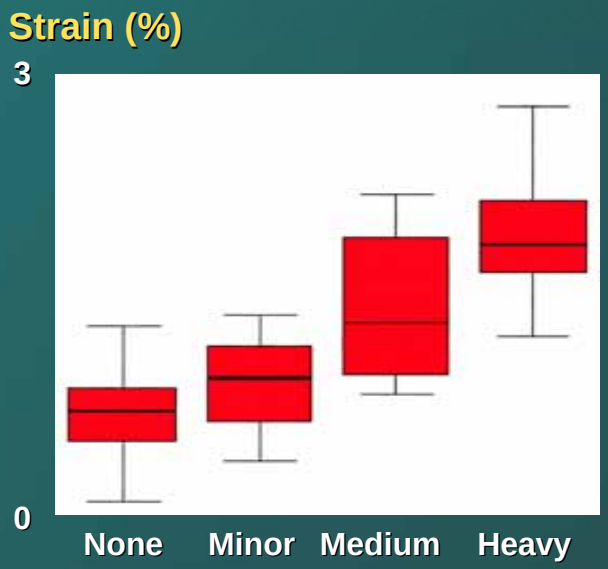


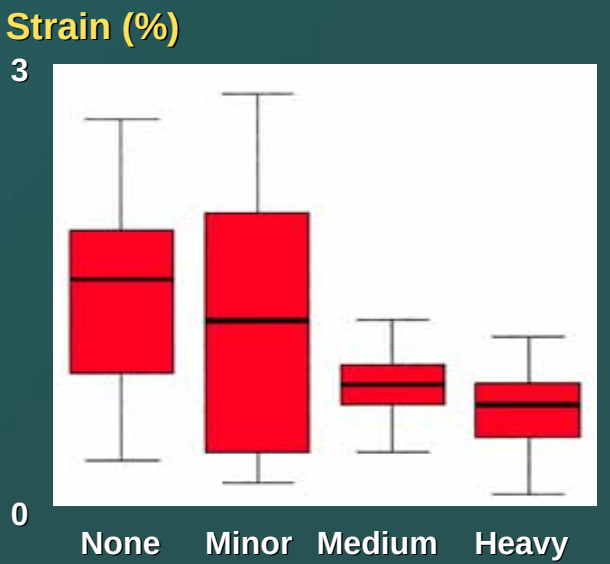
26 vulnerable vs 28 non-vulnerable plaques



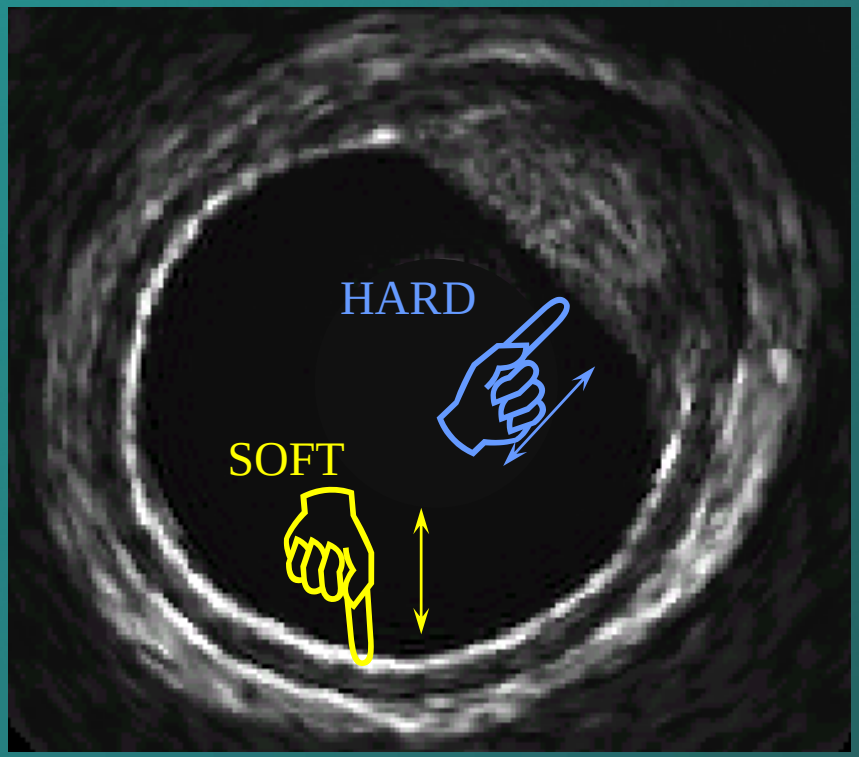


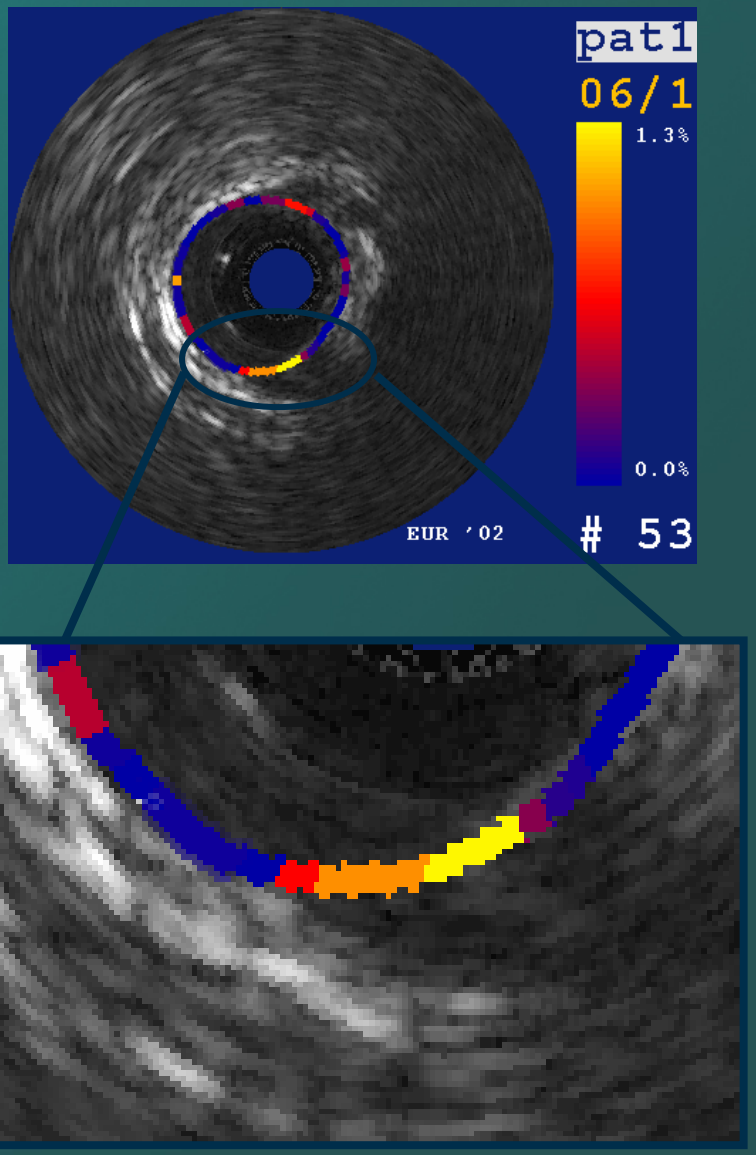






Schaar et al. Circulation 2003;108:2535-41

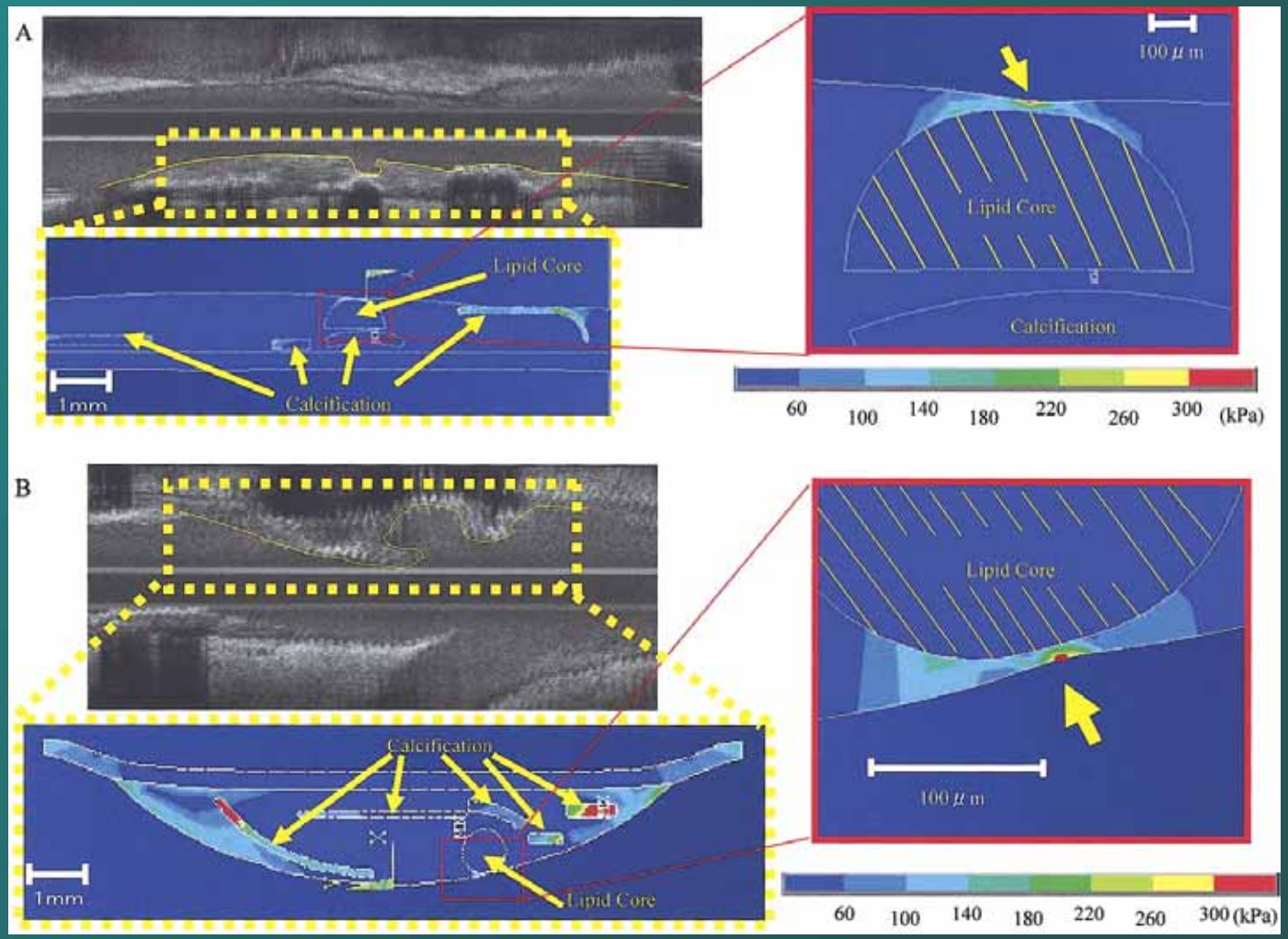




Independent predictors of strain were macrophages (p=0.006) and smooth muscle cells (p=0.0001)

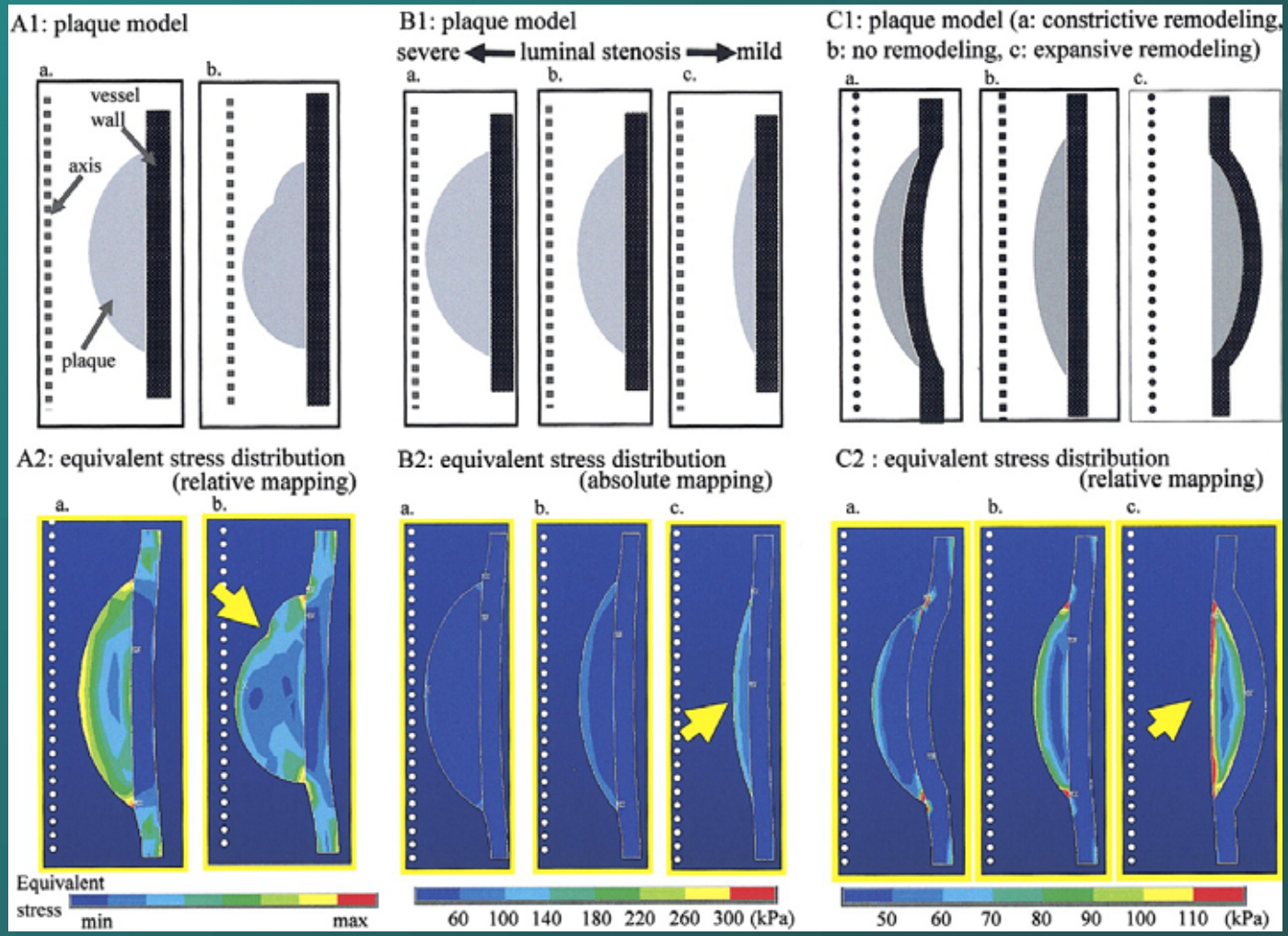
Schaar et al. Circulation 2003;108:2535-41

Three-dimensional IVUS images and color mapping of longitudinal stress distribution assessed using finite element analysis

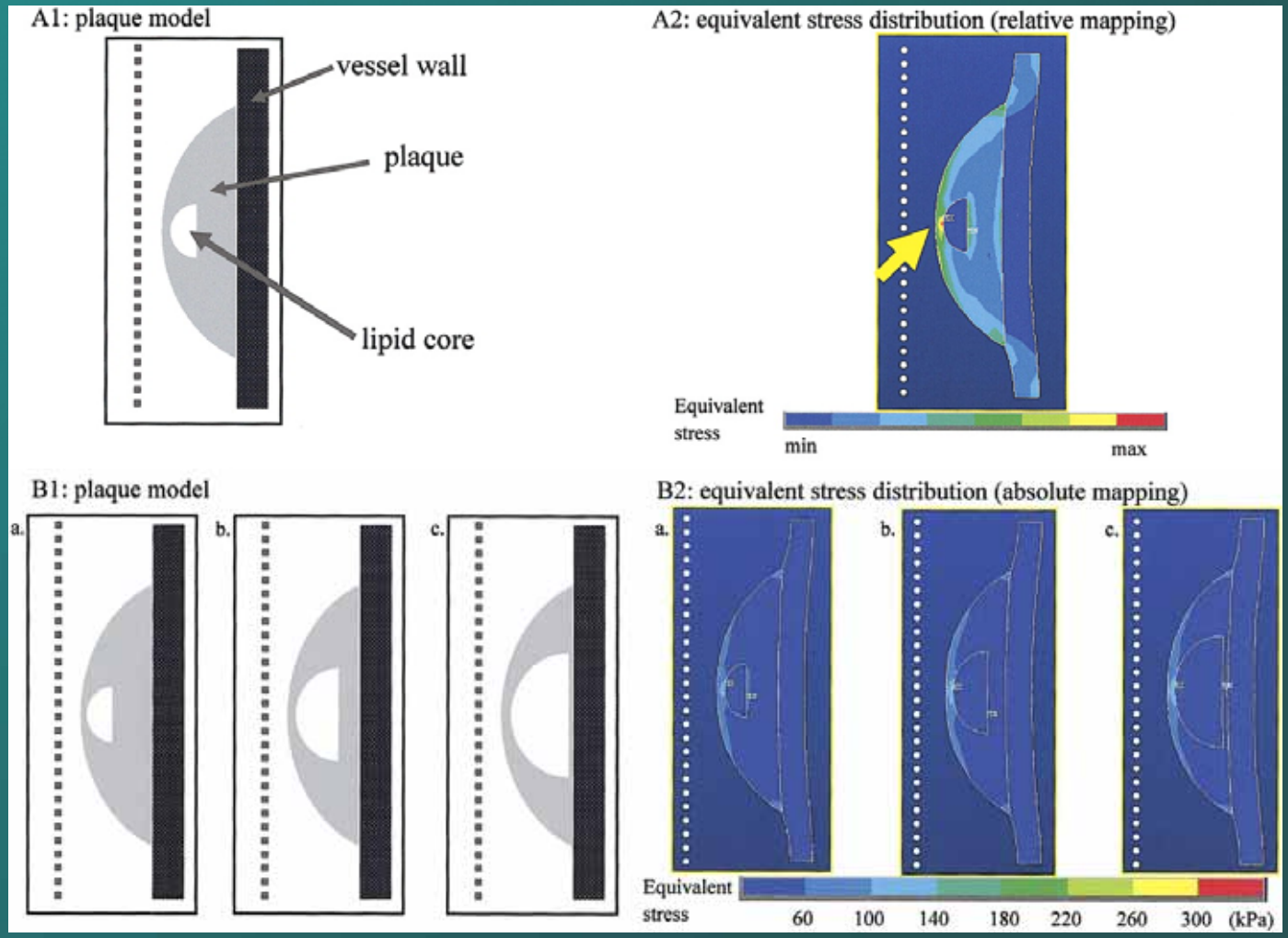


Imoto et al. J Am Coll Cardiol 2005;46:1507-1515

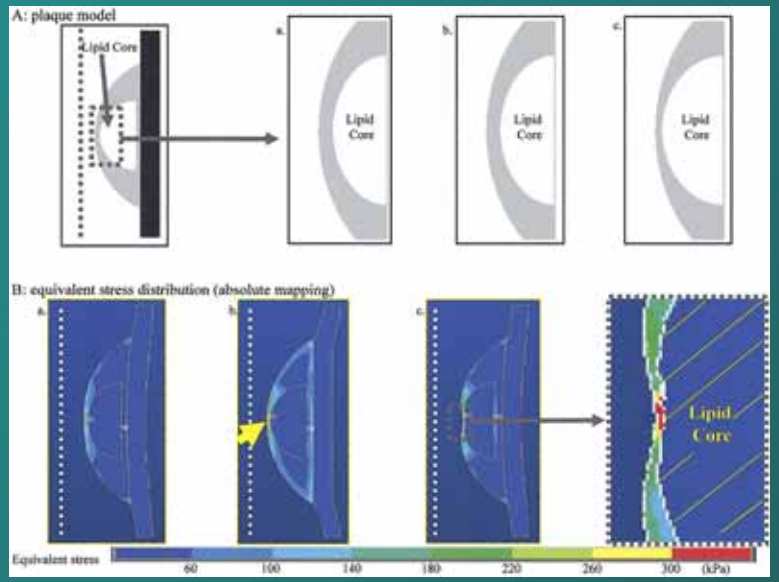
Relationship between stress distribution and plaque shape, luminal stenosis, or vessel remodeling

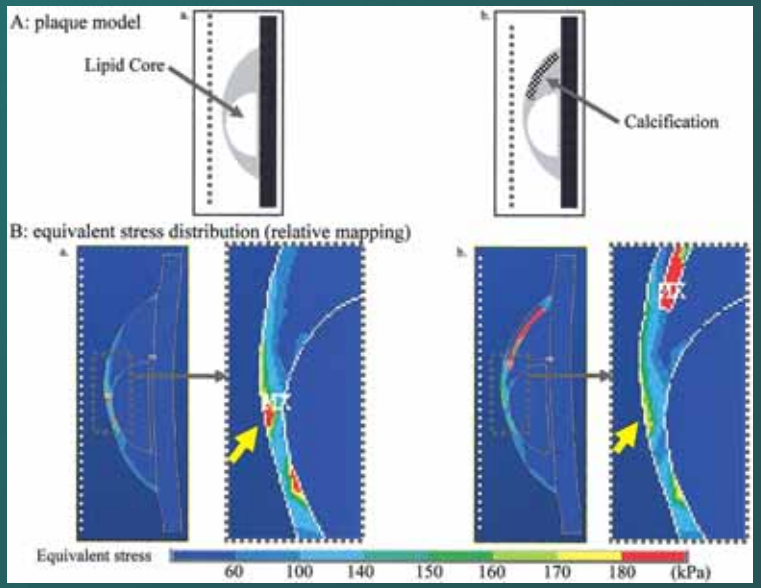


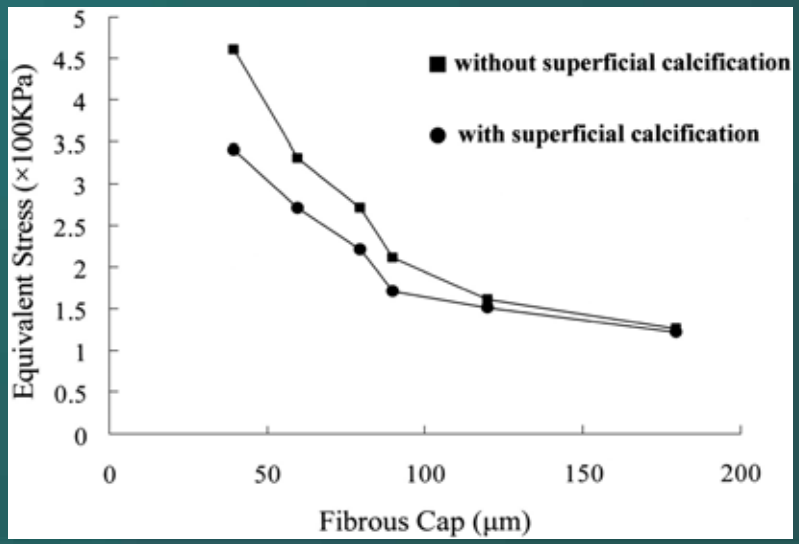
Effect of lipid core on stress distribution

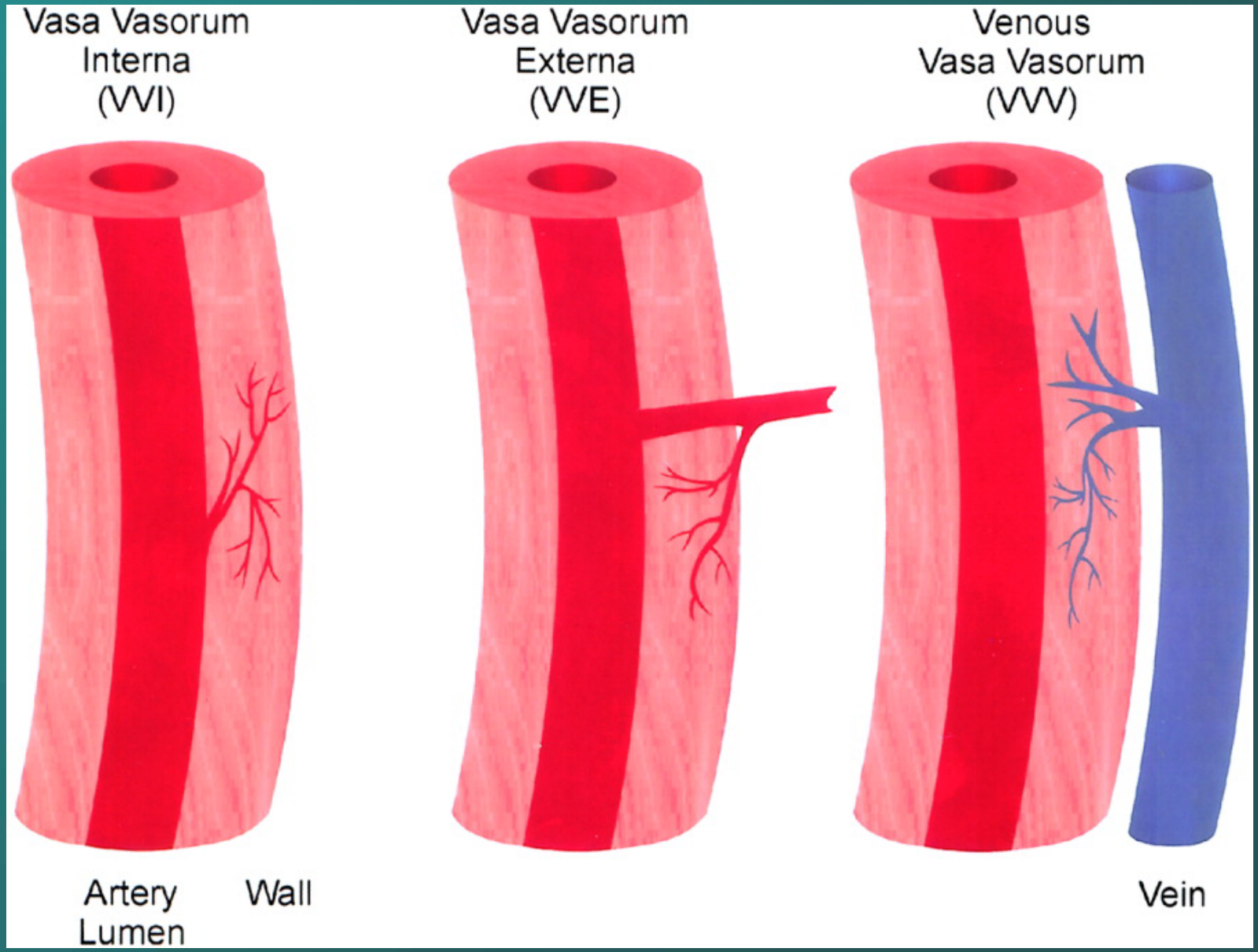


Effect of fibrous cap thickness and surface calcific deposits on stress distribution

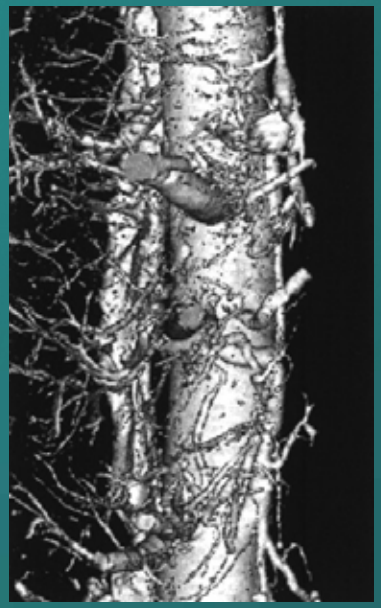




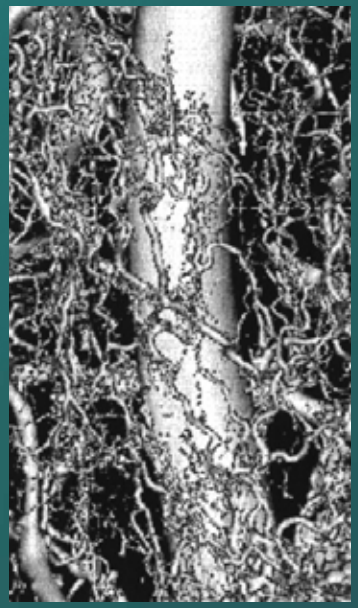



Vasa Vasorum
Interna
(VVI)
Vasa Vasorum
Externa
(VVE)
Venous
Vasa Vasorum
(VVV)
Artery
Lumen
Wall
Vein

Vasovasorum Imaging



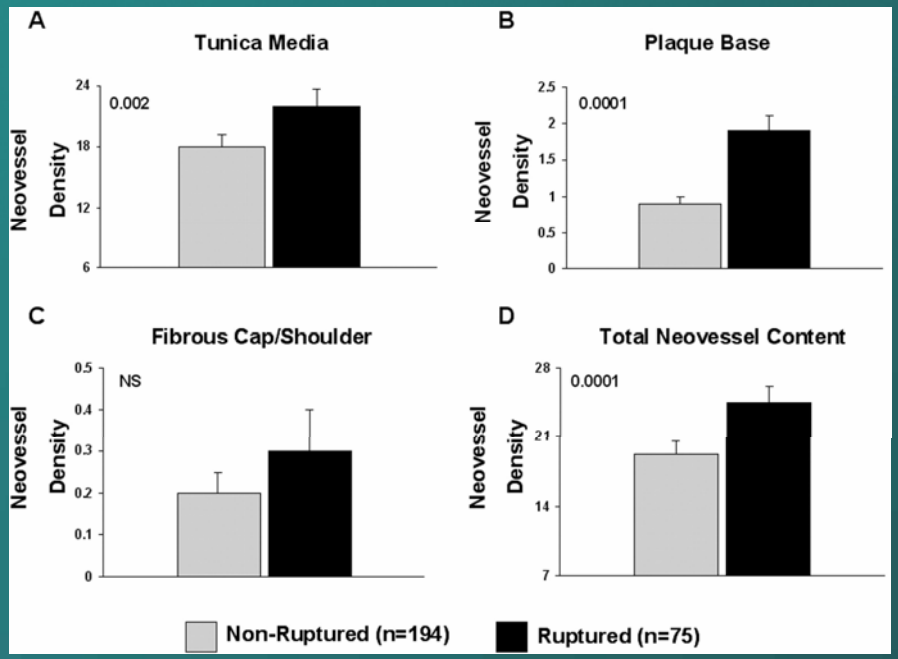
Normal

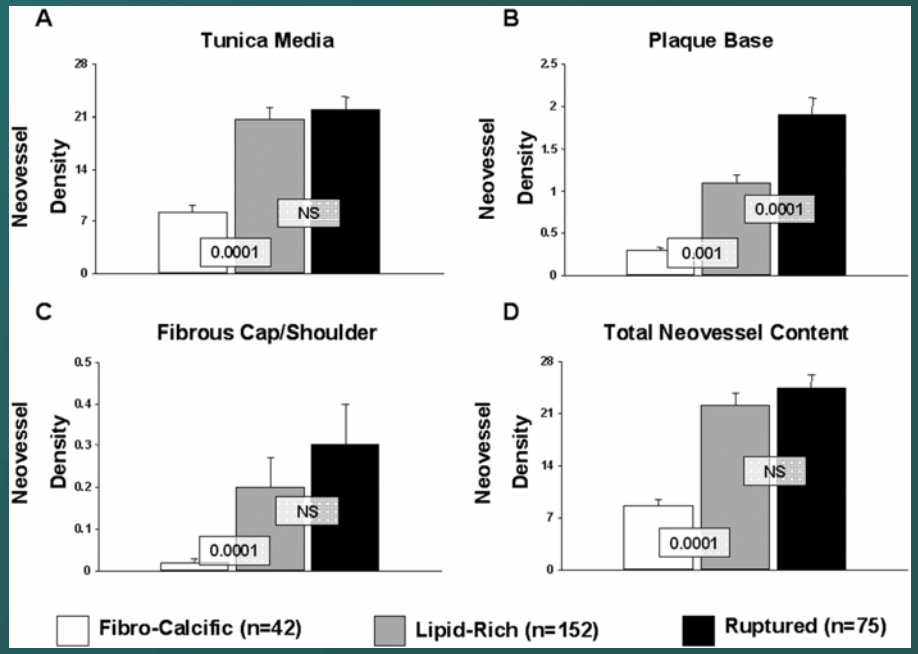


Hypercholesterolemia

Hypercholesterolemia + Statin

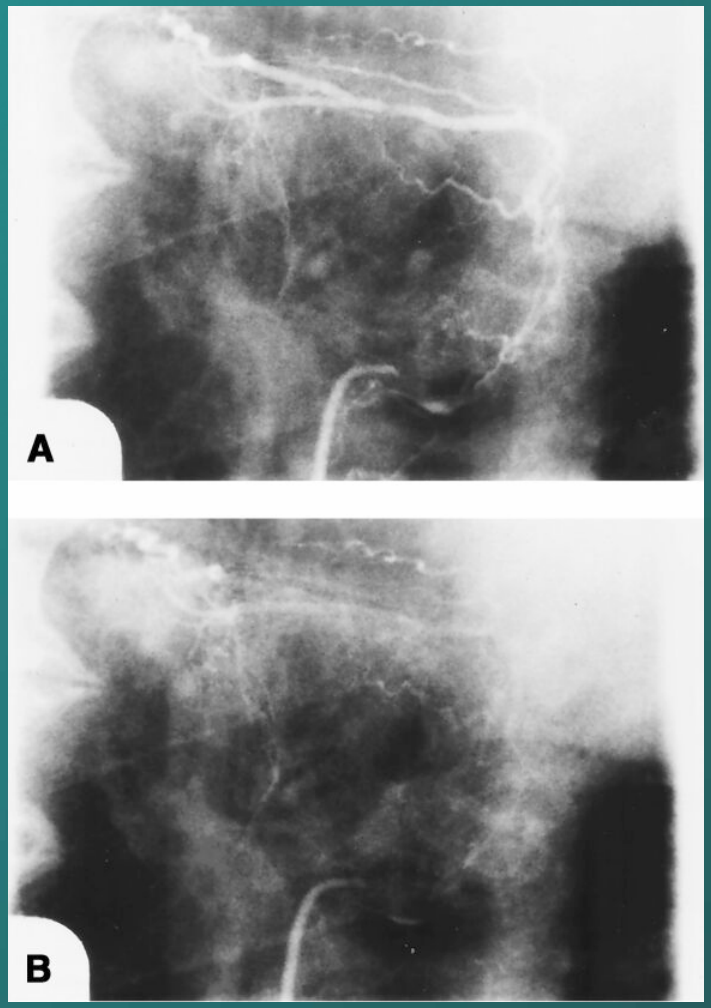
Plaque neovascularization is increased in ruptured atherosclerotic lesions of human aorta





Moreno P et al, Circulation 2004; 110:2032-8

Plaque blush, branch location, and calcification were angiographic predictors of progression of mild to moderate coronary stenoses in 68 patients

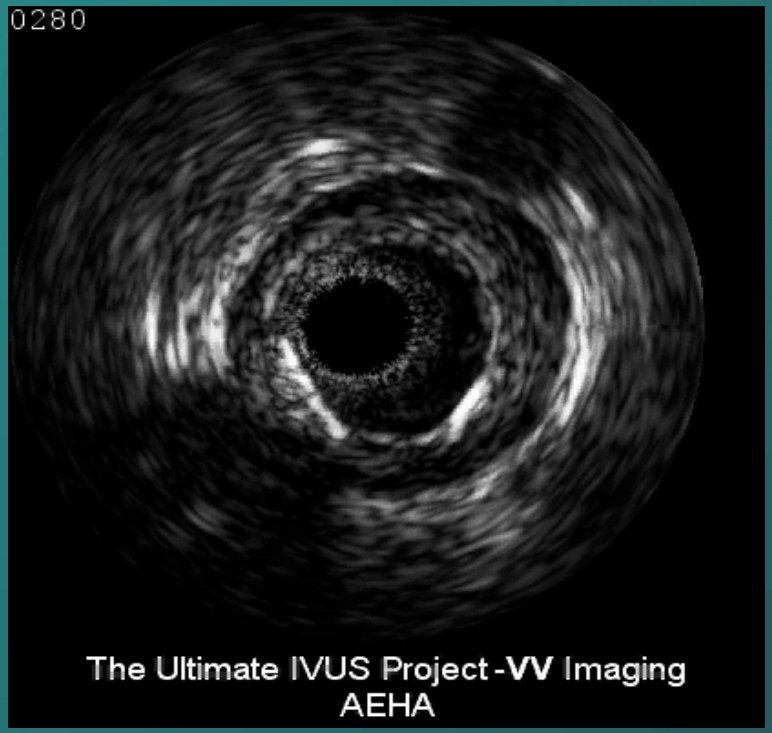


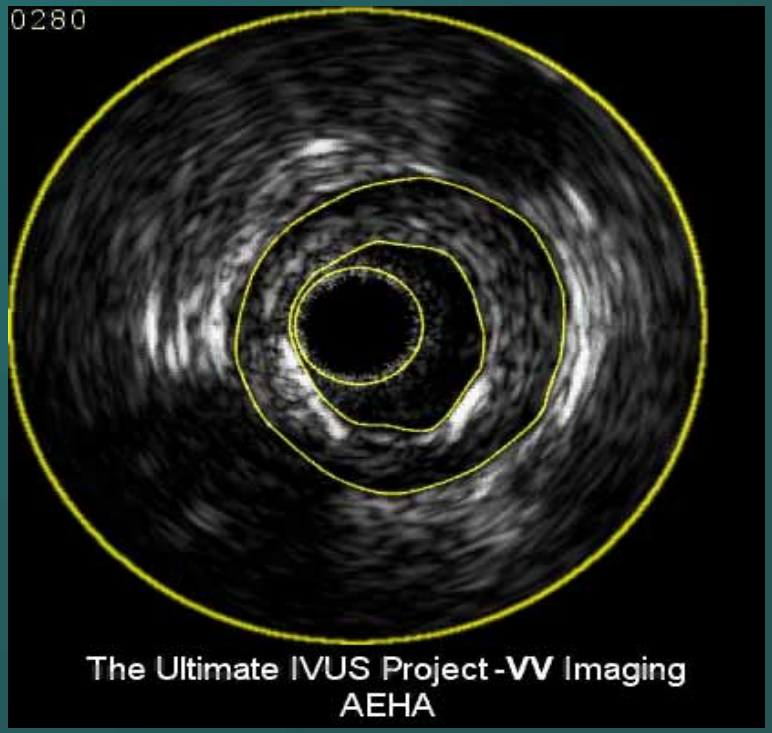
Casscells et al. Am Heart J 2003;145:813-20

Predictors of progression

	OR	p
Plaque blush	12.2	0.0015
Calcification	6.1	0.0235
Branch point	13.9	0.0012

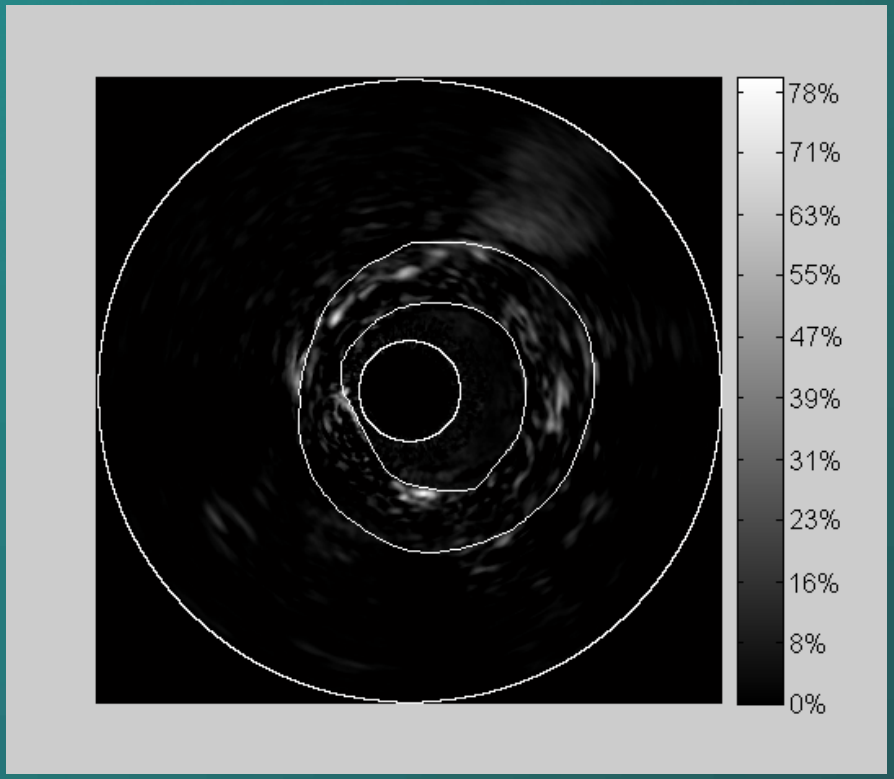
Baseline images are acquired for 20 seconds, and regions of interest are assigned

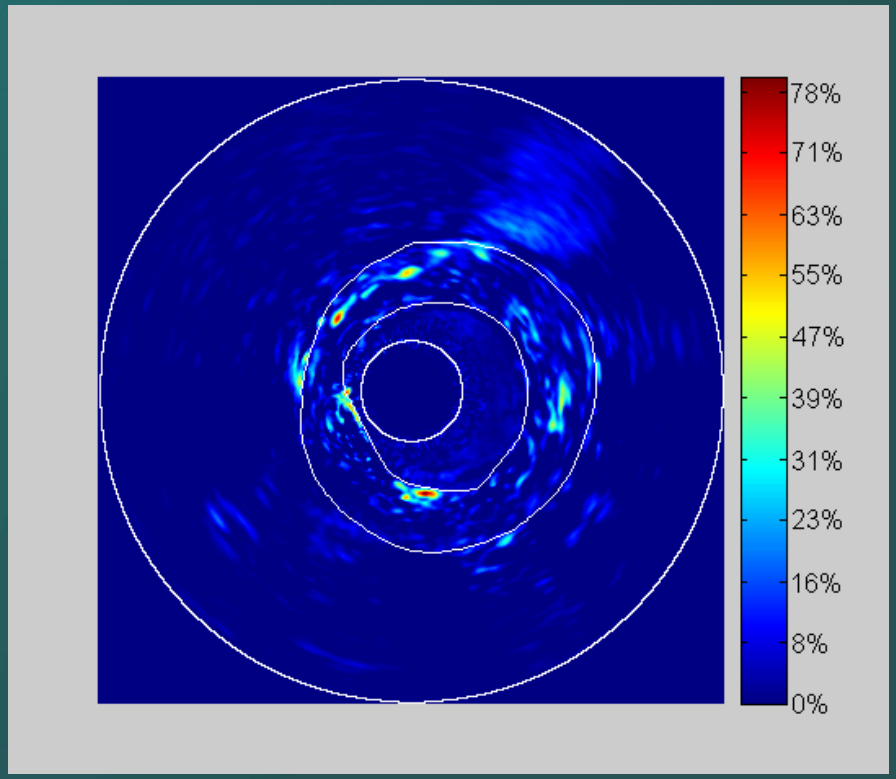


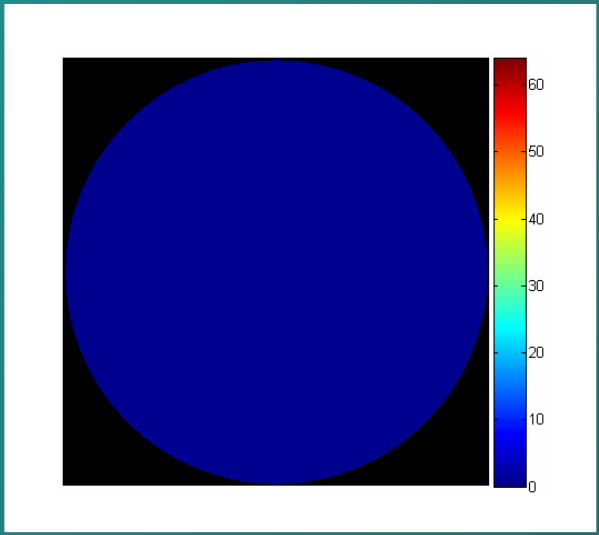


Contrast is injected, images are acquired for 120 seconds post-injection, and baseline images are subtracted

Range of enhancement

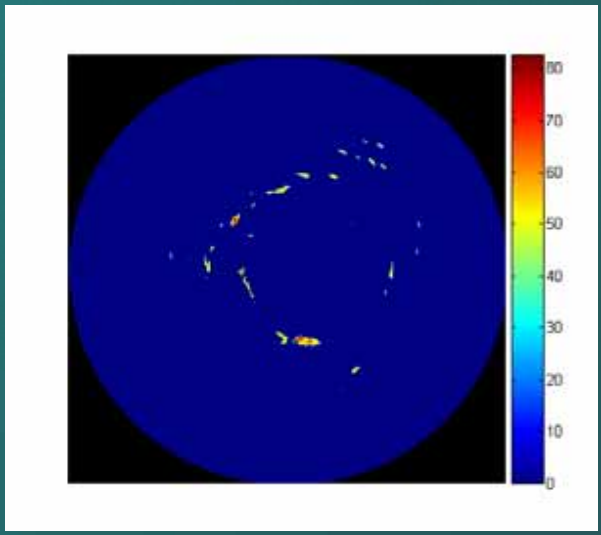






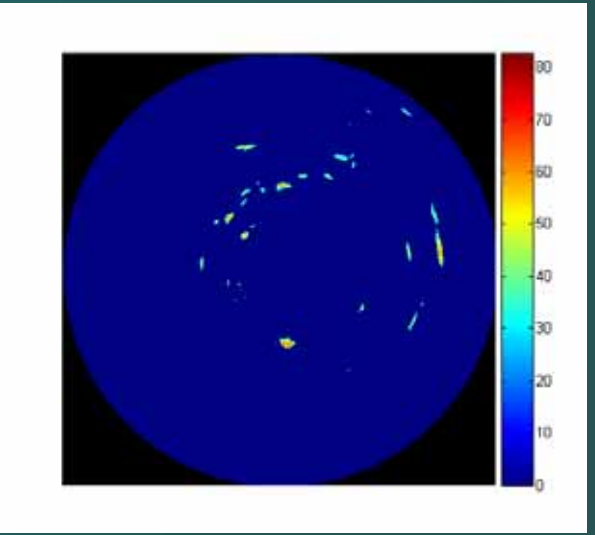
Pre-injection
(Frame #200)

Background motions are cancelled



Peak Injection
(Frame #600)

Lumen subtracted (microbubble shadow effect is not calculated)

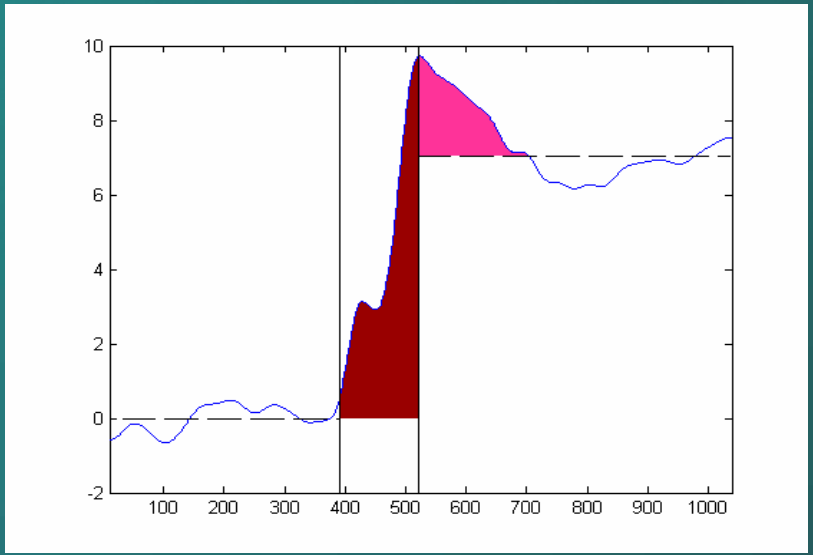


Post-injection
(Frame #800)

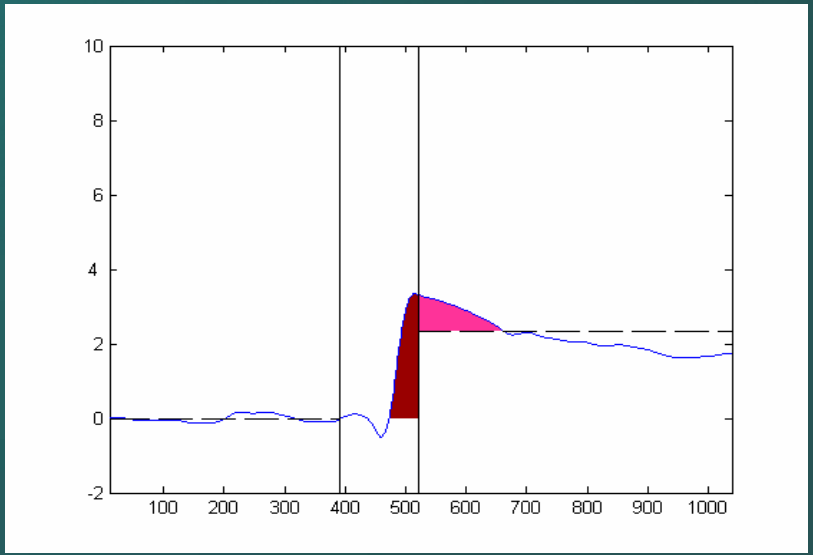
The enhancement lasts for at least 25 seconds.

Time-activity curves with quantitative monitoring of plaque perfusion

Intimo-Medial and Plaque Area



Adventitia Area



The PROSPECT Trial

Providing Regional Observations to Study Predictors of Events in the Coronary Tree

Natural history study in pts with ACS

Multiple imaging techniques

Multiple serum markers

Prolonged follow-up

Principal sponsor: Guidant Corporation

Co-sponsor: Volcano Therapeutics, ?3rd

700 pts with ACS and 1 or 2 vessel CAD undergoing PCI will have QCA of entire coronary tree, culprit artery imaging (post PCI), and both non-culprit arteries also imaged using

IVUS

Virtual histology

Palpography

± Thermography (EU only)

Meds Rx
Aspirin
Plavix 1yr
Statin

F/U: 1 mo, 6 mo, 1 yr
2 yr, ±3-5 yr
(event driven)

Repeat imaging in pts with events

Naghavi et al. Circulation 2003;108:1664-72	Angiography	IVUS+VH+Stress+VV Imaging
Major criteria		
Active inflammation		+
Thin cap with large lipid core		+
Endothelial denudation		
Fissured plaque		±
Stenosis >90%	+	+
Minor criteria		
Superficial calcified nodule		+
Glistening yellow		
Intraplaque hemorrhage		+
Endothelial dysfunction		
Positive remodeling		+
Three vessel imaging	+	±

Conclusion

- Conventional grey scale IVUS cannot detect vulnerable plaques
- Other IVUS based imaging modalities have the potential to detect vulnerable plaques, including
  - VH+IB IVUS
  - Palpography/Stress imaging
  - Vasovasorum Imaging