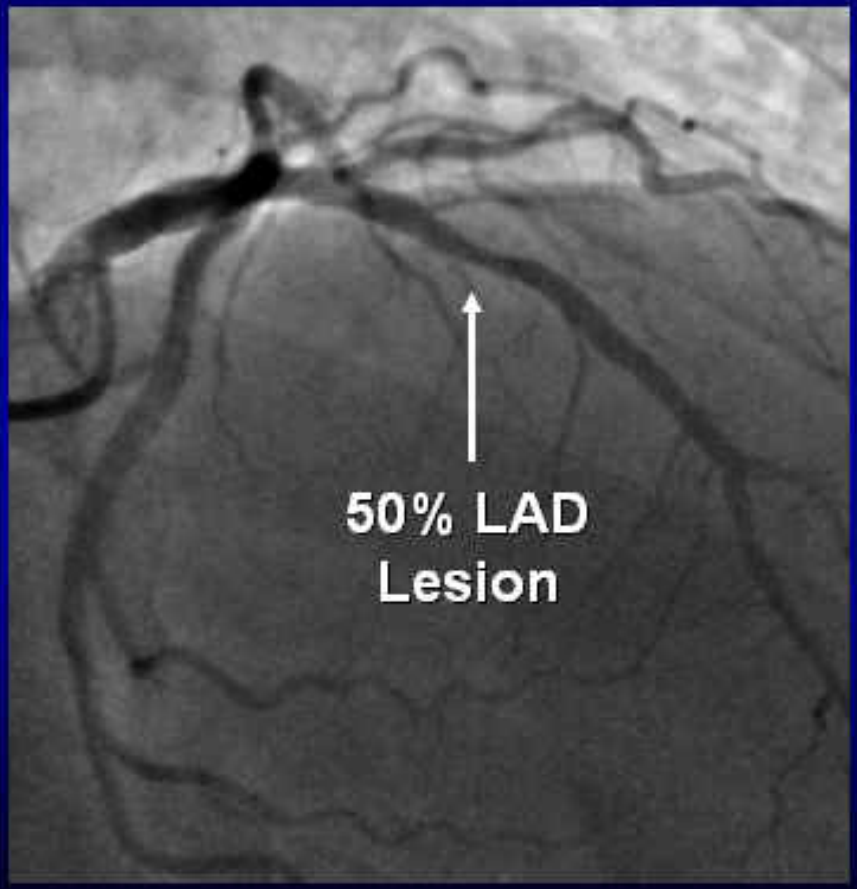
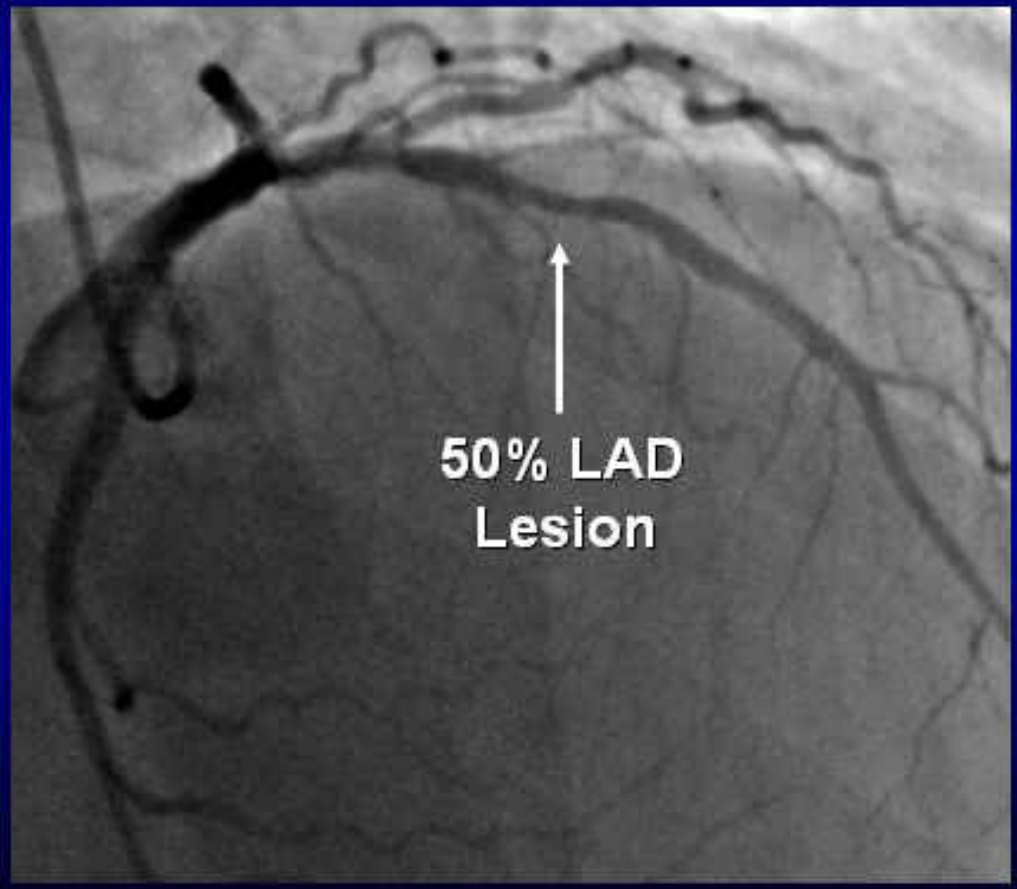
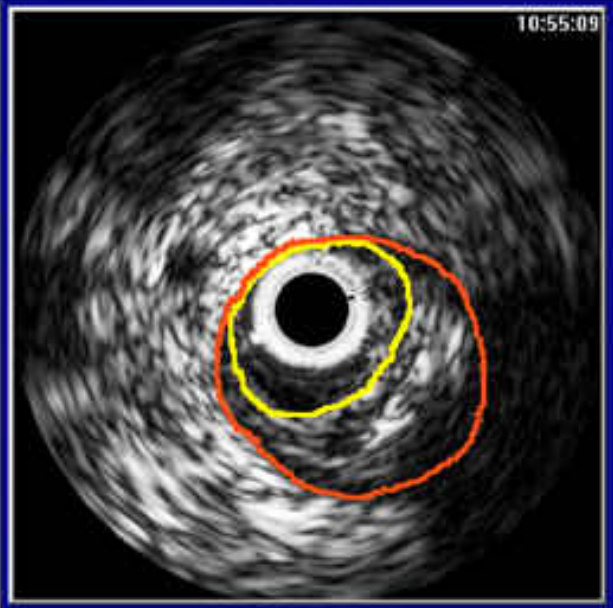
Clinical Examples Using
VIRTUAL HISTOLOGY
Barry D. Rutherford, MD
Angioplasty Summit 2009

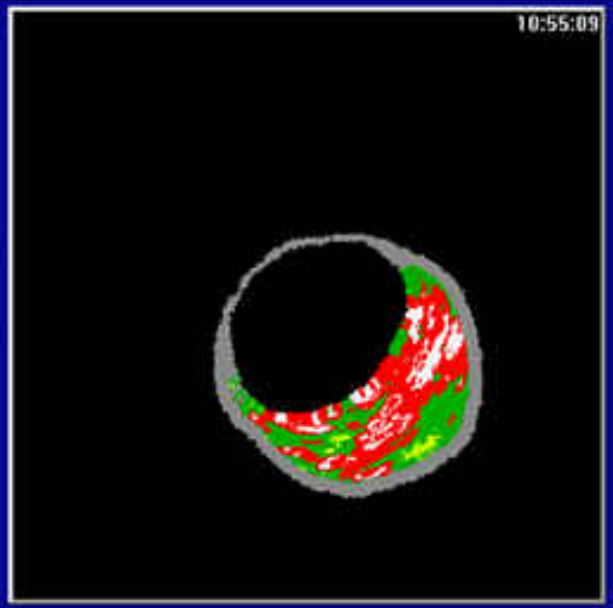
52-yo Male (DB)
Abnormal Nuclear Scan: Anterior Ischemia



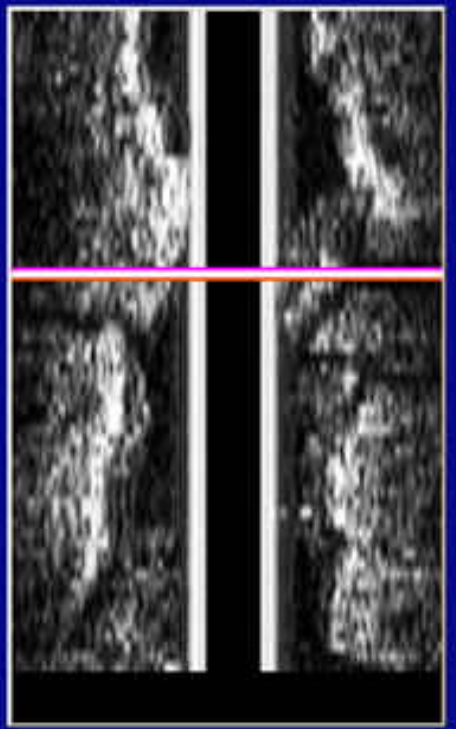


52-yo Male with Abn Nuc Scan (DB)





VL A, Segment: 1

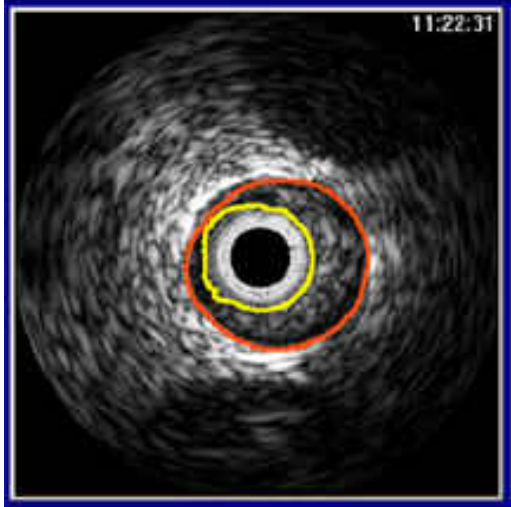


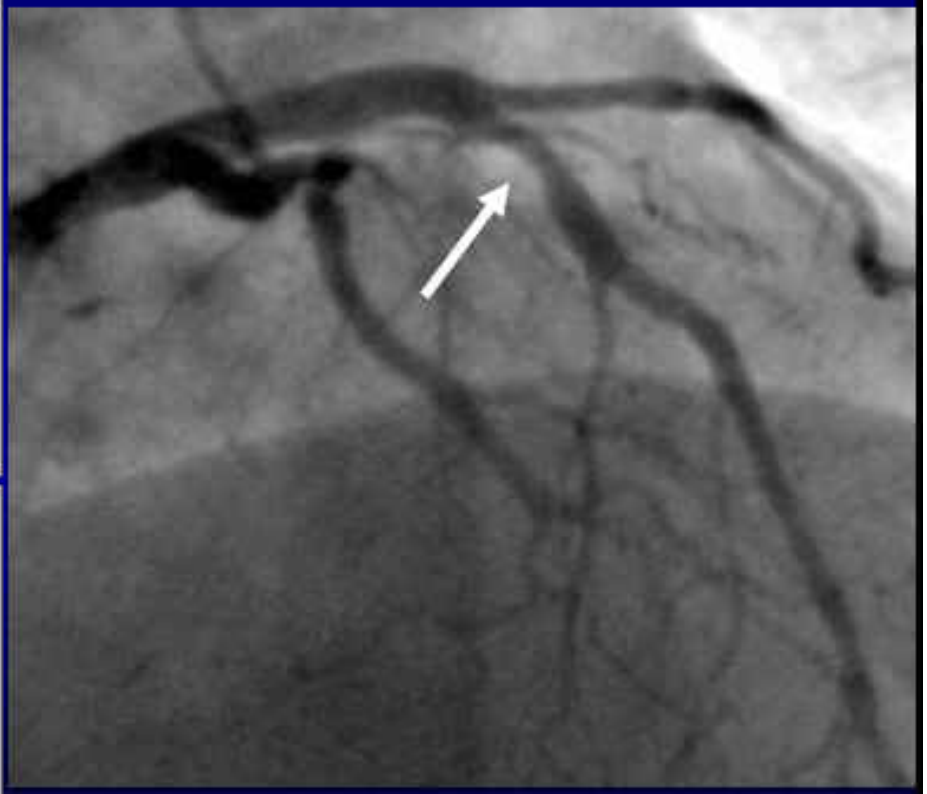
Lumen Area	6.8 mm²	
EEL Area	16.0 mm²	
Plaque Area	9.2 mm²	
% Plaque Burden	58 %	
Fibrous Area	2.2 mm²	35 %
Fibro-Fatty Area	0.2 mm²	3 %
Dense Calcium Area	1.0 mm²	16 %
Necrotic Core Area	2.9 mm²	46 %

More ...

Distal Frame	—	26
Current Frame	—	26
Proximal Frame	—	26

42-Year-Old Male Presenting with UA
Stenting of LADD (CC)

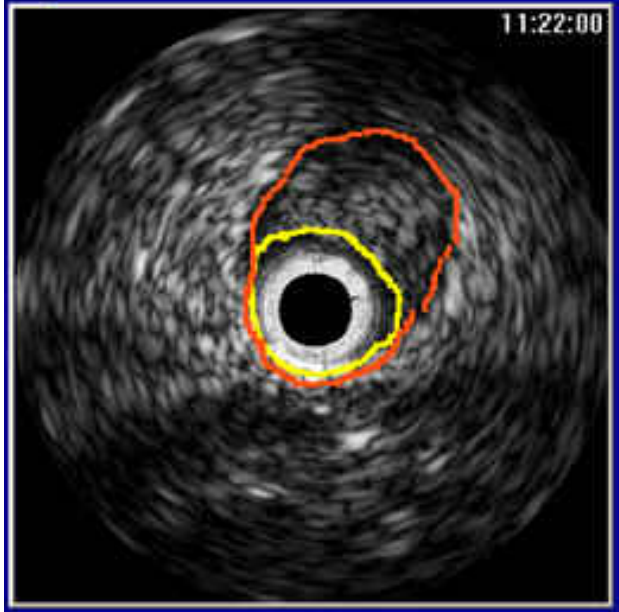


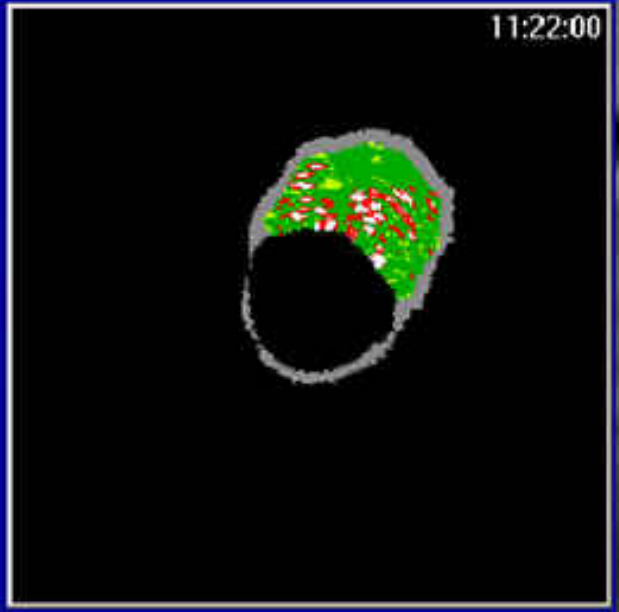


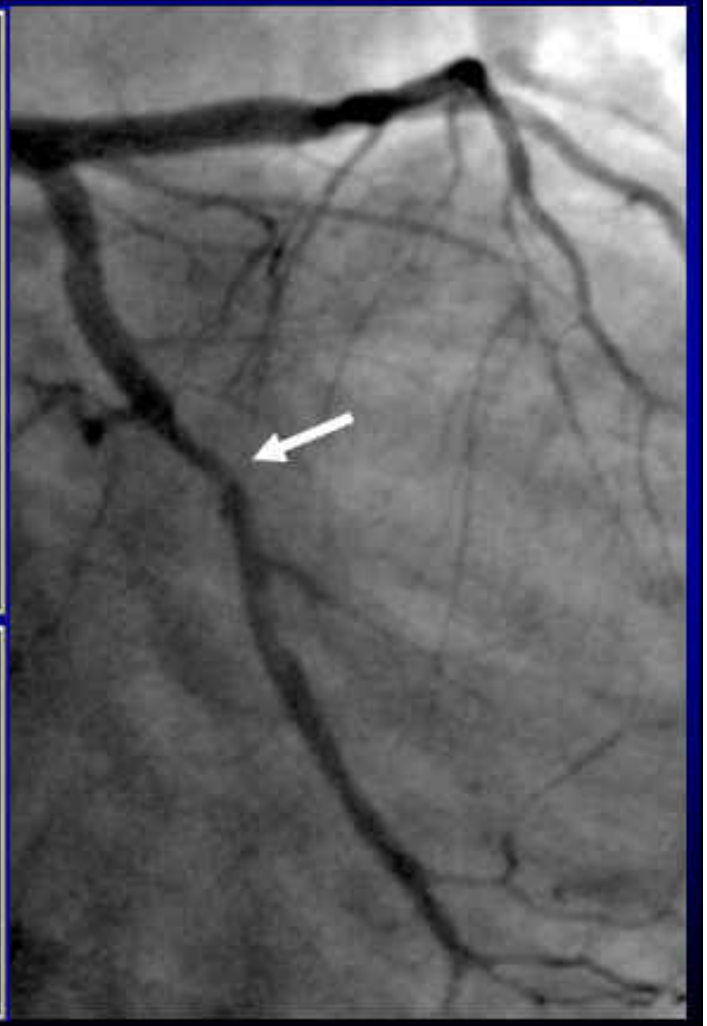
Lumen Area	4.0 mm²	
EEL Area	10.3 mm²	
Plaque Area	6.4 mm²	
% Plaque Burden	62 %	
Fibrous Area	2.3 mm²	63 %
Fibro-Fatty Area	0.1 mm²	4 %
Dense Calcium Area	0.5 mm²	15 %
Necrotic Core Area	0.6 mm²	18 %

More ...

42-Year-Old Male Presenting with UA
Stenting of LADD (CC)



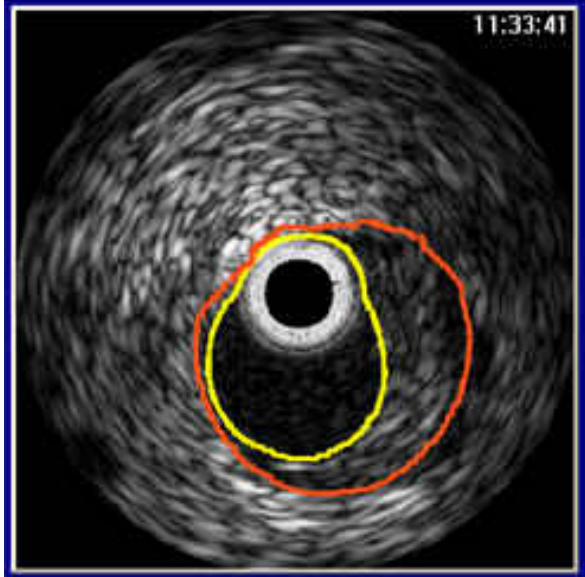


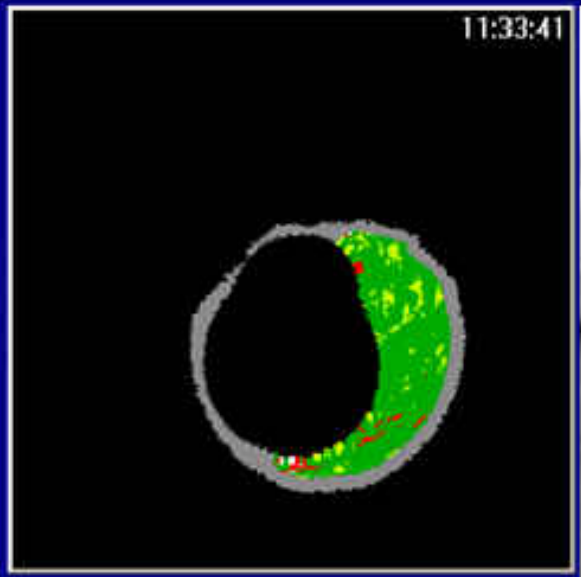


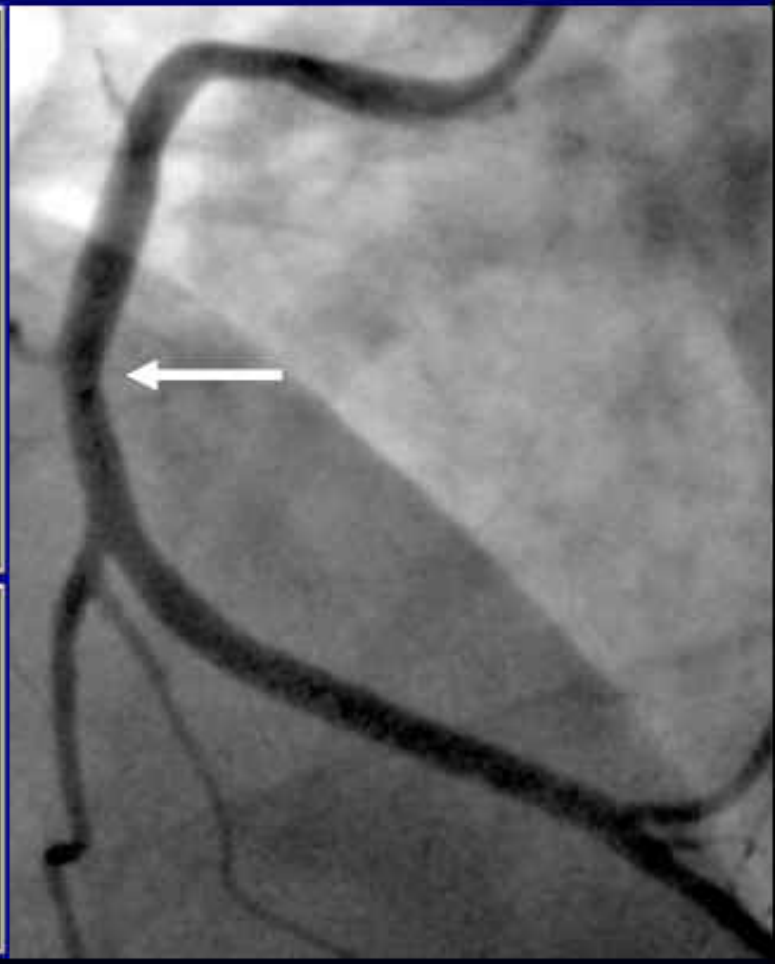
Lumen Area	4.7 mm²	
EEL Area	11.3 mm²	
Plaque Area	6.6 mm²	
% Plaque Burden	58 %	
Fibrous Area	3.1 mm²	70 %
Fibro-Fatty Area	0.3 mm²	7 %
Dense Calcium Area	0.4 mm²	9 %
Necrotic Core Area	0.7 mm²	15 %

More ...

42-Year-Old Male Presenting with UA
Stenting of LADD (CC)



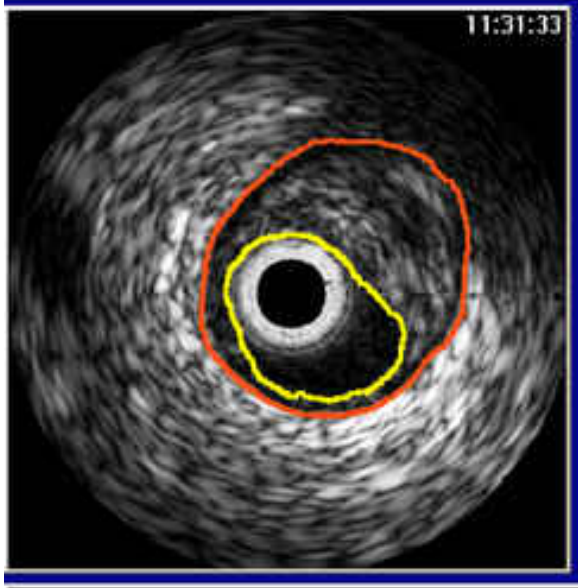


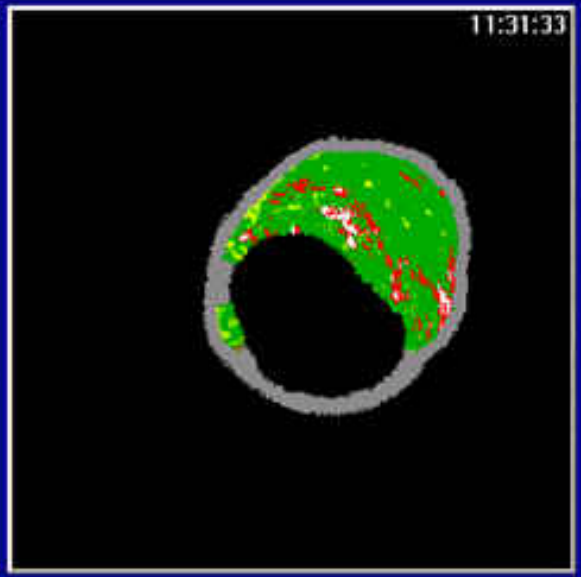


Lumen Area	9.7 mm²	
EEL Area	18.8 mm²	
Plaque Area	9.1 mm²	
% Plaque Burden	49 %	
Fibrous Area	5.0 mm²	86 %
Fibro-Fatty Area	0.6 mm²	10 %
Dense Calcium Area	0.0 mm²	1 %
Necrotic Core Area	0.2 mm²	3 %

More ...

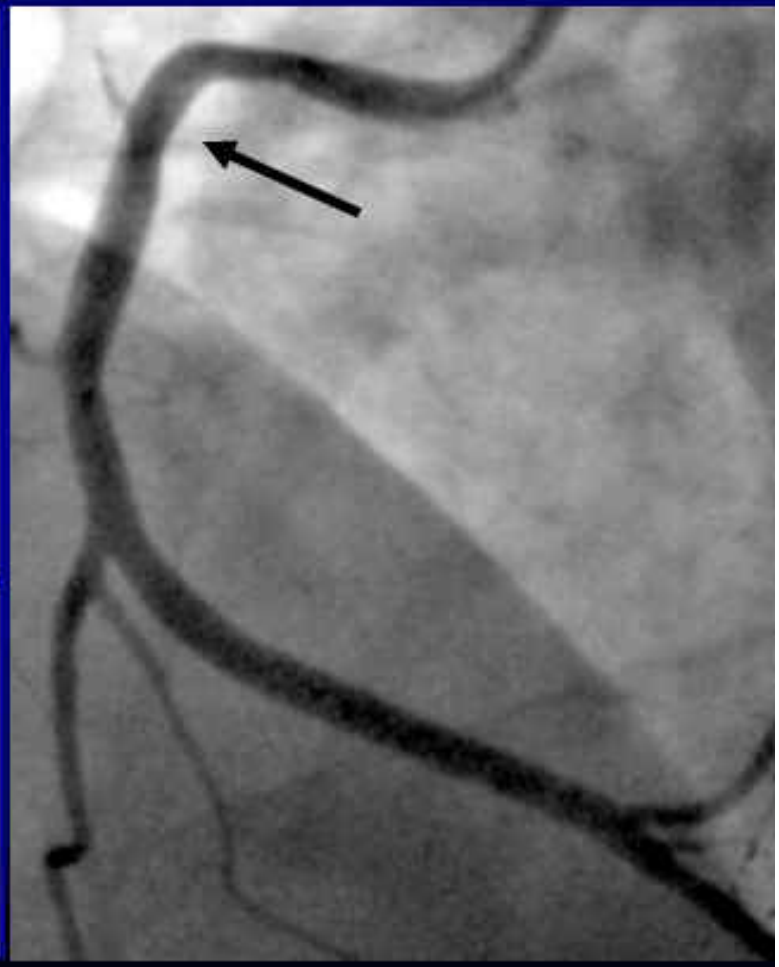
42-Year-Old Male Presenting with UA
Stenting of LADD (CC)

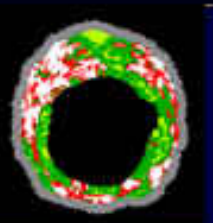




Lumen Area	6.7 mm²	
EEL Area	18.7 mm²	
Plaque Area	11.9 mm²	
% Plaque Burden	64 %	
Fibrous Area	6.4 mm²	81 %
Fibro-Fatty Area	0.4 mm²	5 %
Dense Calcium Area	0.3 mm²	3 %
Necrotic Core Area	0.9 mm²	11 %

More ...





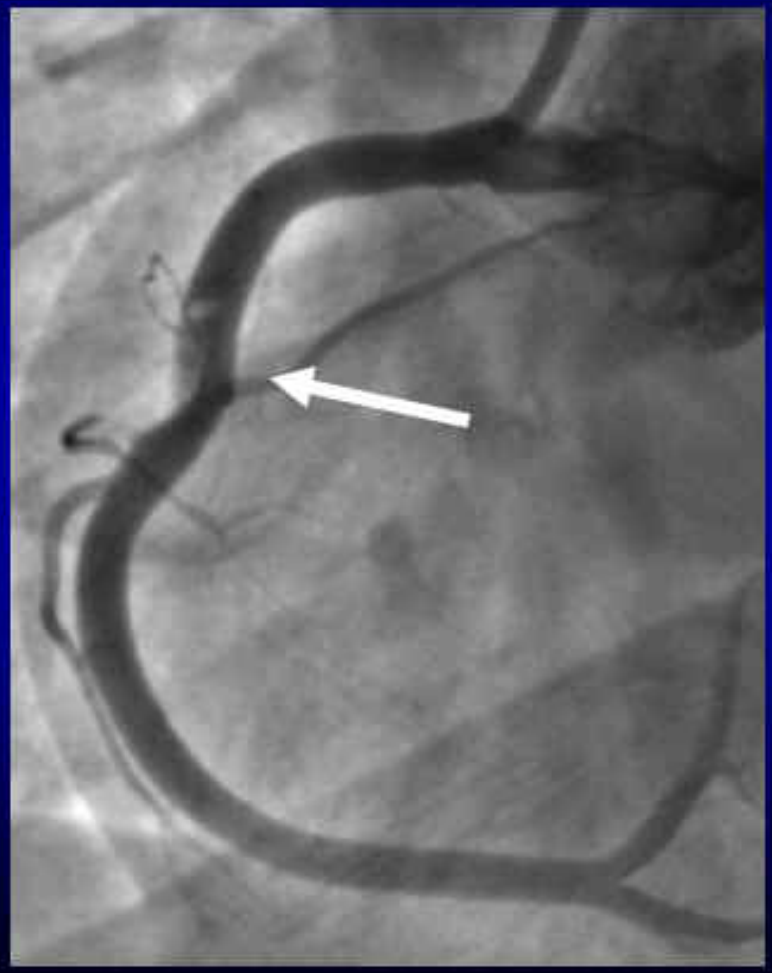
Virtual Histology
Clinical Applications

- Potential to identify vulnerable plaque prior to major clinical events (PROSPECT Trial)

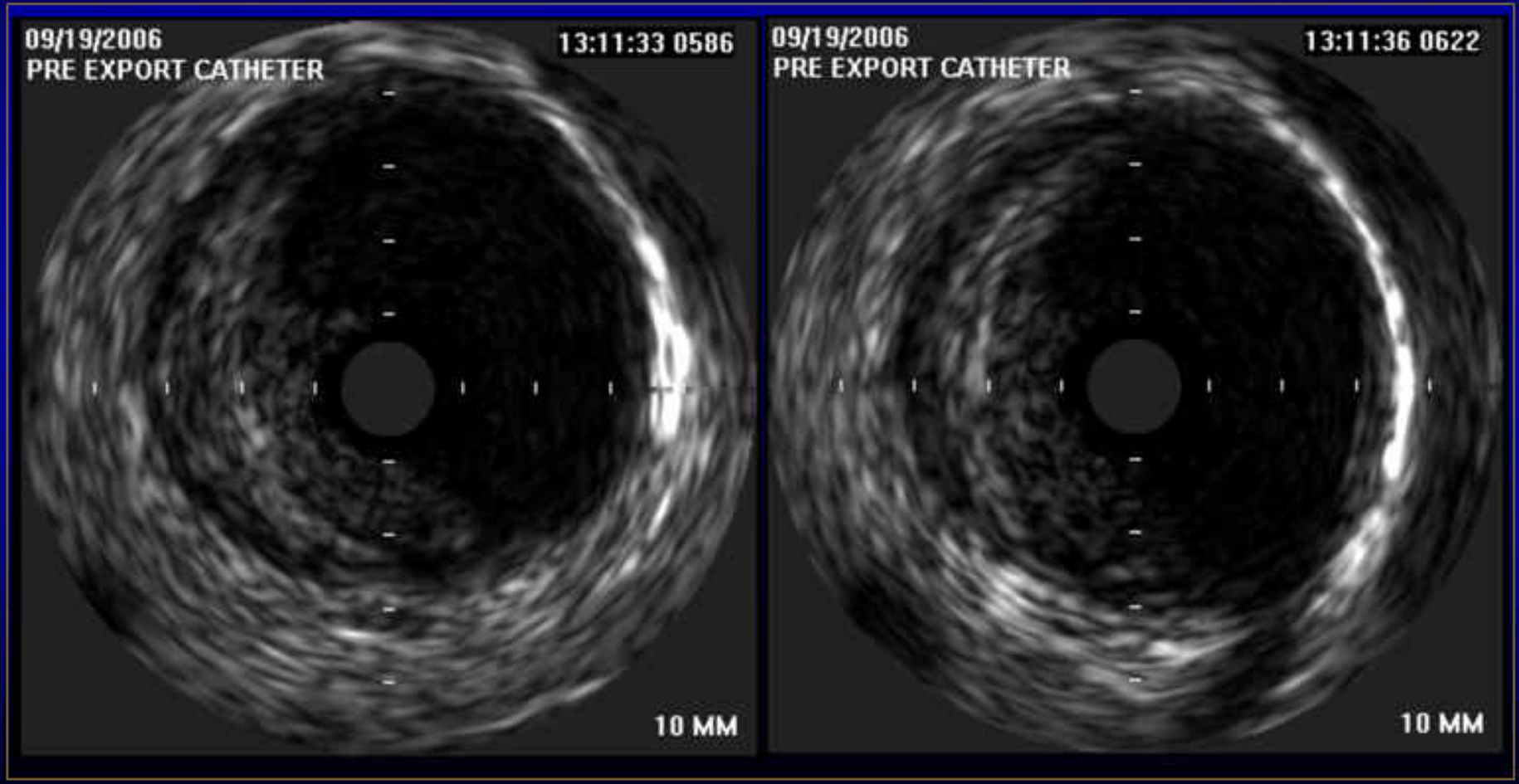
Identify Plaque (10-20% chance of MACE in 12 mths) → **DES / Biodegradable Stent** → **Stabilize**

Identify Plaque (10-20% chance of MACE in 12 mths) → **Intensive Statin Rx** → **Stabilize**

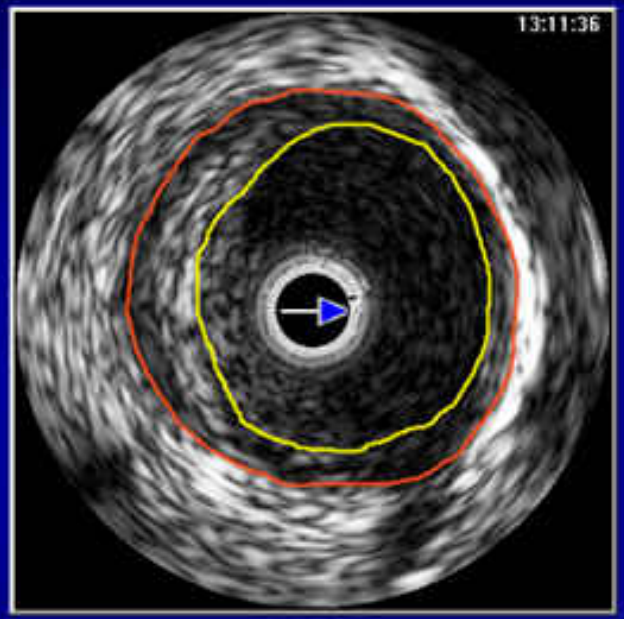
23-Year-Old Male College Football Player Presenting with Chest Pain

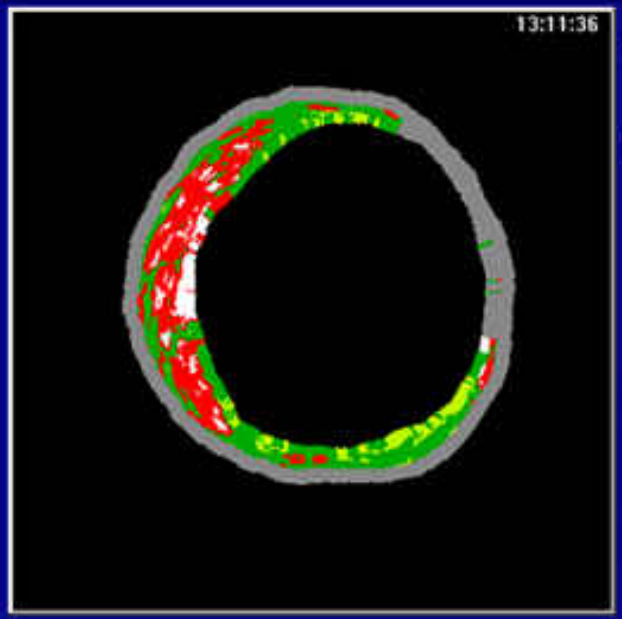


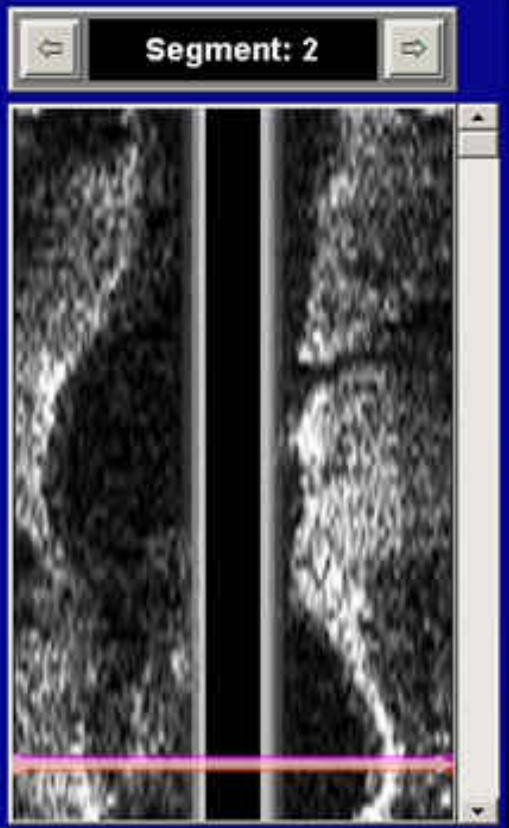
23-Year-Old Male Presenting with Chest Pain Before Use of Export™ Catheter



23-Year-Old Male Presenting with Chest Pain Before Use of Export™ Catheter





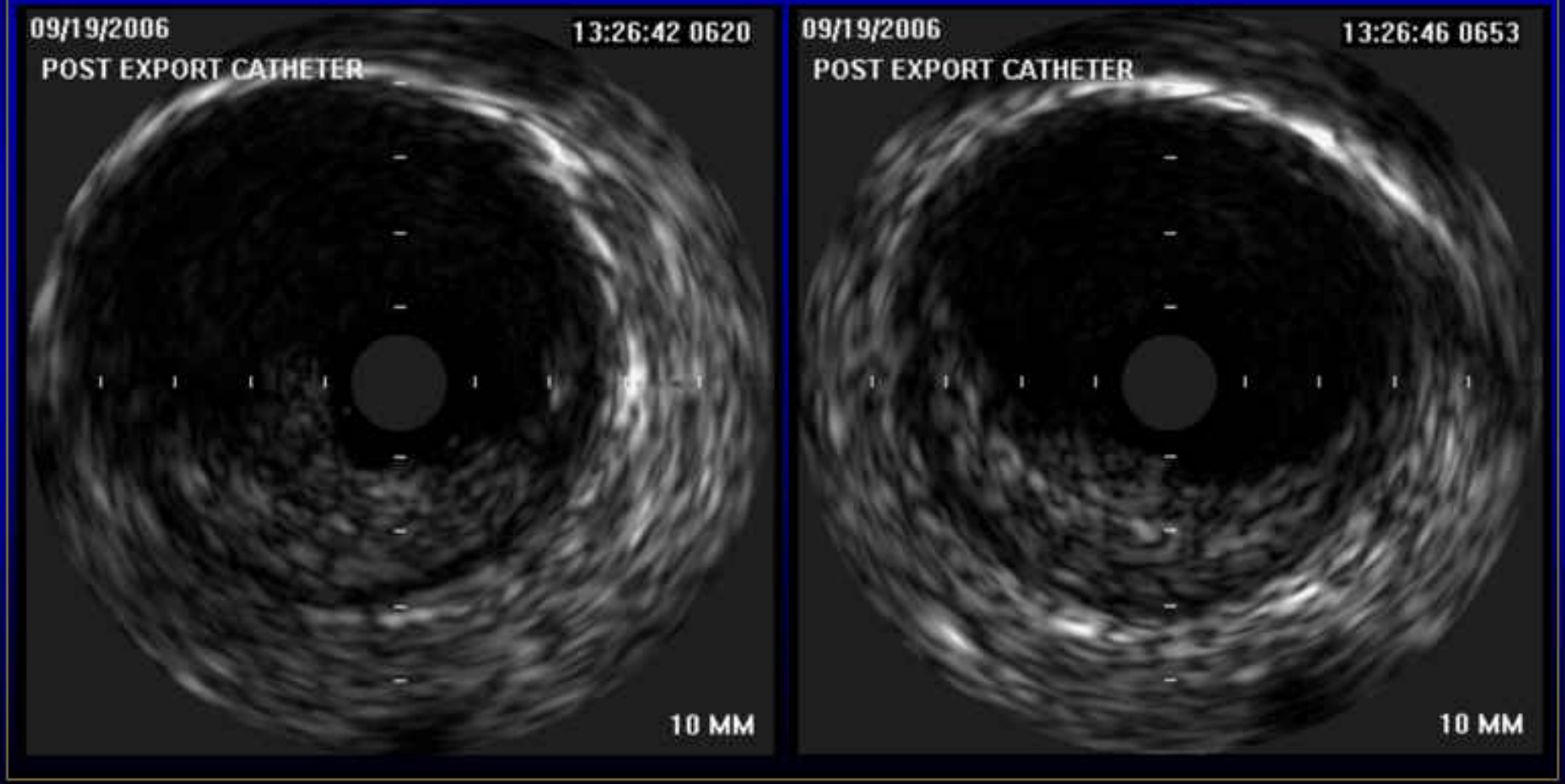


Lumen Area	21.3 mm²	
Vessel Area	35.5 mm²	
Plaque Area	14.2 mm²	
% Plaque Burden	40 %	
FI Green Area	4.0 mm²	47 %
FF Light Green Area	0.8 mm²	9 %
DC White Area	0.8 mm²	10 %
NC Red Area	2.9 mm²	34 %

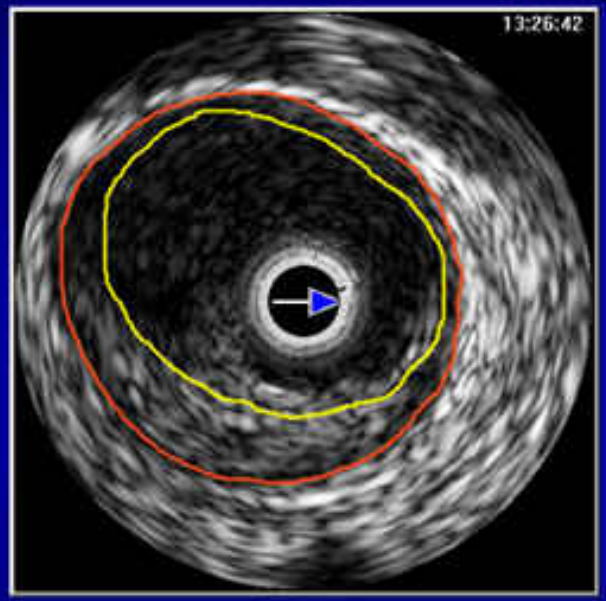
More ...

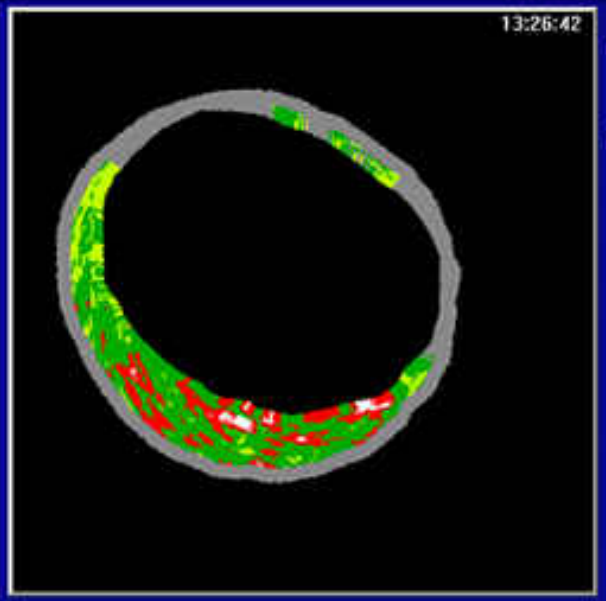
Distal Frame	—	64
Current Frame	—	64
Proximal Frame	—	64

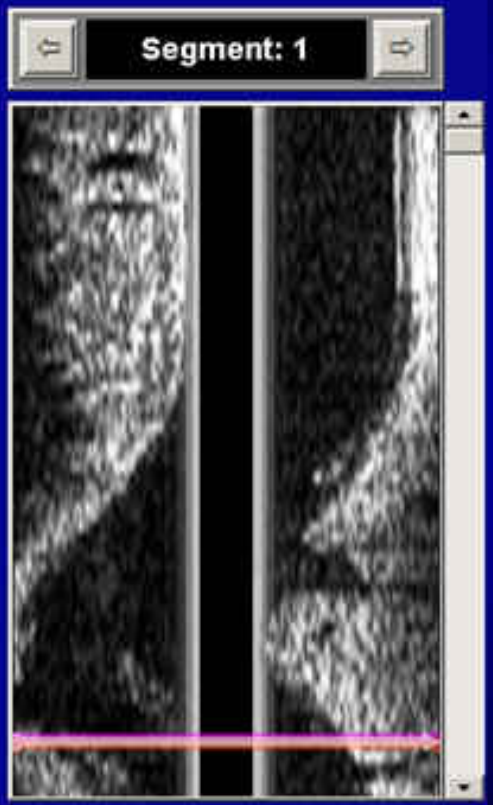
23-Year-Old Male Presenting with Chest Pain After Use of Export™ Catheter



23-Year-Old Male Presenting with Chest Pain After Use of Export™ Catheter







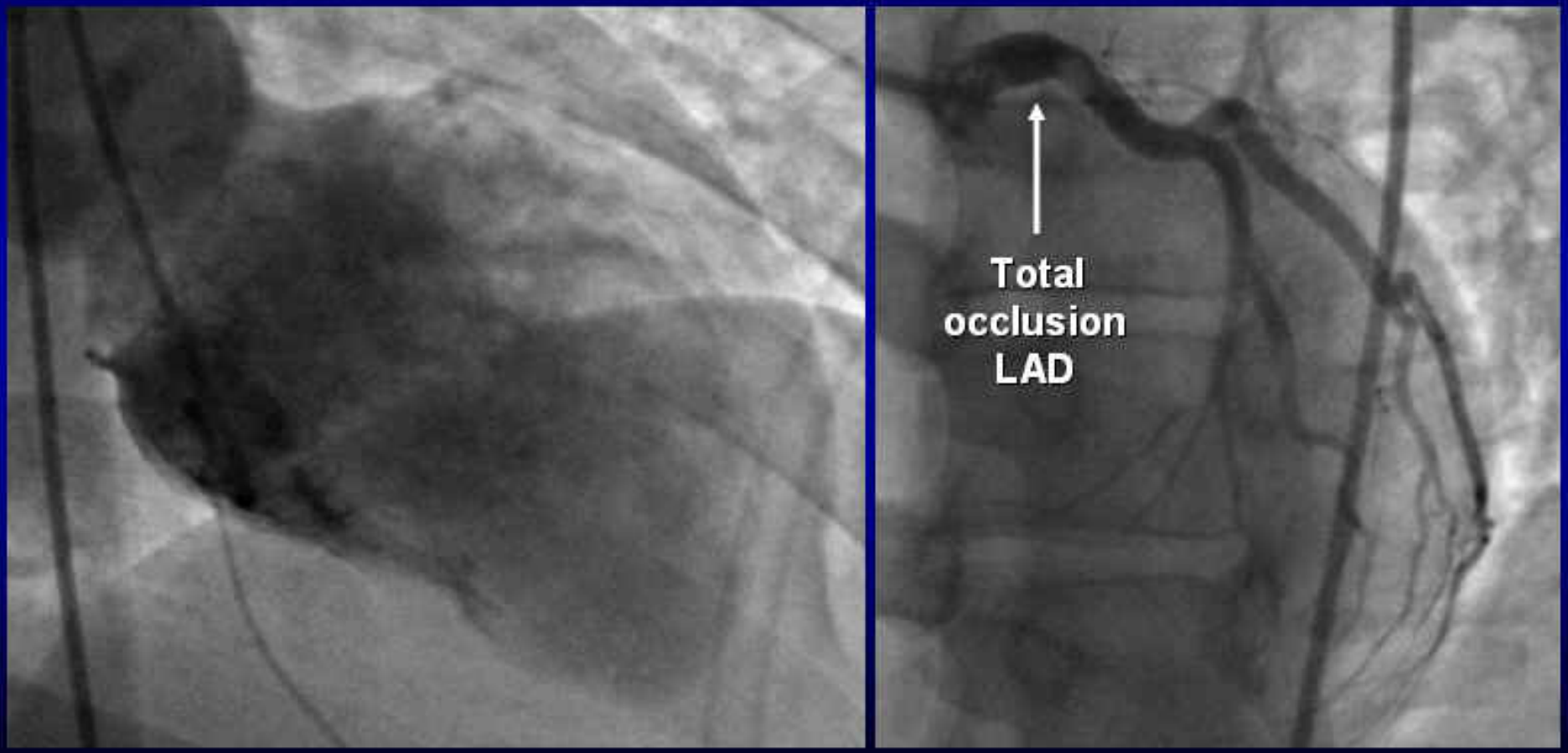
Lumen Area	23.8 mm²	
Vessel Area	37.6 mm²	
Plaque Area	13.9 mm²	
% Plaque Burden	37 %	
FI Green Area	4.8 mm²	61 %
FF Light Green Area	1.1 mm²	15 %
DC White Area	0.2 mm²	3 %
NC Red Area	1.7 mm²	22 %

More ...

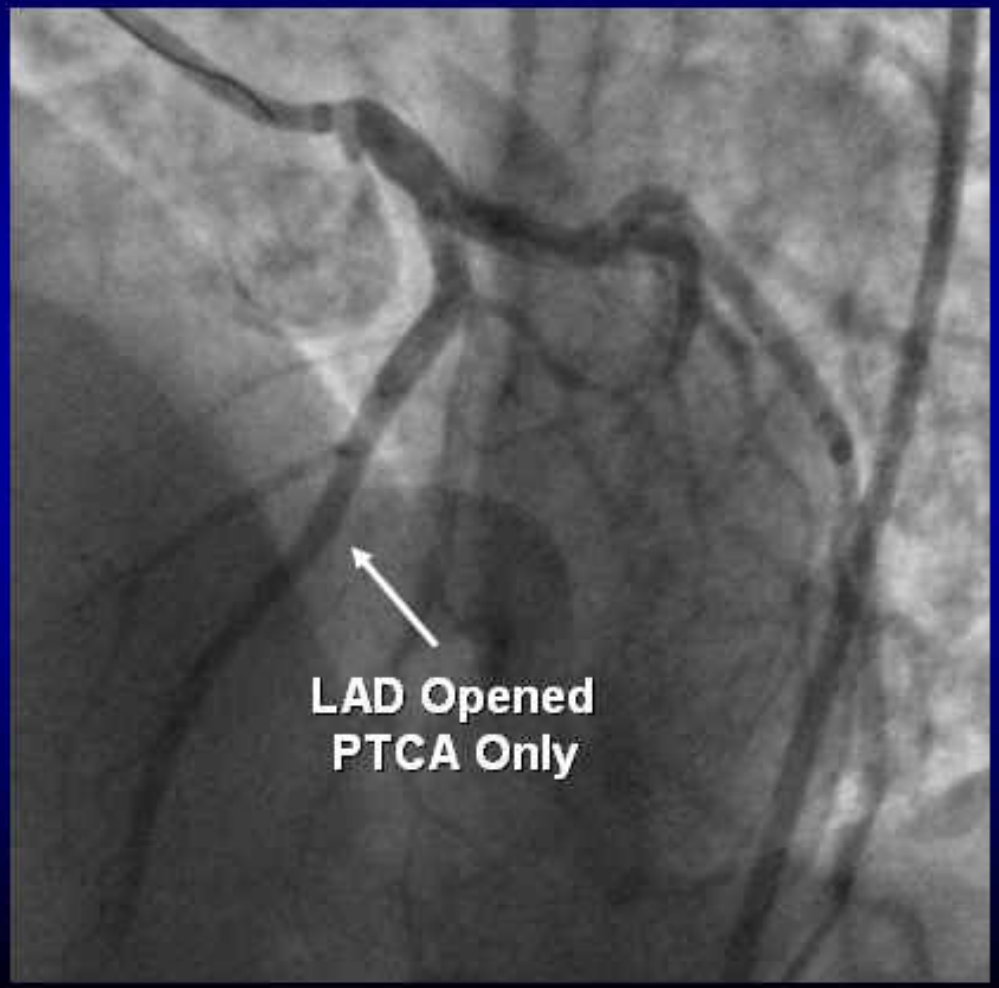
Distal Frame	64
Current Frame	64
Proximal Frame	64

23-Year-Old Male Presenting with Chest Pain After Use of Export™ Catheter

33-Year-Old Male
Acute Anteroseptal Infarct 11-25-06

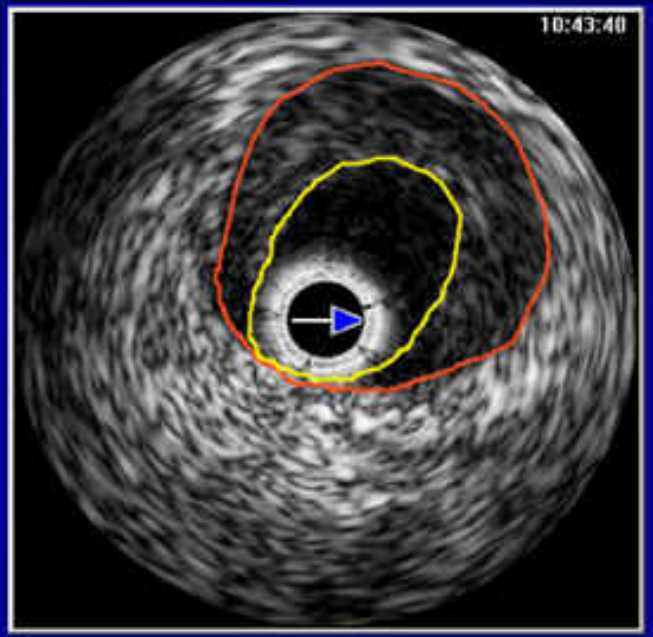


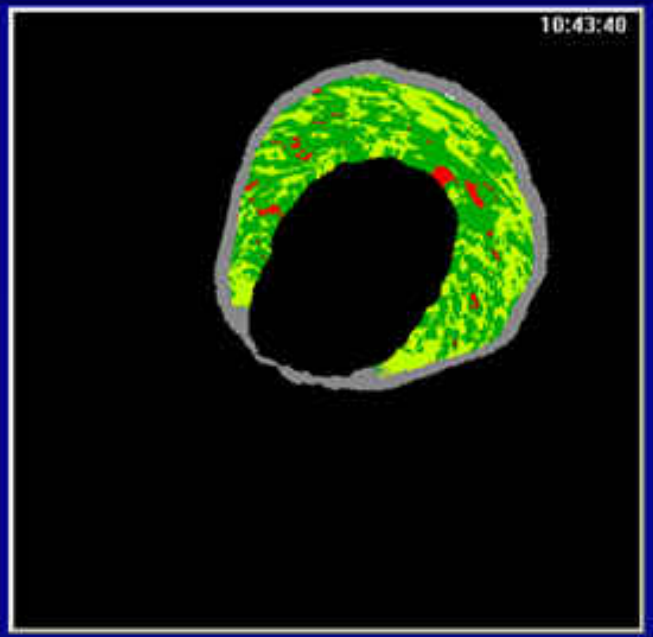
33-Year-Old Male
Acute Anteroseptal Infarct 11-25-06



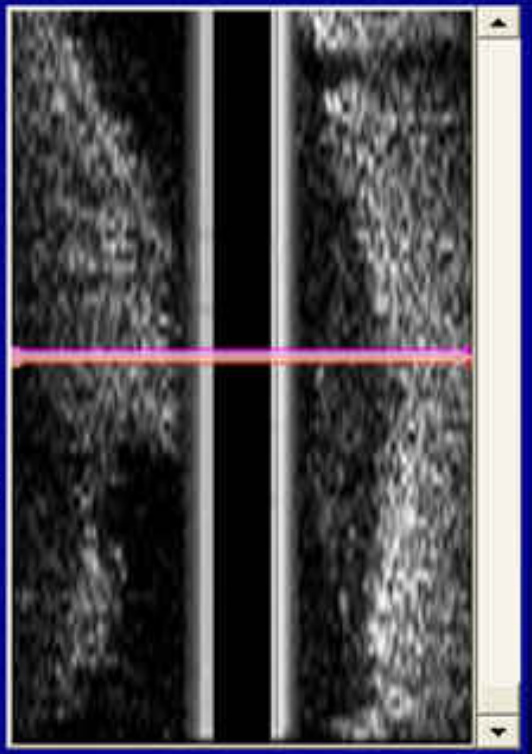
33-yo Male, Acute Anteroseptal Infarct
11-27-06: Follow-up Angio & VH Evaluation

33-yo Male, Acute Anteroseptal Infarct
11-27-06: Follow-up Angio & VH Evaluation





Segment: 1



Lumen Area	9.1 mm²	
Vessel Area	22.9 mm²	
Plaque Area	13.8 mm²	
% Plaque Burden	60 %	
FI Green Area	6.1 mm²	59 %
FF Light Green Area	3.9 mm²	38 %
DC White Area	0.0 mm²	0 %
NC Red Area	0.3 mm²	3 %

More ...

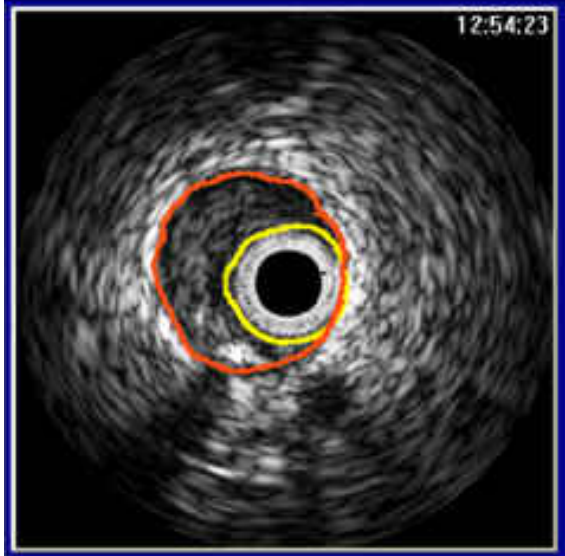
Distal Frame	—	103
Current Frame	—	103
Proximal Frame	—	103

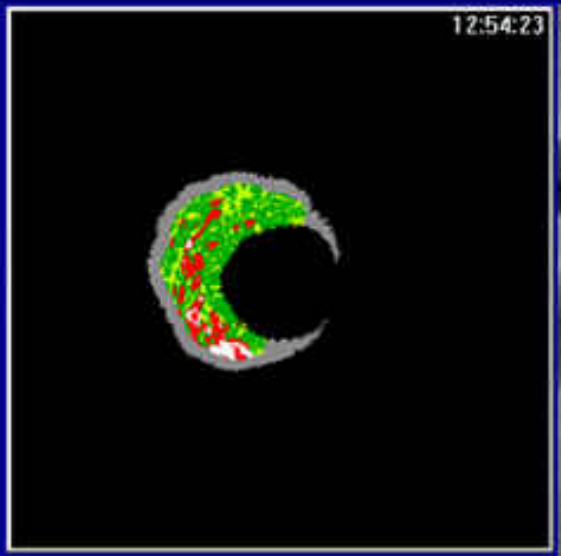
41-Year-Old Female
Acute Anterior STEMI (MD)

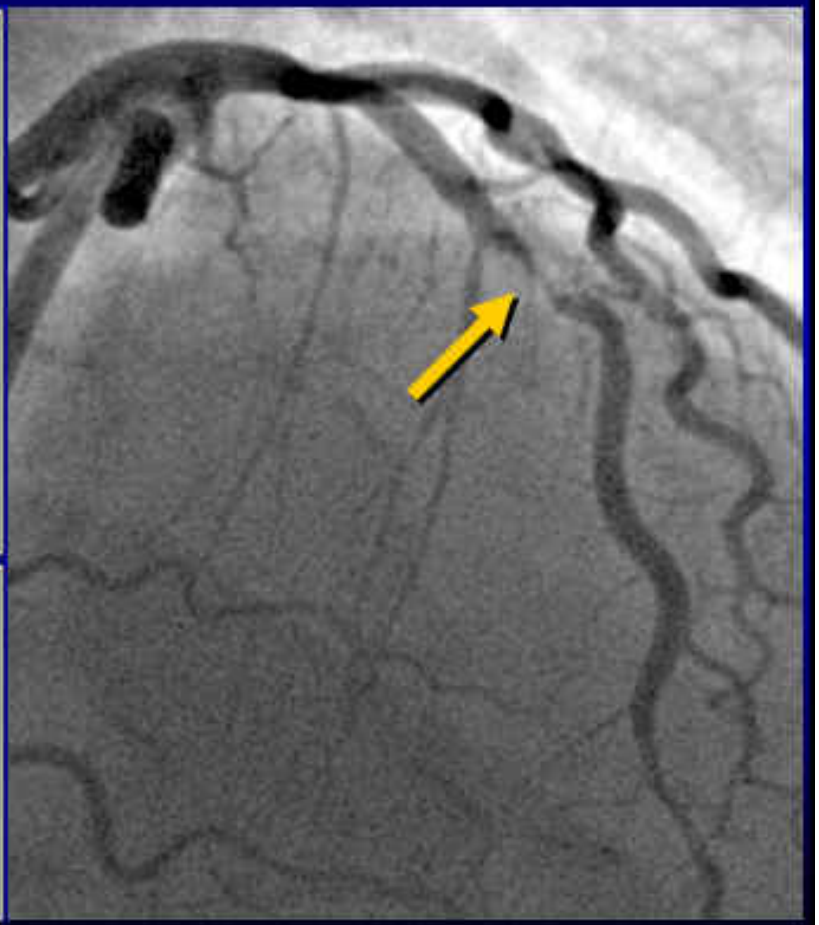
REASON FOR ADMISSION: Chest pain.

HISTORY OF PRESENT ILLNESS: This is a 41-year-old female with multiple cardiac risk factors including diabetes, dyslipidemia, hypertension, and ongoing smoking. She was awakened at 0534 hours with achy chest pain all the way across her chest which was so severe it caused her to sit up and get out of bed. However, she had no nausea, vomiting, or shortness of breath. She went back to bed and managed to get back to sleep.
She woke up at 0730 hours. The pain was still there perhaps a bit worse. She communicated to her husband who brought her to the hospital. Unfortunately, they stopped at McDonald's along the way and she had a bacon, sausage, and cheese egg McMuffin on her way to the hospital. The pain resolved somewhat with eating, although she still had chest pain. In the emergency department, she was noted to have ST elevations on her EKG and was started on aspirin, heparin, and metoprolol with essential resolution of her pain to almost zero and perhaps 1/2 to 1 out of 10.

41-Year-Old Female
Acute Anterior STEMI (MD)



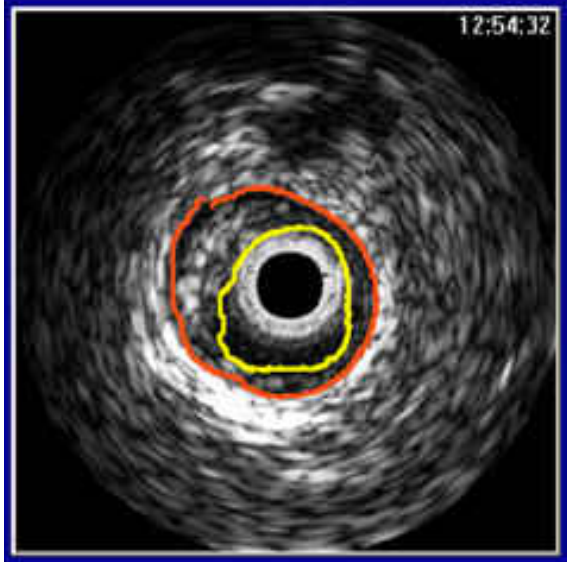


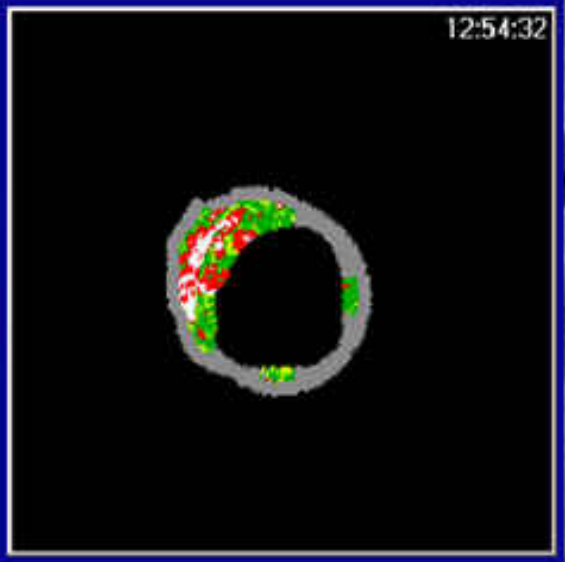


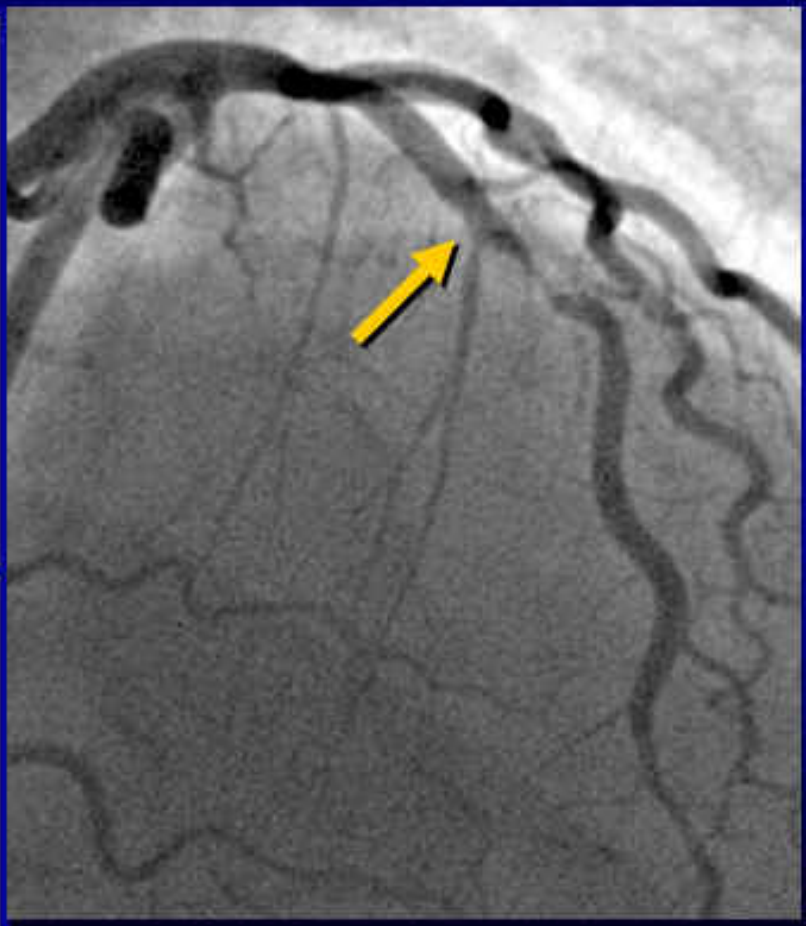
Lumen Area	3.8 mm²	
EEL Area	10.3 mm²	
Plaque Area	6.6 mm²	
% Plaque Burden	63 %	
Fibrous Area	2.6 mm²	58 %
Fibro-Fatty Area	0.8 mm²	19 %
Dense Calcium Area	0.2 mm²	5 %
Necrotic Core Area	0.8 mm²	18 %

More ...

41-Year-Old Female
Acute Anterior STEMI (MD)





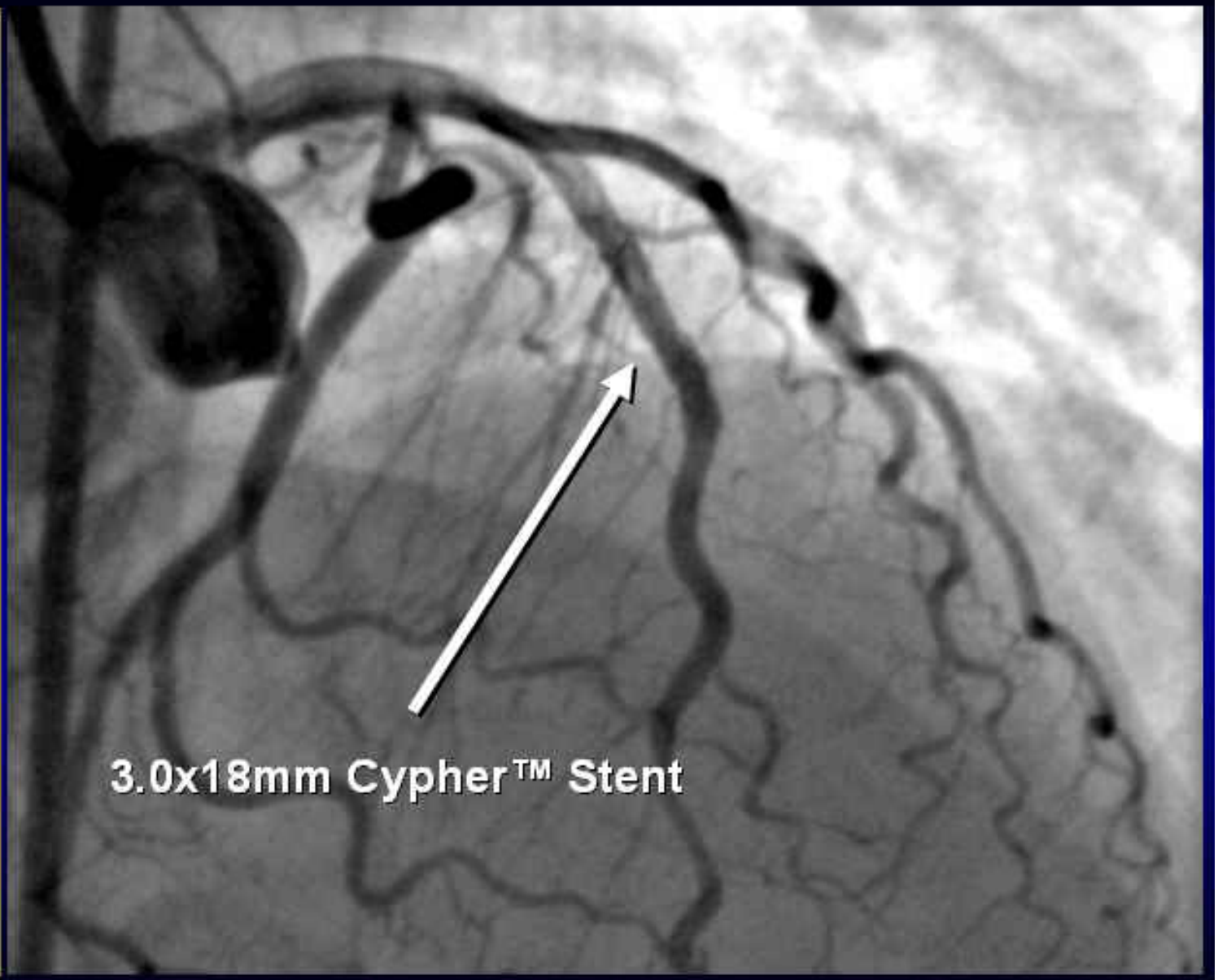


Lumen Area	5.2 mm²	
EEL Area	11.6 mm²	
Plaque Area	6.4 mm²	
% Plaque Burden	55 %	
Fibrous Area	1.4 mm²	45 %
Fibro-Fatty Area	0.4 mm²	14 %
Dense Calcium Area	0.5 mm²	15 %
Necrotic Core Area	0.8 mm²	26 %

More ...

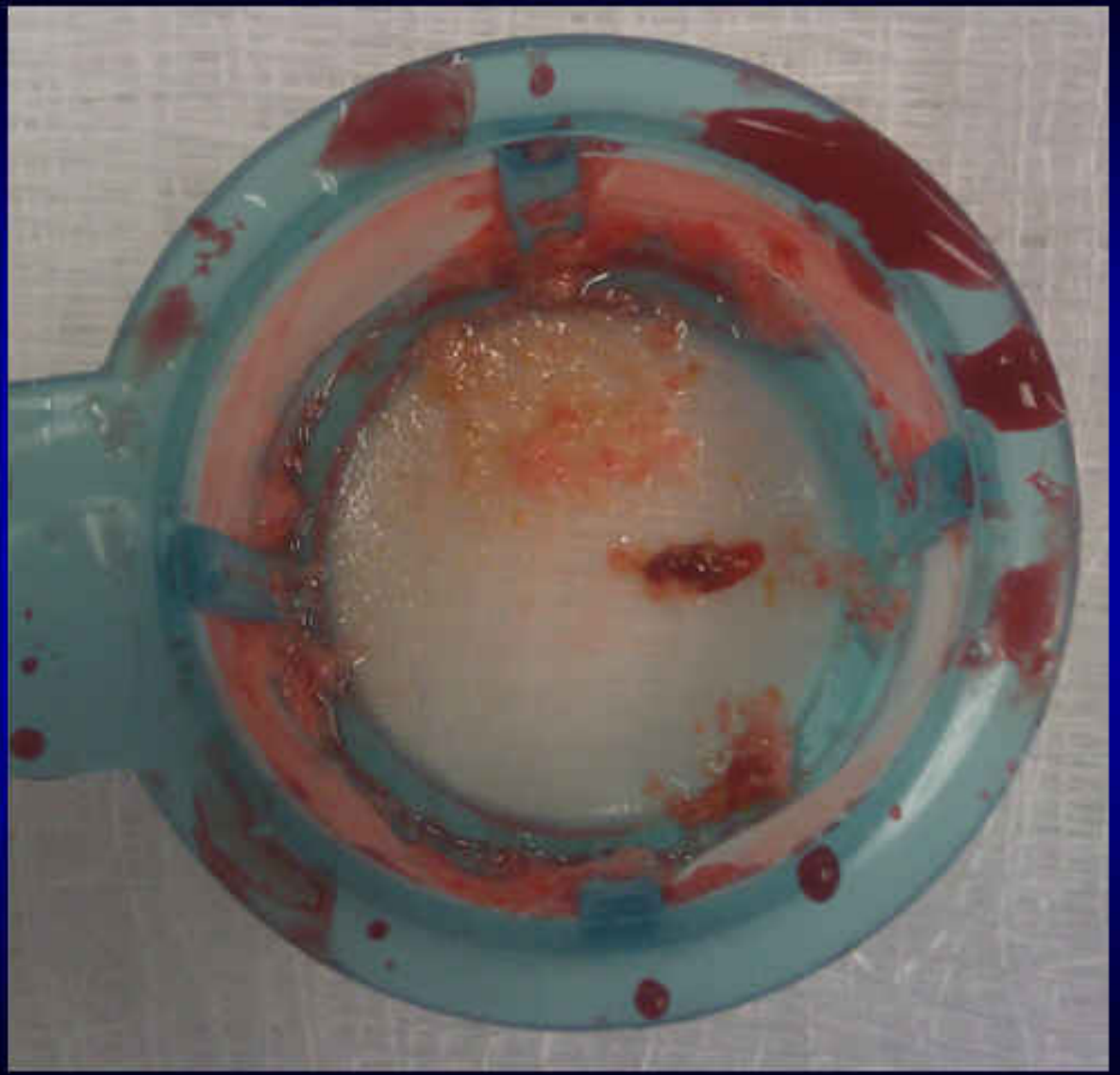
41-yo Female

Acute Anterior STEMI (MD)

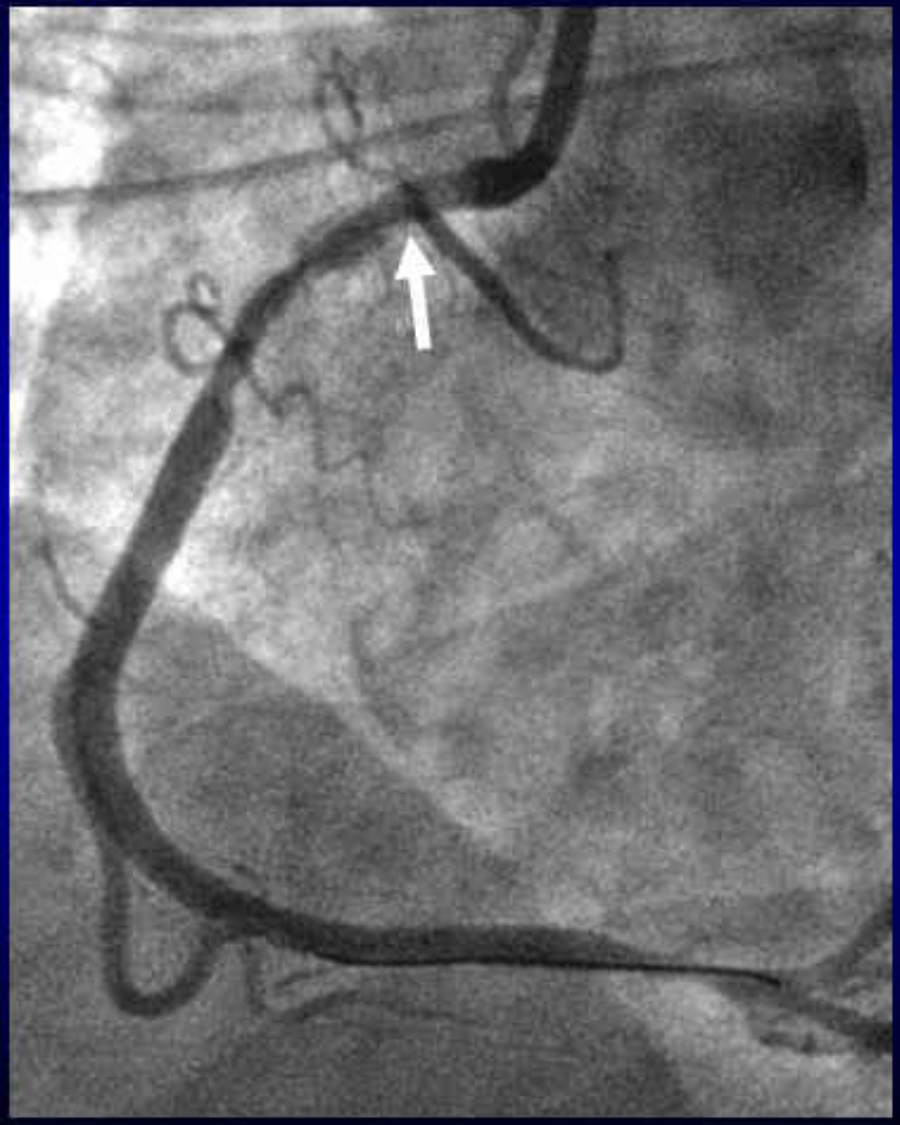


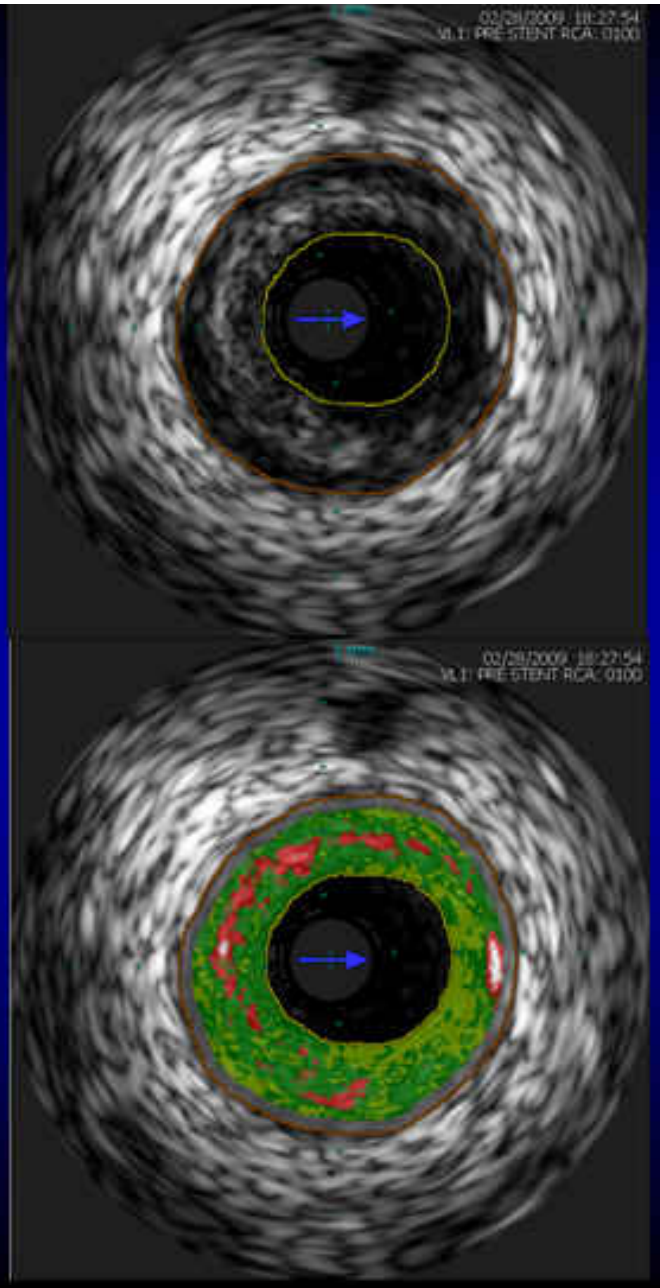
52-yr Male

Acute Inferior MI

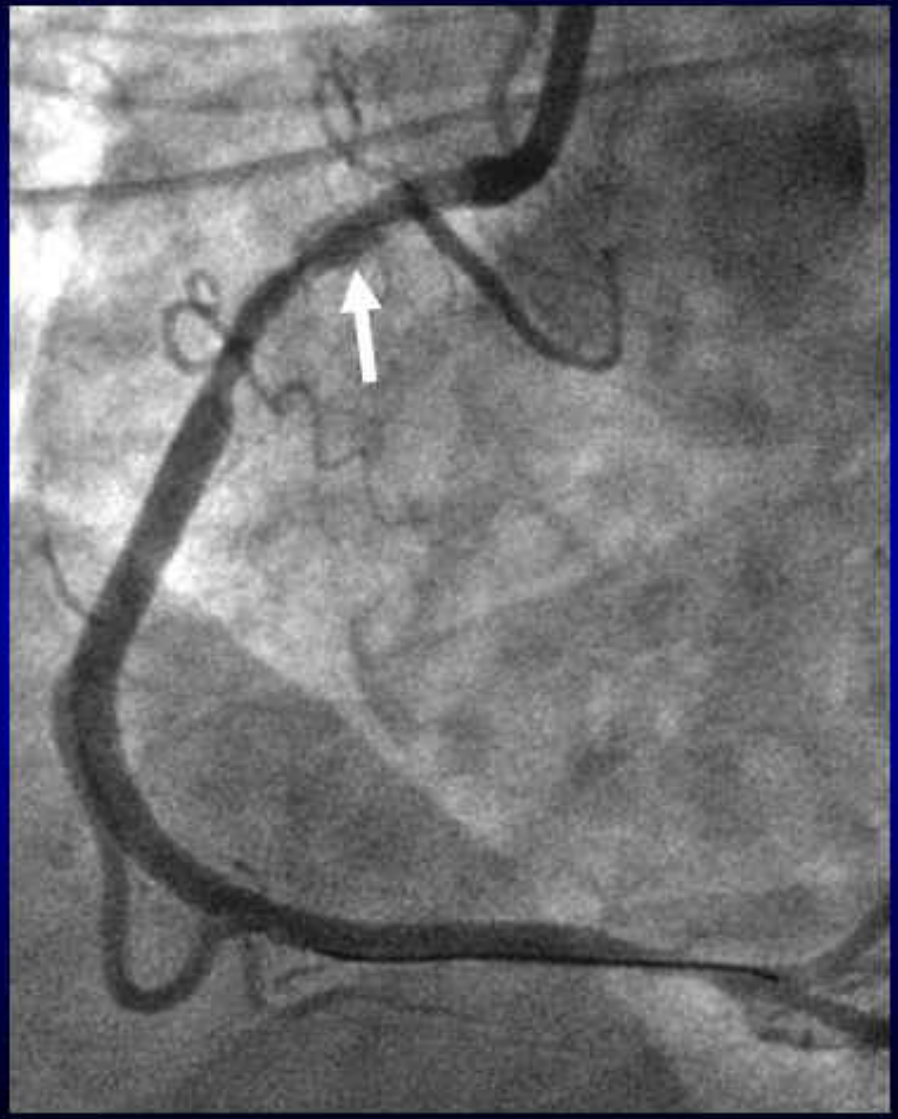


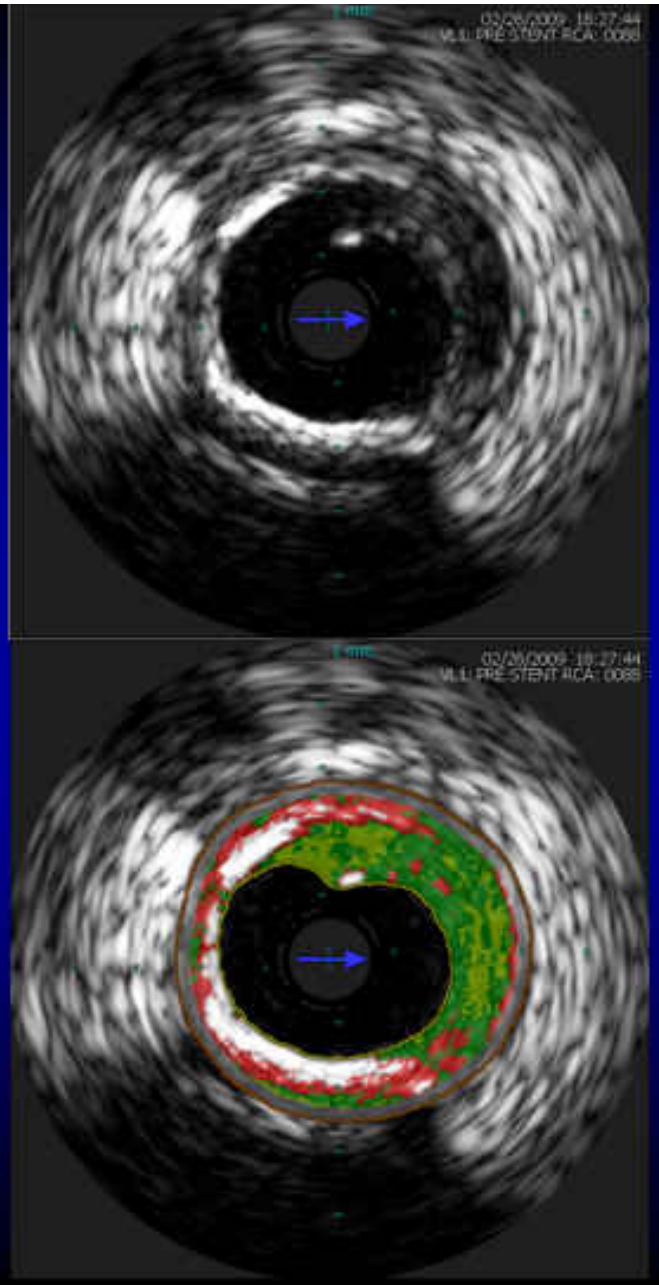
52-yr Male; Acute Inferior MI



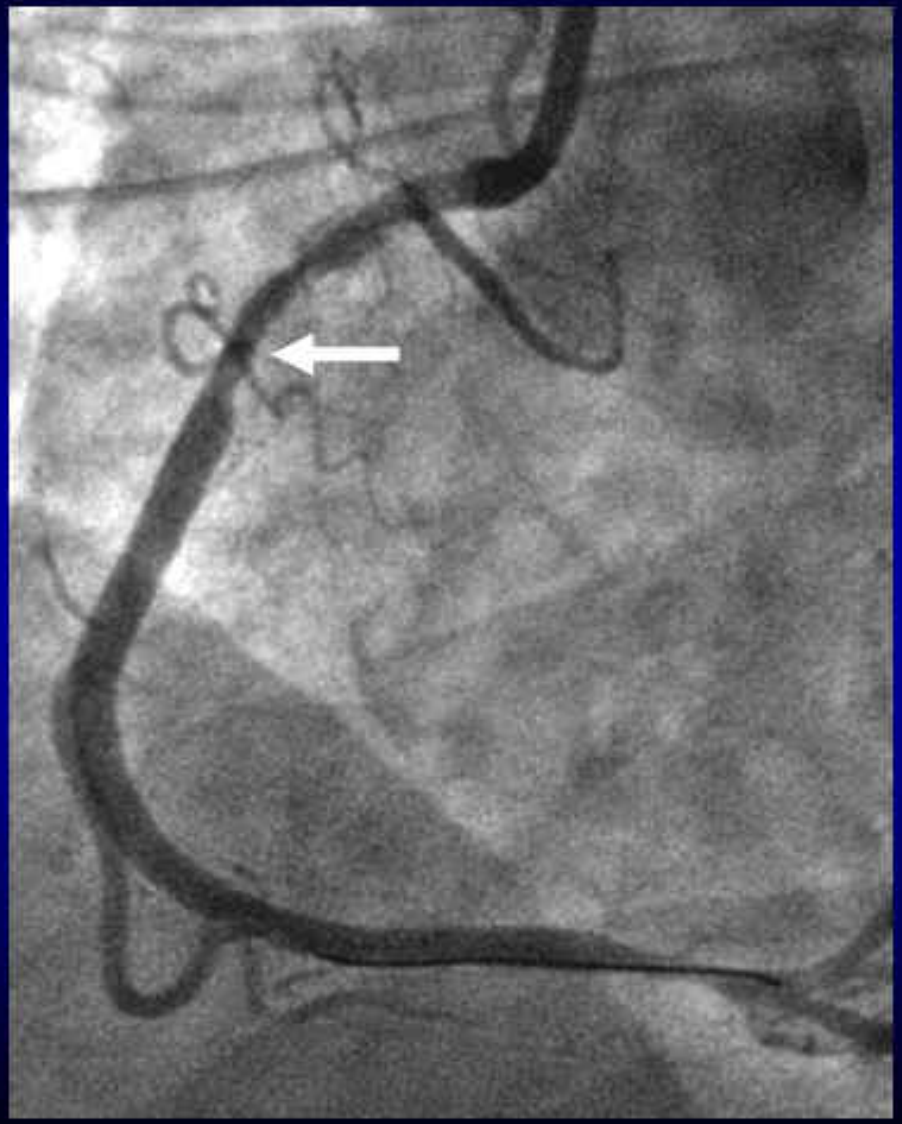


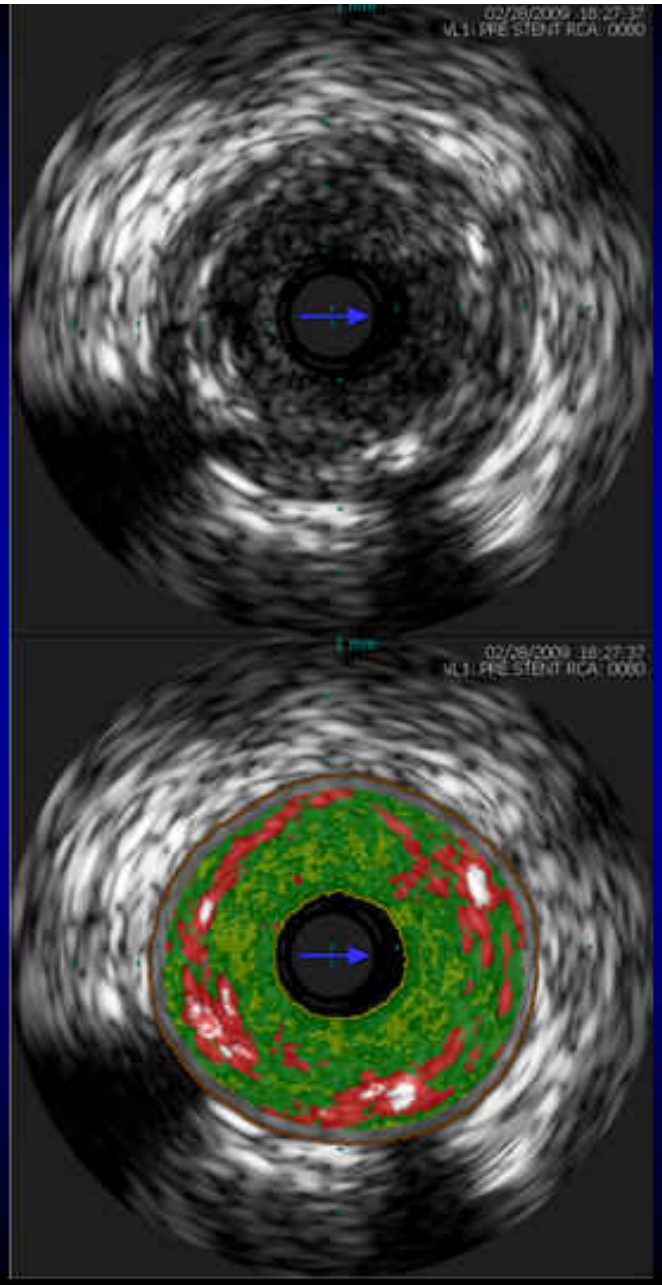
52-yr Male; Acute Inferior MI



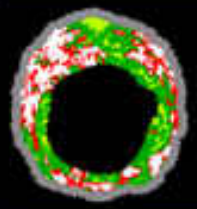


52-yr Male; Acute Inferior MI





EXTRA SLIDES



Virtual Histology
Clinical Applications

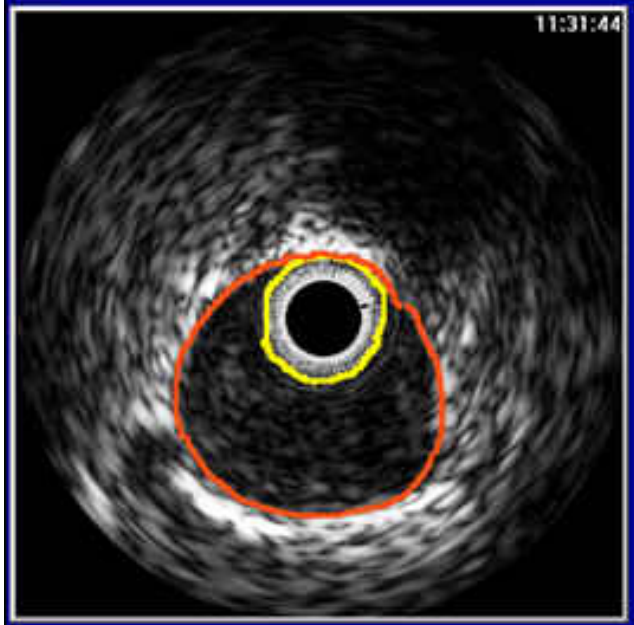
- Good characterization and visualization of plaque composition & volume (plaque burden)
- Careful border recognition to exclude thrombus
- Surprisingly widespread distribution of vulnerable plaques in pts with ACS – relating to both culprit and non-culprit arteries

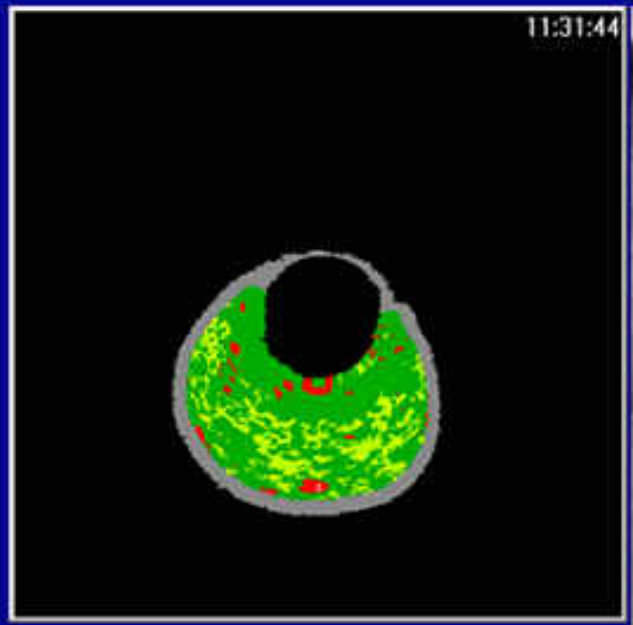
"Systemic Vascular Illness"

Clinical Examples Using Virtual Histology

- Use of VH may guide use of aggressive statin therapy
- Use of VH to extend stent length to cover angiographically silent vulnerable plaque
- Results of clinical trials pending regarding prophylactic stenting of vulnerable plaque

53-Year-Old Male
Acute Anterior Infarct

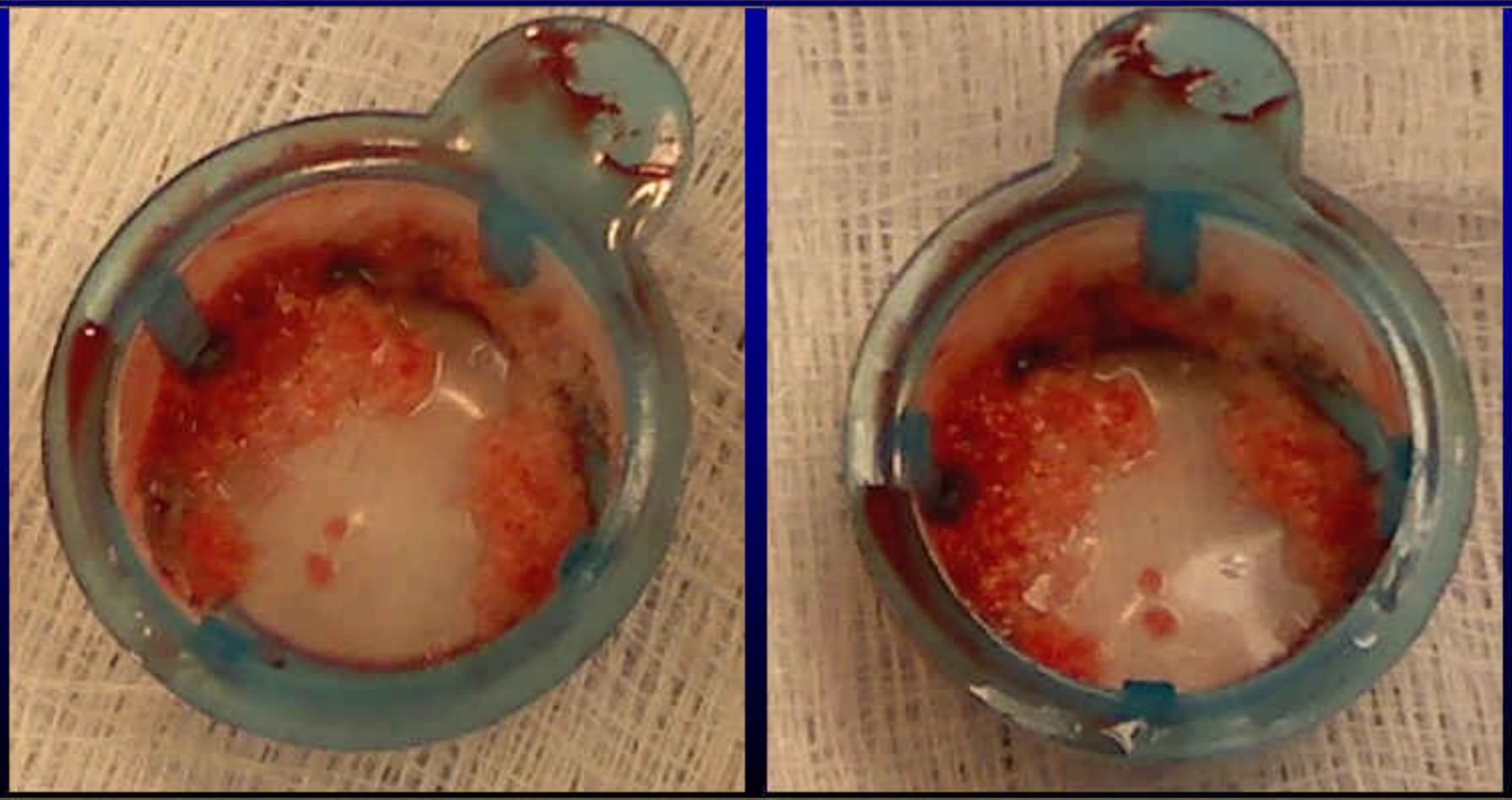




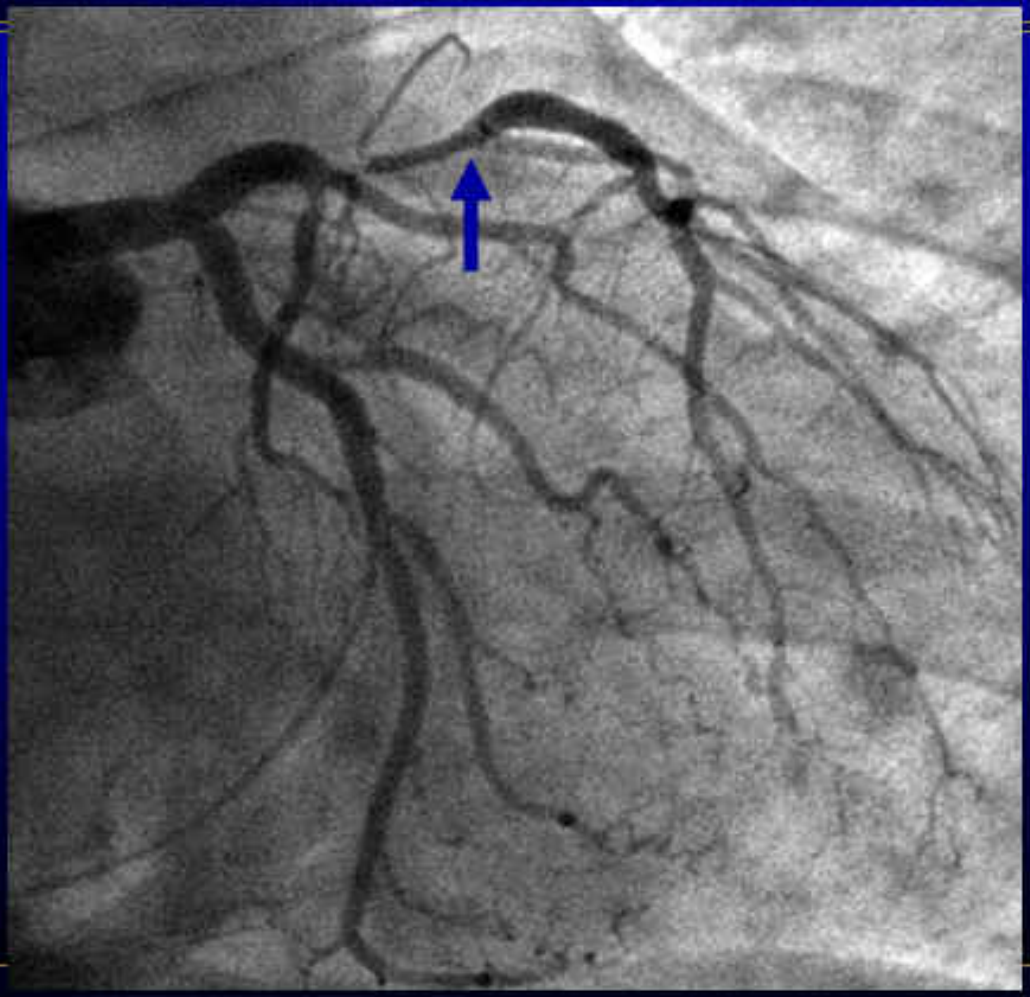
Lumen Area	3.1 mm²	
EEL Area	15.0 mm²	
Plaque Area	11.9 mm²	
% Plaque Burden	79 %	
Fibrous Area	6.8 mm²	75 %
Fibro-Fatty Area	1.8 mm²	20 %
Dense Calcium Area	0.0 mm²	0 %
Necrotic Core Area	0.4 mm²	4 %

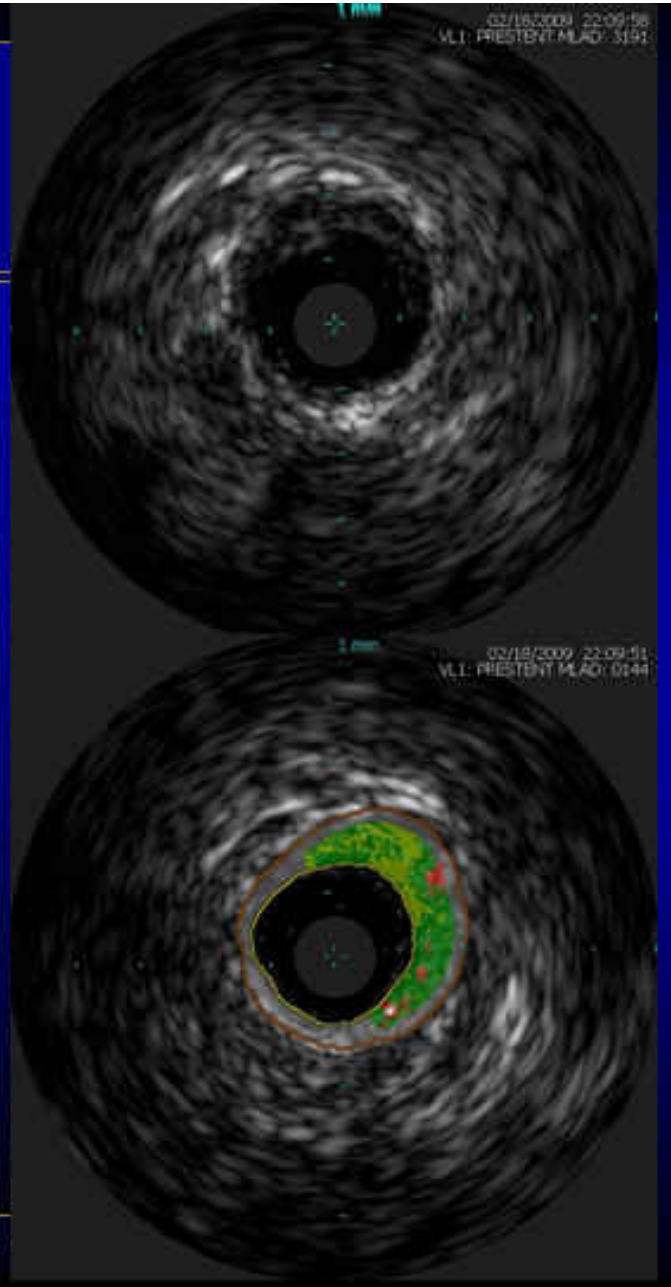
More ...

40-yr Female
Acute Lateral Wall STEMI

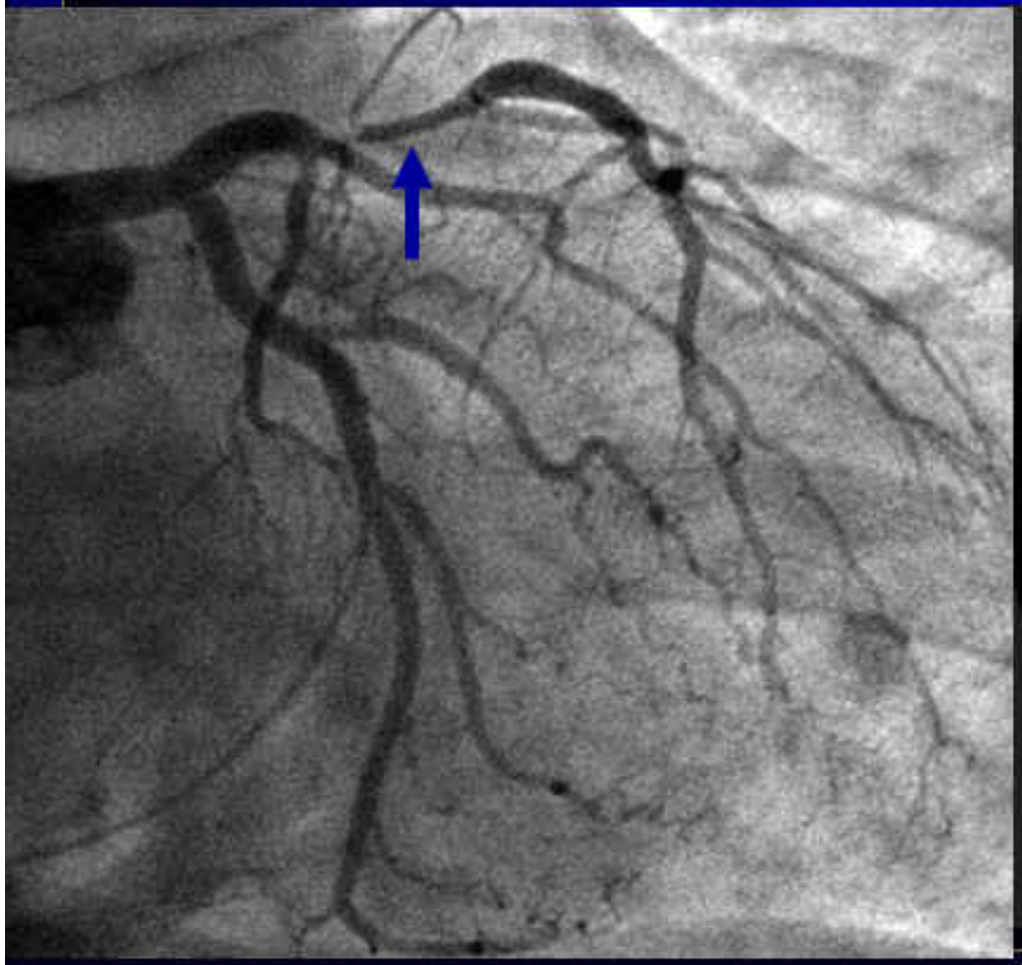


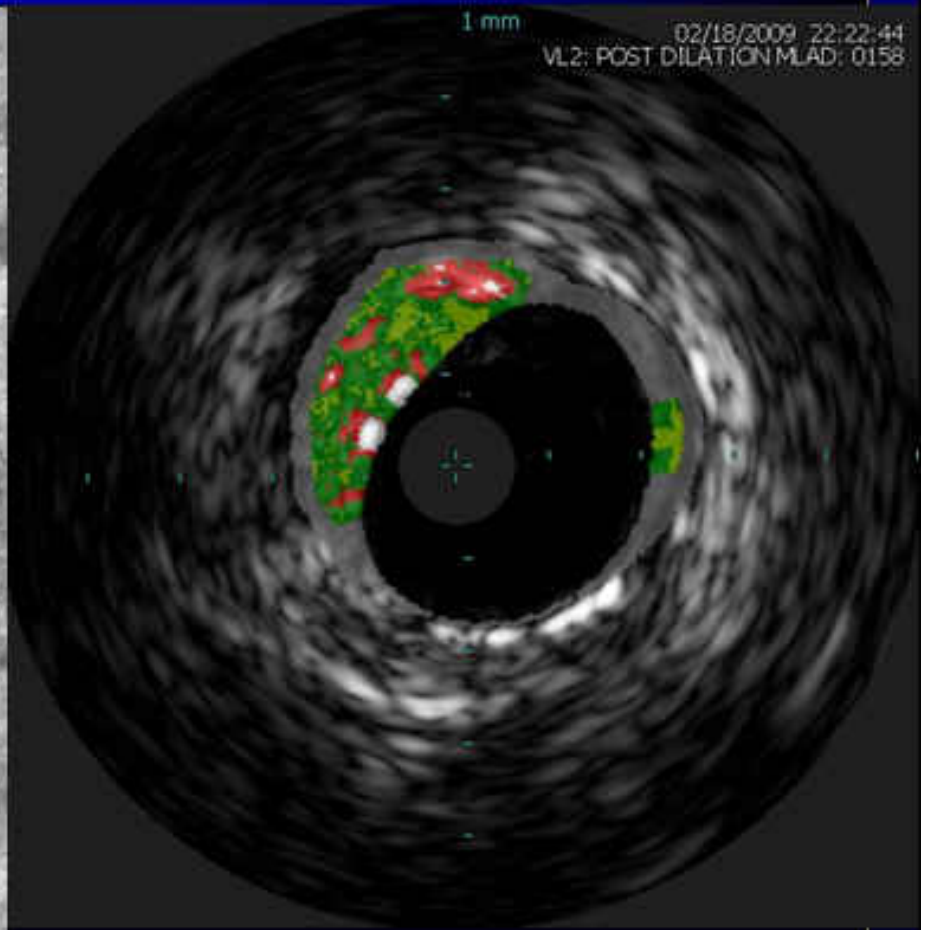
40-yr Female
Acute Lateral Wall STEMI



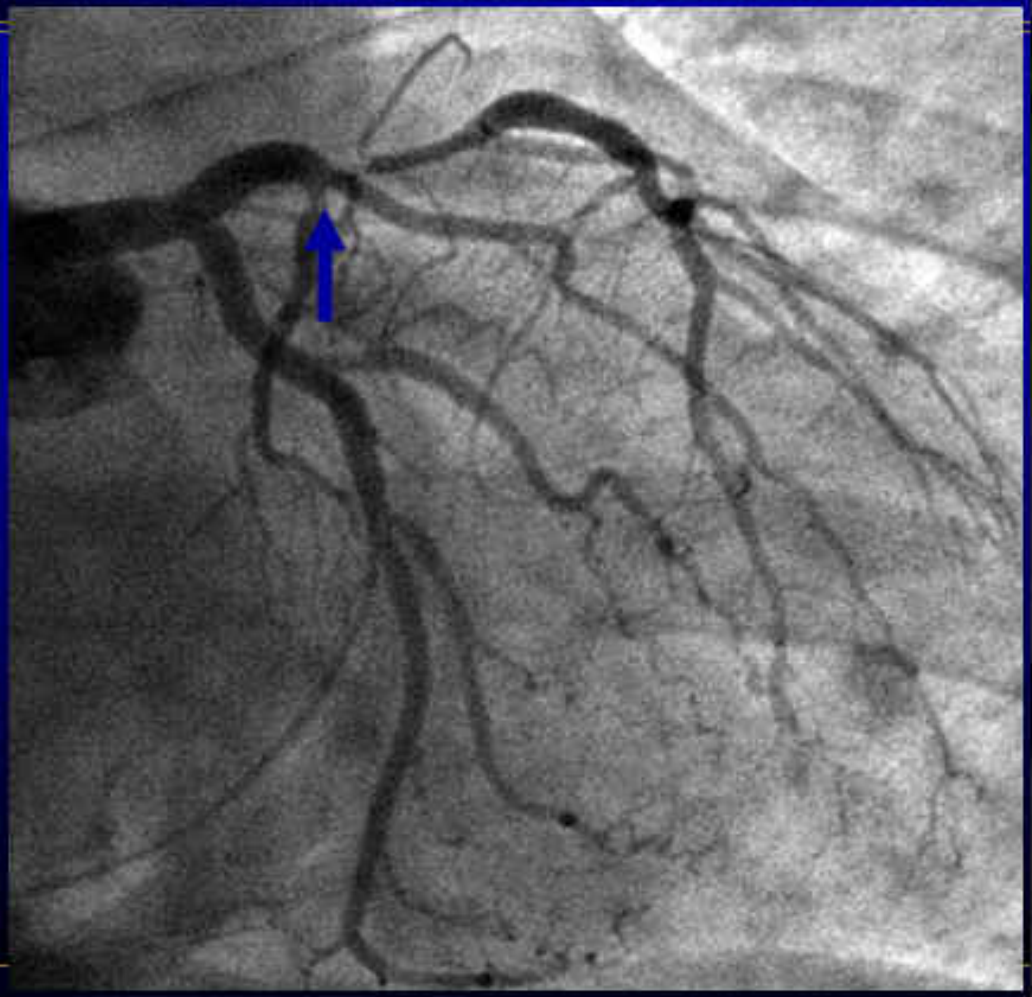


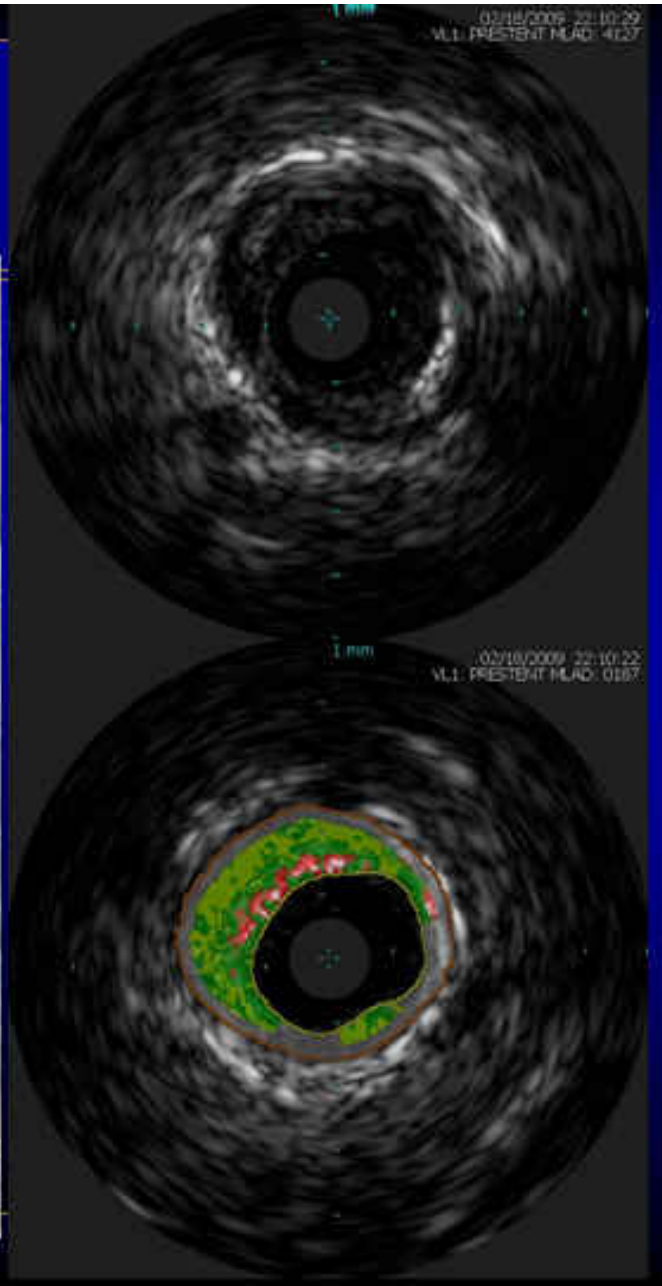
40-yr Female,
Acute Lateral Wall STEMI





40-yr Female
Acute Lateral Wall STEMI





What is Virtual Histology?

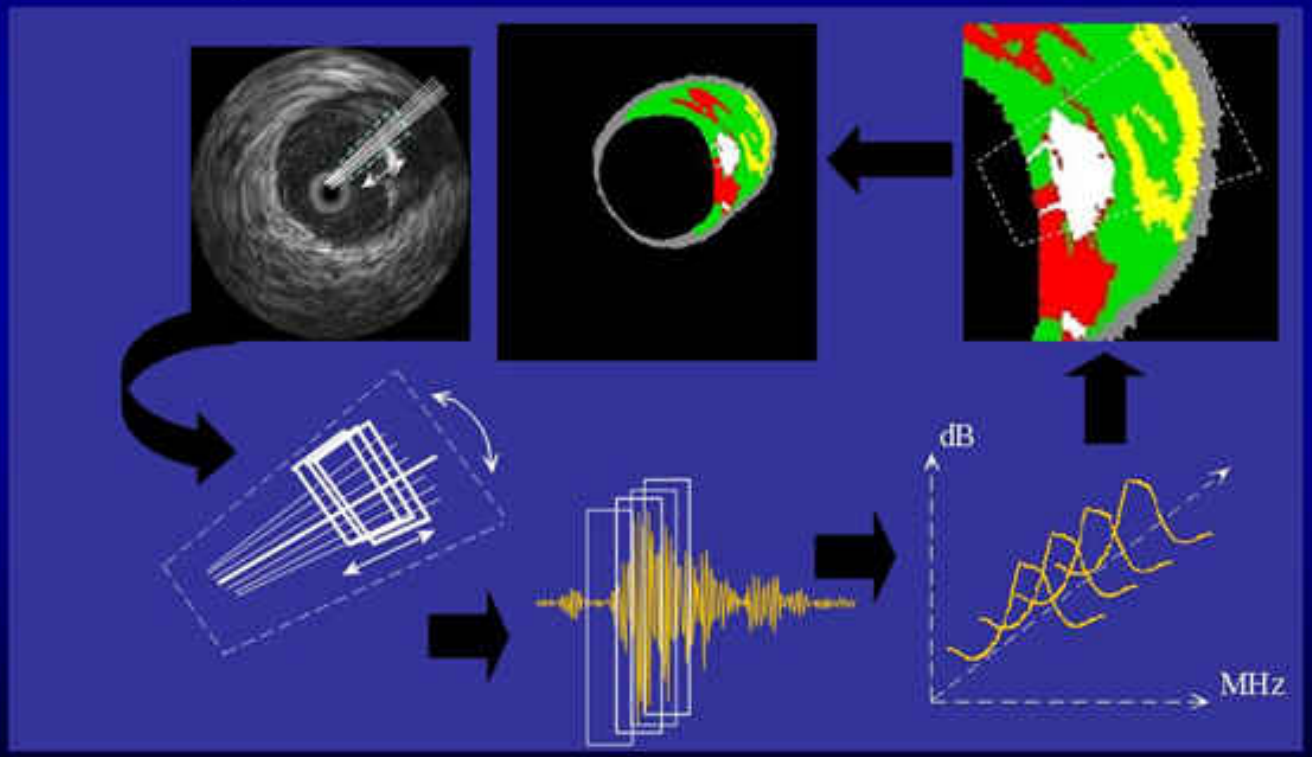
- Real-time plaque characterization and visualization with spectral analysis of intravascular ultrasound data
- Spectral analysis of the backscattered radiofrequency ultrasound signals allows detailed assessment of plaque composition

Anuja Nair, Jon D Klingensmith, D Geoffrey Vince, Cleveland Clinic Foundation

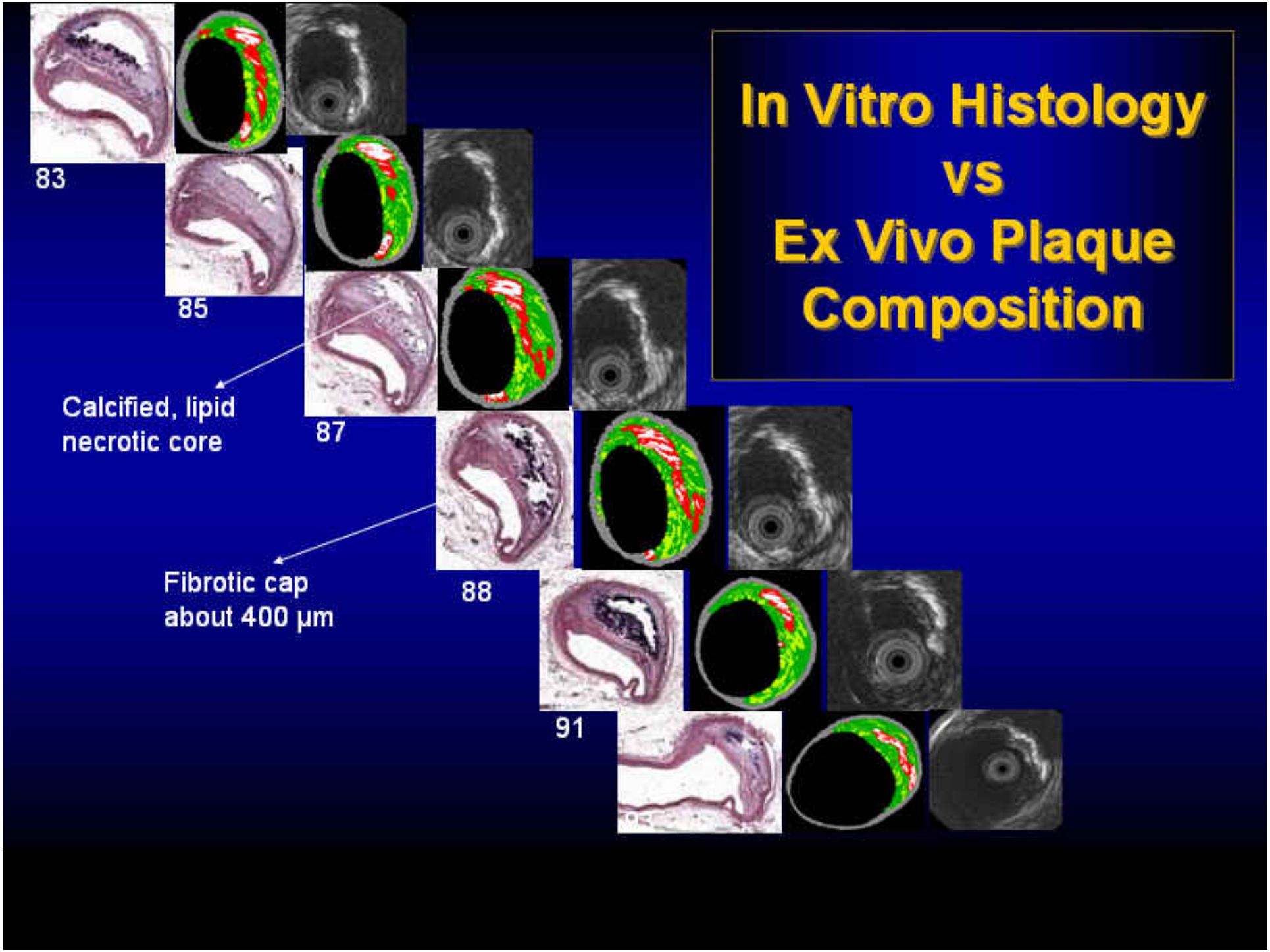
Image Interpretation

The *Volcano IVUS* Program

- In-vivo characterization of plaque composition via advanced spectral analysis



Fibrous; Fibro-lipidic; Lipidic-necrotic; Calcium


In Vitro Histology
vs
Ex Vivo Plaque
Composition
83
85
87
88
91
Calcified, lipid
necrotic core
Fibrotic cap
about 400 µm

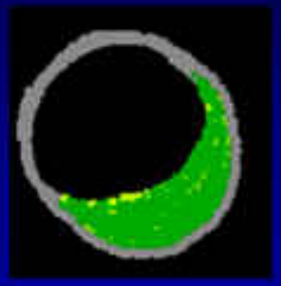
EAGLE EYE JUNE 2005 CLASSIFICATION TREE Accuracy Data:

Slice by Slice VH & Histology Comparison

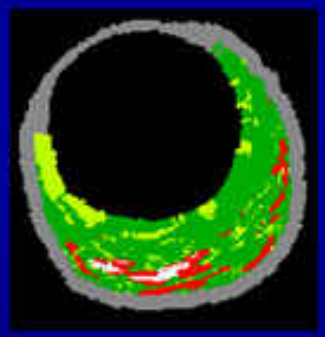
- Overall accuracy for ROIs – 94.96%
- 51 LADs, 115 Artery Sites, 407 Total ROIs

	Sensitivity (%)	Specificity (%)	Predictive Accuracy (%)
Fibrous Tissue (*n*= 162)	83.95	98.78	92.87
Fibro Fatty (*n*= 84)	86.90	95.05	93.37
Necrotic Core (*n*= 69)	97.10	93.79	94.35
Dense Calcium (*n*= 92)	97.83	99.68	99.26

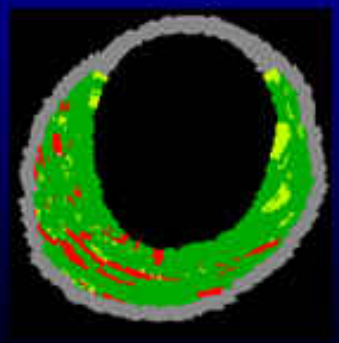
Generally Stable Plaque Types*



"Fibrous" – Plaque nearly all fibrous tissue.



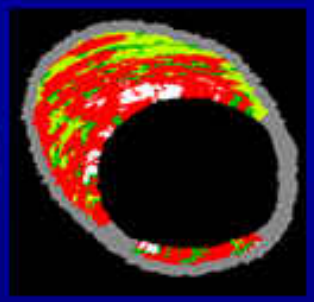
"Fibro-Calcific" – Mainly fibrous with some Dense Calcium. Necrotic Core 3-10%



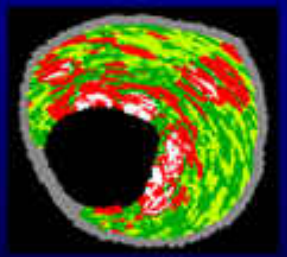
"Pathological Intimal Thickening" –Fibro-Fatty and Fibrous tissue, with Necrotic Core 0-3% due to micro-calcifications within the Fibro-Fatty tissue. Possible progression to risky atheroma.

**Courtesy of Renu Virmani*

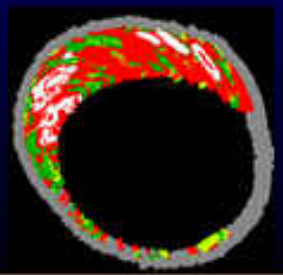
Thin-Cap FibroAtheroma (TCFA)



"Thin Cap Fibro-Atheroma (TCFA)" or "Vulnerable Plaque" - Necrotic Core >10% of total plaque volume *and located at or near the lumen.*



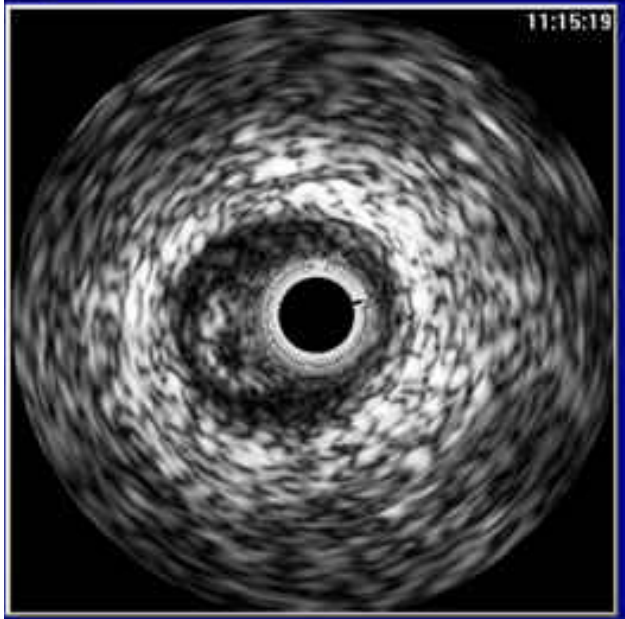
"TCFA with significant narrowing" (≥50% reduction in Cross Sectional Area on IVUS or DS≥25% on angiogram)

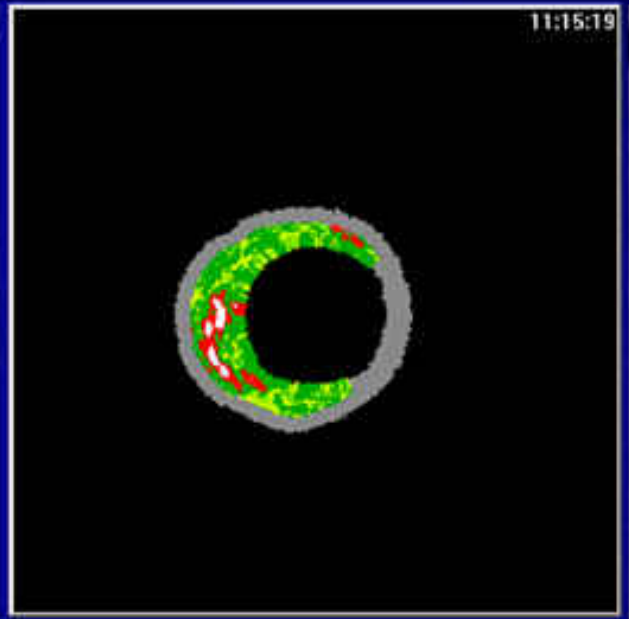


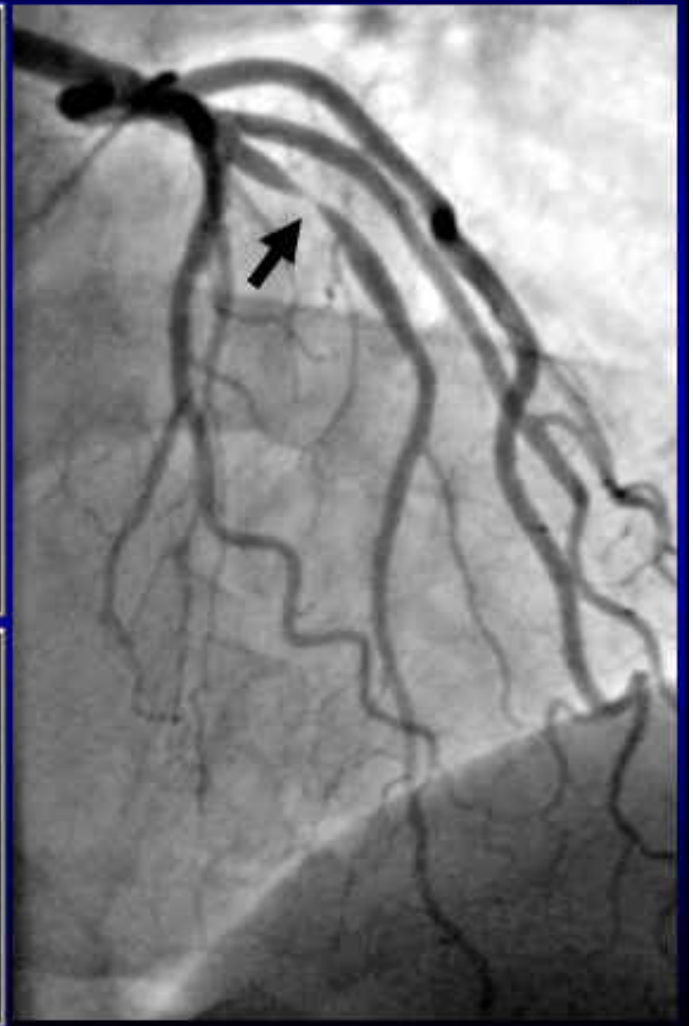
"TCFA without significant narrowing" (<50% area reduction on IVUS or <25% DS on angiogram)

Courtesy of Renu Virmani

53-Year-Old Male
Acute Non-STEMI



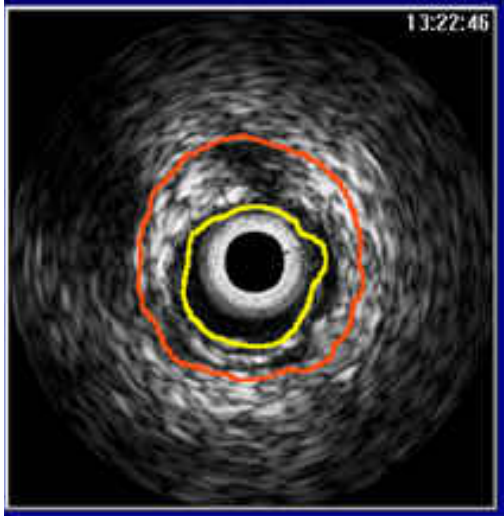


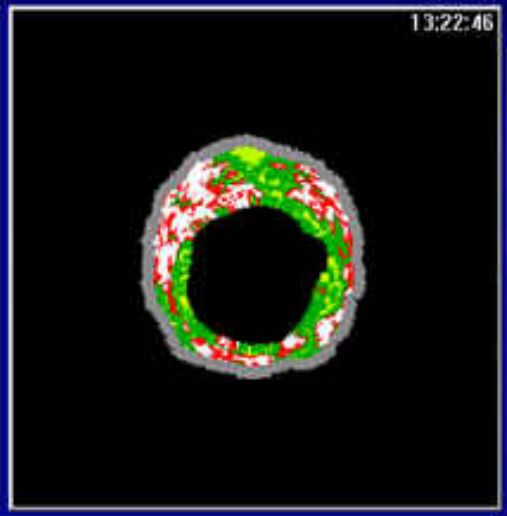


Lumen Area	4.3 mm²	
EEL Area	11.4 mm²	
Plaque Area	7.0 mm²	
% Plaque Burden	62 %	
Fibrous Area	2.4 mm²	62 %
Fibro-Fatty Area	0.8 mm²	21 %
Dense Calcium Area	0.2 mm²	4 %
Necrotic Core Area	0.5 mm²	13 %

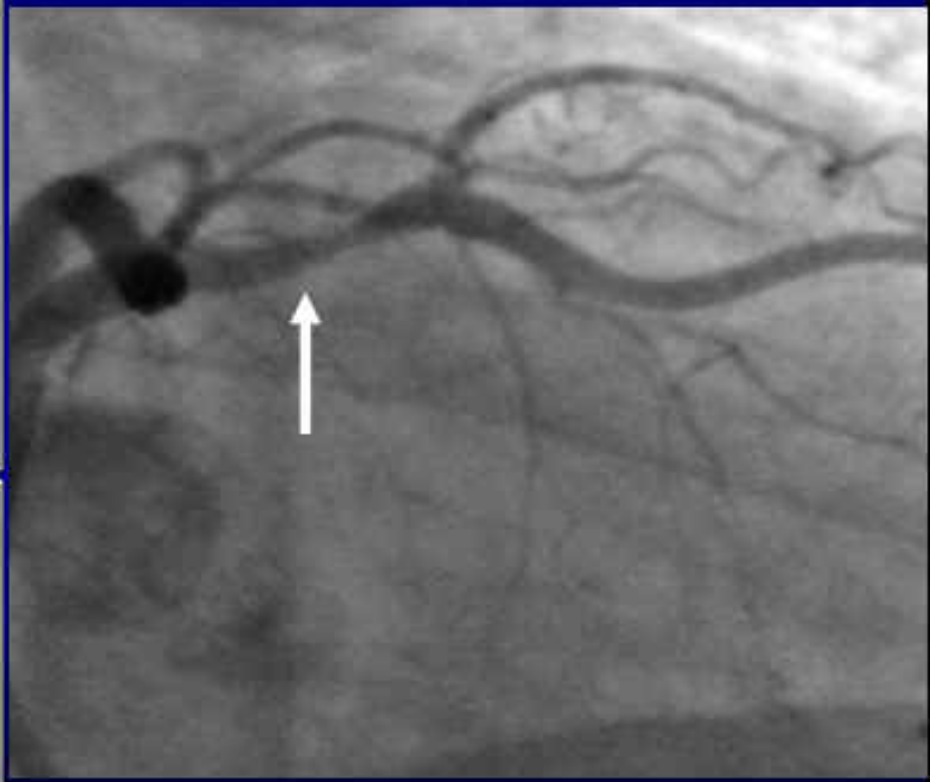
More ...

53-Year-Old Female Presenting with UA

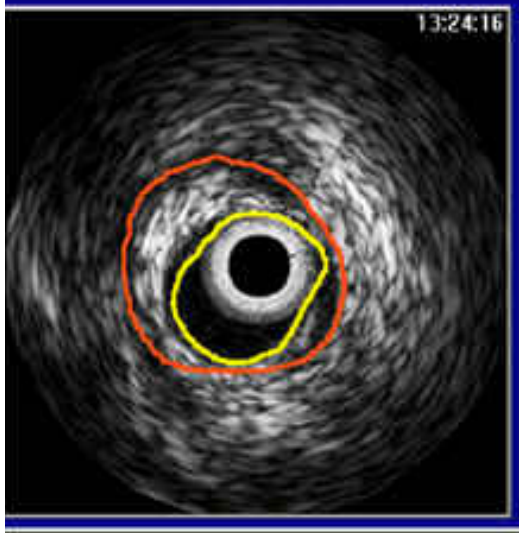


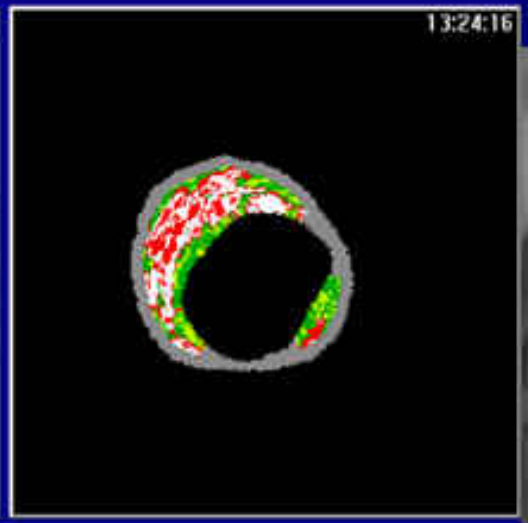


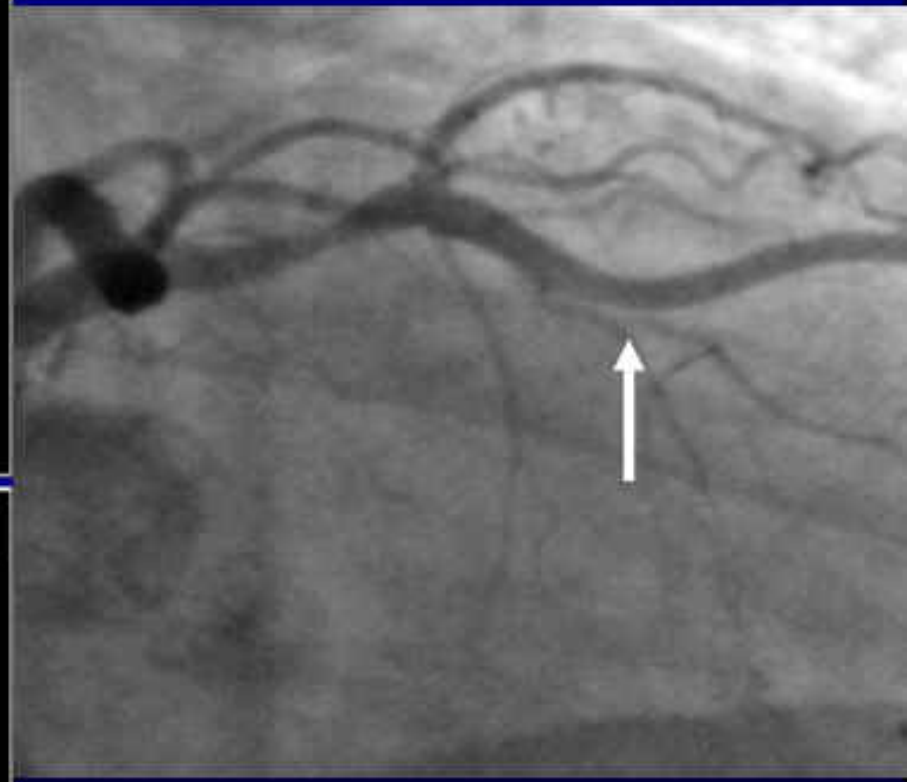
Lumen Area	6.2 mm²	
EEL Area	18.3 mm²	
Plaque Area	12.0 mm²	
% Plaque Burden	66 %	
Fibrous Area	3.5 mm²	42 %
Fibro-Fatty Area	0.8 mm²	9 %
Dense Calcium Area	2.3 mm²	27 %
Necrotic Core Area	1.9 mm²	22 %



53-Year-Old Female Presenting with UA







Lumen Area	6.4 mm²	
EEL Area	15.0 mm²	
Plaque Area	8.7 mm²	
% Plaque Burden	58 %	
Fibrous Area	1.5 mm²	28 %
Fibro-Fatty Area	0.7 mm²	13 %
Dense Calcium Area	1.7 mm²	32 %
Necrotic Core Area	1.4 mm²	27 %

More ...

PROSPECT Study

PI, Dr. Gregg Stone, Guidant, Volcano

3-vessel imaging post PCI of culprit lesion

IVUS

Virtual Histology

↓

F/U: 1 mo, 6 mo, 1 yr, 2 yr, ± 3-5 yr

(event driven)

↓ Meds recommended:
Aspirin, Plavix 1yr, Statin

↓ Repeat imaging
in pts with events

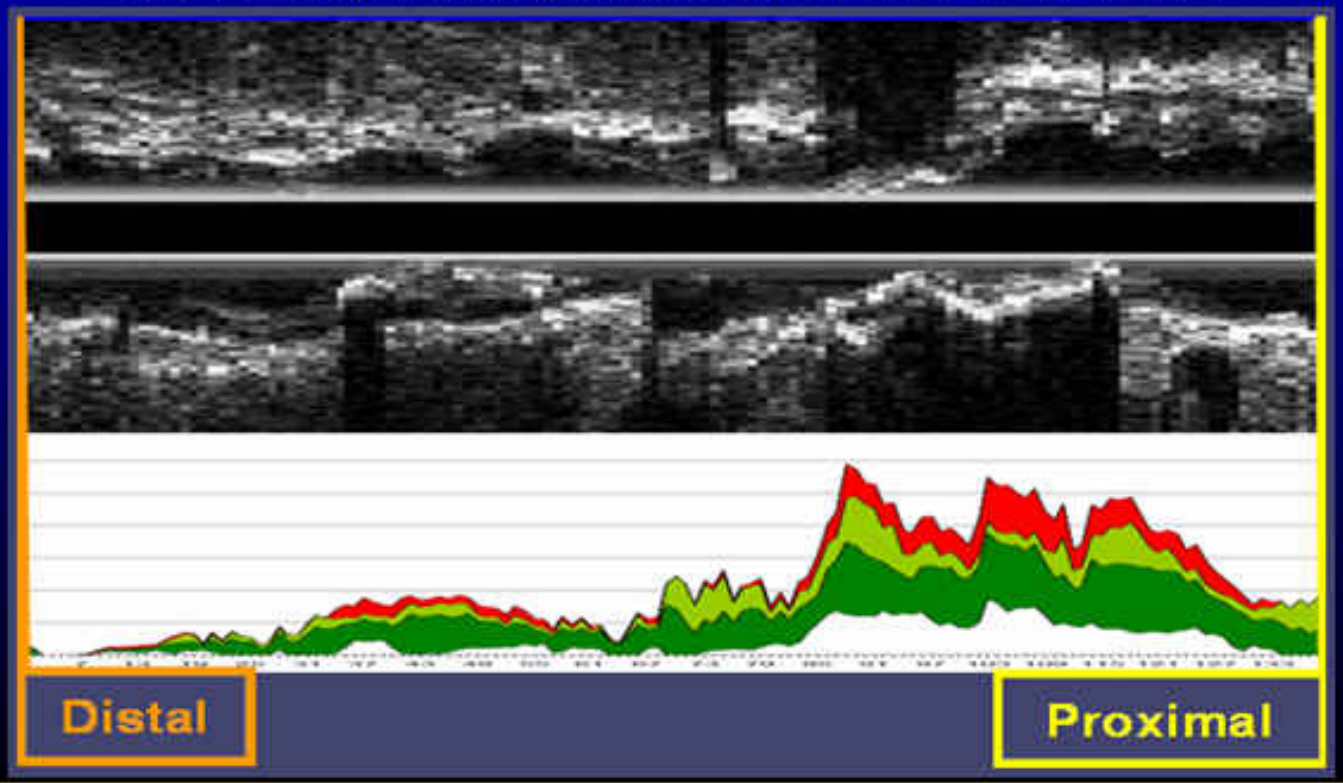
Study Complete = 700 enrolled June 06 (from MAHI = 41)

IVUS-VH Global Registry Background

- Global, prospective, multi-center, non-randomized, cross sectional IVUS registry
- Time period: 2004-2006
- Global registry
  - Planned: 3,000 patients
  - Interim analysis: 990 patients
- 42 centers worldwide
- Materials
  - IVG3 with VH™IVUS Software
  - Eagle Eye™ Catheter
  - TrakBack Pullback / R-100 Pullback Devices

Whole Vessel Analysis
Entire Pullback

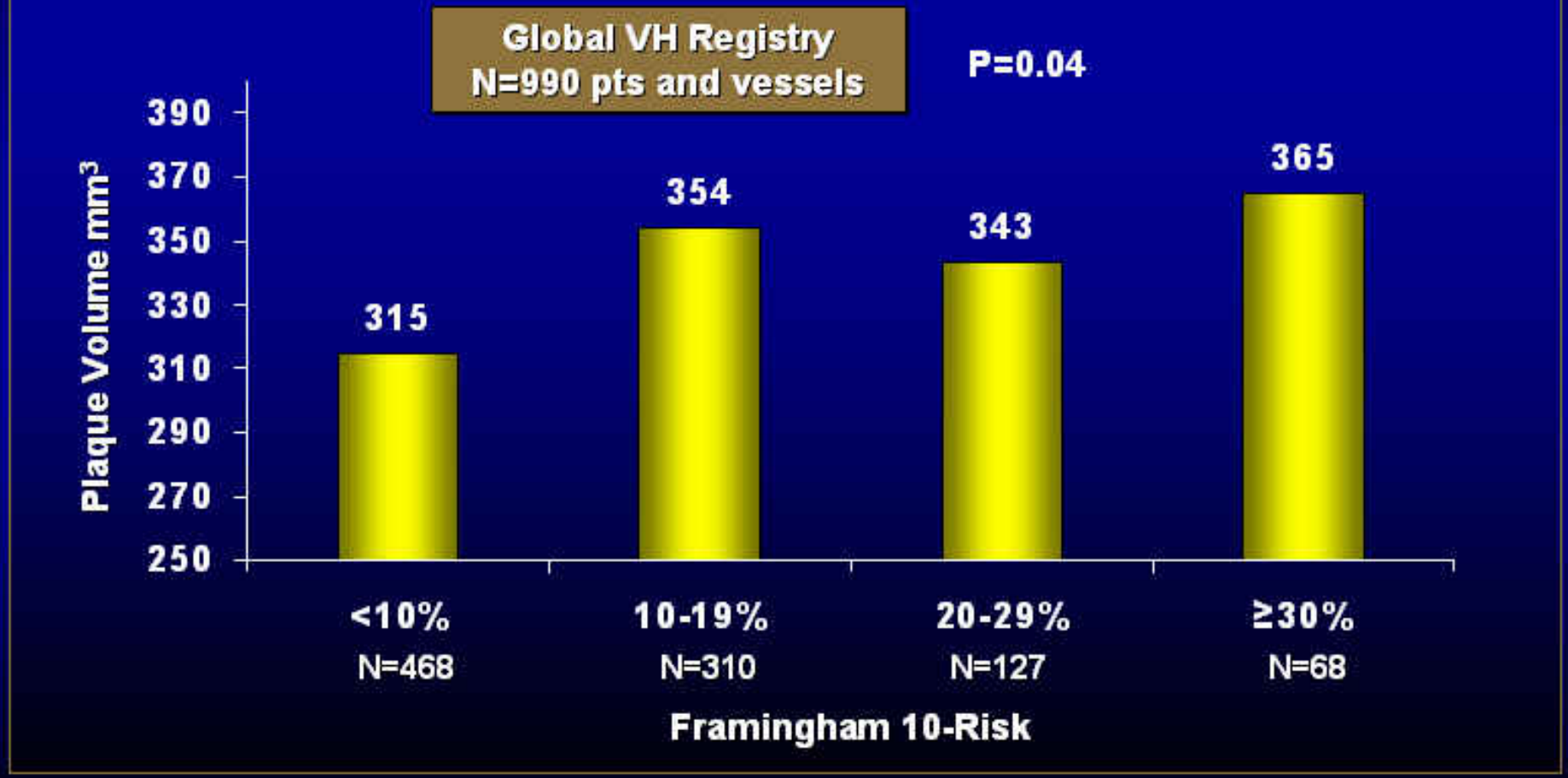
The average Cross Sectional Area (mm^2), total volume (mm^3), and % of total volume of different plaque components, plaque burden, and vessel and lumen diameters of the ENTIRE PULLBACK.



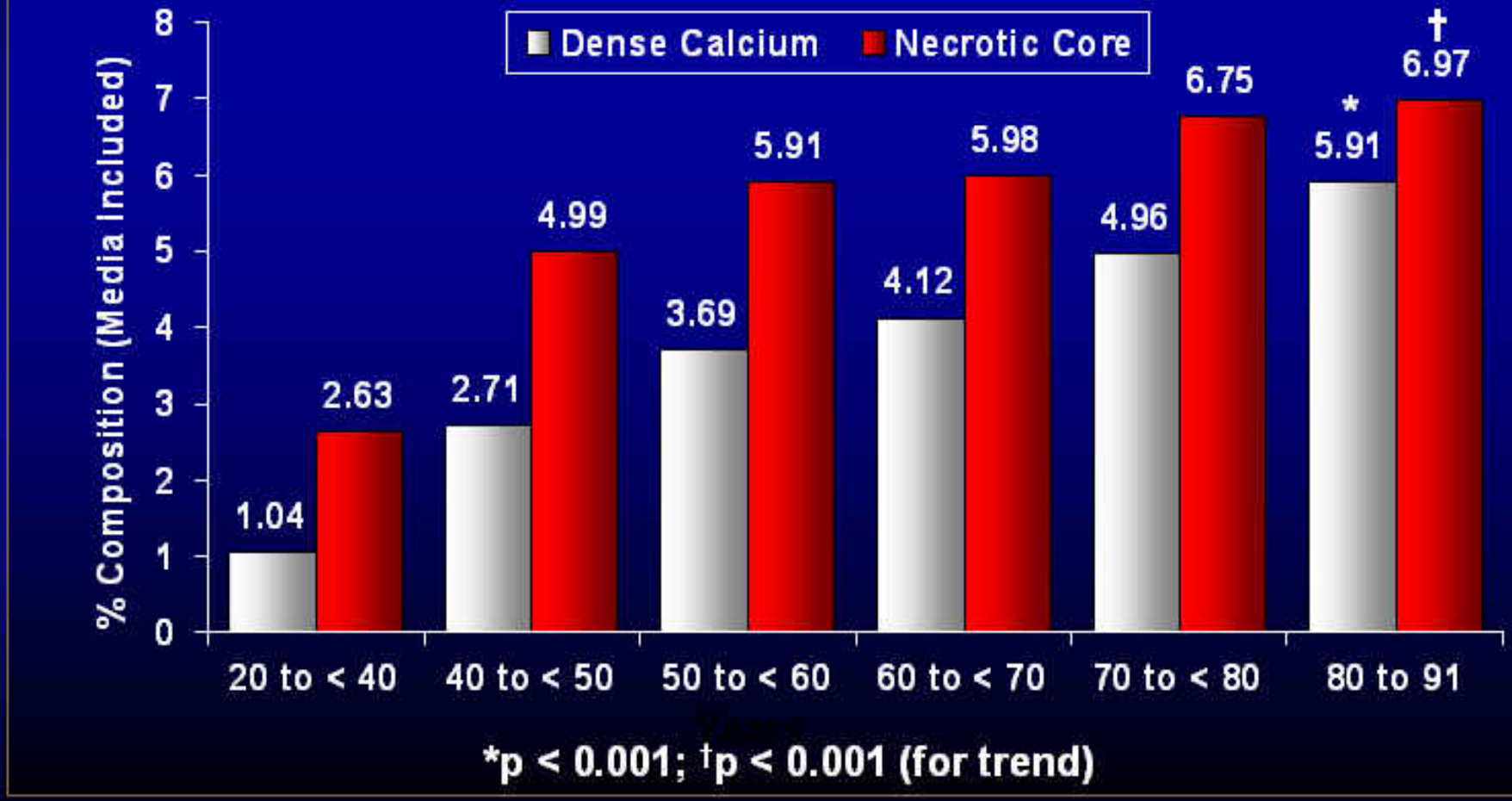
Study Objective

To determine whether plaque composition varies by traditional cardiovascular risk factors

Entire Pull Pack Volumetric Plaque Volume:
FRS Strata

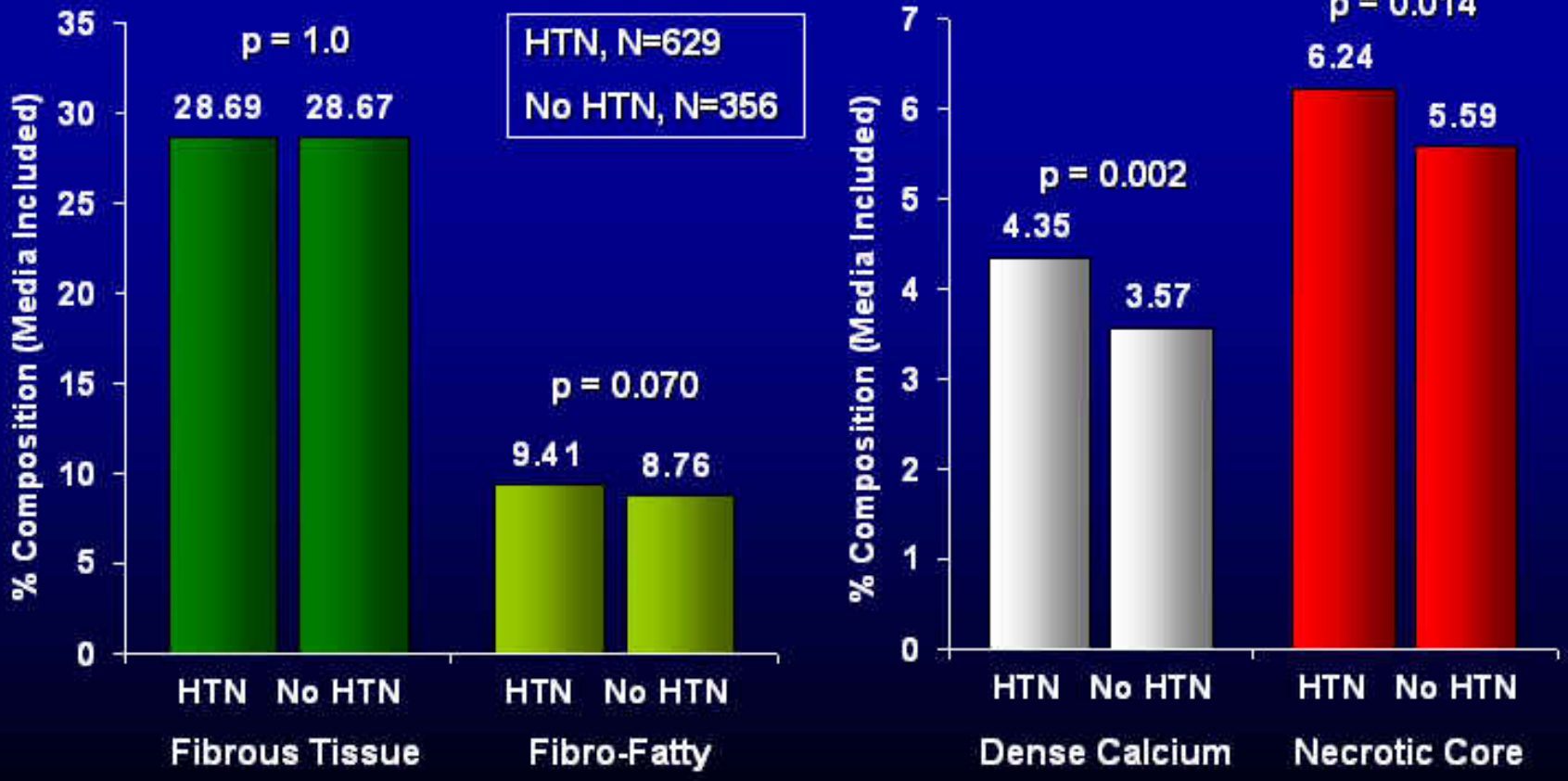


Age

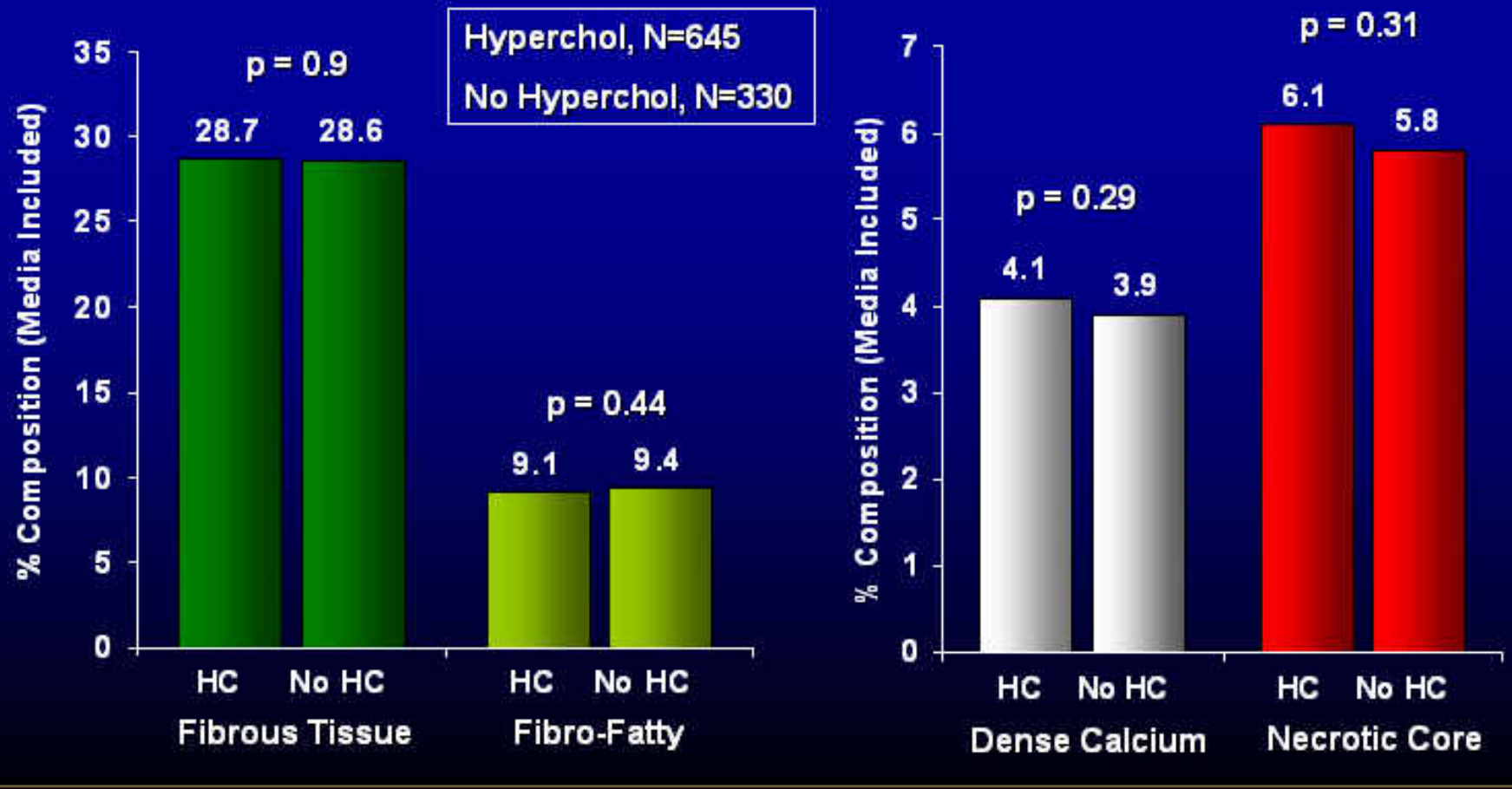


*p < 0.001; †p < 0.001 (for trend)

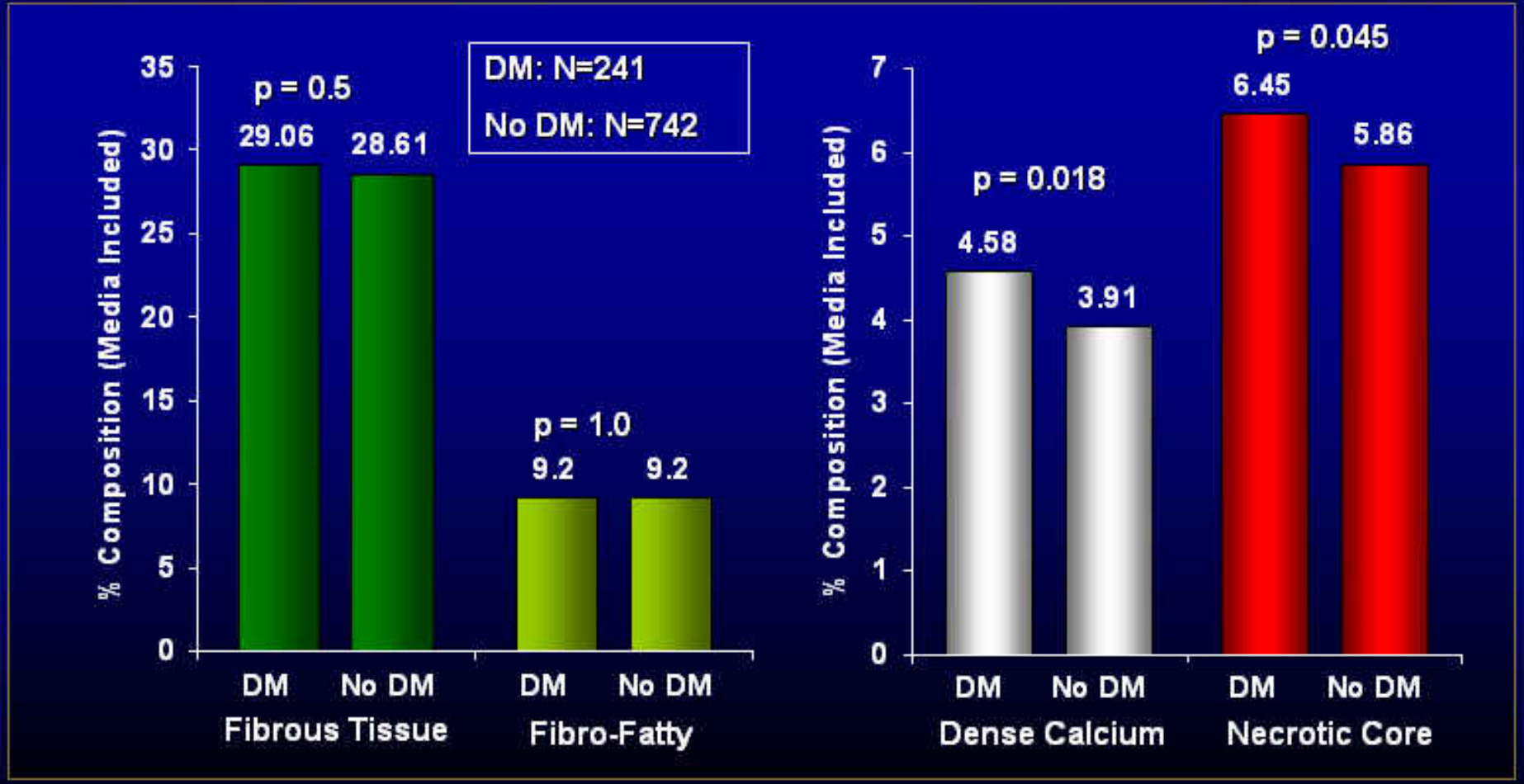
Hypertension



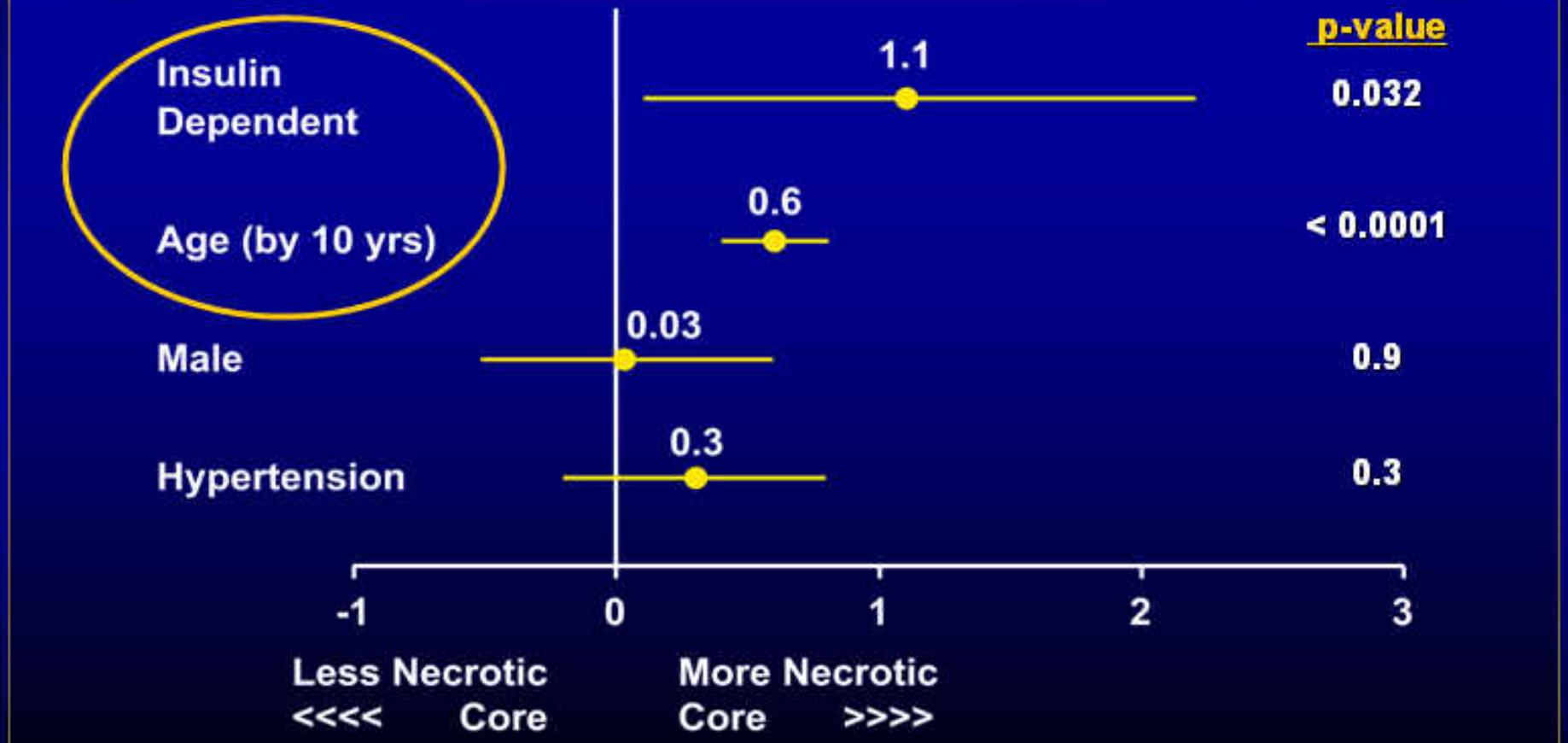
Hypercholesterolemia



Diabetes and Plaque Composition:
Global VH Registry



Multivariable Analysis



These 2 factors account for only 3% of the variance in mean % whole vessel necrotic core.

Conclusions

1. Plaque composition did vary by several traditional cardiovascular risk factors
2. Specifically; age, insulin treated DM, and hypertension were associated with whole vessel mean necrotic core. (Univariate analysis)
3. However, only age and insulin-treated diabetics were multivariable predictors of an increase in whole vessel mean % necrotic core
4. Traditional risk factors account for < 3% of the variability in mean whole vessel necrotic core

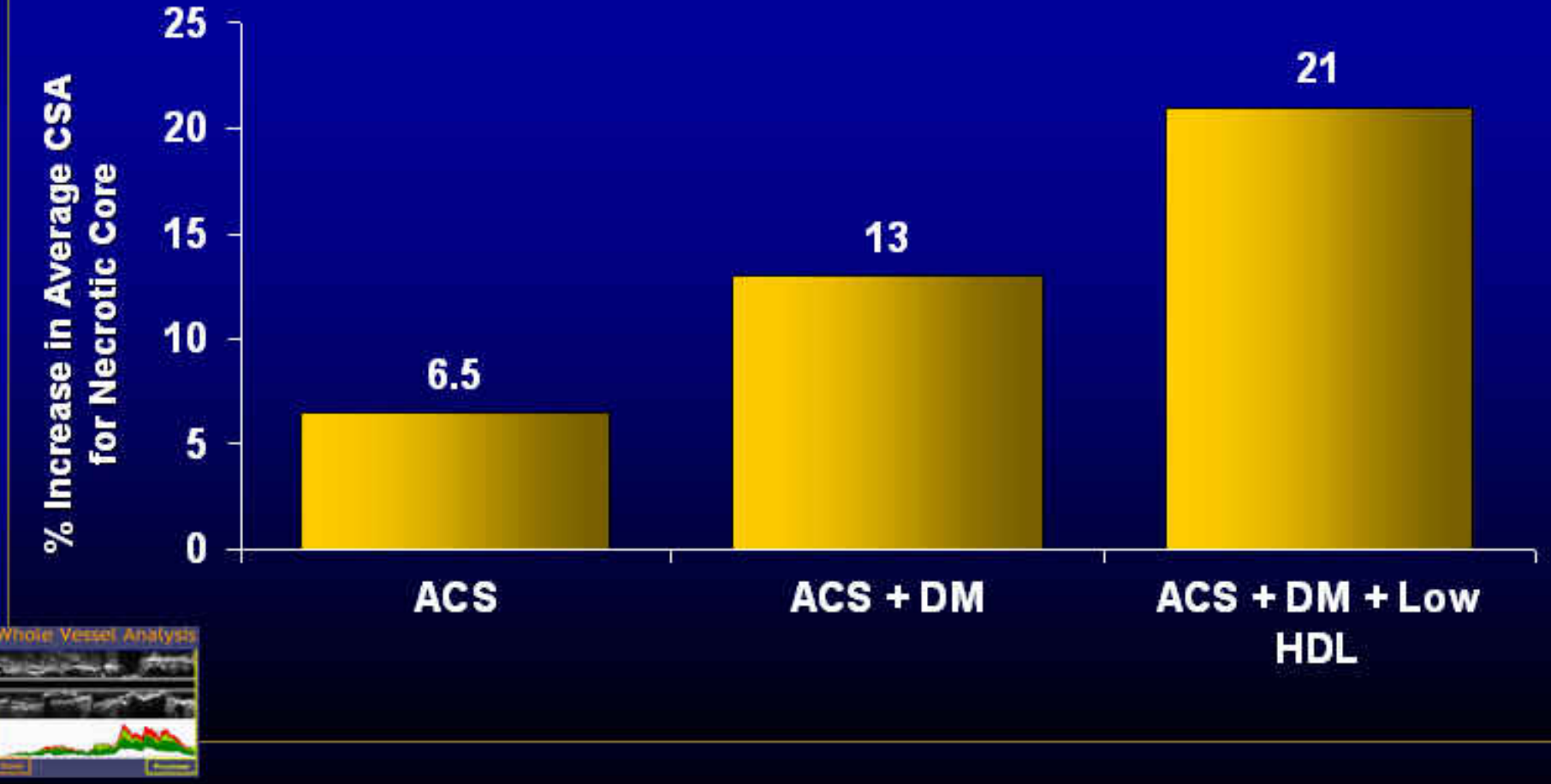
VH Registry:
880 Pts USA & Europe
Entire Pullback Analysis

Description of Predictive Analysis: Predictors of Increase in the Average CSA Necrotic Core

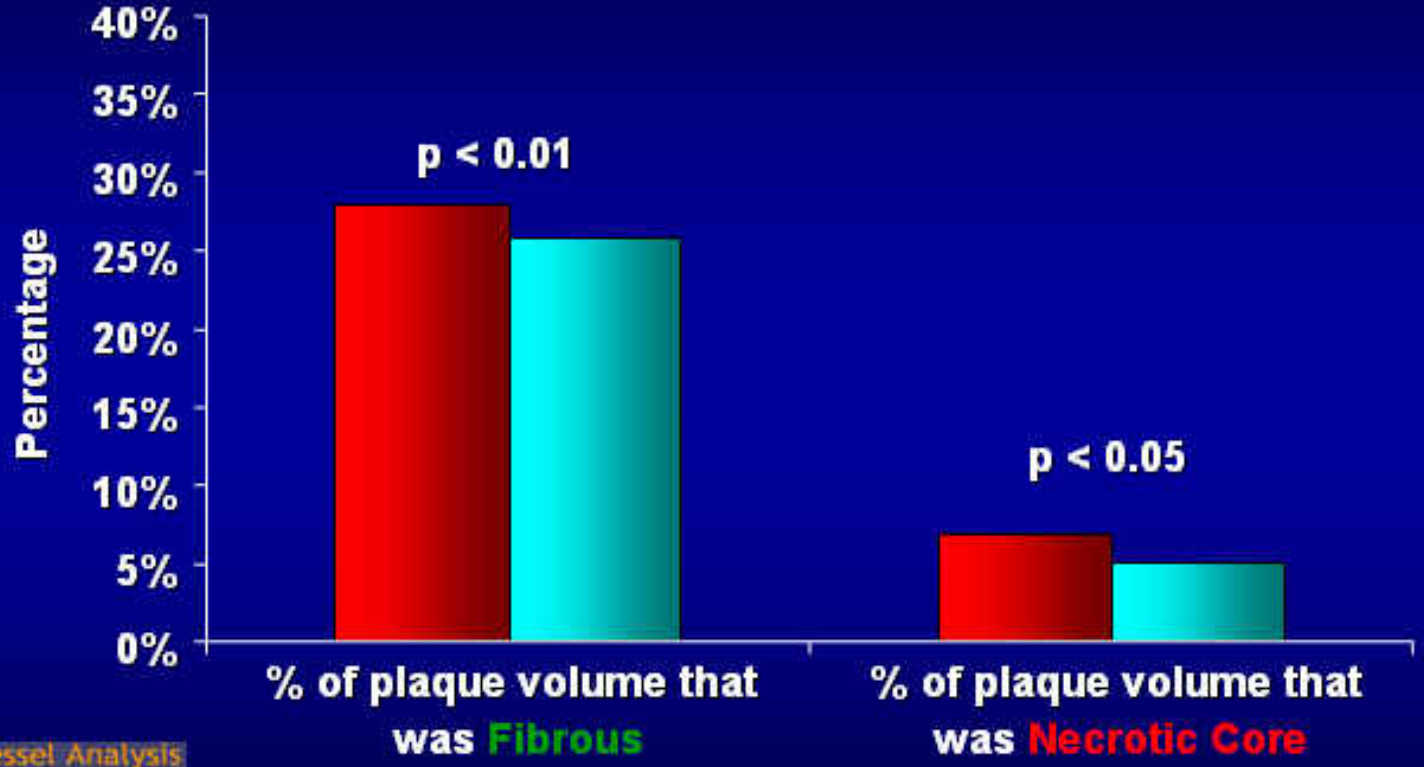
- The following variables were used in a stepwise regression
  - ACS (Y/N)
  - Diabetes (Y/N)
  - Hypertension (Y/N)
  - Prior MI (Y/N)
  - FH of CAD (Y/N)
  - HDL (High/Low)
  - LDL (High/Low)
  - CRP (High/Low)
  - Ischemia (Y/N)
  - Current Smoker (Y/N)

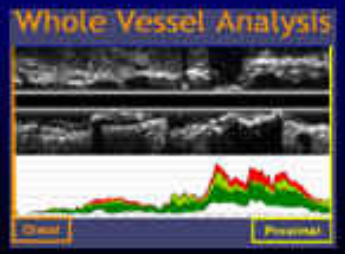
- Variables were allowed to enter the model if they achieve a univariate p-value of ≤ 0.1
- Variables remained in the model if they explain a significant ($p \leq 0.05$) amount of the variation
- Resulting model was confirmed with three types of stepwise model building: forward, backward, and mixed
- Variables remaining were: ACS, Diabetes, and HDL

The CSA of Necrotic Core is Predicted by Key Risk Factors



Patients with MI had Significantly more Fibrosis and Necrotic Core than Patients without MI





Percent of plaque volume that was calcified and fibrofatty were not significant (p>0.05) for MI

Description of Predictive Analysis:
Predictors of Current MI

- The following variables were used in a stepwise regression

- % necrotic core in plaque volume
- cube root [% calcified in plaque vol]
- Sq Rt [% fibro-fatty in plaque vol]
- % of fibrosis in plaque vol
- Log [Ave Necrotic Core CSA]
- Log [Ave Calcified CSA]
- Log [Ave Fibro-Fatty CSA]
- Log [Ave Fibrous CSA]
- Drug or alcohol abuse?
- Current Smoker
- Chronic inflammatory disease?
- Family History of CAD
- Congestive heart failure?
- Prior CABG
- Prior MI
- Lipid Treatment
- Lipid Treatment [Diet/Exercise]
- Diabetes?
- Hypertension?
- Prior cardiac history?
- Gender [F]
- Age years[>=58 & <68]
- Age years[< 58]

VH Registry: 880 Pts USA & Europe
Entire Pullback Analysis

Predictors of AMI

- The strongest predictors of mean CSA Necrotic Core were: diabetes, ACS, Low HDL
- The strongest predictors of current AMI were: high % necrotic core, prior cardiac history, prior CABG, CHF, positive FH

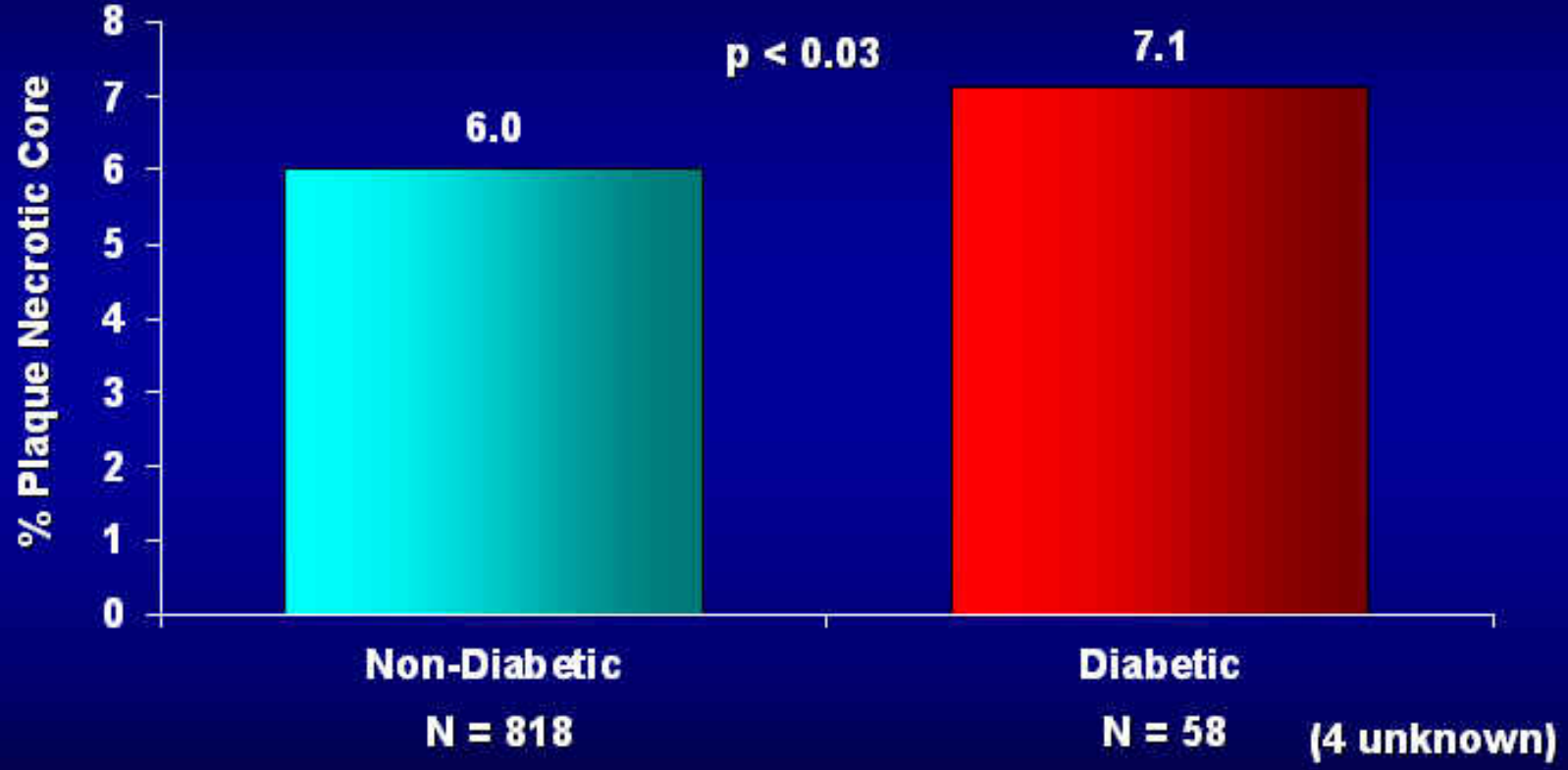
VH Registry: 880 Pts USA & Europe
Entire Pullback Analysis

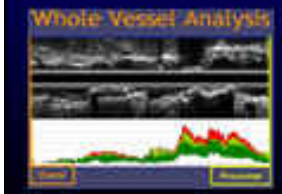
Predictors of AMI (cont)

- The data supports post mortem and epidemiological data of the role of **necrotic core** in identifying pts at risk for AMI

- Targeting **necrotic core** for either systemic medication or local therapy (stent) seems justified to prevent future events

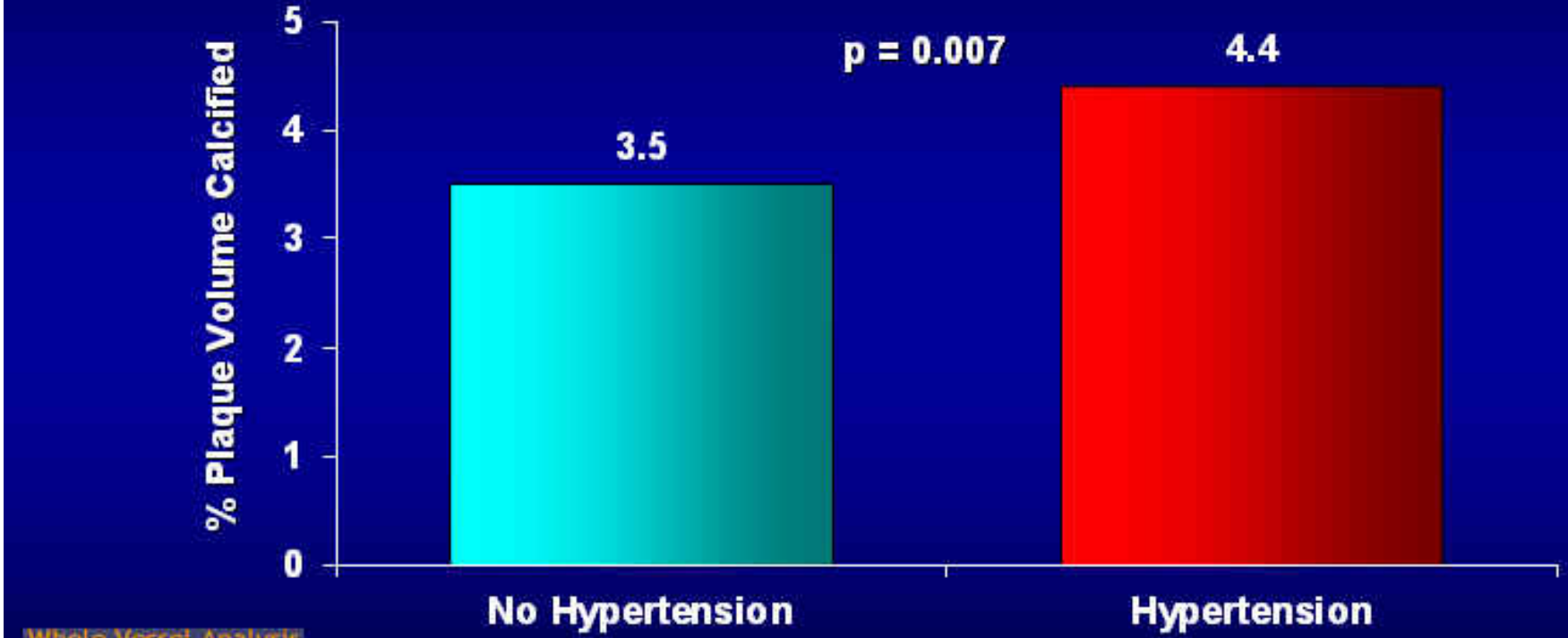
Insulin Dependent Diabetes is Associated with Increased Amount of Necrotic Core

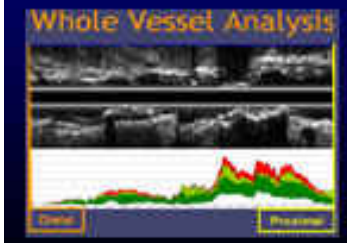




Percent of plaque volume that was calcified, fibrous or fibro-fatty was not significant (p>0.05) for insulin-dependence

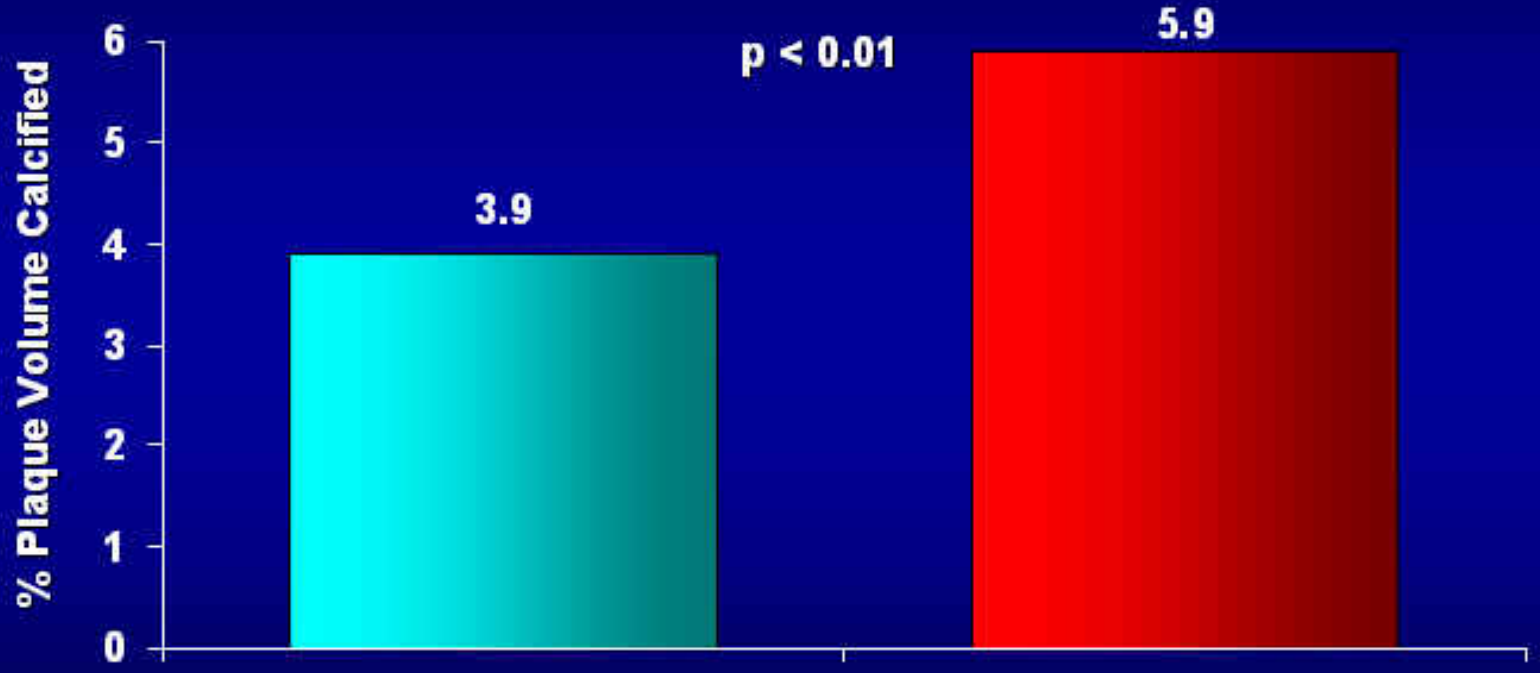
Hypertension is Associated with Increased Amount of Calcium

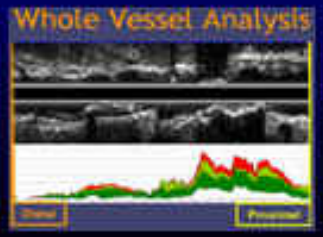




Percent of plaque volume that was fibrous, fibro-fatty or necrotic core was not significant (p>0.05) for HTN

The Arteries of Patients with Prior CABG were Significantly more Calcified than the Arteries of Patients without Previous CABG





Percent of Plaque that was Fibrous and FibroFatty were not significant (p>0.05) for CABG, and borderline for Necrotic Core (p=0.06)

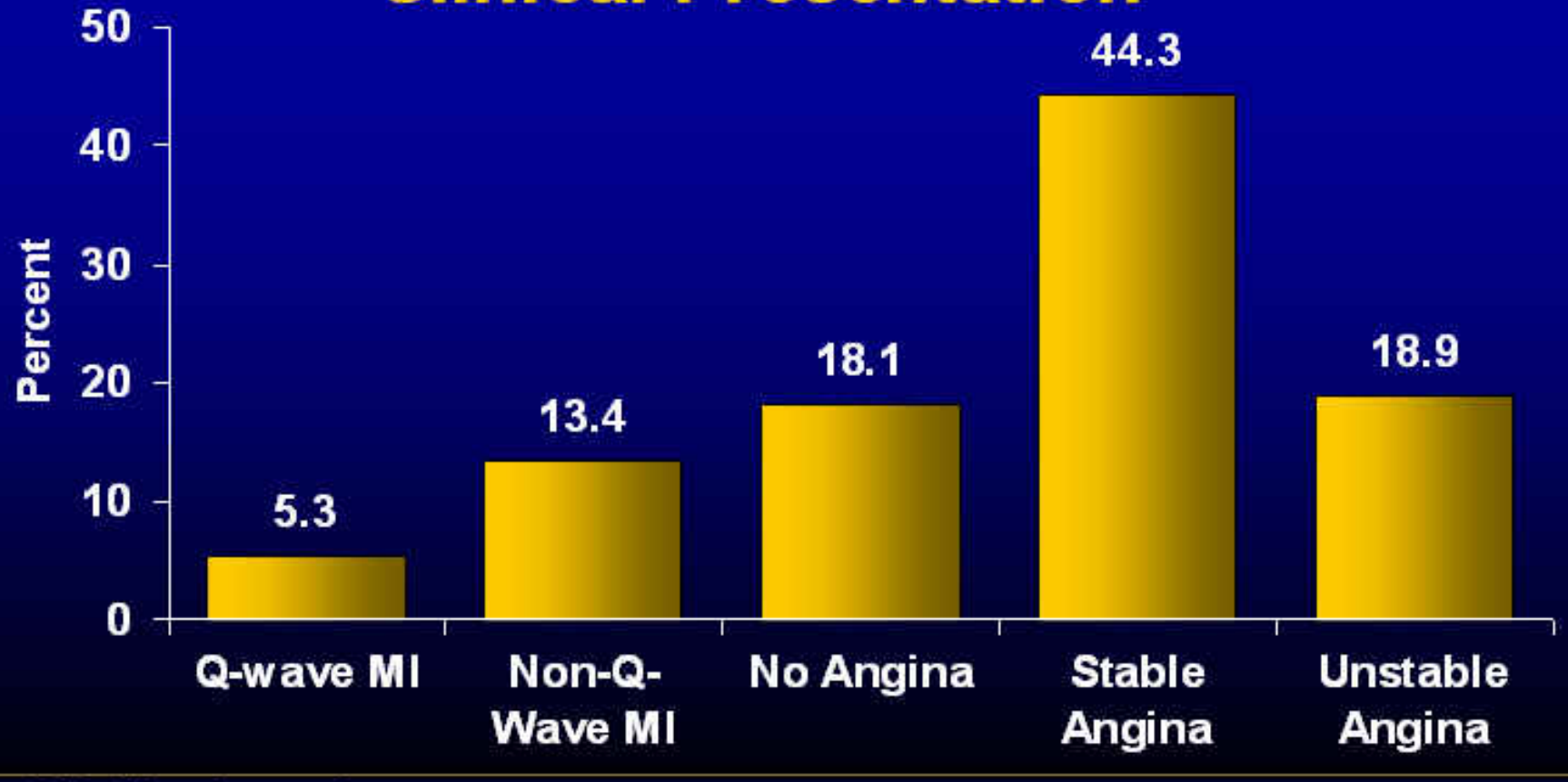
VH Registry: 880 Pts USA & Europe - *Pullback Analysis*
Relationship of Plaque Components to Risk Factors

- Significantly increased Necrotic Core
  - Insulin dependent diabetes
  - Prior cardiac history
  - Prior AMI or CABG
  - Old age, particularly females
- Significantly increased Calcium
  - Older age
  - Congestive Heart Failure
  - Prior Cardiac History or CABG
  - Hypertension
- Significant increase in Fibrosis
  - Prior AMI

VH Registry: 880 Pts USA & Europe

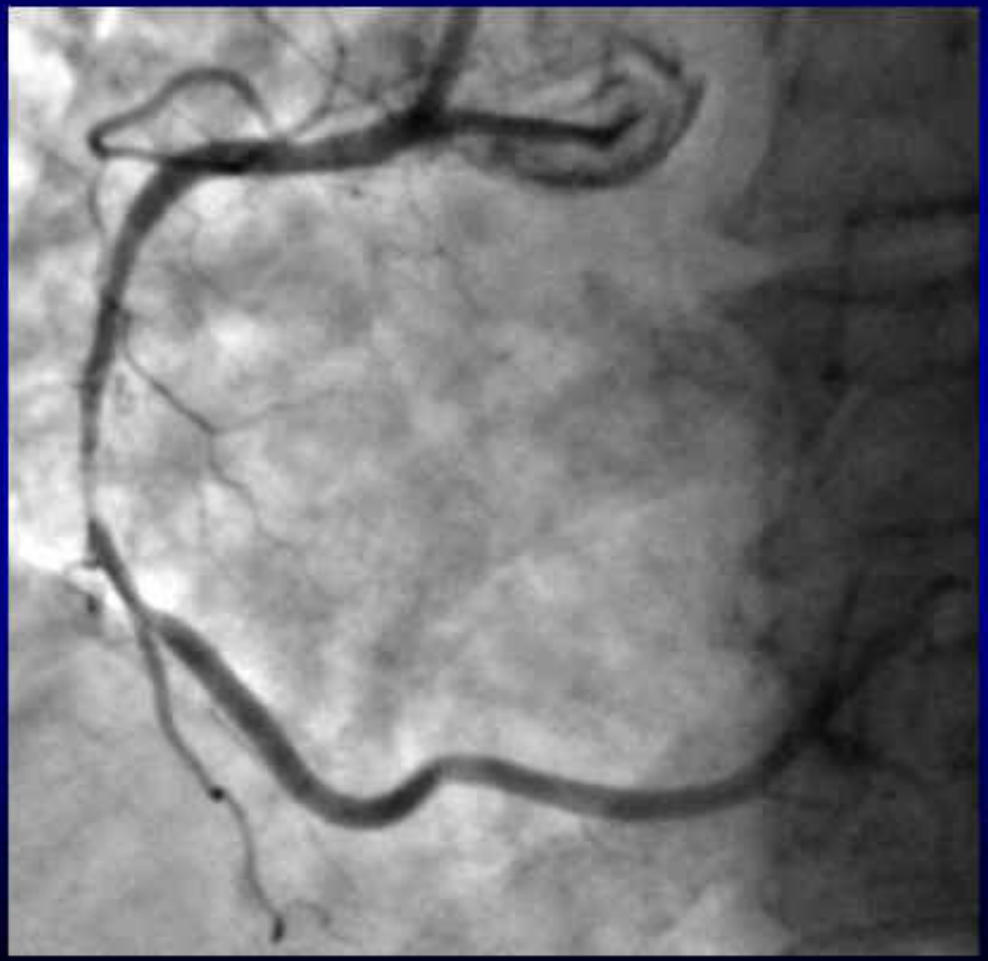
Entire Pullback Analysis

Clinical Presentation

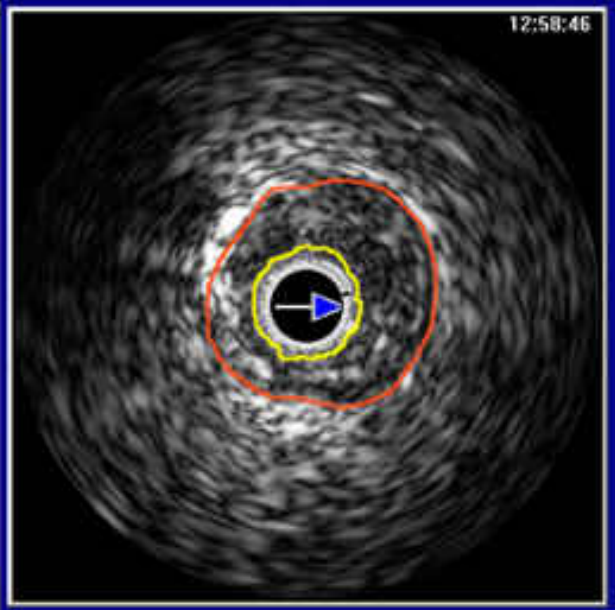


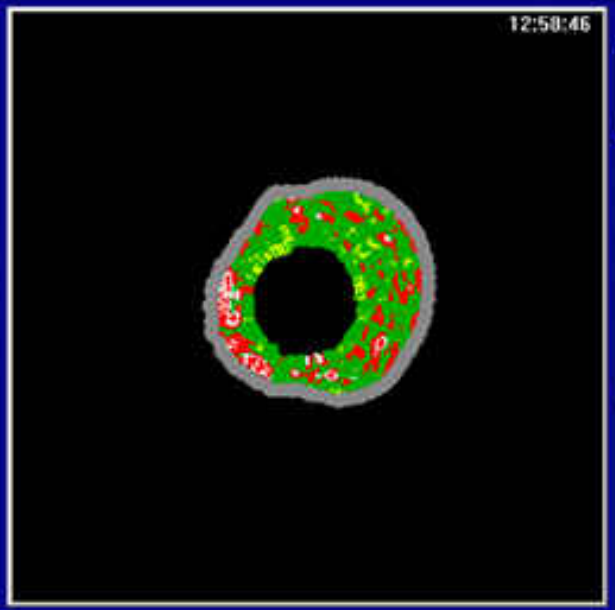
n= 863, (7 unknown)

60-Year-Old Female, Acute Inferior Infarct
Pre Export™ Catheter



60-Year-Old Female, Acute Inferior Infarct
Pre Export™ Catheter

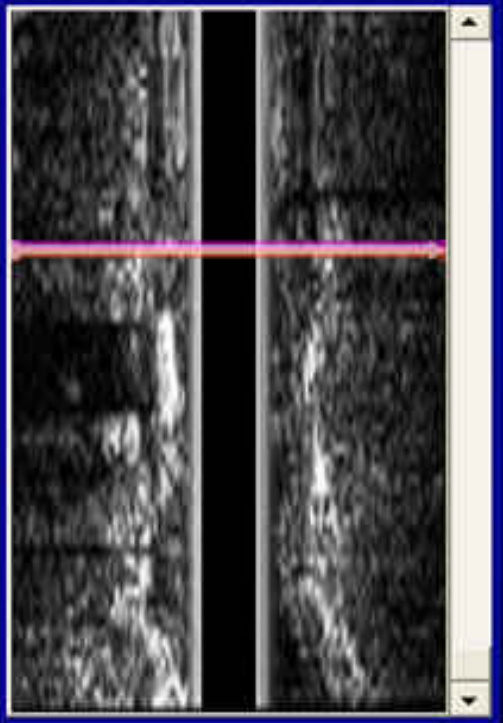




Lumen Area	2.7 mm²	
Vessel Area	12.4 mm²	
Plaque Area	9.7 mm²	
% Plaque Burden	78 %	
FI Green Area	4.6 mm²	67 %
FF Light Green Area	0.4 mm²	6 %
DC White Area	0.3 mm²	4 %
NC Red Area	1.5 mm²	22 %

More ...

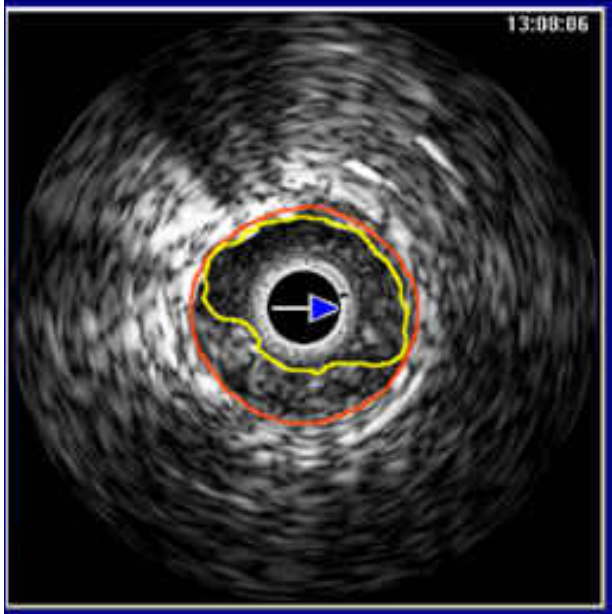
Segment: 3

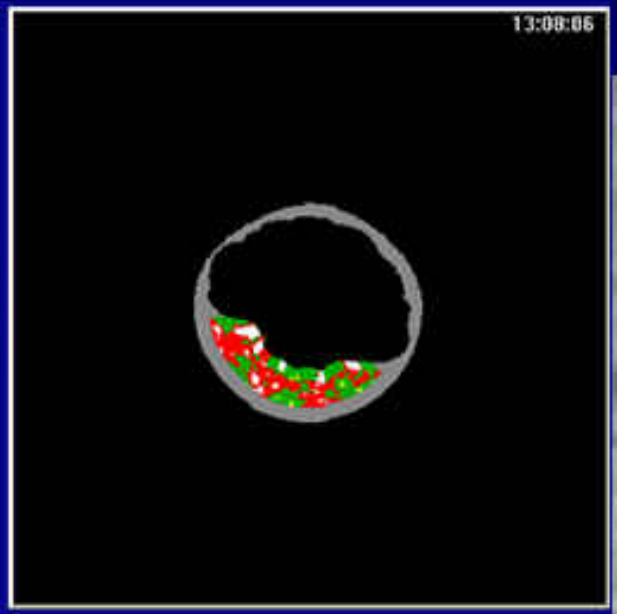


Distal Frame	228
Current Frame	228
Proximal Frame	228

60-Year-Old Female, Acute Inferior Infarct
Post Export™ Catheter

60-Year-Old Female, Acute Inferior Infarct
Post Export™ Catheter – DES in RCA





Lumen Area	6.8 mm²	
Vessel Area	11.3 mm²	
Plaque Area	4.5 mm²	
% Plaque Burden	40 %	
FI Green Area	0.8 mm²	41 %
FF Light Green Area	0.0 mm²	2 %
DC White Area	0.3 mm²	13 %
NC Red Area	0.9 mm²	45 %

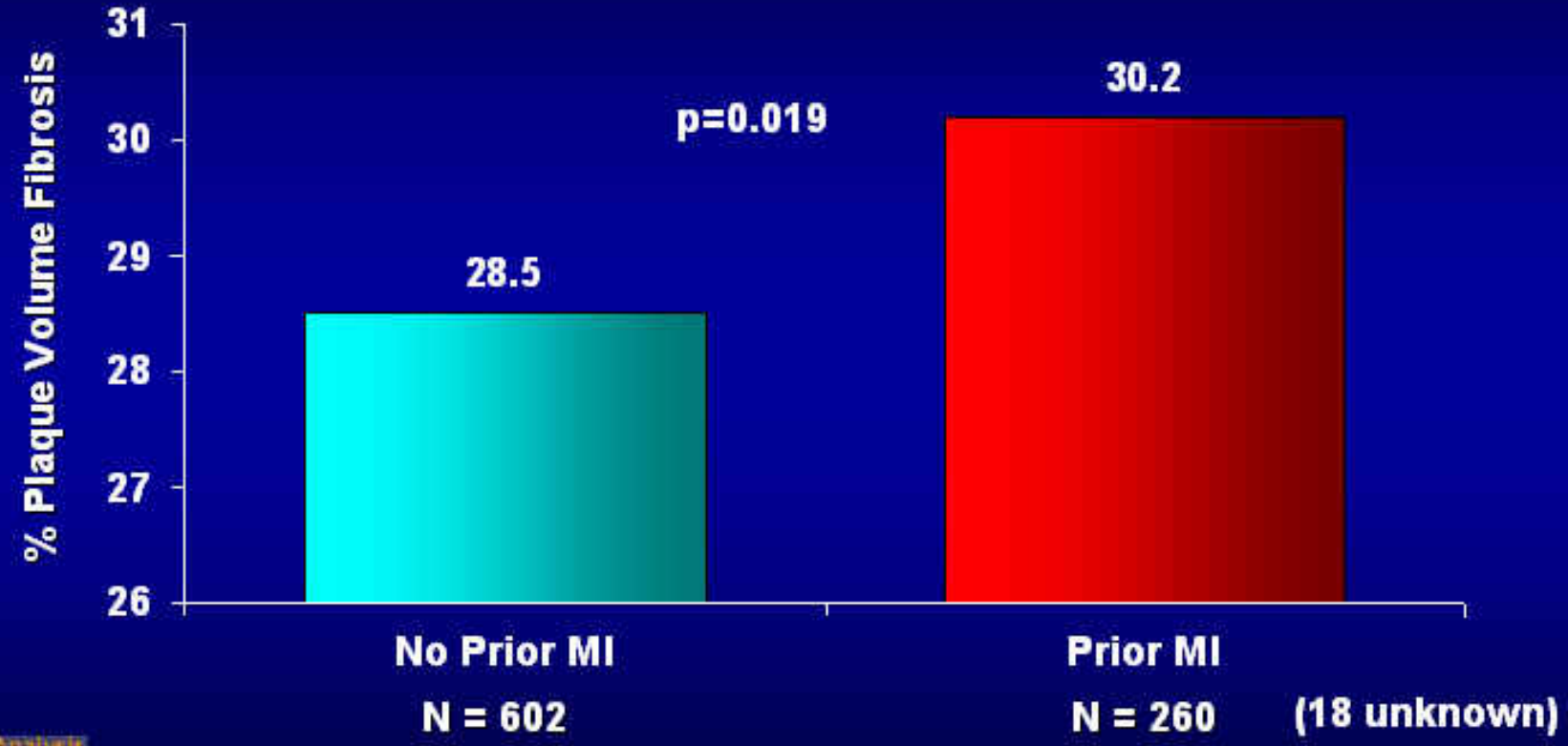
More ...

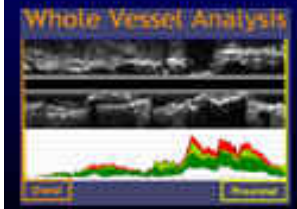
VH Registry: 880 Pts USA & Europe
Entire Pullback Analysis

Relationship of Plaque Components to Risk Factors

- Excellent correlation of *in vivo* plaque composition by VH IVUS and traditional risk factors
- Potential use of in vivo plaque composition to assess risk factor modification

Patients With Prior MI Had Significantly More Fibrosis Than Patients Without Previous MI

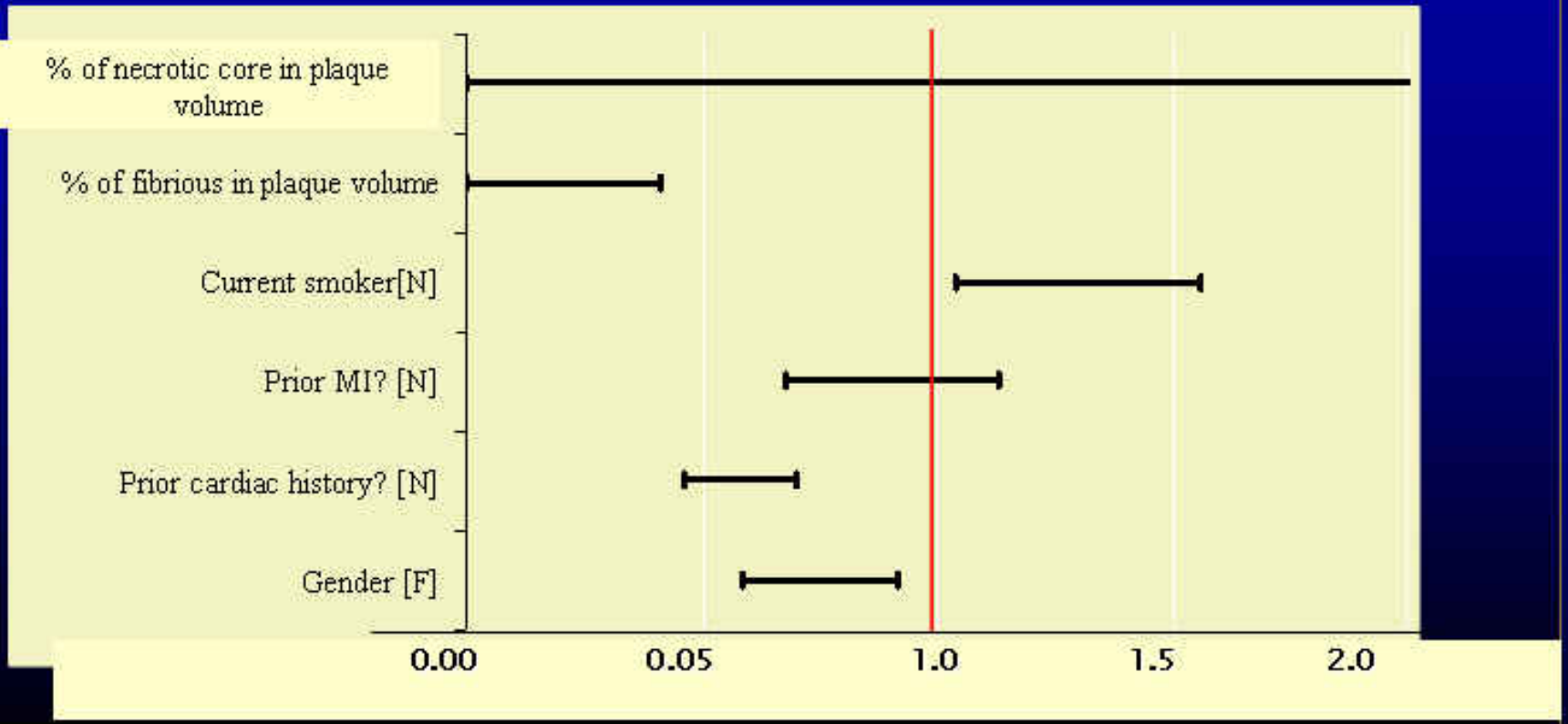




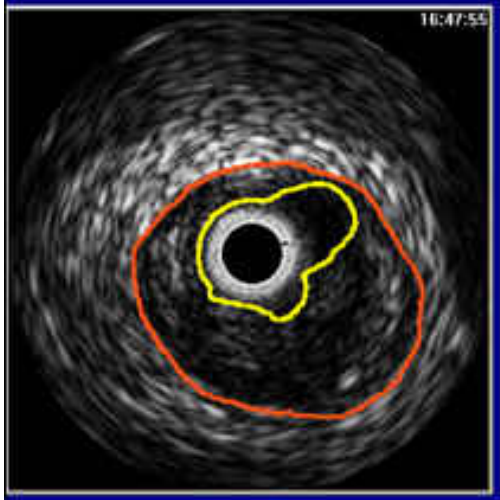
Percent of plaque volume that was fibro-fatty and calcified were not significant (p>0.05) for MI and borderline for necrotic core (p=0.09)

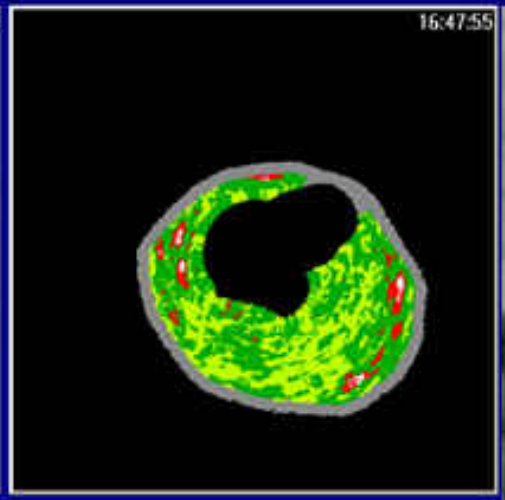
Predictors of Current MI
Results from Stepwise Regression

Strongest Predictors: High % NC, low %F, prior Cardiac History, Male



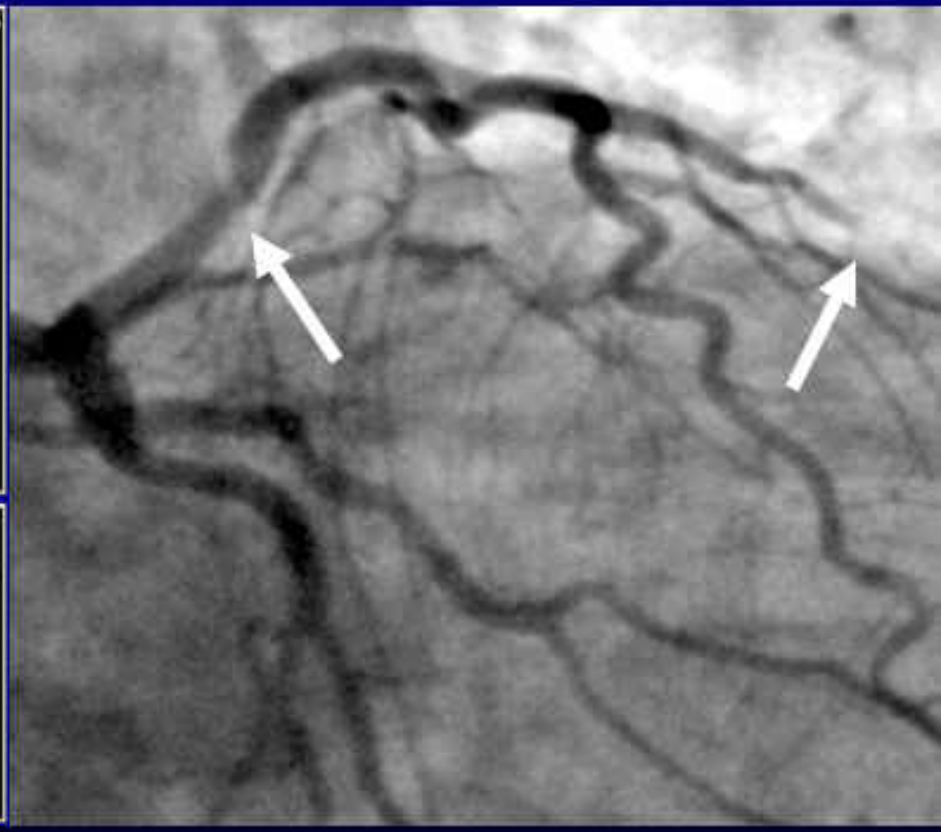
58-Year-Old Male
Acute Lateral Wall Infarct



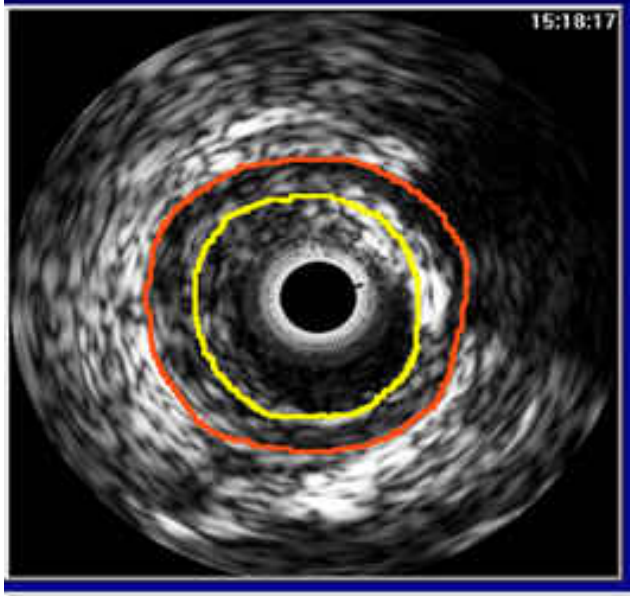


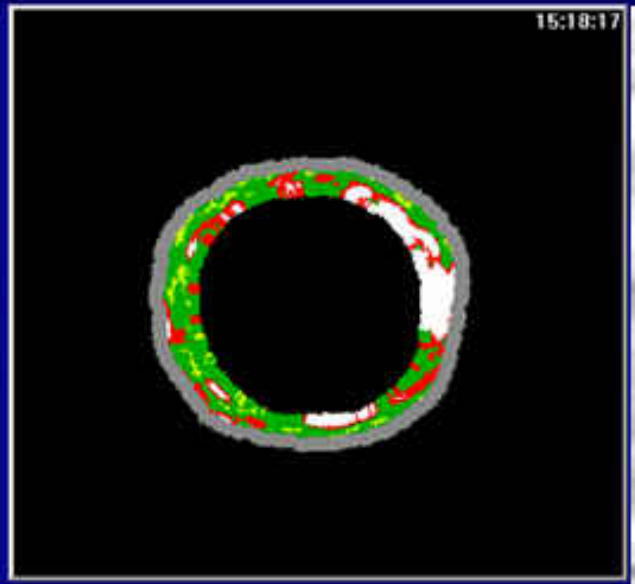
Lumen Area	6.0 mm²	
EEL Area	24.5 mm²	
Plaque Area	18.5 mm²	
% Plaque Burden	76 %	
Fibrous Area	8.2 mm²	57 %
Fibro-Fatty Area	5.2 mm²	36 %
Dense Calcium Area	0.1 mm²	1 %
Necrotic Core Area	0.8 mm²	6 %

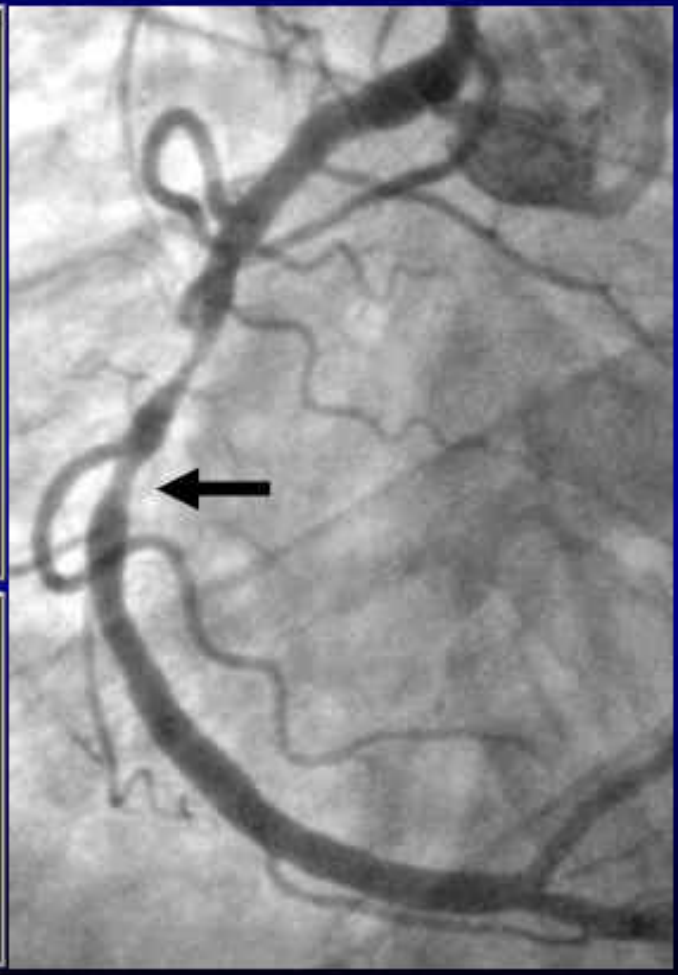
More ...



52-Year-Old Male
Acute Inferior Infarct



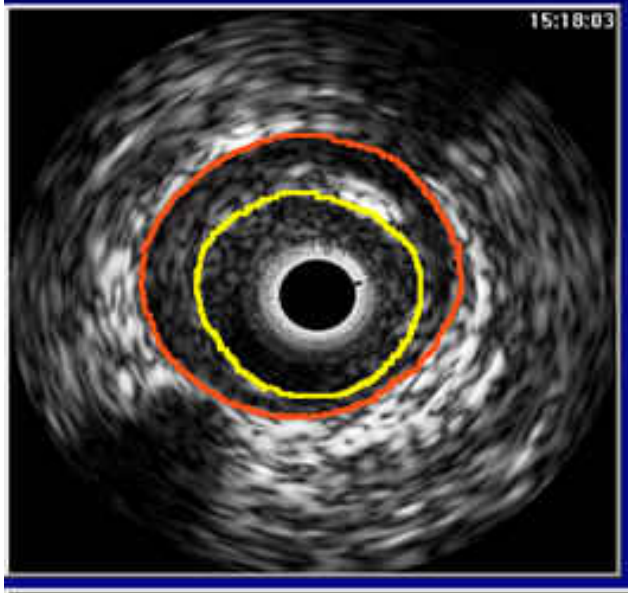


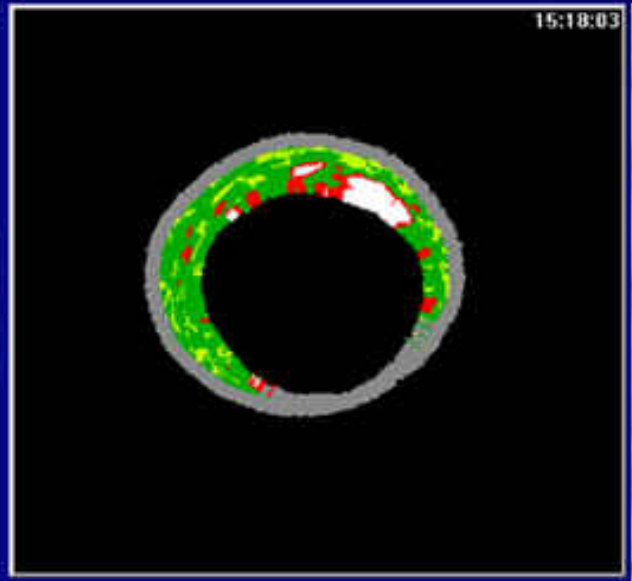


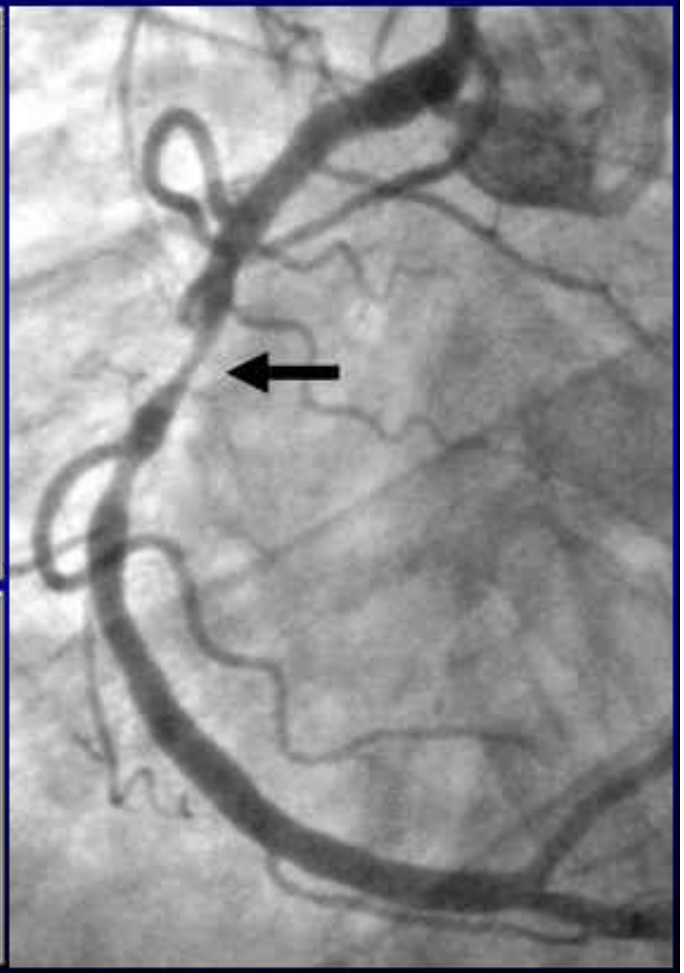
Lumen Area	11.5 mm²	
EEL Area	22.2 mm²	
Plaque Area	10.6 mm²	
% Plaque Burden	48 %	
Fibrous Area	3.4 mm²	51 %
Fibro-Fatty Area	0.5 mm²	7 %
Dense Calcium Area	1.5 mm²	23 %
Necrotic Core Area	1.3 mm²	19 %

More ...

52-Year-Old Male
Acute Inferior Infarct



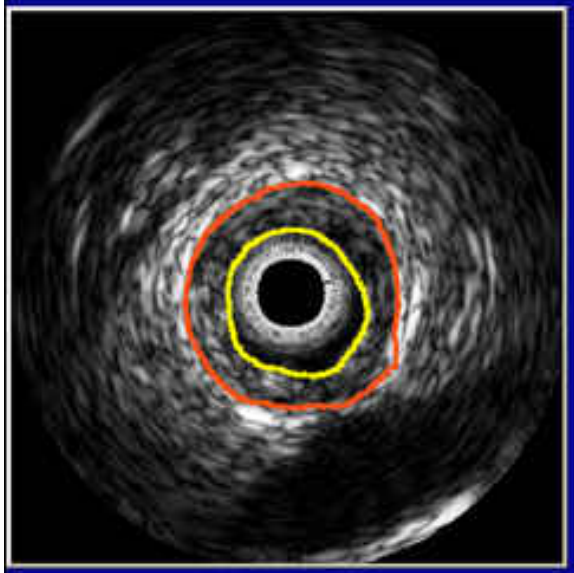


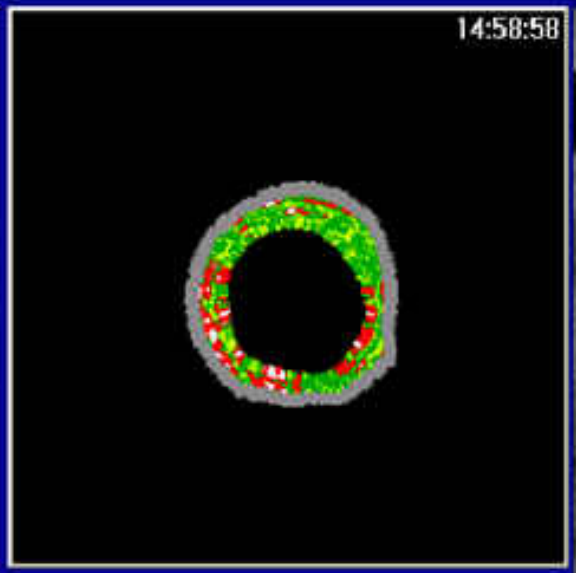


Lumen Area	10.1 mm²	
EEL Area	20.3 mm²	
Plaque Area	10.2 mm²	
% Plaque Burden	50 %	
Fibrous Area	3.9 mm²	64 %
Fibro-Fatty Area	0.8 mm²	14 %
Dense Calcium Area	0.6 mm²	10 %
Necrotic Core Area	0.7 mm²	12 %

More ...

65-Year-Old Male
Acute Inferior STEMI (LB)

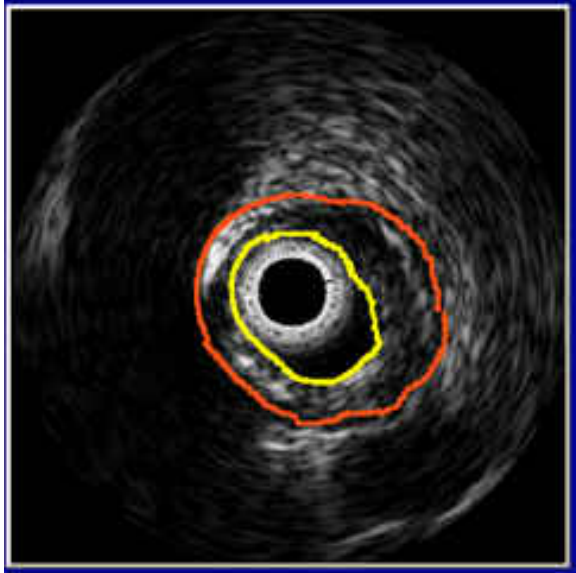


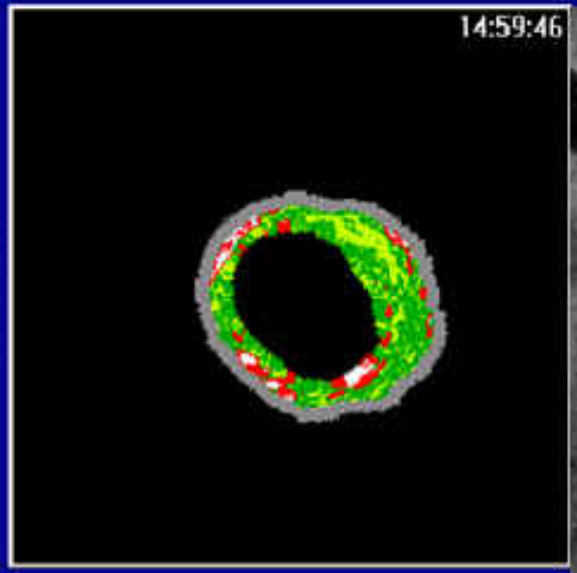


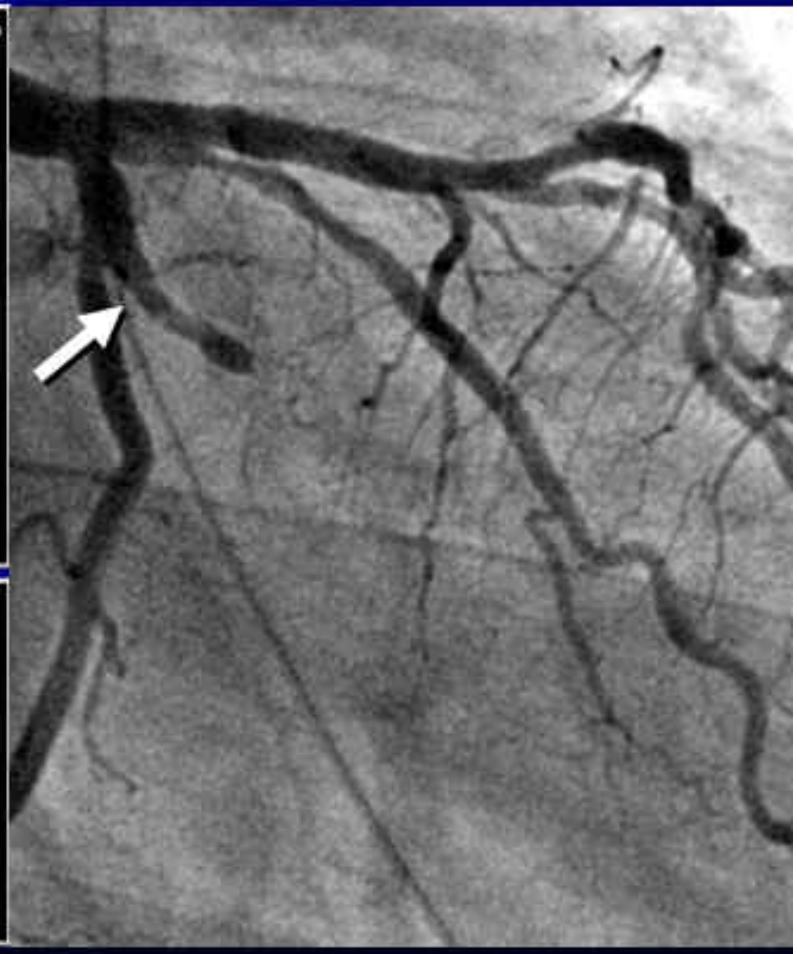
Lumen Area	5.2 mm²	
EEL Area	12.9 mm²	
Plaque Area	7.7 mm²	
% Plaque Burden	60 %	
Fibrous Area	2.5 mm²	52 %
Fibro-Fatty Area	0.9 mm²	19 %
Dense Calcium Area	0.2 mm²	5 %
Necrotic Core Area	1.1 mm²	23 %

More ...

65-Year-Old Male
Acute Inferior STEMI (LB)



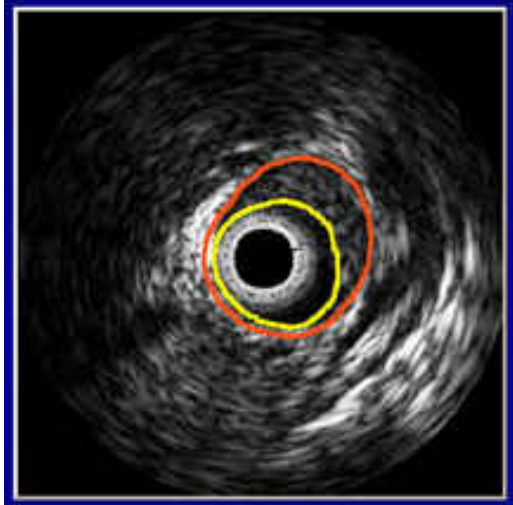


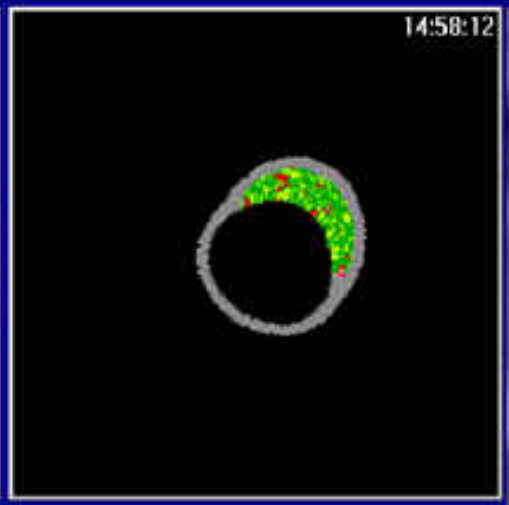


Lumen Area	5.2 mm²	
EEL Area	14.6 mm²	
Plaque Area	9.4 mm²	
% Plaque Burden	64 %	
Fibrous Area	3.6 mm²	57 %
Fibro-Fatty Area	1.5 mm²	23 %
Dense Calcium Area	0.4 mm²	6 %
Necrotic Core Area	0.9 mm²	15 %

More ...

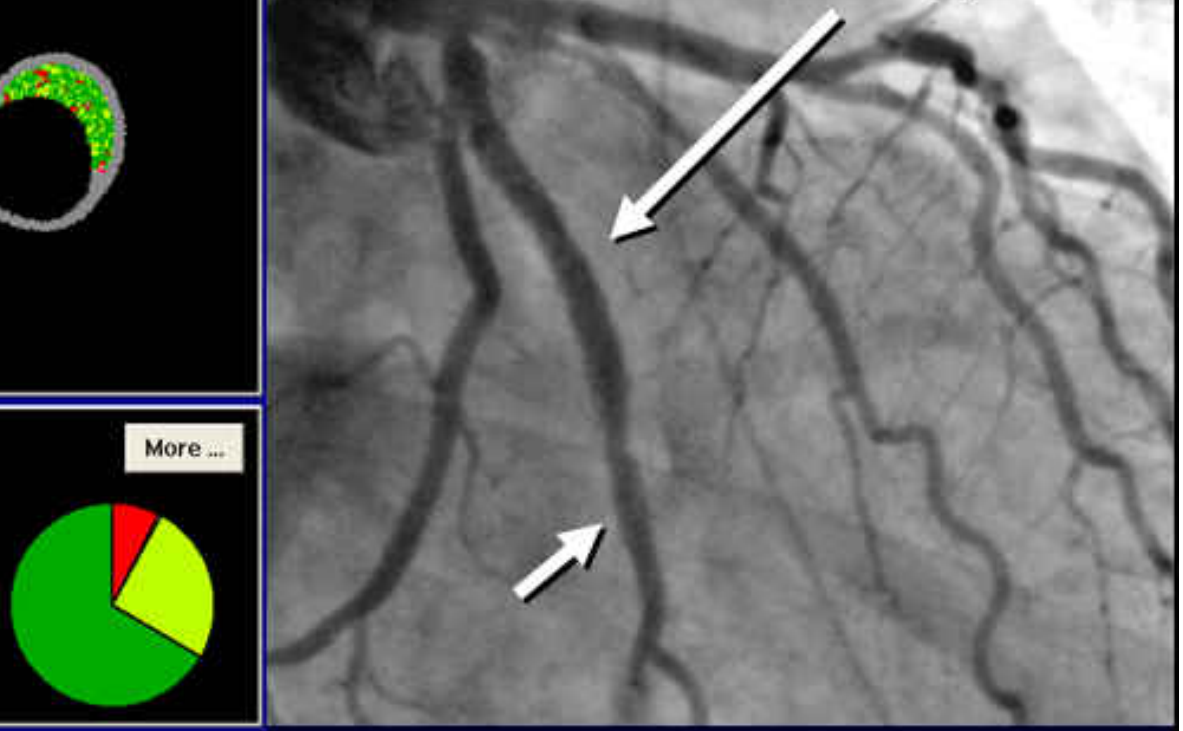
65-Year-Old Male
Acute Inferior STEMI (LB)





Lumen Area	5.2 mm²	
EEL Area	9.7 mm²	
Plaque Area	4.6 mm²	
% Plaque Burden	47 %	
Fibrous Area	1.4 mm²	66 %
Fibro-Fatty Area	0.5 mm²	25 %
Dense Calcium Area	0.0 mm²	0 %
Necrotic Core Area	0.2 mm²	8 %

More ...



IVUS-VH Derived Plaque Phenotyping

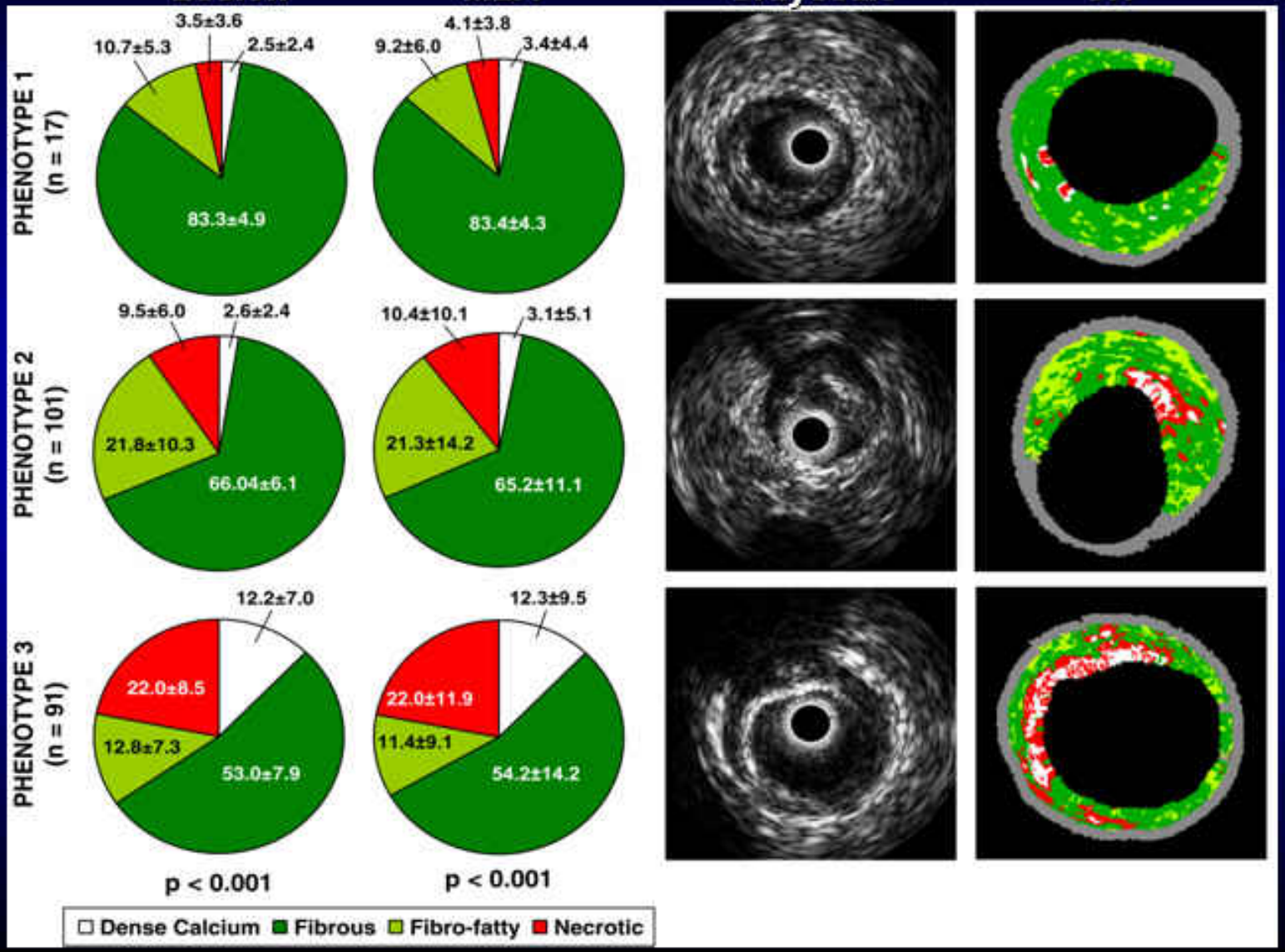
Mid America Heart Institute

- IVUS-VH imaging in 76 pts prior to PCI
  209 lesions of interest evaluated
- 20 MHz catheter (Eagle Eye, Volcano Corp, CA) Automated pullback 0.5 mm/second
- Utilizing a latent class cluster technique, 3 unique phenotypes were identified

IVUS-VH Derived Plaque Phenotyping

	Phenotype 1 (n=17)	Phenotype 2 (n=101)	Phenotype 3 (n=91)	P-value
Segment length (mm)	16.79 ± 12.33	15.06 ± 9.62	17.51 ± 10.55	0.03
Seg vol plaque burden (mm^3)	43.66 ± 6.91	46.41 ± 11.53	50.93 ± 10.31	0.003
MLA plaque burden (%)	52.58 ± 9.82	55.96 ± 14.75	61.48 ± 12.38	0.004
Stenosis at MLA (%)	24.93 ± 19.59	31.28 ± 18.27	37.52 ± 16.97	0.007
MLA vessel EEL CSA (mm^2)	11.13 ± 5.27	15.42 ± 5.85	14.33 ± 4.91	0.009
MLA vessel min diam (mm)	3.42 ± 0.83	4.03 ± 0.80	3.88 ± 0.70	0.009
MLA lumen CSA (mm^2)	5.09 ± 2.23	6.64 ± 3.55	5.35 ± 2.30	0.006
MLA plaque CSA (mm^2)	6.03 ± 3.43	8.78 ± 4.43	8.98 ± 4.05	0.03
Remodeling index at MLA	0.96 ± 0.17	0.94 ± 0.15	0.92 ± 0.16	0.6
Eccentricity	0.43 ± 0.20	0.58 ± 0.19	0.58 ± 0.17	0.06

IVUS-VH Derived Plaque Phenotyping



IVUS-VH Derived Plaque Phenotyping

Conclusions:

- IVUS-VH is a feasible imaging platform to define lesions in target vessels of PCI patients
- There were 1.5 non-culprit lesions for every 1 culprit lesion in target vessels
- Identified 3 distinct phenotypes that differed with respect to composition and plaque burden ($p < 0.001$)
- Tight correlation between lesion phenotype and mean lumen area plaque composition ($p < 0.001$)

IVUS-VH Derived Plaque Phenotyping

Conclusions:

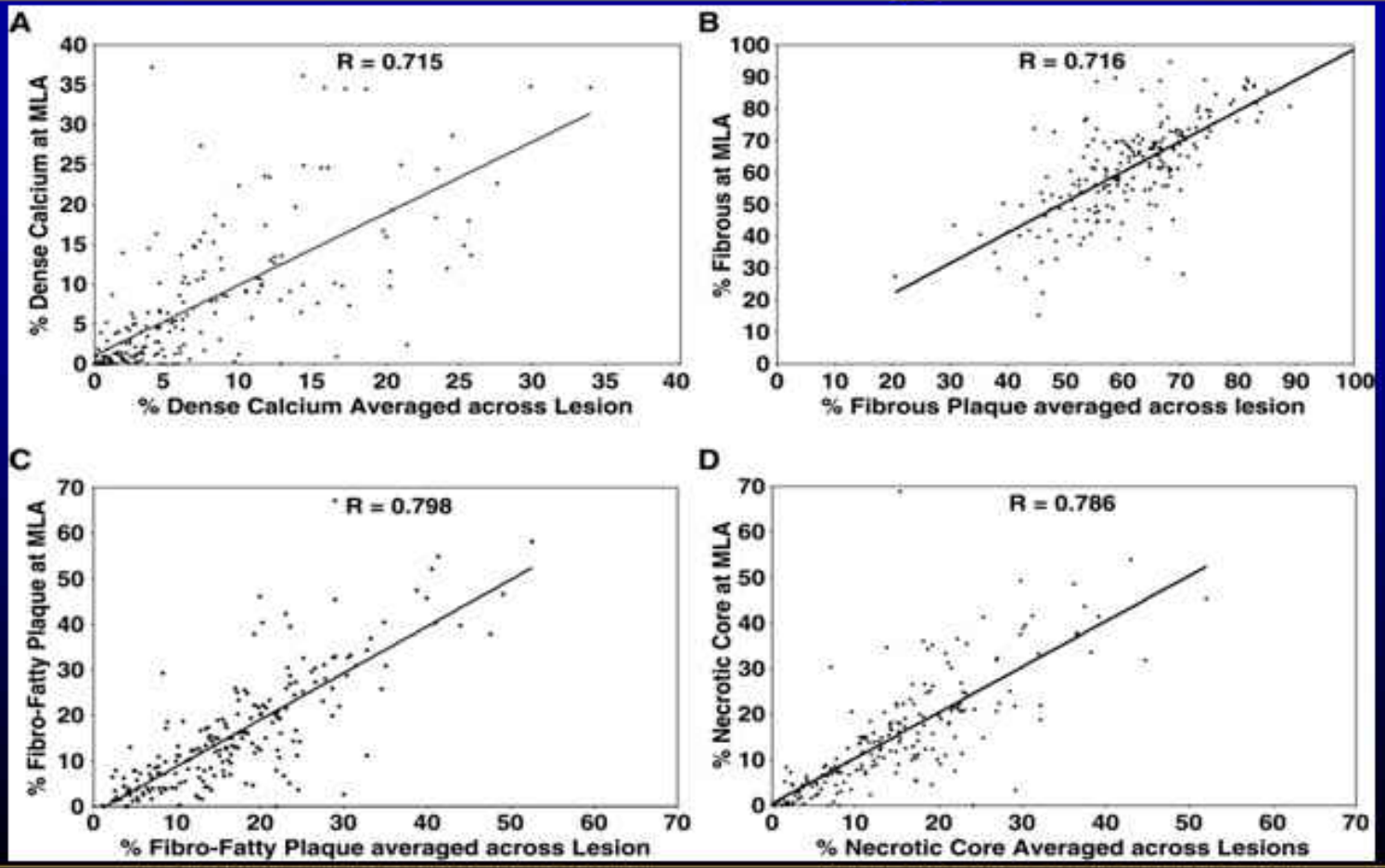
- Among pts with > one lesion:
  - 34 (46%) had lesions of single phenotype
  - 37 (50%) had lesions of two phenotypes
  - 3 (4%) had lesions of three phenotypes
- Trend for clustering of culprit plaques to phenotypes 2 and 3 (p = 0.077)

IVUS-VH Derived Plaque Phenotyping in Coronary Arteries of Patients Undergoing PCI

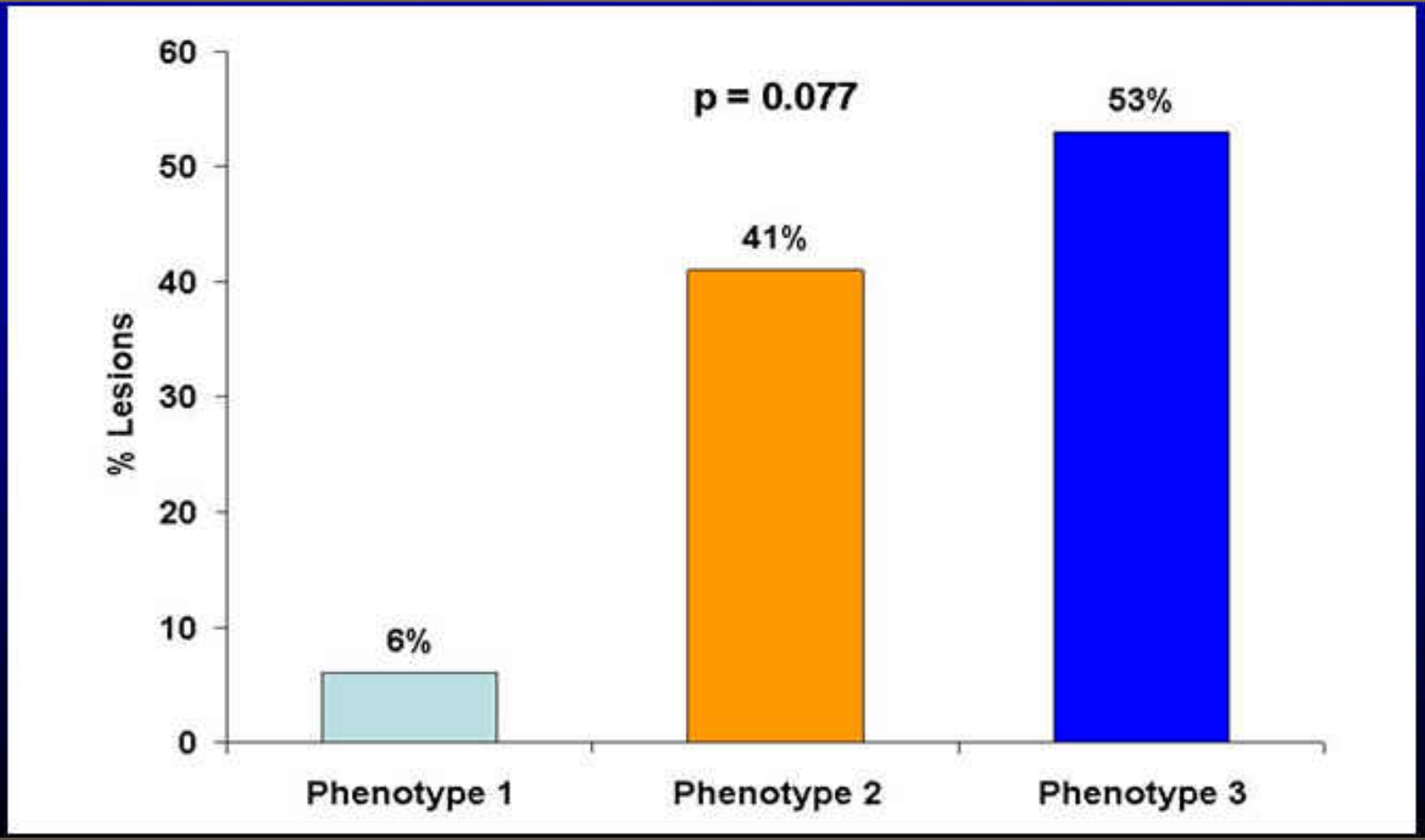
N = 76		N (%)
Age (yrs ± SD)		64.1 ± 11.9
Male		50 (69)
Caucasian		70 (92)
Diabetes		22 (30)
Prior MI		16 (22)
Hypercholesterolemia		62 (85)
CHF		8 (11)
Procedure type:	ACS	32 (42)
	Elective	44 (58)
ACS type:	Unstable angina	12 (37)
	Non-STEMI	7 (22)
	STEMI	13 (41)
Index vessel		209 (100)
	LAD	100 (48)
	LCX	44 (21)
	RCA	65 (31)
Lesions evaluated with IVUS		209 (100)
	Culprit	83 (40)
	Non-culprit	126 (60)

IVUS-VH Derived Plaque Phenotyping in Coronary Arteries of Patients Undergoing PCI

Correlation Between Lesion Segment and MLA



IVUS-VH Derived Plaque Phenotyping in Coronary Arteries of Patients Undergoing PCI



IVUS-VH Derived Plaque Phenotyping in Coronary Arteries of Patients Undergoing PCI

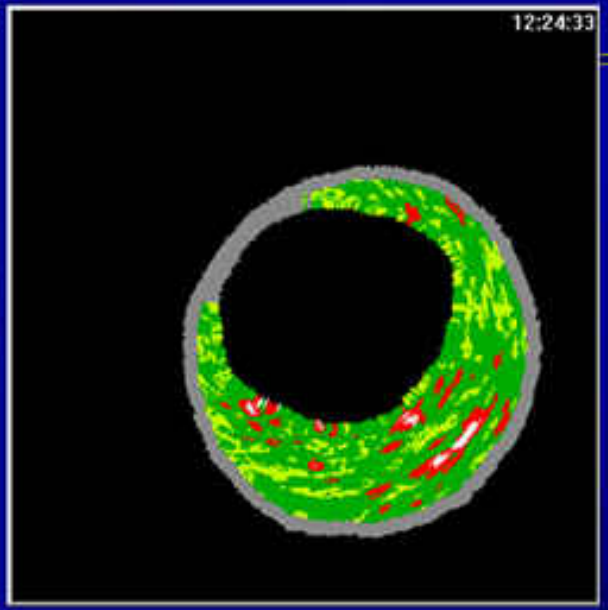
Mid America Heart Institute

- Three experienced, independent IVUS technicians performed quantitative assessment of media-adventitia border, the lumen, lesion of interest, and proximal and distal 5 mm
- Identify 4 basic plaque types
  - Fibrous – dark green
  - Fibro-fatty – light green
  - Dense Ca^{++} – Wwhite
  - Necrotic Core - Red

Clinical Correlates of Virtual Histology
Take-Home Message

- Routine use of IVUS essential for reducing restenosis rates in DES
- Particularly useful if **stented length** ≥ 35-40 mm, **diabetic** patients, and in **multiple vessel** stenting

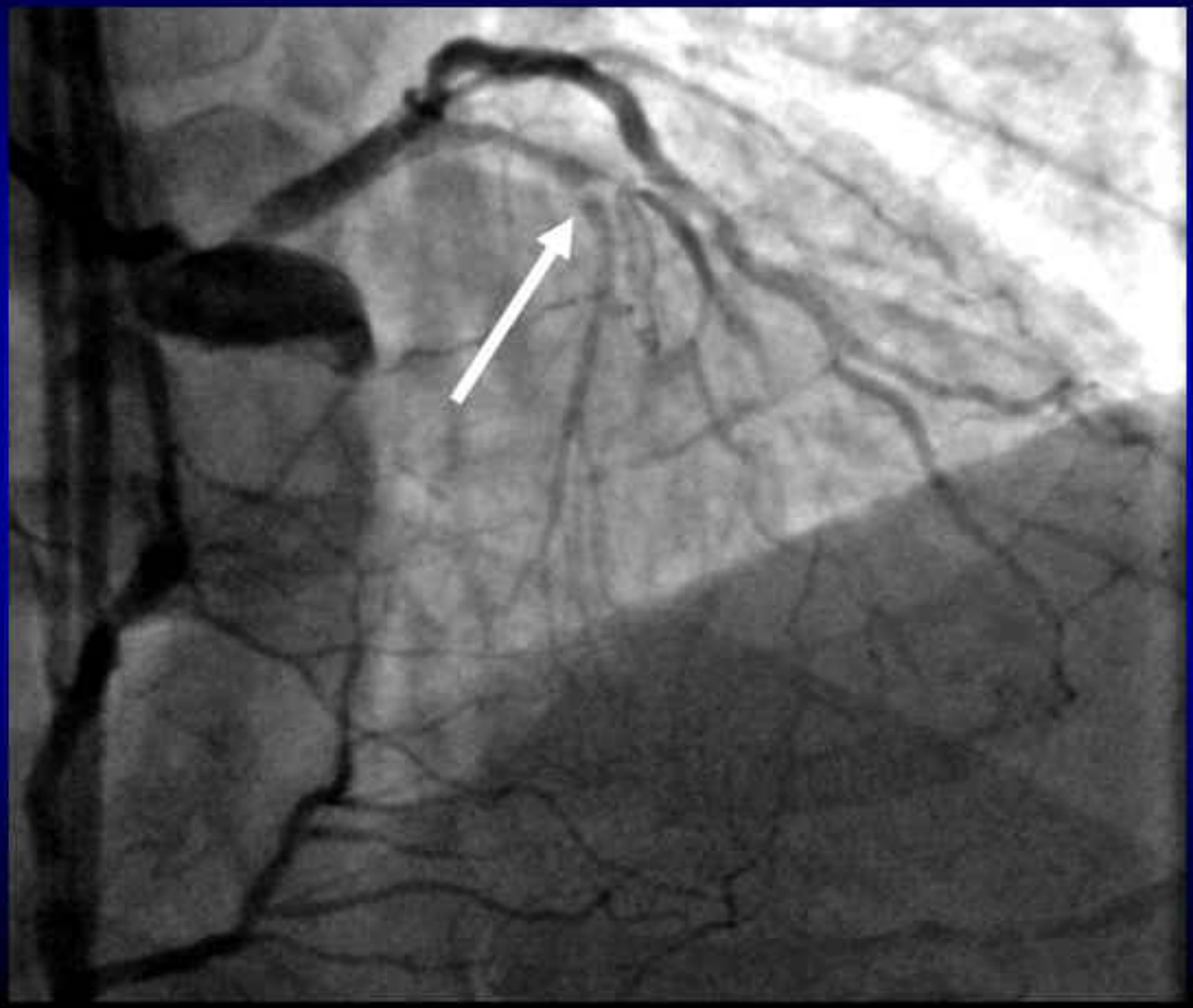
Drinovsky, Lee LCX



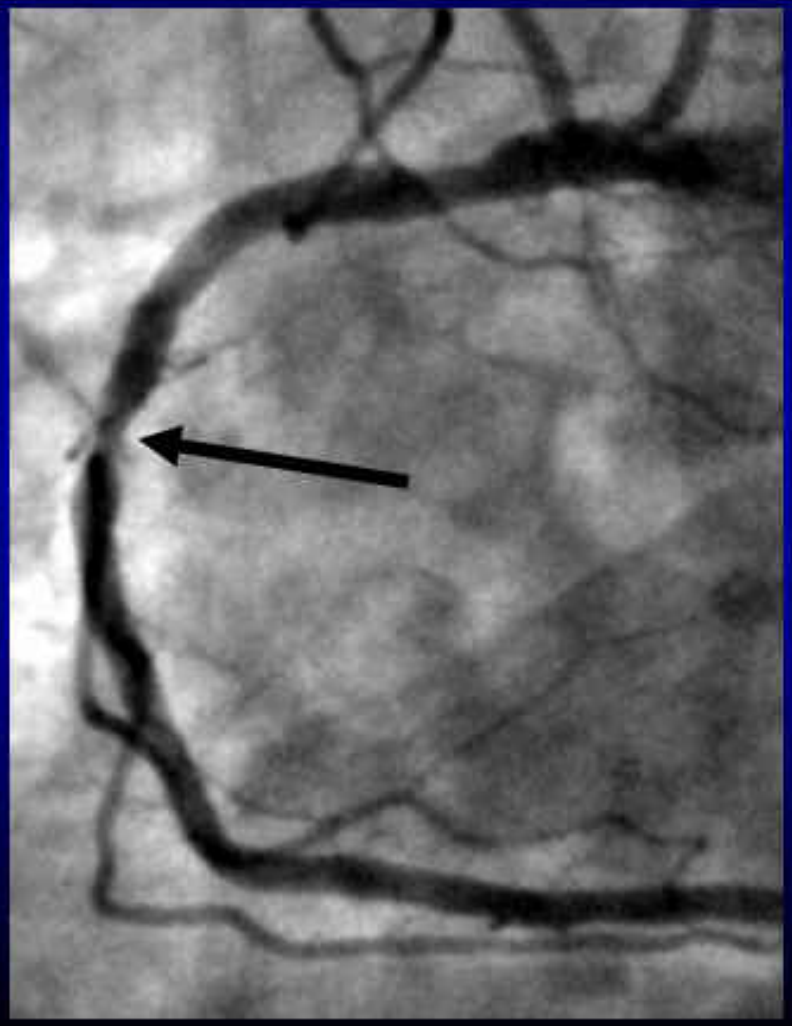
Lumen Area	11.5 mm²	
EEL Area	30.0 mm²	
Plaque Area	18.5 mm²	
% Plaque Burden	62 %	
Fibrous Area	9.7 mm²	71 %
Fibro-Fatty Area	2.6 mm²	19 %
Dense Calcium Area	0.2 mm²	1 %
Necrotic Core Area	1.2 mm²	9 %

More ...

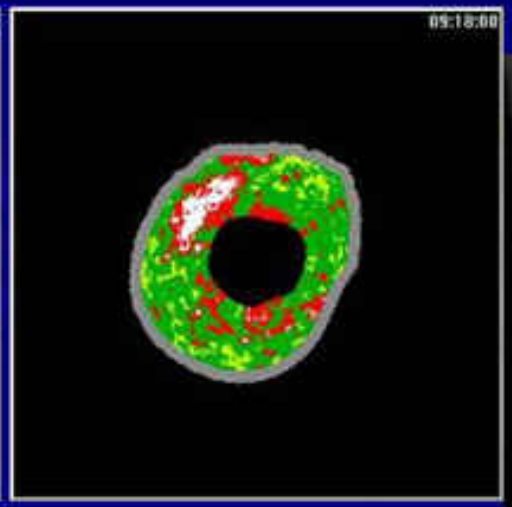
65-Year-Old Male: Unstable Angina

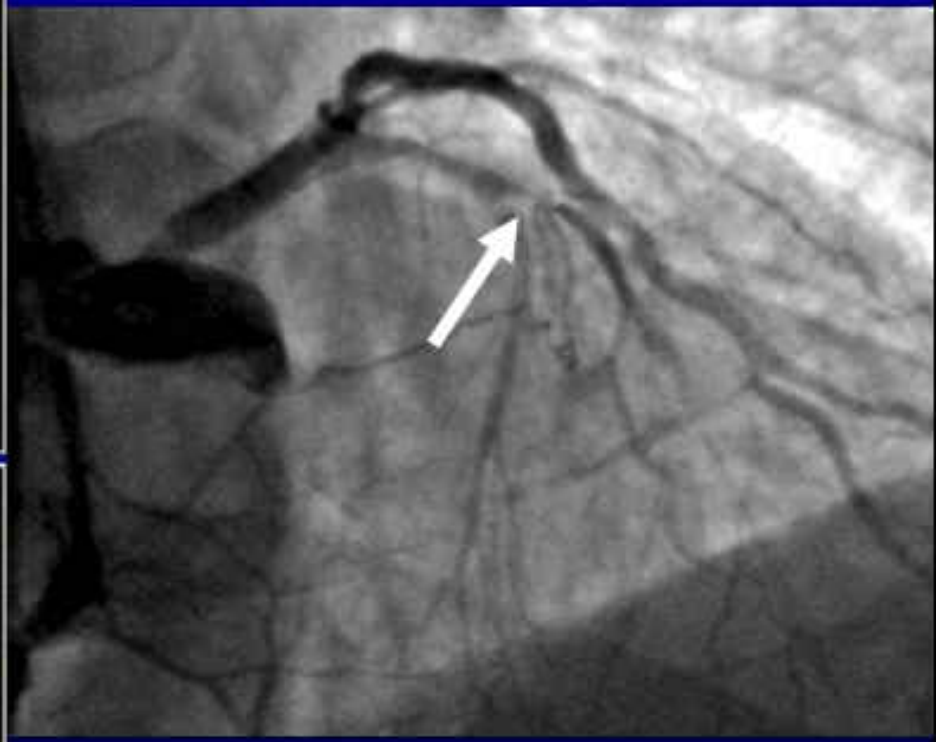


65-Year-Old Male: Unstable Angina



65-Year-Old Male: Unstable Angina

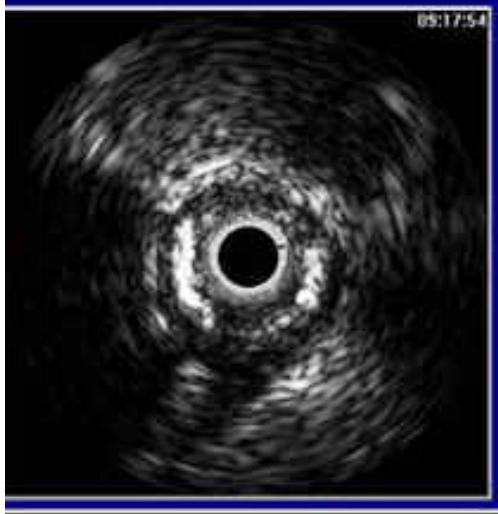


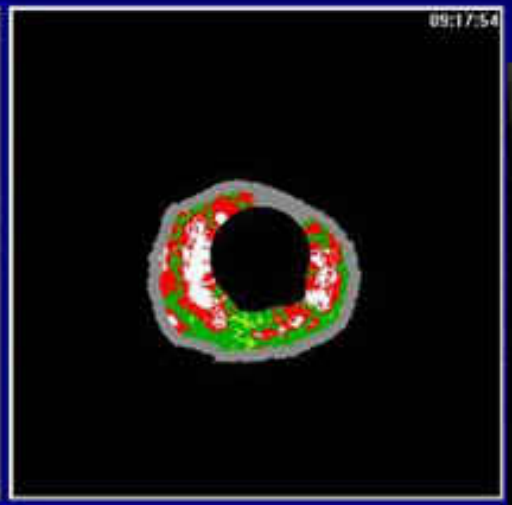


Lumen Area	3.0 mm²	
EEL Area	18.4 mm²	
Plaque Area	15.4 mm²	
% Plaque Burden	84 %	
Fibrous Area	7.3 mm²	61 %
Fibro-Fatty Area	1.3 mm²	11 %
Dense Calcium Area	0.8 mm²	7 %
Necrotic Core Area	2.5 mm²	21 %

More ...

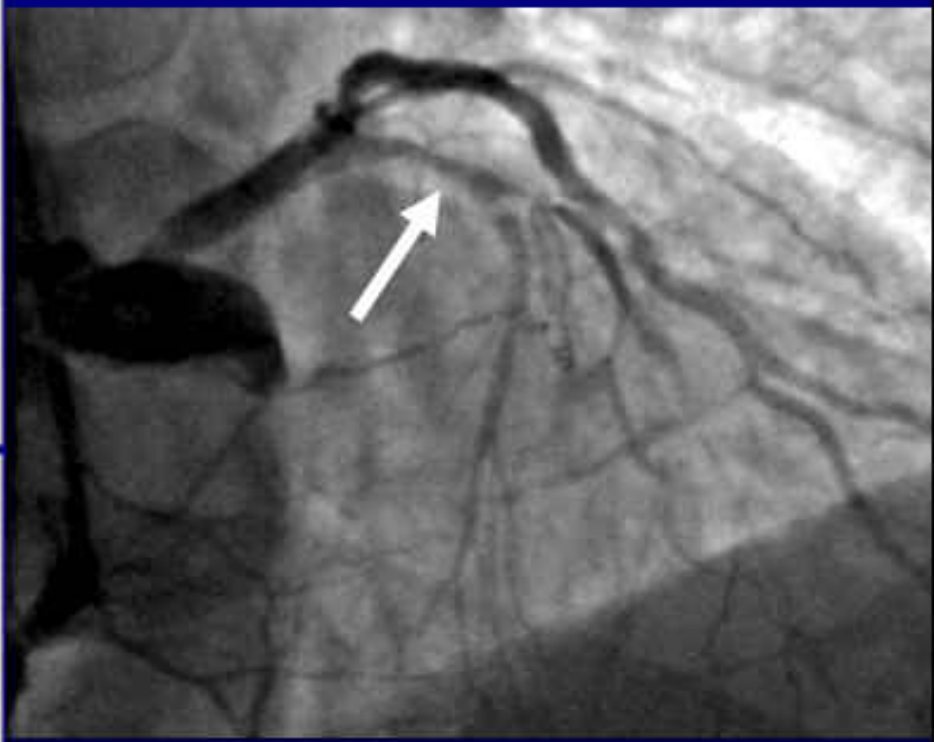
65-Year-Old Male: Unstable Angina



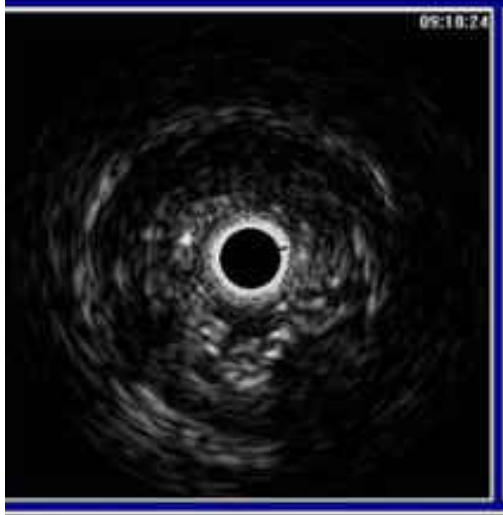


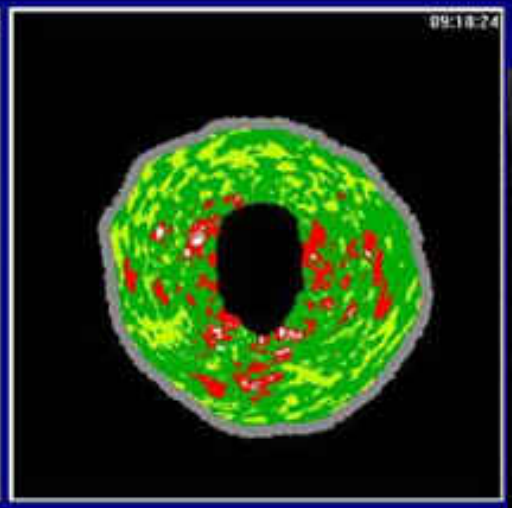
Lumen Area	3.6 mm²	
EEL Area	12.8 mm²	
Plaque Area	9.2 mm²	
% Plaque Burden	72 %	
Fibrous Area	2.2 mm²	36 %
Fibro-Fatty Area	0.1 mm²	2 %
Dense Calcium Area	1.4 mm²	22 %
Necrotic Core Area	2.4 mm²	40 %

More ...



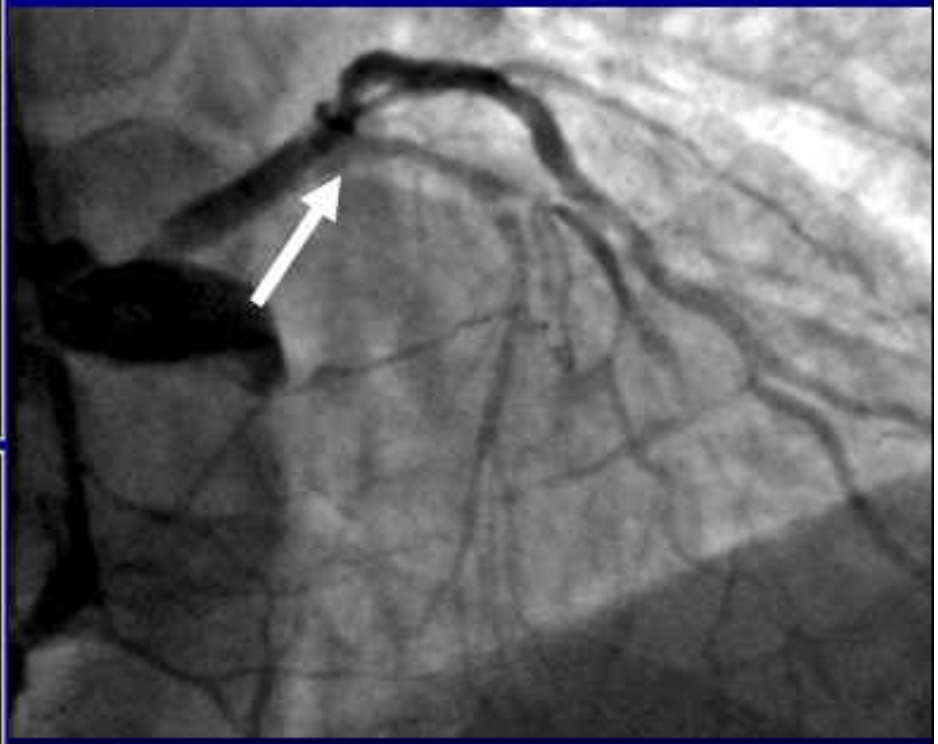
65-Year-Old Male: Unstable Angina



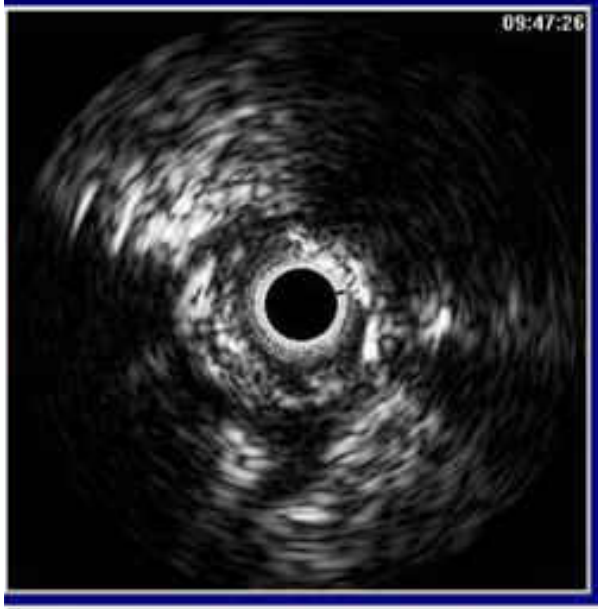


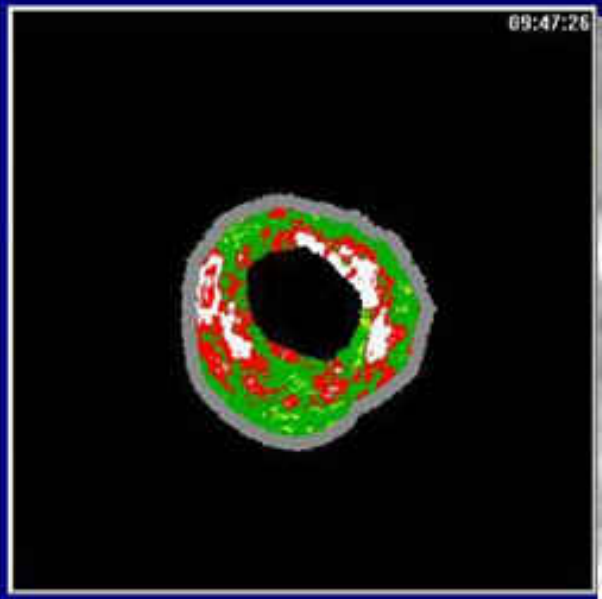
Lumen Area	4.0 mm²	
EEL Area	34.4 mm²	
Plaque Area	30.4 mm²	
% Plaque Burden	88 %	
Fibrous Area	16.9 mm²	66 %
Fibro-Fatty Area	5.1 mm²	20 %
Dense Calcium Area	0.3 mm²	1 %
Necrotic Core Area	3.2 mm²	13 %

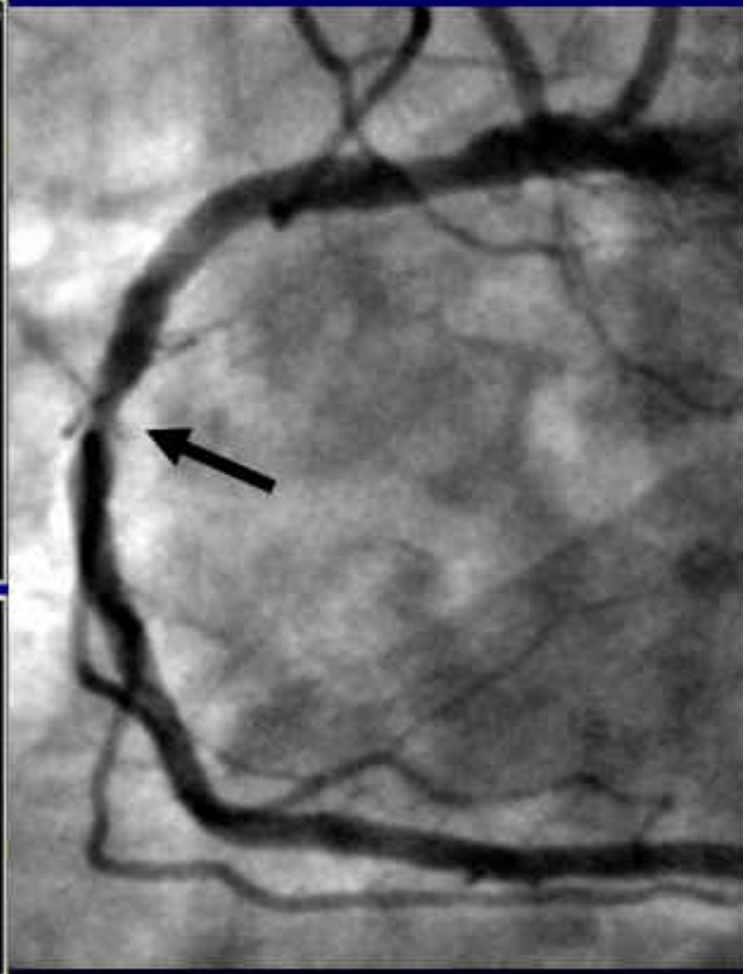
More ...



65-Year-Old Male: Unstable Angina

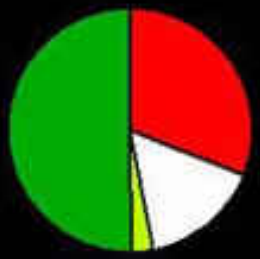




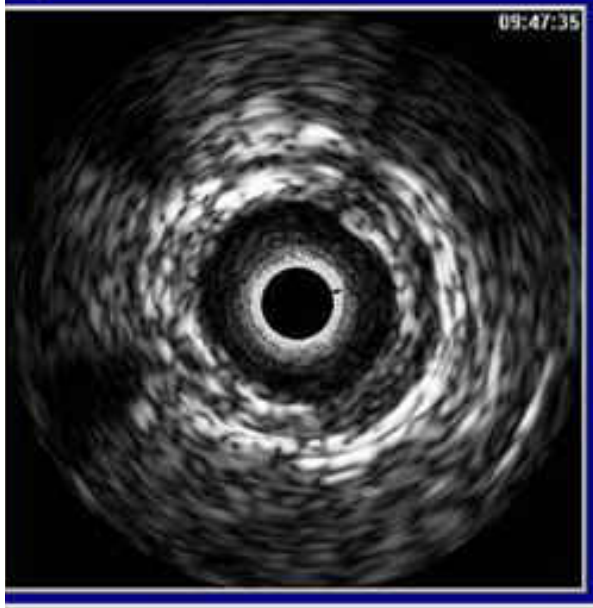


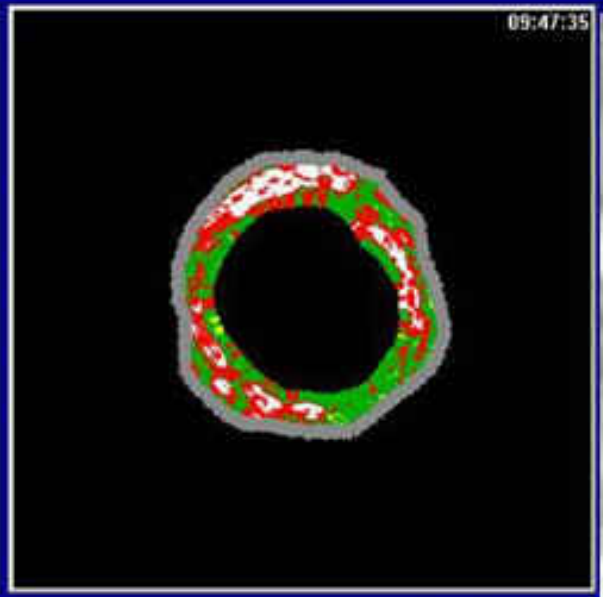
Lumen Area	2.9 mm²	
EEL Area	14.7 mm²	
Plaque Area	11.8 mm²	
% Plaque Burden	80 %	
Fibrous Area	4.3 mm²	50 %
Fibro-Fatty Area	0.3 mm²	3 %
Dense Calcium Area	1.4 mm²	16 %
Necrotic Core Area	2.7 mm²	31 %

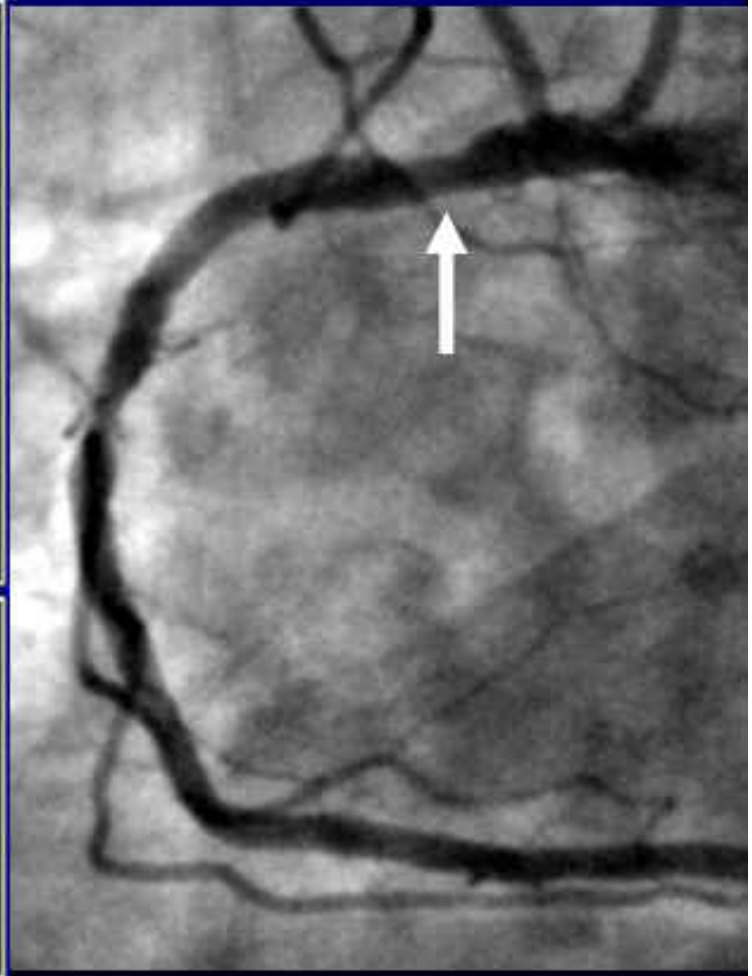
More ...



65-Year-Old Male: Unstable Angina



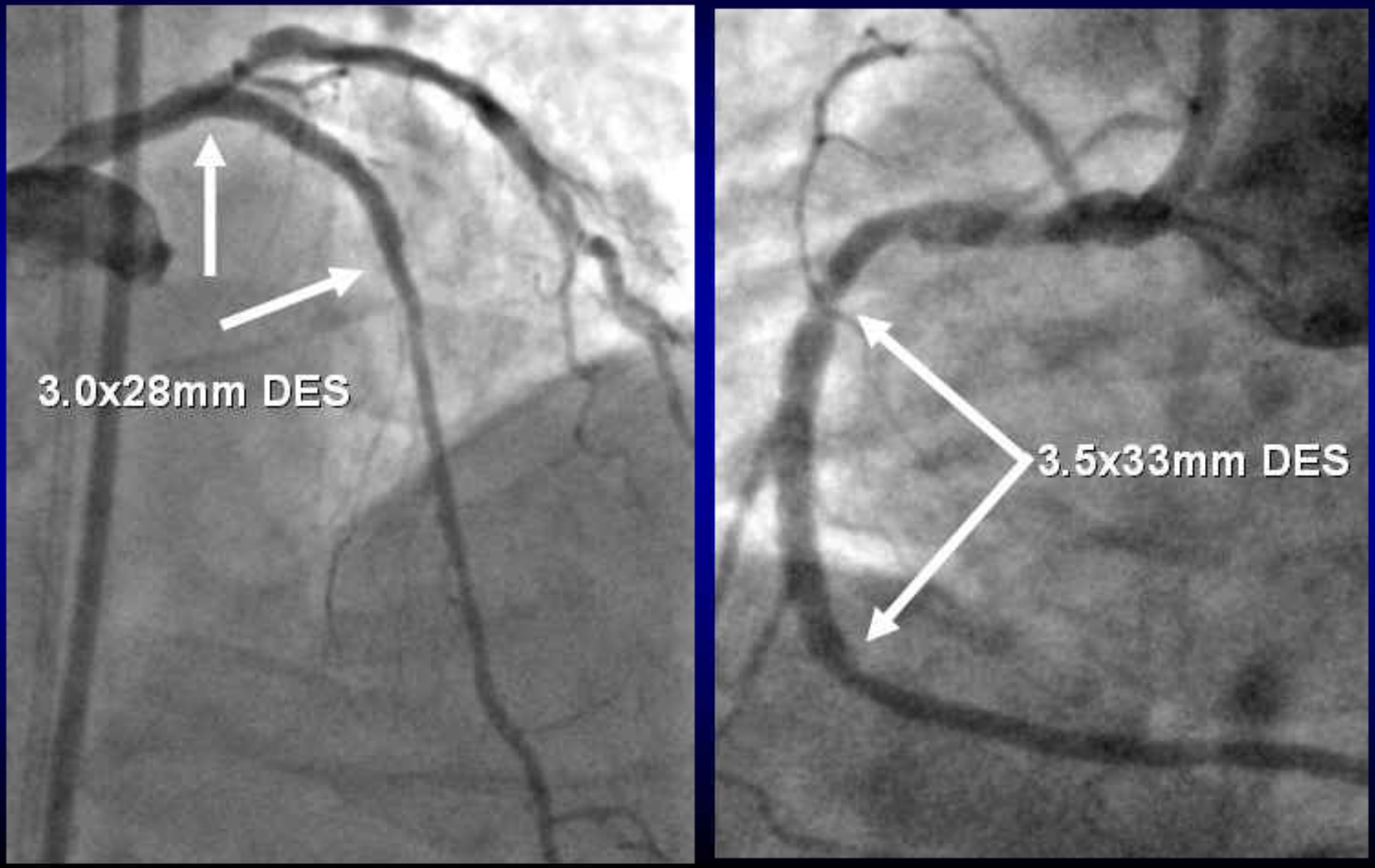




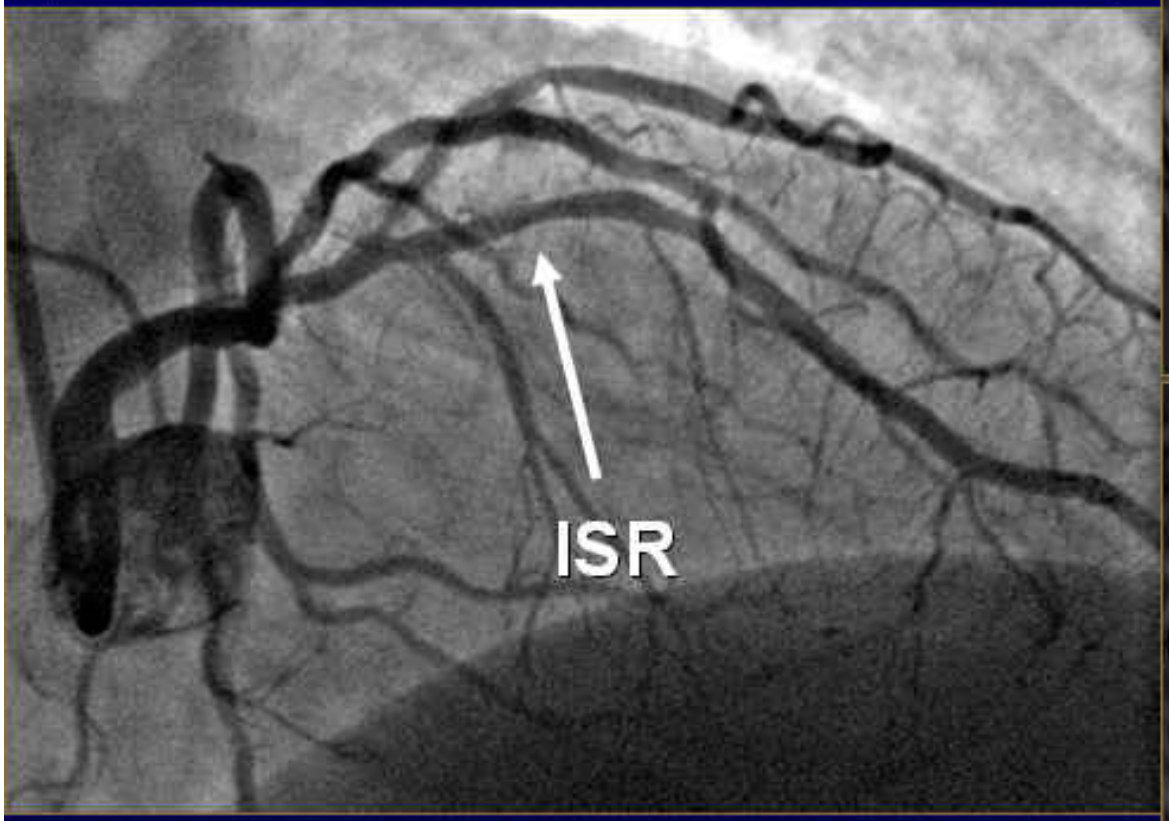
Lumen Area	7.9 mm²	
EEL Area	19.1 mm²	
Plaque Area	11.2 mm²	
% Plaque Burden	59 %	
Fibrous Area	3.3 mm²	43 %
Fibro-Fatty Area	0.1 mm²	2 %
Dense Calcium Area	1.4 mm²	18 %
Necrotic Core Area	2.8 mm²	37 %

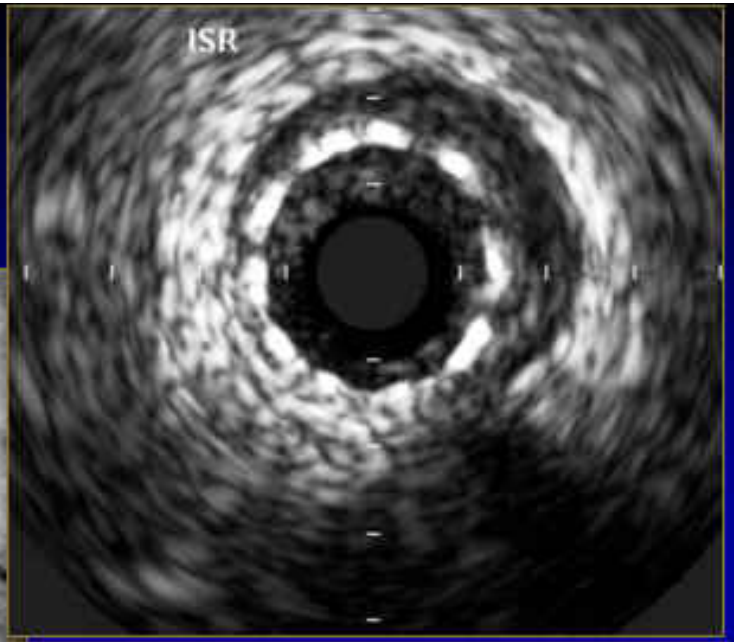
More ...

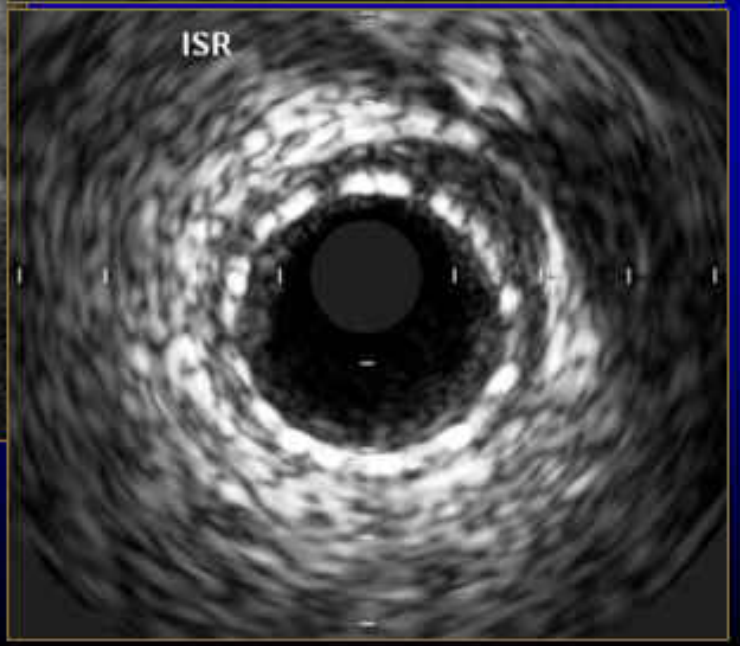
65-Year-Old Male: Unstable Angina



In-Stent Restenosis of DES in LAD





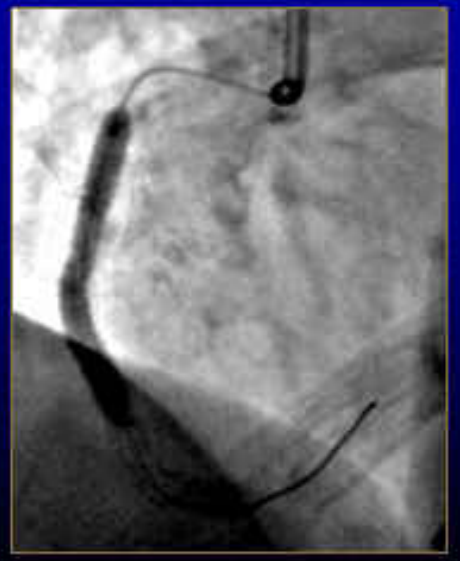


Use of Cypher™ DES in Long, Diffuse Lesions

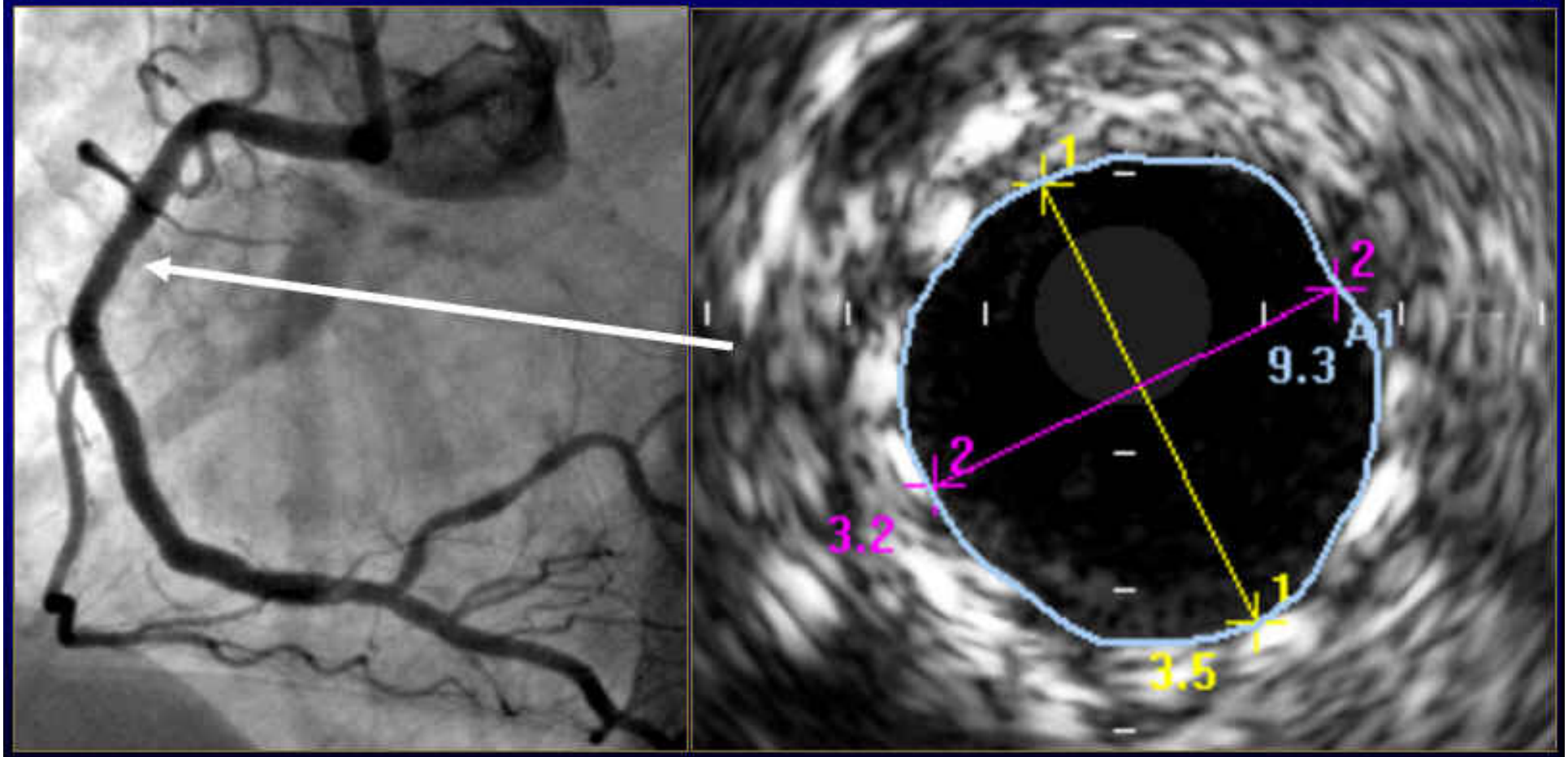
	Restenosis Rate
Stented Length ≥ 46 mm	13.5%
Stented Length < 46 mm	3.5%
Diabetes	9.9%
No Diabetes	6.3%
Multiple Vessel Stenting	12.1%

S.J. Park, Hawaii 2005

“Normal to Normal” DES Stenting



Appropriate Stent Apposition and CSA



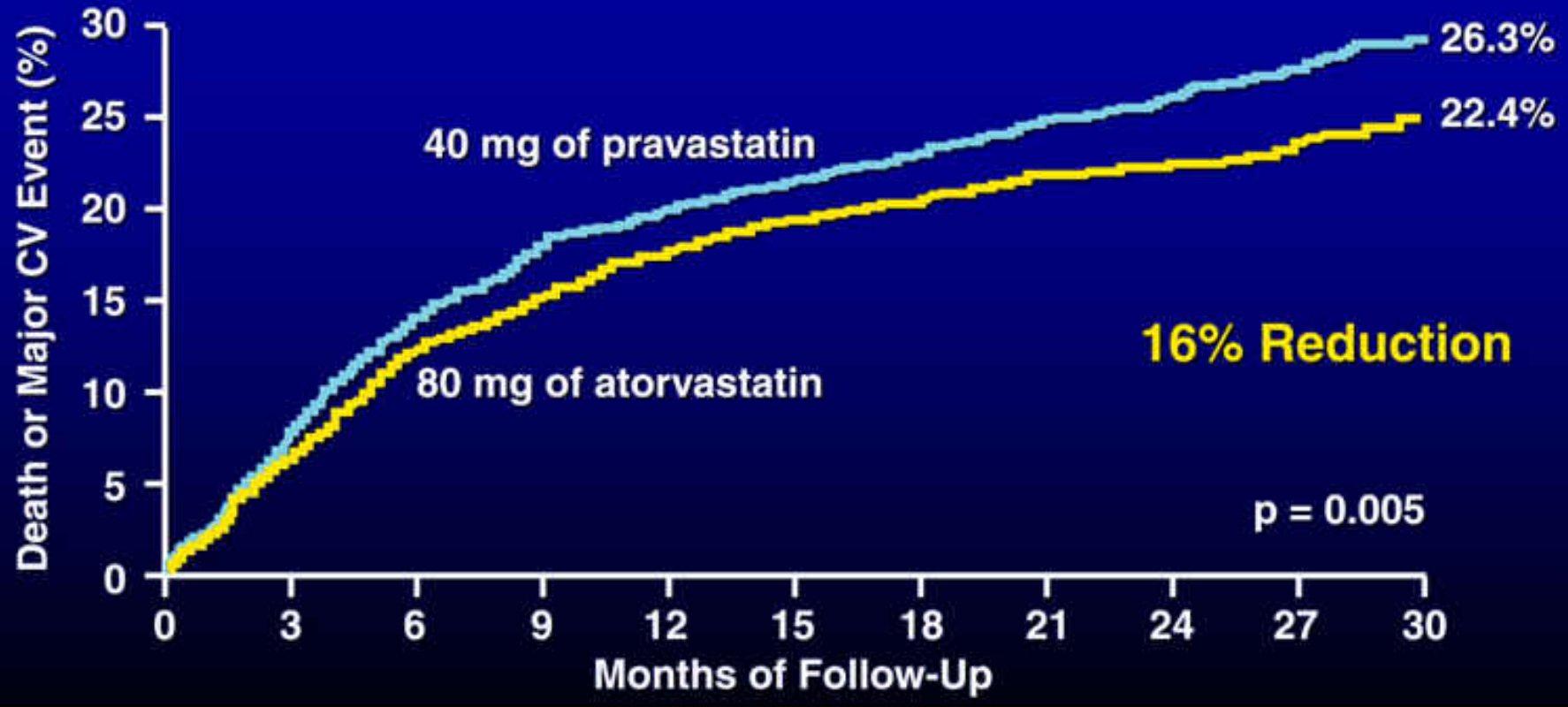
IVUS Guided Stent Deployment

Lower Restenosis Rates in DES Era

PROVE-IT TIMI-22 Trial

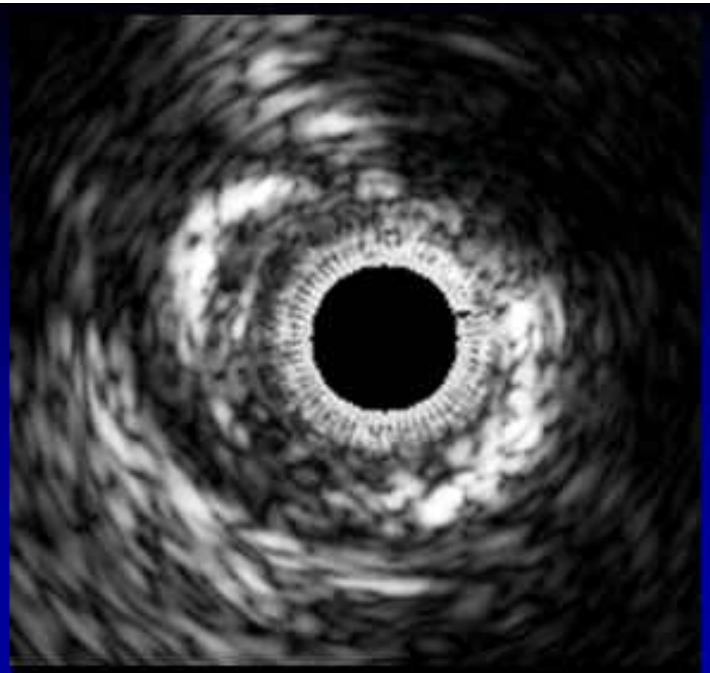
4162 Patients with ACS, F/U 30 Months

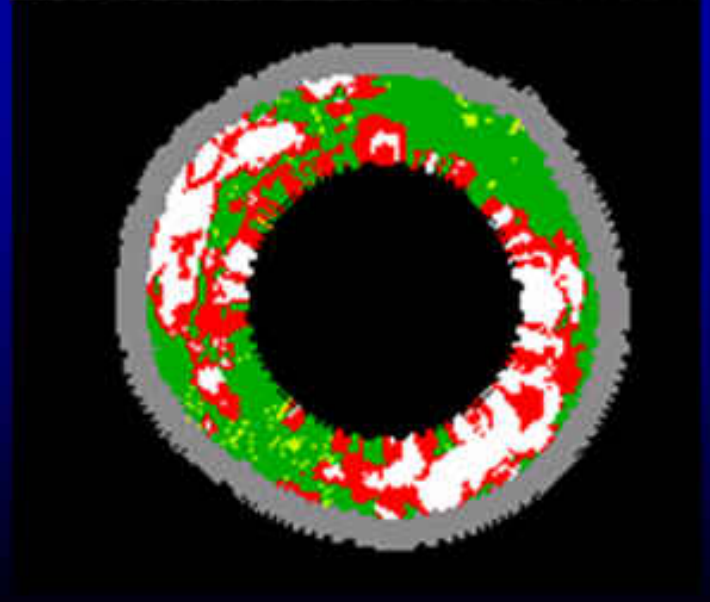
Major Event: *Death, AMI, UA, Rehospitalization, Revascularization, CVA*



C. Cannon et al. NEJM 2004;350:495

Vulnerable Plaque Can Be Modified by Aggressive Statin Therapy or ? Drug Eluting Stents

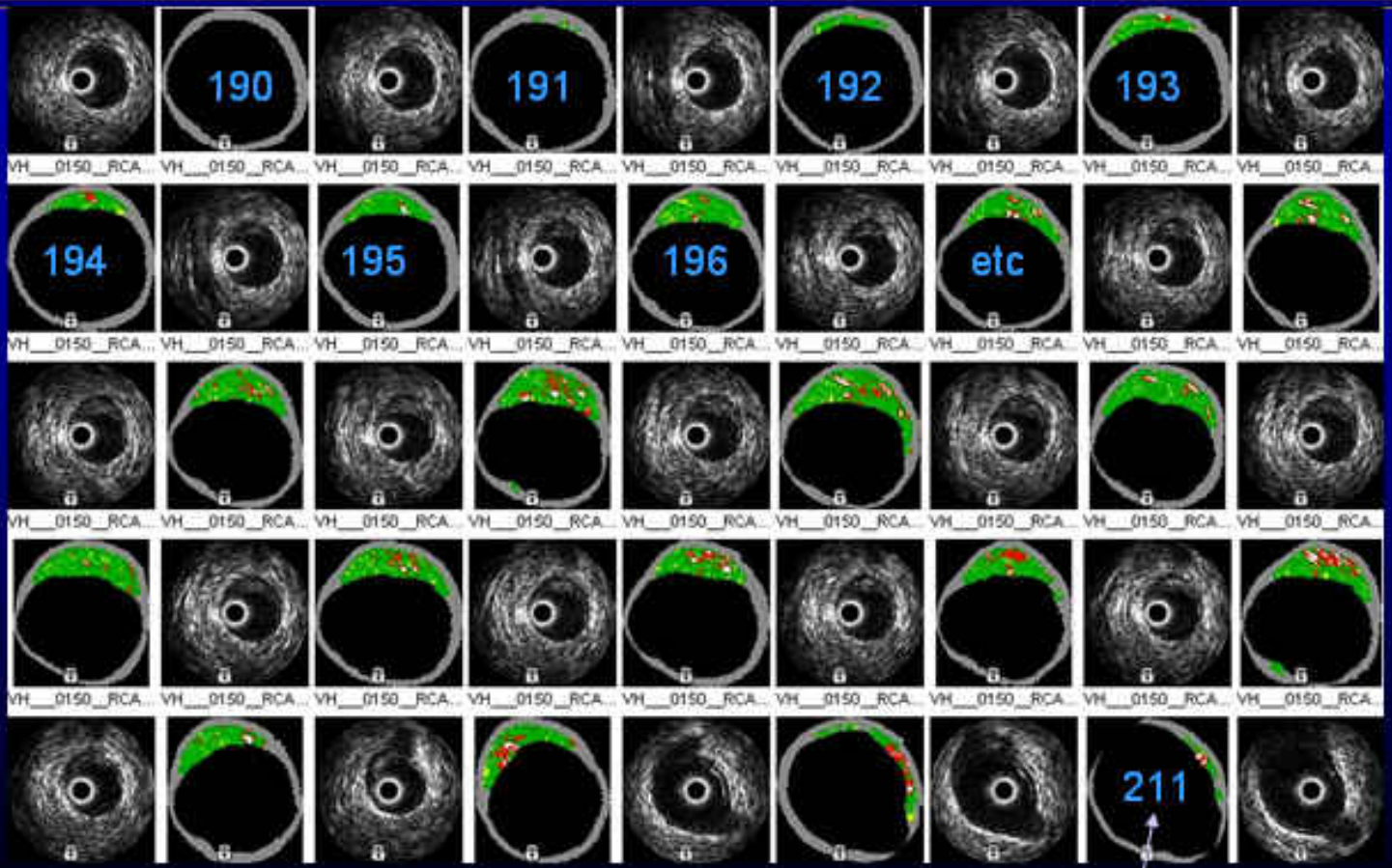




50-Year-Old Male
Acute Inferior STEMI

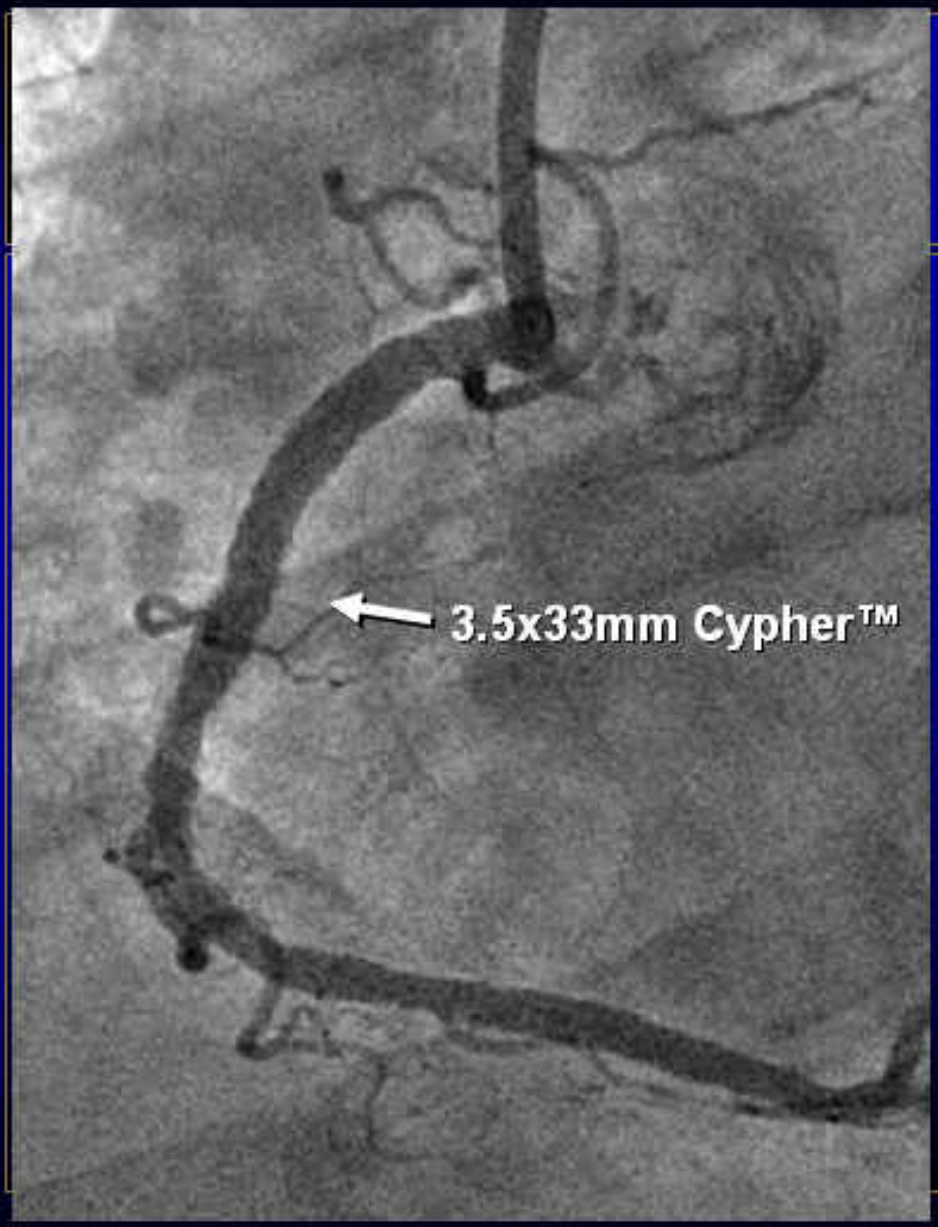
50-Year-Old Male, Acute Inferior STEMI

Proximal RCA, pathological Intimal Thickening



Frame number

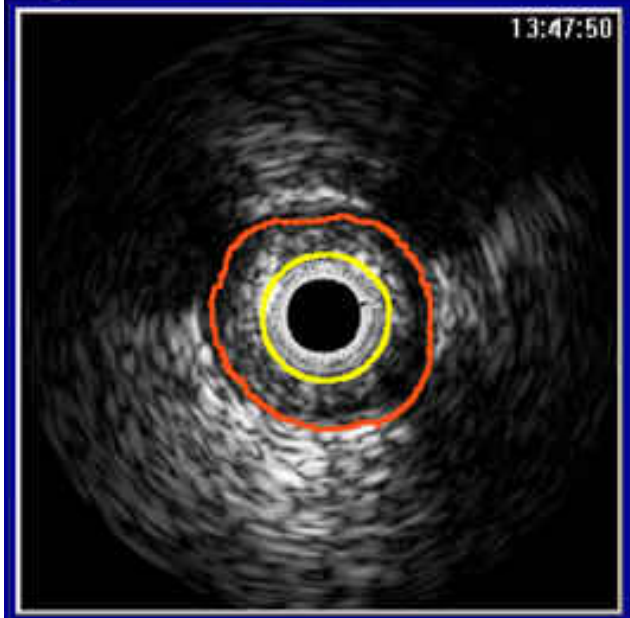
Last, most proximal frame

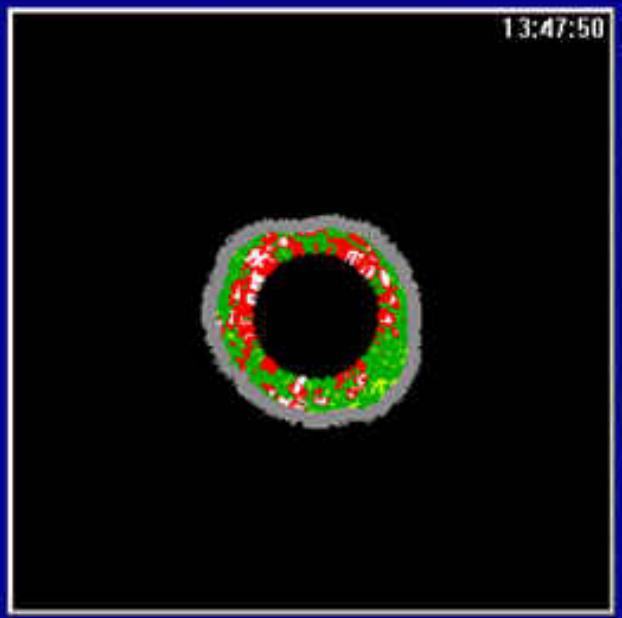


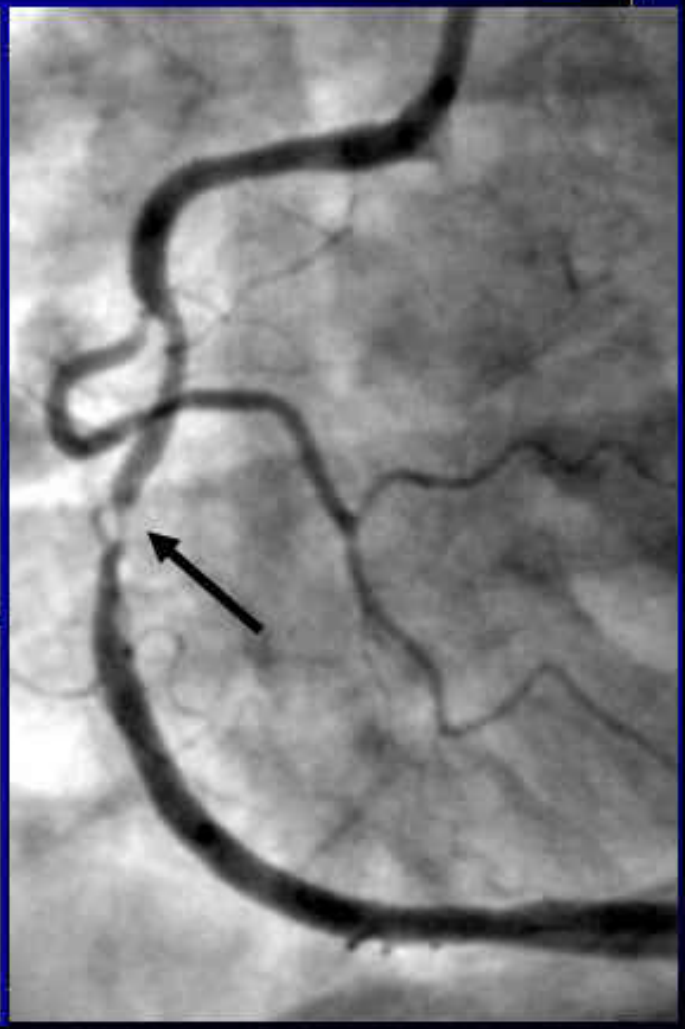
50-Year-Old Male

Acute Inferior STEMI

70-Year-Old Male
Acute Inferior STEMI (WF)







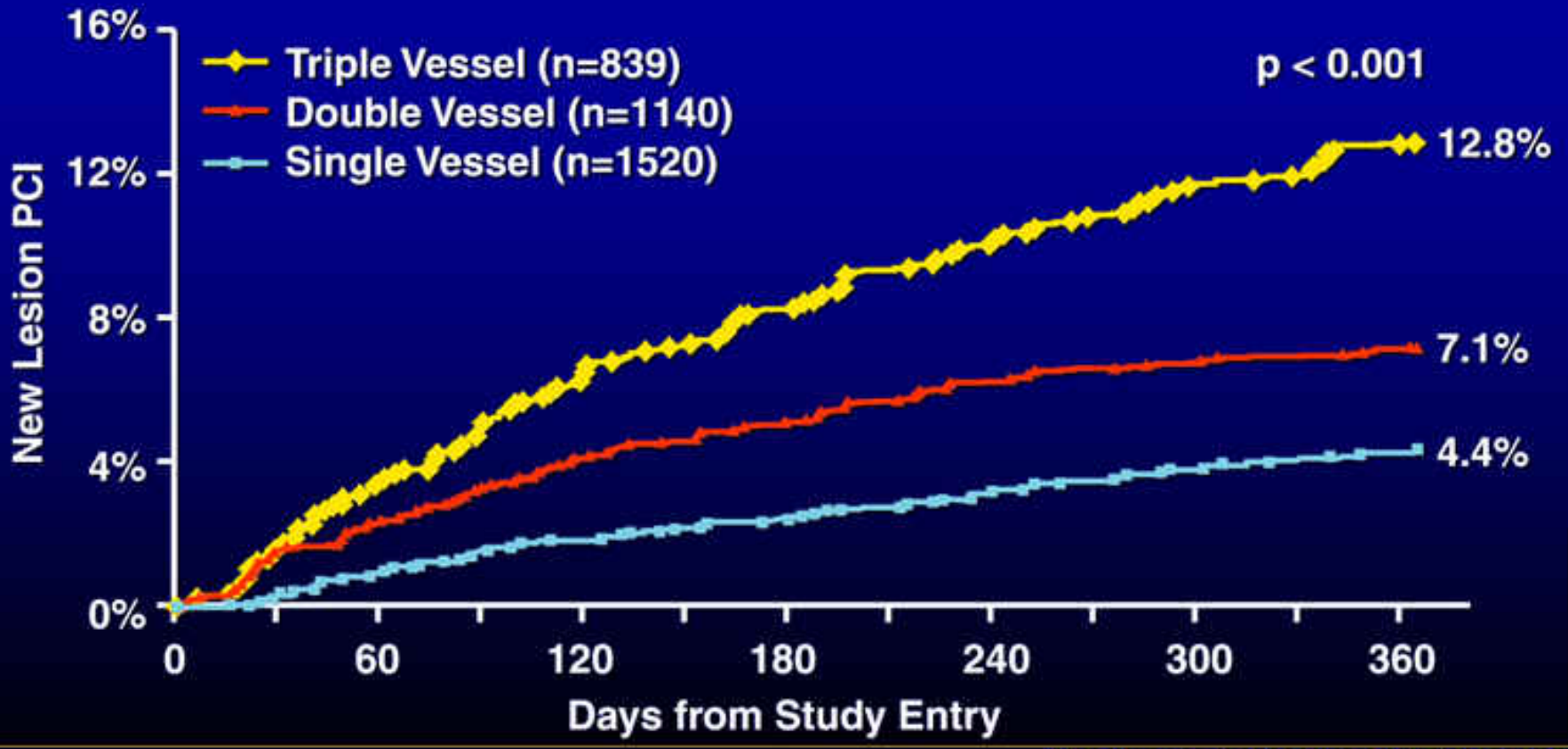
Lumen Area	3.5 mm²	
EEL Area	10.8 mm²	
Plaque Area	7.3 mm²	
% Plaque Burden	67 %	
Fibrous Area	2.5 mm²	53 %
Fibro-Fatty Area	0.2 mm²	4 %
Dense Calcium Area	0.5 mm²	10 %
Necrotic Core Area	1.5 mm²	33 %

More ...

Clinical Progression of Incidental, Asymptomatic Lesions Discovered During Culprit Vessel Coronary Intervention

NHLBI Registry. 3747 pts 1997-99. 1-yr f/u

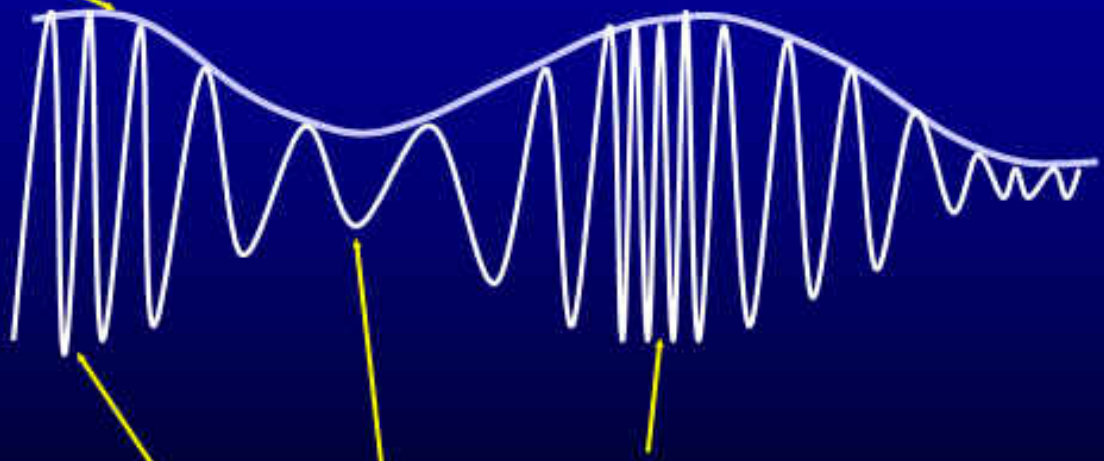
216 pts (5.8%) non-target PCI, mean f/u 163 ± 99 days



R. Glaser et al. Circ 2005;111:143

RF Backscatter from Tissue

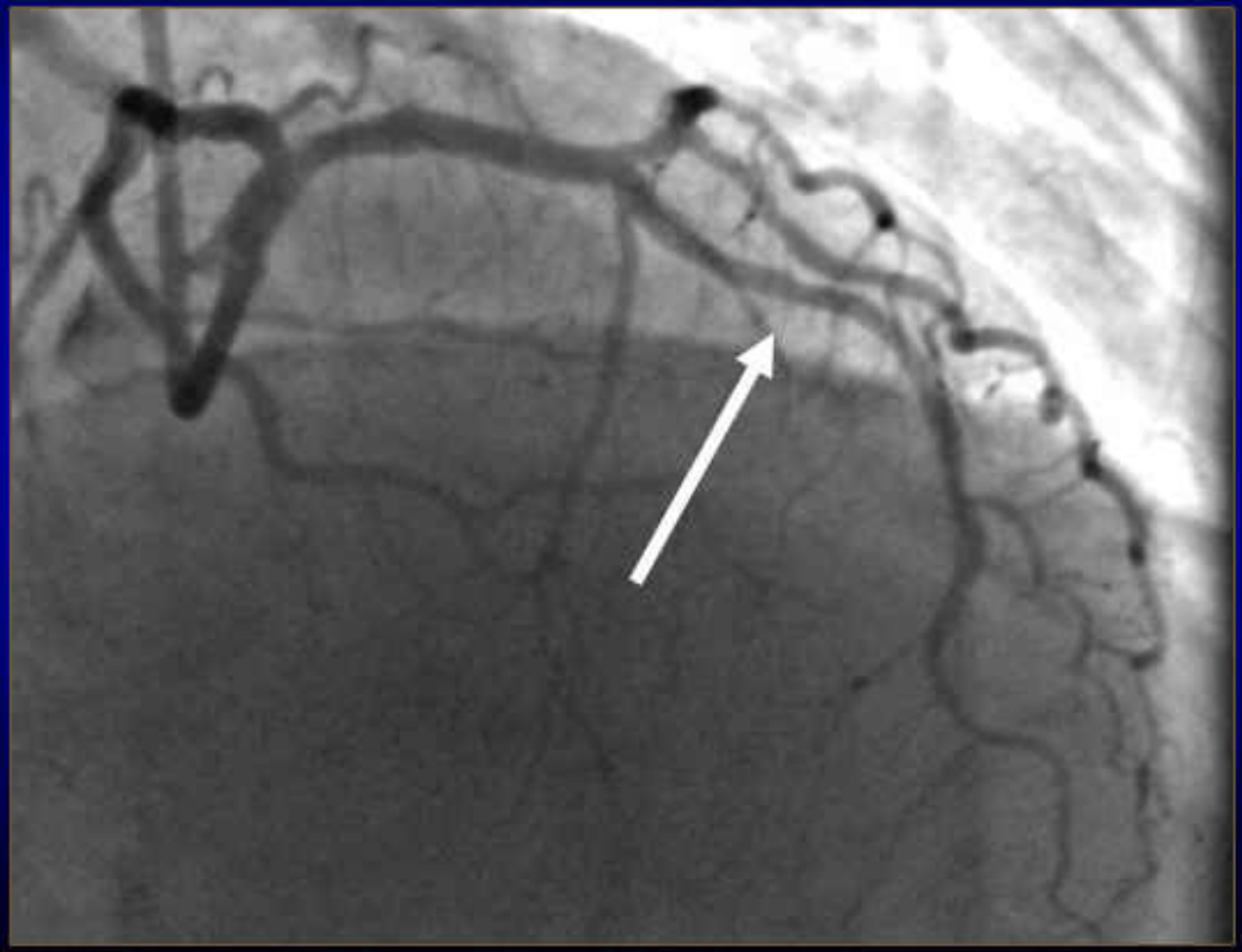
Gray-scale IVUS uses only the amplitude (echo intensity) in formation of the image



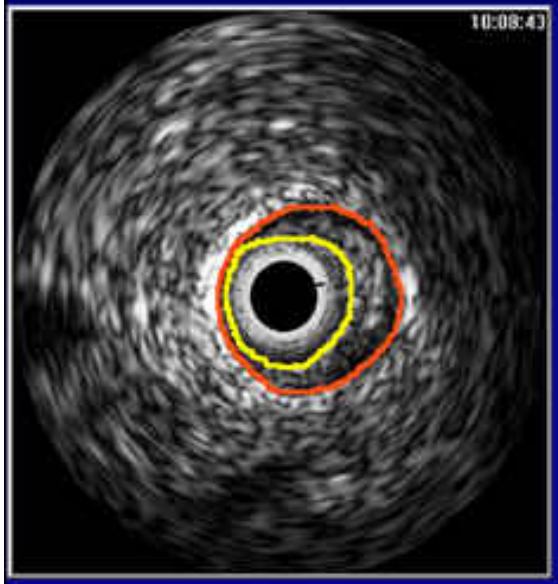
Frequency of echo signal can also vary, depending on the tissue…

Amplitude AND Frequency of Echoes used in Virtual Histology

44-Year-Old Female: Unstable Angina

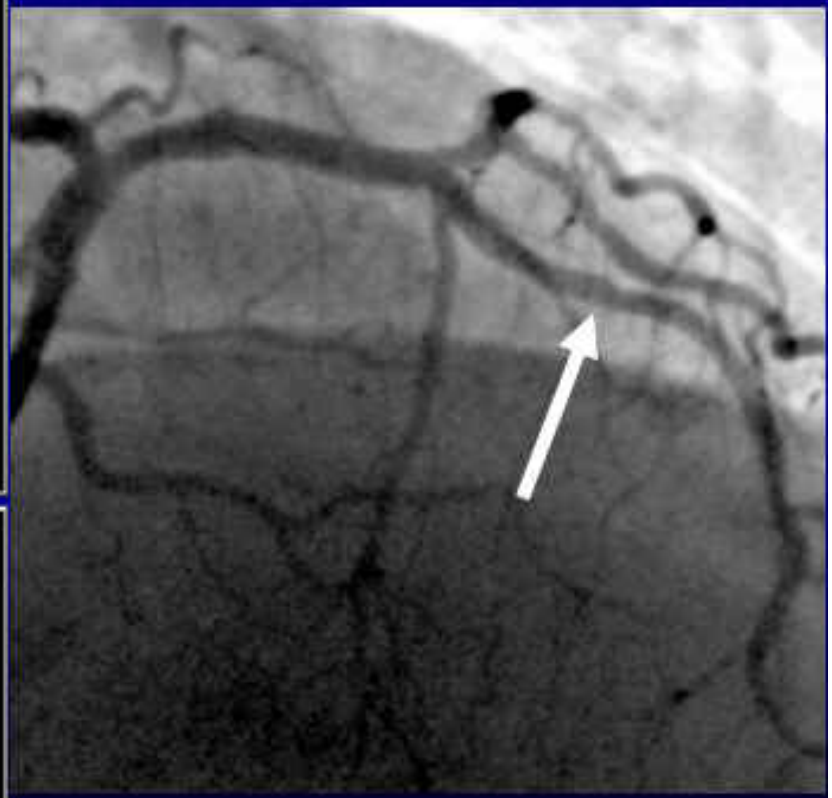


44-Year-Old Female: Unstable Angina

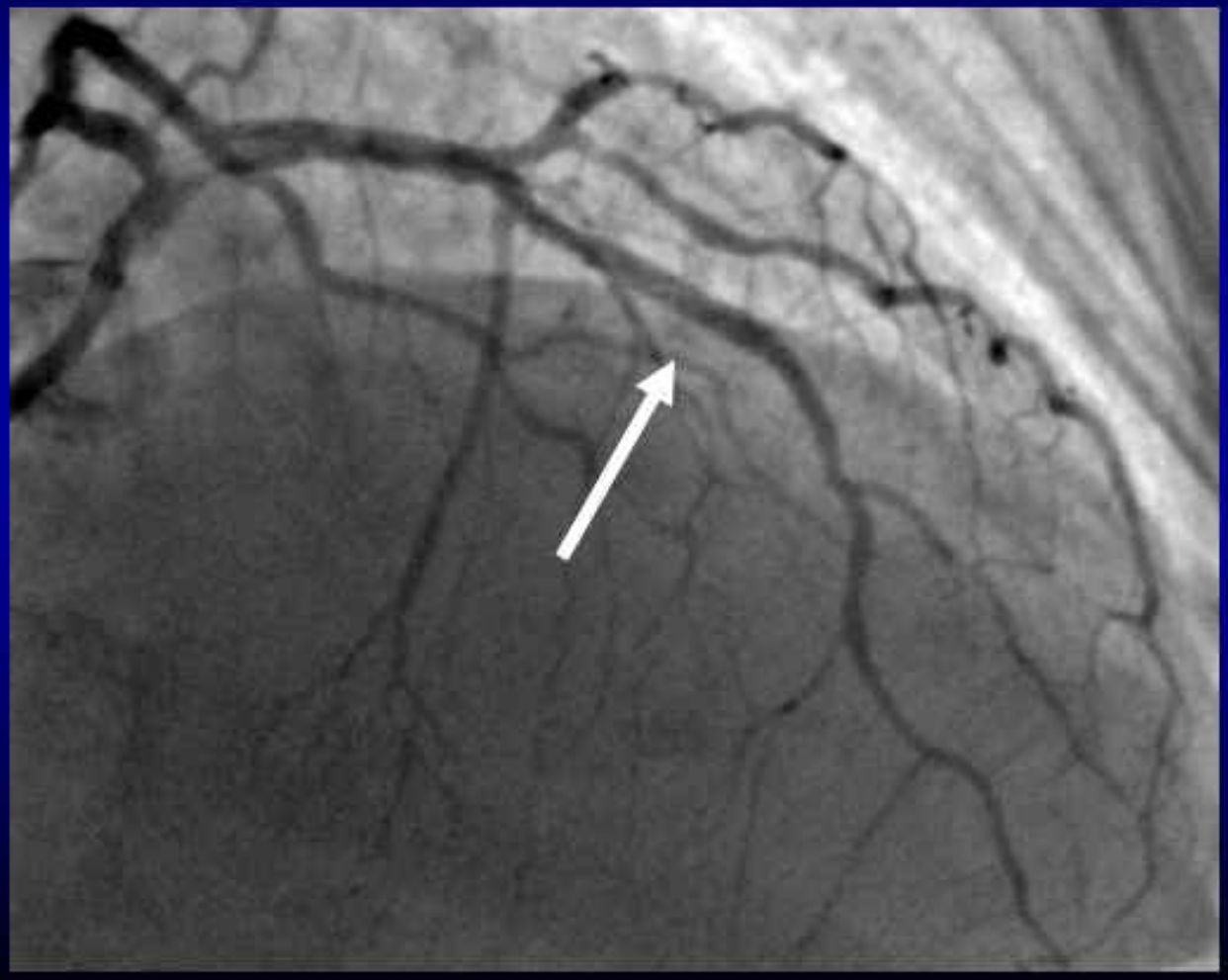


Lumen Area	4.3 mm²	
EEL Area	8.9 mm²	
Plaque Area	4.7 mm²	
% Plaque Burden	52 %	
Fibrous Area	1.4 mm²	66 %
Fibro-Fatty Area	0.0 mm²	1 %
Dense Calcium Area	0.1 mm²	3 %
Necrotic Core Area	0.6 mm²	30 %

More ...



44-Year-Old Female: Unstable Angina



Clinical Progression of Incidental, Asymptomatic Lesions Discovered During Culprit Vessel Coronary Intervention

NHLBI Registry. 3747 pts 1997-99. 1-yr f/u

216 pts (5.8%) non-target PCI,
mean f/u 163 ± 99 days

- 86.9% of lesions requiring repeat PCI ≤ 60% at original study
- Lesions < 50% at initial angio 60.5%
- Lesions > 70% at initial angio 13.4%
- MVD at original angio 76.4%

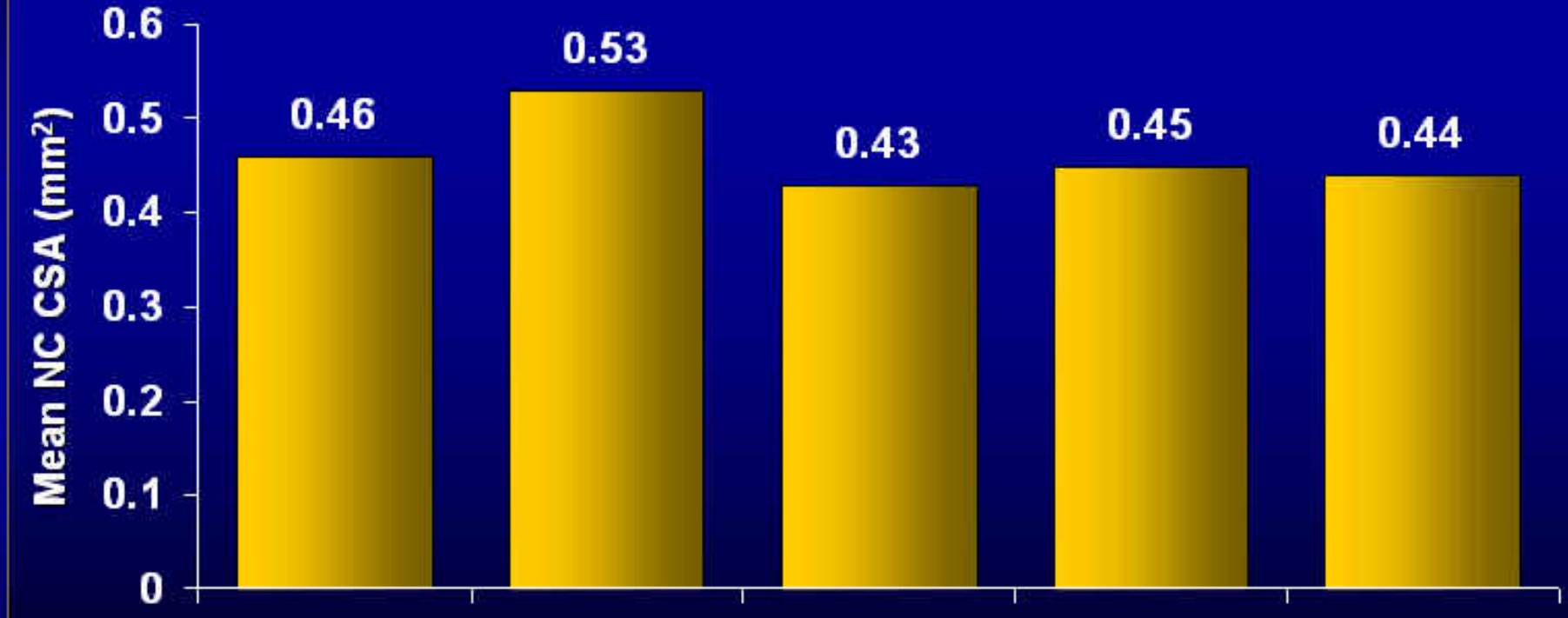
R. Glaser et al. Circ 2005;111:143

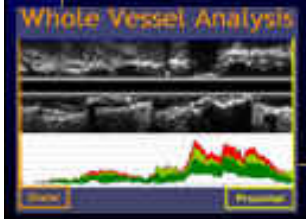
Clinical Progression of Incidental, Asymptomatic Lesions Discovered During Culprit Vessel Coronary Intervention

- Progression in same artery 39%
- Progression in different artery 61%
- Clinical Presentation:
  - Acute Coronary Syndrome 68.5%
  - Stable Angina 24.1%
  - Atypical Symptoms 6.8%

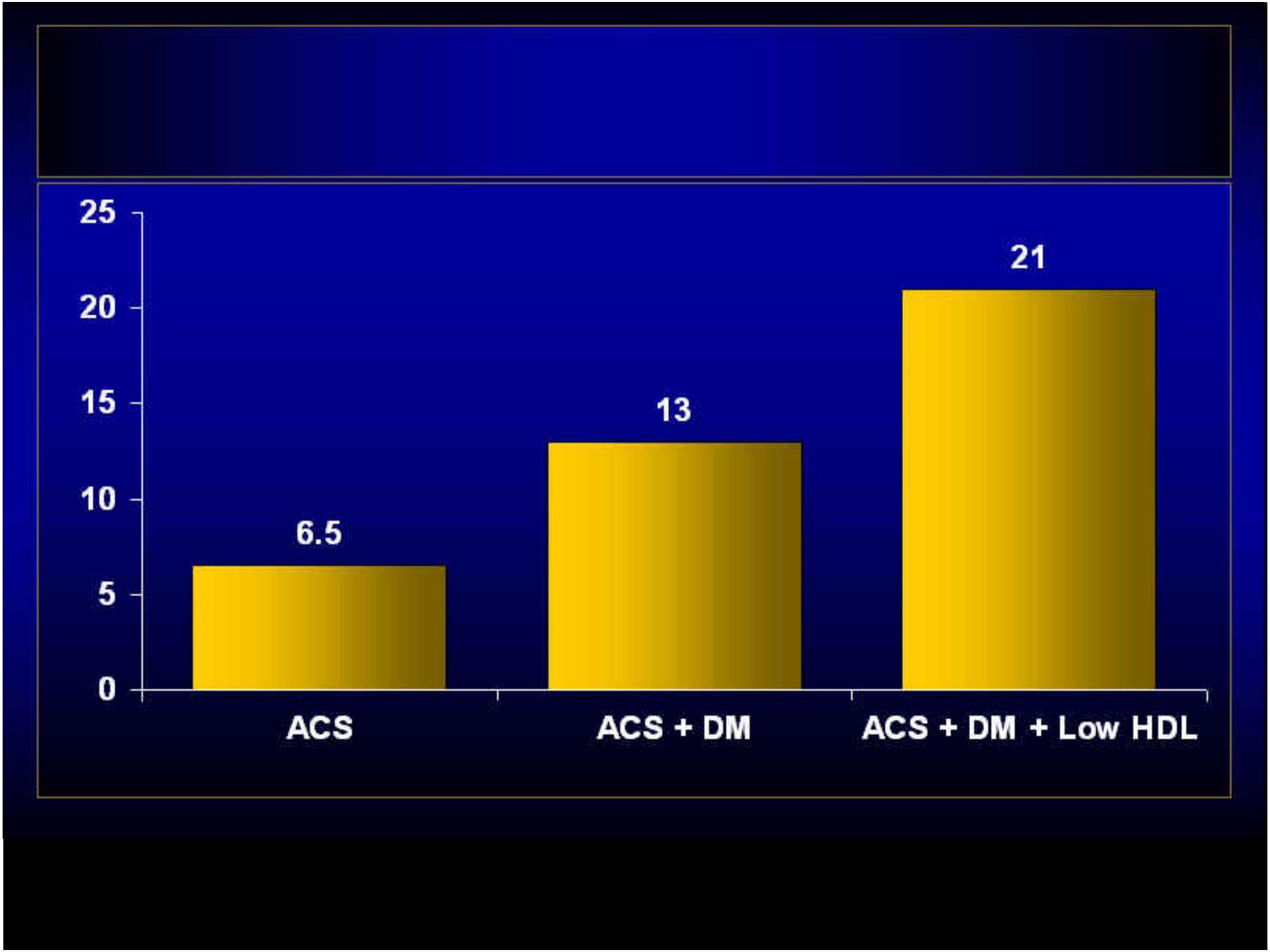
R. Glaser et al. Circ 2005;111:143

Non Q-Wave MI Pts had Highest Mean Necrotic Core CSA, but when Adjusted to Total Plaque Volume, Difference Not Significant



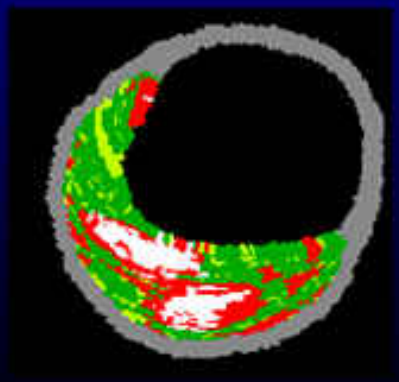


p =0.06 Stable Angina vs. non-Q wave MI


25
20
15
10
5
0
6.5
13
21
ACS
ACS + DM
ACS + DM + Low HDL

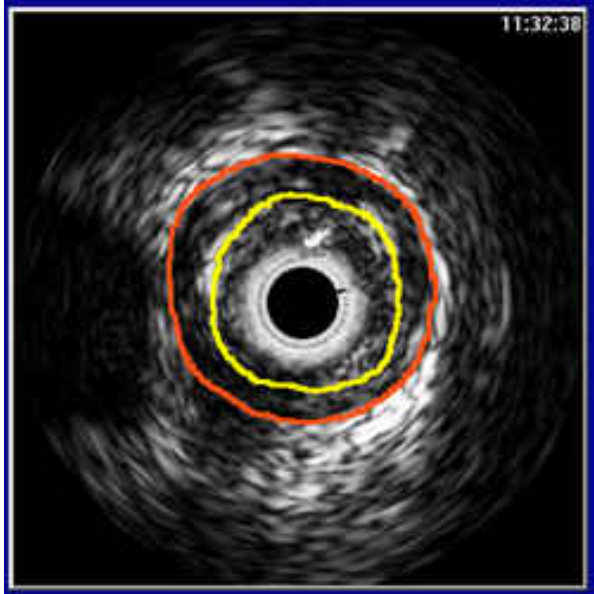
The FibroAtheroma

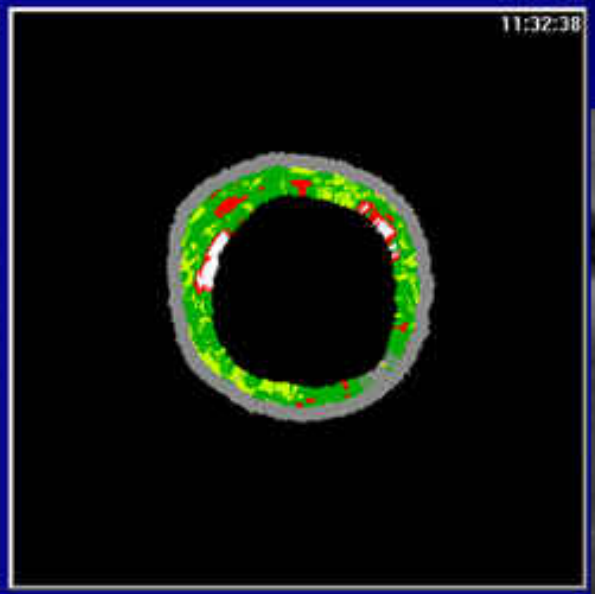
Fibrous and/or Fibro-Fatty plaques with Necrotic Core (>10% of total plaque volume). Goal of using VH to increase the value of IVUS will very likely be in differentiating the Fibro-Atheroma from the other three plaque types.

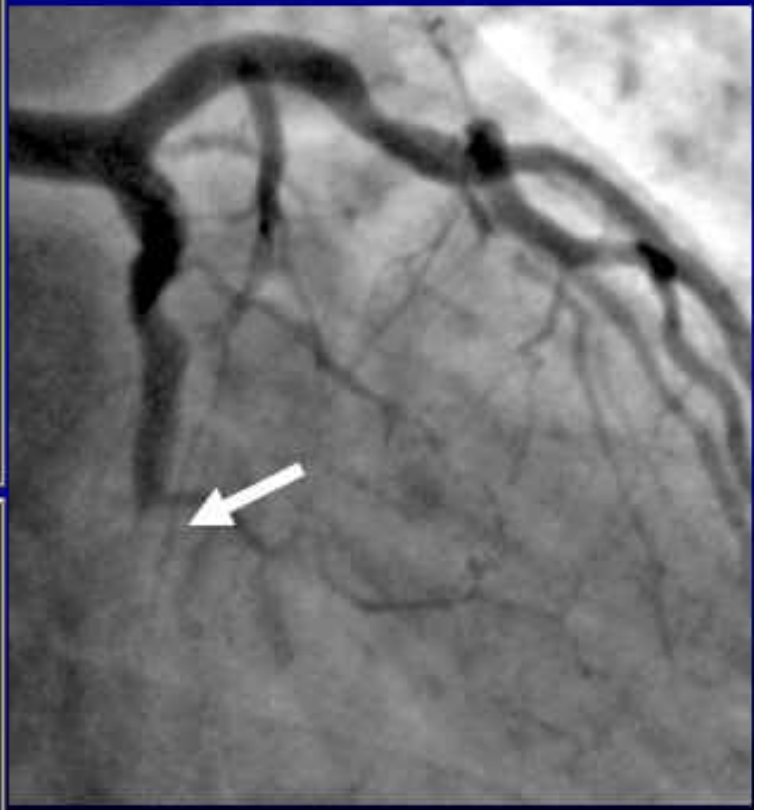


Courtesy of Renu Virmani

63-Year-Old Male
Acute Inferior Wall Infarct – LCX IRA



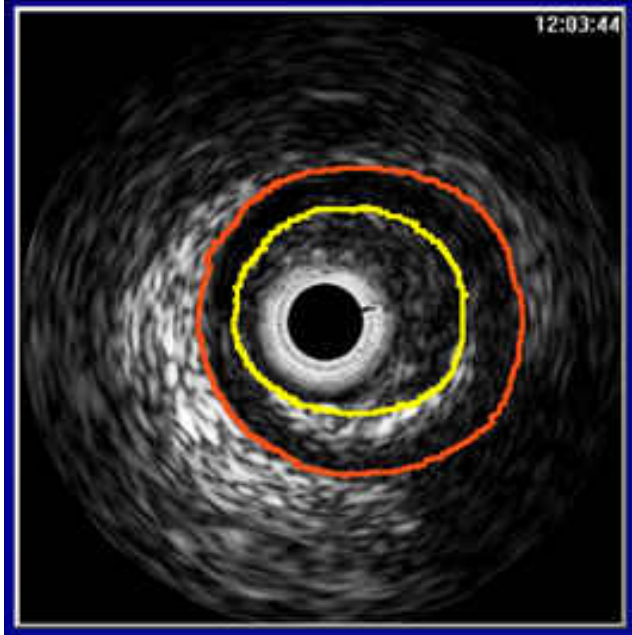


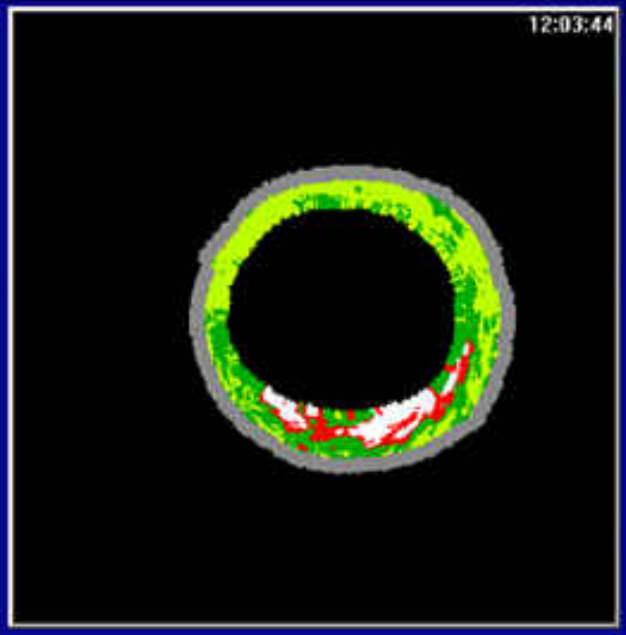


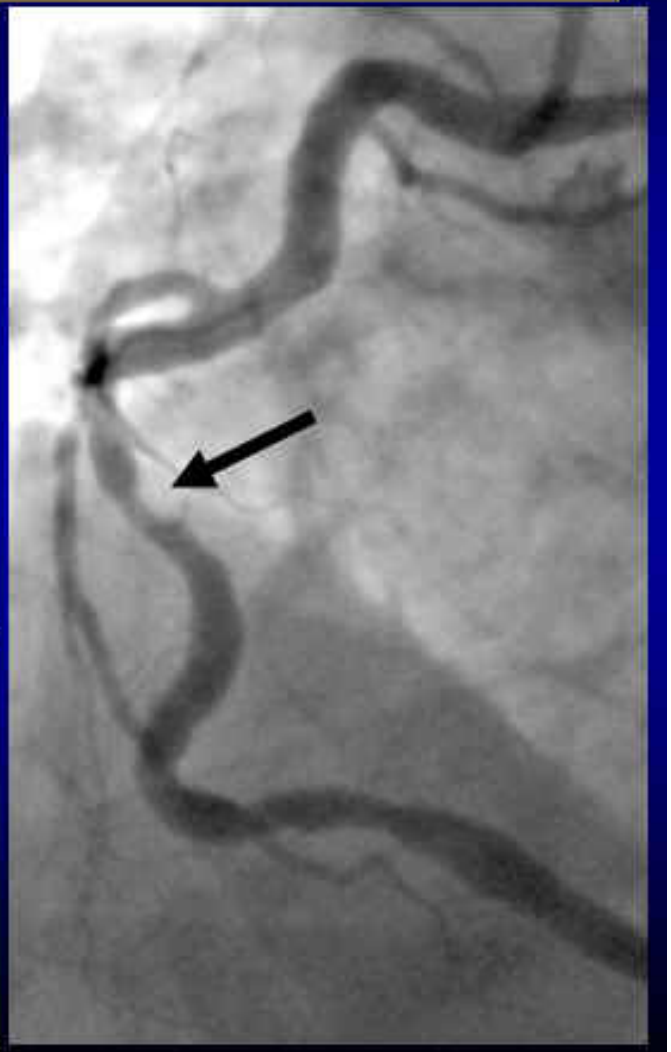
Lumen Area	8.9 mm²	
EEL Area	17.6 mm²	
Plaque Area	8.7 mm²	
% Plaque Burden	50 %	
Fibrous Area	3.2 mm²	63 %
Fibro-Fatty Area	1.1 mm²	21 %
Dense Calcium Area	0.3 mm²	6 %
Necrotic Core Area	0.5 mm²	9 %

More ...

63-Year-Old Male
Acute Inferior Wall Infarct - RCA



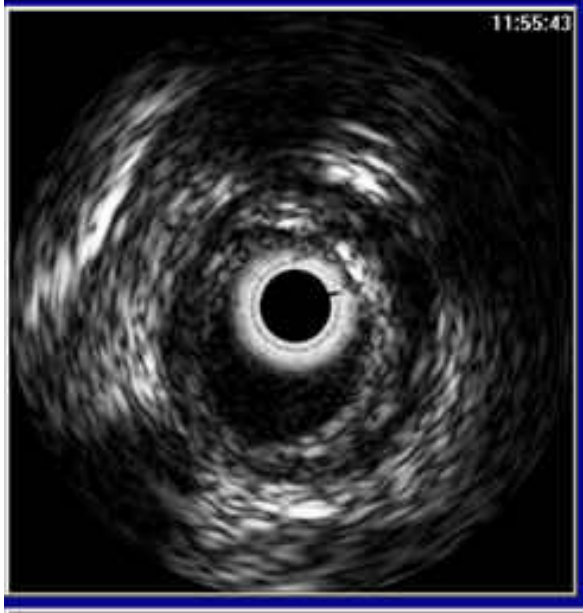


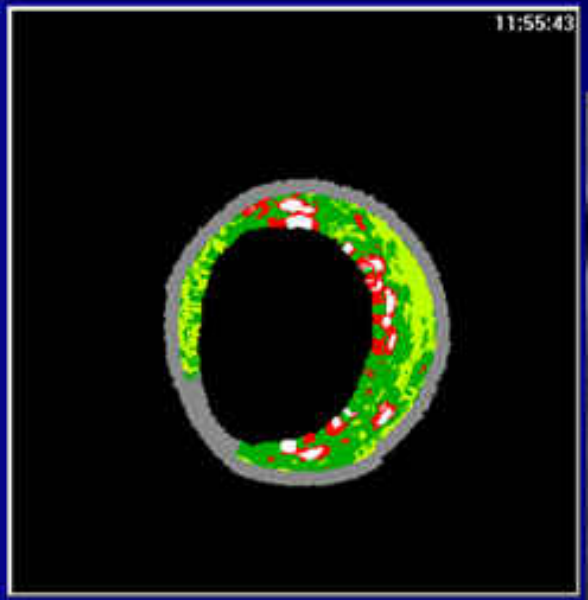


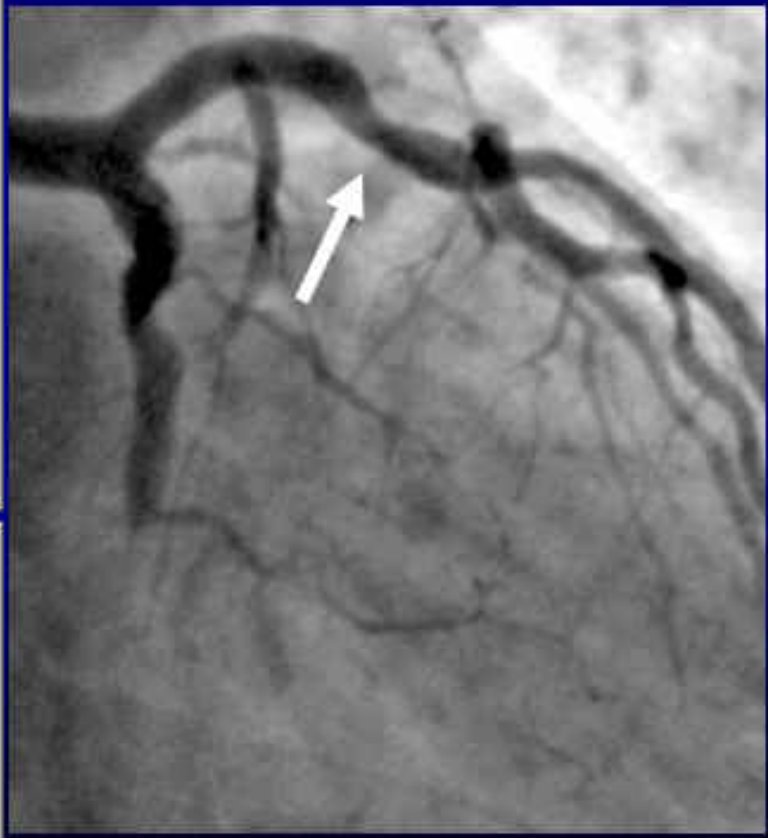
Lumen Area	10.1 mm²	
EEL Area	21.7 mm²	
Plaque Area	11.6 mm²	
% Plaque Burden	54 %	
Fibrous Area	2.8 mm²	36 %
Fibro-Fatty Area	3.4 mm²	44 %
Dense Calcium Area	0.8 mm²	11 %
Necrotic Core Area	0.7 mm²	9 %

More ...

63-Year-Old Male
Acute Inferior Wall Infarct - LAD



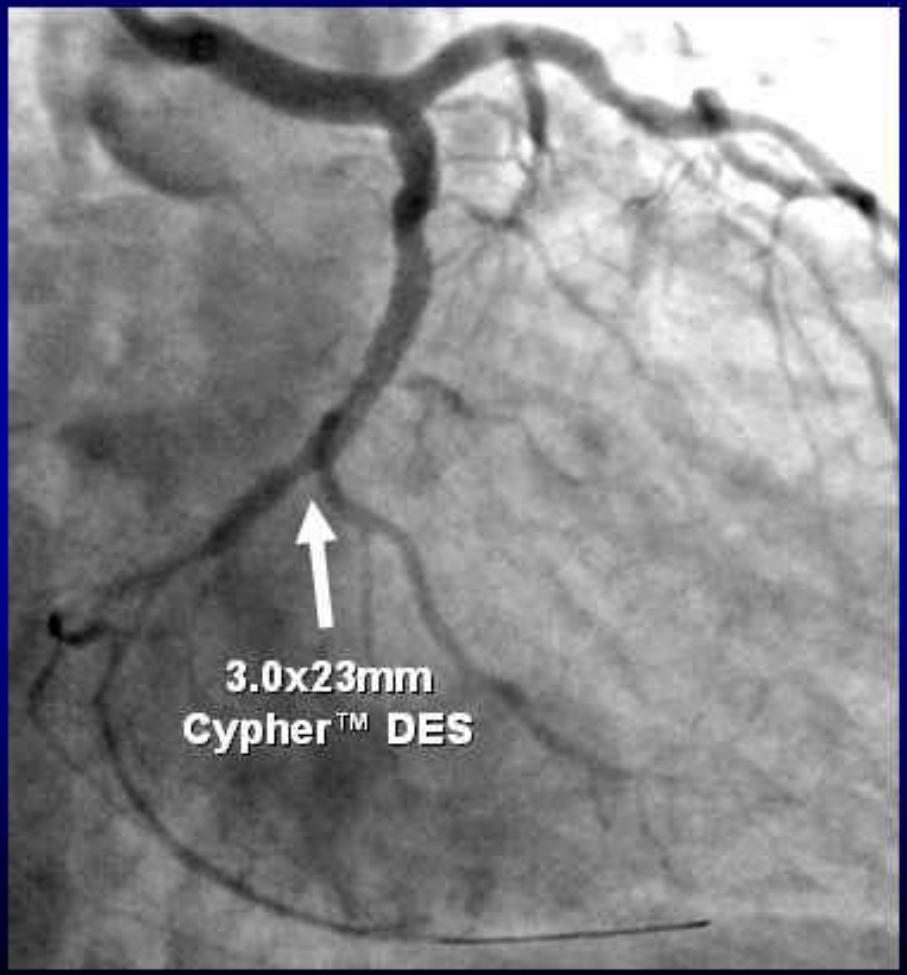


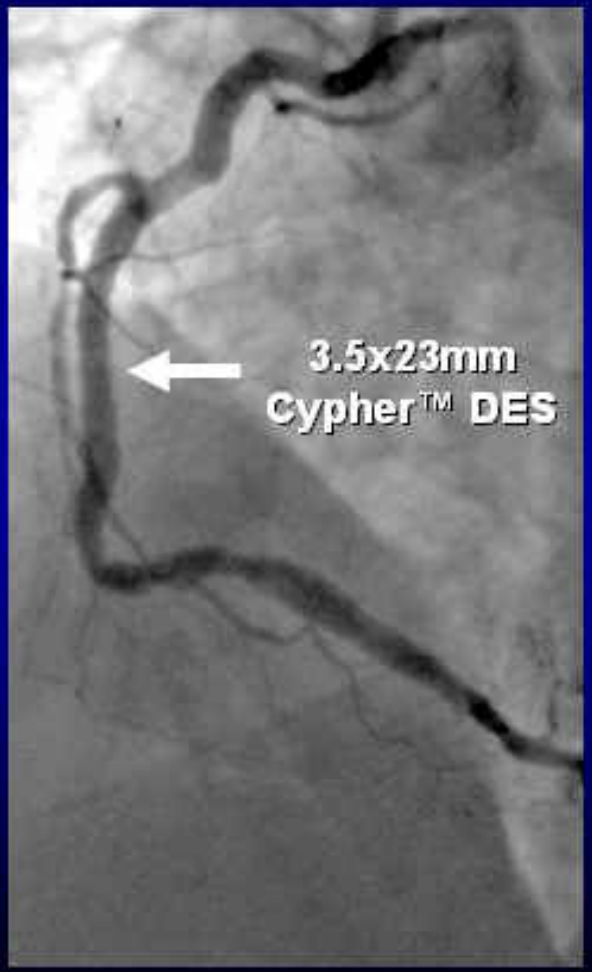


Lumen Area	9.5 mm²	
EEL Area	20.9 mm²	
Plaque Area	11.5 mm²	
% Plaque Burden	55 %	
Fibrous Area	3.9 mm²	52 %
Fibro-Fatty Area	2.0 mm²	27 %
Dense Calcium Area	0.6 mm²	8 %
Necrotic Core Area	1.0 mm²	13 %

More ...

63-Year-Old Male
Acute Inferior Wall Infarct





Clinical Progression of Incidental, Asymptomatic Lesions Discovered During Culprit Vessel Coronary Intervention

NHLBI Registry. 3747 pts 1997-99. 1-yr f/u

216 pts (5.8%) non-target PCI,
mean f/u 163 ± 99 days

- 86.9% of lesions requiring repeat PCI ≤ 60% at original study
- Lesions < 50% at initial angio 60.5%
- Lesions > 70% at initial angio 13.4%
- MVD at original angio 76.4%

R. Glaser et al. Circ 2005;111:143

Clinical Progression of Incidental, Asymptomatic Lesions Discovered During Culprit Vessel Coronary Intervention

- Progression in same artery 39%
- Progression in different artery 61%
- Clinical Presentation:
  - Acute Coronary Syndrome 68.5%
  - Stable Angina 24.1%
  - Atypical Symptoms 6.8%

R. Glaser et al. Circ 2005;111:143

Angiographic Prediction of Vulnerable Plaque Is Not Accurate