

Virtual Histology

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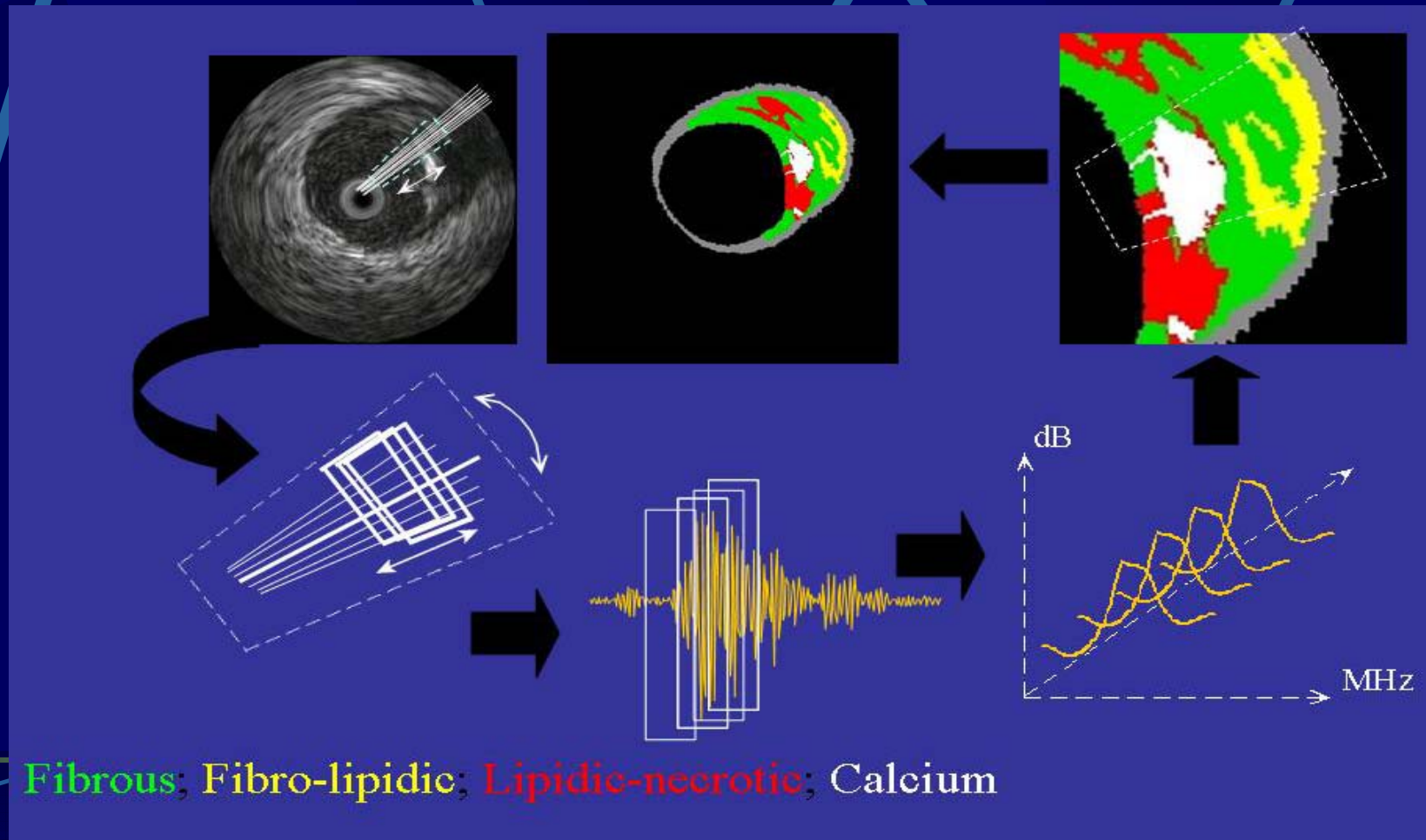
**Division of
Cardiology
Department of
Medicine**



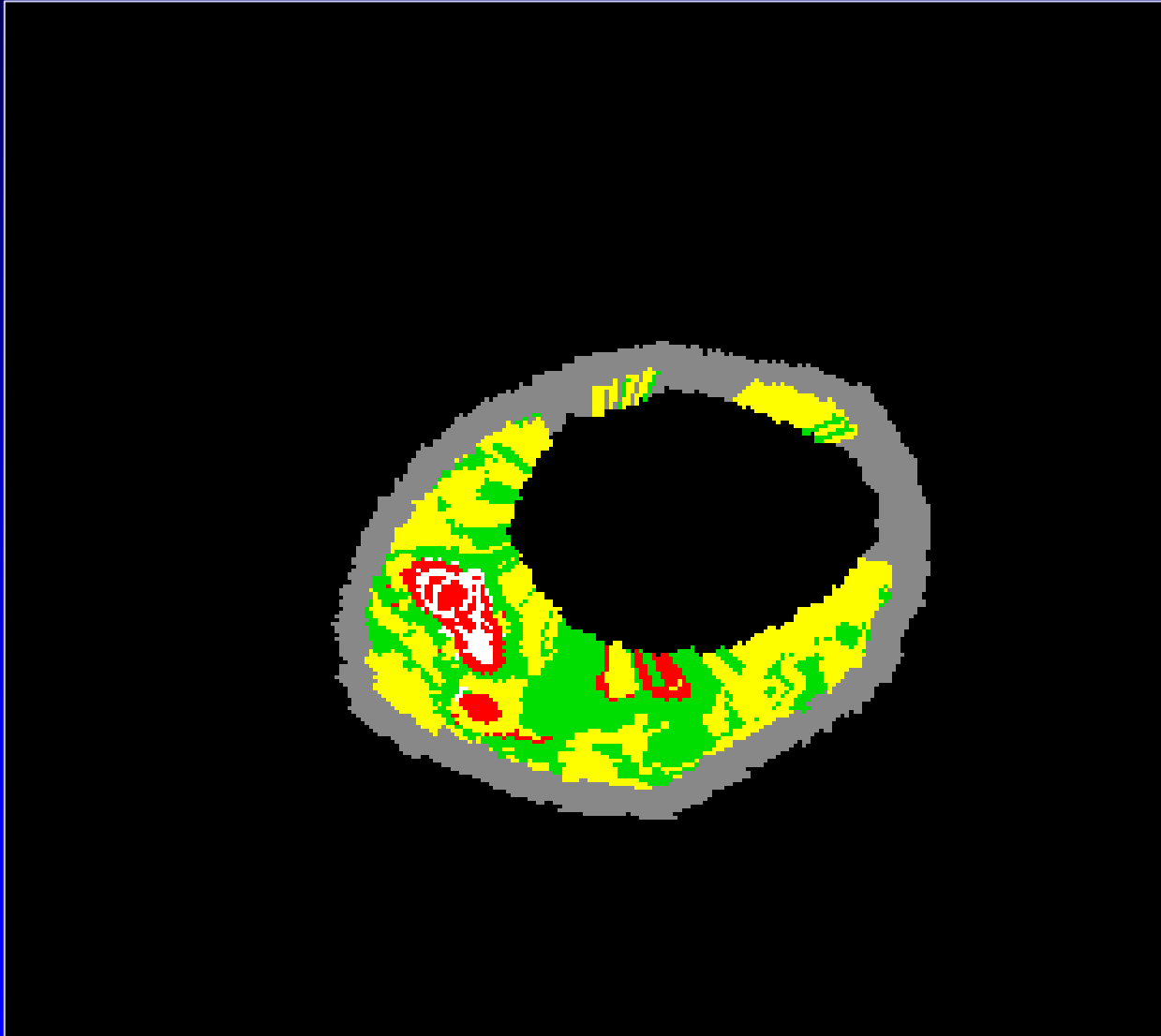
**Queen Elizabeth
Hospital
Hong Kong SAR**

Angioplasty Summit 2007

Virtual histology (VH-IVUS) is a new ultrasound tissue characterization technique, which extends the ability of IVUS through advanced spectral analysis to aid the assessment of plaque composition, and thus may have the potential to identify plaques that are prone to rupture.



VH -- Tissue / Plaque Characterization



Ø Simplified Interpretation

Ø Automated edge detection

Ø Predicted Plaque composition

Ø Calcium 钙化斑块

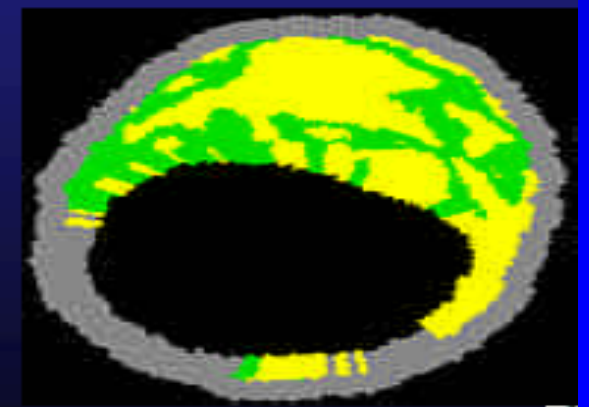
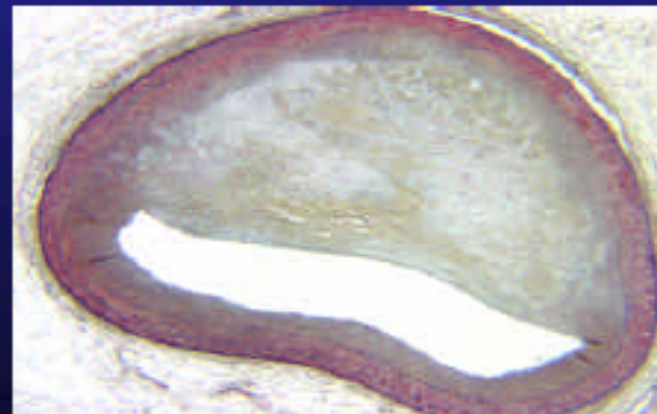
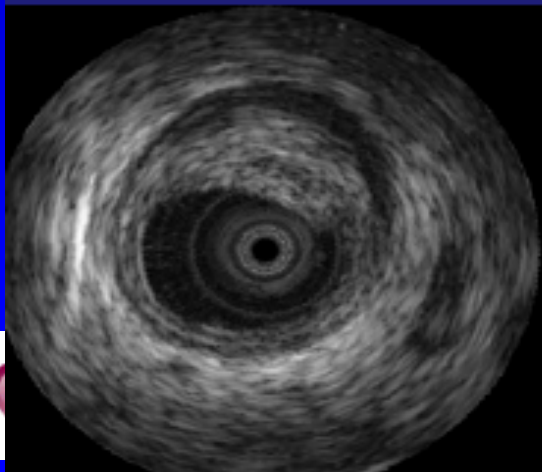
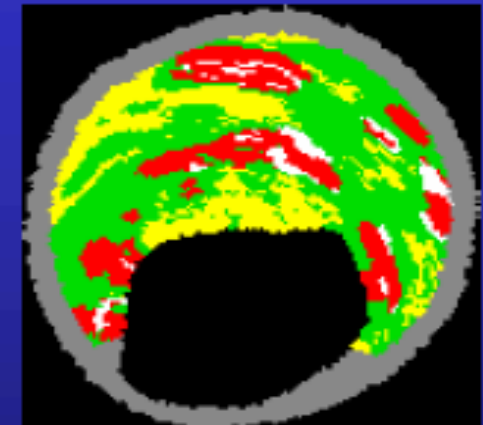
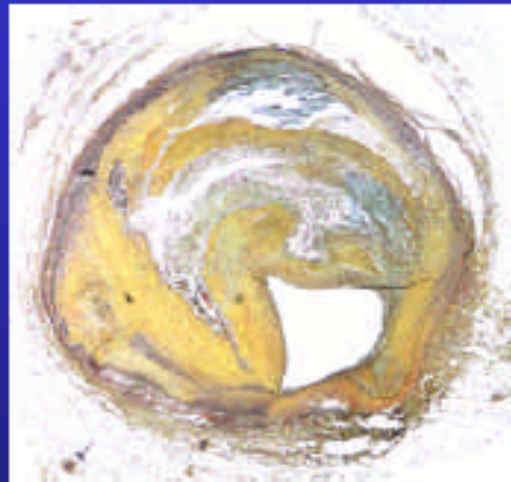
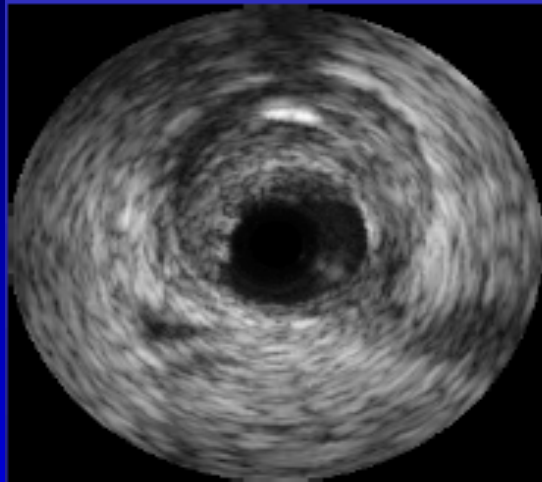
Ø Fibrous 纤维斑块

Ø Fibro-Lipidic 混合性斑块

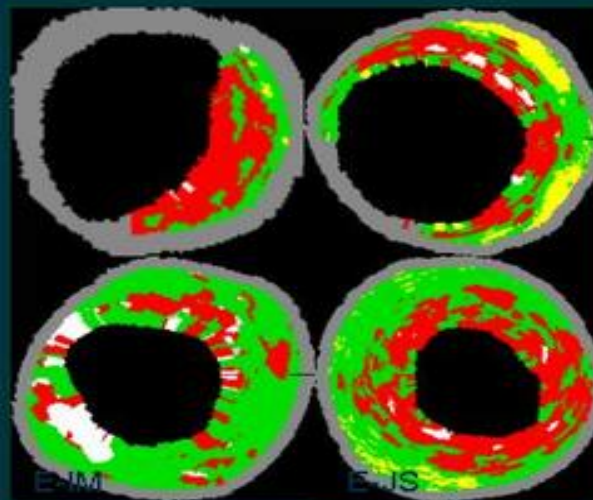
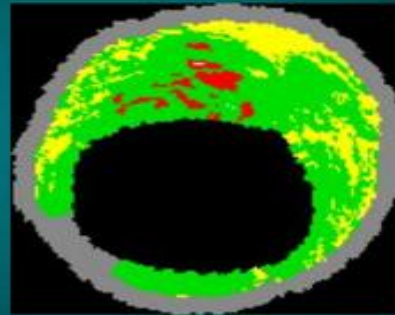
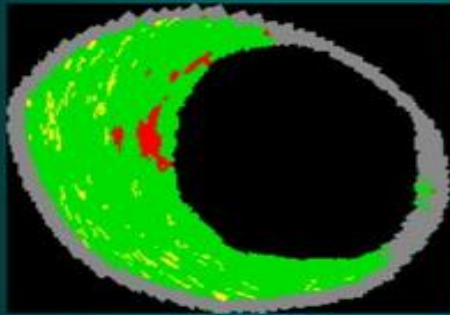
Ø Necrotic 软斑块

Ø Media 中膜

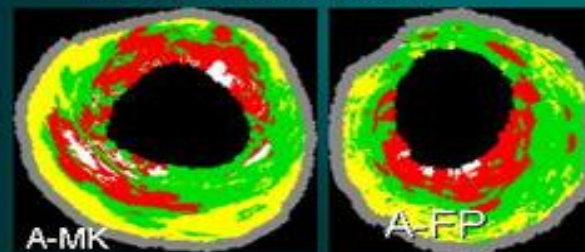
Ability of Gray Scale IVUS to Differentiate Plaque Morphologies



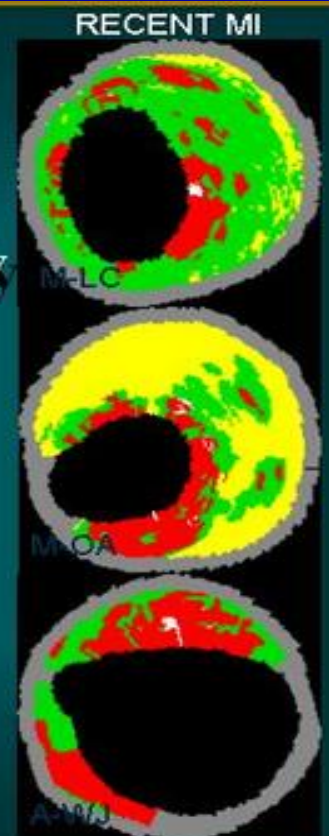
Stable Lesions



UNSTABLE ANGINA



VH Registry
Culprit
Lesion
Sites



RECENT MI



IVUS – derived Thin Cap Fibroatheroma (IDTCFA)

- Criteria :

1/ Necrotic Core – rich

($\geq 10\%$ of Cross sectional area)

2/ Focal

3/ Plaques being in contact with
the lumen

4/ Percent Atheroma Volume

(PAV) $\geq 40\%$



Atherosclerotic Plaque Compositions in Angiographically “Normal” Left Main Coronary Arteries: Insights from Virtual Histology.

MKY Lee, WKT Hau*, KT Chan, D Ho, BCW Cheng, CL Fu, MC Chan, CS Chiang

Division of Cardiology, Queen Elizabeth Hospital, Hong Kong.

*Department of Physiology, Institute of Cardiovascular Medicine and Science,
Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong.

Background

Intravascular ultrasound (IVUS) has been shown to detect **left main coronary artery (LMCA)** disease that is **angiographically silent**, however, no studies have been done to assess the vulnerability and plaque compositions of these kinds of “Angiographically Normal” disease. **TCFAs** which resemble plaque rupture in morphology - a necrotic core with an overlying thin-ruptured cap infiltrated by macrophages, is believed to be the precursor lesion for plaque rupture, which potentially leads to the **thrombosis** that is believed to be the main cause of **sudden coronary death**.

Both in vivo and in vitro validation studies have shown that VH-IVUS has a very high accuracy, varying from 92.9 – 99.3% for the classification of four different plaque components .

Classification Tree

LADs - 51, Sections - 115, ROIs -407

| | Sensitivity | Specificity | Predictive Accuracy |
|-------------------------------|-------------|-------------|---------------------|
| • Fibrous (n=162) | 83.9 | 98.8 | 92.9 |
| • Fibrofatty (n=84) | 86.9 | 95.0 | 93.4 |
| • Necrotic Core (n=69) | 97.1 | 93.8 | 94.3 |
| • Dense Calcium (n=92) | 97.8 | 99.7 | 99.3 |

Objective

The aim of this study was to use VH-IVUS to assess vulnerability and plaque compositions in angiographically insignificant left main coronary artery (LMCA) disease.

Methods:

Patients with stable angina (SA) who underwent LAD interventions and had angiographically normal LMCA were selected for VH-IVUS (Volcano Corp. USA) assessment.

All VH-IVUS studies were performed with a 20Hz solid-state catheter with an automated pullback speed of 1.0mm/s.

IVUS frames with the largest plaque burden together with the two adjacent frames were grabbed for VH-IVUS analysis.

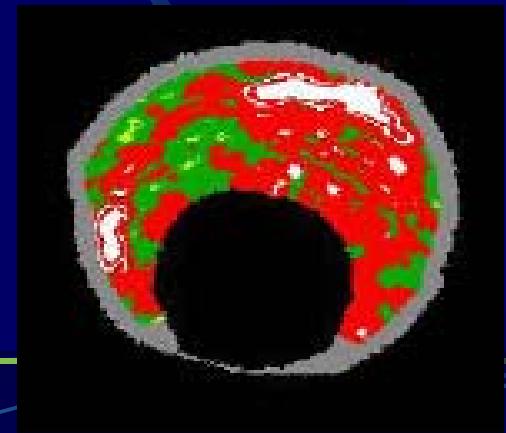
Definiation of High Risk Plaques (TCFA) in Virtual Histology

Previously defined criteria of high-risk plaques were applied to identify those prone to rupture in this study:

- Focal
- Necrotic core-rich $\geq 10\%$ of cross-sectional area
- In direct contact with the lumen
- $\geq 40\%$ atheroma volume.

Per-frame analysis

Per 3 consecutive frames will all characteristics



(Rodriguez-Granillo GA et al. JACC 2005; 46:2038-42)

Inclusion Criteria:

- Patients with SA aged 18 – 85 years old with significant LAD stenosis ($\geq 50\%$) on initial coronary angiography.

Clinical Exclusions:

- Old or recent myocardial infarction
- Heart failure
- Renal failure
- Recommended coronary artery bypass graft surgery

Angiographic Exclusions:

- Visible thrombus
- Chronic total occlusion
- Angiographically significant left main disease
- Small vessel (≤ 2.5 mm in diameter).
- Coronary anatomy that precludes safe IVUS examination of a suitable area of interest.

Patients' Characteristics

No. of Patients : 22

Male Gender : 12 (59%)

Age : 65.1 \pm 8.28 Years Old

Diabetes : 10 (40%)

Stable Angina : 18 (81.81%)

2-Vessels : 5 (22.72%)

LAD : 20

LCX : 3

RCA : 3

No. of Lesions: 46

VH-IVUS Analysis

Garyscale IVUS:

Lumen and Vessel Diameter (mm)

Lumen and Vessel area (mm²)

Percentage Plaque Burden

$$= (\text{Vessel Area} - \text{Lumen Area}) / \text{Vessel Area} \times 100\%$$

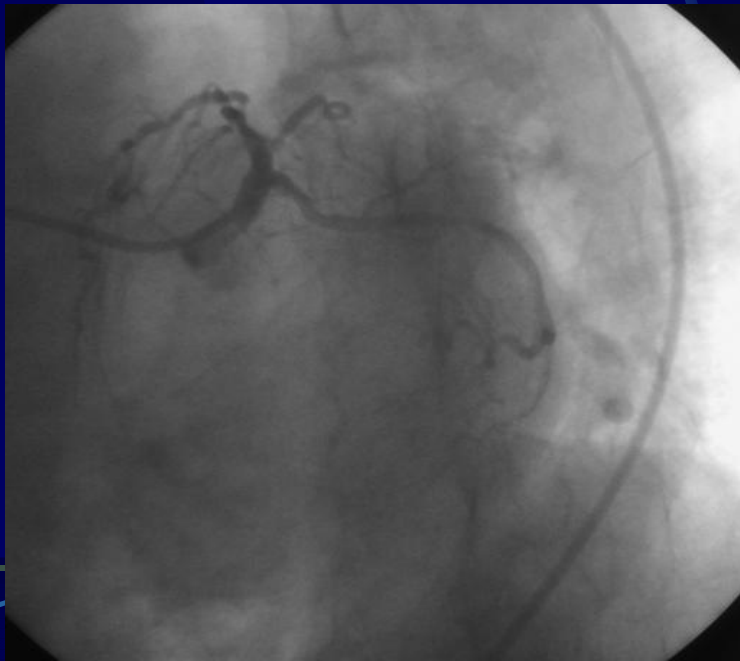
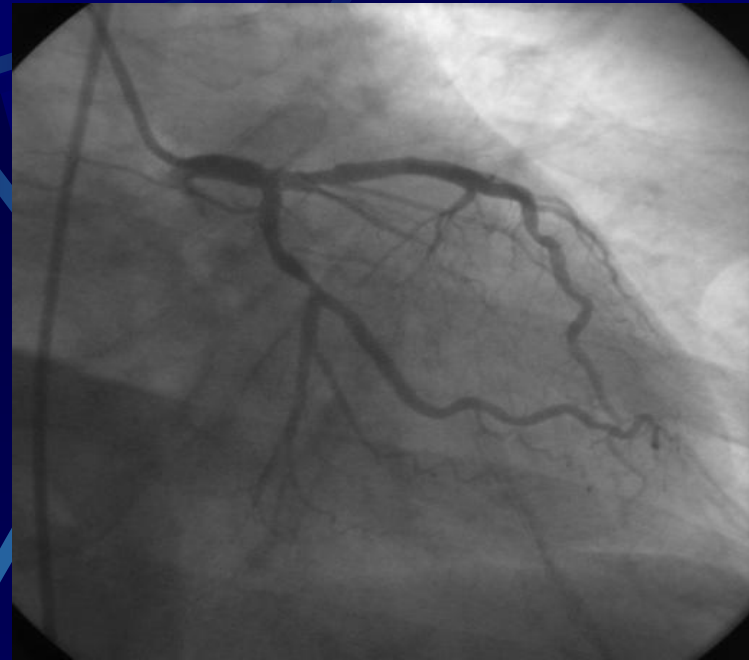
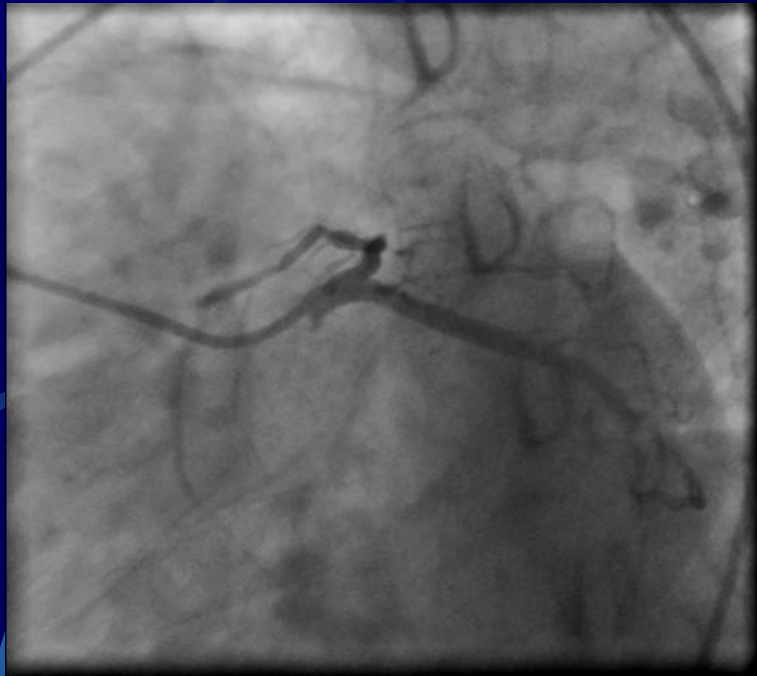
VH-IVUS:

Percentage Fibrous (FI)

Percentage Fibrofatty (FF)

Percentage Dense Calcium (DC)

Percentage Necrotic Core (NC)



Results

IVUS mean Luminal Diameter = 4 ± 0.62 mm

IVUS mean Luminal Area = 13.02 ± 4.06 mm²

IVUS mean Vessel Diameter = 5.34 ± 0.6 mm

IVUS mean Vessel Area = 23.23 ± 4.96 mm²

% Plaque Burden = 44.45 ± 8.49 %

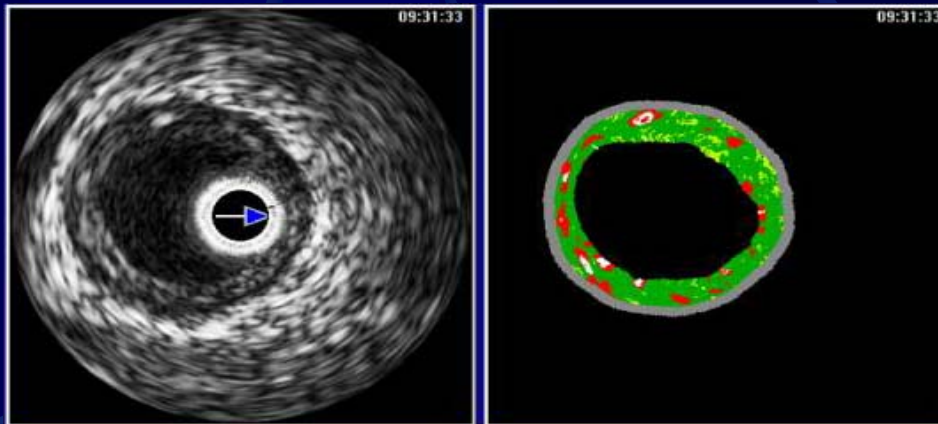
% Fibrous = 62.09 ± 16.06 %

% Fibrofatty = 6.95 ± 5.98 %

% Dense Calcium = 8.23 ± 8.9 %

% Necrotic Core = 22.4 ± 13.6 %

None of the 22 “Angiographically Normal” left main diseases assessed by VH-IVUS fulfill all the 4 criteria of a high-risk plaque previously defined by VH-IVUS.



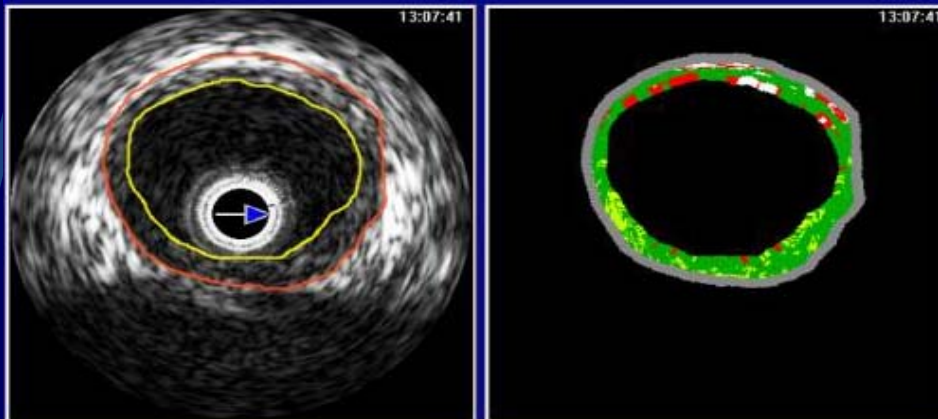
| | | | |
|---------------------|----------------------|------|--|
| Lumen Area | 10.8 mm ² | | |
| Vessel Area | 23.1 mm ² | | |
| Plaque Area | 12.3 mm ² | | |
| % Plaque Burden | 53 % | | |
| FI Green Area | 6.5 mm ² | 77 % | |
| FF Light Green Area | 0.6 mm ² | 8 % | |
| DC White Area | 0.2 mm ² | 3 % | |
| NC Red Area | 1.1 mm ² | 13 % | |



Case 1

- Focal (No)
- Necrotic core-rich $\geq 10\%$ of cross-sectional area (Yes)
- In direct contact with the lumen (No)
- $\geq 40\%$ atheroma volume. (Yes)

Not a high risk Plaque



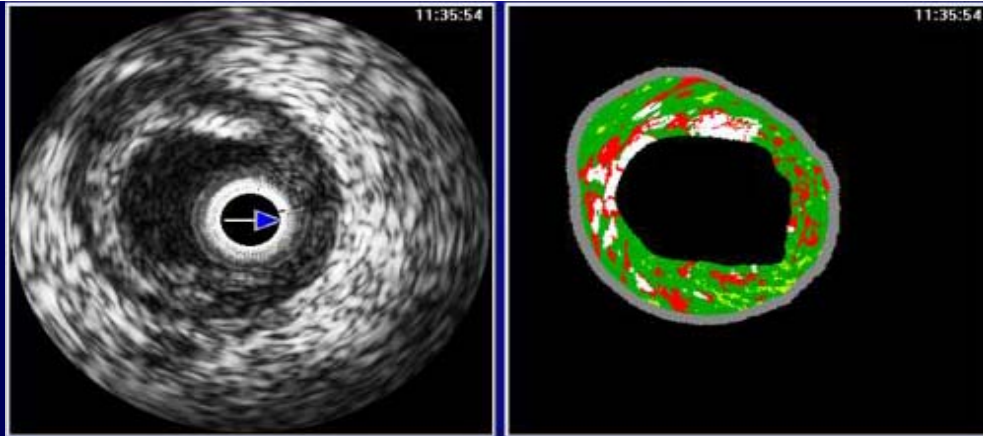
| | | | |
|---------------------|----------------------|------|--|
| Lumen Area | 17.0 mm ² | | |
| Vessel Area | 28.6 mm ² | | |
| Plaque Area | 11.5 mm ² | | |
| % Plaque Burden | 40 % | | |
| FI Green Area | 5.2 mm ² | 72 % | |
| FF Light Green Area | 0.9 mm ² | 12 % | |
| DC White Area | 0.4 mm ² | 6 % | |
| NC Red Area | 0.7 mm ² | 10 % | |



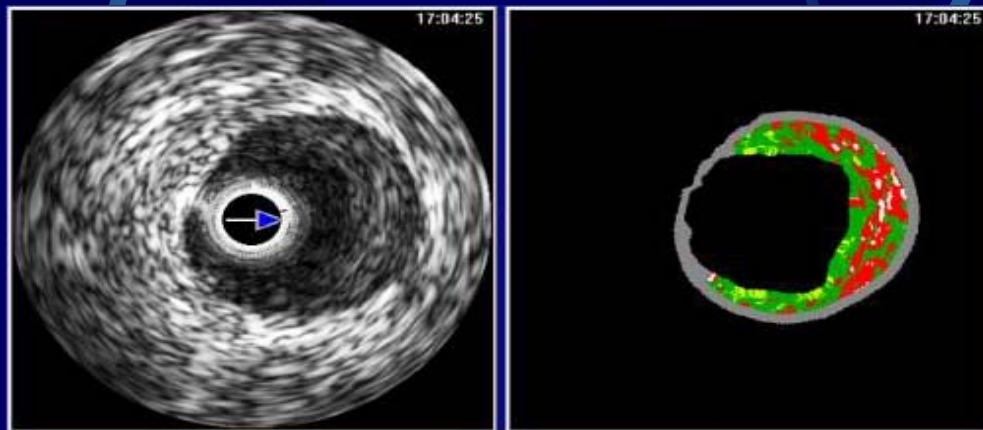
Case 2

- Focal (No)
- Necrotic core-rich $\geq 10\%$ of cross-sectional area (Yes)
- In direct contact with the lumen (No)
- $\geq 40\%$ atheroma volume. (Yes)

Not a high risk Plaque



| | | | |
|---------------------|----------------------|------|--|
| Lumen Area | 9.5 mm ² | | |
| Vessel Area | 27.4 mm ² | | |
| Plaque Area | 17.9 mm ² | | |
| % Plaque Burden | 65 % | | |
| FI Green Area | 8.6 mm ² | 63 % | |
| FF Light Green Area | 0.5 mm ² | 3 % | |
| DC White Area | 1.8 mm ² | 13 % | |
| NC Red Area | 2.8 mm ² | 21 % | |
| | | | |



| | | | |
|---------------------|----------------------|------|--|
| Lumen Area | 9.7 mm ² | | |
| Vessel Area | 20.5 mm ² | | |
| Plaque Area | 10.8 mm ² | | |
| % Plaque Burden | 53 % | | |
| FI Green Area | 3.9 mm ² | 55 % | |
| FF Light Green Area | 0.5 mm ² | 7 % | |
| DC White Area | 0.3 mm ² | 4 % | |
| NC Red Area | 2.4 mm ² | 34 % | |
| | | | |

Case 3

- Focal (No)
- Necrotic core-rich $\geq 10\%$ of cross-sectional area (Yes)
- In direct contact with the lumen (No)
- $\geq 40\%$ atheroma volume. (Yes)

Not a high risk Plaque

Case 4

- Focal (No)
- Necrotic core-rich $\geq 10\%$ of cross-sectional area (Yes)
- In direct contact with the lumen (No)
- $\geq 40\%$ atheroma volume. (Yes)

Not a high risk Plaque

Conclusions

In **stable angina** patients with **LMCA** that appeared **angiographically normal**, even though IVUS revealed a **considerable plaque burden** (up to 60%), these atherosclerotic plaques mainly consisted of fibrous tissue and were generally **stable** in nature.

Composition of Atherosclerotic Plaques in Equivocal Tandem Lesions Along the Left Anterior Descending Artery: Insights from Virtual Histology.

CL Fu, MKY Lee, WKT Hau*, KT Chan, D Ho, BCW Cheng,
MC Chan and CS Chiang.

Division of Cardiology, Queen Elizabeth Hospital, Hong Kong.

*Department of Physiology, Institute of Cardiovascular Medicine and Science,
Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong.

Objective

The purpose of this study was to use Virtual Histology (VH-IVUS) to investigate whether **plaque composition** is related to the **location** of a culprit lesion in a left anterior descending artery (LAD).

Methods:

Patients who underwent LAD interventions and had angiographically visible tandem lesions were selected for VH-IVUS (Volcano Corp.) assessment. VH-IVUS allows reliable characterization of atherosclerotic plaques into four different types: fibrous, fibrofatty, necrotic core and dense calcium.

All VH-IVUS studies were performed using a 20Hz solid-state catheter (EagleEye, Volcano Corp.) with pullback speed of 1.0mm/s.

IVUS frames with the largest plaque burden from each culprit lesion were grabbed for analysis.

Inclusion Criteria:

- Patients aged 18 – 85 years old with tandem LAD stenosis ($\geq 50\%$) on initial coronary angiography.

Clinical Exclusions:

- Old or recent myocardial infarction
- Heart failure
- Renal failure
- Recommended coronary artery bypass graft surgery

Angiographic Exclusions:

- Visible thrombus
- Chronic total occlusion
- Angiographically significant left main disease
- Small vessel (≤ 2.5 mm in diameter).
- Coronary anatomy that precludes safe IVUS examination of a suitable area of interest.

Patients' Characteristics

No. of Patients : 16

Male Gender : 12 (75%)

Age : 65 \pm 10 Years Old

Stable Angina : 13 (81.25%)

Diabetes : 4 (25%)

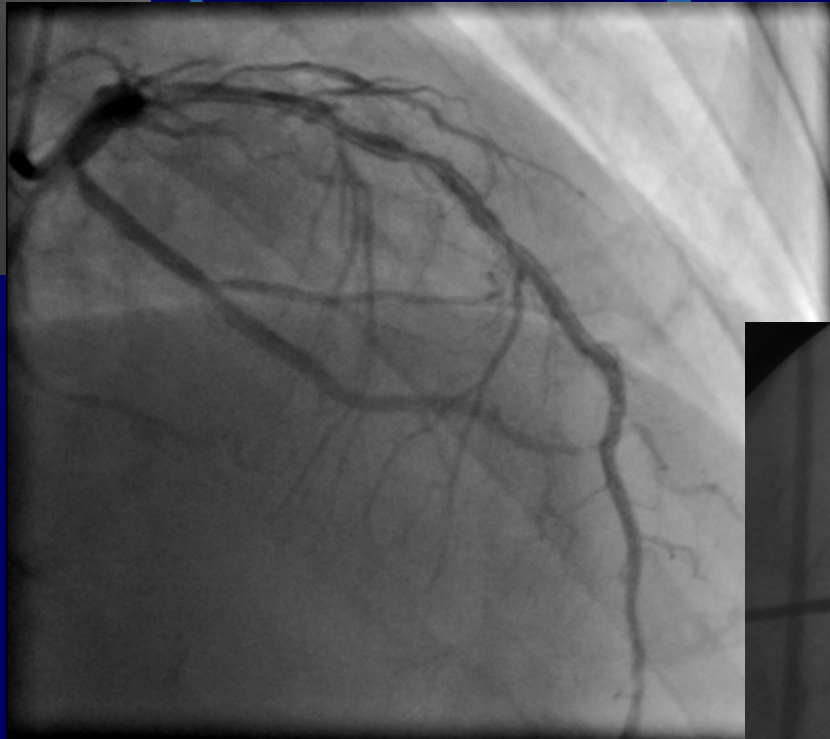
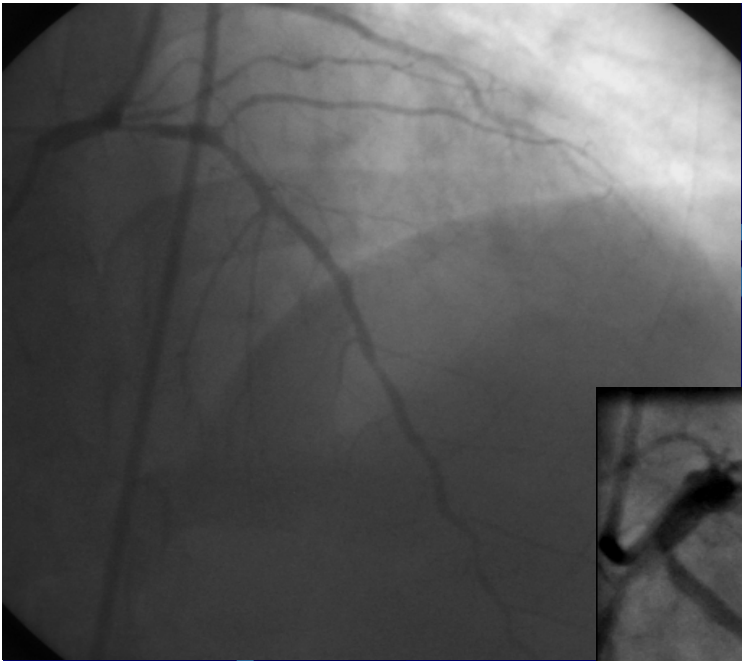
Two Vessels: 5 (31.25%)

LAD: 16

RCA: 2

LCX: 3

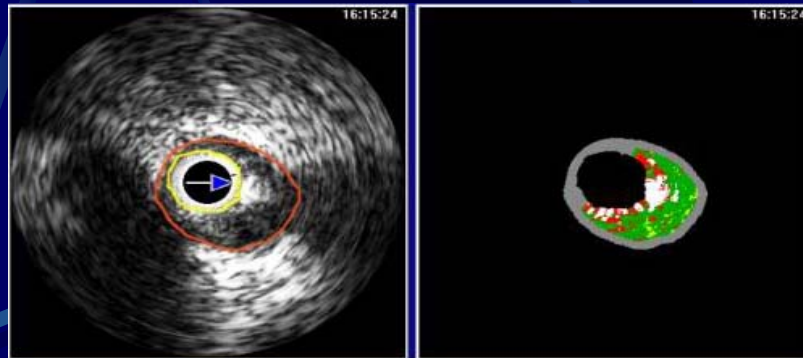
Number of Lesions: 39



Results

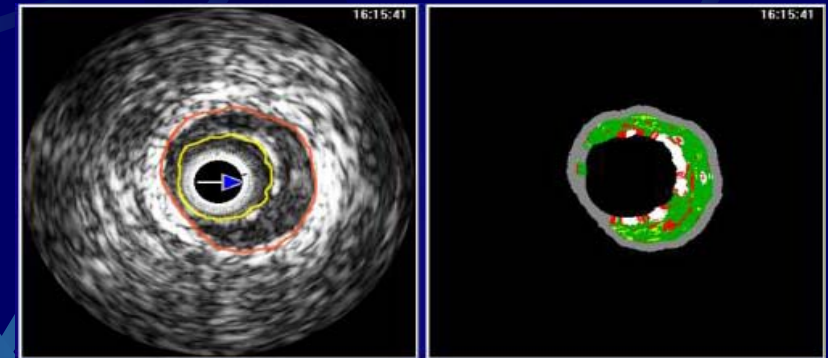
| | Distal Lesion | Proximal Lesion | p value |
|-------------------------------------|----------------------|------------------------|-----------------|
| Lumen Diameter (mm) | 2.14 ± 0.18 | 2.43 ± 0.41 | 0.016 |
| Lumen Area (mm²) | 3.61 ± 0.65 | 4.81 ± 1.66 | 0.011 |
| Vessel Diameter (mm) | 3.61 ± 0.60 | 4.35 ± 0.48 | 0.000573 |
| Vessel Area (mm²) | 10.88 ± 3.63 | 15.43 ± 3.24 | 0.000758 |
| Plaque Area (mm²) | 7.25 ± 3.52 | 10.61 ± 2.65 | 0.0047 |
| % Plaque Burden | 64.25 ± 9.48 | 68.69 ± 8.01 | 0.16 |
| % Fibrous | 51.68 ± 20.60 | 52.94 ± 16.87 | 0.852 |
| % Fibrofatty | 3.81 ± 3.94 | 4.13 ± 2.90 | 0.80 |
| % Calcium | 15.69 ± 12.44 | 13.31 ± 6.70 | 0.506 |
| % Necrotic Core | 28.69 ± 15.12 | 29.25 ± 14.91 | 0.887 |

Case 1



| | | | | |
|---------------------|---------------------|------|--|--|
| Lumen Area | 2.5 mm ² | | | |
| Vessel Area | 9.0 mm ² | | | |
| Plaque Area | 6.5 mm ² | | | |
| % Plaque Burden | 72 % | | | |
| FI Green Area | 2.3 mm ² | 59 % | | |
| FF Light Green Area | 0.2 mm ² | 5 % | | |
| DC White Area | 0.7 mm ² | 19 % | | |
| NC Red Area | 0.6 mm ² | 17 % | | |
| | | | | |

Distal lesion



| | | | | |
|---------------------|----------------------|------|--|--|
| Lumen Area | 4.7 mm ² | | | |
| Vessel Area | 13.0 mm ² | | | |
| Plaque Area | 8.3 mm ² | | | |
| % Plaque Burden | 64 % | | | |
| FI Green Area | 3.4 mm ² | 67 % | | |
| FF Light Green Area | 0.2 mm ² | 4 % | | |
| DC White Area | 0.8 mm ² | 16 % | | |
| NC Red Area | 0.7 mm ² | 13 % | | |
| | | | | |

Proximal lesion

Case 2



| | | | | |
|---------------------|---------------------|------|--|--|
| Lumen Area | 3.4 mm ² | | | |
| Vessel Area | 8.6 mm ² | | | |
| Plaque Area | 5.2 mm ² | | | |
| % Plaque Burden | 61 % | | | |
| FI Green Area | 0.7 mm ² | 24 % | | |
| FF Light Green Area | 0.0 mm ² | 1 % | | |
| DC White Area | 0.6 mm ² | 22 % | | |
| NC Red Area | 1.5 mm ² | 54 % | | |
| | | | | |

Distal lesion



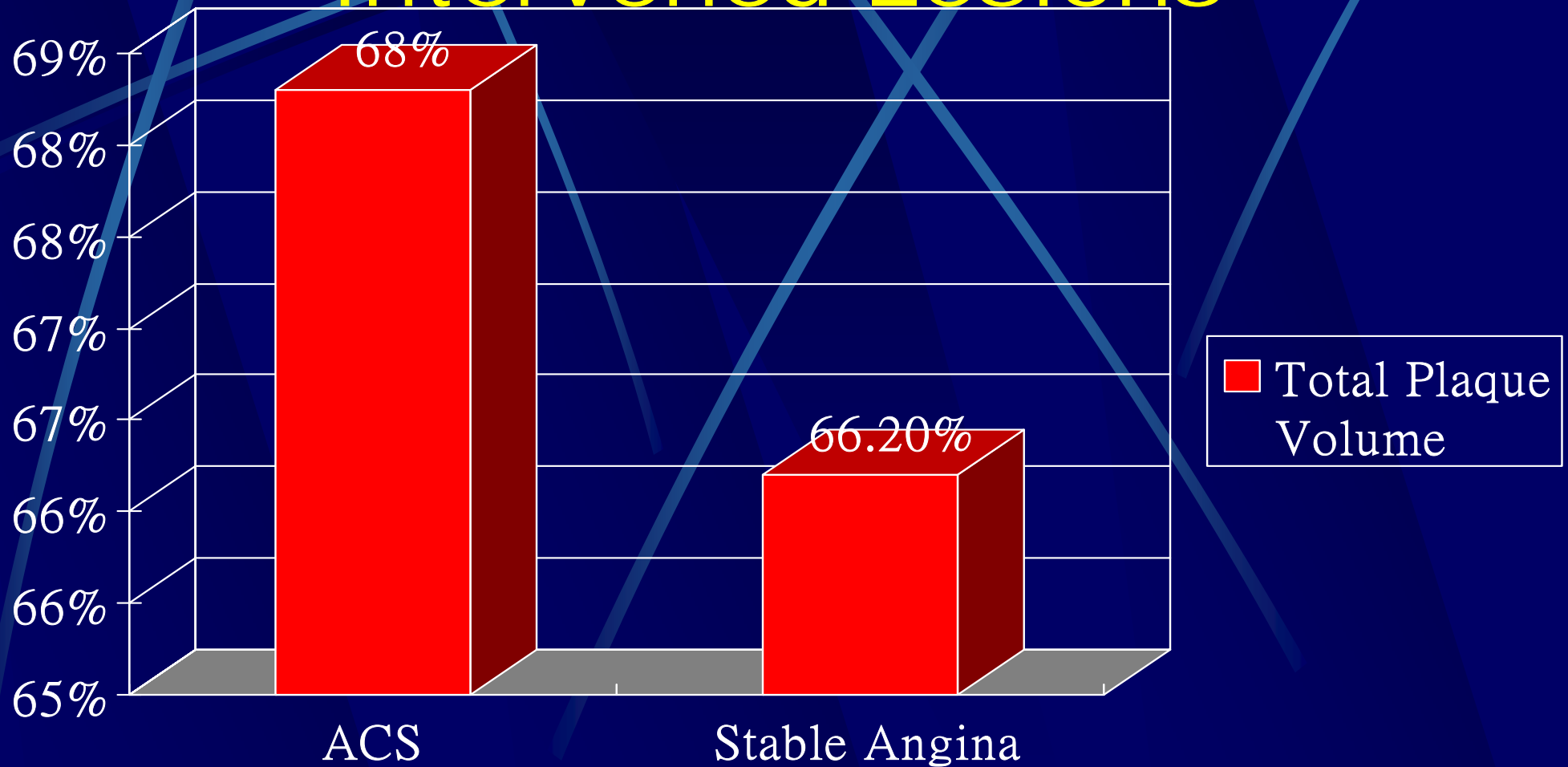
| | | | | |
|---------------------|----------------------|------|--|--|
| Lumen Area | 4.8 mm ² | | | |
| Vessel Area | 11.5 mm ² | | | |
| Plaque Area | 6.6 mm ² | | | |
| % Plaque Burden | 58 % | | | |
| FI Green Area | 1.0 mm ² | 28 % | | |
| FF Light Green Area | 0.0 mm ² | 1 % | | |
| DC White Area | 0.9 mm ² | 23 % | | |
| NC Red Area | 1.8 mm ² | 48 % | | |
| | | | | |

Proximal lesion

Conclusions:

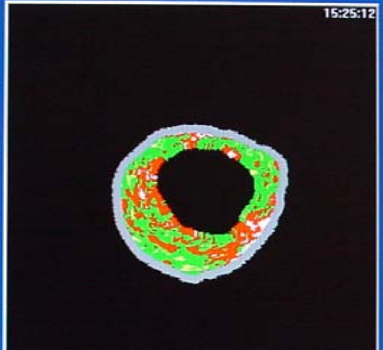
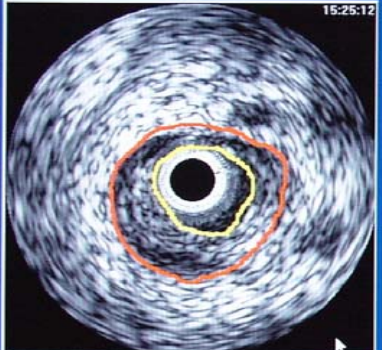
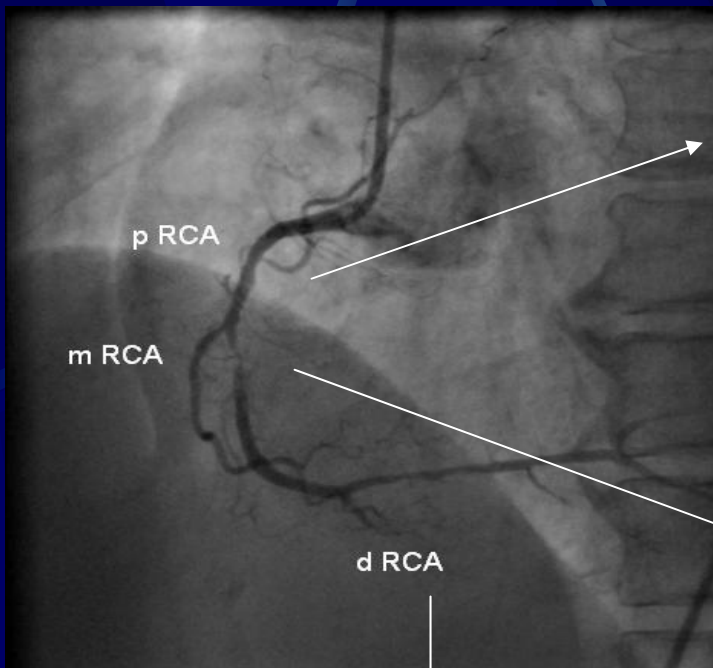
The percentage of plaque burden and plaque composition **did not differ** in relation to the lesion site in the LAD coronary artery, whereas plaque area, luminal diameter/area and vessel diameter/area decreased from proximal to distal position.

Result – Plaque volume of Intervened Lesions



P = NS

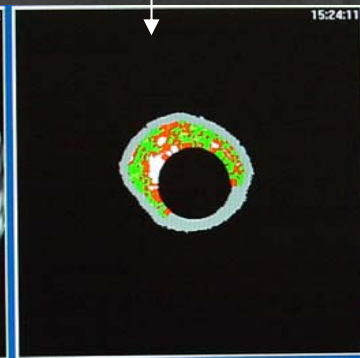
Virtual Histology



| | | |
|--------------------|----------------------|------|
| Lumen Area | 4.9 mm ² | |
| EEL Area | 16.4 mm ² | |
| Plaque Area | 11.4 mm ² | |
| % Plaque Burden | 70 % | |
| Fibrous Area | 4.8 mm ² | 59 % |
| Fibro-Fatty Area | 0.3 mm ² | 4 % |
| Dense Calcium Area | 0.4 mm ² | 4 % |
| Necrotic Core Area | 2.7 mm ² | 33 % |

VL A, Segment: 3

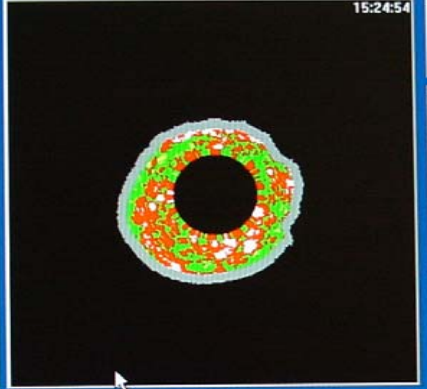
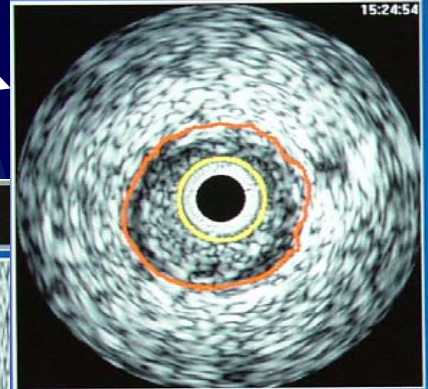
Distal Frame — 141
Current Frame — 141
Proximal Frame — 141



| | | |
|--------------------|---------------------|------|
| Lumen Area | 3.5 mm ² | |
| EEL Area | 9.7 mm ² | |
| Plaque Area | 6.2 mm ² | |
| % Plaque Burden | 64 % | |
| Fibrous Area | 1.7 mm ² | 52 % |
| Fibro-Fatty Area | 0.1 mm ² | 2 % |
| Dense Calcium Area | 0.4 mm ² | 12 % |
| Necrotic Core Area | 1.1 mm ² | 34 % |

VL A, Segment: 5

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

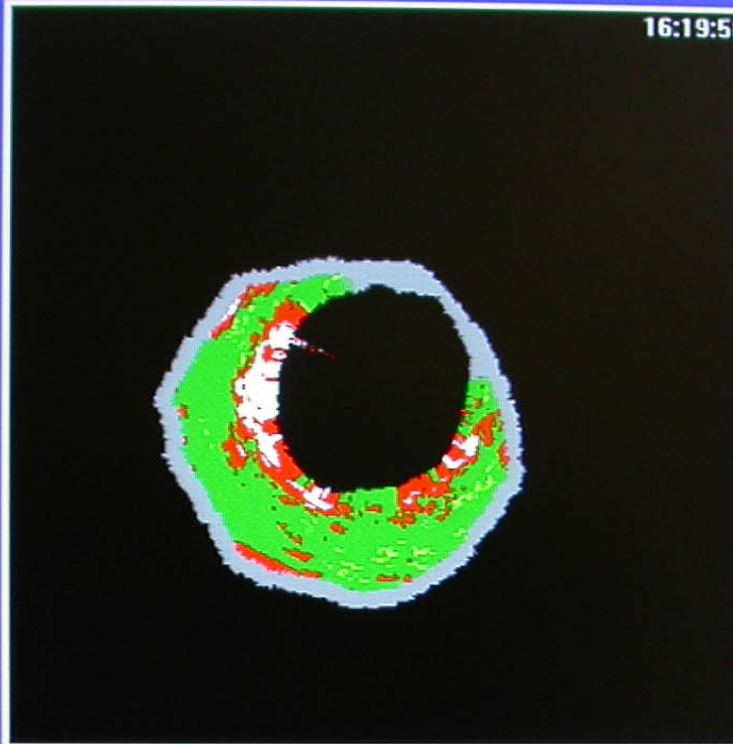
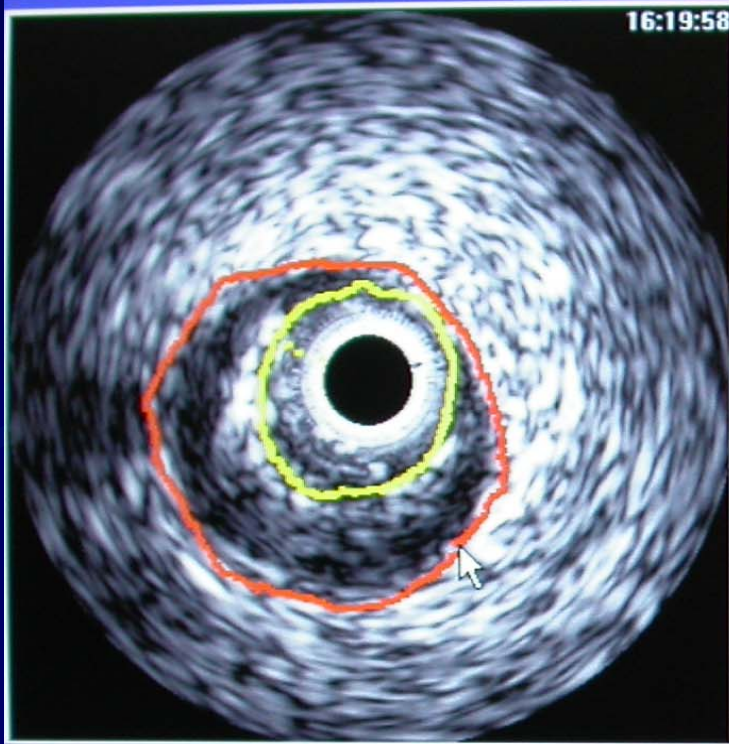


| | | |
|--------------------|----------------------|------|
| Lumen Area | 3.4 mm ² | |
| EEL Area | 15.1 mm ² | |
| Plaque Area | 11.7 mm ² | |
| % Plaque Burden | 77 % | |
| Fibrous Area | 3.8 mm ² | 45 % |
| Fibro-Fatty Area | 0.2 mm ² | 2 % |
| Dense Calcium Area | 0.8 mm ² | 9 % |
| Necrotic Core Area | 3.7 mm ² | 44 % |

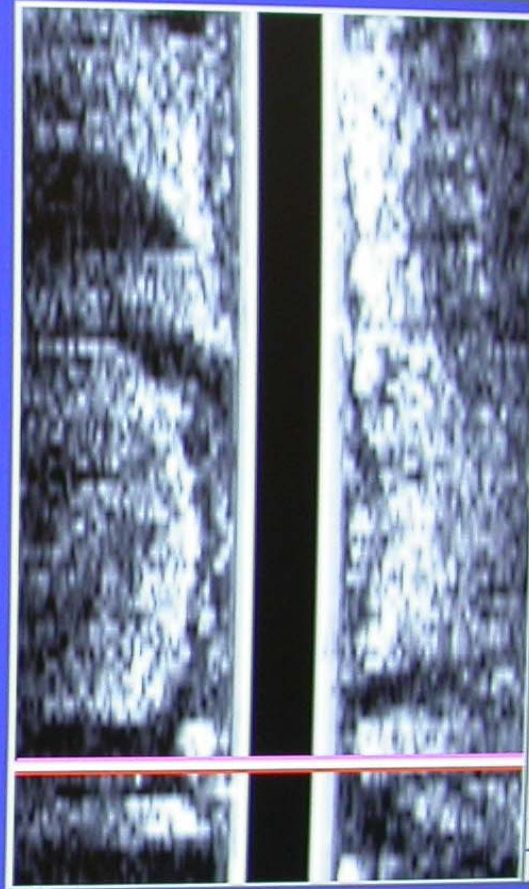
VL A, Segment: 4

Distal Frame — 118
Current Frame — 118
Proximal Frame — 118

ACS patients - urgent PCI



VL B, Segment: 3



| | | |
|--------------------|----------------------|------|
| Lumen Area | 5.9 mm ² | |
| EEL Area | 17.9 mm ² | |
| Plaque Area | 12.0 mm ² | |
| % Plaque Burden | 67 % | |
| Fibrous Area | 5.7 mm ² | 67 % |
| Fibro-Fatty Area | 0.2 mm ² | 2 % |
| Dense Calcium Area | 0.7 mm ² | 9 % |
| Necrotic Core Area | 1.8 mm ² | 22 % |

More ...

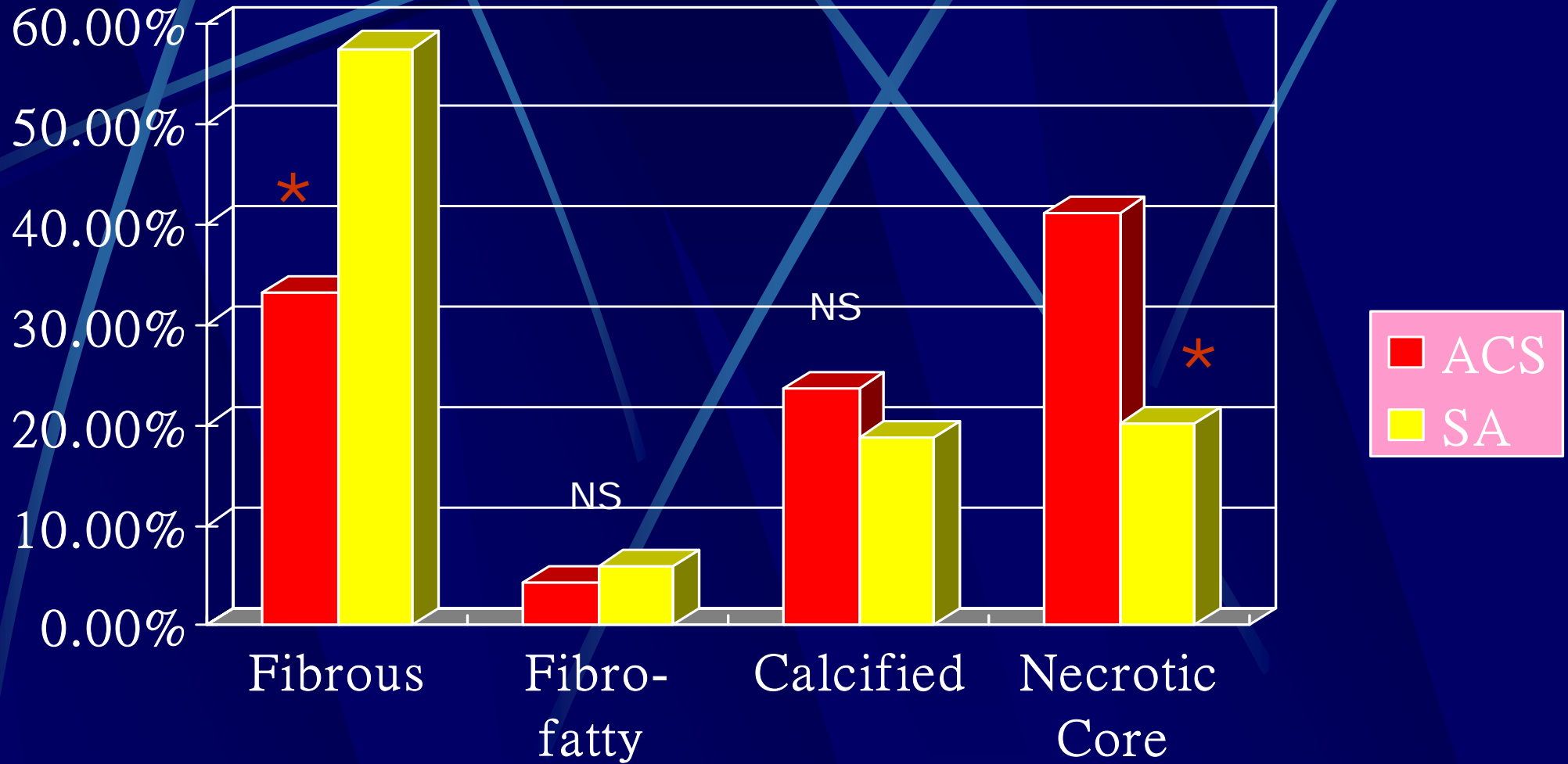
| | | |
|----------------|---|----|
| Distal Frame | — | 92 |
| Current Frame | — | 92 |
| Proximal Frame | — | 92 |

Stable Angina patients – PCI

Plaque Composition

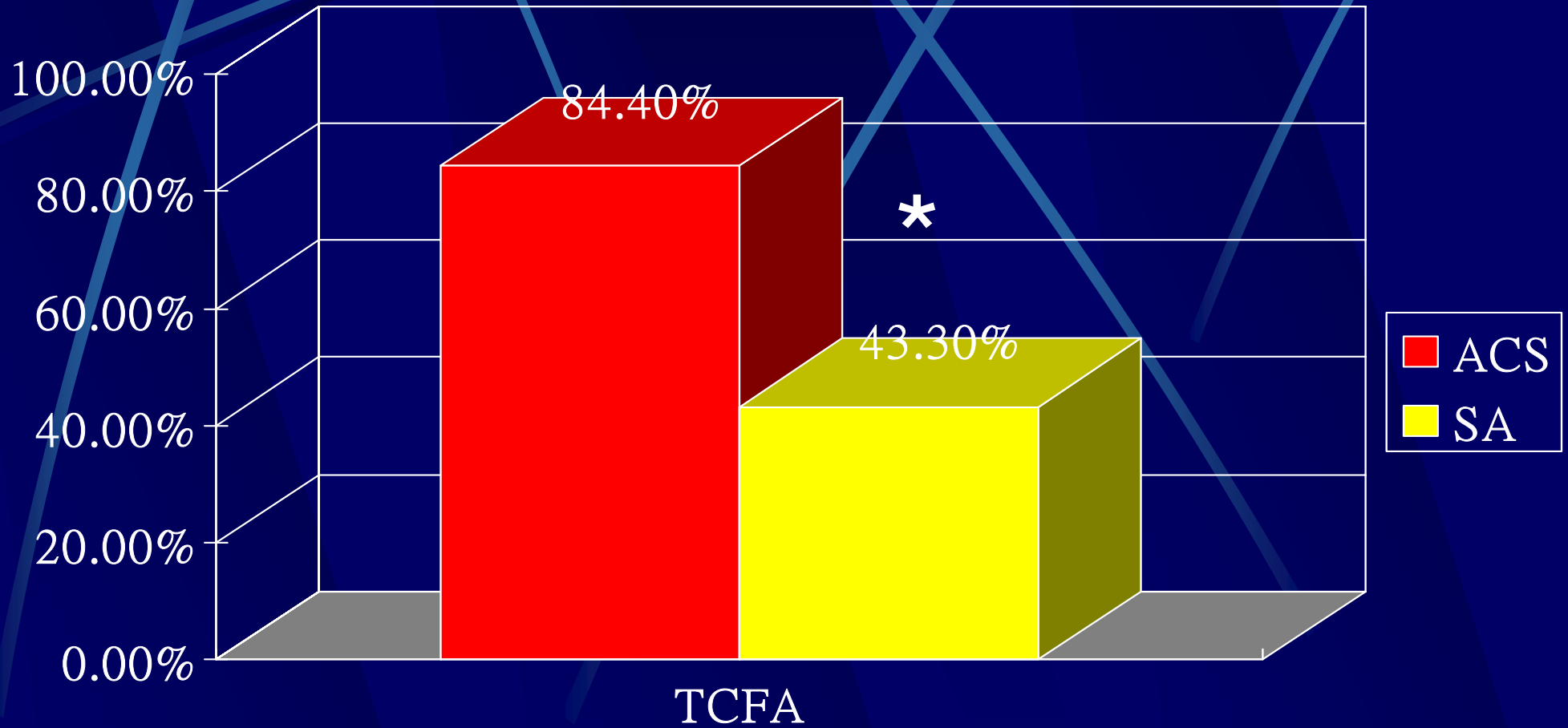
| Plaque Composition | ACS lesions N= 37 | SA Lesions N= 55 | p |
|---------------------------|------------------------------|-----------------------------|----------|
| Fibrous % | 33.1% | 57.5% | S |
| Fibro fatty % | 4.2% | 5.95% | ns |
| Calcified % | 23.6% | 18.7% | ns |
| Necrotic core % | 41.1% | 20.1% | S |

Plaque Composition



* p = Significant

TCFA in lesions



***P < 0.01**

Summary

- Virtual Histology has opened a new horizon in identifying patients at risk
- ?Necrotic core → unstable plaques → more aggressive intervention
- Ongoing clinical trials