Assessment of Vulnerable Plaque by IVUS and VH-IVUS

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## Plaque Morphology of AMI/SCD w/Thrombi

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Plaque Rupture</td>
<td>60% (f) - 80% (m)</td>
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<td>Plaque Erosion</td>
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<tr>
<td>Calcified Nodule</td>
<td>2% - 7%</td>
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</table>

*Images show various morphologies of plaques with thrombi.*
Plaque Rupture & Echolucent Plaque in non-Culprit lesions HORIZONS-AMI

A. Plaque ruptures at baseline (N=29)

- Right (N=15)
- Left anterior descending (N=8)
- Left circumflex (N=4)

B. Echolucent plaques at baseline (N=35)

- Right (N=13)
- Left anterior descending (N=16)
- Left circumflex (N=3)

Doi H et al. Unpublished data
Plaque Rupture

13 Months FU

29

4/11: Healed

7/11: Persisted

9: New

Echolucent Plaque

35

11/25: Disappeared

14/25: Persisted

10: New

Doi H et al. Unpublished data
Calcium Nodule

Data obtained in the CDEV3 Study, Gardner et al, JACC Imaging, 2008, sponsored by InfraReDx, Inc.
• 327 Calcified nodule in 1340 vessels in 572 pts
• Incidence: pt 49.8% (285/572), vessel 18% (241/1340)
• Multiple nodule/vessel 25.3% (61/241)
Distribution of Calcium Nodule

Similar with the distribution of plaque rupture, TCFA

Tam A @ CRF
<table>
<thead>
<tr>
<th>VH-IVUS Classification</th>
<th>Thin-cap FA</th>
<th>Thick-cap FA</th>
<th>PIT</th>
<th>Fibrous</th>
<th>Fibrocalcific</th>
</tr>
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<tbody>
<tr>
<td>More than 10% Confluent Necrotic Core</td>
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<td>NO more than 10% Confluent Necrotic Core</td>
<td>More than 10% Confluent Calcium</td>
<td>More than 15% Fibrofatty</td>
<td></td>
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### Histological Atherosclerosis Classification

<table>
<thead>
<tr>
<th>Nomenclature and main histology</th>
<th>Sequences in progression</th>
<th>Main growth mechanism</th>
<th>Earliest onset</th>
<th>Clinical correlation</th>
</tr>
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<tbody>
<tr>
<td>Type I (initial) lesion</td>
<td>I</td>
<td>isolated macrophage</td>
<td>from first decade</td>
<td>clinically silent</td>
</tr>
<tr>
<td>mainly intracellular lipid</td>
<td>II</td>
<td>foam cells</td>
<td></td>
<td></td>
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<tr>
<td>Type II (fatty streak) lesion</td>
<td>III</td>
<td>mainly by lipid</td>
<td>from third decade</td>
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<tr>
<td>accumulation</td>
<td></td>
<td>extracellular lipid</td>
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<td>Type III (intermediate) lesion</td>
<td>IV</td>
<td>Type II changes &amp; core of extracellular lipid</td>
<td>from fourth decade</td>
<td>clinically silent or overt</td>
</tr>
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<td>Type IV (atheroma) lesion</td>
<td>V</td>
<td>lipid core &amp; fibrotic layer, or multiple lipid cores &amp; fibrotic layers, or mainly calcific, or mainly fibrotic</td>
<td>accelerated smooth muscle and collagen increase</td>
<td></td>
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<td>Type V (fibroatheroma) lesion</td>
<td>VI</td>
<td>surface defect, hematoma-hemorrhage, thrombus</td>
<td>thrombosis, hematoma</td>
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- **Type II lesion**: Macrophage foam cells
  - Adaptive thickening (smooth muscle)
  - Intima
  - Media
- **Type III (preatheroma)**
- **Type IV (atheroma)**
  - Small pools of extracellular lipid
  - Core of extracellular lipid
  - Intima
- **Type V (fibroatheroma)**
- **Type VI (complicated lesion)**
  - Thrombus
  - Fibrous thickening
  - Fissure and hematoma
1. Pathological Intimal Thickening (PIT)
2. Thin cap fibroatheroma (TCFA)
3. Thick cap Fibroatheroma (ThCFA)
4. Fibrous Plaque
5. Fibrocalcific
Pathological Intimal thickening & Fibroatheroma

Pathologic intimal thickening

Fibrous cap atheroma

Necrosis (-)

Necrosis (+)
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[Images of vessel cross-sections with color-coded regions corresponding to the classification criteria.]
“Confluent”
Confluent Necrotic Core

Non-Confluent
Pathological Intimal Thickening

Confluent
Thick Cap Fibroatheroma
Thick cap fibroatheroma

Thin cap fibroatheroma
VH Thin cap fibroatheroma (TCFA)

1. Confluent NC > 10%
2. 30° NC abutting the lumen
3. 3 consecutive frames (=1.5mm in length)

Thin cap < 65 µm (less than the 200 µm resolution of IVUS)
Incidence of NC at the bottom/shoulder of the cavity: 84% (41/49)

1. 129 ruptures in 100 vessels in 97 patients in PROSPECT.
2. Typical plaque rupture=49/129 (38%)

Yang J Unpublished data
Prospect 27731-003: 58 yo man

3/15/05: NSTEMI, PCI of MRCA

3/23/06 (1 year): Unstable angina attributed to LAD

**Index 3/15/05**

QCA MLAD DS 31.1%

**Event 3/23/06**

QCA MLAD DS 100%
PROSPECT 27731-003: Index 3/15/05

Baseline MLAD
QCA: DS 31.1%
IVUS: MLA 3.6 mm²
VH: TCFA

MLAD
1. TCFA
   3.6 46%

PLAD
2. TCFA
   5.7 60%
PROSPECT 82910-012: 52 yo man

2/13/06: NSTEMI, PCI of MLAD

2/6/07 (1 year): NSTEMI attributed to LCX

Index 2/13/06

QCA PLCX DS 38.6%

Event 2/6/07

QCA PLCX DS 71.3%
PROSPECT 82910-012: Index 2/13/06

Baseline PLCX
QCA: DS 38.6%
IVUS: MLA 5.3 mm²
VH: ThCFA

Echolucent Plaque
True or Artificial Necrotic Core?
Necrotic core and Calcium are together **longitudinally**.
Necrotic core and Calcium are together **circumferentially**.
Echolucent Plaque = Vulnerable Plaque?

Fibrous Cap

Necrotic Core?
Echolucent Plaque and VH
Echolucent Plaque and VH

Echolucent Zone
- FT 14 (26%)
- FT+FF 35 (66%)
- FF 4 (8%)

Adjacent to Echolucent Zone
- NC 27 (51%)
- NC+DC 14 (26%)
- FT/FF 10 (19%)
- DC 2 (4%)

VH Phenotype of Echolucent Lesion
- PIT 16 (30%)
- VH-TCFA 3 (6%)
- ThCFA 27 (51%)
- Fibrocalcific 7 (13%)
Attenuated Plaque and VH

Attenuated plaque
P&M: 9.44 mm²
PB: 67.3%

NC area: 1.96 mm²
NC%: 20.8%

Non attenuated plaque
P&M: 8.8 mm²
PB: 61.7%

NC area: 0.54 mm²
NC%: 6.1%

Wu X et al, Am J Cardiol in press
Attenuated Plaque & NC

P<0.001

Incidence (%)

100%

75%

50%

25%

0

1st quartile
(≤ 0.45mm²)

25
(39%)

3
(6%)

Attenuated plaque

Non-attenuated plaque

2nd quartile
(0.45-0.95mm²)

17
(26%)

10
(21%)

3rd quartile
(0.95-1.5mm²)

12
(18%)

18
(38%)

4th quartile
(>1.5mm²)

11
(17%)

16
(34%)

Necrotic core area

Wu X et al, Am J Cardiol in press
Attenuated Plaque

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Attenuated Plaque

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- **Plaque Rupture**: 60% (f) – 80% (m)
- **Plaque Erosion**: 20% (m) – 40% (f)
- **Calcified Nodule**: 2% – 7%
# Comparison between Ruptured thrombosis vs. Erosive thrombosis

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<tr>
<th></th>
<th>No Plaque Rupture (n=23)</th>
<th>Plaque Rupture (n=17)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td><strong>TCFA</strong></td>
<td>73.9%</td>
<td>64.7%</td>
<td>0.53</td>
</tr>
<tr>
<td><strong>MLA site</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumen Area (mm²)</td>
<td>3.5±1.4</td>
<td>3.1±0.6</td>
<td>0.34</td>
</tr>
<tr>
<td>Vessel Area (mm²)</td>
<td>16.0±4.4</td>
<td>20.3±5.5</td>
<td>0.09</td>
</tr>
<tr>
<td>Plaque Burden (%)</td>
<td>78.2±5.5</td>
<td>83.6±4.7</td>
<td>0.002</td>
</tr>
<tr>
<td>Necrotic Core (%)</td>
<td>23.1±11.9</td>
<td>19.1±10.1</td>
<td>0.26</td>
</tr>
<tr>
<td><strong>Maximum NC site</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lumen Area (mm²)</td>
<td>4.8±2.0</td>
<td>5.4±1.7</td>
<td>0.40</td>
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<tr>
<td>Vessel Area (mm²)</td>
<td>16.0±4.3</td>
<td>18.6±5.3</td>
<td>0.11</td>
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<tr>
<td>Plaque Burden (%)</td>
<td>70.3±8.0</td>
<td>70.3±7.9</td>
<td>0.97</td>
</tr>
<tr>
<td>Necrotic Core (%)</td>
<td>34.3±12.9</td>
<td>28.7±9.1</td>
<td>0.13</td>
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Comparison between Ruptured thrombosis vs. Erosive thrombosis

- Pathology -

<table>
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<tr>
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<th>Erosion (n=50)</th>
<th>Rupture (n=65)</th>
<th>p-value</th>
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<tr>
<td>Age (yrs)</td>
<td>43±9</td>
<td>52±10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male</td>
<td>74%</td>
<td>89%</td>
<td>0.03</td>
</tr>
<tr>
<td>Vessel Area (mm²)</td>
<td>9.5±5.2</td>
<td>13.7±6.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Plaque Burden (%)</td>
<td>77.1±13.8</td>
<td>71.3±14.9</td>
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<td>Necrotic Core (%)</td>
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<td>38.3±23.4</td>
<td>&lt;0.0001</td>
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<td>Occlusive Thrombus (%)</td>
<td>52%</td>
<td>46%</td>
<td>0.53</td>
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Vulnerable Plaque?

Pathological Intimal Thickening
Thick Cap FA  Thin Cap FA  Rupture

Echolucent Plaque
Attenuated Plaque
Calcium Nodule

thrombosis