VH-IVUS and OCT; "Clinical Application, Experience, and Future Utility"

Gary S. Mintz, MD

Cardiovascular Research Foundation
New York, NY
What does greyscale IVUS do well?

- Pre-intervention lesion assessment
  - Lesion severity
  - Vessel size and lesion length
  - Overall plaque burden
  - Unusual lesion morphology (i.e., plaque rupture)
  - Calcium
- Guidance of PCI procedures
  - Stent size and length
- Post-intervention lesion assessment
  - Final lumen dimensions
  - Complications
  - Predicting restenosis and subacute stent thrombosis
- Follow-up
  - Mechanisms of restenosis
  - Endpoints in restenosis trials
- Progression/regression
  - Overall plaque burden (although the changes are small!)
What does greyscale IVUS do poorly?

- Pre-intervention lesion assessment
  - 3-D orientation and spatial relationships
  - Plaque composition (except calcium)
  - Vulnerable plaque
  - High risk PCI lesions
  - Thrombus
- Post-intervention lesion assessment
  - Subtle dissections, stent malapposition, plaque prolapse, etc.
  - Thrombus
- Follow-up
  - Subtle malapposition
  - Small amounts of intimal hyperplasia
  - Predicting late events (especially very late stent thrombosis)
- Progression/regression
  - Changes in individual plaque components
Eagle Eye (20MHz Electronic Array Transducer)

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

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Predictive Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrous tissue (n=162)</td>
<td>84.0%</td>
<td>98.8%</td>
<td>92.8%</td>
</tr>
<tr>
<td>Fibrofatty (n=84)</td>
<td>86.9%</td>
<td>95.1%</td>
<td>93.4%</td>
</tr>
<tr>
<td>Necrotic core (n=69)</td>
<td>97.1%</td>
<td>93.8%</td>
<td>94.4%</td>
</tr>
<tr>
<td>Dense calcium (n=92)</td>
<td>97.8%</td>
<td>99.7%</td>
<td>99.3%</td>
</tr>
</tbody>
</table>
Thin Cap Fibroatheroma (TCFA)

“Thin Cap Fibro-Atheroma (TCFA)” or “Vulnerable Plaque” -- Confluent Necrotic Core >10% of total plaque, >33% of lesion circumference at the lumen surface, and present in 3 consecutive frames. Based on the presence or absence of Ca, the length of the NC, or signs of previous ruptures, TCFA can be further sub-classified

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

“Highest Risk TCFA”

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

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

“TCFA without significant narrowing” - plaque burden <50% on IVUS and/or less than 25% narrowing on angiogram.

(Pathologic data suggests that TCFA without significant plaque burden are less “vulnerable”)

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

700 pts with ACS undergoing 1 or 2-vessel PCI followed by 3-vessel imaging
QCA of entire coronary tree
IVUS
Virtual histology
Palpography (n=~350)

Repeat imaging in pts with events
F/U: Until there are 100 VP events

Meds rec
Aspirin
Plavix 1yr
Statin
Repeat biomarkers @ 30 days, 6 months

PI: Gregg W. Stone
Sponsor: Abbott Vascular (Partner: Volcano)
PROSPECT: Baseline Features

N = 697

- STEMI >24 hrs: 30.3%
- NSTEMI: 65.4%
- Unstable angina with ST changes: 4.3%
### PROSPECT: Imaging Summary

Data acquisition (N=697)

<table>
<thead>
<tr>
<th></th>
<th>Angiography</th>
<th>IVUS / VH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N vessels</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Imaged</strong></td>
<td>N=697</td>
<td>N=697</td>
</tr>
<tr>
<td>1, 2, 3</td>
<td>0%, 0%, 100%</td>
<td>1%, 10%, 88%</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>3.0 ± 0</td>
<td>2.84 ± 0.5</td>
</tr>
<tr>
<td><strong>Core lab analyzable</strong></td>
<td>N=697</td>
<td>N=616 (88.4%)</td>
</tr>
<tr>
<td>1, 2, 3</td>
<td>0.1%, 0.4%, 99.4%</td>
<td>14%, 32%, 55%</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>3.0 ± 0</td>
<td>2.42 ± 0.70*</td>
</tr>
<tr>
<td><strong>Length (mm)</strong></td>
<td>446±84</td>
<td>183±76 / 166±70</td>
</tr>
</tbody>
</table>
PROSPECT: Imaging Summary

QCA DS% in 1798 angiographically visible lesions

Mean DS 38.5 ± 15.5%

DS% by QCA

Frequency (%)
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEM area, mm$^2$</td>
<td>16.72 ± 6.36</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>2.82 ± 0.64</td>
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<tr>
<td>Lumen area, mm$^2$</td>
<td>8.89 ± 4.12</td>
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<tr>
<td>Mean LD, mm</td>
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<tr>
<td>Plaque area, mm$^2$</td>
<td>11.29 ± 4.15</td>
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<tr>
<td>MVD, mm</td>
<td>4.04 ± 0.88</td>
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<td>Plaque burden %</td>
<td>47 ± 11</td>
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<tr>
<td>Mean VD, mm</td>
<td>4.45 ± 0.87</td>
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<tr>
<td>MLA, mm$^2$</td>
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<tr>
<td>Max VD, mm</td>
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<td>Lumen ecc.</td>
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By IVUS (in 786 of the 1798 total angiographic lesions)
### PROSPECT: Imaging Summary

**IVUS of angiographic non-culprit lesions**

By IVUS (in 786 of the 1798 total angiographic lesions)

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<th>Parameter</th>
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210 (26.7%) angiographically mild lesions had an MLA <4.0 mm²
IVUS of angiographic non-culprit lesions

By IVUS (in 786 of the 1798 total angiographic lesions)

- EEM area, mm²: 16.72 ± 6.36
- MLD, mm: 2.82 ± 0.64
- Lumen area, mm²: 8.89 ± 4.12
- Mean LD, mm: 3.26 ± 0.72
- Plaque area, mm²: 11.29 ± 4.15
- MVD, mm: 4.04 ± 0.88
- Plaque burden %: 47 ± 11
- Mean VD, mm: 4.45 ± 0.87
- MLA, mm²: 6.36 ± 3.75
- Max VD, mm: 4.90 ± 1.02
- Remodeling index: 0.94 ± 0.16
- Lumen ecc.: 0.93 ± 0.70

210 (26.7%) angiographically mild lesions had an MLA < 4.0 mm²

259 (33.0%) of angiographically visible lesions were NOT considered IVUS lesions (<40% plaque burden or present for <3 frames)
PROSPECT: Baseline features
Presence of $\geq 1$ VH lesion subtypes (2381 lesions in 616 pts)
PROSPECT: Imaging Summary

Per patient incidence of VH-TCFAs

- 28.4% of patients have ≥1 VH-TCFA
- 0.42 ± 0.78 VH-TCFAs per patient (range 0 – 5 per patient)
- Total 266 VH-TCFAs in 616 patients

Lesions/patient per coronary tree

- 71.6% with VH-TCFA lesions
- 17.7% with 1 VH-TCFA
- 7.9% with 2 VH-TCFAs
- 2.3% with 3 VH-TCFAs
- 0.5% with ≥4 VH-TCFAs
Only 24.3% of VH-TCFAs have an MLA ≤4.0mm².
PROSPECT: Acute MI

Pre PCI

Post PCI

POBA

Stent
Mid RCA fibroatheroma

Angiographically near normal

Stent

VH-TCFA
Multiple NC
Length 3.7 mm
F 35%
FF 1%
NC 52%
DC 12%

IVUS MLA: 6.4 mm²
Prox RCA fibroatheroma

Angiographically mild lesion

Stent

2nd VH-TCFA

Single NC
Length 11 mm
F 39%
FF 1%
NC 53%
DC 7%

MLA: 6.1 mm²
Mid LAD fibroatheroma

Angiographically mild lesion

VH-TCFA
Single NC
Length 11 mm
F 40%
FF 7%
NC 42%
DC 11%

MLA: 11.1 mm²
In 81 pts (40 with ACS), the maximum NC was at the MLA in 3%, proximal to the MLA (by 4.1mm) in 61%, and distal to the MLA (by 3.6mm) in 36% with more fibroatheromas at the Maximum NC than at the MLA.
Frequency of the longitudinal geographical miss (GM), with uncovered TCFA at the proximal or distal reference segment of the stent.

Proximal segment

- 40%

Distal segment

- 50%

- 10%
After 4 months
Numerous studies have shown a relationship between the maximum necrotic core and PCI distal embolization

- Kawaguchi et al. J Am Coll Cardiol. 2007;50:1641-6
  - ST re-elevation in 71 patients with STEMI
  - Doppler FloWire high intensity transit signals in 44 patients undergoing elective stenting
- Hong et al. unpublished
  - CK-MB release in 80 patients undergoing elective stenting
- Erbel et al. unpublished
  - Troponin and CK-MB release in 36 patients undergoing elective stenting
- Washington Hospital Center. Unpublished
  - Troponin post elective stenting
Usefulness of VH-IVUS to Predict Distal Embolization in STEMI Patients Undergoing PCI

A total of 71 patients with acute ST-segment elevation myocardial infarction (STEMI) underwent VH-IVUS before stent implantation.

Distal embolization - as assessed by ST-segment re-elevation after stent deployment - was observed in 11 patients and was best predicted by the necrotic core volume determined by VH-IVUS.
The relationship between VH-IVUS coronary plaque components and small embolic particles were studied in 44 patients undergoing elective stenting.

Small embolic particles were detected as high-intensity transient signals (HITS) with a Doppler guidewire. Only the necrotic core was an independent predictor of HITS.

<table>
<thead>
<tr>
<th>Independent Predictors of the Highest HITS Count Tertile by Multivariate Analysis</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EEM CSA, mm²</td>
<td>1.21</td>
<td>0.25-5.73</td>
<td>0.813</td>
</tr>
<tr>
<td>P+M CSA, mm²</td>
<td>0.81</td>
<td>0.17-3.90</td>
<td>0.788</td>
</tr>
<tr>
<td>Dense Calcium, mm²</td>
<td>1.25</td>
<td>0.22-7.21</td>
<td>0.804</td>
</tr>
<tr>
<td>Necrotic core, mm²</td>
<td>4.41</td>
<td>1.03-18.81</td>
<td>0.045</td>
</tr>
</tbody>
</table>
Optical Coherence Tomography (OCT)

The optical analog of IVUS, OCT measures optical reflections.

Transducer (Lens)

Object 1

Object 2

$\Delta d$
<table>
<thead>
<tr>
<th><strong>IVUS</strong></th>
<th><strong>OCT</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Resolution</strong>&lt;br&gt;(axial)</td>
<td>100 - 150 µm</td>
</tr>
<tr>
<td><strong>Resolution</strong>&lt;br&gt;(lateral)</td>
<td>150 - 300 µm</td>
</tr>
<tr>
<td><strong>Size of imaging core</strong></td>
<td>0.8 mm</td>
</tr>
<tr>
<td><strong>Dynamic range</strong></td>
<td>40 - 60 dB</td>
</tr>
<tr>
<td><strong>Frame rate</strong></td>
<td>30 frames/s</td>
</tr>
<tr>
<td><strong>Scan area</strong></td>
<td>10 - 15 mm</td>
</tr>
<tr>
<td><strong>Max. penetration</strong></td>
<td>4 - 8 mm</td>
</tr>
<tr>
<td><strong>Blood clearing</strong></td>
<td>Not required</td>
</tr>
<tr>
<td><strong>Balloon Occlusion</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Flushing</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Pullback</strong></td>
<td>0.5mm/s (no limit)</td>
</tr>
</tbody>
</table>
### In vitro Validation

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>+ Predictive Value</th>
<th>- Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fibrous</strong></td>
<td>.87</td>
<td>.97</td>
<td>.88</td>
<td>.96</td>
</tr>
<tr>
<td><strong>Calcific</strong></td>
<td>.95</td>
<td>1.0</td>
<td>1.0</td>
<td>.95</td>
</tr>
<tr>
<td><strong>Lipid Pool</strong></td>
<td>.92</td>
<td>.94</td>
<td>.81</td>
<td>.97</td>
</tr>
</tbody>
</table>

Interobserver $k = 0.88$; Intraobserver $k = 0.91$

(Yabushita et al. Circulation 2002;106:1640-5)
• **Red thrombus** was identified as high-backscattering protrusions inside the lumen of the artery, with signal-free shadowing in the OCT image.

• **White thrombus** was identified as low-backscattering projections in the OCT image.

Sensitivity = 95%
Specificity = 88%
Positive predictive value = 86%
Negative predictive value = 95%

(Kubo et al. Circulation 2006;114:II-645)
In vivo comparison of OCT and angioscopy in assessing culprit lesions in 30 AMI patients

Plaque rupture

Incidence=73%

Incidence=47%

Incidence=40%

Plaque erosion

Incidence=23%

Incidence=3%

Incidence=0%

(Kubo et al. J Am Coll Cardiol 2007;50:933-9)
Thrombus

(Kubo et al. J Am Coll Cardiol 2007;50:933-9)
OCT vs Angioscopy Assessment of Plaque Vulnerability (n=30)

- White (n=19)
- Light yellow (n=22)
- Yellow (n=21)
- Intense yellow (n=15)

**Fibrous cap thickness (microns)**
- White: 389
- Light yellow: 228
- Yellow: 115
- Intense yellow: 59

**Lipid Rich Plaque (≥2 quadrants)**

<table>
<thead>
<tr>
<th>Lipid (# quadrants)</th>
<th>White</th>
<th>Light Yellow</th>
<th>Yellow</th>
<th>Intense Yellow</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>4</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>7</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>11</td>
<td>9</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

**TCFA**
- 80%

*(Kubo et al. JACC Interventions, in press)*
• Pre-intervention OCT examinations for 3 major coronary arteries using automatic pullback.
• There were 34 acute myocardial infarction and 17 stable angina pectoris patients.
• Total length of the coronary artery imaged by OCT was
  • 72 ± 24mm in the LAD
  • 56 ± 30mm in the LCX
  • 97 ± 31mm in the RCA

(Fujii et al. AHA 2007)
Infarct-artery and non-infarct artery plaques have similar lesion complexity.

- Infarct-artery plaques (n=35):
  - TCFA: 46%
  - Plaque rupture: 11%
  - Thrombus: 23%

- Non-infarct-artery plaques (n=83):
  - TCFA: 41%
  - Plaque rupture: 12%
  - Thrombus: 23%
Location of 82 TCFAs in 34 patients with AMI and 17 patients with stable angina and three vessel OCT: Vulnerable plaques tend to cluster in predictable "hot spots" within the proximal segments of the LAD and LCX and the entire length of the RCA.

(Fujii et al AHA 2007)
Low-pressure occlusion balloon catheter up to 35mm longitudinal imaging runs

Short tip

Dim image of wall

Reflections from blood
<table>
<thead>
<tr>
<th>Feature</th>
<th>IVUS</th>
<th>OCT</th>
<th>OFDI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Resolution</strong></td>
<td>(axial) 100 - 150 μm</td>
<td>(lateral) 150 - 300 μm</td>
<td>10 μm 25 - 40 μm</td>
</tr>
<tr>
<td><strong>Size of imaging core</strong></td>
<td>0.8 mm</td>
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<td>40 - 60 dB</td>
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</tr>
<tr>
<td><strong>Frame rate</strong></td>
<td>30 frames/s</td>
<td>15 frames/s</td>
<td>400 frames/s</td>
</tr>
<tr>
<td><strong>Scan area</strong></td>
<td>10 - 15 mm</td>
<td>6-7 mm</td>
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<td>4 - 8 mm</td>
<td>1 – 1.5 mm</td>
<td>1 – 1.5 mm</td>
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<td><strong>Blood clearing</strong></td>
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<td>Required</td>
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<td><strong>Pullback</strong></td>
<td>0.5mm/s (no limit)</td>
<td>1mm/s (35mm) 30mm/s (90mm)</td>
<td>Required</td>
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In-stent Restenosis
But re-endothelialization is below the resolution of even OCT
Stent Malapposition
OCT vs VH-IVUS
TCFA diagnosis in 126 lesions in 56 pts

VH-IVUS (+) and OCT (-)

VH-IVUS (-) and OCT (+)

VH-IVUS (+) and OCT (+)

(Sawada et al. Eur Heart J, in press)