IV OCT in Clinical CAD
: 1400 patients
Feasibility, Predictability, Preventability, Futurability

Ik-Kyung Jang, MD, PhD
Professor of Medicine, Harvard Medical School
Michael & Kathryn Park Endowed Chair in Cardiology
Disclosure

• Research grant: Abbott Laboratories, Medicure
• Honorarium: Abbott Laboratories
Vulnerable Plaque (High-Risk Plaque)

“A plaque that is prone to disruption, but has not been disrupted yet.”

• Rupture: 60-70%
  – Thin fibrous cap
  – Lipid rich plaque
  – Macrophage
  – Neovascularization
  – Positive remodeling

• Erosion: 30-35%

• Calcified nodule: 3-8%

• Others (SCAD, etc)
# IV Diagnostics for Vulnerable Plaque

<table>
<thead>
<tr>
<th>Modality</th>
<th>Cap</th>
<th>Lipid</th>
<th>МΦ</th>
<th>Microvessels</th>
<th>Remodeling/Plaque burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>GS IVUS</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>VH IVUS</td>
<td>+</td>
<td>++/+++</td>
<td>-</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>NIRS IVUS</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>OCT</td>
<td>+++</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>-</td>
</tr>
</tbody>
</table>

*Ong D, Jang IK. Nature Rev Cardiol 2015*
<table>
<thead>
<tr>
<th></th>
<th>OCT</th>
<th>IVUS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Axial Resolution</strong></td>
<td>12 - 15 μm</td>
<td>100 - 200 μm</td>
</tr>
<tr>
<td><strong>Beam Width</strong></td>
<td>20 – 40 μm</td>
<td>200 – 300 μm</td>
</tr>
<tr>
<td><strong>Frame Rate</strong></td>
<td>100 frames/s</td>
<td>30 frames/s</td>
</tr>
<tr>
<td><strong>Pullback Speed</strong></td>
<td>20 - 30 mm/s</td>
<td>0.5 - 1 mm/s</td>
</tr>
<tr>
<td><strong>Scan Diameter</strong></td>
<td>10 mm</td>
<td>15-20 mm</td>
</tr>
<tr>
<td><strong>Tissue Penetration</strong></td>
<td>1.0 - 2.0 mm</td>
<td>10 mm</td>
</tr>
<tr>
<td><strong>Lines per Frame</strong></td>
<td>500</td>
<td>256</td>
</tr>
<tr>
<td><strong>Lateral Sampling (3mm Artery)</strong></td>
<td>19 μm</td>
<td>225μm</td>
</tr>
<tr>
<td><strong>Blood Clearing</strong></td>
<td>Required</td>
<td>Not Required</td>
</tr>
</tbody>
</table>
Rupture

Erosion

Ca nodule
Local Detection of VP/HRP

• Why trying to detect “vulnerable plaque” using an intravascular modality?

• Only when a local treatment is considered.
# PROSPECT: MACE

## 3-year follow-up, hierarchical

<table>
<thead>
<tr>
<th>Event</th>
<th>All</th>
<th>Culprit lesion related</th>
<th>Non culprit lesion related</th>
<th>Indeterminate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac death</strong></td>
<td>1.9% (12)</td>
<td>0.2% (1)</td>
<td>0% (0)</td>
<td>1.7% (11)</td>
</tr>
<tr>
<td><strong>Cardiac arrest</strong></td>
<td>0.3% (2)</td>
<td>0.3% (2)</td>
<td>0% (0)</td>
<td>0% (0)</td>
</tr>
<tr>
<td><strong>MI (STEMI or NSTEMI)</strong></td>
<td>2.7% (17)</td>
<td>1.7% (11)</td>
<td>1.0% (6)</td>
<td>0.2% (1)</td>
</tr>
<tr>
<td><strong>Rehospitalization for unstable or progressive angina</strong></td>
<td>15.4% (101)</td>
<td>10.4% (69)</td>
<td>10.7% (68)</td>
<td>0.8% (5)</td>
</tr>
<tr>
<td><strong>Composite MACE</strong></td>
<td>20.4% (132)</td>
<td>12.9% (83)</td>
<td>11.6% (74)</td>
<td>2.7% (17)</td>
</tr>
<tr>
<td><strong>Cardiac death, arrest or MI</strong></td>
<td>4.9% (31)</td>
<td>2.2% (14)</td>
<td>1.0% (6)</td>
<td>1.9% (12)</td>
</tr>
</tbody>
</table>
### PROSPECT: Questions

**Was 3-vessel VH-IVUS imaging safe?**

Complications adjudicated to the 3-vessel IVUS imaging procedure (n=697)

<table>
<thead>
<tr>
<th>Complication</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>MI</td>
<td>3 (0.4%)</td>
</tr>
<tr>
<td>- Q-wave (from dissection)</td>
<td>1</td>
</tr>
<tr>
<td>- non Q-wave (from dissection)</td>
<td>2</td>
</tr>
<tr>
<td>PCI or CABG</td>
<td>10 (1.4%)</td>
</tr>
<tr>
<td>- CABG (from perforation)</td>
<td>1</td>
</tr>
<tr>
<td>- CABG (from dissection)</td>
<td>2</td>
</tr>
<tr>
<td>- PCI (from dissection)</td>
<td>9</td>
</tr>
<tr>
<td>Any imaging complication*</td>
<td>11 (1.6%)</td>
</tr>
</tbody>
</table>
PROSPECT: Take home message

• Potential prevention of MI (STEMI + NSTEMI) in 1% of patients undergoing 3 vessel imaging.
• Risk of 3 vessel imaging is 1.6%.
• → 3 vessel imaging is not justified, even in ACS patients.
Daily PCI Practice

- Intravascular imaging is used in 15-90% of PCI cases.
- Focus: culprit lesion – stent optimization
- Information in non-stented area (non-culprit region): not used
Clinical significance of LRP

MGH OCT Registry (NCT01110538)
(20 sites across 6 countries)

Aug 2010 - May 2015
2084 patients with OCT imaging finished at least 1-year F/U

588 patients incomplete imaging of the non-culprit regions.
22 patients with poor image quality.

1474 patients with OCT imaging in the non-culprit region of the target vessel
1474 Patients

495 patients (536 LRP)
Mean F/U period = 26.0±11.4m

979 patients (no LRP)
Mean F/U period = 26.1±11.0m

Culprit lesion related or indeterminate MACE:
12 lipid-rich plaques in 12 patients

19 Patients with non-culprit lesion related MACE (28 LRP)

464 patients with no MACE (496 LRP)
Patient-based Analysis

1474 Patients

495 patients (33.5%) (536 LRP)
Mean F/U period = 26.0±11.4m

979 patients (no LRP)
Mean F/U period = 26.1±11.0m

Culprit lesion related or indeterminate MACE:
12 lipid-rich plaques in 12 patients

19 Patients with non-culprit lesion related MACE (28 LRP)

464 patients with no MACE (496 LRP)
NC-MACE Free Survival Curve

B

Non-culprit Lesion Related MACE Free Survival Curve

At 24-month follow-up
Hazard Ratio (95% CI): 1.984 (0.992 – 3.968)
P(log-rank)=0.048

At 36-month follow-up
Hazard Ratio (95% CI): 1.993 (1.055 – 3.764)
P(log-rank)=0.030

At 48-month follow-up
Hazard Ratio (95% CI): 1.975 (1.046 – 3.731)
P(log-rank)=0.033

Cumulative rate of NC-MACE

No LRP group
LRP group

No. at Risk
Non-LRP 979 956 708 394 52
LRP 495 477 354 193 35
# KM Estimates for Cumulative Number (Rate) of individual MACE in 1474 patients

<table>
<thead>
<tr>
<th>Category</th>
<th>All events</th>
<th>Culprit lesion related</th>
<th>Non-culprit lesion related</th>
<th>Undetermined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Death, n(%)</td>
<td>5 (0.4)</td>
<td>1 (0.1)</td>
<td>0</td>
<td>4 (0.3)</td>
</tr>
<tr>
<td>Acute myocardial infarction, n(%)</td>
<td>21 (1.8)</td>
<td>11 (1.0)</td>
<td>9 (0.7)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>STEMI, n(%)</td>
<td>7 (0.6)</td>
<td>4 (0.4)</td>
<td>2 (0.2)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>NSTEMI, n(%)</td>
<td>14 (1.2)</td>
<td>7 (0.6)</td>
<td>7 (0.6)</td>
<td>0</td>
</tr>
<tr>
<td>Ischemia-driven revascularization, n(%)</td>
<td>66 (6.5)</td>
<td>28 (2.4)</td>
<td>38 (4.3)</td>
<td>0</td>
</tr>
<tr>
<td>Composite cardiac events, n(%)</td>
<td>74 (7.1)</td>
<td>31 (2.6)</td>
<td>38 (4.3)</td>
<td>5 (0.3)</td>
</tr>
</tbody>
</table>
1474 Patients

495 patients (536 LRP)
Mean F/U period = 26.0±11.4m

979 patients (No LRP)
Mean F/U period = 26.1±11.0m

Culprit lesion related or indeterminate MACE:
12 lipid-rich plaques in 12 patients

19 Patients (3.8%) with NC lesion related MACE
(28 LRP)

464 patients with no MACE
(496 LRP)
## Lesion-Level Analysis

<table>
<thead>
<tr>
<th></th>
<th>NC-MACE (n=28)</th>
<th>No MACE (n=496)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Quantitative</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrous cap thickness (μm)</td>
<td>100 ± 64</td>
<td>101 ± 52</td>
<td>0.977</td>
</tr>
<tr>
<td>Lipid length (mm)</td>
<td>9.9 ± 3.6</td>
<td>7.9 ± 4.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean lipid arc (°)</td>
<td>176.7 ± 61.2</td>
<td>166.9 ± 55.7</td>
<td>0.461</td>
</tr>
<tr>
<td>Maximal lipid arc (°)</td>
<td>240.9 ± 78.4</td>
<td>205.1 ± 69.3</td>
<td>0.023</td>
</tr>
<tr>
<td>Lipid index*</td>
<td>1723 ± 880</td>
<td>1411 ± 1139</td>
<td>0.081</td>
</tr>
<tr>
<td>Percent area stenosis (%)</td>
<td>56.7 ± 15.1</td>
<td>47.4 ± 15.4</td>
<td>0.007</td>
</tr>
<tr>
<td>Reference lumen area (mm²)</td>
<td>8.85 ± 4.58</td>
<td>9.75 ± 3.92</td>
<td>0.333</td>
</tr>
</tbody>
</table>

*Lipid index = lipid length x mean lipid arc*
Rate of NC-MACE

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rate of Non-Culprit Lesion Related MACE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid length &gt; 5.9mm</td>
<td>8.0</td>
</tr>
<tr>
<td>Maximal Lipid arc &gt; 192.8°</td>
<td>7.5</td>
</tr>
<tr>
<td>Percent area stenosis &gt; 68.5%</td>
<td>22.7</td>
</tr>
<tr>
<td>Lipid length &gt; 5.9mm + Percent area stenosis &gt; 68.5%</td>
<td>25.7</td>
</tr>
<tr>
<td>Maximal lipid arc &gt; 192.8° + Percent area stenosis &gt; 68.5%</td>
<td>30.4</td>
</tr>
<tr>
<td>Lipid length + Maximal lipid arc + Percent area stenosis</td>
<td>35.0</td>
</tr>
</tbody>
</table>

No. of NC-MACE / No. of present or absent lesions

<table>
<thead>
<tr>
<th>No of present or absent lesions</th>
<th>Hazard Ratio (95%CI) P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>25/314</td>
<td>5.691 (1.718-18.849) 0.001</td>
</tr>
<tr>
<td>3/210</td>
<td>2.493 (1.098-5.662) 0.024</td>
</tr>
<tr>
<td>20/265</td>
<td>10/44</td>
</tr>
<tr>
<td>8/259</td>
<td>18/480</td>
</tr>
<tr>
<td>9/35</td>
<td>19/489</td>
</tr>
<tr>
<td>7/23</td>
<td>7/20</td>
</tr>
</tbody>
</table>

Present | Absent
Plaque-based Analysis

1474 patients

536 LRP
495 patients
Mean F/U period = 26.0±11.4m

12/536 LRP caused MACE (2.4%)
2 STEMI
3 NSTEMI
2 UAP
5 SAP

No LRP
979 patients
Mean F/U period = 26.1±11.0m
Summary

• LRP was found in non-culprit (NC) regions of target vessel in 1/3 of patients.

• Presence of LRP in the NC regions of the target vessel predicts increased risk for future NC-MACE.

• However, MACE was primarily driven by revascularization and not by SCD or AMI.

• Only 0.9% of LRP in the culprit vessel caused AMI (STEMI + NSTEMI) during 4-year F/U.
Study Design

Randomized to treatment (n=80)

- Atorvastatin 60mg (n=40)
- Atorvastatin 20mg (n=40)

6 months OCT and IVUS Follow-up

- Withdrawn (24)
- Poor image (6)
- Image mismatch (4)

12 months OCT and IVUS Follow-up

- (36 plaques/27 patients)
- (30 plaques/19 patients)
LDL-C Levels

AT 20 mg (n = 19)  AT 60 mg (n = 27)

Index 6M F/U 12M F/U

AT 20 mg 115±28 76±28 80±32
AT 60 mg 114±23 66±22 67±21

P<0.001  P=0.520  P=0.730  P<0.001
Fibrous Cap Thickness (FCT)

AT 60 mg (n = 36)
- 61±21 at Index
- 142±91 at 6M F/U
- 186±85 at 12M F/U

AT 20 mg (n = 30)
- 61±18 at Index
- 99±49 at 6M F/U
- 127±68 at 12M F/U

P AT60 vs. AT20
- 0.963 at Index
- 0.022 at 6M F/U
- 0.004 at 12M F/U
Summary (1/2)

• Prevalence of lipid-rich plaque is relatively high (1/3).

• LRP rarely causes SCD/AMI (~ 1%).

• Thin fibrous cap can be rapidly stabilized.
Summary (2/2)

• Pursuit to local detection of vulnerable plaques may not be cost effective, and may increase unnecessary risk.

• Intravascular imaging of vulnerable plaques is not ready for clinical application.
IV OCT in Clinical CAD

- Feasibility: ×
- Predictability: ×
- Preventability: × ×
- Futurability: × ×
Collaborators

Registry
20 sites

MIT
James Fujimoto, PhD

BWH
Peter Libby, MD
Peter Stone, MD

Tsuchiura kyodo, Japan
Taishi Yonetsu, MD

Nara Medical Univ. Japan
Tsunenari Soeda, MD, PhD

Hirosaki Univ. Japan
Takumi Higuma, MD, PhD

Leuven Univ. Belgium
Tom Adriaenssens, MD, PhD

Univ. of Melbourne, Australia
Peter Barlis, MD, PhD
Andrew Ooi, PhD

Catholic Univ. Italy
Filippo Crea, MD
Luigi Biasucci, MD, PhD