Optimizing PCI Outcomes in the Cath Lab: Imaging or Physiology?

Ori Ben-Yehuda, MD, FACC

Cardiovascular Research Foundation

New York, NY
FFR
FFR Reduces Uncertainty in Multi-Vessel CAD

71 yo male with typical angina CCS III and mult. CAD risk factors

Courtesy Dr. M. Kern
Functional PCI

FFR

LCx = 0.88
PCI to Prox LAD
After PCI, residual Mid LAD stenosis - All done?

FFR = 0.68

Courtesy Dr. M. Kern
Without FFR, this patient would have had one unnecessary stent (LCx) and would not have had one necessary stent (mid LAD)

FFR summary:

1. Appropriate need for Stents
2. Objective info re ischemia
3. Helps eliminate uncertainty
4. Answers AUC questions

Courtesy Dr. M. Kern
FFR Accounts for Size of Perfusion Area

- **Normal myocardium**
  - FFR = 0.60
  - 100 → 60

- **Scar tissue**
  - FFR = 0.80
  - 100 → 80
FFR Accounts for Collateral Circulation

Poorly developed collaterals

FFR = 0.70

Pa

Pd

Pv

100

70

0
FFR Accounts for Collateral Circulation

Well developed collaterals

$FFR = 0.85$
FFR pre and post PCI
FFR Based Subsequent Interventions

![Graph showing subsequent interventions with bar chart and line graph]

- Post Dilation: 42%
- Additional Stenting: 33%
- PD+AS: 18%
- IVUS/OCT: 9%

B

- Subsequent Intervention
- Baseline FFR: 0.63±0.14
- Post PCI FFR: 0.78±0.07
- Final FFR: 0.87±0.05

P<0.0001
Post PCI FFR and MACE
Post PCI FFR: Death and TVR

A

Death

Survival probability (%)

FFR > 0.87

FFR ≤ 0.87

P = 0.03

Time (Days)

Number at risk

FFR > 0.87
256

FFR ≤ 0.87
215

B

TVR

Survival probability (%)

FFR > 0.85

FFR ≤ 0.85

P = 0.03

Time (Days)

Number at risk

FFR > 0.85
483

FFR ≤ 0.85
176
Incremental Value of post PCI FFR

**Incremental Prognostic Value**

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Global Chi Square</th>
<th>P = 0.01</th>
<th>P &lt; 0.0001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 1.04(1.01-1.06) p=0.0001</td>
<td>34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes 1.1(0.7-1.5) p=0.7</td>
<td>61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD 1.8(1.2-2.8) p=0.006</td>
<td>1.1(0.7-1.5) p=0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACS 1.6(1.2-2.5) p=0.004</td>
<td>1.6(1.1-2.4) p=0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-vessel Disease</td>
<td>1.6(1.1-2.3) p=0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse Disease</td>
<td>1.9(1.3-2.9) p=0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DES 0.6(0.3-0.9) p=0.01</td>
<td>1.8(1.3-2.9) p=0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent Diameter 0.7(0.4-1.1) p=0.15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stent Length 0.9(0.9-1.01) p=0.26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final FFR ≤ 0.86</td>
<td>1.7(1.1-2.6 p=0.01)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
IVUS
350 patients with 367 intermediate lesions underwent IVUS and FFR
Meta-analysis of 8 Randomized Trials of IVUS vs Angio-Guided DES Implantation

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>#</th>
<th>OR</th>
<th>IVUS MACE</th>
<th>Angio MACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVUS-XLP</td>
<td>2015</td>
<td>1400</td>
<td>0.49</td>
<td>19/700</td>
<td>39/700</td>
</tr>
<tr>
<td>CTO-IVUS</td>
<td>2015</td>
<td>402</td>
<td>0.37</td>
<td>5/201</td>
<td>14/201</td>
</tr>
<tr>
<td>AIR-CTO</td>
<td>2015</td>
<td>230</td>
<td>0.82</td>
<td>25/115</td>
<td>29/115</td>
</tr>
<tr>
<td>Tan-LM</td>
<td>2015</td>
<td>123</td>
<td>0.42</td>
<td>8/61</td>
<td>17/62</td>
</tr>
<tr>
<td>MOZART</td>
<td>2014</td>
<td>83</td>
<td>0.41</td>
<td>2/41</td>
<td>5/42</td>
</tr>
<tr>
<td>RESET</td>
<td>2013</td>
<td>543</td>
<td>0.60</td>
<td>12/269</td>
<td>20/274</td>
</tr>
<tr>
<td>AVIO</td>
<td>2013</td>
<td>284</td>
<td>0.67</td>
<td>24/142</td>
<td>33/142</td>
</tr>
<tr>
<td>Home-DES</td>
<td>2010</td>
<td>210</td>
<td>0.91</td>
<td>11/105</td>
<td>12/105</td>
</tr>
<tr>
<td>OVERALL</td>
<td></td>
<td>3275</td>
<td>0.59</td>
<td>106/1634</td>
<td>169/1641</td>
</tr>
</tbody>
</table>

- IVUS better
- Angio better
- 6.5% 10.3%

<table>
<thead>
<tr>
<th>Event</th>
<th>IVUS events</th>
<th>Angio events</th>
<th>OR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>6.5%</td>
<td>10.3%</td>
<td>0.59</td>
<td>0.46-0.76</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CV mortality</td>
<td>0.5%</td>
<td>1.2%</td>
<td>0.46</td>
<td>0.21-1.00</td>
<td>0.05</td>
</tr>
<tr>
<td>MI</td>
<td>0.9%</td>
<td>1.6%</td>
<td>0.58</td>
<td>0.30-1.11</td>
<td>0.10</td>
</tr>
<tr>
<td>TLR</td>
<td>4.1%</td>
<td>6.6%</td>
<td>0.60</td>
<td>0.43-0.84</td>
<td>0.003</td>
</tr>
<tr>
<td>TVR</td>
<td>5.5%</td>
<td>8.7%</td>
<td>0.61</td>
<td>0.41-0.91</td>
<td>0.02</td>
</tr>
<tr>
<td>ST</td>
<td>0.6%</td>
<td>1.3%</td>
<td>0.49</td>
<td>0.24-0.99</td>
<td>0.04</td>
</tr>
</tbody>
</table>

IVUS-XPL: 1400 pts with long lesions (EES length ≥28 mm) randomized to IVUS vs angio guidance.
Primary end point: MACE (cardiac death, target-lesion related MI, and ischemia-driven TLR)

Primary End Point – Intention to Treat Analysis

HR 0.48 (95% CI, 0.28-0.83)
Log-rank P = 0.007

<table>
<thead>
<tr>
<th>Time Since Randomization, months</th>
<th>Angiography-guidance</th>
<th>IVUS-guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>6</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>9</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>12</td>
<td>5.8%</td>
<td>2.9%</td>
</tr>
</tbody>
</table>

No. at risk
Angiography arm 700 673 660 643 624
IVUS arm 700 671 665 654 641

Hong et al. JAMA 2015;314:2155-63
IVUS-XPL: 1400 pts with long lesions (EES length ≥28 mm) randomized to IVUS vs angio guidance. Primary end point: MACE (cardiac death, target-lesion related MI, and ischemia-driven TLR)

<table>
<thead>
<tr>
<th>Cross-over</th>
<th>IVUS-guidance (n=700)</th>
<th>Angiography-guidance (n=700)</th>
<th>Hazard ratio (95% CI)</th>
<th>Log-Rank P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary End Point</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MACE</td>
<td>19 (2.9%)</td>
<td>39 (5.8%)</td>
<td>0.48 (0.28–0.83)</td>
<td>.007</td>
</tr>
<tr>
<td>Secondary End Point</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac death</td>
<td>3 (0.4%)</td>
<td>5 (0.7%)</td>
<td>0.60 (0.14-2.52)</td>
<td>.48</td>
</tr>
<tr>
<td>Target lesion related MI</td>
<td>0</td>
<td>1 (0.1%)</td>
<td>-</td>
<td>.32</td>
</tr>
<tr>
<td>Ischemia-driven TLR</td>
<td>17 (2.5%)</td>
<td>33 (5.0%)</td>
<td>0.51 (0.28-0.91)</td>
<td>.02</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>2 (0.3%)</td>
<td>2 (0.3%)</td>
<td>1.00 (0.14-7.10)</td>
<td>1.00</td>
</tr>
<tr>
<td>Acute</td>
<td>1 (0.1%)</td>
<td>1 (0.1%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sub-acute</td>
<td>1 (0.1%)</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Late</td>
<td>0</td>
<td>1 (0.1%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Hong et al. JAMA 2015;314:2155-63
Primary End Point in IVUS Guidance

HR, 0.31 (95% CI, 0.11-0.86)
Log-rank P = .017

Event Rate, %

Patients not meeting IVUS-criteria for stent optimization

Patients meeting IVUS-criteria for stent optimization

No. at risk
Not meeting criteria 315 299 297 394 285
Meeting criteria 363 362 345 338 334

Time Since Randomization, months

Hong et al. JAMA 2015;314:2155-63
IVUS technology has been clinically available for over 20+ years. Yet . . .

- Technology and image quality have not improved in the last 10+ years.
- Poor spatial resolution and catheter-to-catheter imaging inconsistency are problematic.
- Current IVUS systems are not capable of resolving structures <100 μm (and maybe <150μm) in size.
- Often requires expert interpretation, inhibits confidence in new users, and is a primary obstacle to maximizing growth and adoption of IVUS technology.
OCT can show...

- Plaque Composition
- Lesion length
- Stent Diameter
- Adequate expansion
- Edge Dissection
- Malapposition
- Tissue Protrusion
PCI Optimization using OCT

Acquire the image
High quality image allows planning for PCI optimization

Assess plaque composition
Determines your vessel preparation

Identify reference segments
Stent from normal to normal

Choose stent size
Size by the smallest mean EEL to EEL diameter of your reference segments

Determine expansion/MSA
Small increases in MSA lead to major improvements in outcome

Rule out geographic miss
Angiographic co-registration can eliminate geographic miss

Determine apposition
Treatment is based on location (ostial) and relationship to underexpansion

Identify edge dissections
Treatment is based on location (proximal vs distal), arc, length and flow

Identify tissue protrusion
Treatment is based on whether it impairs effective flow area
Stent Diameter

How Big?

**Lumen**
MLD 3.0mm
MSA ($\pi r^2$) = 7.07mm²

**Mid-wall**
MWD 3.1mm
MSA ($\pi r^2$) = 7.55mm²

**External Elastic Lamina**
EELD 3.2mm
MSA ($\pi r^2$) = 8.04mm²
Why the External Elastic Lamina on OCT?

OPUS-CLASS (Phantom vs OCT vs IVUS)

Kubo et al. iJACC 2013;6(10):1095-1104
Why the External Elastic Lamina on OCT?

**Histology**
- MLD 3.0mm

**OCT**
- MLD 3.0mm
- 3.0mm Stent
  - 7.1mm²

**IVUS**
- MLD 3.3mm
- 3.25mm stent
  - 8.5mm²
Size Matters

Final Minimum Stent Area (mm²) vs. Restenosis (%) for different Stent Lengths (mm):

- 3-3.9 mm²: 40% Restenosis
- 4.8-5.7 mm²: 35% Restenosis
- 6.6-7.5 mm²: 30% Restenosis
- 8.4-9.3 mm²: 25% Restenosis
- 10.2-11.1 mm²: 20% Restenosis

* indicates statistical significance compared to other groups.

Source: de Feyter et al. Circulation 1999;100:1777-83
OCT vs. IVUS
ILUMIEN II
Retrospective comparison of OCT-guidance in ILUMIEN I and IVUS-guidance in ADAPT-DES

ILUMIEN I
418 pts enrolled

Lesions excluded:
- Poor quality (n=45)
- Not received by core lab (n=12)
- BRS (n=5)
- Inconsistent data (n=2)

Randomly chosen 1 lesion per patient

Overall study population (n=940)
354 patients, 354 lesions

1:1 Propensity matching

1:1 Propensity matched groups (n=572)
286 patients, 286 lesions

ADAPT-DES
2,179 pts enrolled in IVUS substudy

Lesions excluded:
- No QCA available (n=1043)
- STEMI (n=378)
- In-stent restenosis (n=191)
- No reference available (n=179)
- Left main (n=99)
- Poor image quality or media issue (n=77)
- Chronic total occlusion (n=75)
- Saphenous vein graft (n=66)
- Unreliable pullback (n=66)
- Not received by core lab (n=12)

2,179 pts enrolled in IVUS substudy
354 patients, 354 lesions

Randomly chosen 1 lesion per patient

Overall study population (n=940)
586 patients, 586 lesions

1:1 Propensity matching

1:1 Propensity matched groups (n=572)
286 patients, 286 lesions

RVD, lesion length, calcification, reference segment availability
ILUMIEN II: Endpoints

Primary endpoint

- Post-PCI stent expansion (%) defined as the minimum stent area (MSA) divided by the mean reference lumen area
  
  • Assessed by OCT in ILUMIEN I and by IVUS in ADAPT-DES

Secondary endpoints

- IVUS and OCT core lab measures
  
  • Mean stent expansion (defined as stent volume/stent length divided by the mean reference lumen area)
  
  • Prevalence of major edge dissection (≥3 mm in length)
  
  • Prevalence of major stent malapposition defined as malapposition distance/luminal diameter ≥20%

- Angiographic core lab measures (independent of technique)
  
  • Post-PCI MLD, mean lumen diameter, %DS and acute gain
OCT Imaging and Quantitative Analysis

- St. Jude OCT catheter with automatic pullback (C7 Dragonfly)
- OCT analysis performed at an independent core laboratory (CRF)

\[ \text{% stent expansion} = \frac{\text{MSA}}{\text{average of reference lumen area}} \times 100 \]

\[ 102.8\% = \frac{7.70}{[(6.96+8.02)/2]} \times 100 \]
IVUS Imaging and Quantitative Analysis

- Volcano Eagle Eye IVUS catheter (20MHz) with automatic pullback
  - IVUS analysis at independent core laboratory (CRF)

```
% stent expansion = MSA / average of reference lumen area
75.0% = 7.2 / [(8.1 + 11.1)/2]*100
```
Examples of Major Post Stent Findings

Major:
- Malapposition: Distance/lumen >20%
- Tissue protrusion: >10%
- Stent edge dissection: Length ≥3 mm

OCT

IVUS
**Ilumien II: Cumulative Frequency Distribution of Minimum Stent Expansion**

OCT: 72.8% [63.3, 81.3]  
IVUS: 70.6% [62.3, 78.8]  

$P=0.29$
<table>
<thead>
<tr>
<th>Finding</th>
<th>OCT guidance (n=286)</th>
<th>IVUS guidance (n=286)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any finding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Malapposition</td>
<td>76 (26.6%)</td>
<td>39 (13.6%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>- Tissue protrusion</td>
<td>182 (63.6%)</td>
<td>78 (27.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>- Stent edge dissection</td>
<td>66 (23.1%)</td>
<td>15 (5.2%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Major finding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Malap distance/lumen &gt;20%</td>
<td>4 (1.4%)</td>
<td>2 (0.7%)</td>
<td>0.69</td>
</tr>
<tr>
<td>- Tissue protrusion &gt;10%</td>
<td>33 (11.5%)</td>
<td>23 (8.0%)</td>
<td>0.17</td>
</tr>
<tr>
<td>- Dissection with length ≥3 mm</td>
<td>7 (2.4%)</td>
<td>3 (1.0%)</td>
<td>0.29</td>
</tr>
</tbody>
</table>
ILUMIEN II: Conclusions

- In the present comparison of pts undergoing OCT-guided stenting from ILUMIEN I and IVUS-guided stenting from ADAPT-DES, OCT-guidance was associated with comparable stent expansion, slightly greater in-segment %DS, and similar rates of major stent malapposition, tissue protrusion, and stent edge dissection as IVUS-guidance.

- The results of angiography-guided, IVUS-guided and OCT-guided stent implantation are currently being evaluated in the prospective, multicenter ILUMIEN III: OPTIMIZE PCI randomized trial.
ILUMIEN III RANDOMIZED CONTROLLED TRIAL
OCT VS. IVUS VS. ANGIOGRAPHY GUIDANCE

Angiography

Identification of study lesion

Randomization to IVUS or Angiography or OCT guided PCI

IVUS Guided PCI

Pre-PCI IVUS

IVUS guided PCI, per "local standard practice"

Post-PCI IVUS

OCT Guided PCI

Pre-PCI OCT

OCT Stent Sizing Guidance, per study protocol

OCT guided PCI to Acute Procedural Success

Angiography Guided PCI

Pre-PCI Angiography

Angiography guided PCI, per "local standard practice"

Post-PCI Angiography

Post-PCI OCT, blinded to investigator

OCT Guided PCI

Pre-PCI OCT

OCT guided PCI to Acute Procedural Success

Post-PCI OCT

Post-PCI OCT, blinded to investigator

Procedure Complete
Pre-PCI OCT
Dilation with 1.5-2.0mm balloon to adequately visualize distal reference if degree of lumen obstruction would interfere with distal clearance of blood or if initial OCT is suboptimal.

Stent Sizing

Stent Implantation

Angiographic success?
• 0% diameter stenosis

Post-PCI OCT

Target MSA criteria achieved?

No

Post-dilation

No

Post-dilation

Procedure Complete

Final OCT imaging
Results at TCT 2016 in Washington DC