DES Implantation in Long Diffuse Lesion

Can We Reach Optimal Stent Expansion With Conventional Stent Delivery System?

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CPIS 2007
FIM .. 4 year follow-up

Pre
Post
4 Months
12 months
24 months
48 months

Sousa JE et al.
Are Drug-Eluting Stents Changing Your Daily Practice?

After 24 months of DES for all patients, the point of no return has been reached and we will not come back to bare stent.

Thank you
DES changes our pattern of PCI

**DES Procedure**

- **Simple De Novo Lesions**
- **Chronic Total Occlusion**
- **Bifs**
- **Ostial Disease**
- **Diffuse Disease**
- **Calcified Lesions**
- **Multi Vessel Disease**

**More Complex Lesions**
- Small Vessels
- Diabetic Patients
DES failure in the real worlds ..

- Target vessel failure
  Angiographic binary restenosis < 11.9% - 16.5%*
  Clinical restenosis or TLR < 8.3% – 12.0%*

- Stent thrombosis < 2.0%

  * in diabetic patients

Data from REALITY, SIRTAX, ISAR-DIABETES
The Goal of PCI with DES

- Reduce target vessel failure
  - Restenosis
  - TLR/TVR

- Maintain long-term lower MACE rates
Is pre or post-DES dilation needed?

- Hypothesis
  - Optimize stent expansion

"Bigger is still Better" in DES era?

following DES deployment with and without pre or postdilation.
## Predictors of Restenosis and Target Vessel Revascularization after SES Implantation

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>Angiographic variables</th>
<th>Procedural variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>Small reference vessel diameter</td>
<td>Long stent length</td>
</tr>
<tr>
<td></td>
<td>Ostial location</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non–left anterior descending artery lesion</td>
<td>Small stent diameter or minimal stent area (MSA) by IVUS</td>
</tr>
<tr>
<td></td>
<td>In-stent restenosis</td>
<td></td>
</tr>
</tbody>
</table>
IVUS analysis of Cypher failure

- 27 Cypher failure vs. 29 non-restenotic control
  - Diabetes 52% vs. 14% p<0.01
  - Unstable angina 22% vs. 0% p<0.01
  - Ostial location 19% vs. 0% p<0.05

- IVUS findings
  - Minimal Stent Area (mm$^2$) 4.5 ± 1.7 vs. 6.5 ± 1.6 p<0.01
  - Stent underexpansion (<5mm$^2$) 67% vs. 21% p<0.01
What is the smallest acceptable minimum stent area?

**Bare Metal Stents**

F/U MLA > 4.0 mm² (%)

Minimum stent area (mm²)

- 6.5* (predictive value = 56%)


**Cypher**

F/U MLA > 4.0 mm² (%)

Minimum stent area (mm²)

- 5.0** (predictive value = 90%)

**CPIS 2007**
Late Loss and “Headroom” to Restenosis

- Late loss “headroom” is the space of extra late loss available for higher risk cohorts
- Headroom highest for large MSA and low in-stent late loss stent systems
Mean Late Loss and Risk of Restenosis

Mauri L, Orav JE, Kuntz RE. Circulation 2005; 111: 3435-3442
## Multivariable Predictors of in-Stent Late Loss

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Effect estimate (mm)</th>
<th>SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent type (sirolimus eluting vs bare metal)</td>
<td>-0.79</td>
<td>0.029</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.16</td>
<td>0.028</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lesion length (per 10 mm)</td>
<td>0.17</td>
<td>0.019</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Acute gain (per mm)</td>
<td>0.17</td>
<td>0.029</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Residual % diameter stenosis (per 1%)</td>
<td>-0.0097</td>
<td>0.0014</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Reference vessel diameter (per mm)</td>
<td>-0.044</td>
<td>0.028</td>
<td>0.12</td>
</tr>
</tbody>
</table>

*Mauri et al: Circulation 112:2833, 2005*
Late Loss and “Headroom” to Restenosis

- MLD < 1.5 mm
- Late Loss Headroom:
  - 0.55 mm
  - 0.35 mm
  - 0.15 mm
- RVD 3.0 mm
- Stent 3.0 mm
- MLL 0.2 mm
- MLL 0.4 mm
- MLL 0.6 mm
Late Loss and “Headroom” to Restenosis

The bigger, the better

The increased “headroom” provided by optimal DES expansion and lower late loss confers particular benefits in high-risk patients with the diabetes, small vessel, and more complex lesions.

Late Loss Headroom
0.30 mm
0.10 mm
-0.10 mm
RVD 3.0 mm with suboptimal stent expansion
Predictors of Drug-Eluting Stent Thrombosis

Clinical variables
- Diabetes
- Renal failure
- Low ejection fraction

Angiographic variables
- Bifurcation lesions

Procedural variables
- Use of multiple stents
- Use of long stents
- Small final stent area (MSA) by IVUS
- Stent underexpansion
- Residual reference segment stenosis

Postprocedural variables
- Premature discontinuation of antiplatelet therapy
Predictor of Cypher thrombosis

- 2,575 patients were treated with 4,722 Cypher stents.
- 21 (0.8%) had stent thrombosis of whom 15 had IVUS
- 12/15 SES thrombosis lesions has stent CSA <5.0mm² (vs 13/45 controls)

*Residual edge stenosis = edge lumen CSA <4.0mm² & plaque burden >70%.

Fujii et al. JACC 2005;45:995-998
Why is optimal DES expansion and apposition important ..

- Uniform stent apposition facilitates uniform drug absorption into endothelial tissue
- Incomplete apposition may contribute to thrombosis formation & SAT’s
- Stent underexpansion may increase risk for restenosis
- Optimal stent apposition may reduce target vessel revascularization (TVR)

4. Leon, M. The basic “tips and tricks” for DES implantation; TCT 2003 presentation
5. The TAXUS Stent Directions for Use
Optimal stent deployment* is only achieved in 29% of patients with current stent delivery systems; usually due to inability of stent delivery balloon to expand fully the stent to nominal size (n=256).

*MSD≥90% of average reference lumen diameter
POSTIT Trial

71% of patients did NOT have optimum stent expansion

There are NO angiographic predictors of sub-optimal apposition, including:
- Lesion Length
- % Stenosis
- Type of Stent
- RVD

POSTIT Trial, Brodie et al, Catheterization and Cardiovasc Int 2003;59:184
What causes sub-optimal stent apposition?

A) Was the SDS (balloon) undersized for the target vessel?  NO

B) Was balloon deployment pressure too low?  NO

C) Does the semi-compliant balloon with SDS not provide the necessary force to reach optimal stent apposition?  YES

“With post-dilatation using non-compliant balloons, the frequency of achieving optimum stent deployment doubles and there are significant increases in MSA – maximum stent apposition.

These data stress the continued need for adjunctive balloon post-dilatation with appropriate stent expansion balloons.”¹

¹POSTIT Trial, Brodie et al, Catheterization and Cardiovasc Int 2003;59:184
Compliance of current stent delivery system

![Graph showing the compliance of different stent delivery systems with inflation pressure. The graph compares balloon diameters at various inflation pressures for DES1, DES2, and HPB.]
Balloon compliance and dilation force

Compliant

High dilation force
More vessel injury

Non Compliant

Low dilation force and
Stent Underexpansion

\[ F = \frac{\text{Pressure} \times \text{Diameter}}{2 \times \text{Wall Thickness}} \]
Balloon inflation pressure and dilation force

No Preparation

3.2mm Vessel
90% Stenosis

Pressure x Diameter
2 x Wall Thickness

F = \frac{\text{Pressure} \times \text{Diameter}}{2 \times \text{Wall Thickness}}

\begin{align*}
\frac{6 \text{ atm} \times 0.32\text{mm}}{2 \times 1.44\text{mm}} &= 0.67 \text{ atm} \\
\frac{6 \text{ atm} \times 2.5\text{mm}}{2 \times 0.35\text{mm}} &= 21.43 \text{ atm}
\end{align*}
Which lesions need preparation before DES? ..

When to pre-dilate?

- Simple De Novo Lesions
- Chronic Total Occlusion
- Bifurcation Disease
- Ostial Disease
- Diffuse Disease
- Calcified Lesions
- Multi Vessel Disease

The More Complex Lesions and

- Tips for pre-dilatation
  - Undersize balloon (0.5-1.0mm)
  - Select balloon shorter than length of stent
  - Focal, calcified lesions – Cutting balloon may be beneficial

Leon, M. The basic “tips and tricks” for DES implantation; TCT 2003 presentation
Long Diffuse Lesion  
FFR and IVUS-guided DES Implantation

• PCI with current semi-compliant stent delivery system (SDS) in long diffuse lesion may result in stretching of the balloon around the lesion rather than concentrating the force at the lesion and cannot achieve optimal stent expansion.

• Conventional PCI in long diffuse lesion based on the visual angiographic estimation of stenosis may poorly correlate with anatomic and physiologic significance.
### Optimal stent implantation in DES era; Observations from the TAXUS IV

<table>
<thead>
<tr>
<th>TAXUS Stent MDP Groups</th>
<th>&lt;14 atm</th>
<th>14–16 atm</th>
<th>&gt;16 atm</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDP (atm)</td>
<td>11.6</td>
<td>14.2</td>
<td>17.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>22.3%</td>
<td>22.2%</td>
<td>24.9%</td>
<td>0.73</td>
</tr>
<tr>
<td>RVD (mm)</td>
<td>2.63</td>
<td>2.75</td>
<td>2.84</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>13.11</td>
<td>13.32</td>
<td>13.56</td>
<td>0.75</td>
</tr>
<tr>
<td>Acute gain (mm)</td>
<td>1.13</td>
<td>1.33</td>
<td>1.43</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Poststent analysis segment diameter stenosis</td>
<td>20.8%</td>
<td>19.4%</td>
<td>18.1%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

### 9-month Angiographic Measures

<table>
<thead>
<tr>
<th></th>
<th>&lt;14 atm</th>
<th>14–16 atm</th>
<th>&gt;16 atm</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Late loss (mm), analysis segment</td>
<td>0.26</td>
<td>0.21</td>
<td>0.23</td>
<td>0.74</td>
</tr>
<tr>
<td>Binary restenosis, in-stent</td>
<td>11.1%*</td>
<td>3.5%</td>
<td>3.8%</td>
<td>0.06</td>
</tr>
<tr>
<td>Binary restenosis, analysis segment</td>
<td>13.9%†</td>
<td>5.9%</td>
<td>6.1%</td>
<td>0.10</td>
</tr>
</tbody>
</table>

### 1-year clinical outcomes

<table>
<thead>
<tr>
<th></th>
<th>&lt;14 atm</th>
<th>14–16 atm</th>
<th>&gt;16 atm</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subacute thrombosis</td>
<td>1.1%</td>
<td>0.0%</td>
<td>0.7%</td>
<td>0.39</td>
</tr>
<tr>
<td>Target vessel revascularization</td>
<td>10.2%†</td>
<td>6.8%</td>
<td>5.4%</td>
<td>0.16</td>
</tr>
<tr>
<td>Major adverse cardiac events</td>
<td>14.9%*</td>
<td>10.4%</td>
<td>8.6%</td>
<td>0.11</td>
</tr>
</tbody>
</table>

*p <0.04 vs >16 atm.
†P = 0.06 vs >16 atm.
Study Purpose

• Evaluate the incidence of suboptimal stent expansion with current drug SDS in long diffuse lesion.

• Evaluate effectiveness of post-stent adjuvant high-pressure non-compliant balloon dilatation.

• Identify the factors which was related with the suboptimal stent expansion.
Study Population

• Inclusion Criteria
  – 37 consecutive angina patients, 41 de novo lesions
  – % DS on QCA >50% with evidence of myocardial ischemia
  – Stent length > 32mm
  – Informed consents for IVUS and FFR measurement.

• Exclusion Criteria
  – Restenotic lesion
  – Acute myocardial infarction or prior myocardial infarction
  – LV dysfunction: LVEF < 55%
  – Left main disease
  – Significant cardiac arrhythmia hampering physiologic study

SJ Tahk, MH Yoon, et al. CCT 2006
Methods

Pre PCI  Stenting with SDS  Adjunctive High Pressure
(at RBP: 16-18 atm)  (Quantum at 20-22 atm)

if Post Stent FFR<0.95

IVUS  IVUS  IVUS
FFR  FFR  FFR

Pressure measurement: RADI Medical System, Uppsala, Sweden
IVUS: 40MHz Atlantis™ SR Pro, Galaxy 2 Ultrasound Imaging System, Boston Scientific Corporation, Natick, MA, USA

SJ Tahk, MH Yoon, et al. CCT 2006
Baseline Characteristics (n=37)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61.4 ± 8.4</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>30 (81.1%)</td>
</tr>
<tr>
<td>Clinical Presentation</td>
<td></td>
</tr>
<tr>
<td>Stable Angina</td>
<td>16 (43.2%)</td>
</tr>
<tr>
<td>Unstable Angina</td>
<td>21 (56.8%)</td>
</tr>
<tr>
<td>Coronary Risk Factors</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>16 (43.2%)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>15 (40.5%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>10 (27.0%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>7 (18.9%)</td>
</tr>
<tr>
<td>Coronary Artery Studied (LAD/LCX/RCA)</td>
<td>30 / 2 / 9</td>
</tr>
<tr>
<td>Extent of CAD (1/2/3 VD)</td>
<td>21 / 9 / 11</td>
</tr>
</tbody>
</table>

SJ Tahk, MH Yoon, et al. CCT 2006
Results

41 Lesions

Stenting with Current SDS at RBP

FFR ≥ 0.95

8 Lesions (19.5%)

MLA $7.0 \pm 1.9 \text{ mm}^2$

%DS $13.7 \pm 1.2 \%$

MLA < 5 mm²: (1)

FFR < 0.95

33 Lesions (80.5%)

MLA $5.5 \pm 1.4 \text{ mm}^2$

%DS $27.0 \pm 12.9 \%$

MLA < 5 mm²: (14)

Adjunctive High Pressure

16 Lesions (39.0%)

MLA $7.0 \pm 2.0 \text{ mm}^2$

%DS $6.1 \pm 2.2 \%$

MLA < 5 mm²: (0)

24 Lesions (58.5%)

MLA $7.0 \pm 1.9 \text{ mm}^2$

%DS $5.9 \pm 2.3 \%$

MLA < 5 mm²: (1)

FFR < 0.95

17 Lesions (41.5%)

MLA $5.9 \pm 2.1 \text{ mm}^2$

%DS $9.8 \pm 6.3 \%$

MLA < 5 mm²: (7)

* 15/41 (36.5%) lesions could not reach MLA>5.0mm² on IVIS with SDS at RBP

** 8/41 (19.5%) lesions could not reach MLA>5.0mm² on IVIS with HP dilatation
## Angiographic and Procedural Findings

<table>
<thead>
<tr>
<th></th>
<th>Group A (FFR ≥ 0.95, n=8)</th>
<th>Group B (FFR &lt; 0.95, n=33)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-Stent</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>0.57 ± 0.11</td>
<td>0.59 ± 0.19</td>
<td>0.819</td>
</tr>
<tr>
<td>DS (%)</td>
<td>81.1 ± 4.5</td>
<td>81.5 ± 5.6</td>
<td>0.880</td>
</tr>
<tr>
<td><strong>Post-Stent</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>2.80 ± 0.46</td>
<td>2.32 ± 0.47</td>
<td>0.014</td>
</tr>
<tr>
<td>DS (%)</td>
<td>13.8 ± 12.1</td>
<td>27.0 ± 12.9</td>
<td>0.025</td>
</tr>
<tr>
<td>Reference Diameter (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal</td>
<td>3.40 ± 0.17</td>
<td>3.40 ± 0.26</td>
<td>0.911</td>
</tr>
<tr>
<td>Distal</td>
<td>2.95 ± 0.14</td>
<td>3.0 ± 0.28</td>
<td>0.607</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>42.9 ± 10.4</td>
<td>52.3 ± 11.9</td>
<td>0.047</td>
</tr>
<tr>
<td>Stent number</td>
<td>1.75 ± 0.46</td>
<td>2.0 ± 0.56</td>
<td>0.250</td>
</tr>
<tr>
<td>Stent length (mm)</td>
<td>48.6 ± 58.7</td>
<td>58.7 ± 15.4</td>
<td>0.075</td>
</tr>
</tbody>
</table>

SJ Tahk, MH Yoon, et al. CCT 2006
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<th>Group A (FFR ≥ 0.95, n=8)</th>
<th>Group B (FFR &lt; 0.95, n=33)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-stent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLA (mm²)</td>
<td>2.44 ± 0.60</td>
<td>1.57 ± 0.56</td>
<td>0.001</td>
</tr>
<tr>
<td>AS (%)</td>
<td>74.2 ± 10.1</td>
<td>82.8 ± 6.0</td>
<td>0.007</td>
</tr>
<tr>
<td>Post-stent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLA (mm²)</td>
<td>7.01 ± 1.89</td>
<td>5.53 ± 1.36</td>
<td>0.016</td>
</tr>
<tr>
<td>AS (%)</td>
<td>27.4 ± 12.8</td>
<td>38.9 ± 16.7</td>
<td>0.098</td>
</tr>
<tr>
<td>Ref Lumen Area (mm²)</td>
<td>10.6 ± 3.9</td>
<td>9.2 ± 1.8</td>
<td>0.157</td>
</tr>
<tr>
<td>VA at Lesion (mm²)</td>
<td>12.1 ± 3.6</td>
<td>10.8 ± 2.3</td>
<td>0.204</td>
</tr>
<tr>
<td>Plaque Burden</td>
<td>78.9 ± 7.3</td>
<td>85.0 ± 5.4</td>
<td>0.020</td>
</tr>
<tr>
<td>Ref Vessel Area (mm²)</td>
<td>13.4 ± 4.6</td>
<td>13.4 ± 3.0</td>
<td>0.992</td>
</tr>
<tr>
<td>Remodeling Index</td>
<td>0.93 ± 0.10</td>
<td>0.82 ± 0.15</td>
<td>0.085</td>
</tr>
</tbody>
</table>

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## IVUS Findings

<table>
<thead>
<tr>
<th></th>
<th>Group A (FFR ≥ 0.95, n=8)</th>
<th>Group B (FFR &lt; 0.95, n=33)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Plaque Characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft/Mixed</td>
<td>6 (75%)</td>
<td>13 (39.4%)</td>
<td>0.115</td>
</tr>
<tr>
<td>Fibrous/Fibrocalcific</td>
<td>2 (25%)</td>
<td>20 (60.6%)</td>
<td></td>
</tr>
<tr>
<td>Calcium Arc Grading</td>
<td>0.75 ± 1.39</td>
<td>1.30 ± 1.49</td>
<td>0.346</td>
</tr>
<tr>
<td>Eccentricity</td>
<td>0.24 ± 0.18</td>
<td>0.17 ± 0.16</td>
<td>0.334</td>
</tr>
</tbody>
</table>

SJ Tahk, MH Yoon, et al. CCT 2006
## Independent Predictor for Suboptimal Stent Expansion

### Coefficients

<table>
<thead>
<tr>
<th>Model</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Std. Error</td>
<td>Beta</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>(Constant)</td>
<td>1.220</td>
<td>.599</td>
<td>2.038</td>
</tr>
<tr>
<td></td>
<td>L_LENGTH</td>
<td>.007</td>
<td>.006</td>
<td>.196</td>
</tr>
<tr>
<td></td>
<td>PLAQ_C</td>
<td>.055</td>
<td>.155</td>
<td>.065</td>
</tr>
<tr>
<td></td>
<td>REMOD_IX</td>
<td>−.408</td>
<td>.486</td>
<td>−.138</td>
</tr>
<tr>
<td></td>
<td>MINLA</td>
<td>−.274</td>
<td>.110</td>
<td>−.435</td>
</tr>
</tbody>
</table>

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*a. Dependent Variable: G_95*

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*SJ Tahk, MH Yoon, et al. CCT 2006*
Summary

- After DES implantation with current SDS at RBP in long diffuse lesions; 80.5% could not reached FFR $\geq 0.95$, which was known as functionally successful result after BMS deployment. 36.5% could not reached MLA>5.0mm$^2$, which was known as the smallest acceptable minimum stent area with DES.

- After high pressure ballooning with non-compliant balloon at 20-22 atm; 41.5% and 19.5% of long diffuse lesions could not meet successful functional criteria (FFR $\geq 0.95$) and IVUS criteria (MLA>5.0mm$^2$), respectively.

- Factors associated with suboptimal stent expansion with current SDS were lesion length, plaque burden, and minimal lumen area.

- Independent IVUS predictors for suboptimal stent expansion was minimal lumen area.

SJ Tahk, MH Yoon, et al. CCT 2006
Conclusion

• Routine adjunctive high-pressure ballooning might be required to achieve optimal functional and anatomic stent expansion, in number of long diffuse coronary stenoses.

• FFR and IVUS-guided PCI could potentially improve the procedural precision and decrease the rate of target vessel failure in DES era. However, the role of physiologic and IVUS study in DES era needs more randomized trials.

• Do not forget old lessons even in DES era.
Optimal DES Implantation in Long Diffuse Lesion

- Appropriate lesion preparation

- Adjunctive High Pressure Dilatation with Non Compliant HP Balloon

Thank You for Attention