Current status of in-stent restenosis treatment in the SFA

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The problem of ISR

Cellular reaction
Extra-cellular matrix (ECM) > 50% of total volume (Thrombus)

Inoue S et al, JVS 2002;35:672-678
The problem of ISR

• Mechanism of luminal gain (PTA coronary ISR)
  – Tissue compression
  – Extrusion of tissue out of stent
  – Additional stent expansion (upto 56 % of total luminal gain)

• NB additional stent expansion not possible in SE stents

Mehran R et al, Am J Cardiol 1996;78:618-622
The problem of ISR

• Volumetric IVUS analysis (coronary)
  – PTA provides good acute luminal gain (intra-stent volume decrease 50%)
  – After short delay (ca. ½ hour) increase in intra-stent volume (32%)

• Underscores need for tissue ablation

Albertal M et al, Am J Cardiol 2005;95:751-754
Treatment modalities for ISR

- Cutting-balloon angioplasty
- Cryoplasty
- Brachytherapy
- DES
- Relining
- Atherectomy
- DCB angioplasty
- Combination therapy of atherectomy and DCB angioplasty
Treatment modalities for ISR

- Cutting-balloon angioplasty
- Cryoplasty
  - Brachytherapy
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  - Relining
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ISR and brachytherapy

**Re-188**
- N = 90
- ISR length = 24.6 cm
- PP 6 months 95.2%
- PP 12 months 79.8%

**Iridium 192**
- N = 42
- ISR length = 23.5 cm
- PP 12 months 75.2%
- PP 24 months 73.7%

Werner M et al, JET 2012;19:467-475
Ho KJ et al, JVS 2017;65:734-743
ISR and DES

**ZILVER Global**

N= 119
ISR length = 13.3 cm

PP 1 yr 78.8%
fTLR 2 yr 60.8%

**Zephyr**

N= 119 vs. 133 (stenosis vs. occlusion)

Benefit of DES doubtful in absence of total occlusion

**Tomoi**

N= 110 (21 DES)
ISR length = 22.8

fTLR 2 yr 27.1 vs 85.7%

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Murata N et al, JET 2016;23:642-647
Tomoi Y et al, JET 2016;23:461-467
ISR and covered stents

**RELINE**

RCT PTA vs. CS  
N= 44 vs. 39  
ISR length = 19 vs. 17.3 cm

PP at 1 year PTA 28% CS 74.8%  
fTLR at 12 months PTA 42.2% CS 79.9%

Bosiers M et al, JET 2015;22:1-10
ISR and DCB-registries

**DCB in SFA-ISR**
- N = 39
- ISR length = 8.3 cm
- 70.3% Primary Patency at 2y

**DEBATE ISR**
- N = 44
- 100% DM, 75% CLI
- ISR length = 13.2 cm

Virga V et al. JACC Cardiovasc Int 2014;7:411-415
Liistro F et al. JET 2014;21:1-8
ISR and DCB-registries

**PLAISIR**

N = 55
ISR length = 8.6 cm

- fTLR 18 months 90.2%

**INPACT GLOBAL**

N = 149
ISR length = 17.2 cm

- PP 12 months 88.7%
- fTLR12 months 92.7%

Bague N et al EJVES 2017;53:106-113
Brodmann M et al JACC Cardiovasc Interventions 2017;;10:2113-2123
ISR and DCB-RCT’s

**FAIR**
RCT DCB vs. PTA  
N= 119  
ISR length = 8.2 cm

- **62.5%**  
  (25/40)

- **29.5%**  
  (13/44)

\[ p = 0.004 \]

**ISAR-PEBIS**
RCT DCB vs. PTA  
N=70  
ISR length = 13.2/14.6 cm

Krankenberg H et al, Circulation 2015;132:2230-2236
Ott I et al, J Am Heart Association 2017;6:e006321
ISR and DCB-class effect?

- PACUBA (Freeway)
- Lesion length
  - 17.3±11.3 cm DCB
  - 18.4 ± 8.8 cm PTA

ISR and DCB-meta-analysis

ISR and DCB

- Lesion length 132±86 mm (DCB)
- At 3 year follow-up complete catch-up
- No difference between DCB and POBA

Liistro F et al. JET 2014;21:1-8
Grotti S et al. JET 2015;23:52-57
ISR and ELA

**PATENT**
Registry  
N= 90  
ISR length = 12.3 cm  
f TLR-Class I 54.5%  
-Class II 27.6%  
-Class III 24%

**EXCITE**
RCT ELA+PTA vs. PTA  
N=250 (169/81)  
ISR length = 19.6/19.3 cm

Schmidt A et al, JET 2014;21:52-60  
Dippel E et al JACC Cardiovasc Int 2015;8:92-101
ISR and ELA/DCB

RCT
N= 48
ISR length = 22.4/25.9 cm
All Tosaka class 3

12-month Primary Patency: 66.7% vs. 37.5%
(p= 0.01)

Registry
N=25 (FU 5 yrs)
ISR length = 10.5 cm
Tosaka I n=6
Tosaka II n=0
Tosaka III n=20

<table>
<thead>
<tr>
<th>Primary Patency</th>
<th>Freedom from TLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>88.0%</td>
<td>89.7%</td>
</tr>
<tr>
<td>78.2%</td>
<td>85.9%</td>
</tr>
<tr>
<td>71.7%</td>
<td>76.4%</td>
</tr>
<tr>
<td>71.7%</td>
<td>76.4%</td>
</tr>
<tr>
<td>62.7%</td>
<td>70%</td>
</tr>
</tbody>
</table>

Registry ELA/DCB vs ELA/PTA
N=112
Bailout stenting
laser/DCB 31.7% vs laser/PTA 58%, p=0.006

Table 3. Twelve-Month Kaplan-Meier Estimates of Outcomes.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Laser + DCB</th>
<th>Laser + BA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent occlusion</td>
<td>13.3</td>
<td>43.1</td>
<td>0.003</td>
</tr>
<tr>
<td>TLR</td>
<td>27.5</td>
<td>49.5</td>
<td>0.043</td>
</tr>
<tr>
<td>Bypass</td>
<td>8.3</td>
<td>5.3</td>
<td>0.9</td>
</tr>
<tr>
<td>Limb loss</td>
<td>5.2</td>
<td>2.6</td>
<td>0.5</td>
</tr>
<tr>
<td>MALE</td>
<td>12.4</td>
<td>16.6</td>
<td>0.6</td>
</tr>
<tr>
<td>MACCE</td>
<td>8.8</td>
<td>8.8</td>
<td>&gt;0.9</td>
</tr>
<tr>
<td>Mortality</td>
<td>6.8</td>
<td>8.8</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Abbreviations: BA, balloon angioplasty; DCB, drug-coated balloons; MACCE, major adverse cardiac or cerebrovascular events; MALE, major adverse limb events; TLR, target lesion revascularization.

Gandini R et al, JET 2013;20:805-813
Kokkinidis DG et al. JET 2018;25:81-88
Perspective (cf. DCB alone @ 3 years)

\[ \Delta = 16.4\% \]

Freedom from TLR

Grotti S et al. JET 2015;23:52-57
Conclusions

• The treatment of in-stent restenosis with conventional balloon angioplasty yields poor short-term results that can be improved by using DCB technology.

• DCB treatment shows a catch-up phenomenon after 3 years.

• Treatment of long femoral in-stent restenosis with a combination of laser debulking and DCB shows excellent short-term results and good long-term results.
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