TECHNICAL ASPECTS OF TREATING FISTULAS WITH IN.PACT DCB

Konstantinos Katsanos, MSc, MD, PhD, EBIR

Interventional Radiologist
Patras University Hospital, Rion, Greece
& Guy’s and St. Thomas’ Hospitals, London, UK
Conflicts of interest

- Honoraria from MEDTRONIC, BOSTON SCI
- Research grants from MEDTRONIC, ABBOTT
Angioplasty outcomes

Bittl JA, JACC Cardiovascular Interventions 2010 and Courtesy Prof TAY Kiang Hiong – RCT of Cutting Balloon Angioplasty (CBA) vs High Pressure Balloon Angioplasty (HPBA) in Haemodialysis AV Access
Vessel restenosis

- Coronary angioplasty: ~ 10% @ 9 months
- Carotid angioplasty: ~ 10% @ 1 year
- Iliac angioplasty: ~ 30% @ 5 years
- Femoral angioplasty: ~ 50% @ 2 years
- AV-Fistula angioplasty: ~ 50% @ 1 year
- AV-Graft angioplasty: ~ 50% @ 6 months
Fluid dynamics: Wall shear stress

Proximal Artery

AV Anastomosis

Proximal Vein
AV-shunt restenosis

- Veins **ARE NOT** Arteries *(anatomy)*
- ESRD causes **endothelial dysfunction** *(uremia + oxidative stress + inflammation)*
- **Constrictive / negative remodelling** *(impaired vasodilation + increased shear stress)*

*Diskin CJ, Blood Purification, 2010*
Venous neointima / myointima

<table>
<thead>
<tr>
<th></th>
<th>Actin</th>
<th>Desmin</th>
<th>Vimentin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smooth muscle cells (mix)</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Myofibroblasts</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Fibroblasts</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Roy-Chaudhury Prabir et al. Nephrol Dial transplant 2009
Rationale for DCB in dialysis

- Juxta-anastomotic lesions of native AV fistulas are usually related to intimal hyperplasia especially for anastomotic and venous stenosis \[^1\]

- **Animal data** support the benefit of local antiproliferative drugs such as sirolimus & paclitaxel to decrease neointimal hyperplasia at the venous side of hemodialysis access \[^2,3,4\]

---

## Randomized controlled DCB

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design</strong></td>
<td>Prospective, randomized, single centre</td>
<td>Prospective, randomized, single centre</td>
<td>Prospective, randomized, single centre</td>
</tr>
<tr>
<td><strong>Devices</strong></td>
<td>IN.PACT DCB vs. High-pressure PTA</td>
<td>IN.PACT DCB vs. High Pressure PTA</td>
<td>SeQuent Please vs. POBA</td>
</tr>
<tr>
<td><strong># Patients</strong></td>
<td>40 (1:1)</td>
<td>40 (1:1)</td>
<td>10 (20 lesions; 1:1)</td>
</tr>
<tr>
<td><strong>Primary Endpoint</strong></td>
<td>Primary Patency 6M / 12M</td>
<td>TLR-free survival</td>
<td>Freedom from TLR (FTLR)</td>
</tr>
<tr>
<td><strong>Access type</strong></td>
<td>AVF and AVG</td>
<td>AVF</td>
<td>AVF</td>
</tr>
</tbody>
</table>
| **Outcomes: DCB vs. control** | 6M: 70% vs 25%  
12M: 35% vs 5%  
p < 0.001 | TLR-free survival: 308 vs 161 days  
p = 0.04 | FTLR: 251T vs. 103T  
6M PP 70% vs. 0%  
12M PP 20% vs. 0%  
p < 0.01 |

---

DCB case example
DCB case example
Post 6mm high pressure

What next?
Post 8mm high pressure

What next?
DCB application

1:1 sizing
No geographic miss
Meta-analysis of failing dialysis

### 1.2.1 Cutting balloons

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Af tab et al. 2014</td>
<td>24</td>
<td>36</td>
<td>14</td>
<td>35</td>
<td>8.4%</td>
<td>3.00 [1.14, 7.90]</td>
<td></td>
</tr>
<tr>
<td>Rasuleh et al. 2015</td>
<td>2</td>
<td>18</td>
<td>5</td>
<td>19</td>
<td>3.8%</td>
<td>0.35 [0.06, 2.10]</td>
<td></td>
</tr>
<tr>
<td>Saleh et al. 2014</td>
<td>150</td>
<td>316</td>
<td>127</td>
<td>307</td>
<td>14.8%</td>
<td>1.28 [0.93, 1.76]</td>
<td></td>
</tr>
<tr>
<td>Vesely et al. 2005</td>
<td>83</td>
<td>173</td>
<td>68</td>
<td>167</td>
<td>13.7%</td>
<td>1.34 [0.87, 2.06]</td>
<td></td>
</tr>
<tr>
<td>Wu et al. 2008</td>
<td>25</td>
<td>35</td>
<td>15</td>
<td>35</td>
<td>8.2%</td>
<td>3.33 [1.23, 9.00]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>578</strong></td>
<td><strong>563</strong></td>
<td><strong>58.8%</strong></td>
<td></td>
<td></td>
<td><strong>1.55 [1.02, 2.36]</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Heterogeneity:** Tau² = 0.10; Chi² = 7.95, df = 4 (P = 0.09); I² = 50%
**Test for overall effect:** Z = 2.03 (P = 0.04)

### 1.2.2 Covered stents

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carmona et al. 2016</td>
<td>14</td>
<td>33</td>
<td>1</td>
<td>11</td>
<td>2.8%</td>
<td>7.37 [0.84, 64.43]</td>
<td></td>
</tr>
<tr>
<td>Haskal et al. 2016</td>
<td>37</td>
<td>138</td>
<td>18</td>
<td>132</td>
<td>11.7%</td>
<td>2.32 [1.24, 4.33]</td>
<td></td>
</tr>
<tr>
<td>Karnabatidis et al. 2013</td>
<td>21</td>
<td>35</td>
<td>2</td>
<td>20</td>
<td>4.5%</td>
<td>13.50 [2.70, 67.52]</td>
<td></td>
</tr>
<tr>
<td>Rajan et al. 2015</td>
<td>2</td>
<td>9</td>
<td>0</td>
<td>5</td>
<td>1.4%</td>
<td>3.67 [0.15, 92.65]</td>
<td></td>
</tr>
<tr>
<td>Vesely et al. 2016</td>
<td>75</td>
<td>145</td>
<td>51</td>
<td>148</td>
<td>13.3%</td>
<td>2.04 [1.27, 3.26]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>360</strong></td>
<td><strong>316</strong></td>
<td><strong>33.7%</strong></td>
<td></td>
<td></td>
<td><strong>2.85 [1.63, 4.98]</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Heterogeneity:** Tau² = 0.12; Chi² = 6.05, df = 4 (P = 0.20); I² = 34%
**Test for overall effect:** Z = 3.66 (P = 0.0002)

### 1.2.3 Paclitaxel-coated balloons

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kitrou et al. 2014</td>
<td>7</td>
<td>20</td>
<td>1</td>
<td>20</td>
<td>2.7%</td>
<td>10.23 [1.12, 93.34]</td>
<td></td>
</tr>
<tr>
<td>Kitrou et al. 2015</td>
<td>4</td>
<td>20</td>
<td>0</td>
<td>20</td>
<td>1.6%</td>
<td>11.18 [0.56, 222.98]</td>
<td></td>
</tr>
<tr>
<td>Lai et al. 2014</td>
<td>2</td>
<td>10</td>
<td>0</td>
<td>10</td>
<td>1.5%</td>
<td>6.18 [0.26, 146.78]</td>
<td></td>
</tr>
<tr>
<td>Massmann et al. 2015</td>
<td>7</td>
<td>10</td>
<td>7</td>
<td>15</td>
<td>4.2%</td>
<td>2.67 [0.49, 14.46]</td>
<td></td>
</tr>
<tr>
<td>Swinnen et al. 2015</td>
<td>26</td>
<td>37</td>
<td>7</td>
<td>37</td>
<td>7.4%</td>
<td>10.13 [3.43, 29.93]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>97</strong></td>
<td><strong>102</strong></td>
<td><strong>17.5%</strong></td>
<td></td>
<td></td>
<td><strong>7.42 [3.38, 16.29]</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Heterogeneity:** Tau² = 0.00; Chi² = 1.89, df = 4 (P = 0.76); I² = 0%
**Test for overall effect:** Z = 5.00 (P < 0.00001)

**Total (95% CI)**

<table>
<thead>
<tr>
<th>Total Events</th>
<th>1035</th>
<th>981</th>
<th>100.0%</th>
<th>2.60 [1.74, 3.88]</th>
</tr>
</thead>
</table>

**Total events**

| Total Events | 479 | 316 |

**Heterogeneity:** Tau² = 0.28; Chi² = 35.21, df = 14 (P = 0.001); I² = 60%
**Test for overall effect:** Z = 4.66 (P < 0.00001)
**Test for subgroup differences:** Chi² = 12.43, df = 2 (P = 0.002), I² = 83.9%
Failing brachiocephalic
5-mm pre-dil & 6-mm
Plain angioplasty result
DCB application
Final result - thrill restored
Forearm fistulae
Fore-arm radiocephalic
Crossing to artery
Vessel dilatation - preparation

3.5mm compliant

5mm 24 Atm

5mm 30 Atm
Central veins
IVUS: In-stent restenosis

Homogeneous hypoechoic ISR
Cross-sectional areas
Quantitative analysis (↓72%)
Dysfunctional dialysis graft
IVUS pull-back study
12mm high-pressure
Post 12-mm
16-mm high pressure
Lumen area gain

- **8-mm** → 27mm²
  +50% ↓ +150% ↓

- **12-mm** → 67mm²
  +33% ↓ +100% ↓

- **16-mm** → 130mm²
IN.PACT AV Access IDE Trial

Design:

✓ Prospective
✓ Global, Multicentre
✓ Randomized (1:1)
✓ Corelab
✓ Clinical Events Committee

• Prospective, global, multicenter, randomized, single-blinded study
• ~30 Global Sites (US, Japan & New Zealand)
• 330 patients
• 24 month follow-up
• 1:1 randomization
• Lesions up to 10 cm in length in the AVF

Purpose:
Evaluate the safety and efficacy of the IN.PACT™ AV Access DCB compared to PTA for treatment of subjects presenting with de-novo or non-stented restenotic obstructive lesions of native AVF in the upper extremity.

Primary Safety Endpoint: Serious Adverse Event Rate through 30 Days\(^1\)

Primary Efficacy Endpoint: Primary Patency Rate through 6 Months\(^2\)

Principal Investigators:
• Robert Lookstein, MD (New York, USA)
• Andrew Holden (Auckland, New Zealand)
• Hiroaki Haruguchi, MD (Tokyo, Japan)

\(^1\) Defined as the Serious Adverse Event (SAE) rate involving the AV access circuit through 30 days post-procedure. \(^2\) Defined as freedom from clinically-driven target lesion revascularization (CD-TLR) or access circuit thrombosis measured at 6 months post-procedure.
TECHNICAL ASPECTS OF TREATING FISTULAS WITH IN.PACT DCB

Konstantinos Katsanos, MSc, MD, PhD, EBIR

Interventional Radiologist
Patras University Hospital, Rion, Greece
& Guy’s and St. Thomas’ Hospitals, London, UK