DCB’s are Here to Stay: What Do We know About Performance So Far?

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DISCLOSURES

Peter Schneider, MD

• Intellectual Property/Patents: Cook Medical
• Consultant/Advisory Board: Abbott, Medtronic, Cardinal Health
Timing of SFA Restenosis

Coronary DES Technology in the US

Jonas et al, Cathet Cardiovasc Interv, 2007

% ≥ 1 DES
% only BMS

BMS
n = 1798 lesions

DES
n = 3061 lesions

p < 0.001
81% reduction

2.2%
Current Approach: Managing Lower Extremity Occlusive Disease

Drug mediated technologies is disrupting this paradigm.

TASC
Currently “implant based”
Multiple competitive technologies

Rutherford class
Angiosomal anatomy
Runoff
Currently “balloon based”
Femoral-popliteal Patency
These are the curves we need to disrupt

RCT Data: PTA, stent, DES, stent-graft

- PTA
- Stent
- Stent-graft
- DES

Lesion length (cm)

12-month Primary Patency

- RCTs
- Resilient
- FACT
- 4EVER
- Durability
- Astron
- Zilver PTX
- Vienna
- Vienna-3

Stent-graft RCTs
- Viper
- Vibrant
- Viastar
SFA: Late Lumen Loss
6 Different Paclitaxel DCB Preparations

Angiogram at 6 months: substantially less loss of lumen size
Why Paclitaxel?

- Mechanism: slowly dissolving particles in the vessel wall, transferred to wall during balloon inflation.
- Cytostatic agent - acts on microtubules.
- Intravascular dose for tumor is 300 mg.
- Single dose of 70 mg has no adverse effect.
- Maximum dose on a balloon is 10 mg.

### Downstream Effects in Animal Experiments

50, S, vasculitis, 10x
40, L, scar, 10x
3 µg/mm²
2 x 5µg/mm²
Uncoated

<table>
<thead>
<tr>
<th>DCB</th>
<th>Dose (µg/mm²)</th>
<th>Excipient</th>
</tr>
</thead>
<tbody>
<tr>
<td>IN.PACT</td>
<td>3.5</td>
<td>Urea</td>
</tr>
<tr>
<td>LUTONIX</td>
<td>2.0</td>
<td>Polysorbate and Sorbitol</td>
</tr>
<tr>
<td>STELLAREX</td>
<td>2.0</td>
<td>Polyethylene Glycol</td>
</tr>
<tr>
<td>PASSEO 18 LUX</td>
<td>3.0</td>
<td>Butyryl-tri-hexyl Citrate</td>
</tr>
<tr>
<td>ADVANCE 18 PTX</td>
<td>3.0</td>
<td>none</td>
</tr>
<tr>
<td>ELUTAX</td>
<td>2.2</td>
<td>dextrane</td>
</tr>
<tr>
<td>FREEWAY</td>
<td>3.0</td>
<td>shelloic acid</td>
</tr>
<tr>
<td>LEGFLOW</td>
<td>3.0</td>
<td>shelloic acid</td>
</tr>
<tr>
<td>RANGER</td>
<td>2.0</td>
<td>citrate ester</td>
</tr>
<tr>
<td>LUMINOR</td>
<td>3.0</td>
<td>unknown</td>
</tr>
<tr>
<td>SeQuent Please</td>
<td>3.0</td>
<td>Iopromide</td>
</tr>
<tr>
<td>Biopath</td>
<td>3.0</td>
<td>Shellac</td>
</tr>
</tbody>
</table>

Paclitaxel Coated Balloon Evolution

More crystallinity = better transfer to wall = more particulate

- Macro-Crystalline
- Amorphous Coating
- Hybrid Coating
- Crystalline Aggregate
- Micro-Crystalline
- Nano-Encapsulation

Courtesy of J Granada

PNEC-SEATTLE.ORG
Solid phase paclitaxel is embedded in the vessel wall, creating “reservoirs” that provide sustained release of drug over time.

From R Vermani, Charing Cross 2016
12 Month Patency
RCTs of DCB vs PTA

Lyden, TCT 2016

Illumenate

- DCB 82.3% @ day 365
- PTA 70.9% @ day 365

Rosenfield et al. NEJM 2015;373:145

Levant

- DCB 82.3% @ day 365
- PTA 70.9% @ day 410

Proportions-based difference was 65.2% for DCB vs. 52.6% for standard PTA → 12.6% difference
Primary Patency at 3 Years

![Graph showing Primary Patency over time with DCB and PTA comparison.](image)

- **Log-rank P < 0.001**
- **DCB**
- **PTA**

**Number at risk**
- DCB: 220, 213, 192, 149, 121
- PTA: 111, 108, 69, 52, 41

Krisnan, VIVA 2016
Femoral-popliteal Patency

DCB Randomized Trials

- PTA
- DES
- DCB
- No implant!
Technique of DCB Angioplasty

Pre-dilate: 1mm smaller diameter

DCB inflation: balloon to artery ratio of at least 1:1, maintain inflation 3 minutes

Post-dilate: Focal for residual stenosis

Bailout: Spot stent in the case of dissection

Where Does the Drug Go?

<table>
<thead>
<tr>
<th>Source of Drug Loss</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wash off during transit</td>
<td>5-30%</td>
</tr>
<tr>
<td>Lost in runoff during balloon inflation</td>
<td>40-70%</td>
</tr>
<tr>
<td>Transferred to artery wall</td>
<td>5-20%</td>
</tr>
<tr>
<td>Drug on used balloon</td>
<td>0-30%</td>
</tr>
</tbody>
</table>
What About TASC C/D?

Lesions >15cm (TASC C&D only)
Mean lesion length 24cm
65.3% occlusions
Primary patency at 1 year = 79.2%

Lesions >10cm
Mean lesion length 19cm
53% occlusions
Primary patency at 1 year:
DCB = 76.1%
DES = 69.6%

Schmidt et al. JACC Cardiovasc Interv 2016;9;715

Micari et al. JACC Cardiovasc Interv 2016;9;950

Zeller et al. J Endovasc Ther 2014;21;359
Femoral-popliteal Patency

What About TASC C/D?

12-month Primary Patency vs Lesion length (cm)

- PTA
- Stent
- Stent-graft
- Atherectomy
- DES
- DCB
- Woven nitinol

DCB for TASC C/D

Registries:
- IN.PACT Global
- Leipzig
- Bad Krozingen
- Italy
What About DCB Below-the-Knee?

<table>
<thead>
<tr>
<th></th>
<th>DCB</th>
<th>PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3m Angiographic FU</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restenosis (&gt;50%)</td>
<td>27%</td>
<td>69%</td>
</tr>
<tr>
<td>Full-segment Resten.</td>
<td>10%</td>
<td>56%</td>
</tr>
<tr>
<td>Restenosis Length</td>
<td>64 mm</td>
<td>155 mm</td>
</tr>
</tbody>
</table>

Mean lesion length 17-18cm

Schmidt CCI 2010;76:1047
Schmidt JACC 2011;58:1105
IN.PACT DEEP Trial
Randomized DCB vs PTA for BTK Revascularization in CLI

• 358 subjects in 13 centers
• Randomized 2:1-DEB to PTA
• Rutherford 4-6 (>80% R5)

<table>
<thead>
<tr>
<th>12 Month Results</th>
<th>DCB</th>
<th>PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLR</td>
<td>9.2%</td>
<td>13.1%</td>
</tr>
<tr>
<td>Amputation</td>
<td>8.8%</td>
<td>3.6%</td>
</tr>
<tr>
<td>Wound healing</td>
<td>73.8%</td>
<td>76.9%</td>
</tr>
<tr>
<td>Amputation Free Survival</td>
<td>81.1%</td>
<td>89.2%</td>
</tr>
</tbody>
</table>

Zeller et al. JACC 2014;64:1568
IN.PACT DEEP
What went wrong?

• Device-coated in the deflated state
• Drug-paclitaxel does not have a good track record in small arteries (coronary)
• Trial design-wound care not standardized, imaging cohort too small
• Serendipity-PTA group was best results ever
BIOLUX P-II Prospective RCT
Biotronik Paclitaxel DCB vs POBA

A  TLR

B  Loss of patency

Zeller et al. JACC: Cardiovasc Interv 2015;8:1614
### Trial Summary

**PRIMARY ENDPOINTS**
- Safety at 30 days
- Limb salvage & primary patency at 12 months

**NUMBER OF PATIENTS/SITES**
- 320 randomized patients at 55 global sites

**FOLLOW-UP**
- **Clinical**: 1, 6, 12, 24, and 36 Months
- **Duplex Ultrasound (DUS)**: 1, 6, 12, 24, & 36 months
- **Angiography**: 12 months
- **Telephone**: 48 and 60 Months

**NATIONAL PRINCIPAL INVESTIGATORS**
- Patrick Geraghty: Washington University, St. Louis, MO
- Jihad Mustapha: Metro Health Hospital, Wyoming, MI
- Marianne Brodmann: Medical University Graz, Austria

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398 patients randomized
End point moved to 6 months

Randomized 2:1 versus POBA
Permits treatment of 2 tibial arteries
Combined lesion length up to 32cm
Core labs
Angiographic subset at one-year
Pathology of BTK Arteries

- Medial calcification-is it a barrier?
- Diffuse intimal thickening
- We routinely underdilate
- Response to PTA-fewer dissections
- Overall dose if multiple vessels are treated
- Is paclitaxel too toxic for small arteries?
DCB’s Are Here to Stay

Conclusion

• DCBs have a role in femoral-popliteal algorithm.
• Moving toward standard of care.
• Just the beginning.
• Multiple other applications in development.
• Optimistic about BTK.