Drug Eluting balloon: what We are learning?

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when to avoid using a stent

- Intrastent restenosis
- Small vessel diameter
- Bifurcated lesion

However, the primary patency of POBA is not the right solution.
PTA Randomized Data

- Most studied interventional technique
- 9 cm lesion average ~40% primary patency at 1 yr
- Patency appears to be dependent on lesion length

<table>
<thead>
<tr>
<th>Study/Author</th>
<th>Year</th>
<th>No. of Limbs</th>
<th>Lesion Length (cm)</th>
<th>% Occlusions</th>
<th>Primary Patency (years / %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAST</td>
<td>2007</td>
<td>121</td>
<td>4.4</td>
<td>25</td>
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<td>RESILIENT</td>
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<td>18.5</td>
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<td>VIENNA</td>
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<td>31</td>
<td>37 (1) 31 (2)</td>
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<td>ASTRON</td>
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<td>39</td>
<td>7.1</td>
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<td>Kougias</td>
<td>2009</td>
<td>57</td>
<td>19.0</td>
<td>100</td>
<td>28</td>
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<tr>
<td>Saxon</td>
<td>2008</td>
<td>100</td>
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<td>29</td>
<td>40</td>
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<tr>
<td>VIENNA-3</td>
<td>2005</td>
<td>46</td>
<td>10.3</td>
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<td>47 (1) 39 (2)</td>
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<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>487</strong></td>
<td><strong>9</strong></td>
<td><strong>39</strong></td>
<td><strong>40 (1) 35 (2)</strong></td>
</tr>
</tbody>
</table>
DEB: new approach of endovascular therapy saves the cost of stenting?

- Fundamental and potential benefits of DEBs
- Component of DEBs
- Results @1 Y @ 2 Y
- Cost efficiency
- what we can be certain. What we have to demonstrate.
principles and benefits expected

- marked improvement in restenosis rate
- Reduced of Late lumen loss
- Reduced TLR (target lesion of revascularisation)
- Reproducible technique
- Length lesions repair
- Product adapted to the different vessels
- No foreign body
Component DEB

- **Active agent**
  - Paclitaxel (2-3µg/mm²)
    - Blocks proper microtubal formation - Inhibits cell division AND migration
    - Paclitaxel inhibits platelet derived growth factor (PDGF) mediated vascular smooth muscle cell migration to the intima
    - Paclitaxel inhibits extracellular matrix secretion and breakdown
    - Paclitaxel selectively inhibits proliferation of SMC
  - Paclitaxel does not inhibit endothelium cells
Component DEB

- **Excipient: good properties**
  - Controls Ptx integrity and drug loss during transport until location.
  - Facilitates Tissue uptake to:
    - increase exposure
    - accelerate Ptx release and transfert vessel wall
    - allow to achieve therapeutic drug levels
  - safe (including decompositif)
Challenges ahead with DEB

• Coating must be uniform, stable, predictable

• the transfer of drugs must be effective thereby with a suitable excipient to reduce drug dose

• the integrity of the system including its transport to the lesion should ensure effective administration: loading tool.

• Balloon profile is also important, especially for crossing difficult lesions
What do we really need?

Stayed effective drug ($\geq 28$ days)

The delivery of paclitaxel in suitable form, allows rapid penetration of the active ingredient in the intima, followed by prolonged elution intimal to media to limit neointimal hyperplasia.
Coating Integrity: Particulate Loss

- DCBs were delivered in a peripheral track model with fluid recirculation.
- Particulates lost downstream were collected with a 5 µm polycarbonate filter and are shown as green dots.
Besoin de réintervention sur la lésion cible après une angioplastie

Les études randomisées montrent 75% de réduction de TLR avec un ballon actif

**DEB : significative clinic benefit**
3 key words

• COATING

• LOADING TOOL

• DELIVERY SYSTEM (BALLOON PLATEFORM)
What we learned different studies

Thunder :


.RCT

.3 arm/

.Ptx 3 microg

.154 patients with SFA and Popliteal stenosis or occlusion

.main aim: LLL(6 months)

.second points: Angiographic restenosis; TLR; Additional stenting
What we learned
differents studies

- **Thunder results**
  - LLL: 0.4% vs 1.7 mm P< 0.001
  - Resténosis: 17% vs 44% P<0.001
  - TLR: -4% vs 37% p<0.001 @6months
  - TLR: -10% vs 48% p<0.001 @ 1Y
  - TLR: -15% vs 52% p<0.001 @ 2Y
  - Add stenting: -4% vs 22%
What we learned different studies

- **Pacifier:** Circ Cardiovasc Interv. 2012;5:831-840
  - RCT
  - 2 arm: DEB vs POBA
  - Ptx 3 microg/excipient: uréa
  - 85 patients/ 91 lesions of femoropoplitéal stenosis or occlusion
  - Main aim: LLL
  - Second points:
    - Binary resténosis
    - TLR
    - Major adverse event
What we learned differsnt studies

- Pacifier results:
  - LLL: 0.01mm vs 0.65mm (p = 0.0014) to the benefit of DEB
  - Binary restenosis: 8.65% vs 32.4% @ 6 months (p = 0.01)
  - TLR:
    - 7.1% vs 21.4% @ 6 months
    - 7.1% vs 27.9% @ 1 Y

  Major adverse event: DEB < POBA
What we learned different studies

- Fempac trial: - Circulation. 2008; 118: 1358-1365
  - RCT
  - DEB VS POBA: 3 Microg Ptx
  - 87 patients with femoropopliteal lesions (mean length: 5.7cm/19% occlusion)
  - Main aim: LLL
  - Second points:
    - Restenosis
    - Improve clinic
What we learned different studies

• Fempac results:
  o LLL : 0.5 mm vs 1.0 mm (p=0.031) lower DEB vs POBA

• Restenosis:
  o Restenosis 19% vs 47%, p=0.035 @ 6 months
  o Improvement rutherford score: better in ptx treated group
  o Same difference between groups @18 months @2 Y
What we learned different studies

- Levant 1: JACC; Cardiovascular Interventions, vol7, No1, 2014: 10-9
  - RCT
  - DEB vs POBA Ptx: 2 µG
  - 101 patients enrolled (lesion length: 8 cm / 42% occlusion) with de novo stenosis or occlusion
    - If unsuccessful predilatation: stented then randomized to DEB vs POBA
  - Main aim: LLL
  - Second points:
What we learned
differsents studies

• **Levant1 results:**
  
  • LLL: significantly reduced in DEB Group@ 6 months
    - All subjects (39 DEB/35 POBA): 0.46 mm vs 1.07 mm (p=0.016)
    - Balloon group (31 DEB/24 POBA): 0.45 mm vs 1.19 mm (p=0.024)
    - Stent group (8 DEB/11 POBA): 0.45 mm vs 0.9 mm (p=0.34)
  
  • Freedom from loss of patency, thrombosis, amputations, death
    - 65% in DEB group vs 50% in POBA group @1Y
    - 62% in DEB group vs 45% in POBA group @2Y
What we learned differently studies

- Illuminate FIH : Catheterization and Cardiovascular Interventions, 23 fév. 2015,

- prospective, multicenter, single arm study
- 80 patients (50 with predilatation +DEB/30 DEB only)

- Results:
  - TLR: 10%@1Y AND 14.2% @2Y
  - PRIMARY PATENCY: 89.5%@1Y AND 80.3% @2Y

Independent evaluation by duplex central laboratories and angiographic and a committee of clinical incidents.
Late lumen loss: significative reduction
Savings using DEB vs comparators (pour une population de patients avec claudication intermittente)

Kearns et al; British Journal of Surgery 2013; 100: 1180–1188

Cost-effectiveness analysis of enhancements to angioplasty for infrainguinal arterial disease

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- Cryoplasty
- Stent-graft
- Endovascular brachytherapy
- PTA with primary drug-eluting stents
- PTA with primary bare metal stents
- PTA, no bail-out stenting
- PTA with bail-out bare metal stents
- PTA with bail-out drug-eluting stents

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Savings using DEB vs comparators (per patient with IC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTA with bail-out drug-eluting stents</td>
<td>€ 416</td>
</tr>
<tr>
<td>PTA with bail-out bare metal stents</td>
<td>€ 2 327</td>
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<tr>
<td>PTA, no bail-out stenting</td>
<td>€ 2 504</td>
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<tr>
<td>PTA with primary bare metal stents</td>
<td>€ 2 792</td>
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<td>PTA with primary drug-eluting stents</td>
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<tr>
<td>Stent-graft</td>
<td>€ 4 140</td>
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<tr>
<td>Cryoplasty</td>
<td>€ 5 803</td>
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</tbody>
</table>
What we can be certain

- A stable coating with a minimal loss of drug

- A product to give an efficiency of paclitaxel to the arterial wall as an effective stay with the product.

- A transfer of effective drugs and a drug coating ensures the integrity, thanks to a subtle manufacturing technology a uniform and predictable treatment

- Coated balloon ≠ active balloon
What we can be certain

• DEB seems better than POBA

• Stent are better than POBA

• 3rd generation stent are Better than BMS
What we can be demonstrate

• What is the role of each product in the treatment of femoropopliteal lesions?

• Many questions arise:
  o Should we systematically predilatation before using a DEB?
  o should we only use the DEB to treat restenosis?
  o In case of dissection, which stent to use?
  o What is the role of drug-coated stents?
  o If DEB + stenting, should be done PTA + DEB + stent or PTA + stent + DEB?
  o What is the place of the 3rd generation of stents and covered stents?
  o And biodegradable stents?
  o ...
What we can be demonstrate

• We are at the beginning of new concepts (3rd generation stent / DEB / Coated stent). We can not draw any firm conclusions. We need studies and long-term results.

• Need for better understanding of the SFA
  o to characterize the hemodynamics and behaviour of each segment
  o Understand the constraints between as segments transition

• SFA is an engineering challenge
Our bigger challenge: restenosis
The good flow
And where to find the good flow?

BORDEAUX

Perspectives 2015
Are drug devices efficient?

Educational (crash) live in box (aortic and peripheral)