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

Study/Author	Year	No. of Limbs	Lesion Length (cm)	% Occlusions	Primary Patency (years / %) 1	2
FAST	2007	121	4.4	25	61	
RESILIENT	2010	72	6.4	18.5	37	
VIENNA	2006	52	9.3	31	37	31
ASTRON	2009	39	7.1	39	29	
Kougias	2009	57	19.0	100	28	
Saxon	2008	100	7.0	29	40	
VIENNA-3	2005	46	10.3	28	47	39
Total		***487***	***9***	***39***	***40***	***35***

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.
-

principies and benefits expected

- marked improvement in restenosis rate
- Reduced of Late lumen loss
- Reduced TLR (target lesion of revascualrisation)
- 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

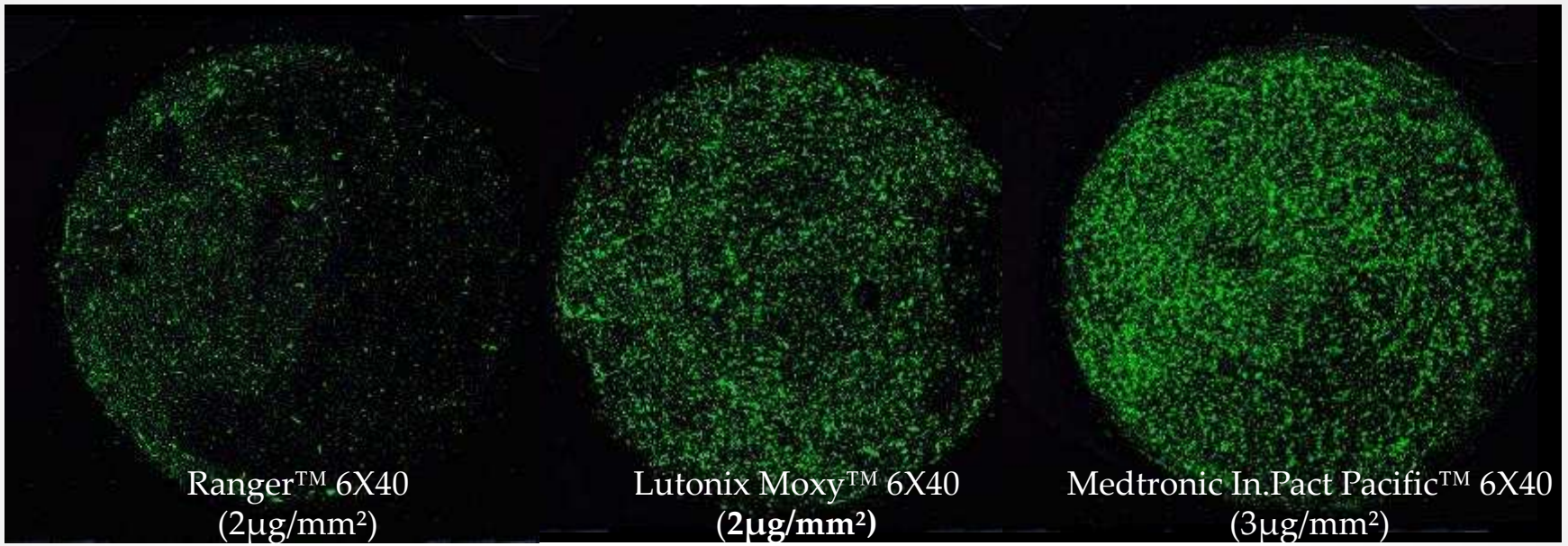
- Coating must be uniform, stable, predictable
- the transfer of drugs must be effective thereby with a suitable excipient to reduce drug dose
- the integrity of the system including its transport to the lesion should ensure effective administration: loading tool.
- Balloon profile is also important, especially for crossing difficult lesions

What do we really need?

Stayed effective drug (≥ 28 days)

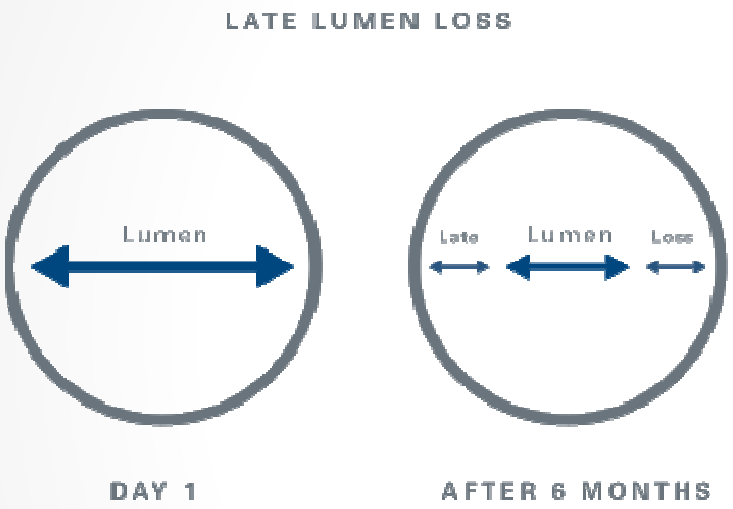
The delivery of paclitaxel in suitable form, allows rapid penetration of the active ingredient in the intima, followed by prolonged elution intimal to media to limit neointimal hyperplasia.

Coating Integrity: Particulate Loss

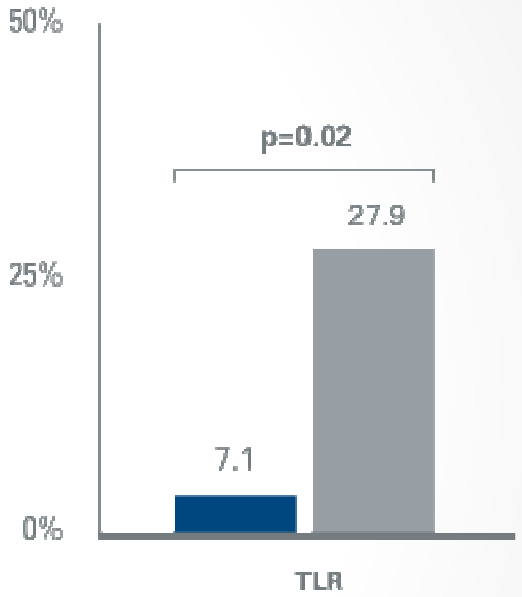


- DCBs were delivered in a peripheral track model with fluid recirculation
- Particulates lost downstream were collected with a 5 µm polycarbonate filter and are shown as green dots

DEB : significative clinic benefit



Besoin de réintervention sur la lésion cible après une angioplastie



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

3 key words

- COATING
- LOADING TOOL
- DELIVERY SYSTEM (BALLOON PLATEFORM)

What we learned differents studies

Thunder :

1-N Engl J Med 2008;358:689-99

.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 differents studies

- **Pacifier:** Circ Cardiovasc Interv. 2012;5:831-840
  - **RCT**
  - **2 arm:DEB vs POBA**
  - **Ptx 3microg/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 differents 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 differents 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 differents studies

- **Fempac results:**
  - **LLL : 0,5 mm vs 1,0 mm (p=0.031) lower DEB vs POBA**
  - **Restenosis:**
    - **Restenosis 19% vs 47%, p=0.035 @ 6 months**
    - **Improvement rutherford score : better in ptx treated group**
    - **Same difference between groups @18 months @2 Y**

What we learned differents 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 unsuccesfull predilatation: stented then randomized to DEB vs POBA

  - Main aim: LLL
  - Second points :

What we learned differents studies

- **Levant1 results:**

- **LLL: significantly reduced in DEB Group@ 6 months**
  - **All subjects (39 DEB/35 POBA): 0,46 mm vs 1,07mm (p=0.016)**
  - **Balloon group (31 DEB/ 24 POBA): 0,45 mm vs 1,19mm (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 differents studies

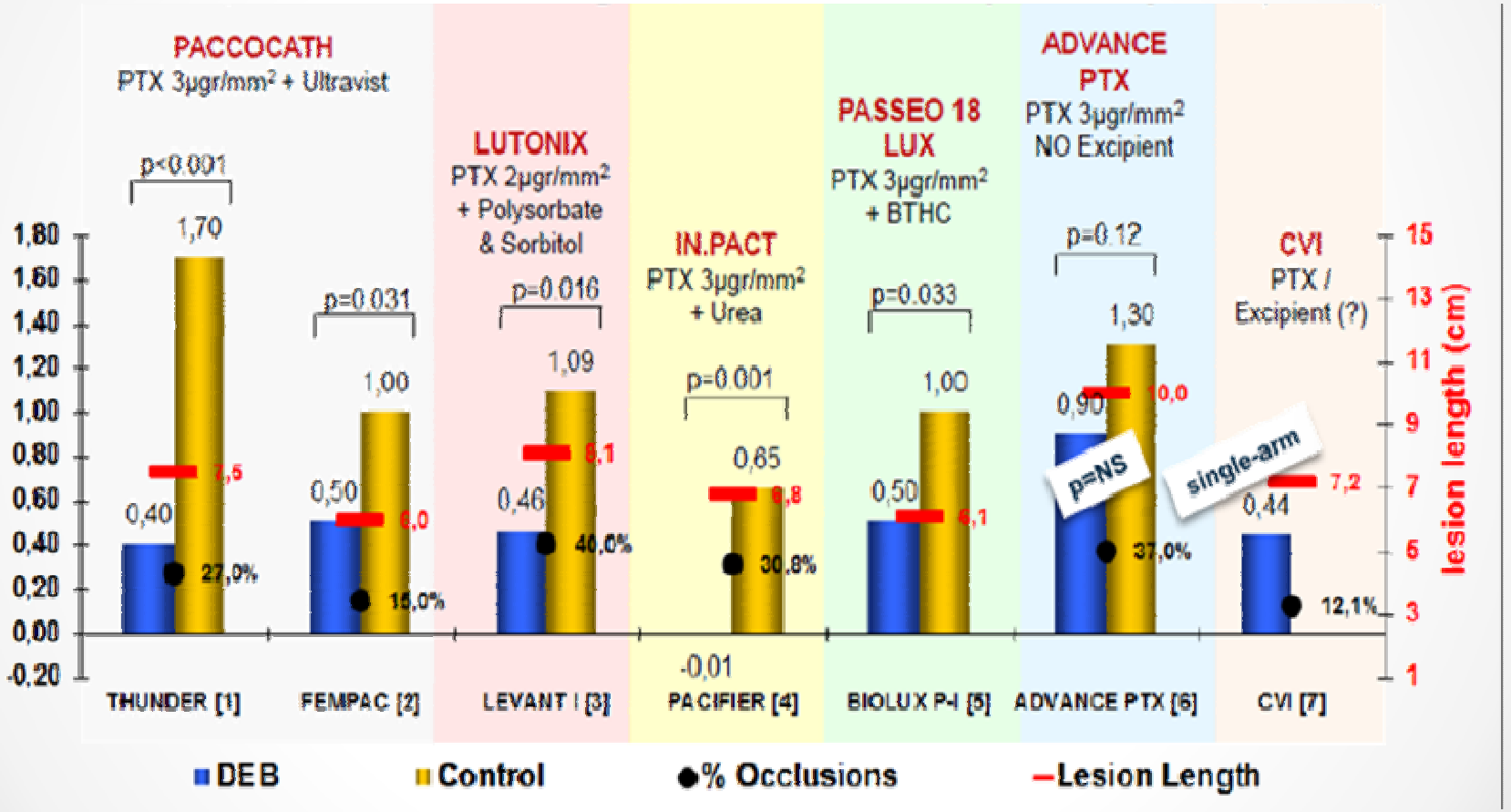
- Illuminate FIH :Catheterization and Cardiovascular Interventions, 23 fév. 2015,

- 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)

Original article

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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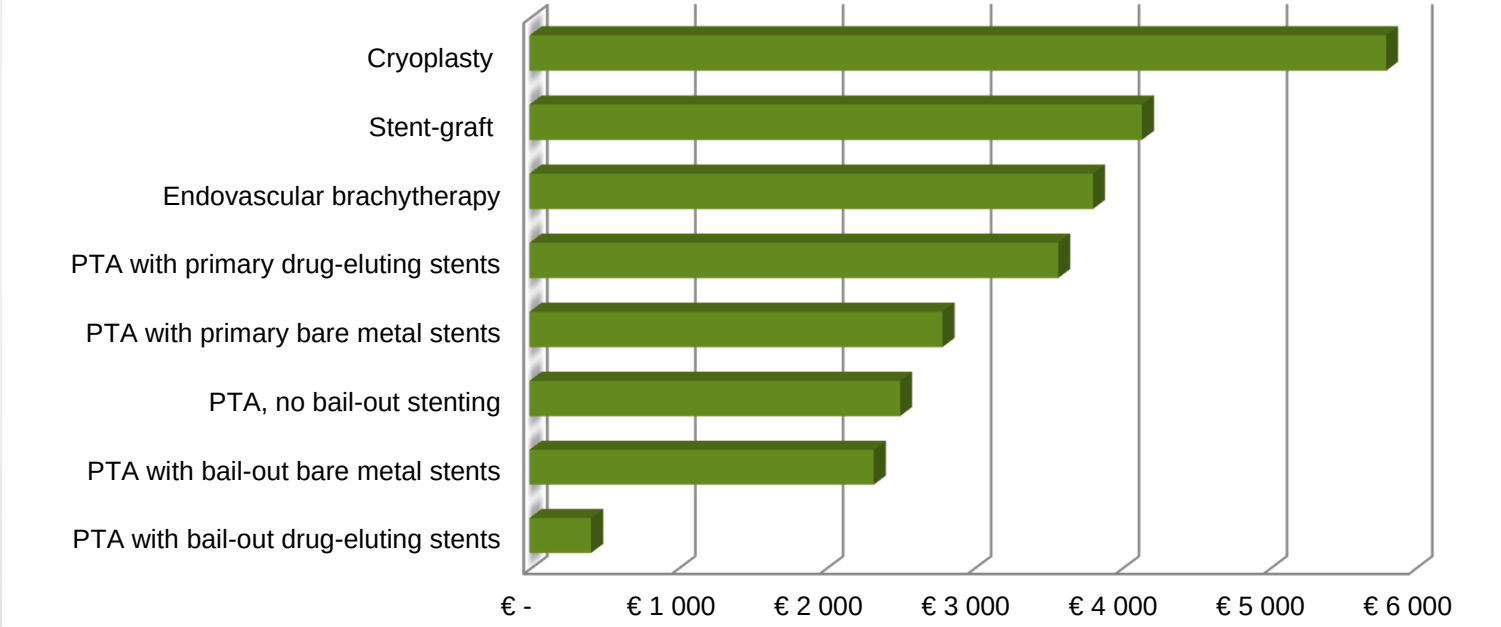

	PTA with bail-out drug-eluting stents	PTA with bail-out bare metal stents	PTA, no bail-out stenting	PTA with primary bare metal stents	PTA with primary drug-eluting stents	Endovascular brachytherapy	Stent-graft	Cryoplasty
Savings using DEB vs comparators (per patient with IC)	€ 416	€ 2 327	€ 2 504	€ 2 792	€ 3 574	€ 3 809	€ 4 140	€ 5 803

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

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
  - to characterize the hemodynamics and behaviour of each segment
  - 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

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Are drug devices efficient?

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

Simultaneous translation

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