A Future Concept for Drug Delivery: The Mercator Bullfrog Technology

Dierk Scheinert, MD
Universitätsklinikum Leipzig AöR
Leipzig, Germany
Disclosure

Speaker name: Dierk Scheinert

I have the following potential conflicts of interest to report:

Consulting: Abbott, Angioslide, Atheromed, Biotronik, Boston Scientific, Cook Medical, Cordis, Covidien, CR Bard, Gardia Medical, Hemoteq, Intact Vascular Inc., Medtronic, Ostial Inc, TriReme Medical, Trivascular, Upstream Peripheral Technologies

Stockholder: IDEV Technologies
The Bullfrog® Micro-Infusion Device (Mercator MedSystems)
Bullfrog Device Features

• Microneedle is 34 Ga (0.007”) diameter; smaller than most suture needles, so insertion does not injure the vessel
• Needle is constantly sheathed during manipulation to prevent scratching the vessel
• Balloon self-adjusts to a range of vessel diameters (2-4 mm, 3-6 mm or 4-8 mm)
• Balloon inflation limited to 2 atm to prevent barotrauma
• Contrast co-delivered with drug confirms real-time procedural success
Bullfrog Adventitial Infusion

Pre-Revascularization  Post-Revascularization  Post-Infusion

20% contrast, 80% drug
Bullfrog Adventitial Infusion

Pre-Revascularization

Post-Revascularization

Post-Infusion
Without Angio  With Angio

20% contrast, 80% drug
Bullfrog Adventitial Infusion

Example Cases

(Controlled Extravasation of Drug)
Revascularization Injures the Deep Layers of the Artery

• What is seen during vascular intervention

• What is affected during vascular intervention
Restenosis Summary

INJURY

- Stretching
- Denudation
- Recoil
- Injury response programs
- Leukocyte adherence
- Phenotypic switch: quiescent → proliferative and synthetic

Negative remodeling

- Neointima
- Migration
- Myofibroblast proliferation
- Fibrosis

Microvascular networks
- Paracrine factors

Lumen loss

Media
- Lumen

Adventitia
- Neointima

Perivascular tissue
- Tissue
Restenosis Begins with Inflammation

Timeframe:
- Hours to Days
- Weeks
- Months

Agents:
- Dexamethasone
- Paclitaxel, -limus compounds

INJURY → INFLAMMATION, RECRUITMENT → PROLIFERATION, MIGRATION → FIBROSIS, HYPERPLASIA
Clinical Hypothesis: Adventitial delivery of dexamethasone at the time of peripheral artery endovascular revascularization reduces inflammation and improves long-term patency*

DANCE-Pilot study results
- 20 patients with average lesion length 8.9cm
- 6-month primary patency: 89% (17/19)
- 1-year primary patency: 81% (13/16)

Patency After 1 Year F/U

390 Day (1 year ± 1 month) Primary Patency Rates in SFA-POP Trials

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=20</td>
<td>N=220</td>
</tr>
<tr>
<td>81.3%</td>
<td>49.5%</td>
</tr>
<tr>
<td>N=111</td>
<td>N=264</td>
</tr>
<tr>
<td>78.4%</td>
<td>65.2%</td>
</tr>
<tr>
<td>N=135</td>
<td></td>
</tr>
<tr>
<td>52.6%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lesion length (cm)</th>
<th>DANCE Pilot (Owens)</th>
<th>In.PACT SFA (Tepe, MEET 2014)</th>
<th>LEVANT 2 (FDA Panel 2014)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8.9</td>
<td>8.9</td>
<td>6.3</td>
</tr>
<tr>
<td>% total occlusions</td>
<td>50%</td>
<td>26%</td>
<td>21%</td>
</tr>
<tr>
<td>% popliteals</td>
<td>45%</td>
<td>7%</td>
<td>5%</td>
</tr>
<tr>
<td>% R2</td>
<td>15%</td>
<td>38%</td>
<td>29%</td>
</tr>
<tr>
<td>% R3</td>
<td>65%</td>
<td>57%</td>
<td>63%</td>
</tr>
<tr>
<td>% R4</td>
<td>15%</td>
<td>5%</td>
<td>8%</td>
</tr>
</tbody>
</table>
PAD Trials Utilizing Bullfrog

**DANCE**
- N=300
- Baseline angiogram and biomarker blood draw (1/3 of pts)
- 150 PTA
- 150 atherectomy
- Adventitial DEX treatment
- 24-hour blood draw for Δ biomarkers (1/3 of pts)
- 1-month blood draw for Δ biomarkers (1/3 of pts)
- Clinical, hemodynamic and duplex U/S follow-up at 6, 12, 18, 24 months

**DANCE-R**
- N≈1,000
- Long lesions
- ISR
- Rutherford 5
- Revascularization
- Adventitial DEX treatment
- Clinical, hemodynamic and duplex U/S follow-up at 12 months

**LIMBO (2 Trials)**
- Beginning Q1 2015
- N≈1,000
- Baseline angiogram and biomarker blood draw
- 100 PTA and 100 ATX revascularization (2 trials)
- 50 controls (each)
- 50 DEX treatment (each)
- 24-hour blood draw for Δ biomarkers
- 1-month blood draw for Δ biomarkers
- Clinical, hemodynamic and angiographic follow-up at 6 months
Summary

• The adventitia holds advantages for drug delivery: large volume drug depot possible
• The Bullfrog Device is safe, straightforward, and already regulated in Europe and U.S.
• Standard anti-inflammatory medication is available
• Large body of clinical evidence is being generated in PAD therapy with Bullfrog and dexamethasone
A Future Concept for Drug Delivery: The Mercator Bullfrog Technology

Dierk Scheinert, MD
Universitätsklinikum Leipzig AöR
Leipzig, Germany