Role of Specialty Balloons in Treating CLI

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• Spectranetics

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• Bard
• Tri-Reme
• Mercator
• Astra Zeneca
• Cook
The Complexity of CLI

Arterial plaque reduces blood flow to peripheral tissues

Tissue necrosis can occur distal to site of arterial obstruction
CLI - DEFINITION

• Critical Limb Ischemia
  – Progressive disease marked by rest pain and/or development of ulcers/gangrene

Inter-Society Consensus for the Management of PAD (TASC II) ¹

- Flat pulse volume waveform
- Chronic ischemic rest pain
- Systolic ankle pressure <50mm Hg
- Ulceration or gangrene of the foot or toes
- Toe pressure <30 mm Hg
- ABI ≤0.40

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The best way to cope with trouble is to stay out of it as much as possible.

— Jack Nicklaus —
Peripheral Arterial Disease

1. **Atherosclerosis**
   - Mixed morphology with areas of compact calcium.
   - Complex Morphologies
     - Must remove the broad spectrum of morphologies
     - Embolization risk
   - Intimal Calcium
     - Increased risk of perforation
     - Severe calcification

2. **Medial Calcium**
   - Concentric sheets of calcium, hardening the vessel.
   - Inaccessible by mechanical means
     - Cannot be safely removed by any atherectomy device
   - Reduces safety and efficacy of mechanical treatments
     - Vessel stiffness increases risk of intrusion into medial/adventitial layer
   - Indistinguishable on angiography
     - Often ‘grouped’ with intimal calcium
     - Prevalence may overestimate ‘treatable’ intimal calcium

3. **Restenosis**
   - Soft, aqueous neointimal hyperplasia tissue, with areas of thrombus.
   - Widely Prevalent
     - 50% interv. case load
     - Poor patency rates after many interventions
   - Never Ending Cycle
     - Repeated intervention continues restenotic cycle
   - Mechanical Intervention
     - Largely Ineffective
     - Morphology difficult to treat mechanically
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Problems with POBA

Torsional Stress

Radial Stress

Figure 1. Torsional stress can be imparted on the vessel wall through a twisting motion when a plain balloon unfolds during inflation.

Figure 3. Radial stress outwardly expands the vessel wall when a plain balloon unfolds during inflation.
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Longitudinal Stress

Figure 2. Longitudinal stress elongates the vessel wall when a plain balloon unfolds during inflation.
I think this calls for a number 3 rake.
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Focused Force Balloons

Fletxtome™ Cutting Balloon™ Device

The combination of the Cutting Balloon Device non-compliant balloon material AND atherotome blades resulted in:

1. Reduced vessel stretching and injury by scoring for precise dilatation.\(^2\)\(^3\)

2. Maximum lumen gain via plaque compression using lower pressure.\(^4\)\(^5\)

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Stainless steel micro-surgical blades:
- Flexpoints every 5 mm on the 30 mm and 15 mm lengths
- Working height of blades 0.005”

Atheromas with flexpoints assist in tracking to lesions that may have been previously out of reach.
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VascuTrak Focused Force
AngioSculpt Scoring Balloon

• AngioSculpt is a scoring balloon catheter consisting of two main components:
  • Angioplasty balloon catheter
    • semi-compliant nylon balloon,
    • coaxial nylon shaft,
    • 2 radiopaque markerbands
  • Scoring element
    • laser-cut Nitinol hypotube
    • helical configuration
Scoring Mechanism of Action

• AngioSculpt offers 3 distinct benefits with one device:
  • Precision
  • Predictable Power
  • Safety
Precision

- Rectangular edges of scoring element “lock” the device in place
- Minimal device slippage\(^1\)

Power

• The leading edges are designed to drive outward expansion with up to ~15-25 times the force of a conventional balloon\(^1\)

• The helical nitinol element creates a large initial luminal expansion\(^2\)

\(^1\) AngioSculpt Study Plan: ST-1197 (2008), on file at AngioScore
Safety

• Post scoring, outward forces are designed to be equivalent to that of a conventional balloon

• Low dissection rates\textsuperscript{1,2}

• Low rate of adjunctive PTA stenting\textsuperscript{1,2}

\textsuperscript{1} Kiesz RS, Scheinert D, Peeters PJ et al. Results from the international registry of the AngioSculpt Scoring Balloon Catheter for the treatment of infra-popliteal disease. J Am Coll Cardiol. 2008;51;10(suppl B);75.

European Registry: Infra-popliteal Disease
Study Design & Demographics

• Multi-center prospective registry
• Study population: patients scheduled for percutaneous intervention of infra-popliteal arteries or planned amputation
• Reference vessel diameter: 1.5 – 3.5 mm
• 42 patients at 5 sites
• Follow-up per institutional protocol

European Registry: Infra-popliteal Disease Results

• 42 patients and 56 lesions treated
• Age 75.2 + 8.4 years, 59.5% male
• CLI (Rutherford > 4) present in 38 patients (90.5%)
• Moderate/severe calcium present in 73% of lesions
• Lesion length: 33.9 + 42.2 mm
• AngioSculpt® successfully deployed in 55/56 lesions (98.2%)
• AngioSculpt used as primary therapy in 50/56 lesions (89.3%)

International Multi-Center Registry
Infra-Popliteal Disease

- N= 93 patients (131 lesions)
- Successful deployment in 99.2% of lesions
- Used without adjunctive stenting in 88.6% of lesions
- Low dissection rate of 9.9%
- No significant device slippage
- Zero perforations

 Belgian Infra-Popliteal Registry

- Two clinical sites
- Enrolled 31 CLI (Rutherford 4-5) pts with 36 lesions
- Reference vessel diameter: 2.0 – 4.0 mm
- Single vessel run-off
- Age 76 (54-91) yrs, males 54.8%
- Endpoints
  - Safety: 1-month complication-free survival
  - Efficacy: 1-year limb salvage and primary patency

Belgian Infra-popliteal Registry Results

• Successful AngioSculpt® deployment in all patients
• Stand-alone treatment in 64.5%
• Adjunctive stenting in 35.5%
• Post-AngioSculpt dissections in 9.7% (all minor)
• No perforations
• 1-month complication-free survival 96.8%
  • (one percutaneous re-intervention within the first month)
• 1-year primary patency 61.0%
• 1-year limb salvage 86.3%

Chocolate Platform for Controlled Inflation
Chocolate Platform for Controlled Inflation

• Controlled dilatation to help reduce dissections, minimize vessel wall trauma and edge injury
Chocolate PTA

- Predictable luminal gain with unique pillows and grooves design
- Reduced dog-boning with uniform inflation
- Demonstrated low rates of dissection and bailout stenting
- Concentric secondary profile, allowing use in multiple lesions per patient
Chocolate BAR Study

490 patients enrolled across 33 sites

Procedural Success\(^{(1)}\)

<table>
<thead>
<tr>
<th></th>
<th>ATK (2) patients</th>
<th>BTK (3) patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment was conducted without major dissection</td>
<td>98%</td>
<td>97%</td>
</tr>
<tr>
<td>Achieved less than 30% diameter stenosis</td>
<td>90%</td>
<td>94%</td>
</tr>
<tr>
<td>Bail-out stenting was not required</td>
<td>94%</td>
<td>96%</td>
</tr>
</tbody>
</table>

Clinical Outcomes\(^{(1)}\) 6 months

<table>
<thead>
<tr>
<th></th>
<th>ATK (2) patients</th>
<th>BTK (3) patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Re-intervention of the limbs was not required</td>
<td>89%</td>
<td>91%</td>
</tr>
<tr>
<td>Limb preservation</td>
<td>96%</td>
<td>97%</td>
</tr>
</tbody>
</table>

Reference: 1. Site-reported interim data on file with TriReme Medical, LLC.

Notes:

(1) These data are interim only. Follow up is not complete on all patients and final outcomes may change.
(2) ATK patients are patients with atherosclerotic disease mainly in above-the-knee vessels.
(3) BTK patients are patients with atherosclerotic disease mainly in below-the-knee vessels.
Interrupting the Cascade at Inflammation

Cell recruitment

Inflammation

– cytokine expression

Proliferation Neointima
Lumen Loss

ATVB 2011;31:1530-1539
Bullfrog Micro-Infusion Device

20% contrast 80% dexamethasone
Injection 1 @ 21cm: 0.5 ml (not in frame)

Injection 2 @ 17cm: 1.0 ml

Injection 3 @ 13.5cm: 1.0 ml

Injection 4 @ 9cm: 1.0 ml

After 3 minutes, diffusion up, down, and around >15cm of SFA

Payload visualization
Bullfrog Drug Delivery

Pre-Revascularization

Post-Revascularization

Post-Infusion

20% contrast, 80% drug

Bullfrog Delivery of Dexamethasone
Mercator DANCE Study for PAD

• Above the Knee Study
• Drug added to PTA or Atherectomy
• Data competitive to Drug Coated Balloon
• Enrollment complete 12/2015 285 patients at 35 US Sites
Mercator LIMBO Studies for CLI

- Below the Knee Study
- Restenosis Indication
- Prospective Randomized Controlled Trials with Biomarkers
- Drug in addition to ATX (U.S.) or PTA (Germany)
- PTA opened in 1/2016
- ATX to open in 6/2016
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DEBATE BTK (PRELIMINARY RESULTS)*

12 MONTHS RESULTS (ANGIOGRAPHIC AND CLINICAL)

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Standard PTA</th>
<th>IN.PACT DEB</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>3</td>
<td>90%</td>
<td>95%</td>
</tr>
<tr>
<td>6</td>
<td>80%</td>
<td>85%</td>
</tr>
<tr>
<td>9</td>
<td>70%</td>
<td>75%</td>
</tr>
<tr>
<td>12</td>
<td>60%</td>
<td>65%</td>
</tr>
</tbody>
</table>

CONCLUSION

By preliminary study results, DEB was superior in all 12 months compared with BTK and showed improved freedom from amputation compared with BTK in the minimization of these events in diabetic patients with CLI.

Freedom from Amputation

Time After Initial Procedure (Days)
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Lutonix DCB Catheter Technology

- Low paclitaxel drug-load balloon with 2µg / mm²
- IV approved carriers of polysorbate & sorbitol
- Coating thickness: ±1.3 micron
- Coating applied while balloon is inflated

![Graph showing comparison between Drug-coated balloon and Standard angioplasty balloon over time with P<0.001](image-url)
I've always made a total effort, even when the odds seemed entirely against me. I never quit trying; I never felt that I didn't have a chance to win.

— Arnold Palmer —

AZQuotes
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