Lower Extremity Interventions: The Cutting Edge

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Disclosures

• None.
Outline

• Background on Angioplasty and Stenting in the Legs

• New Approaches to Lower Extremity Interventions
  - Atherectomy: Excisional, Rotational, and Laser
  - Drug Coated Balloons
  - Drug Eluting Stents

• The Future: How Do We Choose a Device for a Specific Patient or Lesion?
Indications for Lower Extremity Interventions

- **Claudication**
  - Exertional calf pain that limits activity
  - May significantly impact quality of life
  - Medical therapy and walking program are first line of management

- **Critical Limb Ischemia**
  - Advanced arterial insufficiency resulting rest pain or non-healing ulceration.
  - At risk for major amputation.
Critical Limb Ischemia (CLI)

• Advanced PAD resulting in breakdown of the skin (ulcers or gangrene) or pain in the foot even at rest
  
  • Stage III or IV of Fontaine classification

  • Rutherford Categories 4, 5, and 6
Why Don’t We Just Stent Everyone?

• If it works in the heart, why not in the legs?
  ▪ Longer lesions
    • Higher rates of restenosis
    • Need for re-intervention
  ▪ Greater potential for fracture
  ▪ Heavy calcification

• Stents are generally better than balloon angioplasty, but are not always the answer.
Stenting vs. Balloon Angioplasty

12 months restenosis vs. lesion length

Data from randomised trials

- PTA + provisional stent
- Stent

Lesion length (cm)
Current Status of Stents for Lower Extremities

- Most data is for shorter lesions (under 150 mm).

- Restenosis rate of stents depends significantly on lesion length.

- New developments in stent technology will lead to incremental improvements
  - Covered stents, new cell types
Stent Evolution

- Enhanced Flexibility by:
  - Reduction of cell interconnections
  - Spiral orientation of interconnections
TIGRIS Stent

Clinically Proven Stent Frame
Nitinol wire

ePTFE Interconnecting Structure
CARMEDA Bioactive Surface
VIABAHN Covered Stent
SUPERA stents – Unbreakable?
Stents for the Lower Extremity: Conclusions

• For lesions > 40 mm, stents are superior to balloon angioplasty.

• Early generation stents had high rates of restenosis and risk of fracture.

• Newer stent designs have much lower fracture rates and less restenosis.
Atherectomy – Let’s Just Cut it Out!

- Large, bulky lesions with excessive calcium limit the utility of angioplasty and stents.

- Debulking can “prepare” the lesion for other treatments.

- Atherectomy also useful for “no stent” zones.
Device Evolution

Predator 360° 1.25 mm crown

Diamondback 360° 1.25 mm crown

3X 2.25mm Crown (0.350” Long)

Gen1A 2.25mm Solid Crown (0.400” Long)
Excimer Laser

**Technical Improvements:**

- New Catheter Designs –
  - Turbo Elite
  - Turbo Tandem
  - 0.9 mm
  - Cross-Pilot support catheter

- Saline Flush

<table>
<thead>
<tr>
<th>Attribute</th>
<th>TURBO elite™</th>
<th>CLiRpath® TURBO</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model Number</td>
<td>417-152</td>
<td>317-152</td>
<td></td>
</tr>
<tr>
<td>Number of Fibers</td>
<td>182</td>
<td>136</td>
<td>More fibers</td>
</tr>
<tr>
<td>Active Area</td>
<td>0.53mm²</td>
<td>0.39mm²</td>
<td>33.8% more active area</td>
</tr>
<tr>
<td>Max. Output Energy</td>
<td>31.8mJ</td>
<td>25.2mJ</td>
<td>26.2% more energy</td>
</tr>
<tr>
<td>Sheath Compatibility</td>
<td>5F</td>
<td>5F</td>
<td></td>
</tr>
<tr>
<td>Max. Guidewire Compatibility</td>
<td>0.018”</td>
<td>0.018”</td>
<td></td>
</tr>
<tr>
<td>Working Length</td>
<td>150 cm</td>
<td>150 cm</td>
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</table>
• Challenging Lesion Type #1: Severe Calcium
Turbohawk Calcium Cutter
Orbital Atherectomy

Speed = Lumen

- Increased speed and/or increased mass increase the centrifugal force
- Greater centrifugal force creates bigger lumens

2.0 mm crown at 80k RPMs

2.0 mm crown at 200k RPMs
Dealing With Calcium: Orbital Atherectomy
Orbital Atherectomy Below the Knee
• Challenging Lesion Type #2: Bulky Lesions/ Long Segment Occlusions
• 54 year old male
• Long standing diabetes mellitus
• ESRD on hemodialysis
• Claudication with minimal ambulation and ischemic rest pain (Rutherford 4)
• Referred for angiography and possible intervention
What’s the best treatment strategy?

Diffuse SFA Disease
Decrease in patency as lesions get longer
Limited data available in medium to long lesion lengths
Long SFA Occlusion
Following Laser and PTA
• Challenging Lesion Type #3: “The No-Stent Zones”
Common Femoral Artery

Rest Pain
2 Prior Fem-Pop bypasses

Following Excisional Atherectomy
What’s the Data for Atherectomy?

• Most studies have been case series reporting outcomes similar to stenting.

• DEFINITIVE Trial recently presented.

• Silverhawk excisional atherectomy for patients with claudication or critical limb ischemia.

• Trial also specifically examined patients with diabetes.
Study Design & Primary Endpoints

800 patients
47 centers

Claudicants (RCC 1-3)
598 patients*

Primary patency by Duplex US at 12 mos

CLI (RCC 4-6)
201 patients

Freedom from major unplanned amputation at 12 mos

*1 censored due to informed consent violation
### Lesion Assessment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Claudication (RCC 1-3)</th>
<th>CLI (RCC 4-6)</th>
<th>All Subjects (RCC 1-6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>598</td>
<td>201</td>
<td>799</td>
</tr>
<tr>
<td>Number of Lesions</td>
<td>743</td>
<td>279</td>
<td>1022</td>
</tr>
<tr>
<td>Mean Length (cm)</td>
<td>7.5</td>
<td>7.2</td>
<td>7.4</td>
</tr>
<tr>
<td>Baseline Stenosis (%)</td>
<td>73</td>
<td>76</td>
<td>74</td>
</tr>
<tr>
<td>Occlusions (%)</td>
<td>17</td>
<td>30</td>
<td>21</td>
</tr>
</tbody>
</table>

Anatomic location based on proximal edge of lesion treatment, % (N)

<table>
<thead>
<tr>
<th>Location</th>
<th>Claudication (RCC 1-3)</th>
<th>CLI (RCC 4-6)</th>
<th>All Subjects (RCC 1-6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SFA</td>
<td>72% (536)</td>
<td>48% (135)</td>
<td>66% (671)</td>
</tr>
<tr>
<td>Popliteal</td>
<td>15% (114)</td>
<td>17% (48)</td>
<td>16% (162)</td>
</tr>
<tr>
<td>Infrapopliteal</td>
<td>13% (93)</td>
<td>34% (96)</td>
<td>18% (189)</td>
</tr>
</tbody>
</table>
Excellent Patency in Diabetics

DEFINITIVE LE Primary Patency by Diabetes (Claudicants)

Diabetes mellitus

No
Yes

Diabetics
Non-Diabetics

Primary Patency, %

Days

p=0.98
Atherectomy: General Conclusions

• Atherectomy offers advantage of plaque modification and removal (excisional atherectomy).

• Useful tool for difficult to treat lesions and areas.

• Consider excisional atherectomy in diabetics.

• Need more data in comparison to other treatments.
Drug Coated Balloons – The Answer to Restenosis?

• Balloon angioplasty can achieve excellent immediate results in selected cases, but associated with high rates of restenosis.

• Local delivery of anti-restenotic drug could prevent restenosis without needing to leave a stent behind.
Drug Coated Balloons

- Currently approved in Europe, under investigation in USA.

- All available versions deliver paclitaxel to local area where balloon is inflated.

- Paclitaxel is lipophilic $\rightarrow$ migrates into local cells and inhibits cell proliferation.
## Multiple DCBs Under Development

<table>
<thead>
<tr>
<th>Company</th>
<th>Device Name</th>
<th>Balloon Drug Load</th>
<th>Carrier</th>
<th>Randomized FIM Data</th>
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<tbody>
<tr>
<td>Lutonix</td>
<td>Moxy DCB</td>
<td>2 µg/mm²</td>
<td>Undisclosed</td>
<td>Yes</td>
</tr>
<tr>
<td>Medrad-Possis</td>
<td>Cotavance</td>
<td>3 µg/mm²</td>
<td>Iopromide</td>
<td>Yes</td>
</tr>
<tr>
<td>Medtronic/Invatec</td>
<td>In.Pact</td>
<td>3 µg/mm²</td>
<td>Urea</td>
<td>No</td>
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<tr>
<td>Biotronik</td>
<td>Pantera Lux, Passeo 18</td>
<td>3 µg/mm²</td>
<td>BTHC</td>
<td>No</td>
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<tr>
<td>B. Braun</td>
<td>Sequent Please</td>
<td>3 µg/mm²</td>
<td>Iopromide</td>
<td>Yes</td>
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<tr>
<td>Eurocor</td>
<td>DIOR II</td>
<td>3 µg/mm²</td>
<td>Shellac</td>
<td>No</td>
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<tr>
<td>Aachen Resonance</td>
<td>Elutax</td>
<td>3 µg/mm²</td>
<td>Unknown</td>
<td>No</td>
</tr>
<tr>
<td>Blue Medical</td>
<td>Protégé</td>
<td>3 µg/mm²</td>
<td>Unknown</td>
<td>No</td>
</tr>
<tr>
<td>Cook Medical</td>
<td>Advance 18 PTX</td>
<td>3 µg/mm²</td>
<td>Undisclosed</td>
<td>No</td>
</tr>
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Local Delivery Reduces Restenosis: THUNDER trial

<table>
<thead>
<tr>
<th></th>
<th>Mean (%)</th>
<th>n</th>
<th>N</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncoated BA</td>
<td>44.7</td>
<td>21</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Uncoated BA / Paclitaxel i.a</td>
<td>45.4</td>
<td>22</td>
<td>39</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Paccocath</td>
<td>17.1</td>
<td>7</td>
<td>41</td>
<td></td>
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Limitations of Drug-Coated Balloons

- Still require bailout stenting if significant dissection (10-20% of the time).

- Most trials were for short, less calcified lesions.

- Best application may be to below-knee arteries or for in-stent restenosis.
Drug-Eluting Stents: Catching Up With the Coronaries

• Initial studies of drug-eluting stents in the leg were disappointing.
  - Partly reflected early stent design and higher rate of stent fractures.

• Zilver PTX stent is a paclitaxel-eluting stent for the superficial femoral artery.

• Recently approved in USA.
Palitaxel-Eluting Zilver Stent

- Elutes paclitaxel at 3 mcg/mm² on its outer surface.

- Paclitaxel inhibits microtubule formation → local suppression of neointimal hyperplasia.
24-Month Paclitaxel Effect
Patency (PSVR < 2.0): Provisional Zilver PTX vs. BMS

![Graph showing primary patency over months with Provisional Zilver PTX and Provisional Bare Zilver comparing at 24 months with 81.2% and 62.7% respectively, and 50% reduction in Restenosis Rate for Zilver PTX compared to Bare Zilver.]

<table>
<thead>
<tr>
<th>Provisional Group</th>
<th>24-month Restenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zilver PTX</td>
<td>18.8% Reduction</td>
</tr>
<tr>
<td>Bare Zilver</td>
<td>37.3%</td>
</tr>
</tbody>
</table>

$p < 0.01$
Drug Coated Stents for Long Lesions

Zilver® PTX® stenting effectively treats long SFA lesions

Mean lesion length
22.6 cm
Drug Eluting Stents in the SFA: Coming Soon to a Cath Lab Near You
Putting it All Together

• Multiple treatment options for lower extremity disease:
  - Balloon only
  - Stents
  - Atherectomy
  - Drug Coated Balloons (investigational)
  - Drug Eluting Stents
No one device is best for all applications.

- Common femoral or popliteal: consider atherectomy
- Heavy calcification: excisional or orbital atherectomy
- Restenosis: Drug coated balloon or drug-eluting stent?

- More comparative data will help with decision making.
The Future: Best of Both Worlds?

- Combination of atherectomy with drug coated balloons.
- Better acute results, long term inhibition of restenosis.
- No device left behind.
Questions?