Optimizing BTK Angioplasty: Dissections Matter!

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Disclosures: Dr. Andrew Holden

- Dr. Holden is a Medical Advisory Board Member for Medtronic, Boston Scientific, and Gore
- Dr. Holden is a Clinical Investigator for Medtronic, Boston Scientific, Gore, Abbott, Cagent, Endologix, Intact Vascular, Shockwave, Bard, Cook, Endospan, Intervene, Spectranetics, TriReme, Merit, Reflow, Terumo, Surmodics
- No other relevant disclosures
Differences in Lesion Morphology: Above and Below the Knee

Above the Knee

- Multiple plaque types
- Thrombus
- Medium to large vessels
  - 4 – 7 mm

Below the Knee

- More commonly calcified
- Tortuous anatomy
- Small vessels: 1.5 – 3.5 mm
- Long lesion lengths

Bishop Ann Vasc Surg 2008
Zeller LINC 2019
Below-the-Knee Angiography: Technique

• Be meticulous in technique:
  – Assess femoro-popliteal inflow
  – Separate/identify 4 BTK segments:
    • Tibioperoneal trunk
    • Anterior tibial
    • Posterior tibial
    • Peroneal
  – Assess pedal outflow:
    • Delineate continuation of AT into DP, and
    • PT to plantar artery

Image: Yokoi 2012
Challenges with Below-the-Knee Angiography

- **Vessel size assessment:**
  - Calcification and extent of disease alter the accuracy of quantitative angiography\(^1\)
  - Lumen size is particularly underestimated (≥34%) in BTK vessels\(^2,3\)
- **Bone interference**
- **Small vessel caliber**
- **Vessel overlap**

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\(^1\) Kashyap, *J Endovasc Ther* 2008
\(^2\) Arthurs, *J Vasc Surg* 2010
\(^3\) Shammas 2018
Challenges with Below-the-Knee Angioplasty

- Mechanisms of early BTK angioplasty failure$^{1,2}$
  - Smaller vessels, longer lesions
  - Multivessel and bifurcation disease
  - Residual stenosis/calcium/recoil
  - Balloon undersizing
  - Dissection
    - Very common in BTK angioplasty
    - Action of subintimal recanalization$^2$

$^1$Geary RL Epidemiology and Pathogenesis of Restenosis 2007
$^2$Bakker LINC 2019
Image: Shammas 2018
Appropriate Balloon Sizing in Infra-popliteal Arteries

- More complete dilation = more durable result (particularly when associated by dissection)\(^1\)

- Naturally, larger balloon size leads to larger balloon diameter
  - Too much = dissection
  - BTK dissection is different: lesions tend to be inelastic and break, rather than stretch\(^2,3\)

\(^1\)Geary 2007  \(^2\)Bakker 2019 (top)  \(^3\)Shammas 2019 (bottom)
Pathophysiology-Based Guidelines for BTK Angioplasty

- Aggressive dilation with balloon-vessel ratio >1:1
- Long inflations (≥3 minutes)
- Consider aggressive vessel preparation (atherectomy, lithoplasty, etc.)
- Consider peri- and post-interventional vasodilation? Cilostazol?
- Don’t leave a focal dissection
Dissection after BTK Angioplasty

Reported in **up to 30.7%** of BTK balloon angioplasty procedures

Rates of post-PTA dissection are thought to be underestimated in BTK arteries due to small vessel caliber and overlap of bony structures

<table>
<thead>
<tr>
<th>Procedure</th>
<th>PTA Rate</th>
<th>DCB Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>DEBELLUM</td>
<td>15.0%</td>
<td>30.7%</td>
</tr>
<tr>
<td>IN.PACT® DEEP</td>
<td>12.3%</td>
<td>19.2%</td>
</tr>
</tbody>
</table>

1. Fanelli, J Cardiovasc Surg 2014
2. Zeller, J Am Coll Cardiol 2014
3. Razavi, J Vasc Interv Radiol 2014

Image: Brodmann Catheter Cardiovasc Interv 2018

IN.PACT® is a registered trademark of Medtronic, Inc.
Correlation Between Arterial Dissection and Restenosis

- 89 patients with BTK intervention
- 6-month follow up (clinical, Duplex)
- Residual stenosis > 50% in 40% patients
- Most residual stenosis due to dissection
- Dissection was the major predictor of restenosis

Schillinger, Radiology 2002
Limited Options for BTK Dissection Repair

Prolonged Inflation
• No data for infrapopliteal arteries

Stenting
• No approved BTK implants in US
  – Off-label use of coronary stents
• BTK arteries are susceptible to external crushing, especially the posterior tibial artery

Native PT @ baseline
w/external compression

1Schneider, LINC 2017
Tack® Implants
• Four pre-loaded nitinol implants (with gold RO markers)
• 6mm deployed length
• Each implant self-sizes to tapering BTK anatomy
  – 1.5 – 4.5mm RVD

OTW Delivery System
• 4F / 0.014”
• 150cm working length
• Accurate (≤1mm) deployment

Caution: Investigational Device
Tack Endovascular System (4F) is limited by Federal (United States) law to investigational use. Not approved for sale in the United States.
BTK Dissection Repair

2 Grade C dissections after PTA with standard balloon

Dissections resolved with Tack implants
**Prospective, single-arm study**

<table>
<thead>
<tr>
<th>Population</th>
<th>Subjects with CLI (RCC 4-5) and angiographic evidence of a dissection post-PTA requiring repair in the mid, distal popliteal, tibial and/or peroneal arteries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrollment Complete</td>
<td>233 subjects at 41 sites in US, Europe, and New Zealand</td>
</tr>
</tbody>
</table>
| Primary Endpoints | Safety: MALE + POD at 30 days  
Efficacy: MALE at 6 months + POD at 30 days |

**Pivotal IDE study of the Tack Endovascular System in the treatment of patients with Critical Limb Ischemia**
TOBA II BTK Study Design and Endpoints

Prospective, single-arm pivotal IDE study

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| Primary Endpoints | • Safety: MALE + POD at 30d  
• Efficacy: freedom from MALE at 6m + POD at 30d |
| Secondary Endpoints | • Tacked segment patency at 6 months (DUS flow/no flow)  
• Target limb salvage at 6 months |
| Key Observational Endpoints | • Dissection resolution  
• Freedom from CD-TLR  
• Target lesion patency  
• Changes from baseline:  
  - Rutherford  
  - Wound status  
  - Quality of life |

MALE + POD: composite of all-cause death, above-ankle target limb amputation, or major re-intervention to the target lesion(s), defined as new bypass graft, jump/interposition graft revision, or thrombectomy / thrombolysis
SUCCESSFUL DEPLOYMENT OF THE TOBA II BTK TACK DELIVERY
(ITT population, core lab adjudicated)

*Device success* 96.5% (303/314)

*Bail out stent rate* 1.3% (3/233)

*Within Tacked segment* 0.4% (1/233)

Tack deployment site

<table>
<thead>
<tr>
<th>Site</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior tibial</td>
<td>44%</td>
</tr>
<tr>
<td>Peroneal</td>
<td>18%</td>
</tr>
<tr>
<td>Posterior tibial</td>
<td>17%</td>
</tr>
<tr>
<td>Tibioperoneal trunk</td>
<td>11%</td>
</tr>
<tr>
<td>Popliteal</td>
<td>10%</td>
</tr>
</tbody>
</table>

*successful deployment of the Tack(s) at the intended target site(s) and withdrawal of the delivery catheter from the introducer sheath (per device)
TOBA II BTK Pivotal Results

• Successfully met primary and secondary endpoints
  – 98.7% freedom from MALE + POD at 30 days
  – 95.6% freedom from MALE at 6m + POD at 30 days

• Demonstrated that the Tack implant repaired 100% of BTK dissections, with:
  – 87.3% 6m K-M target lesion patency
  – 92.0% 6m K-M freedom from CD-TLR
  – 73.8% of wounds healed or improved at 6 months
  – 95.7% 6m K-M amputation-free survival
TOBA II BTK Pivotal Results
6M K-M Tacked Segment and Lesion Patency (ITT population)

**Tacked Segment Patency:** 87.7%
**Target Lesion Patency:** 87.3%

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*DUS flow or no flow at 6m; Tacked segment: Tack implant + 5mm of artery proximal and distal; Tacks w/in 1cm are considered same segment

†DUS flow or no flow at 6m in PTA treated length
TOBA II BTK Pivotal Results
Limb Salvage and Freedom from CD-TLR
(ITT population)

6m K-M Target Limb Salvage: 98.6%

<table>
<thead>
<tr>
<th>Days</th>
<th>ff Maj Amp (95% CI)</th>
<th>At Risk</th>
</tr>
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<tbody>
<tr>
<td>30</td>
<td>99.1% (97.9%, 100%)</td>
<td>225</td>
</tr>
<tr>
<td>180</td>
<td>98.8% (97.1%, 100%)</td>
<td>163</td>
</tr>
<tr>
<td>210</td>
<td>98.0% (96.0%, 100%)</td>
<td>112</td>
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6m K-M Freedom from CD-TLR: 92.0%

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<th>Days</th>
<th>ff CD-TLR (95% CI)</th>
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<tr>
<td>30</td>
<td>100% (100%, 100%)</td>
<td>225</td>
</tr>
<tr>
<td>180</td>
<td>92.0% (88.3%, 95.8%)</td>
<td>152</td>
</tr>
<tr>
<td>210</td>
<td>88.7% (84.1%, 93.3%)</td>
<td>105</td>
</tr>
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TOBA II BTK Pivotal Results

All-Cause Mortality, Amputation-Free Survival
(ITT population)

6m K-M Survival: 97.0%

<table>
<thead>
<tr>
<th>Days</th>
<th>Survival (95% CI)</th>
<th>At Risk</th>
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<tr>
<td>30</td>
<td>99.6% (98.7%,100%)</td>
<td>225</td>
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<tr>
<td>180</td>
<td>97.0% (94.7%, 99.4%)</td>
<td>173</td>
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<tr>
<td>210</td>
<td>94.3% (90.9%, 97.8%)</td>
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6m K-M Amputation-Free Survival: 95.7%

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<th>Days</th>
<th>AFS* (95% CI)</th>
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Conclusions

• BTK angioplasty is different than ATK:
  • Goals for treatment (limb salvage vs. patency)
  • Vessels (undersizing vs. appropriate sizing)
  • Morphology (calcium vs. plaque)

• Post-Infrapopliteal PTA Dissections:
  – Occur often, yet frequently missed or underestimated
  – Can have substantial clinical impact, with limited tools for repair

• Tack Endovascular System:
  – Shows positive results at 6 months
  – With less metal, less force
  – Preserves future treatment options
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