Therapeutic Solutions for BAD in CLI

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Disclosures

- Consultant
  - Cook Medical
  - Daiichi Sankyo
  - Lake Region Medical
  - Volcano
  - Bard
  - Terumo
- Speaker
  - Abbott Vascular
  - CSI
  - Cook Medical
  - Spectranetics
- Research
  - Boston Scientific
  - CloSys
  - Daiichi Sankyo
  - Cordis
  - Medtronic
  - Volcano
Big Arterial Disease (BAD) in CLI
BTK Endovascular Intervention Failure

- **Dissection**
  - Prevent – Vessel Preparation
  - Treat - Tack

- **Recoil**
  - Prevent – Vessel Preparation (Focal Force Balloons, atherectomy, IVL)
  - Treat – Biologics (Vonapanitase)

- **Restenosis**
  - Prevent/Treat – Biologics with direct drug delivery
    - Paclitaxel ?
    - Others
Current BTK Treatments for Dissections

Lack of effective treatment options

- **BMS**
  - Evaluated in shorter lesions (mean length 47mm\(^1\), 189mm\(^2\))
  - Multiple implants per lesion (1.2\(^2\))
  - Stent fractures (1.2\(^1\))

- **DES**
  - Evaluated in shorter lesions (mean length 47mm\(^1\), 159mm\(^2\), 26.9mm\(^3\))
  - Multiple implants per lesion (1.5\(^1\), 1.1\(^2\))
  - Stent fractures (0.9\(^3\))
  - Requires patients to be on long term dual antiplatelet therapy

\(^1\)Rocha-Singh, *Catheter and Cardio Inte* 80:1042-1051.
\(^3\)Scheinert, *JACC*, 60(22):2290-5.
Implant:
- Nitinol with Gold RO markers
- Unique anchoring system to prevent migration

Catheter:
- 4 Tack® implants per 4 Fr delivery system
- Pin-Pull delivery technique is highly familiar to clinicians
- Standard over the wire delivery system
- Design permits high accuracy Tack deployment

The 6 Fr. Tack Endovascular System™ is CE Mark Authorized under EC Directive 93/42/EEC. (4 Fr. System CE Mark pending)
Tack and Tack Endovascular System™ are trademarks of Intact Vascular, Inc.
Not Available for Sale or Use in the United States.
Case Study: Baseline

- 63yr male
- History:
  - IDDM, HTN, hyperlipidemia, CAD, CKD
- Presentation:
  - Superficial plantar heel wound
Angioplasty

Multiple balloons and inflations required:

- **2.5/200**
  - 60 sec @ 16 atm x 6 inflations
- **3.0/200**
  - 60 sec @ 16 atm x 2 inflations
- **4.0/220**
  - 60 sec @ 14 atm x 2 inflations
Post-PTA Result

• Is there a dissection present?
• If so, would you treat it?
  – How?
4 Tack Implants Deployed

Video

Reference

Deployment
How Shockwave Creates Localized Lithotripsy

High Speed Sonic Pressure Wave Created Safely Inside Integrated Balloon

1. **Unfocused lithotripsy energy** is created at the emitters which are contained in a fluid filled coupler.

2. Electrical energy is delivered to the emitter, initiating the steam bubble, which expands & collapses – creating **sonic pressure waves**.

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**Video**: Actuation of Single Pulse (20µs/frame)
Case Example

- 78 y/o male with a history of DM, CAD, HTN, hyperlipidemia

- Presenting with medial plantar wound which is not healing
Initial Angiogram

*Plantar wound*
TP trunk
Ostial PT
Proximal Peroneal
Posterior Tibial/TP Trunk/Peroneal Intervention

4.0x60mm Shockwave IVL
Post Intervention
Most BTK vessels undergo significant elastic recoil following angioplasty.

Medial calcification produces vessel recoil and restenosis.

1) Baumann et al, Early recoil after balloon angioplasty of tibial artery obstructions in patients with critical limb ischemia, J Endovasc Ther 2014
2) Guzman et al, Tibial artery calcification as a marker of amputation risk in patients with PAD, JACC 2008
3) Zettervall et al, Association of arterial calcification with CLI in patients with PAD, J Vasc Surg 2017
4) Mustapha et al, One-Month Duplex Ultrasound Evaluation of Vessel Recoil After Tibial Peripheral Vascular Intervention for Critical Limb Ischemia Predicts 12m TLR, AMP 2017
Tibial US after 1 Month is Predictive of Reintervention at 12 Months

Recoil and vessel diameter were significant predictors of re-intervention within 12 months, for every 10% recoil, odds ratio 12.76 (95%CI: 11.51-14.22), p<0.001
The Bullfrog® Micro-Infusion Device

- Adventitial drug delivery – where drug is most needed
- Microneedle precision – simple dosage control and unlimited payload
- Not limited to one drug
- No lost drug during transit of device (unlike coated products)
- Three balloon sizes treats full range of peripheral arteries:
  - 2-4 mm
  - 3-6 mm
  - 4-8 mm
- Contrast medium co-administered to track injections and provide complete coverage
Targeting the Restenosis Cascade

Restenosis results from the inflammatory cascade:

- **Hours**
  - Injury
- **Days**
  - Endovascular procedure
  - Transcription
  - Signaling
  - Recruitment
- **Weeks**
  - Migration
  - Proliferation
- **Months**
  - Hyperplasia / Narrowing

Sirolimus and its analogs have shown the ability to decrease inflammation and reduce cellular proliferation, targeting multiple aspects of the restenosis cascade.

Dexamethasone: Upstream targeting of the early restenosis process limits downstream restenosis, allows healing and resolution.
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CEA what else?
Pro: Carotid Endarterectomy (CEA)

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