Therapeutic Solutions for BAD in CLI

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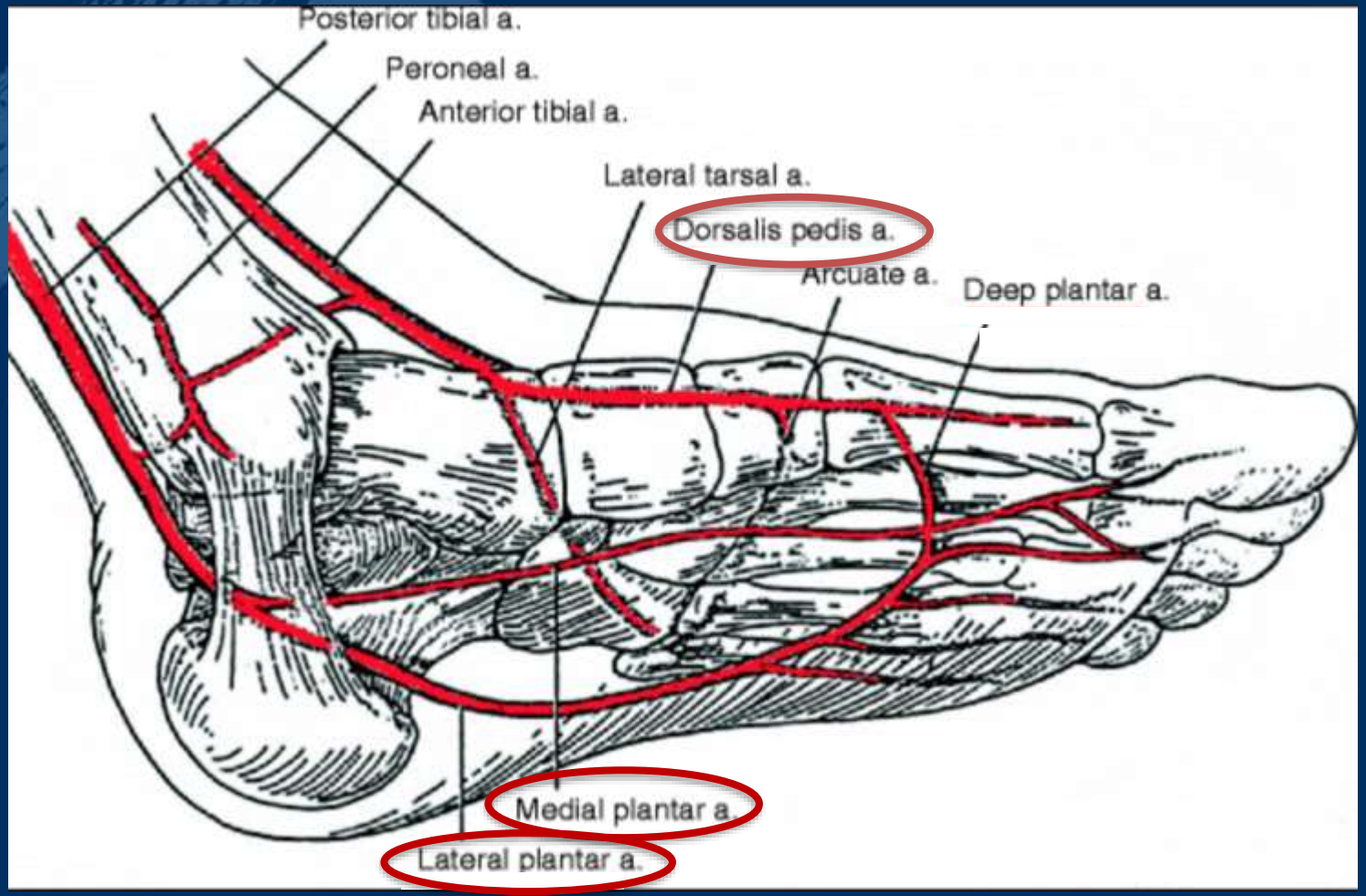
Disclosures

- 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.
[2]Bosiers, *J Vasc Surg*, 55(2):390-398.
[3]Scheinert, *JACC*, 60(22):2290-5.

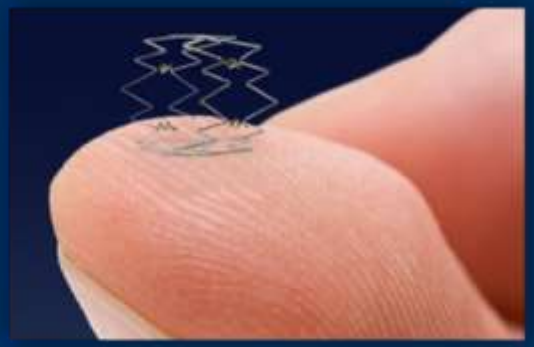
Tack Endovascular System™

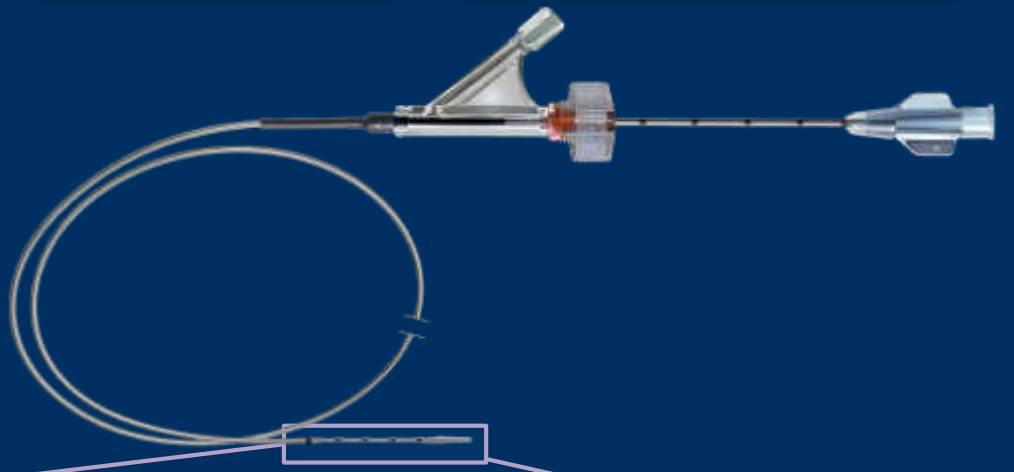
Implant:

- 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





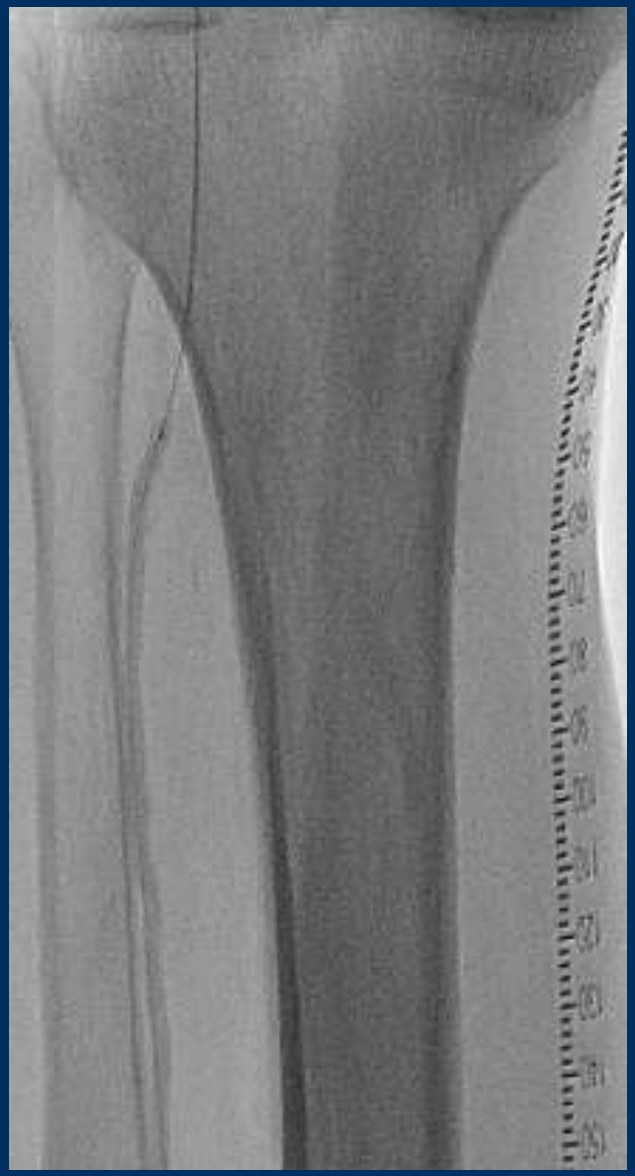
Case Study: Baseline

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

Angioplasty

Multiple balloons and inflations required:

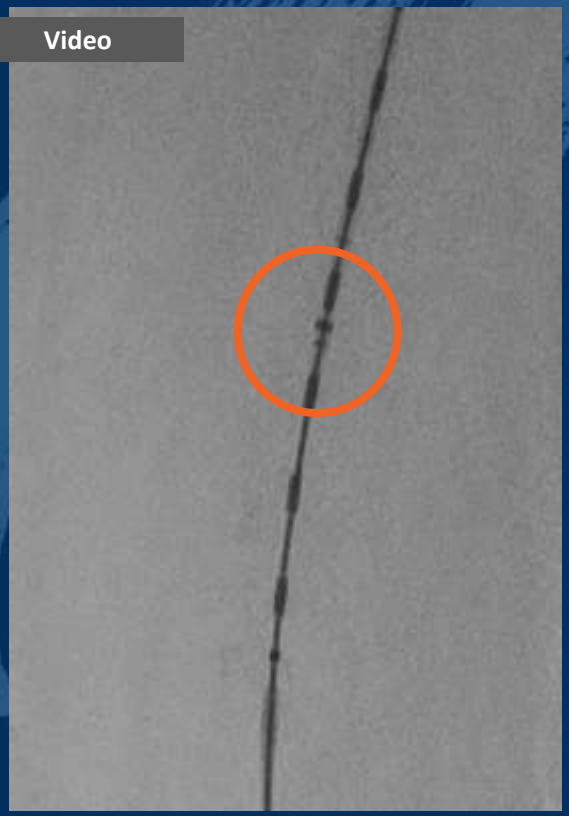
- 2.5/200
  - 60 sec @ 16 atm x 6 inflations
- 3.0/200
  - 60 sec @ 16 atm x 2 inflations
- 4.0/220
  - 60 sec @ 14 atm x 2 inflations

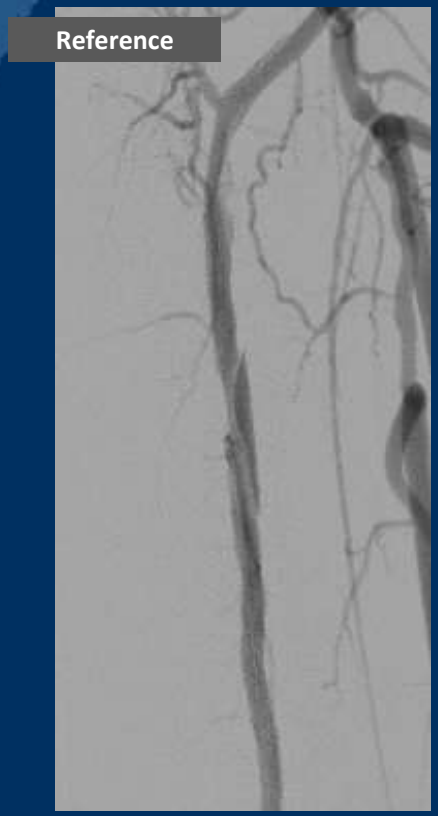


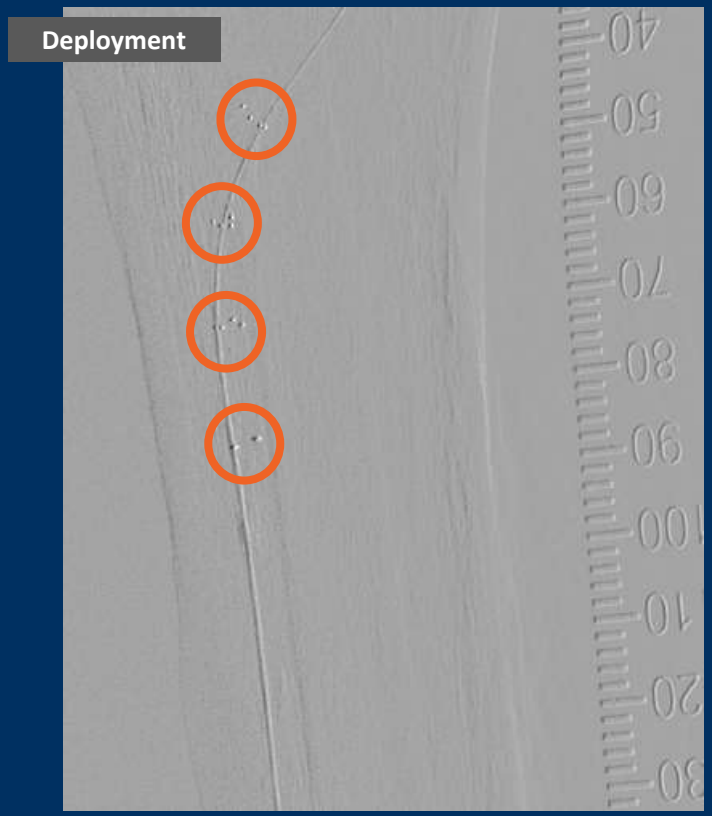
Post-PTA Result

- Is there a dissection present?
- If so, would you treat it?
  - How?

4 Tack Implants Deployed







Final Result

Baseline

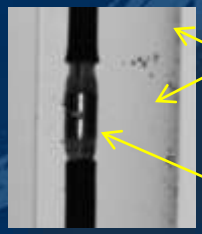
Post-PTA

Final

How Shockwave Creates Localized Lithotripsy

High Speed Sonic Pressure Wave Created Safely Inside Integrated Balloon

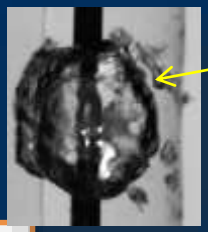
1 **Unfocused lithotripsy energy** is created at the emitters which are contained in a fluid filled coupler



Fluid filled Balloon

Emitter

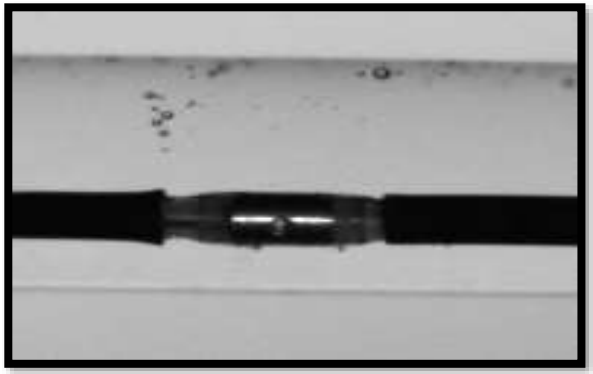
2 Electrical energy is delivered to the emitter, initiating the steam bubble, which expand & collapses – creating **sonic pressure waves**.



Bubble expands-collapses

Sonic Pressure Waves

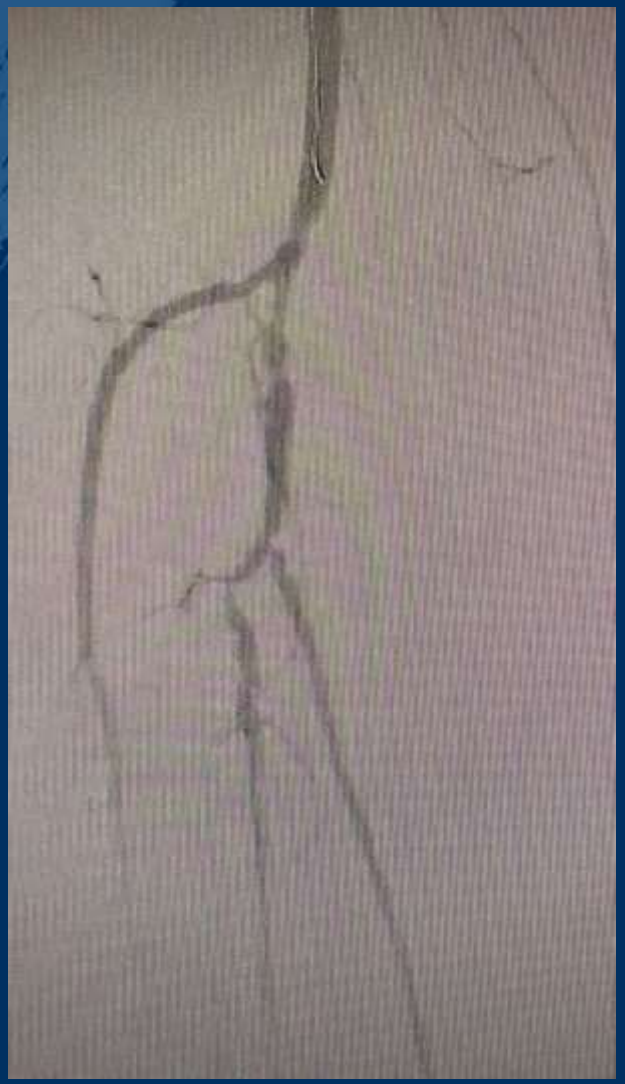
***Video*: Actuation of Single Pulse (20µs/frame)**



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

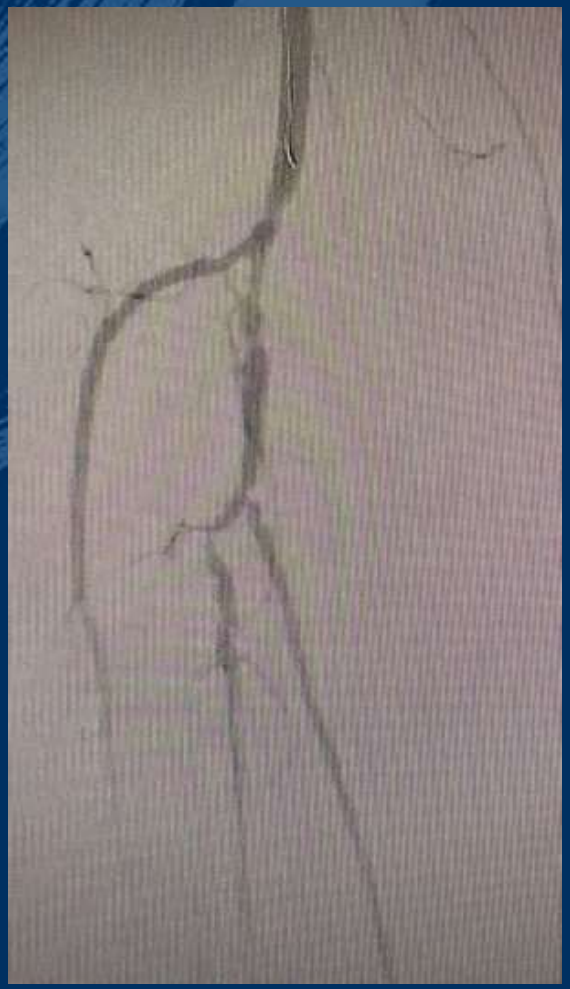
Ostial PT

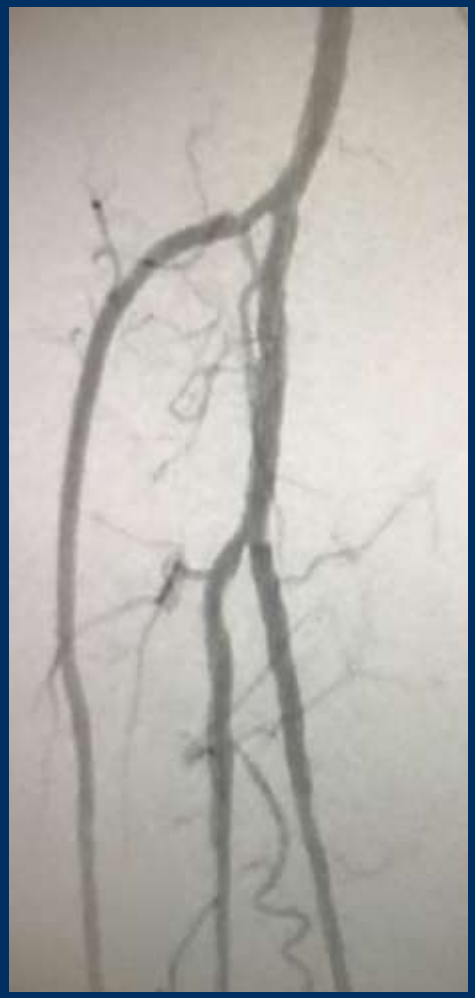
Proximal Peroneal

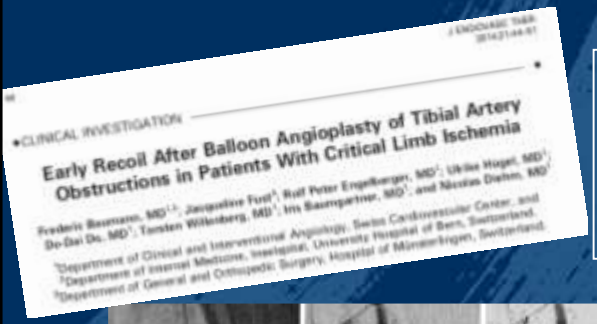
Posterior Tibial/TP Trunk/ Peroneal Intervention

4.0x60mm Shockwave IVL

Post Intervention



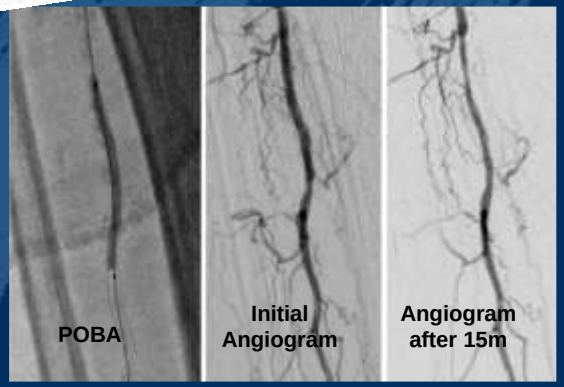


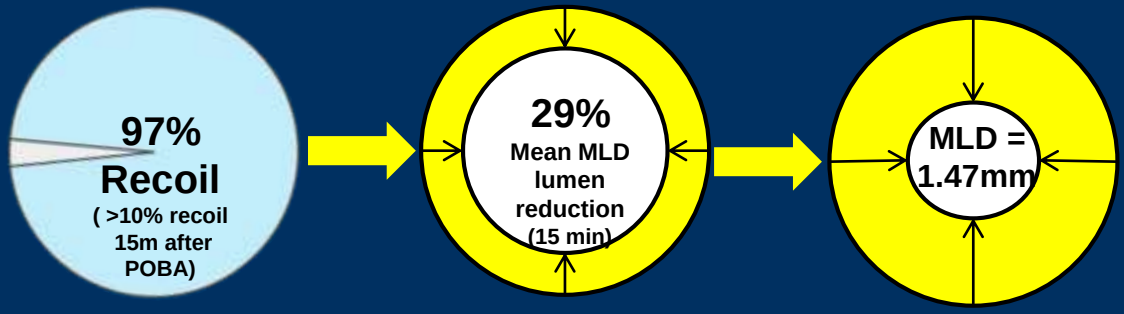


CLINICAL INVESTIGATION

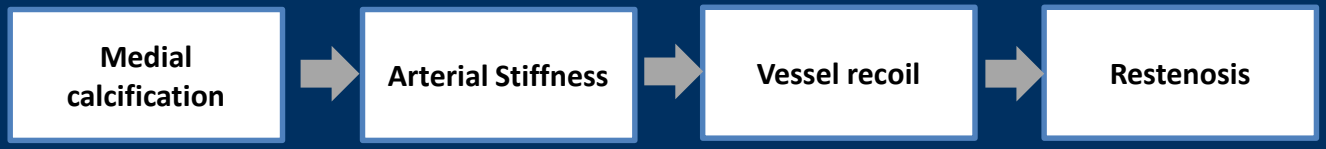
Early Recoil After Balloon Angioplasty of Tibial Artery Obstructions in Patients With Critical Limb Ischemia

Most BTK vessels undergo significant elastic recoil following angioplasty



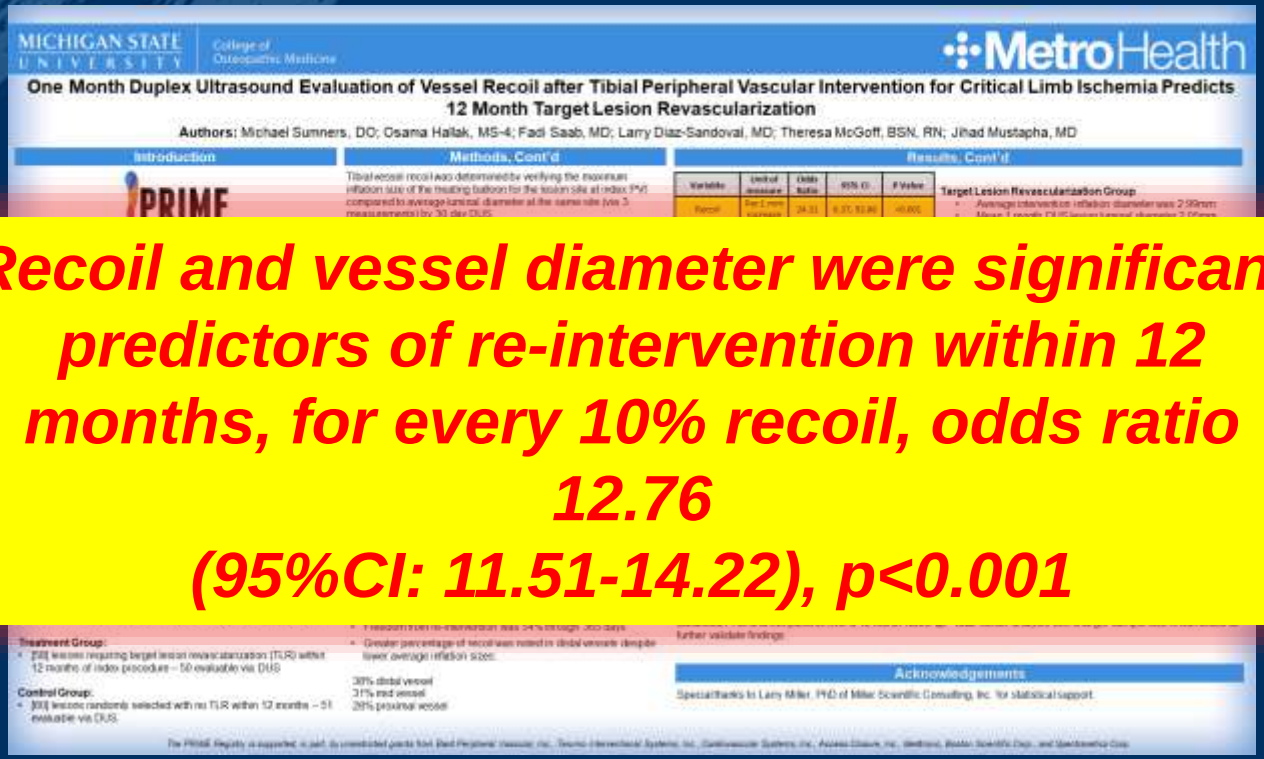


Medial calcification produces vessel recoil and restenosis[2,3,4]



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


MICHIGAN STATE UNIVERSITY College of Osteopathic Medicine

MetroHealth

One Month Duplex Ultrasound Evaluation of Vessel Recoil after Tibial Peripheral Vascular Intervention for Critical Limb Ischemia Predicts 12 Month Target Lesion Revascularization

Authors: Michael Sumners, DO; Osama Hallak, MS-4; Fadi Saab, MD; Larry Diaz-Sandoval, MD; Theresa McGoff, BSN, RN; Jihad Mustapha, MD

Introduction

PRIME

Methods, Cont'd

Tibial vessel recoil was determined be verifying the maximum inflation size of the treating balloon for the lesion site at index PVI compared to average luminal diameter at the same site (via 3 measurements) by 30 day DUS.

Results, Cont'd

Variable	Critical Measure	Odds Ratio	95% CI	P Value
Recoil	Per 1 mm increase	24.11	6.37, 93.80	<0.001

Target Lesion Revascularization Group

- Average intervention inflation diameter was 2.99mm

Treatment Group:

- [XX] lesions requiring target lesion revascularization (TLR) within 12 months of index procedure – 50 evaluable via DUS

Control Group:

- [XX] lesions randomly selected with no TLR within 12 months – 51 evaluable via DUS

- Freedom from re-intervention was 94% through 365 days
- Greater percentage of recoil was noted in distal vessels despite lower average inflation sizes

38% distal vessel
31% mid vessel
28% proximal vessel

further validate findings

Acknowledgements

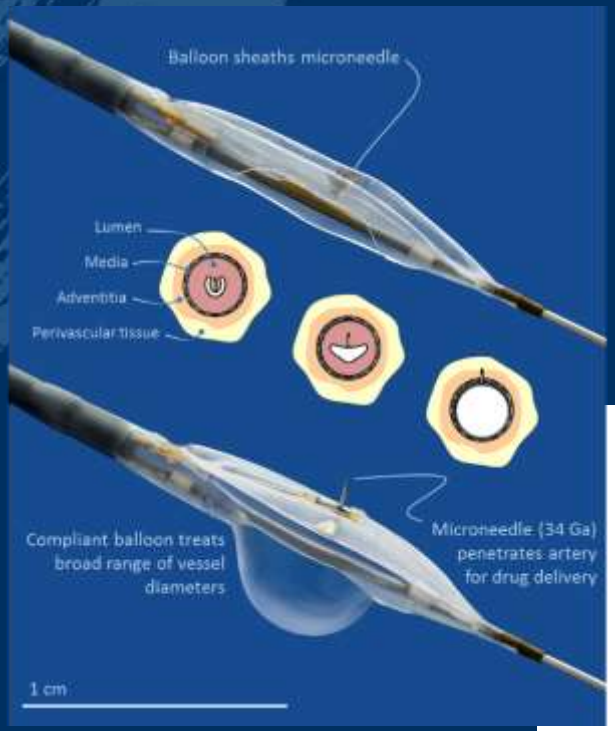
Special thanks to Larry Miller, PhD of Miller Scientific Consulting, Inc. for statistical support.

The PRIME Registry is supported, in part, by unrestricted grants from [illegible]

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

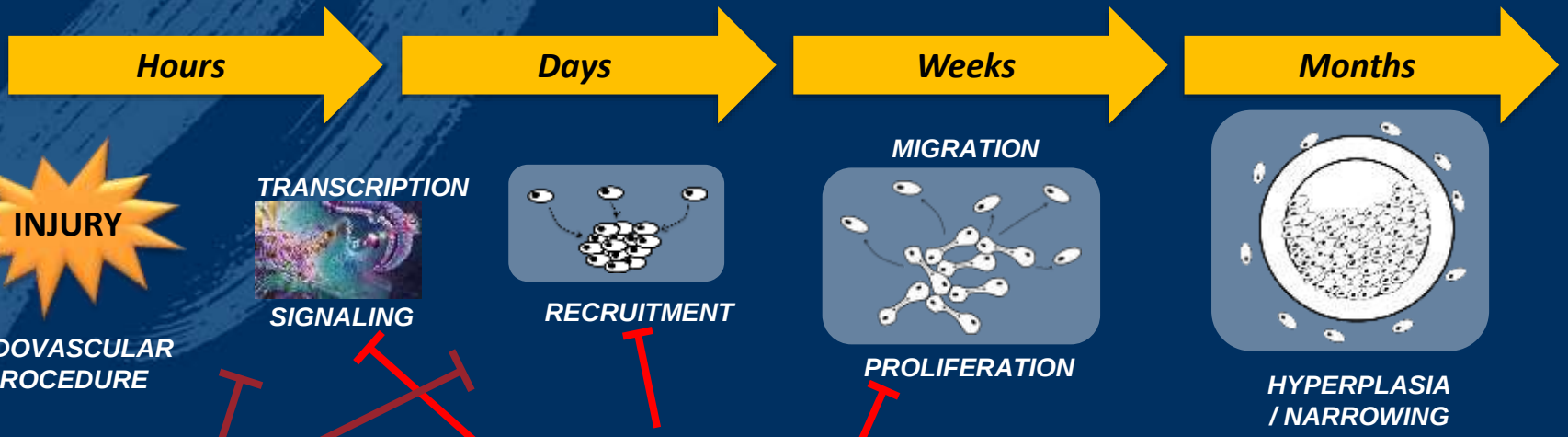
The Bullfrog® Micro-Infusion Device

- 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:



Dexamethasone: Upstream targeting of the early restenosis process limits downstream restenosis, allows healing and resolution

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

Therapeutic Solutions for BAD in CLI

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CEA what else?
Pro: Carotid Endarterectomy (CEA)

Prof. Dr. med. Ernst Weigang

Academic Hospital Hubertus Berlin, Germany