Multidisciplinary Insights on CLTI

Applying New Data Below the Knee

Supported by an educational grant from Shockwave IVL

Faculty

- **Andrew Holden, ONZM, MBChB, FRANZCR, EBIR**
  Director of Northern Region Interventional Radiology Service
  Auckland City Hospital
  Te Toka Tumai, New Zealand
- **Michael Siah, MD**
  Vascular Surgeon, Director of Limb Salvage, Assistant Professor of Surgery
  UT Southwestern Medical Center
  Dallas, TX
- **Gabriela Velazquez, MD, FACS, DFSVS, RPVI**
  Interim Chair, Associate Professor
  Director Vascular Surgery Training Programs
  Department of Vascular and Endovascular Surgery
  Wake Forest University School of Medicine
  Winston-Salem, NC
- **Constantino S. Peña, MD, FSIR**
  Medical Director of Vascular Imaging
  Miami Cardiac & Vascular Institute
  Miami, FL

Faculty Disclosures

- **Andrew Holden, MBChB, FRANZCR**
  Advisory Board: Boston Scientific; Gore; Medtronic; Clinical Investigator: Abbott; Artivion; Bard-BD; Biotronik; Boston Scientific; Cagent; Cook; Cordis; Efemoral; Endospan; FluidX; Gore; Inari; LifeSeal; Medtronic; Merit; Nectero; Penumbra; Reflow Medical; R3 Vascular; Shape Memory; Shockwave; Terumo

- **Michael Siah, MD**
  Advisory Board, Consultant: Abbott; Cagent; Contego; Inari; Philips; Shockwave

- **Gabriela Velazquez, MD, FACS, DFSVS, RPVI**
  Speakers Bureau: Gore; Penumbra

- **Constantino S. Peña, MD, FSIR**
  BD Bard: Consultant |BD Bard: Speaker's Bureau |Biotronix: Consultant |Biotronix: Speaker's Bureau |Cagent: Other Financial or Material Support |Cook Medical: Speaker's Bureau |Cordis: Consultant |Cordis: Speaker's Bureau |Penumbra: Speaker's Bureau |Philips Healthcare: Consultant |Shockwave: Speaker's Bureau |Surmodics: Advisory Board

Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration)
  - Applicable CME staff have no relationships to disclose relating to the subject matter of this activity
  - This activity has been independently reviewed for balance

- This CME activity includes brand names for participant clarity purposes only. No product promotion or recommendation should be inferred

Learning Objectives

- Describe the clinical presentation, pathophysiology, and disease burden of chronic limb-threatening ischemia (CLTI)
- Evaluate current evidence and emerging data on below-the-knee (BTK) and below-the-ankle (BTA) interventions for CLTI
- Apply case-based insights to clinical practice by reviewing real-world BTK and BTA revascularization

CLTI = chronic limb-threatening ischemia; BTK = below-the-knee; BTA = below-the-ankle.

Welcome and Introduction

Andrew Holden, ONZM, MBChB, FRANZCR, EBIR
Director of Northern Region Interventional Radiology Service
Auckland City Hospital
Te Toka Tumai, New Zealand

Chronic Limb-Threatening Ischemia (CLTI)

CLTI is the most severe manifestation of late-stage PAD characterized by ischemic rest pain and/or tissue loss

Prevalence

Up to 22 million people affected worldwide

- CLTI patients represent ~10-11% of PAD patients[1]

Clinical Burden

Associated with high comorbidity burden and poor limb and life-related outcomes[2]

[1]Farber, et al. *Br J Surg*. 2024;111(2) [2]Gornik, et al. *Circulation*. 2024;149(24)e1313-e1410.

Clinical and Anatomical Complexity in CLTI

PATIENT PRESENTATION

Diabetes & CKD are key comorbidities in CLTI patients

~50-70%
CLTI patients with Diabetes[1-3]

~25-55%
CLTI patients with CKD[2,4,5]

SYMPTOMATIC REST PAIN OR TISSUE LOSS[6]

LESION COMPLEXITIES

Small Vessels

Long Diffuse

Early Recoil

COMMONLY MODERATE/SEVERE CALCIFICATION[4]

TREATMENT CHALLENGES

Achieving distal perfusion

Maintaining patency

Wound Healing

MULTIDISCPLINARY CARE VITAL TO PREVENT LIMB LOSS[3]

[1]Callegari, et al. *J Vasc Surg*. 2025;82(4):1401-1411. [2]Menard, et al. *J Vasc Surg*. 2023;78(3):711-718.25. [3]Fereydooni, et al. *Vasc Med.* 2020;25(1):78-87. [4]Rivera, et al. *Cardiorenal Med*. 2024;14(1):533-542.
[5]Soon, et al. *Vasc Specialist Int*. 2021;37:13. [6]Hawkins, et al. *JSCAI*. 2022;1(3):100015. [7]Mustapha JA, et al. *Circ CV Interventions*. 2016;9e003468.

CLTI-Related Amputations Are Associated with High Mortality Rates and Cost

U.S. Prevalence

4 million
people affected[1]

500-1,000 new cases annually per million individuals & growing[2]

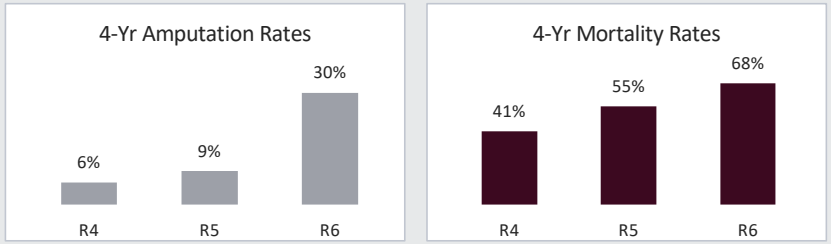
U.S. Major Amputation Rates

70,000
annual amputations[3]

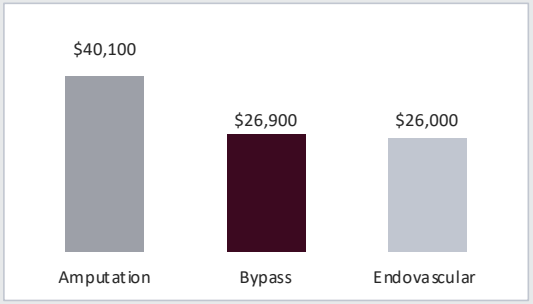
$13 billion
in direct costs[4]

$25 billion
in total costs[4]

CLTI Amputation Results in Higher Mortality[5]



Amputation Costs 35% More Than Revascularization[5]



[1]Torres, et al. *Crit Limb Ischemia.* 2023. [2]Teraa, et al. *Am Heart Assn*. 2016;5(2):e002938. [3]Yost, et al. *Endovasc Today*. 2014. [4]Yost, et al. *Endovasc Today.* 2021 [5]Yost, et al. The Sage Group, 2019.

Current Treatment Paradigm in CLTI

Circulation

CLINICAL PRACTICE GUIDELINES

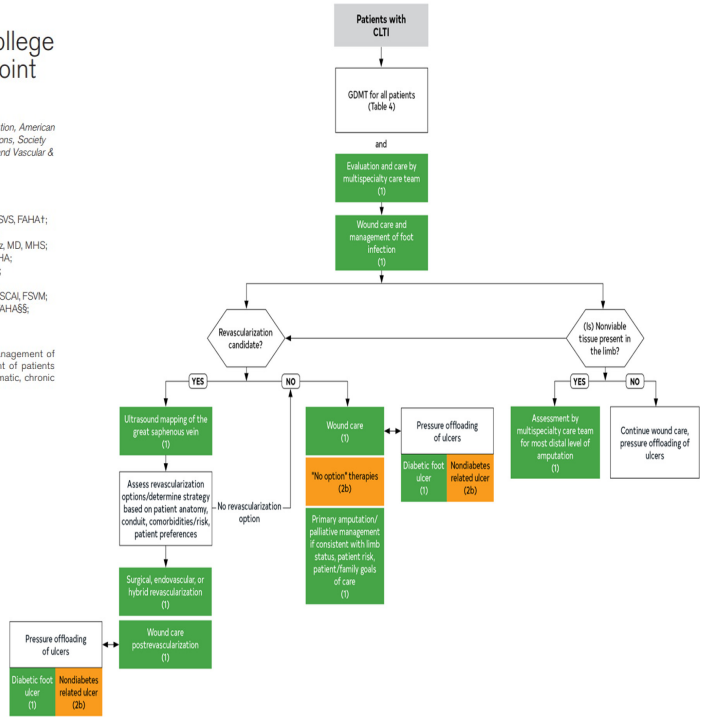
2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Developed in Collaboration With and Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Podiatric Medical Association, Association of Black Cardiologists, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine, Society for Vascular Nursing, Society for Vascular Surgery, Society of Interventional Radiology, and Vascular & Endovascular Surgery Society

Writing Committee Members*

Heather L. Gornik, MD, FAHA, MSVM, Chair; Herbert D. Aronow, MD, MPH, FACC, FSCAI, FSVM, Co-Vice-Chair; Philip P. Goodney, MD, MS, DFSVS, Co-Vice-Chair; Shipra Arya, MD, SM; Luke Packard Brewster, MD, PhD, MA, RVT, DFSVS, FAHA†; Lori Byrd, MSN†; Venita Chandra, MD§; Douglas E. Drachman, MD, FACC, FSCAI; Jennifer M. Eaves, DNP, MSN, RN; Jonathan K. Ehrman, PhD, FACC, FAHA, FAACVPR‖; John N. Evans, DPM¶; Thomas S.D. Getchius; J. Antonio Gutiérrez, MD, MHS; Beau M. Hawkins, MD, FACC, FSCAI, FSVM; Connie N. Hess, MD, MHS, FACC, FAHA, FSCAI; Karen J. Ho, MD, FAHA; W. Schuyler Jones, MD, FACC#; Esther S.H. Kim, MD, MPH, FAHA, FSVM**; Scott Kinlay, MBBS, PhD, FACC, FAHA; Lee Kirksey, MD, MBA††; Debra Kohlman-Trigoboff, RN, MS, ACNP-BC, CVN; Chandler A. Long, MD; Amy West Pollak, MD, MSc, FAHA; Saher S. Sabri, MD; Lawrence B. Sadwin‡; Eric A. Secemsky, MD, MSc, FACC, FAHA, FSCAI, FSVM; Maya Serhal, MD, FACC; Mehdi H. Shishehbor, DO, MPH, PhD, FACC, FSVM‡‡; Diane Treat-Jacobson, PhD, RN, MSVM, FAHA§§; Luke R. Wilkins, MD, FSIR‖‖

AIM: The "2024 ACC/AHA/AACVPR/APMA/ABC/SCAI/SVM/SVN/SVS/SIR/VESS Guideline for the Management of Lower Extremity Peripheral Artery Disease" provides recommendations to guide clinicians in the treatment of patients with lower extremity peripheral artery disease across its multiple clinical presentation subsets (ie, asymptomatic, chronic symptomatic, chronic limb-threatening ischemia, and acute limb ischemia).



Key Takeaways

- **Multispecialty care team**
  - Focus on wound healing, limb preservation, and survival
- **Revascularization is central to salvage limb, if feasible**
  - Endovascular, surgical, or hybrid individualized strategy
- **Adjunctive care**
  - Ongoing foot/wound care alongside revascularization and medical therapy for optimal outcomes
- **Amputation is selective**
  - Often a last-resort strategy, favoring the most distal functional level

[1]Gornik, et al. *Circulation.* 2024;149(24):e1313-e1410.

Vascular Calcification in Peripheral Arterial

Peripheral Artery Disease (PAD):

US Prevalence[1]

12.4 Million

Interventional Procedures[2]

850 Thousand

Complex, Calcified Lesions[3,4]

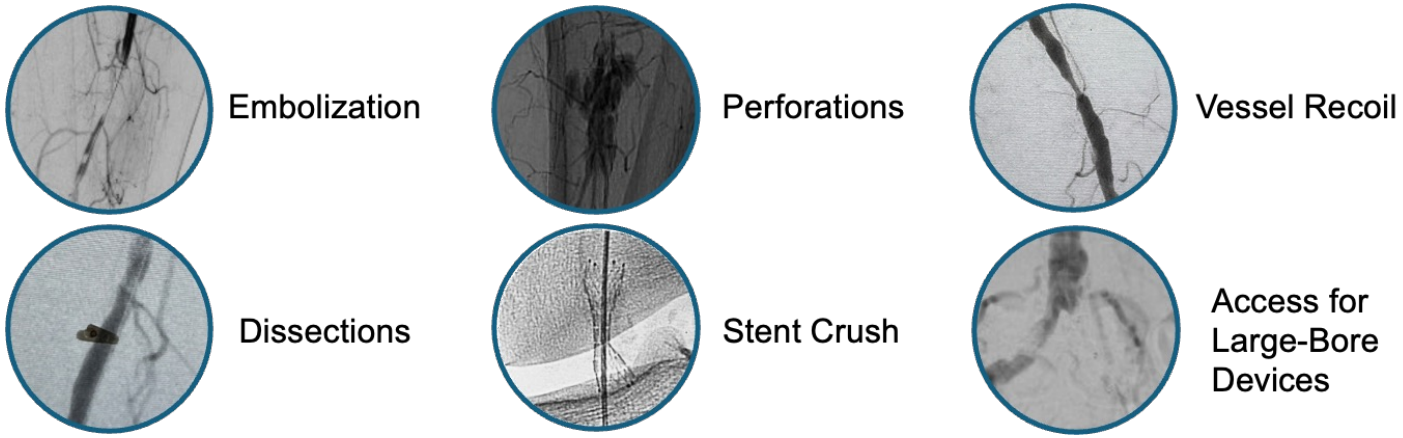
40-70 Percent

Calcified arteries resist expansion, resulting in more complications and vessel damage

1Martin et al. Circulation 2025; 151(8), e41–e660; 2. Decision Resources Group. Peripheral Vascular Devices 2020; 3. Summation of data from Sage Report: "Prevalence and Significance of Calcium, Vulnerable Plaque, and Plaque Morphology in Peripheral Artery Disease (PAD)", Mary L. Yost, The Sage Group 2016; 4. Soor et al. Peripheral Vascular Disease: Who Gets It and Why? A Histomorphological Analysis of 261 Arterial Segments from 58 Cases. Pathology. 2008.

Calcified Lesions

- More likely to have sub-optimal results and complications after standard endovascular therapies



A technology is needed to address these gaps

1Katsanos K, et al. *Cardiovasc Intervent Radiol*. 2017;40:964-977.

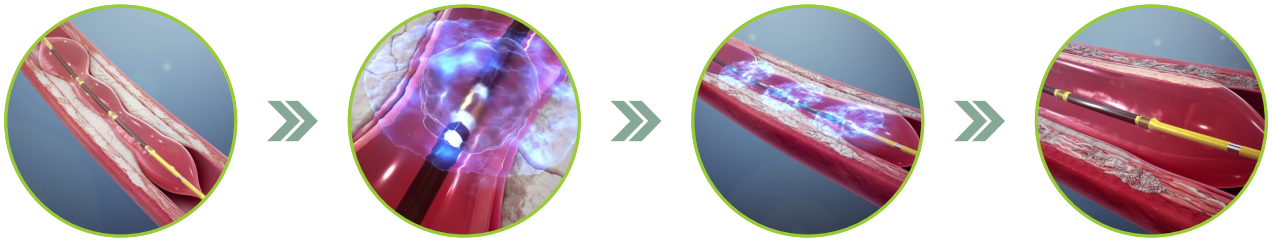
Shockwave Intravascular Lithotripsy Mechanism

Shockwave IVL

Each pulse delivers an effective pressure of **~50 atm**

Balloon maintained at a **low inflation** pressure

Fractures both **superficial** and **deep** calcium

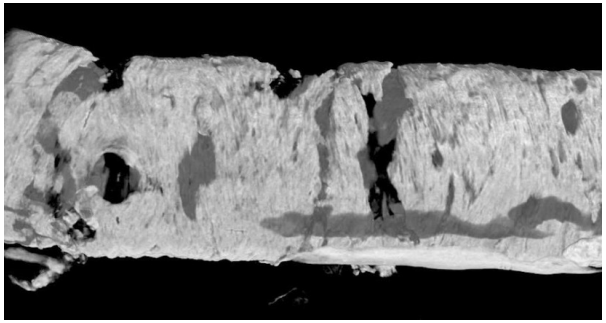


Deliver catheter and inflate to low pressure

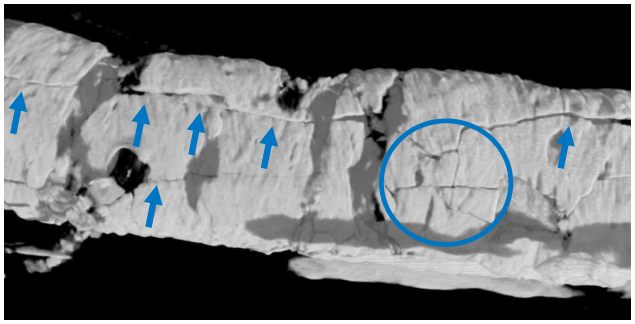
Generate ultrasonic acoustic pressure waves using lithotripsy

Crack calcium

Safely expand the vessel



Pre-IVL Treatment*



Post-IVL Treatment*

*Micro-CT scan analysis: R. Virmani, CV Path Institute

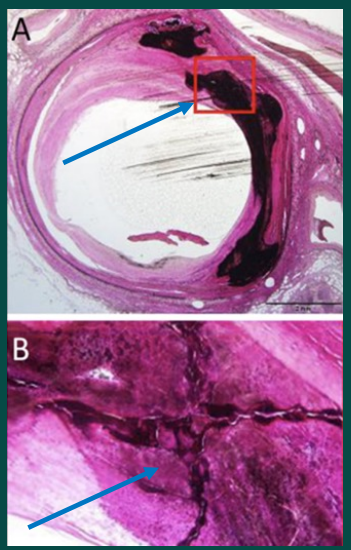
Shockwave IVL MOA Enables Treatment of Both Superficial and Deep Calcium

Safely selects and modifies both superficial and deep calcium[1]

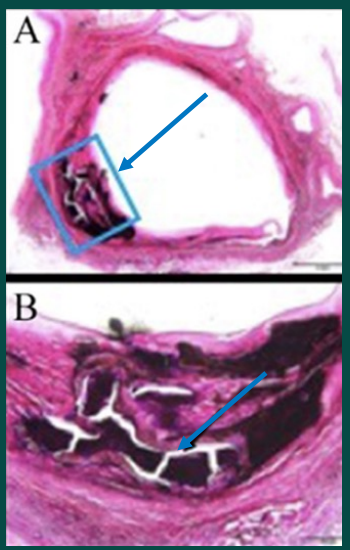
A) Cross-Sectional Histological Images

B) High-power magnification of images in A

Microfractures in Superficial calcium



Microfractures in Deep calcium



[1]Kereiakes, et al. *J Am Coll Cardiol Interv*. 2021;14(12):1275-1292.

Peripheral IVL Clinical Programs
>1,800 patients enrolled globally

	Disrupt PAD I	Disrupt PAD II	Disrupt BTK	Disrupt PAD III RCT	Disrupt PAD III OS	Disrupt PAD +	Disrupt BTK II
Status	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment completed	Ongoing
Study design	Single arm, safety & performance	Single arm, safety & effectiveness	Single arm, pilot	RCT, safety & effectiveness	Single arm, observational study	Single arm, safety & performance	Single arm, safety & performance
Vessel beds	SFA, Pop	SFA, Pop	BTK	SFA, Pop	Iliac, CFA, SFA, Pop, BTK	Iliac, CFA, SFA, Pop, BTK	BTK
Study conduct*	CEC, ACL	CEC, ACL	ACL	CEC, ACL	ACL	CEC, ACL	CEC, ACL
# of patients/sites	35/3	60/8	20/3	306/45	1,373/30	37/8	250/42
Regions	NZ, EU	NZ, EU	NZ, EU	US, NZ, EU	US, NZ, EU	AUS, NZ, US	US, EU

*CEC: Independent clinical events committee; ACL: Angiographic core lab

Study Design

Prospective, multicenter, single-blind, observational study

NCT02923193

Objective

Assess "real-world" periprocedural outcomes of IVL for treatment of calcified, stenotic, peripheral arteries

Key Inclusion

RC 2-6

Moderate-severe calcification*

Ilio-femoral, femoral, popliteal and infrapopliteal arteries

Angiographic Core Laboratory

Yale Cardiovascular Research Group

New Haven, CT

November 2017 – June 2021

30 sites, 3 countries

N = 1,373 patients, 1,677 lesions

↓

IVL treatment ± adjunctive technology†

↓

1,531/1,677 lesions (91.3%)

Evaluable angiographic core lab data could be cross-referenced with site-reported information

↓

N = 1,262 patients

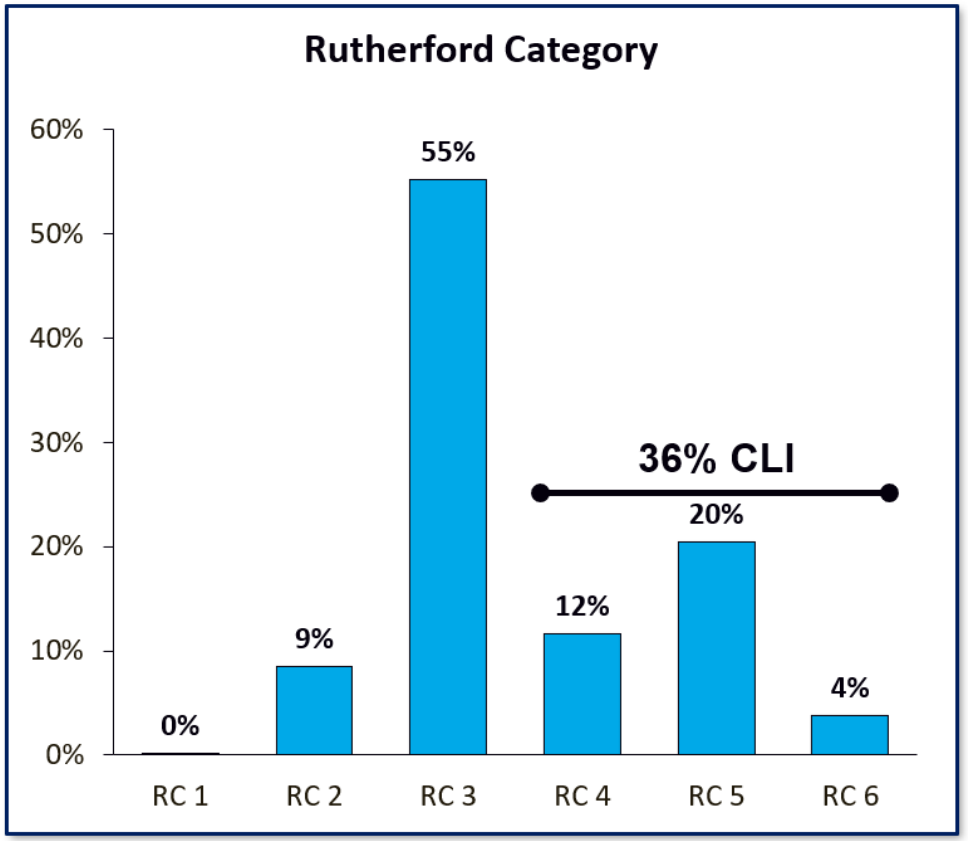
N = 1,531 lesions (core lab assessment)

*Presence of fluoroscopic evidence of calcification: 1) on parallel sides of the vessel and 2) extending > 50% the length of the lesion if lesion is ≥50mm in length; or extending for minimum of 20mm if lesion is <50mm in length.

†At the operator's discretion

Baseline Characteristics

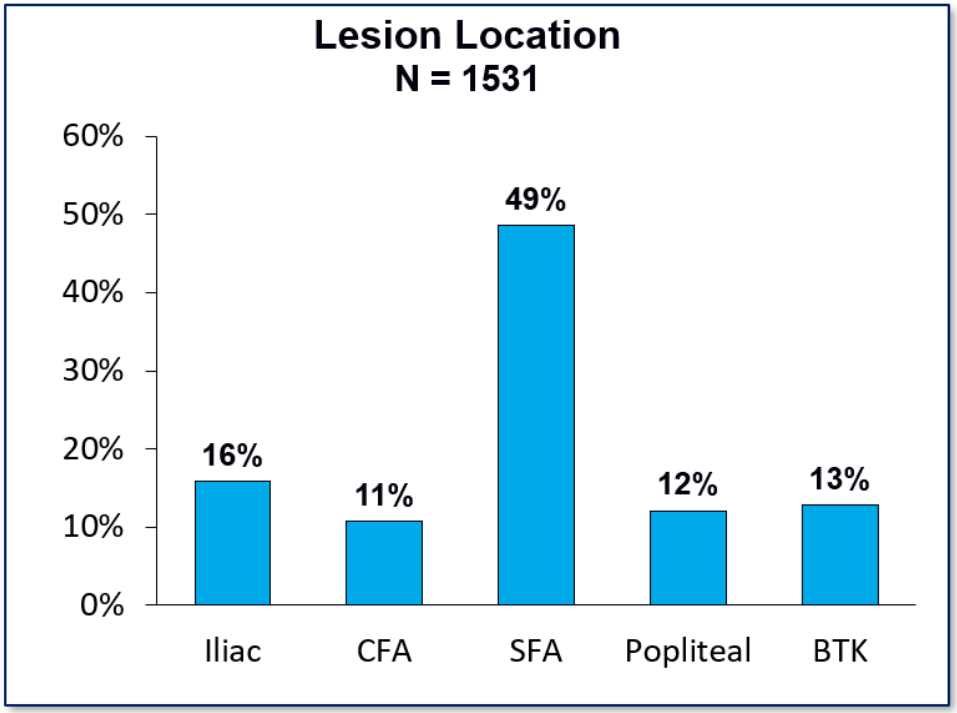
Characteristic	Patients N=1262
Age	71.9 ± 9.0
Male	70.1%
Hypertension	94%
Hyperlipidemia	89%
Diabetes Mellitus	56%
Coronary artery disease	65%
Smoker	78%
Prior MI	24%
CVA or TIA	15%
Renal Insufficiency	27%
On Dialysis	30%
ABI	0.7 ± 0.3



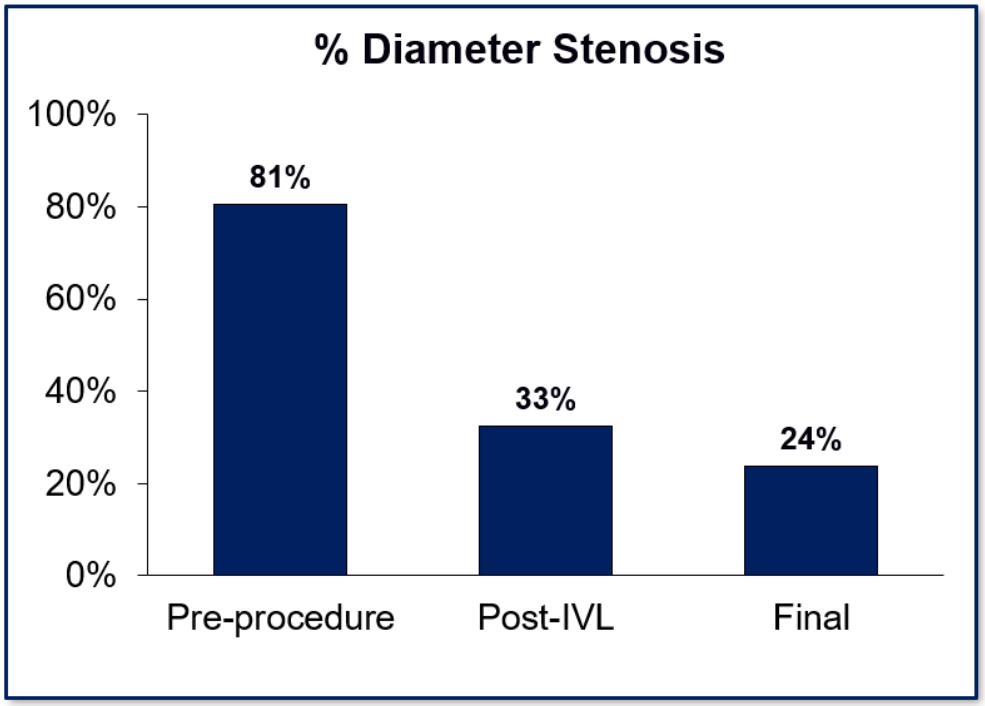
Baseline Lesions Characteristics
Core Lab Adjudicated

Characteristic	Lesions N=1531
Lesions per Patient	1.2 ± 0.5
Reference Vessel Diameter, mm	5.5 ± 1.7
Minimum Lumen Diameter, mm	1.1 ± 1.1
Diameter Stenosis, %	81% ± 18%
CTO, %	31%
Lesion Length, mm	93.5 ± 74.3
Lesion Length ≥150mm	19%
Calcified Length, mm	114.8 ± 90.4
Moderate-Severe Calcification*	90%
Eccentric	20%

*PARC definition of calcium severity



Angiographic Outcomes
Core Lab Adjudicated

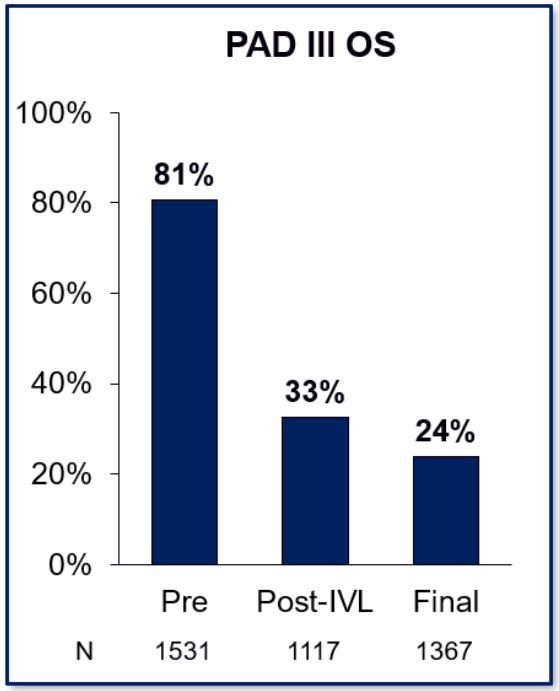


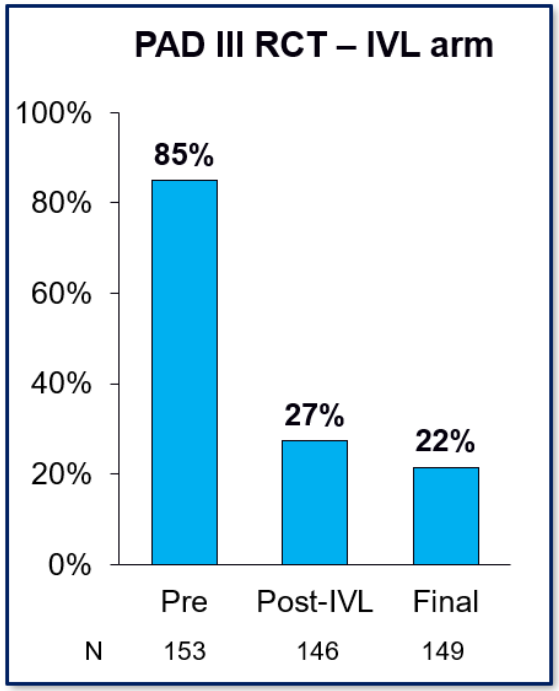
Complications	Post-IVL N=1119	Final N=1367
Dissections D-F	2.2%*	0.7%
Perforation	0.4%†	0.2%
Distal Emboli	0.1%	**0%**
Slow Flow/No Reflow	0.2%	**0%**
Abrupt Closure	**0%**	**0%**
Thrombus	0.1%	**0%**

*22/25 ≥grade D dissections occurred in CTO lesions
†4 perforation events treated with stenting with no serious adverse events

Consistent reduction in diameter stenosis with low rates of angiographic complications

Consistent Outcomes with PAD III RCT Core Lab Adjudicated





Complications	PAD III OS N=1367	PAD III RCT N=149*
Dissections D-F	0.7%	0%
Perforation	0.2%	0%
Distal Emboli	**0%**	0%
Slow Flow/ No Reflow	**0%**	0%
Abrupt Closure	**0%**	0%
Thrombus	**0%**	0%

*Tepe et al. *JACC: Cardiovasc Interv* 2021.

Consistent outcomes between clinical trial and 'real world' environments

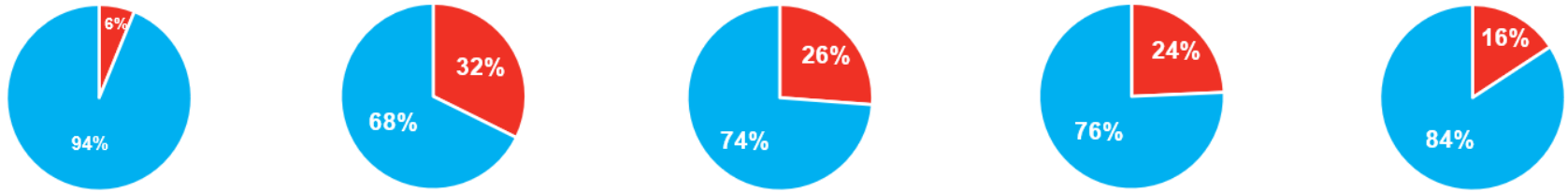
Adjunctive Therapy across Vessel Beds
Operator's Discretion

	Iliac	CFA	SFA	Popliteal	BTK
N (%), lesions	242 (16%)	164 (11%)	744 (49%)	185 (12%)	196 (13%)
Mod-sev Ca†	93%	95%	92%	81%	82%
Lesion length	56.8 ± 41.0 mm	53.6 ± 53.1 mm	127.3 ± 81.6 mm	72.5 ± 49.3 mm	64.8 ± 51.8 mm

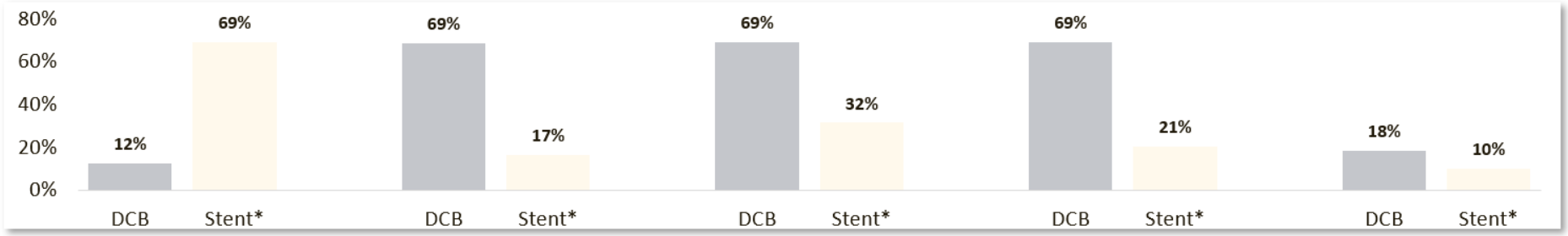
Adjunctive Ca modification

IVL only‡

IVL with atherectomy or specialty balloon



Definitive therapy



†PARC definition. ‡IVL without atherectomy or specialty balloon. *Drug-eluting, bare-metal, or covered stent.

Peripheral IVL Clinical Programs
>1,800 patients enrolled globally

	Disrupt PAD I	Disrupt PAD II	Disrupt BTK	Disrupt PAD III RCT	Disrupt PAD III OS	Disrupt PAD +	Disrupt BTK II
Status	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment completed	Enrollment completed	Ongoing
Study design	Single arm, safety & performance	Single arm, safety & effectiveness	Single arm, pilot	RCT, safety & effectiveness	Single arm, observational study	Single arm, safety & performance	Single arm, safety & performance
Vessel beds	SFA, Pop	SFA, Pop	BTK	SFA, Pop	Iliac, CFA, SFA, Pop, BTK	Iliac, CFA, SFA, Pop, BTK	BTK
Study conduct*	CEC, ACL	CEC, ACL	ACL	CEC, ACL	ACL	CEC, ACL	CEC, ACL
# of patients/sites	35/3	60/8	20/3	306/45	1,373/30	37/8	250/42
Regions	NZ, EU	NZ, EU	NZ, EU	US, NZ, EU	US, NZ, EU	AUS, NZ, US	US, EU

*CEC: Independent clinical events committee; ACL: Angiographic core lab

DISRUPT BTK II Study: IVL Device Usage

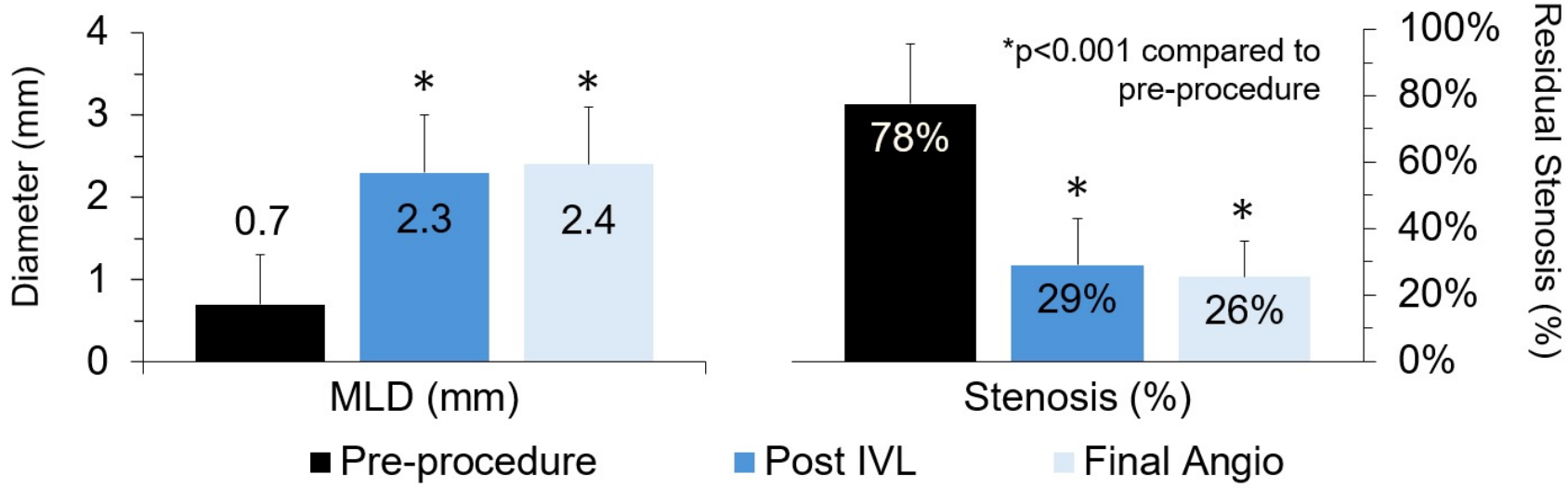
M5+		**26.5% (92/347)**
	3.5 x 60 mm	15.3% (53/347)
	4.0 x 60 mm	7.8% (27/347)
	4.5 x 60 mm	3.5% (12/347)
S4		**73.5% (255/347)**
	2.5 x 40 mm^2	25.1% (87/347)
	3.0 x 40 mm	27.4% (95/347)
	3.5 x 40 mm	10.4% (36/347)
	4.0 x 40 mm	10.7% (37/347)

[1] The Table represents unique devices utilized. [2] 2.5 x 40 mm catheter was used on second target lesion which was also used on a non-target lesion and is not captured in the table

DISRUPT TK II Study

Thirty-day outcomes from the Disrupt PAD BTK II study of the Shockwave Intravascular Lithotripsy System for treatment of calcified below-the-knee peripheral arterial disease

Venita Chandra, MD,[a] Alexandra J. Lansky, MD,[b] Sameh Sayfo, MD,[c] Nicolas W. Shammas, MD, MS,[d] Peter Soukas, MD,[e] James Park, MD,[f] Michael Siah, MD,[f] Anvar Babaev, MD,[g] Ryan Shields, MS,[h] Nick E. J. West, MD,[h] *and* Ehrin Armstrong, MD, FACC,[i] *Palo Alto and Santa Clara, CA; New Haven, CT; Plano and Dallas TX; Davenport, IA; Providence, RI; NY; and Thornton, CO*

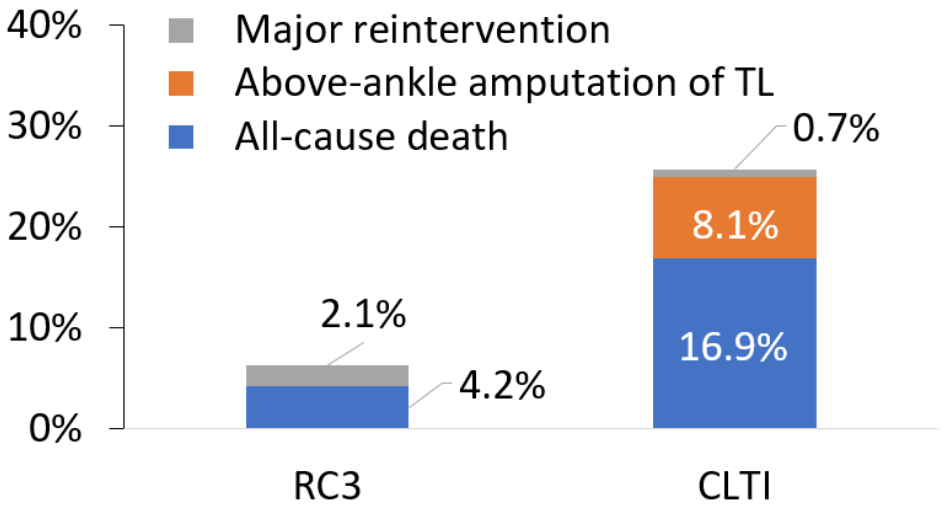


Chandra V, et al. *J Vasc Surg*. 2025;81(3):710-719.

12-Month Outcomes from DISRUPT BTK II

Low Rates of Reintervention, Amputation, and Significant Symptomatic Improvements

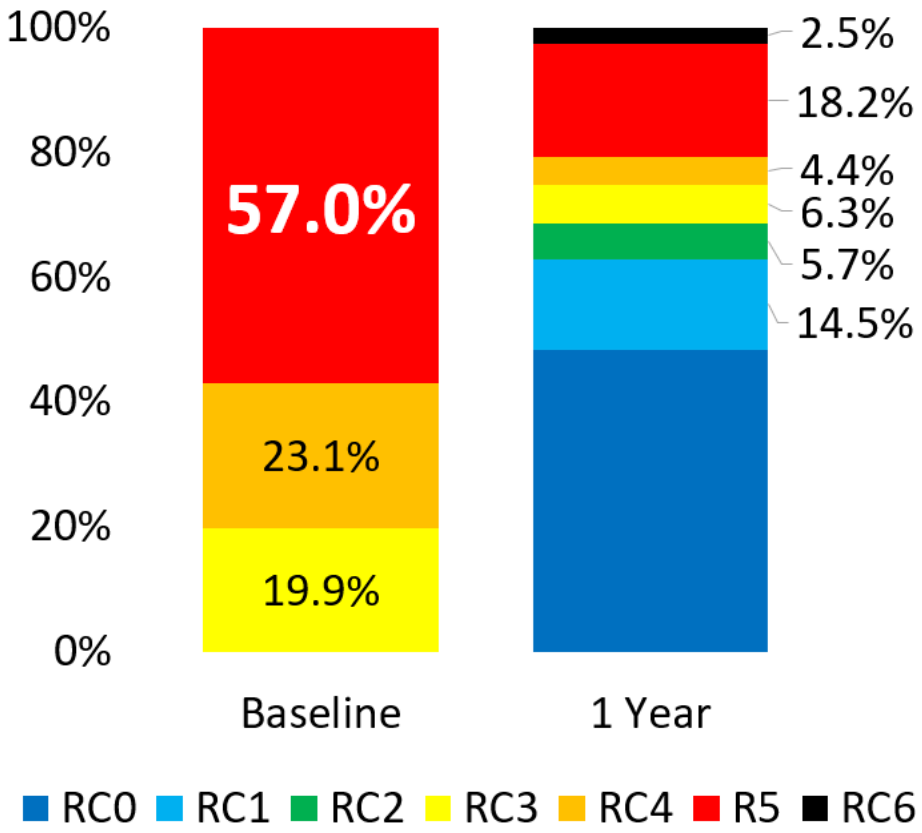
Primary Patency	67.1%
KM Freedom from CD-TLR	84.5%
KM Freedom from Major Amputation	94.8%



Primary Patency defined as the absence of both total occlusion in all of the target lesion flow pathway, as well as any CEC adjudicated CD-TLR

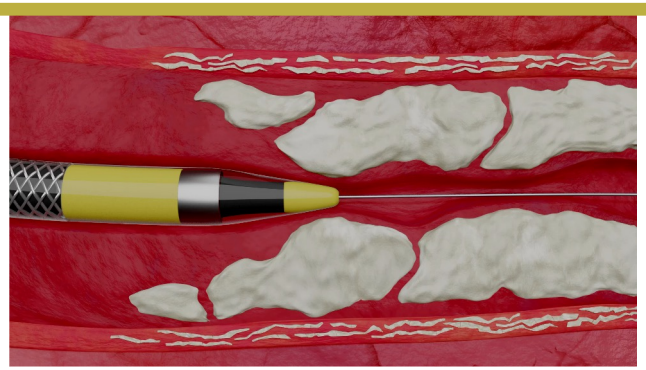
12-Month Outcomes from DISRUPT BTK II

Low Rates of Reintervention, Amputation, and Significant Symptomatic Improvements



Primary Patency defined as the absence of both total occlusion in all of the target lesion flow pathway, as well as any CEC adjudicated CD-TLR

New IVL Catheters for Patient-Specific Treatment

	IVL Action (Animations NOT to Scale)	Treatment Steps
E8 (Balloon-based IVL)		1. Deliver catheter and inflate balloon to low pressure 2. Sonic pressure waves generated from IVL emitters in balloon modify calcium 3. Expand vessel
Javelin (Non-balloon- based IVL)		1. Deliver catheter 2. Sonic pressure waves generated at distally positioned IVL emitter 3. Modify calcium and advance across lesion 4. Post dilatation

E8 Catheter Design

80mm enhanced polymer balloon is durable and provides longer treatment zone

150cm catheter length for difficult-to-reach lesions

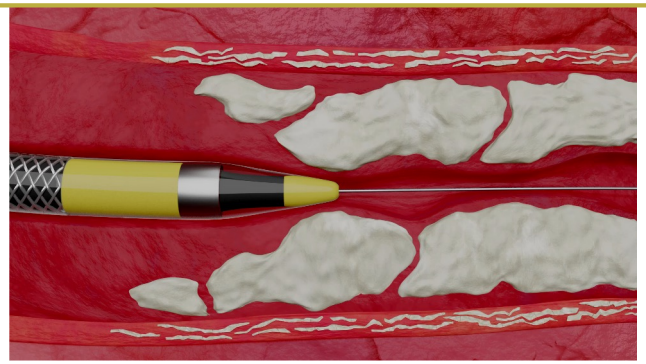
Tip constructed with lower durometer material and smoother entry profile

2Hz pulse rate for faster treatment time

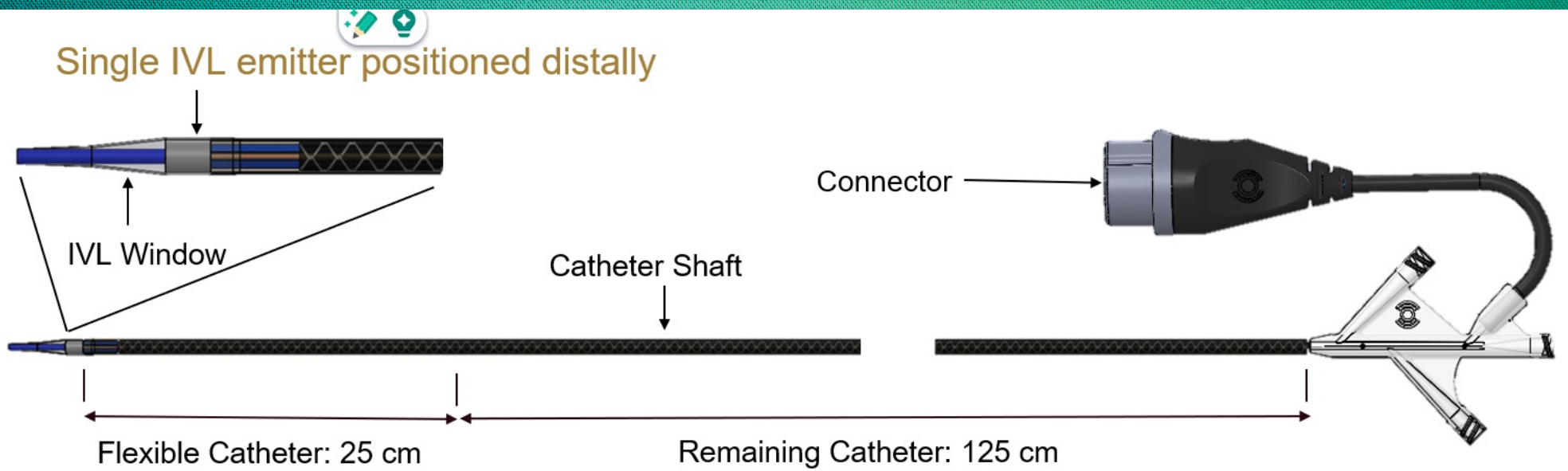
Key Features

- 150 cm / 5F & 6F sheath compatible
- 2.5-6.0mm balloon diameters
- 400 Pulses total (10 cycles at 40 pulses/cycle)
- 45cm hydrophilic coated length (compared to 15cm on S4 and no coating on M5+)
- Compatible with existing Shockwave generators

New IVL Catheters for Patient-Specific Treatment

	IVL Action (Animations NOT to Scale)	Treatment Steps
E8 (Balloon-based IVL)		1. Deliver catheter and inflate balloon to low pressure 2. Sonic pressure waves generated from IVL emitters in balloon modify calcium 3. Expand vessel
Javelin (Non-balloon- based IVL)		1. Deliver catheter 2. Sonic pressure waves generated at distally positioned IVL emitter 3. Modify calcium and advance across lesion 4. Post dilatation

Javelin Peripheral IVL Catheter

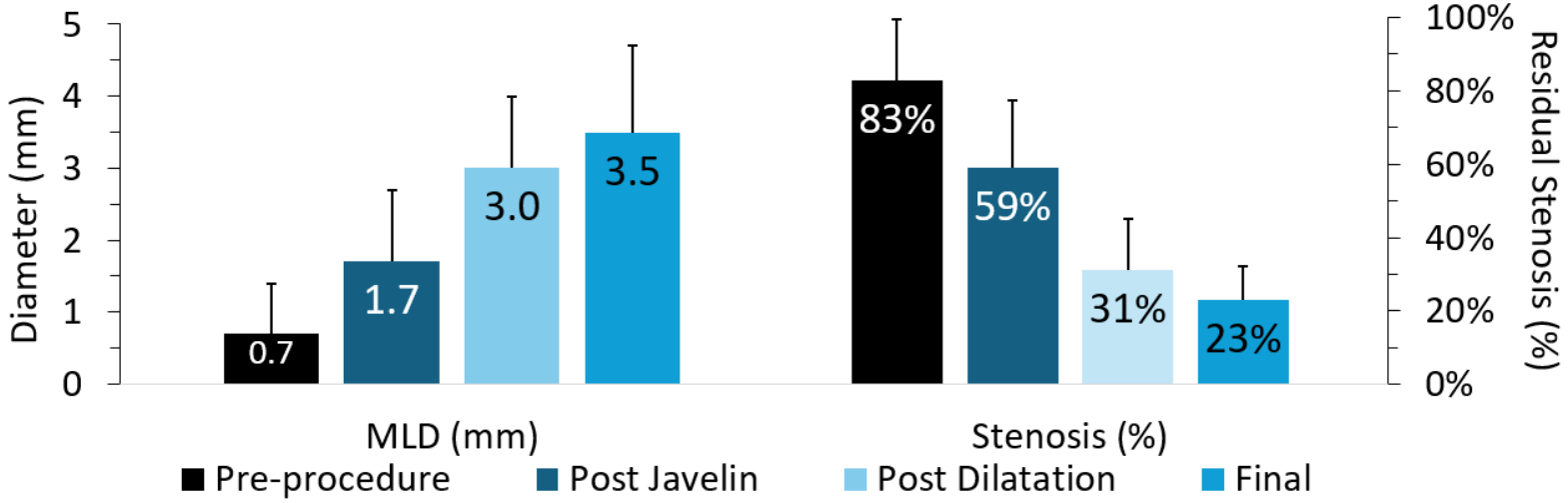


Key Features:

- 150 cm / 5F / 0.014" OTW System
- 1.5 mm Crossing Profile
- 50 cm Hydrophilic Coated
- 120 Pulses total (12 cycles at 10 pulses/cycle)
- Compatible with existing Shockwave generators
- Non-balloon-based catheter

FORWARD PAD IDE and Feasibility Studies

Primary Effectiveness Endpoint	Final RS of ≤50% without flow-limiting dissection	**99.0%** (PG 85%; 95%CI: 94.4%-100%, p<0.0001)
Primary Safety Endpoint	MAE at 30 days	**1.1%** (PG 11.2%; 95%CI: 0.0%-6.0%, p=0.0012)
Secondary Endpoint	Final RS of ≤30% without flow-limiting dissection	**78.6%** (95%CI: 69.1%-86.2%)



Corl, et al. *JACC Cardiovasc Interv.* 2025;18(3):398-399.

12-Month Outcomes from FORWARD PAD Studies

- Low rates of unplanned TL major amputation and cardiovascular death at 1 yr
- Favorable 1-yr primary, primary-assisted, and secondary patency results given high-risk patient population

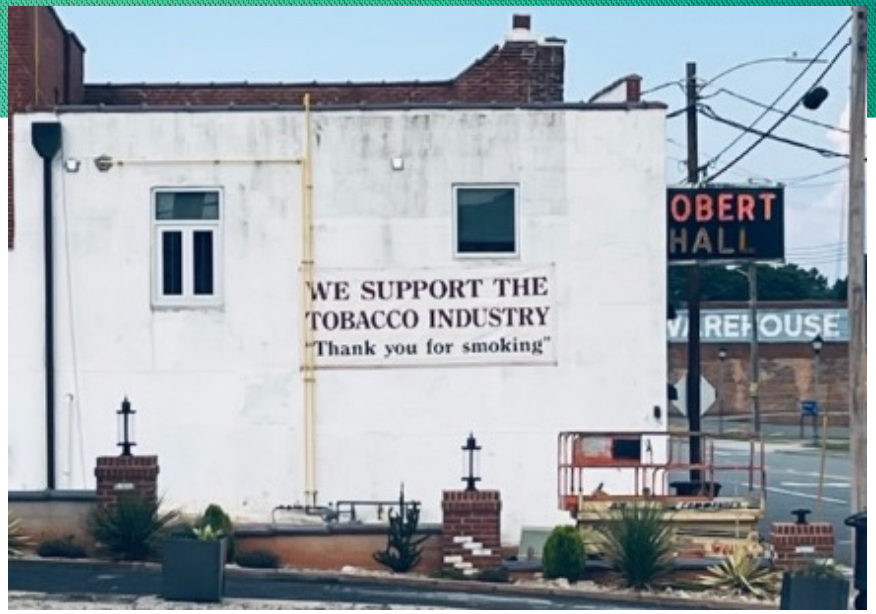
Major Adverse Events	18.6% (19/102)
Cardiovascular death	3.9% (4/102)
Unplanned TL major amputation	1.0% (1/102)
CD-TLR	14.7% (15/102)

ATK	Primary Patency	72.7% (40/55)
	Primary Assisted Patency[1]	74.5% (41/55)
	Secondary Patency[2]	76.4% (42/55)
BTK	Primary Patency	61.5% (24/39)
	Primary Assisted Patency[1]	78.4% (29/37)
	Secondary Patency[2]	88.6% (31/35)

[1]Primary assisted patency defined as freedom from diameter stenosis (>=50 atk, total occlusion in btk) determined by DUS and freedom from CD-TLR performed for 100% stenosis. [2]Secondary patency defined as freedom from diameter stenosis (>=50 atk, total occlusion in btk) determined by DUS regardless of additional intervention. Both definitions based on Stoner et al. *J Vasc Surg*. 2016 Jul;64(1):e1-e21.

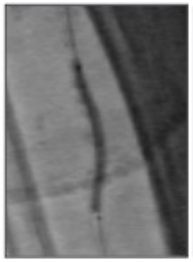
Bringing BTK Evidence to Life:
Real-World Case Insights

Gabriela Velazquez, MD, FACS, DFSVS, RPVI
Interim Chair, Associate Professor
Director Vascular Surgery Training Programs
Department of Vascular and Endovascular Surgery
Wake Forest University School of Medicine
Winston-Salem, NC


WE SUPPORT THE
TOBACCO INDUSTRY
"Thank you for smoking"
OBERT
HALL

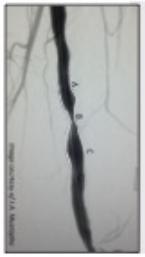
Bringing BTK Evidence to Life: Real-World Case Insights

Technologies We Have Used Historically in Calcified Lesions



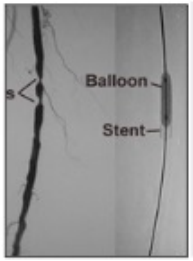
PTA and Specialty Balloons

- PTA is the **standard of care** for BTK, due to simplicity and **ability for retreatment**[1]
- PTA can cause **significant complications and suboptimal outcomes**[2]
- Limited data on MOA and effectiveness of specialty balloons



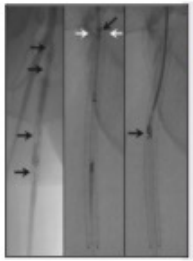
DCB

- **No patency or amputation benefit** vs. POBA in 5 RCTs that mostly excluded calcium[3]
- Drug uptake limited by deep calcium[3]



BMS and DES

- Benefit with DES in **short and minimally calcified lesions**; long stents have not shown patency benefit[4]
- Stenting limits future treatment options and is typically reserved for bail-out after complications[4]



Atherectomy

- Reduces but does not eliminate serious complications[5,6]
- Does not impact **deep calcium**
- Considered improvement vs. PTA for acute outcomes
- Not global standard of care due to learning curve and minimal wound healing evidence in CLI patients[7]

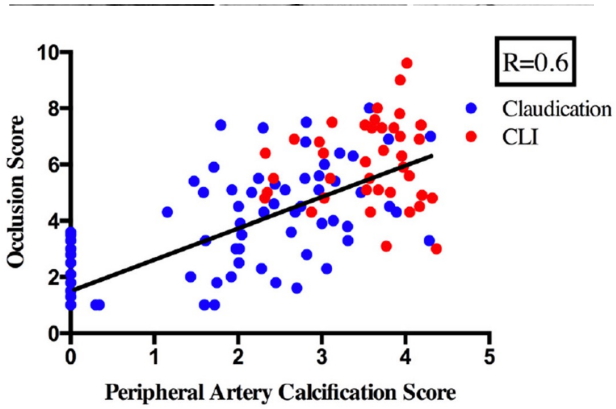
DRS

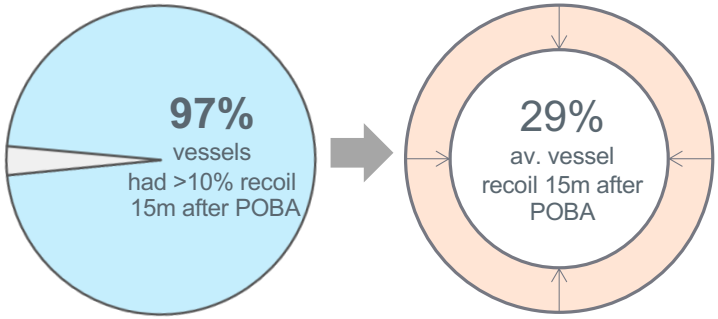
- Promising initial data to support drug-eluting + scaffold technology
- Data limitations = **short lesions & non-calcified lesions**
- Appropriate lesion prep prior to implantation essential

1. Rocha-Singh et al., Peripheral arterial calcification: prevalence, mechanism, detection, and clinical implications, Catheter Cardiovasc Interv, 2014
2. Mustapha et al., Percutaneous Transluminal Angioplasty in Patients With Infrapopliteal Arterial Disease, Circ Cardiovasc Interv 2016
3. Cassese et al., Drug-Coated Balloons for Revascularization of Infrapopliteal Arteries, JACC Cardiovasc Interv 2016
4. Fehing AJ, Krahn M, Nelson L, et al. Preventing leg amputations in critical limb ischemia with below-the-knee drug-eluting stents: the PARADISE (Preventing Amputations Using Drug-Eluting Stents) trial. J Am Coll Cardiol. 2010;55:1580-1589
5. Baumann et al., The Importance of Patency in Patients with Critical Limb Ischemia Undergoing Endovascular Revascularization for Infrapopliteal Arterial Disease, Front Cardiovasc Med 2014
6. Abdullah et al., Percutaneous angioplasty versus atherectomy for treatment of symptomatic infra-popliteal arterial disease, Cardiovasc Revasc Med 2017
7. Azar et al., Atherectomy-Associated Complications in the Southern California Vascular Outcomes Improvement Collaborative, Ann Vasc Surg 2017

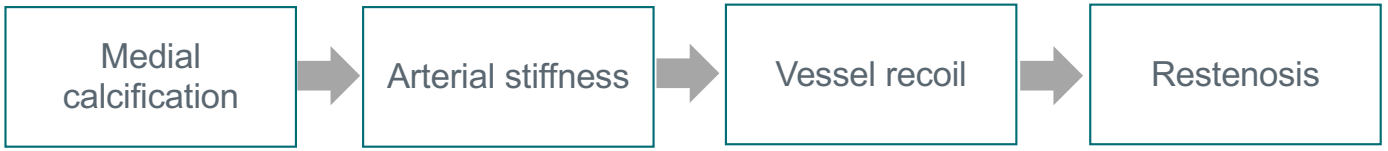
Challenges Associated with Tibial Angioplasty

Significant elastic recoil following angioplasty due to vascular calcification





Medial calcification produces vessel recoil and restenosis



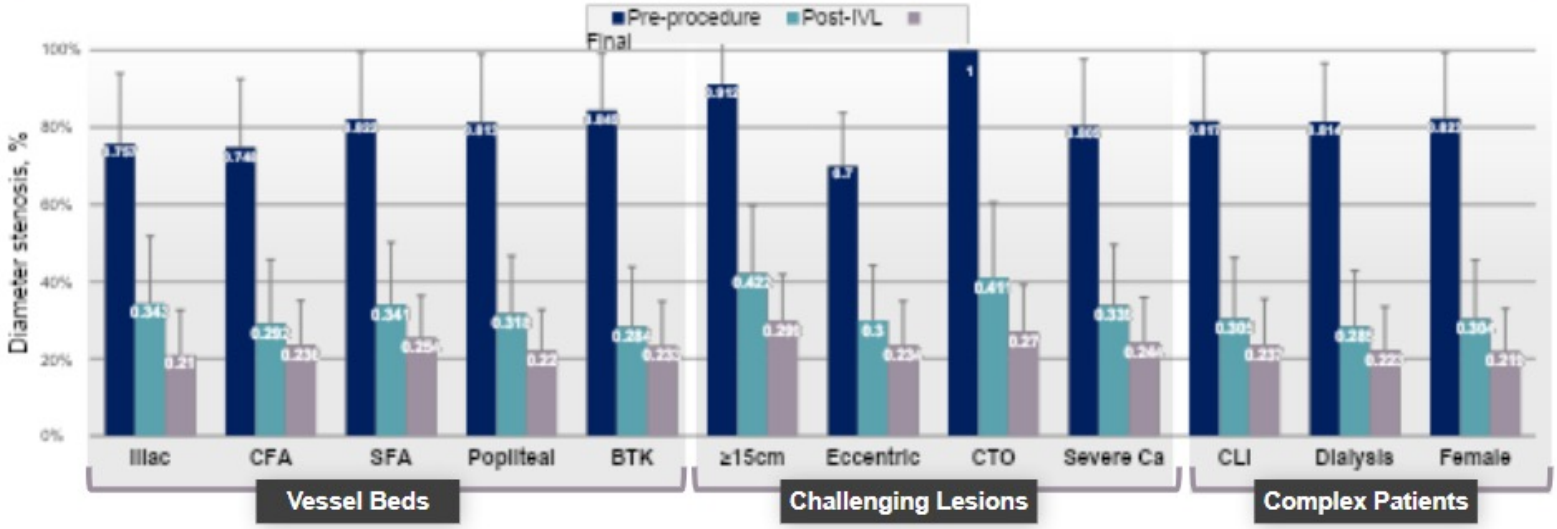
Zettervall, et al. Association of arterial calcification with CLI in patients with PAD. *J Vasc Surg.* 2017.

Predictable Outcomes in Challenging Situations

DISRUPT PAD III OS

Predictably consistent results across vessel beds, challenging lesions, and complex patients

Majority of stenosis reduction from IVL treatment



Armstrong E. Late Breaking Clinical Trial and Shockwave Symposium, VIVA 2022. Data on file at Shockwave Medical.

Bringing BTK Evidence to Life: Real-World Case Insights

Clinical Insights in a Challenging Patient Cohort

In a challenging patient cohort, IVL was shown to be a safe and effective treatment of challenging calcific lesions BTK with minimal need for provisional stenting

Confirmed Safety	Confirmed Effectiveness	Minimal Provisional Stenting
		
1.9% Post-IVL | **1.0%** Final	**29%** Post-IVL | **26%** Final	**4.9%** Total | **2.3%*** Provisional
Total Serious Angiographic Complications	Avg. Residual Stenosis	Stent/Tack Implant

*Remaining Stent/Tack implants were part of physicians' standard algorithm

Holden A, CIRSE Late Breaking Clinical Trial 2024

Conclusions

DISRUPT BTK II Study represents complex patients with challenging lesions below-the-knee
- **Patients with wounds at baseline:** 46%
- **CLTI patients:** 80%
- **Diabetes Mellitus:** 70%
- **Moderate-to-Severely calcified lesions:** 85%

IVL was confirmed to be a safe treatment option in a challenging patient and lesion cohort
- **Angiographic complication rate:** 1.9% Post-IVL and 1.0% at Final

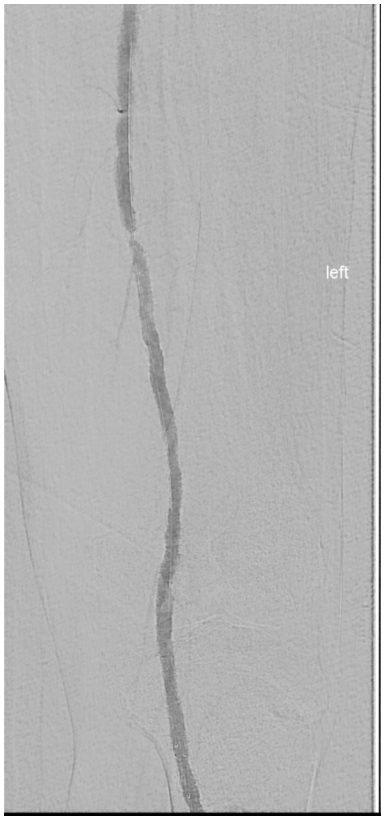
IVL was confirmed to be effective at reducing lesion stenosis with minimal additional treatment therapy
- **Average residual stenosis:** 29% Post-IVL and 26% at Final
- **No pre-dilatation:** 65%
- **No post-dilatation:** 65%
- **Stents/Tack implant:** 4.9%, **Provisional Stent/Tack implant:** 2.3%

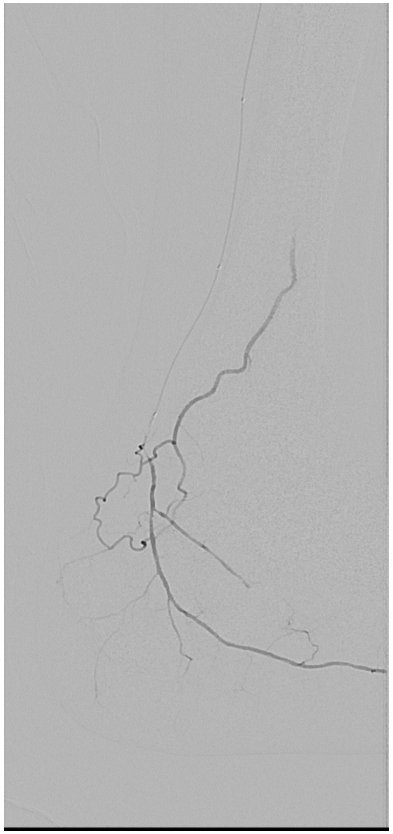
Future BTK II data to include 30-day, 6-month, 1-Year, and 2-Year follow-up

In summary, in a challenging patient cohort, IVL was shown to be a safe and effective treatment of challenging calcific lesions BTK with minimal need for provisional stenting

Holden A, CIRSE Late Breaking Clinical Trial 2024

Bringing BTK Evidence to Life: Real-World Case Insights





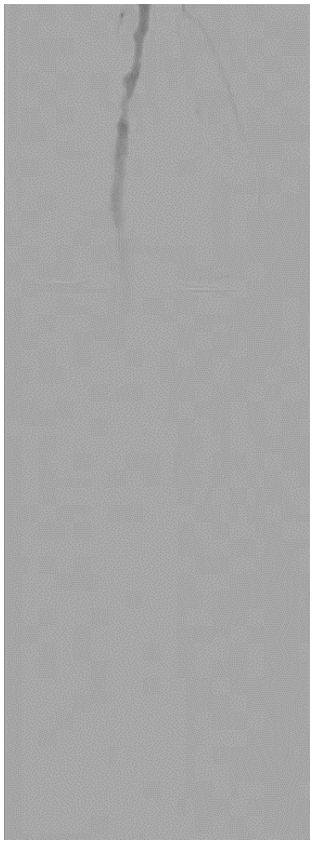
- 82 yo male
- ESRD, DM, HTN, CAD, COPD
- 2nd toe ulcer
- Single vessel peroneal runoff
- Reconstitution of lateral plantar artery

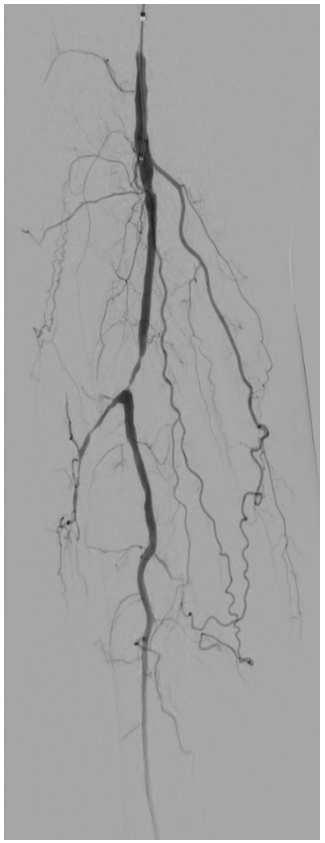
- 6 followed by 7mm Shockwave IVL
- Followed by 7mm DCB

- Armada XT to help cross lesion
- Nanocross tapered balloon
- Serration angioplasty 3mm

Bringing BTK Evidence to Life: Real-World Case Insights

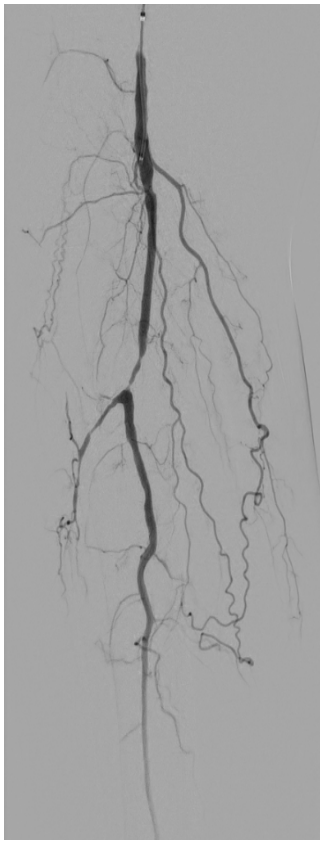
- 72 yo male
- DM, HTN, HLD
- 6 mo right great toe wound
- Failed wound care





Bringing BTK Evidence to Life: Real-World Case Insights

- Once through and through AT access proceeded with 2-2.5 nanocross predilation
- Followed by 3 and 3.5 Serranator in AT and pop
- 4mm DCB in distal popliteal artery



Results of Balloon Angioplasty (PTA) for BTK

PTA has demonstrated[1]

- \+ High rate of clinical improvement
- – Low short-term patency
- – High reintervention rate

PTA 3-month CLI outcomes assessed by angiography[1]

(N=62 limbs, 183mm mean BTK lesion length)

- 31% patency
- 31% restenosis >50%
- 38% re-occlusion rate

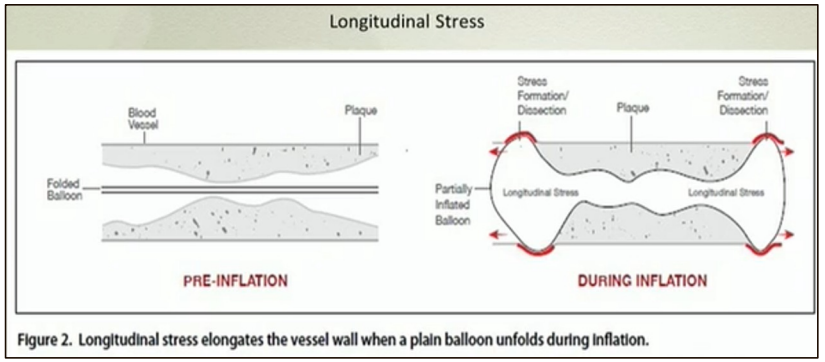
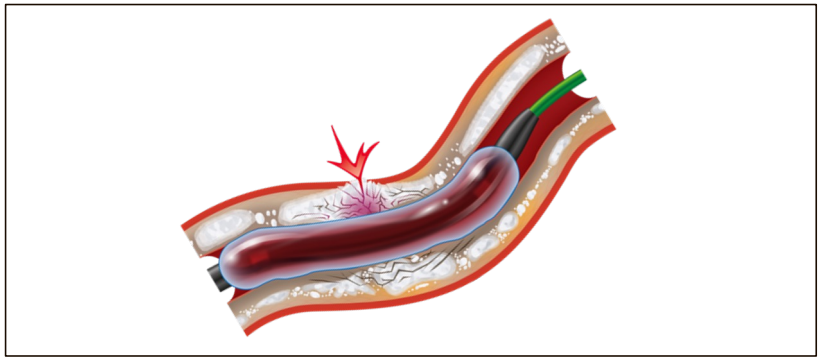


Figure 2. Longitudinal stress elongates the vessel wall when a plain balloon unfolds during inflation.



1 Schmidt A. *Catheter Cardiovasc Intervent.* 2010;76:1047-1054.

PAD III OS BTK Cohort:
IVL Treatment of Calcified Infrapopliteal Arteries

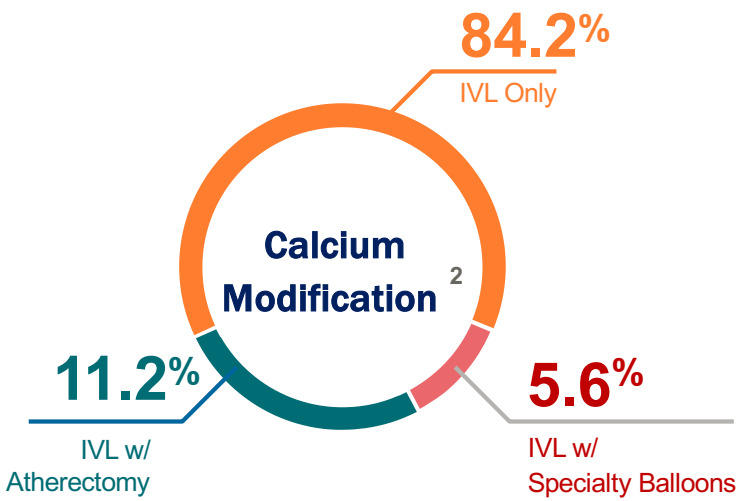
Assessing real-world procedural outcomes of Shockwave IVL treatment of calcified BTK lesions[1]

196
BTK Lesions Treated with IVL[3]

70%
CLI Patients

35%
Chronic Total Occlusions

- The PAD III OS BTK Analysis **represents the use of the Shockwave IVL** catheters in heavily calcified BTK lesions
- There is no per protocol treatment algorithm for calcium modification or definitive therapy; it is at the **operator's discretion**
- IVL was the stand-alone calcium modification tool in 84.2% of subjects treated
- DCBs and stents were used as definitive therapy **in 26% of cases post calcium modification**
- Angiographic data were **core-lab adjudicated**

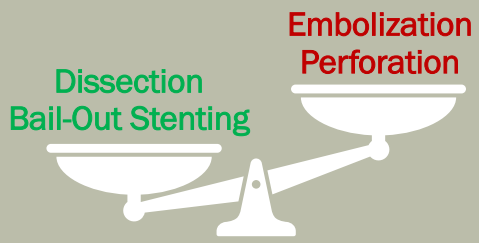


1 Armstrong E. VIVA Late Breaking Clinical Trial 2022 | 3 Adams, et al. *JEVT*. 2020;27(3):473-480. Armstrong E. VIVA IVL Symposium 2022. 2 Calcium Modification may also include pre- or post-dilatation with PTA
3 Final data for n=152 (not all 196 lesions); Data on file at Shockwave Medical

Atherectomy in BTK Revascularization

Atherectomy may reduce, but does not eliminate, acute complications and failures

Atherectomy tends to reduce bail-out stent use but may increase embolic risk.[1,2]



Atherectomy has no short- or long-term advantages to POBA in CLI patients according to meta-analysis.[3]

"PTA and Atherectomy were associated with similar outcomes in terms of dissection, residual stenosis, mortality, and amputation."

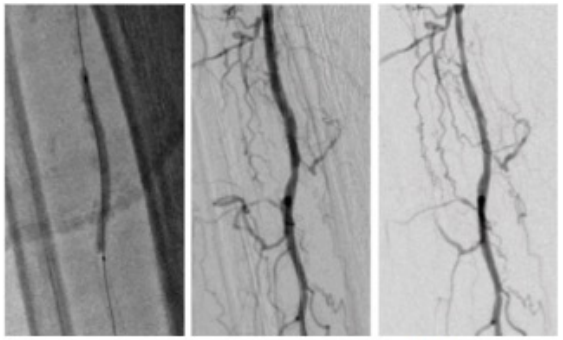
- Severe angiographic complications occur in ~10% CLI patients in large cohort registries[1,2]
- Mustapha, et al. (n=553 lesions)
  - 9.3% severe angiographic complications in CLI patients
    - 4.6% bail-out stenting
- Azar, et al. (n=729 procedures)
  - 12% severe angiographic complications in CLI patients
    - 7% dissection rate
    - 2% perforation rate
    - 3% embolization

1 Azar, et al. Atherectomy-Associated Complications in the Southern California Vascular Outcomes Improvement Collaborative. *Ann Vasc Surg.* 2017. 2 Mustapha, et al. LIBERTY 360 Data, LINC 2018.
3 Abdullah, et al. Percutaneous angioplasty versus atherectomy for treatment of symptomatic infra-popliteal arterial disease. *Cardio Revasc Med.* 2017.

BTK Intervention is Complicated by Calcium

Possible complications for BTK therapy

- Dissections leading to bail-out stenting, increasing costs and limiting future options[1]
- Poor vessel expansion limiting acute gain[2]
- Acute recoil limiting acute gain and reducing patency[3]



POBA | Initial Angiogram | Angiogram after 15m

15 min Results 15 min after POBA

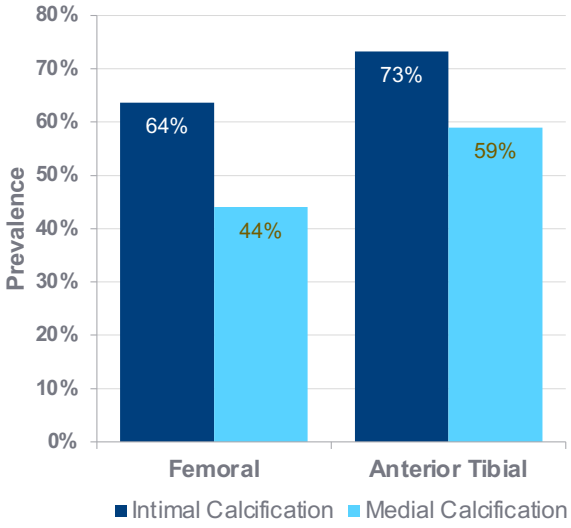
97% of vessels recoiled

29% average vessel recoil

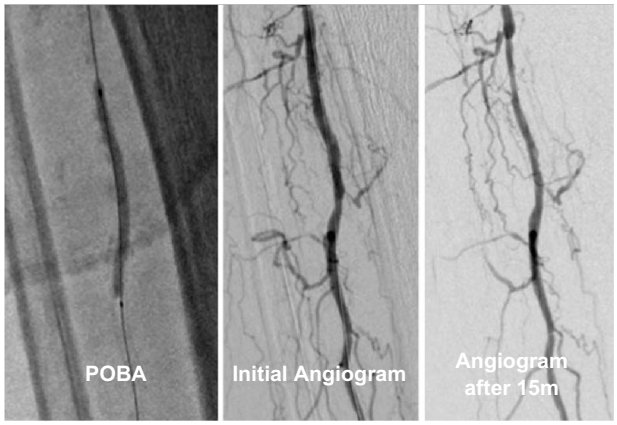
1 Fitzgerald et al., Contribution of localized calcium deposits to dissection after angioplasty. An observational study using intravascular ultrasound, *Circulation* 1992
2 Rocha-Singh et al., Peripheral arterial calcification: prevalence, mechanism, detection, and clinical implications, *Catheter Cardiovasc Interv*, 2014
3 Baumann et al., Early recoil after balloon angioplasty of tibial artery obstructions in patients with critical limb ischemia, *J Endovasc Ther* 2014

Medial Calcium Drives Vessel Recoil

Both intimal and medial calcium are more prevalent in BTK arteries[1]



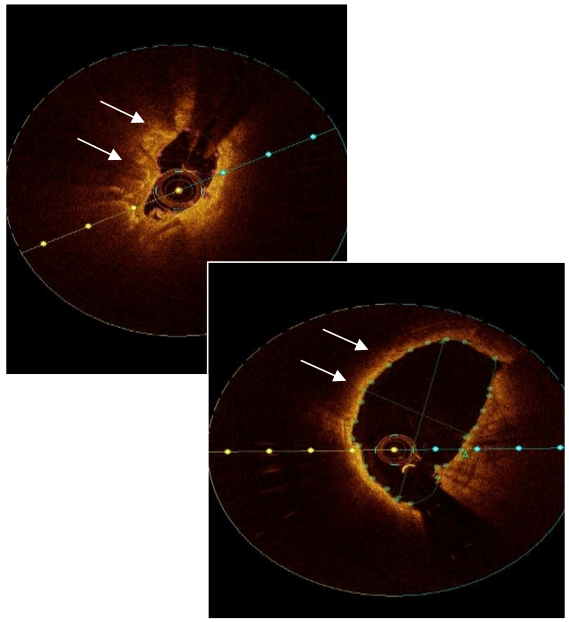
Medial calcification produces vessel recoil, which drives poor outcomes[2,3,4]



Recoil 15m after PTA

~30%

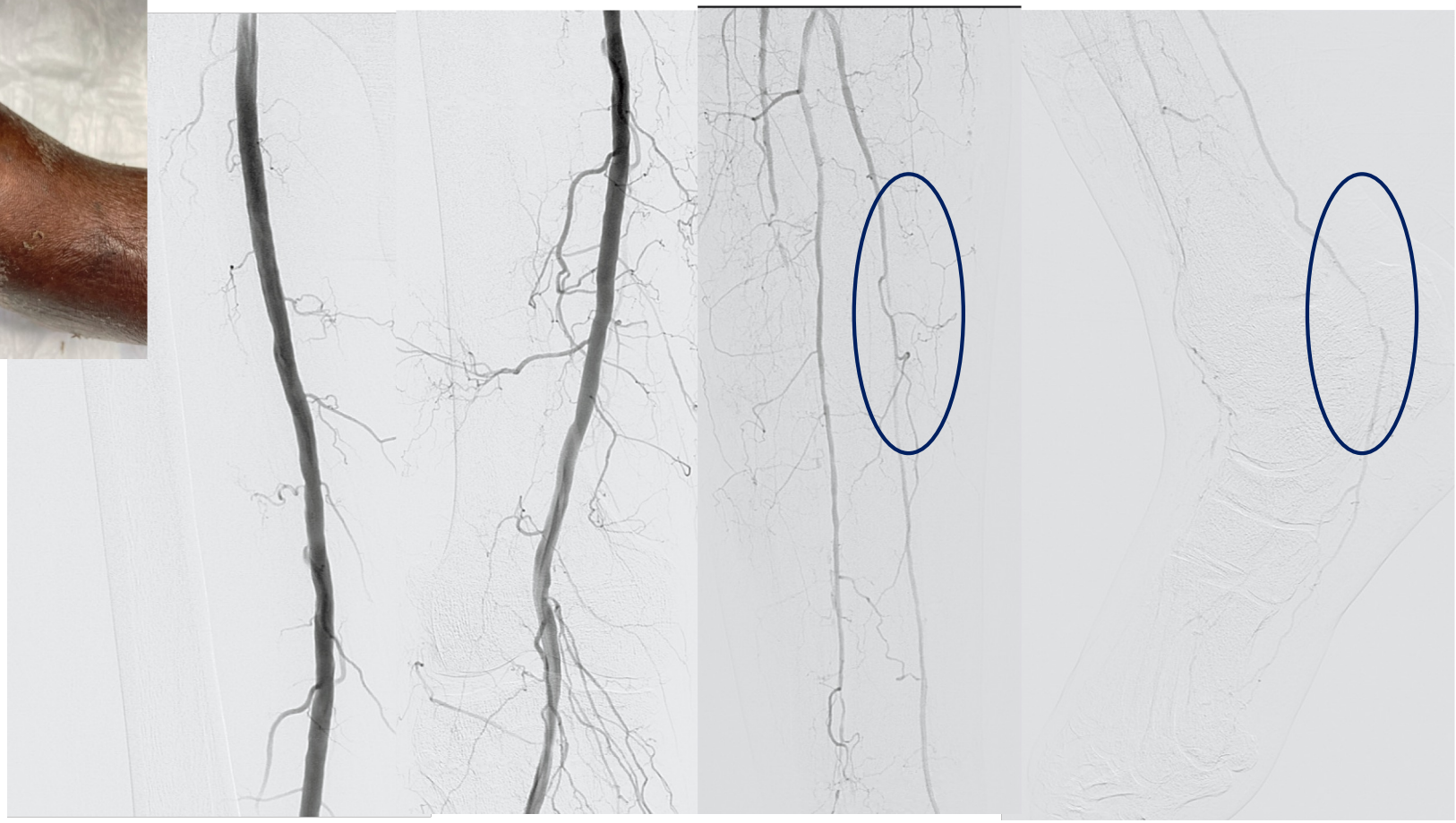
Intravascular lithotripsy impacts medial calcium[5]



1 Soor, et al. Peripheral vascular disease: who gets it and why? *Pathology.* 2008. 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. 5 Holden A, DISRUPT PAD II IVUS Substudy, Presented at LINC 2018.

ESRD + Tibial Calcification

- 63y Male, ESRD, with 3 months 1st toe wound not healing. Known TBI 0.29, calcified vessels, toe pressure 36.



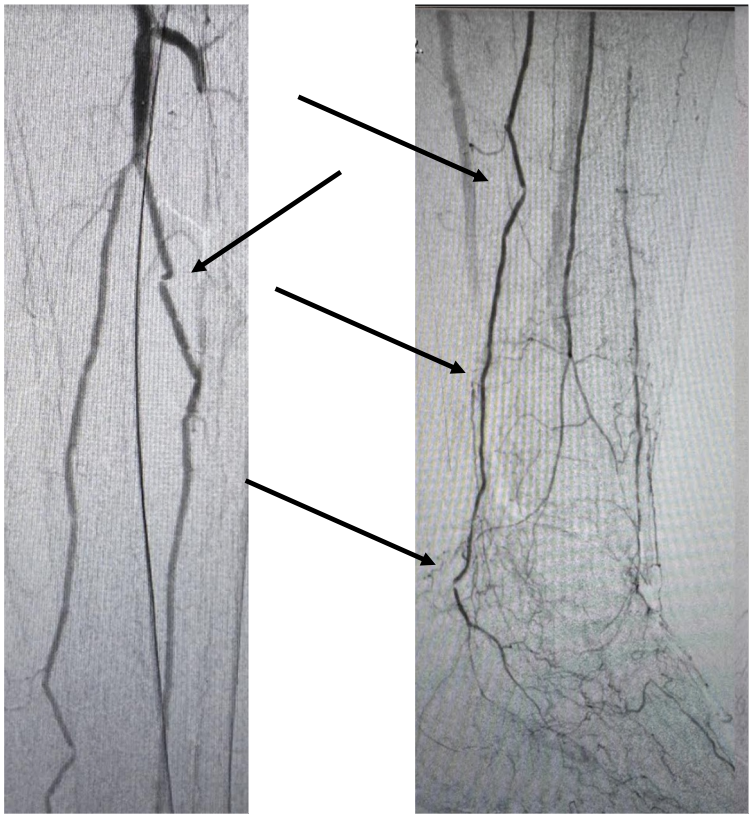
ESRD = end-stage renal disease.

Tibial Angioplasty 2.5mm Shockwave Followed by 2.5mm and 3mm POBA

POBA = plain-old balloon angioplasty.

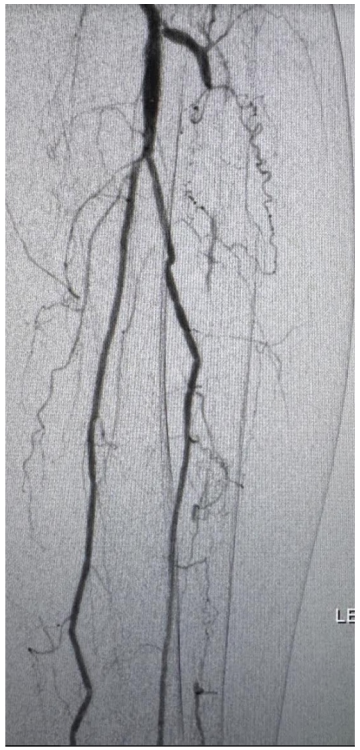
Bringing BTK Evidence to Life: Real-World Case Insights

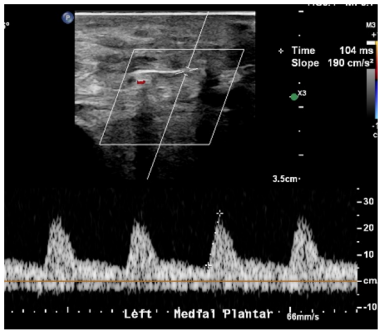
- 53y Male ESRD, DM with non-healing L foot wounds and prior laser atherectomy, DCB popliteal, PTA TPT and PT
- ABI non-compressible/TBI unobtainable
- Monophasic waveforms throughout with PAT Class IV

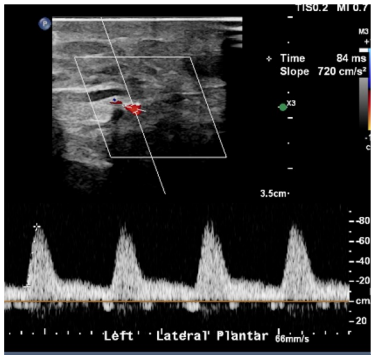


ESRD = end-stage renal disease; DCB = drug-coated balloon; PTA = percutaneous transluminal angioplasty; ABI = ankle-brachial index; TBI = toe-brachial index.

Heavily Calcified Tibial Disease







- 3mm E8 entire PT and prox Pe

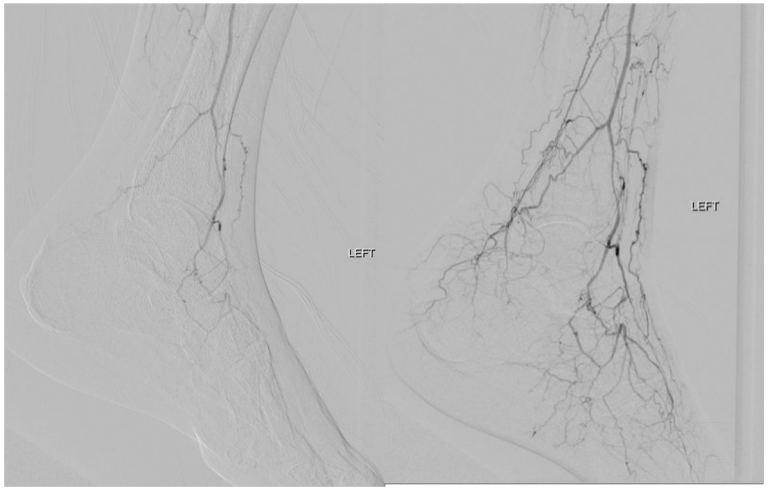
Heavily Calcified Tibial Disease

- 96y Male with CHF, contralateral AKA presents with superficial wound of the L foot
- TBI .2/PAT Class IV
- Monophasic waveform in DP and peroneal only

Heavily Calcified Tibial Disease

3x80 E8-peroneal

6x80
E8-popliteal

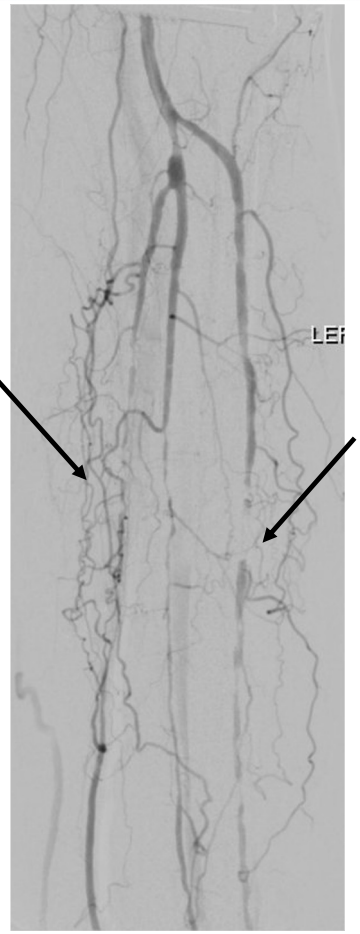


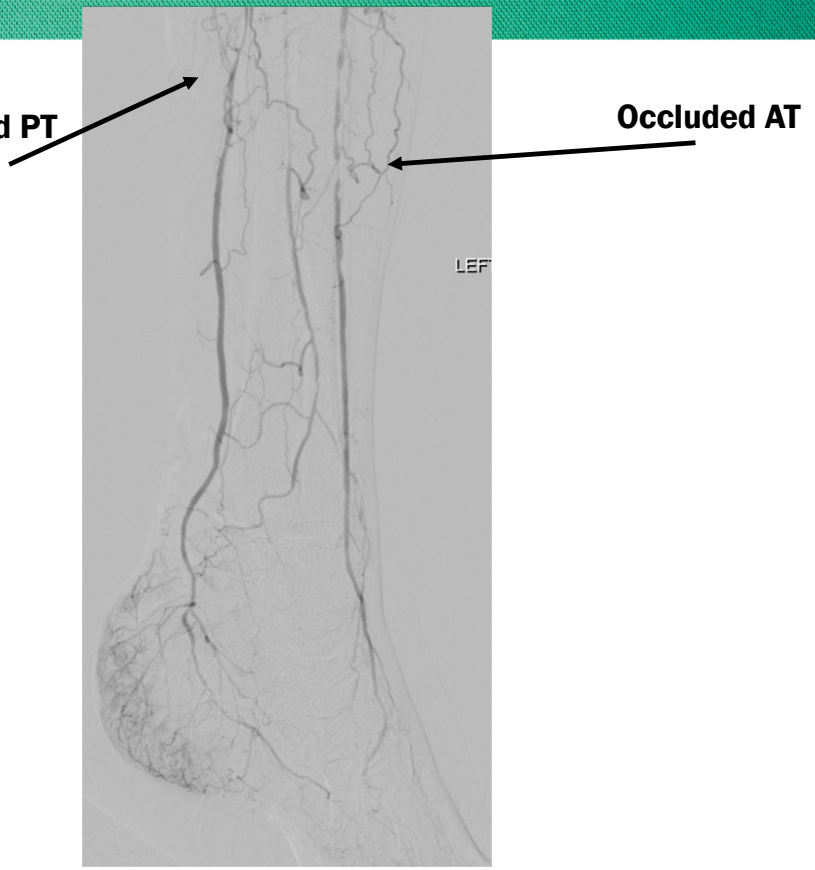
Post Intervention — Foot

Heavily Calcified Tibial Disease

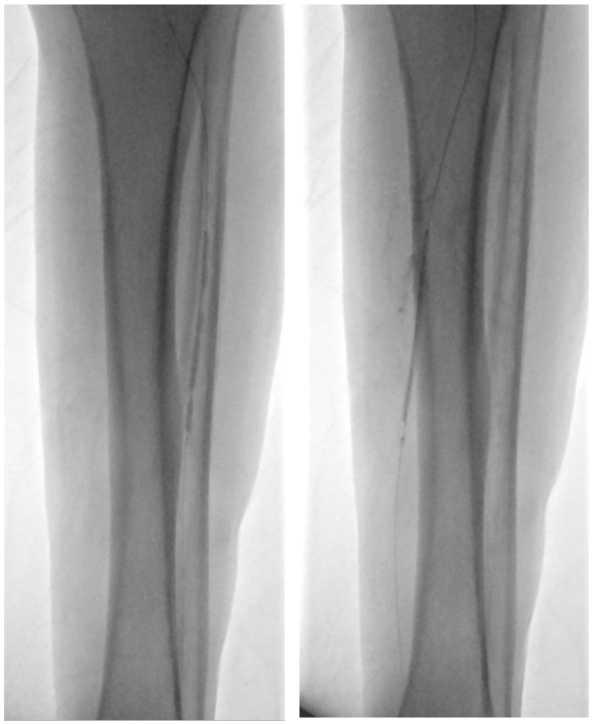
- 68y Male s/p CVA, EF 20%, DM presents with 3rd toe gangrene
- TBI unobtainable/PAT Class III/IV
- Palpable popliteal, Monophasic waveform in DP and PT

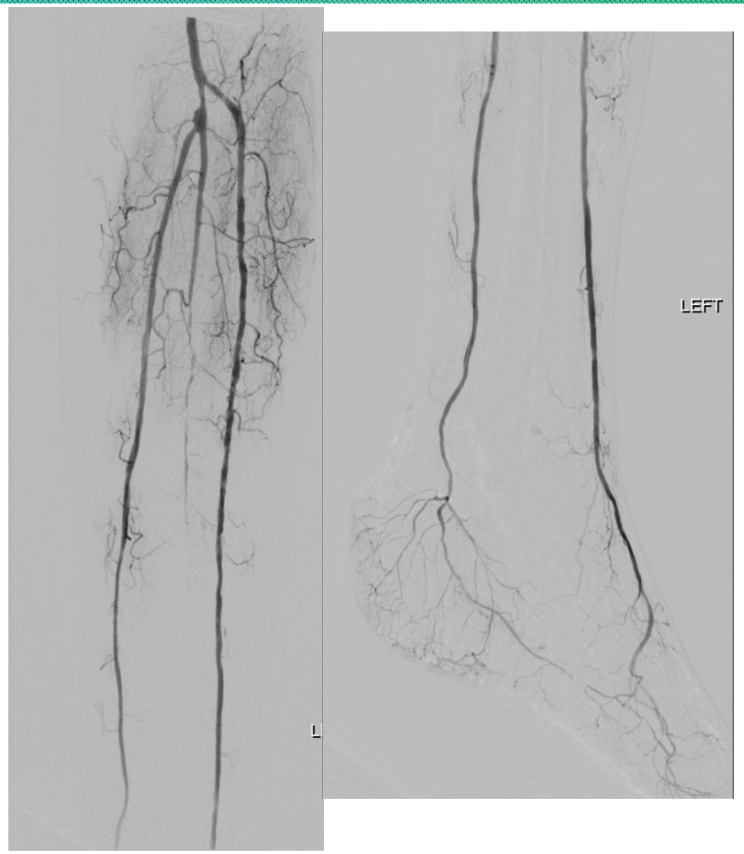
Heavily Calcified Tibial Disease



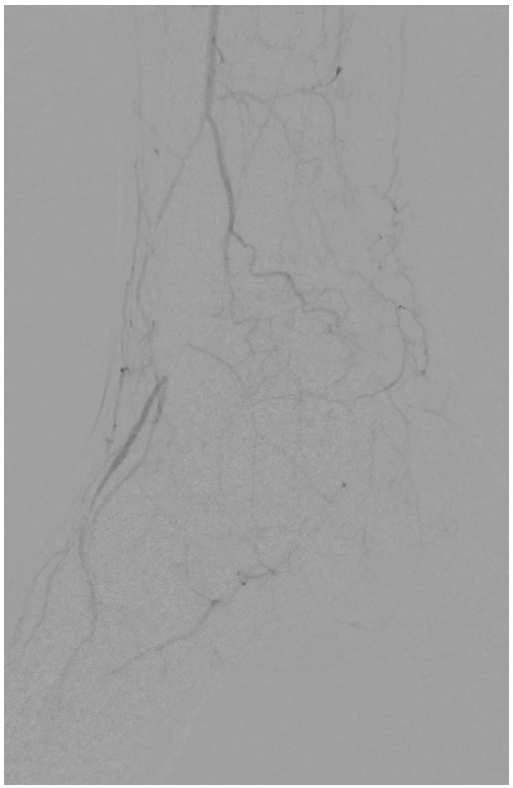


Heavily Calcified Tibial Disease: 3mm E8 AT and PT





Bringing BTK Evidence to Life: Real World Case Insights



Pedal Access:

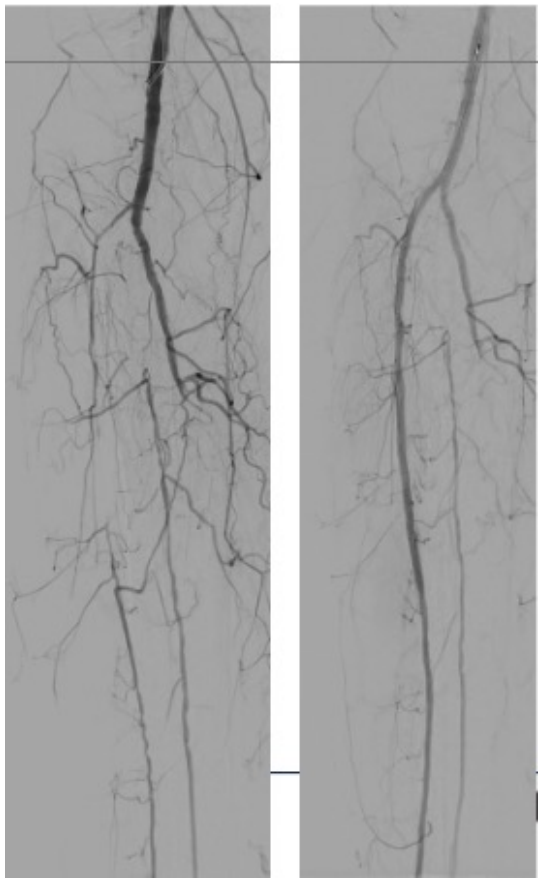
BTK CTO Recanalization

- Where to access when recanalizing a tibial?
  - 2-4cm distal to reconstitution
    - Running room to engage occlusion
    - Decrease likelihood of injuring the collateralization
  - Preserve distal bypass target
  - .018 or .014 glide advantage/command ES immediately

Bringing BTK Evidence to Life: Real World Case Insights

BTK Occlusive Lesions:
Access and Sheaths

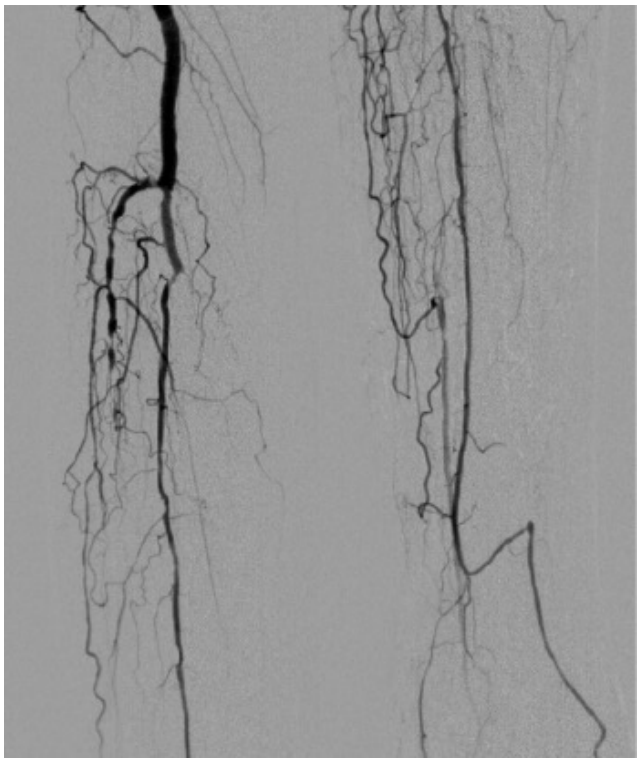
- Sheath support at the below-knee pop
  - Antegrade CFA/SFA access
    - 25cm or 45cm sheath
  - Up and over
    - 6Fr or 7Fr 90cm
    - 4Fr from within the shorter sheath



Bringing BTK Evidence to Life: Real World Case Insights

BTK Occlusive Lesions: Crossing Techniques

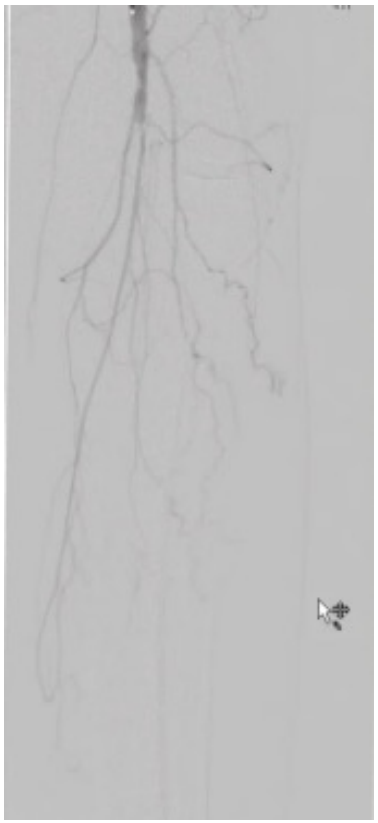
- Start: 018 command wire and 018 angled CXI
- Attempt to stay true lumen with tibial
  - Calcifications
  - Once engaged, should travel easily
  - Islands of patent vessel- check true lumen
- Will often transition to .014 wire mid/distal
- Create tri-axial system to improve pushability



Bringing BTK Evidence to Life: Real World Case Insights

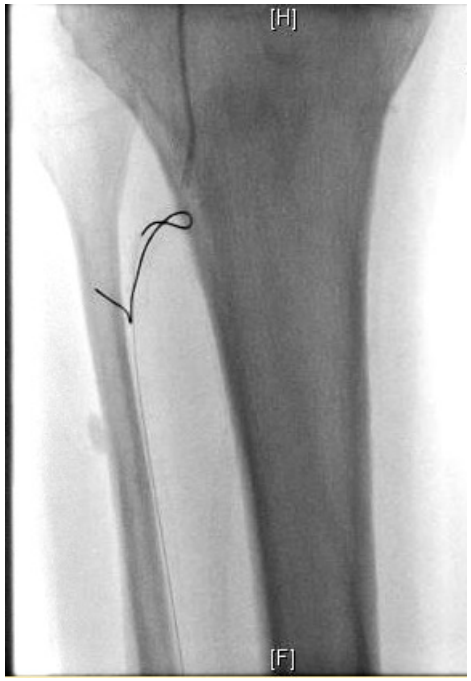
BTK Occlusive Lesions:
Crossing Techniques, What to Engage Antegrade?

- If origin of occluded vessel is patent, will attempt antegrade
- Occluded BK or origins of vessels
  - 7Fr sheath
  - Will try to cross into a re-constituted peroneal and PT antegrade
- If origin of AT occluded, will access retrograde pedal
- Always try to remain true lumen
- Be mindful of origins of tibials and bifurcations
- Assess what collaterals are feeding the reconstitution of the foot and preserve, especially if only 1 vessel reconstitutes on the foot



Bringing BTK Evidence to Life: Real World Case Insights

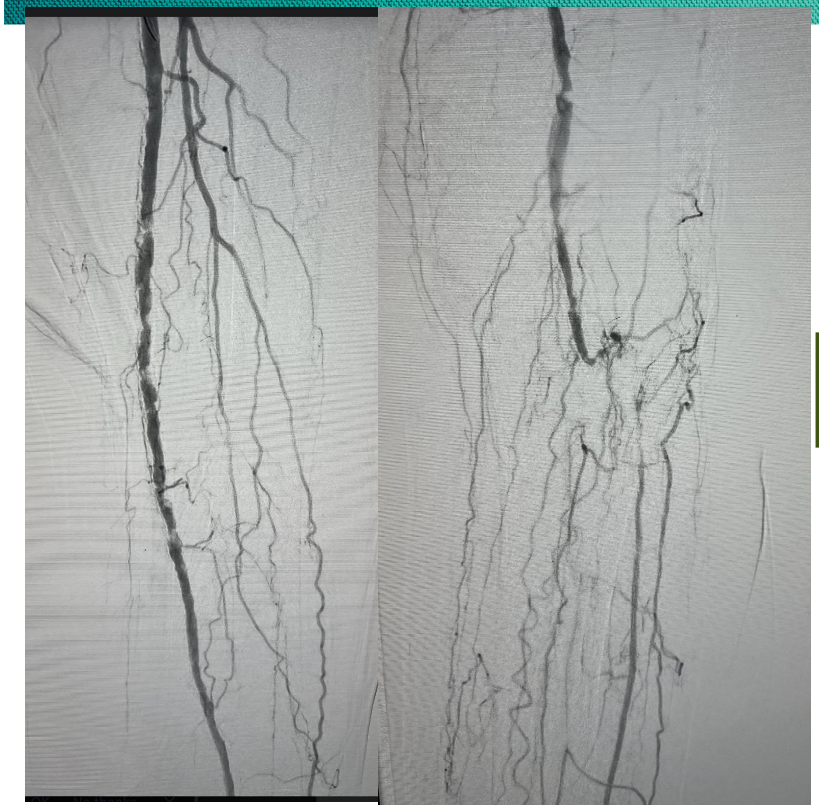
Ultrasound-guided DP puncture

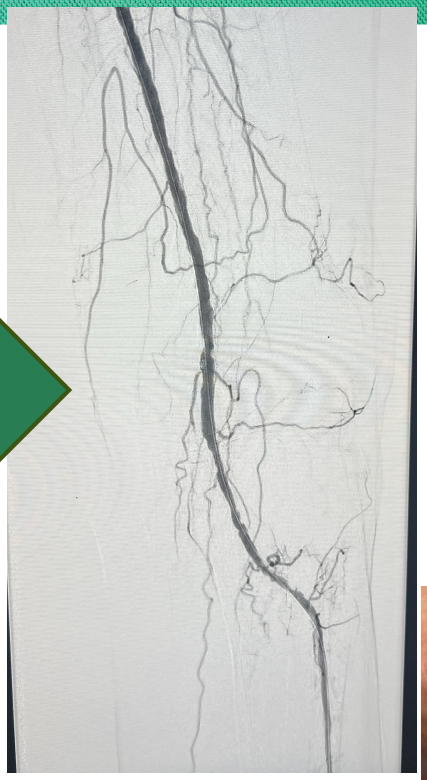


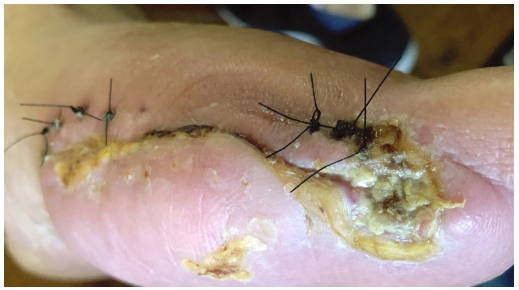
Advanced wire captured in catheter allowing through and through access and angioplasty of occlusion

60y Male with R BKA + CTLI

- Primary caregiver for his mother walks with a prosthesis without pain until 3 months ago. Developed wound metatarsal head, needed Ray amputation.
  - ABI 0.67 on the left , diminished forefoot and toe waveforms
- PMHx
  - Severe cardiomyopathy + heart failure + AICD+ Afib with RVR + prior CABG
  - COPD (quit smoking 7 yrs ago)
- PSHx- Right BKA 5 yrs ago
  - CABG with GSV 5 yrs ago
- ASA, statin, apixiban





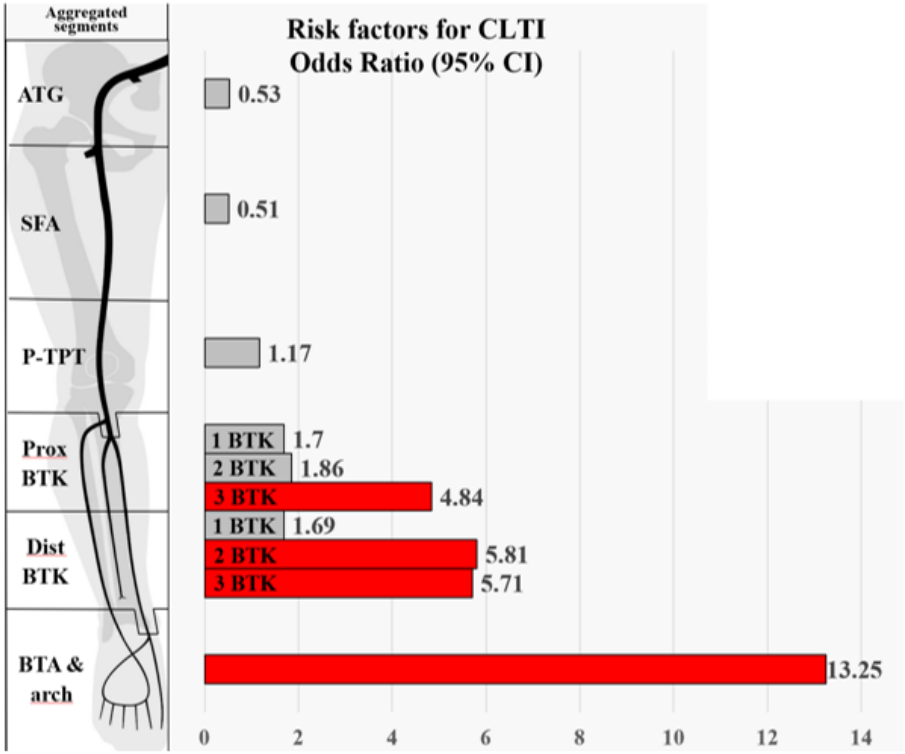


Bring Evidence and Technique: BTA Cases that Inform Practice

Michael Siah, MD
Vascular Surgeon, Director of Limb Salvage,
Assistant Professor of Surgery
UT Southwestern Medical Center
Dallas, TX

Below the Ankle Importance

- Proximal arterial disease less correlated with CLTI development
- BTA disease and arch disease have a significant role in CLTI



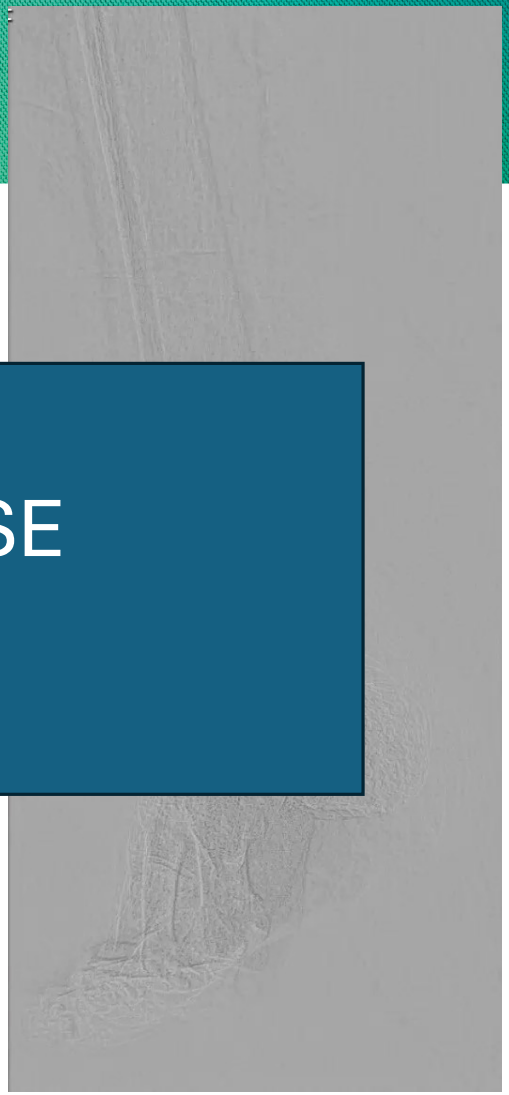
Slide courtesy of Roberto Ferraressi

Pedal Artery Interventions? Why?

- Perfusion is essential component of limb salvage

SHOULD WE PERFORM THESE INTERVENTIONS?

- No RCT data
- No level 1 recommendations
- Potential risks may theoretically increase risk of limb loss

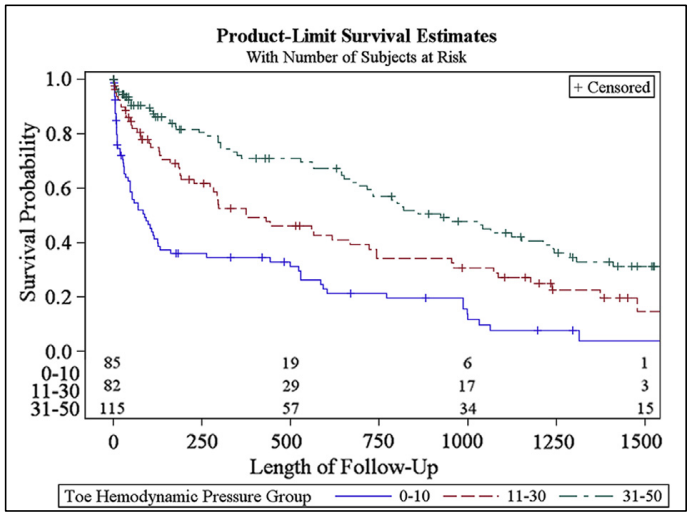


Patients with Very Low Foot Perfusion Tend to Lose their Limb

AFS lower with decreased toe pressure

Toe pressure <10mm Hg:
1-year AFS 35%

31% underwent intervention but did not achieve hemodynamic improvement.



TP 31-50 mm Hg

TP 11-30 mm Hg

TP <10 mm Hg

Table IV. Kaplan-Meier amputation-free survival (AFS) by revised toe hemodynamic pressure group (N = 282 limbs)

Toe pressure ≤50 mm Hg	*6 months*	*1 year*	*2 years*	*3 years*
Overall	0.64 (0.031)	0.54 (0.032)	0.41 (0.033)	0.28 (0.032)
TP 31-50 mm Hg (group 0, n = 115)	0.82 (0.040)	0.71 (0.048)	0.58 (0.053)	0.44 (0.056)
TP 11-30 mm Hg (group 1, n = 82)	0.69 (0.054)	0.53 (0.060)	0.38 (0.060)	0.27 (0.057)
TP 0-10 mm Hg (group 2, n = 85)	0.36 (0.055)	0.35 (0.055)	0.21 (0.050)	0.08 (0.036)

Vallabhaneni, et al. *J Vasc Surg.* 2016;63:105.

J Cardiovasc Surg (Torino). 2009 Jun;50(3):331-7.

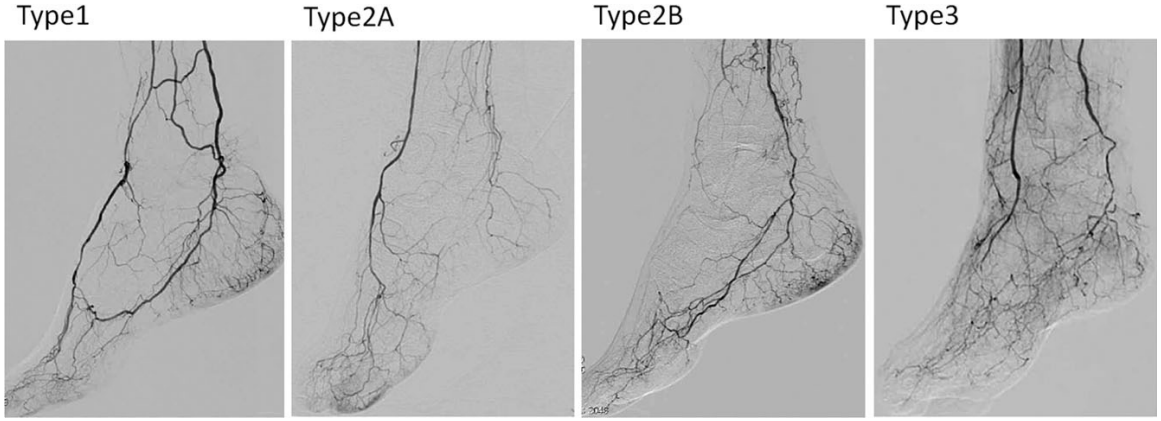
Clinical results of below-the knee intervention using pedal-plantar loop technique for the revascularization of foot arteries

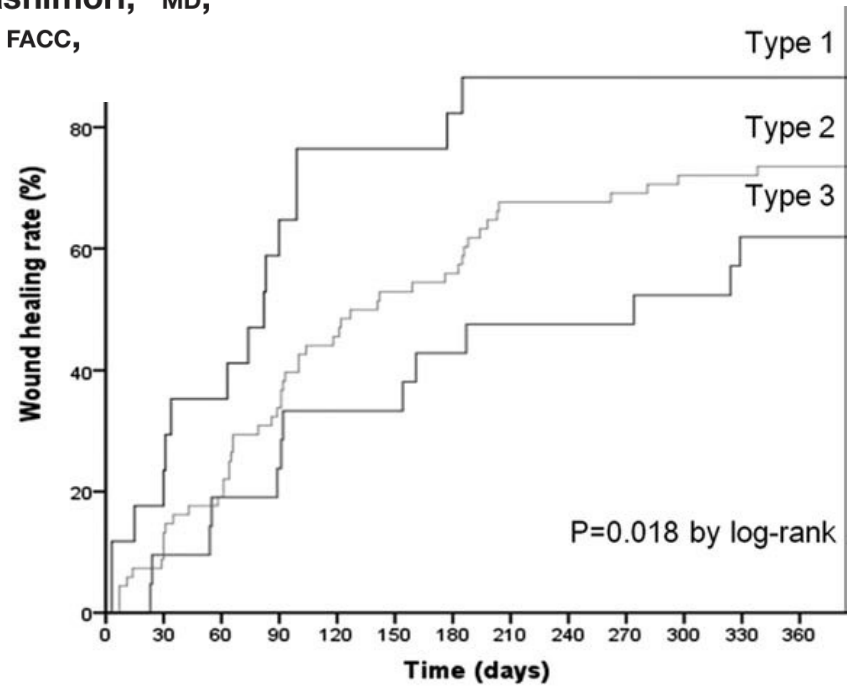
M Manzi [1], M Fusaro, T Ceccacci, G Erente, L Dalla Paola, E Brocco

- 2006-2007 → 1331 consecutive patients
  - 135 stenotic and CTO BTA
  - 85% technical success
  - Functional status improved and maintained for 1 yr
  - Demonstrated BTA interventions in CLTI are safe, feasible, and positive in short term

Predictors of Adverse Clinical Outcomes After Successful Infrapopliteal Intervention

Osami Kawarada,[1,2,3*] MD, FSCAI, Masahiko Fujihara,[2] MD, Akihiro Higashimori,[2] MD, Yoshiaki Yokoi,[2] MD, PhD, FSCAI, FACC, Yasuhiro Honda,[3] MD, FAHA, FACC, and Peter J. Fitzgerald,[3] MD, PhD, FACC





Worse pedal artery disease = lower rate of wound healing

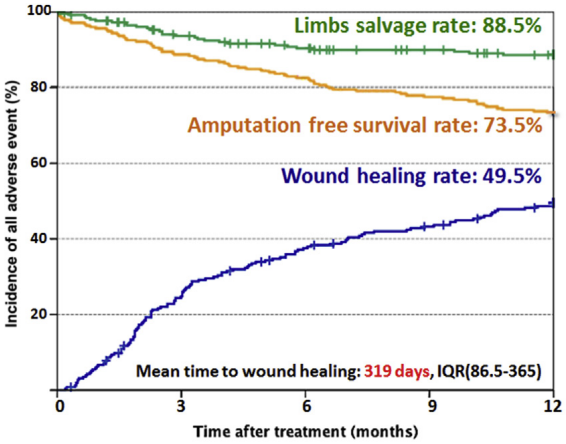
Kawarada, et al. *Catheter Cardiovasc Interv*. 2012;80:861.

Clinical Outcomes of Pedal Artery Angioplasty for Patients With Ischemic Wounds

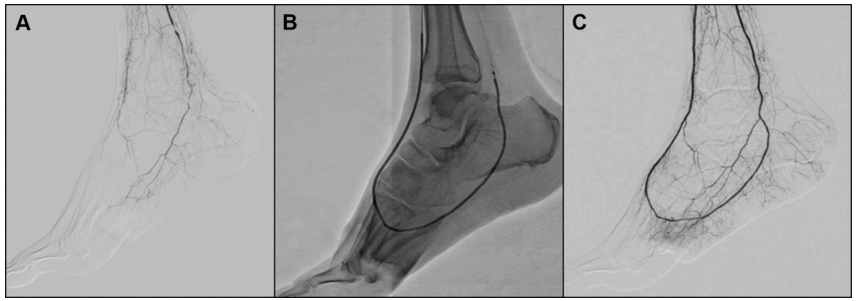
Results From the Multicenter RENDEZVOUS Registry

Tatsuya Nakama, MD,[a] Nozomi Watanabe, MD,[a] Takuya Haraguchi, MD,[b] Hiroshi Sakamoto, MD,[c] Daisuke Kamoi, MD,[d] Yoshinori Tsubakimoto, MD,[c] Kenji Ogata, MD,[a] Katsuhiko Satoh, MD,[b] Kazushi Urasawa, MD,[b] Hiroshi Andoh, MD,[c] Hiroshi Fujita, MD,[c] Yoshisato Shibata, MD[a]

CLTI Patients N=257



Interval (months)		0	3	6	9	12
Limbs salvage rate (n=257)	at risk	257	229	213	200	189
	%	100.0	93.6	90.3	89.8	88.5
Amputation free survival rate (n=257)	at risk	257	229	213	200	189
	%	100.0	89.1	82.9	77.8	73.5
Wound healing rate (n=257)	at risk	257	190	155	138	120
	%	100.0	24.8	37.5	43.2	49.5

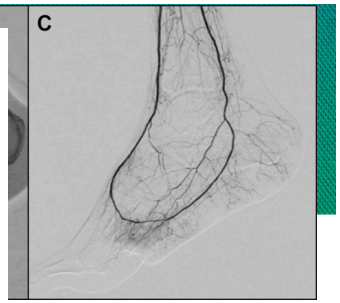


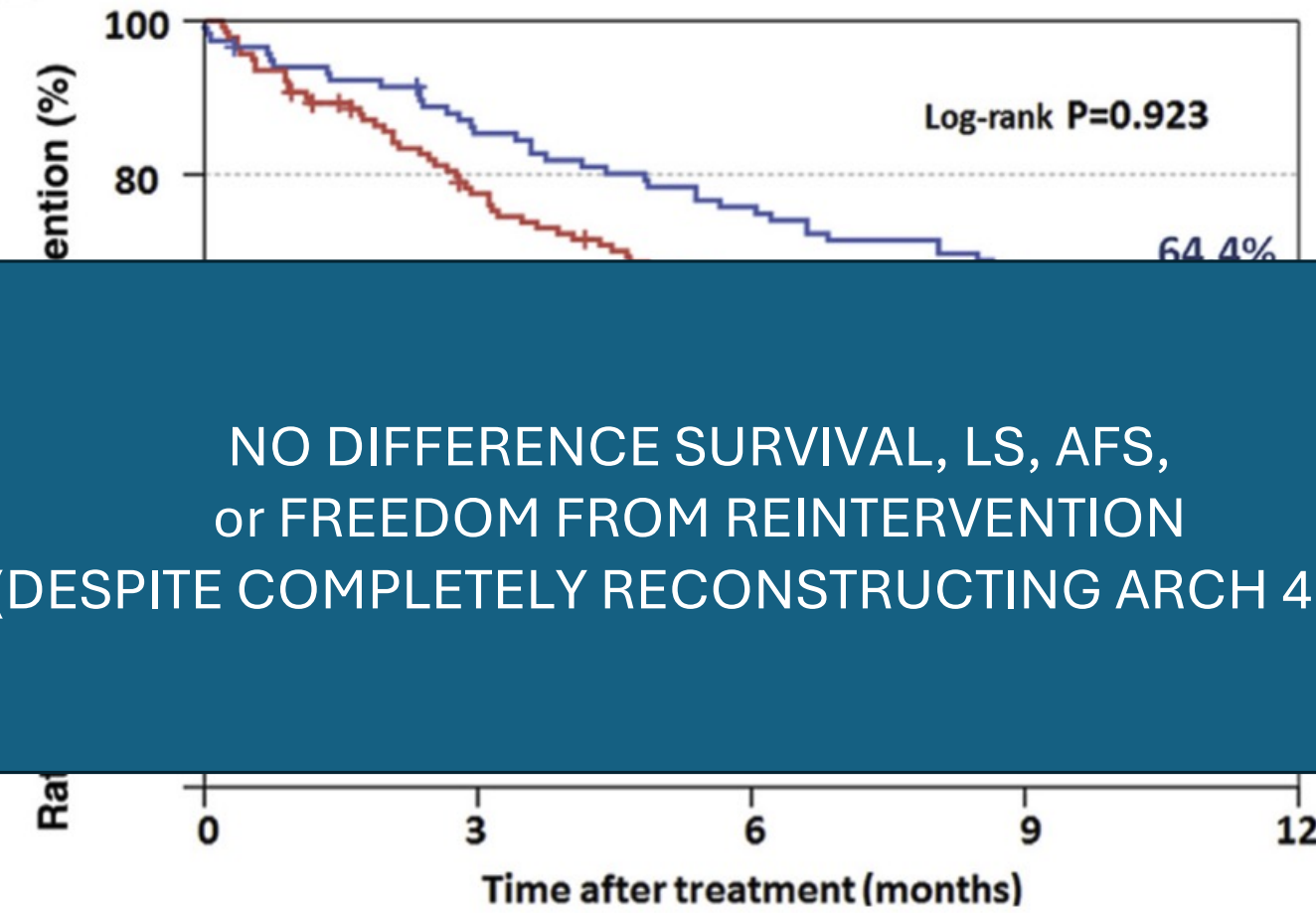
The limb salvage rate was 88.5%, the amputation-free survival rate was 73.5%, and the rate of wound healing was 49.5% (standard errors did not exceed 10%). Median time to wound healing was 319 days (interquartile range: 86.5 to 365 days).

Nakama, et al. *JACC: Cardiovasc Interv.* 2017;10:79.

Clinical Outcome
Pedal Artery Ang
Patients With Isc
Results From the Mu

Tatsuya Nakama, MD,[a] Nozomi Wa
Daisuke Kamoi, MD,[d] Yoshinori Tsu
Hiroshi Andoh, MD,[c] Hiroshi Fujita



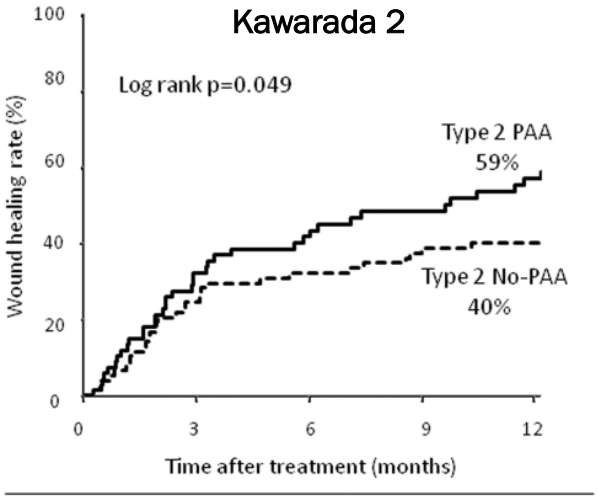


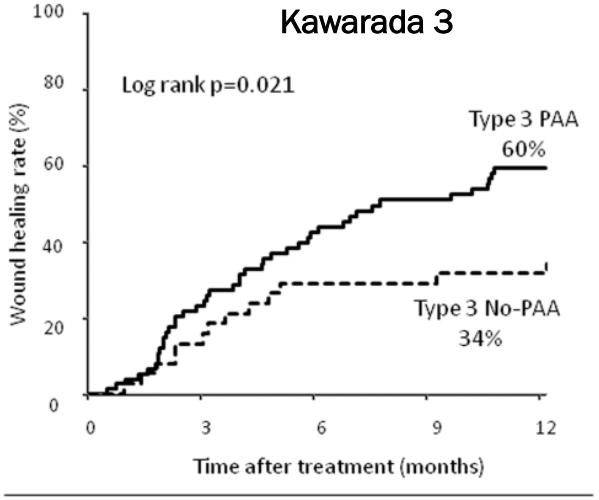
NO DIFFERENCE SURVIVAL, LS, AFS,
or FREEDOM FROM REINTERVENTION
(DESPITE COMPLETELY RECONSTRUCTING ARCH 45%)

Nakama, et al. *JACC: Cardiovasc Interv* 2017;10:79.

Outcomes of Pedal Artery Angioplasty Are Independent of the Severity of Inframalleolar Disease: A Subanalysis of the Multicenter RENDEZVOUS Registry

Yoshinori Tsubakimoto, MD, PhD[1], Tatsuya Nakama, MD[2], Daisuke Kamoi, MD[3], Hiroshi Andoh, MD[4], and Kazushi Urasawa, MD, PhD[5]

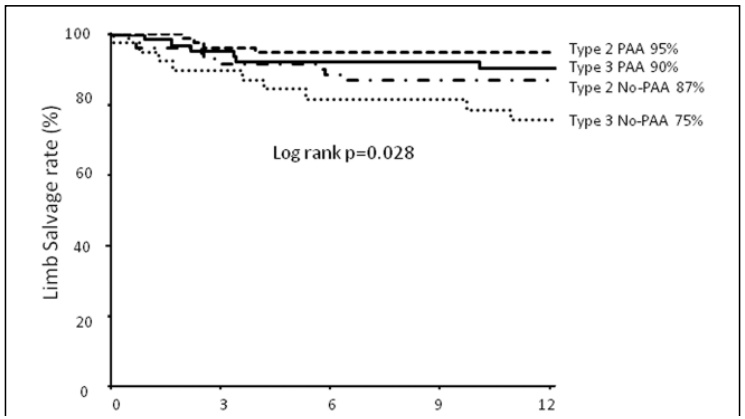




Wound healing

257 consecutive CLTI patients: pedal angioplasty in 140

Technical success 88% and 90% in severe



Limb salvage

Tsubakimoto, et al. *J Endovasc Ther*. 2020;27:186-193.

SO in 2025

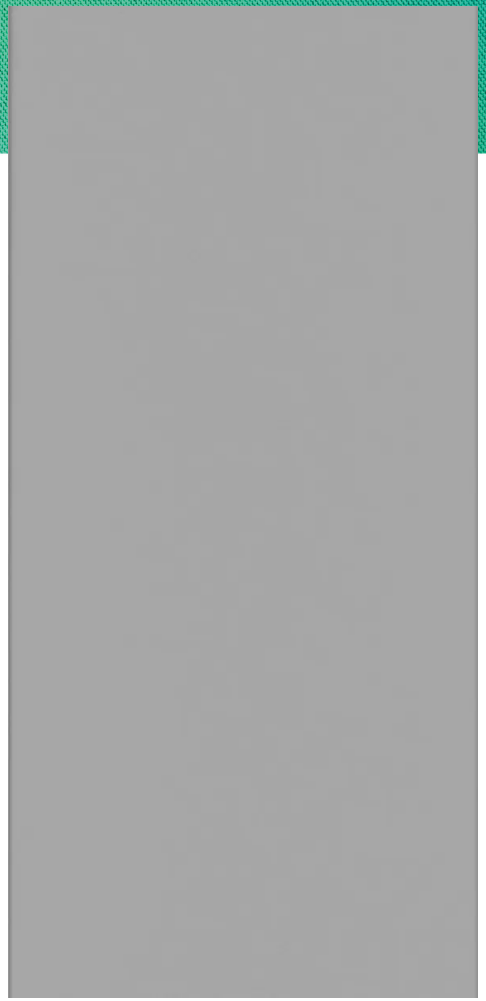
- BTA Angioplasty is “sexy”
  - No RCT data BUT they are SAFE
  - But provides marginal benefit compared to BTK (alone) angioplasty
  - May improve time to wound healing… but it still takes A LONG TIME
  - Furthermore, challenging to differentiate what success looks like?
    - No algorithm
    - Marginal hemodynamic effect
    - Difficult to assess results
    - No viable bailout
    - No clear limb salvage benefit

BTA Interventions

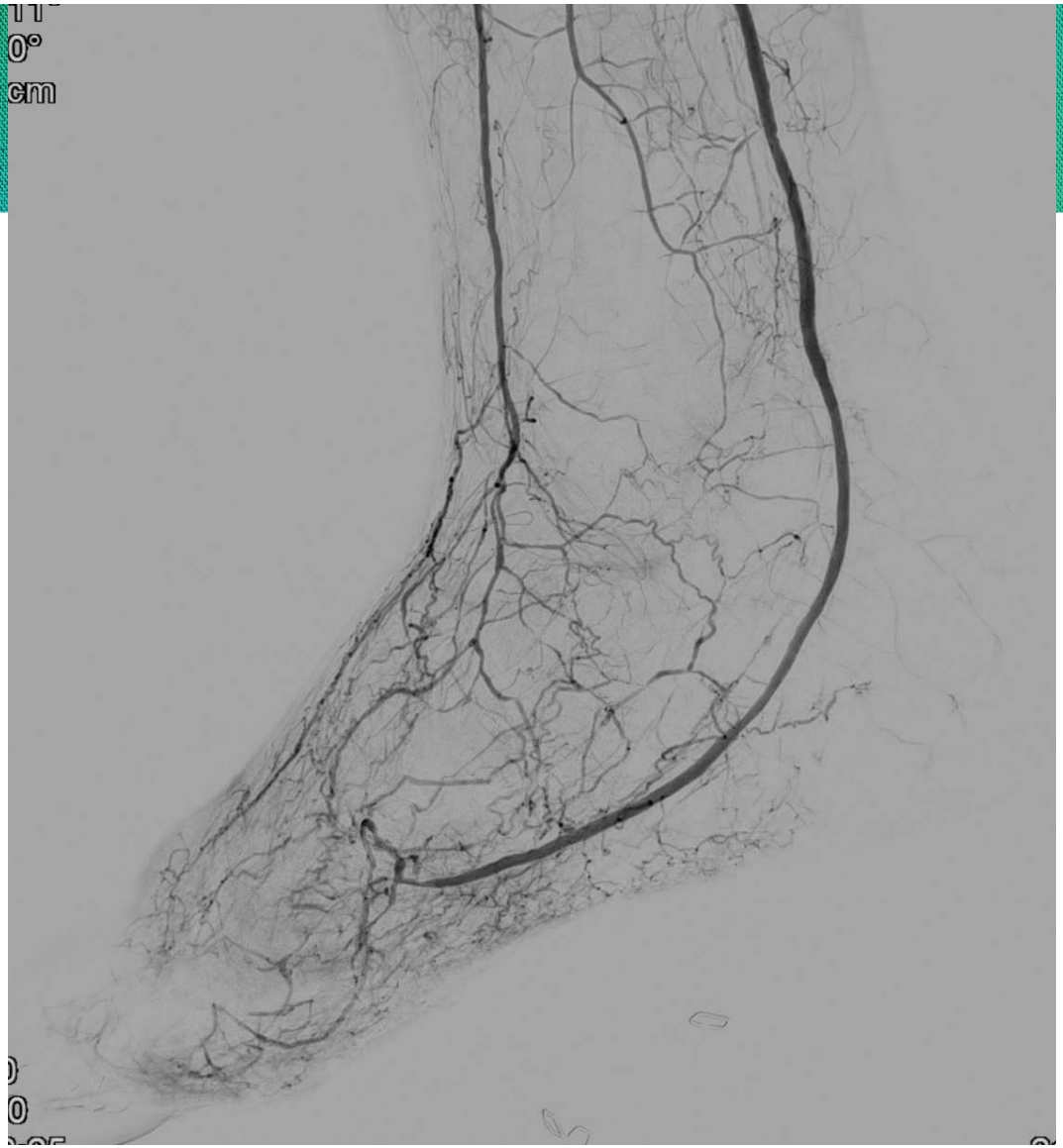
- Setting patient expectations CRITICAL preoperatively
  - Chance for failure
  - Chance to WORSEN their problem
  - Limited bailouts
    - Discuss DVA
  - Patency issues
- Planning is KEY
- Prep EVERYTHING

Case 1

- 78y F with non-healing RLE foot ulceration
  - CAD, ESRD, CHF
  - ABI NC
  - TP 22 mm Hg

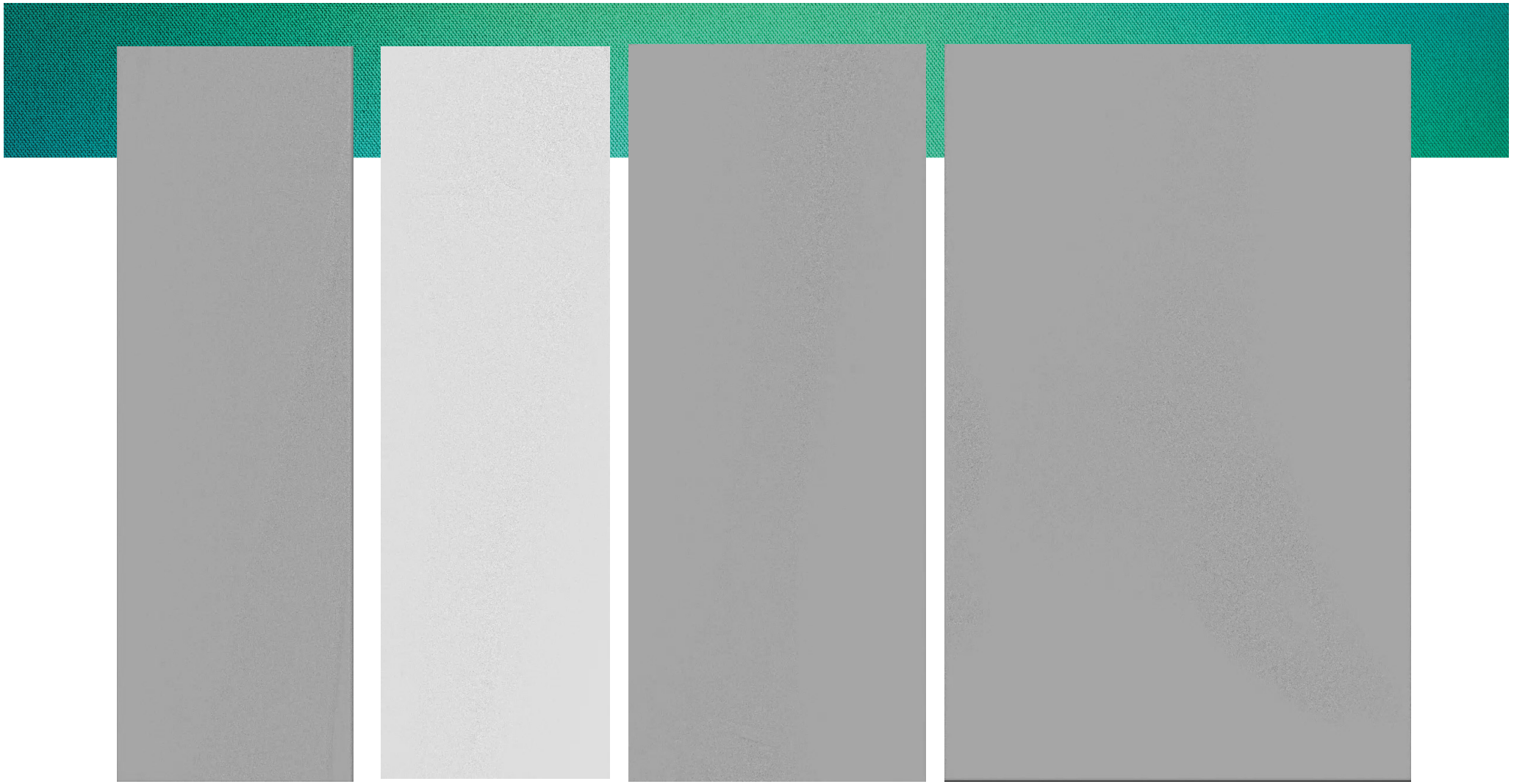


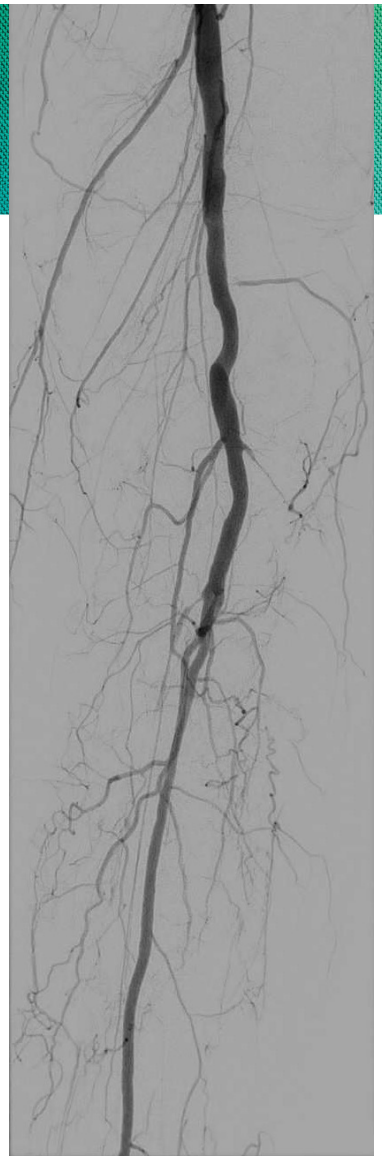
E8 3x80

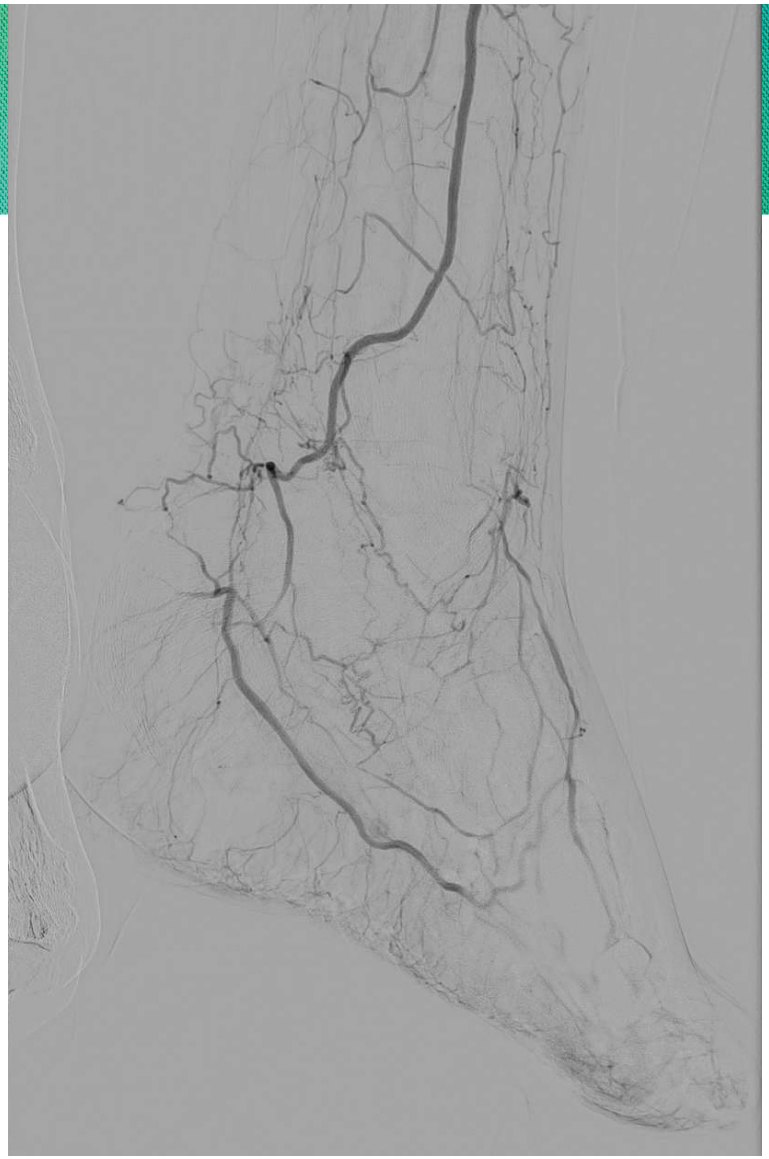

0°
cm

Case 2

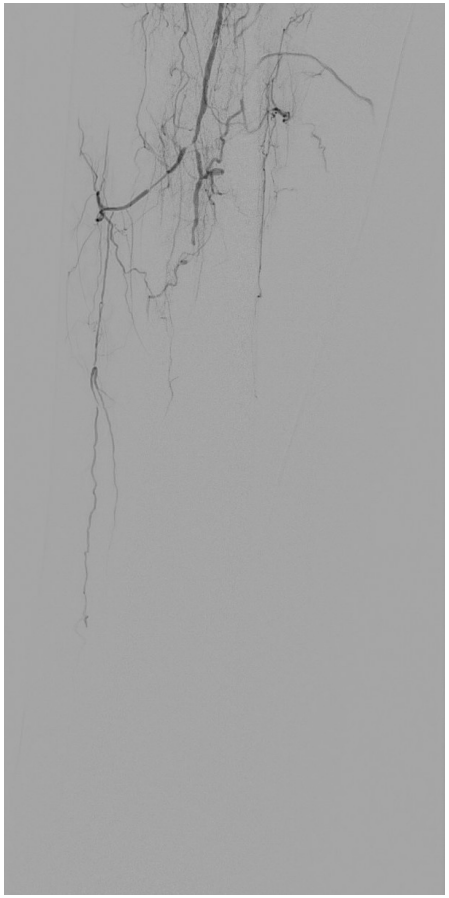
- 71y M w/DM, HTN, CKD, CAD, and non-healing left hallux ulceration
- ABI BLE 1.0
  - LLE TP: 24 mm Hg
  - LLE TBI: .2





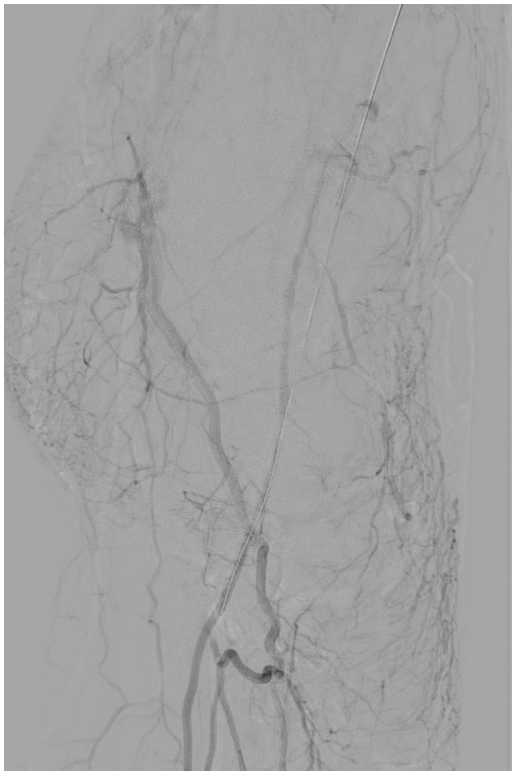


OK try to cross PT CTO → LP artery



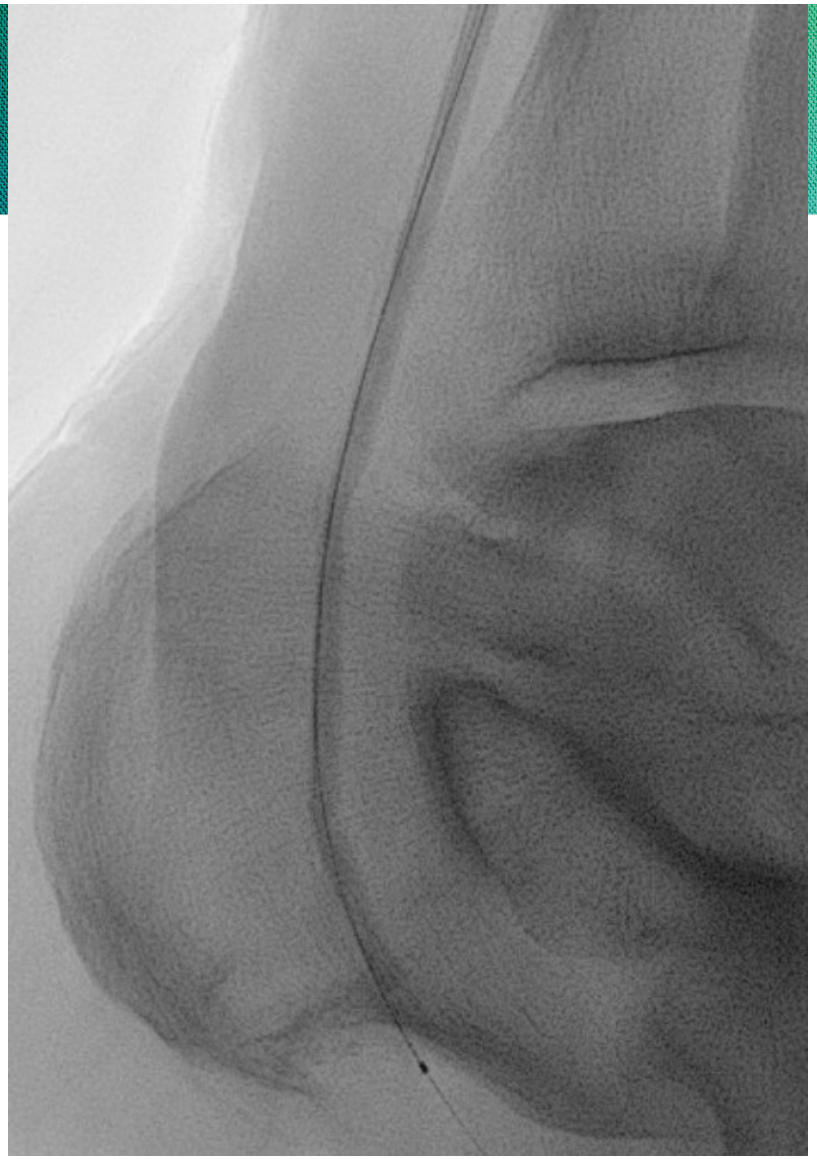
Let's Do Something... Alternative

- Antegrade DP access
- 0.014 wire + 0.018 cath
- "Surf" the loop
- Get body floss!

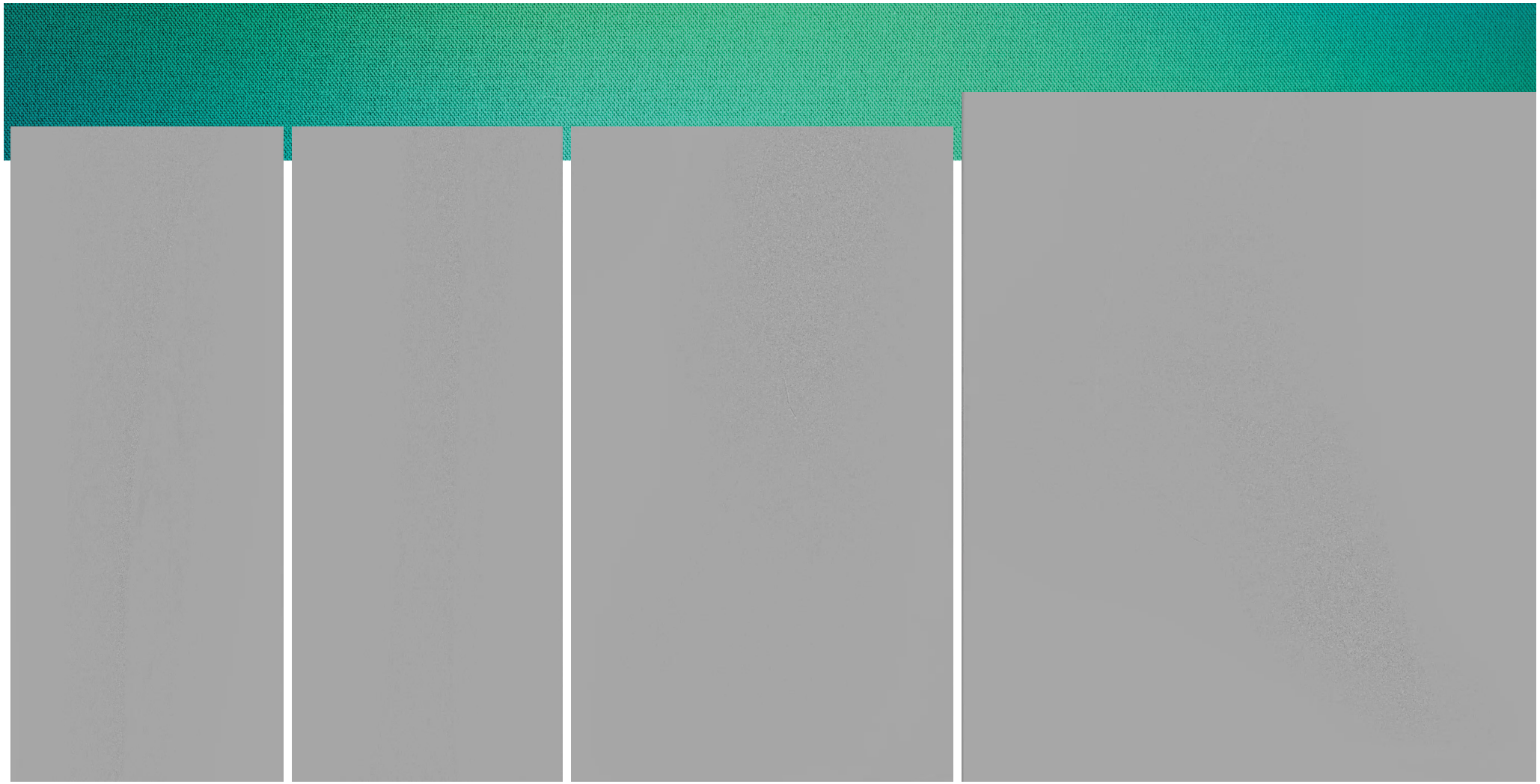


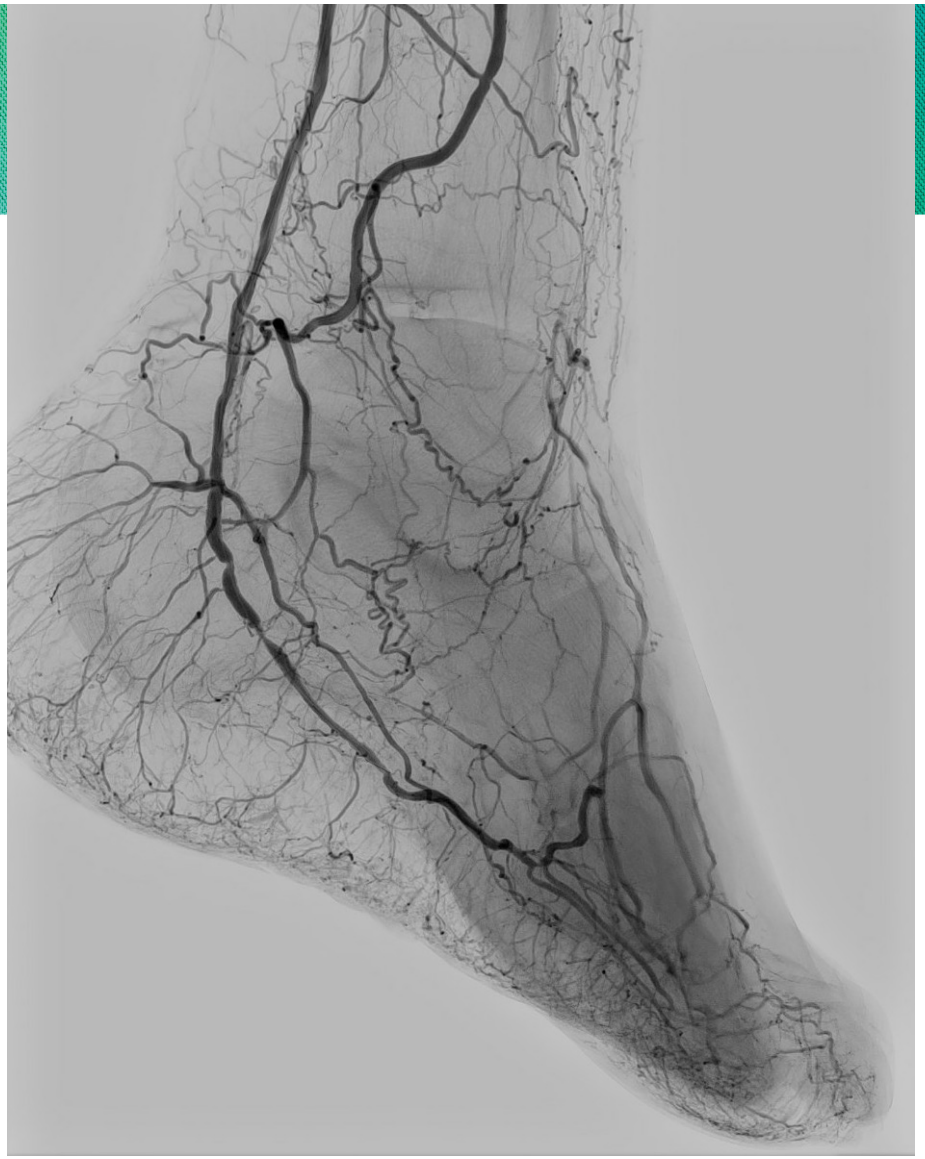
Vessel PREP

Javelin IVL

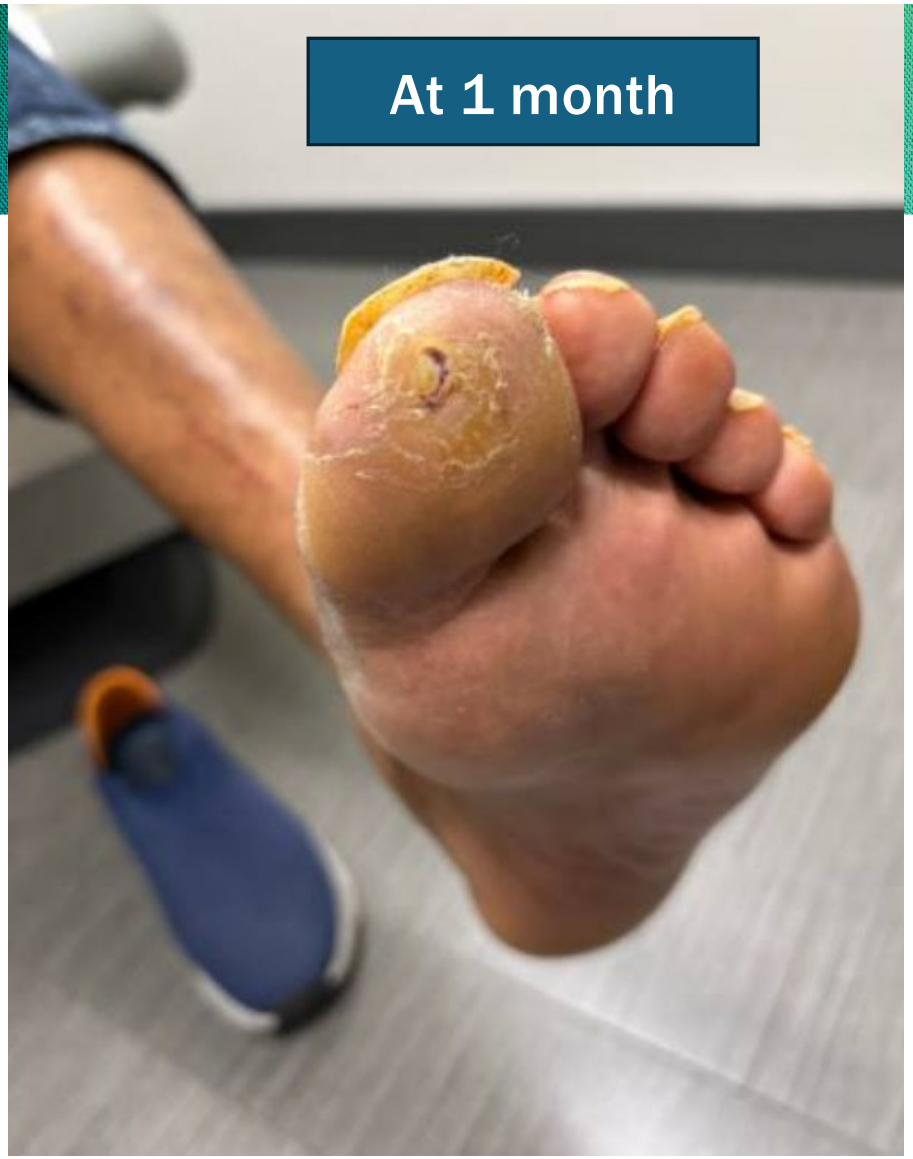


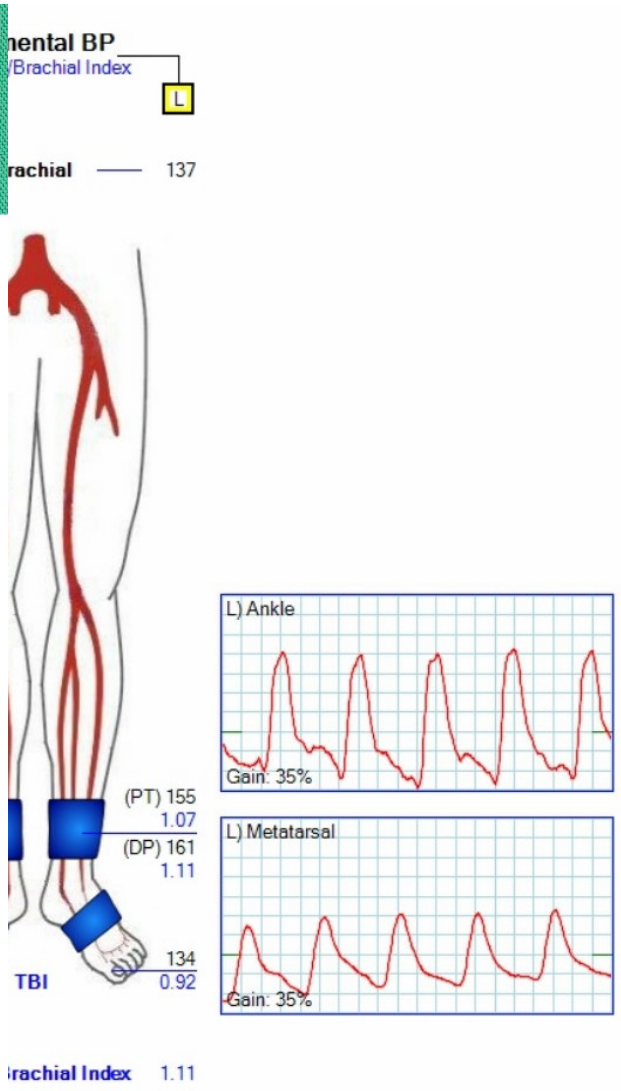
3x120 specialty balloon





At 1 month




nental BP
/Brachial Index
L
rachial 137
(PT) 155
1.07
(DP) 161
1.11
134
0.92
TBI
rachial Index 1.11
L) Ankle
Gain: 35%
L) Metatarsal
Gain: 35%

Conclusion

- BTA interventions are a REQUIRED part of any CLTI interventionalist's tool bag
- No RCT data, BUT they are SAFE
- May improve time to wound healing, but it MAY take A LONG TIME
- Keys to success
  - Find the tools that work for YOU and become comfortable with them
  - Be aggressive… these interventions COULD be the only thing standing in the way of your patient undergoing amputation

Thank You