How I Do It:

Treating Complex, Below-the-Knee Disease

Supported by an educational grant from Shockwave Medical

Faculty

- **Karan Garg, MD** — Associate Professor of Surgery, Division of Vascular Surgery, NYU Langone Medical Center; Bellevue Hospital Center; Manhattan Veterans Affair Hospital; New York, NY
- **Liz Genovese, MD, MS, FACS** — Assistant Professor of Surgery; Penn Advanced Limb Preservation Program — Director at HUP; Division of Vascular Surgery and Endovascular Therapy, University of Pennsylvania; Philadelphia, PA
- **Constantino Peña, MD, FAHA, FSCCT, FSIR** — Associate Clinical Professor, FIU Herbert Wertheim College of Medicine; Section Chief, Interventional Radiologist, and Medical Director of Vascular Imaging, Miami Cardiac & Vascular Institute; Miami, FL
- **Sameh Sayfo, MD** — Endovascular Fellowship Program Director, Baylor Scott & White The Heart Hospital Plano; Assistant Professor A&M School of Medicine; Plano, TX

Faculty Disclosures

- **Karan Garg, MD** — Cook, Gore, Shockwave
- **Elizabeth Genovese, MD, MS, FACS, RPVI** — Abbott Medical, Boston Scientific Corporation, Cook Inc. Inari, Penumbra Inc., Philips, Shockwave Medical, W. L. Gore— Speaker's Bureau; Boston Scientific Corporation, Cook Inc., Philips — Advisory Board; Boston Scientific Corporation, Cook Inc., Shockwave Medical— Consultant; Boston Scientific Corporation— Grant/Research Support; Philips— Advisory Board
- **Constantino Peña, MD, FAHA, FSCCT, FSIR** — Consultant: Avanos; Cook Medical; Cordis; Philips Medical; Scientific Advisory Board: Asahi; Medtronic; Speakers Bureau: BD (Bard); Cook Medical; Penumbra; Shockwave; Terumo; Investor: Cagent Medical
- **Sameh Sayfo, MD** — Consultant, Speakers Bureau: AngioDynamics; Boston Scientific; Philips; Shockwave Medical

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 may include brand names for participant clarity purposes only. No product promotion or recommendation should be inferred.

Learning Objectives

- Assess the calcification within the vessel to determine an appropriate treatment plan and technology
- Understand the mechanisms of action of new technology for below-the-knee (BTK) calcification
- Analyze available data that supports treatment options in BTK arteries

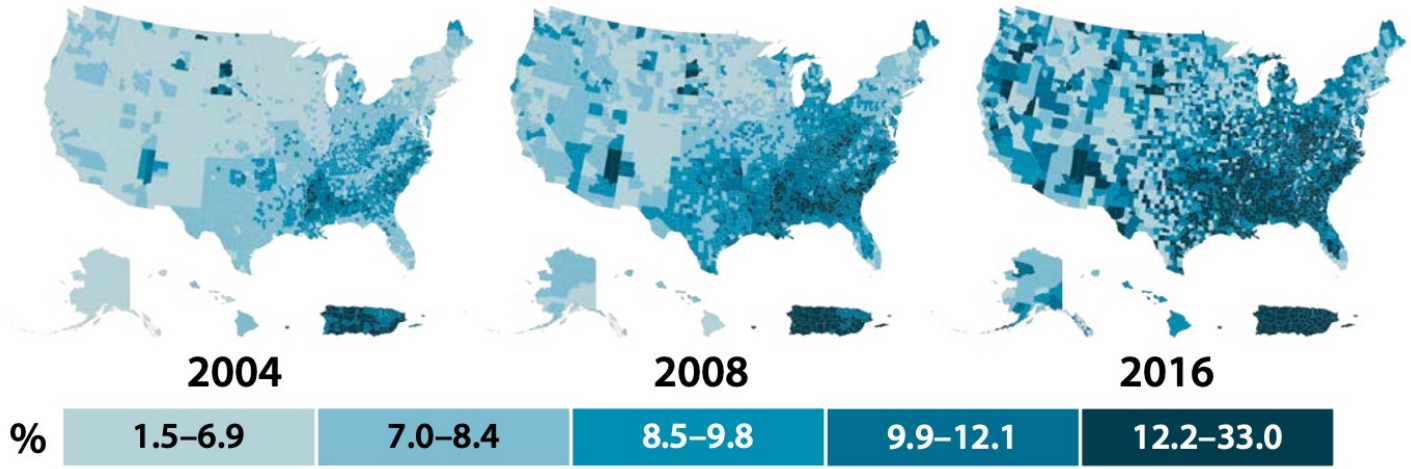
BTK = below-the-knee.

Introduction to Below-the-Knee Calcification

Liz Genovese, MD, MS, FACS
Assistant Professor of Surgery
Penn Advanced Limb Preservation Program — Director at HUP
Division of Vascular Surgery and Endovascular Therapy
University of Pennsylvania
Philadelphia, PA

Epidemic of Diabetes in the United States

- 13.0% of all U.S. adults (34 million) have diabetes
- Percentage of adults with diabetes increases with age, reaching 26.8% among those aged ≥65 yrs



CDC. National Diabetes Statistics Report. 2020.

Impact of Diabetes on Peripheral Arterial Disease

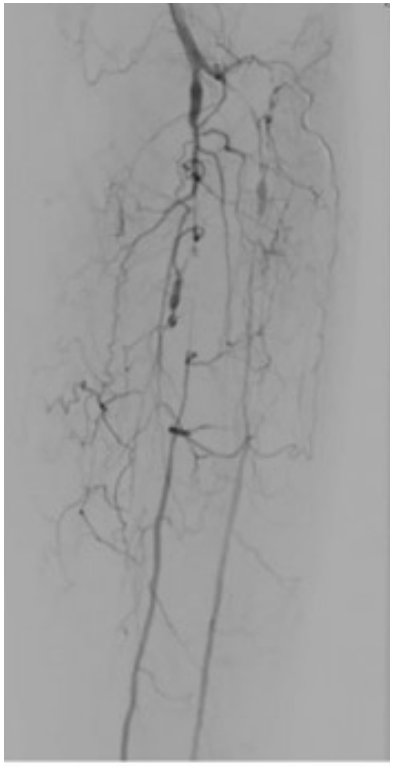
- Increased rates of peripheral arterial disease (PAD)
  - High associated rates of concomitant neuropathy, decreased wound healing capability, infection
- Increased medial calcinosis
- Increases risk of chronic kidney disease (CKD)

Increasing prevalence of highly calcific infrainguinal occlusive disease, infrapopliteal disease, and outflow disease

PAD = peripheral arterial disease; CKD = chronic kidney disease.

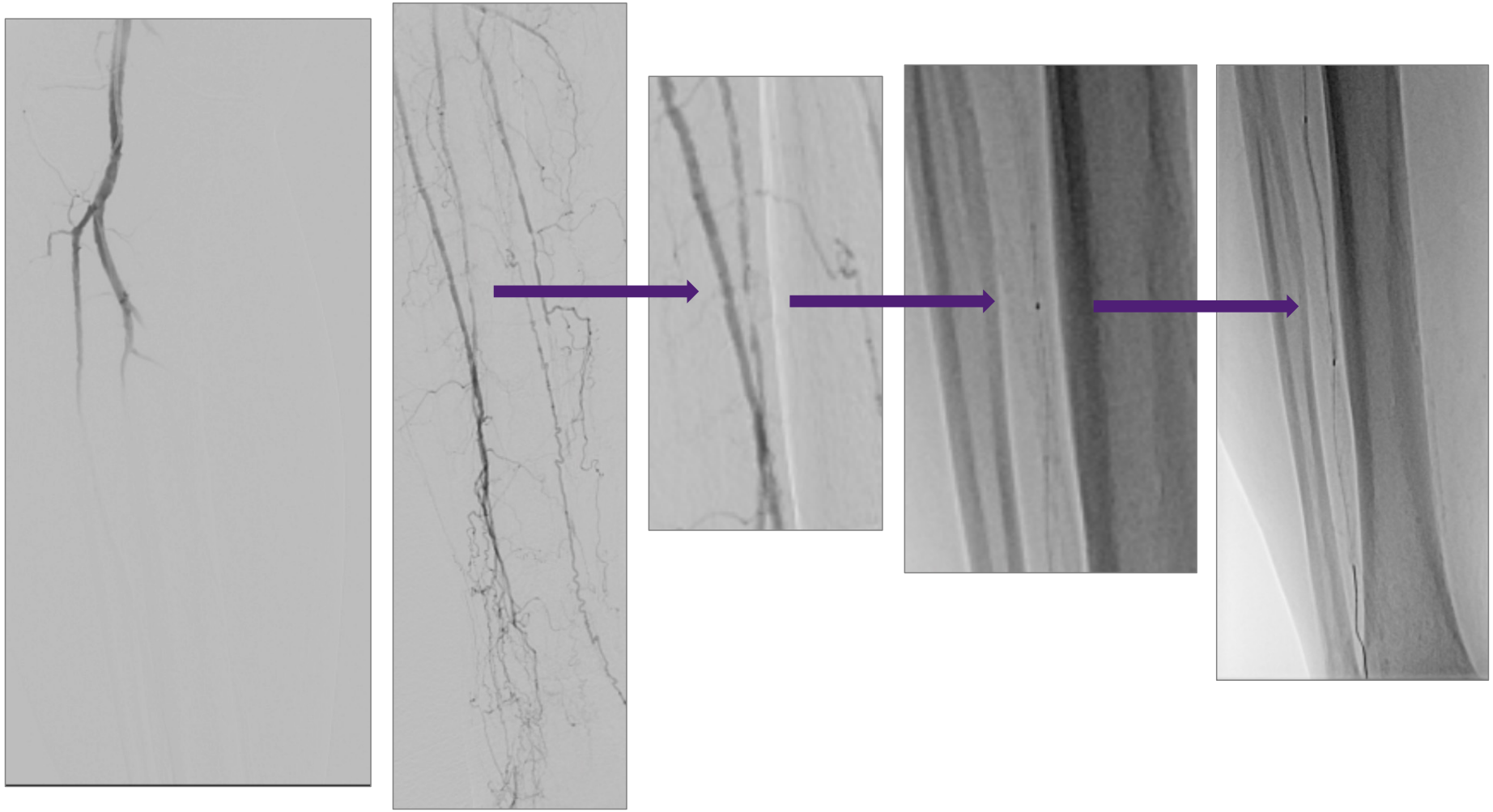
Conte MS, et al. GVG Writing Group. *J Vasc Surg*. 2019;69(6S):3S-125S. Erratum in: *J Vasc Surg*. 2019;70(2):662.

Highly Calcified Below-the-Knee Disease

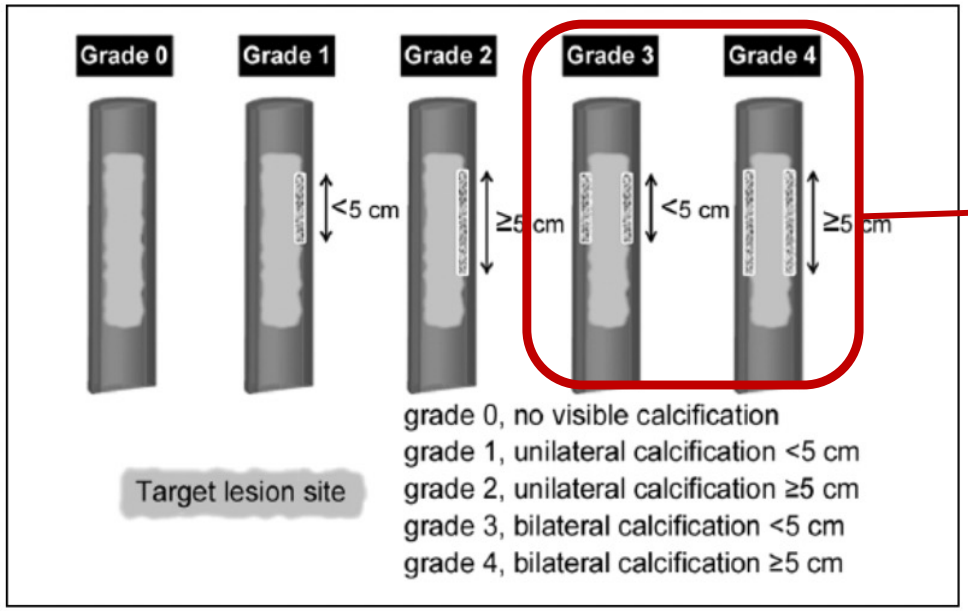


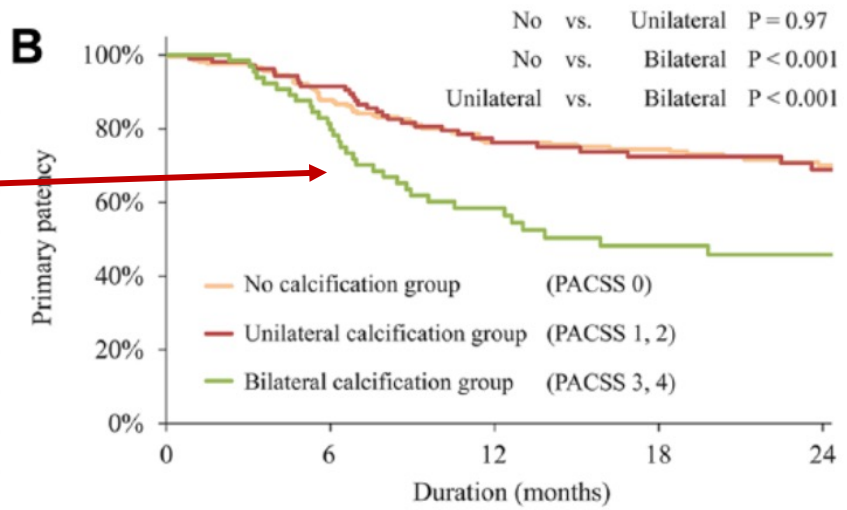
- Difficulty with lesion crossing
- Poor luminal gain
- Dissection
- Recoil
- Poor stent wall apposition

Mustapha JA, et al. *Circ Cardiovasc Interv*. 2016;9(5):e003468.



Impact of Peripheral Arterial Calcification Scoring System (PACSS) on Outcomes

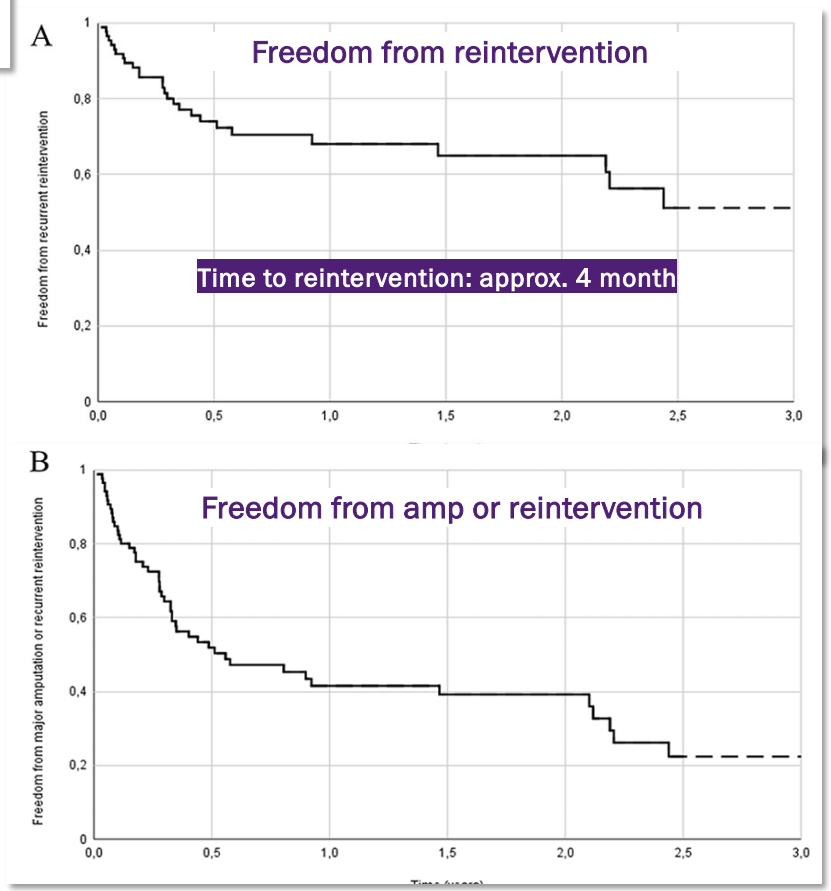


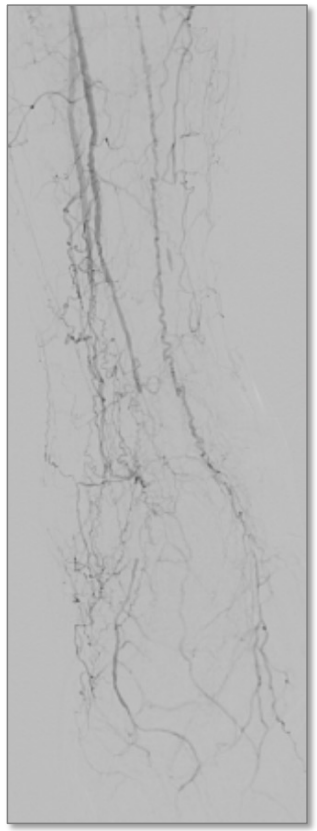


Okuno S, et al. *J Endovasc Ther*. 2016;23(5):731-737.

Outcomes and Patency of Endovascular Infrapopliteal Reinterventions in Patients With Chronic Limb-Threatening Ischemia

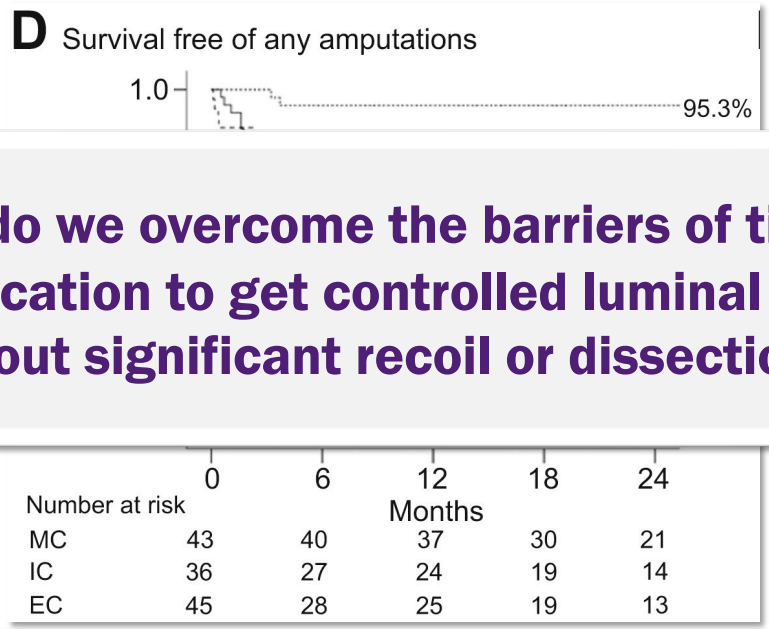
	n=81
Male sex	53 (65%)
Age (years)	78.0 [68.0, 83.0]
BMI (kg/m^2)	26.8 [23.7, 29.5]
ASA	
• 2	7 (9%)
• 3	65 (80%)
• 4	4 (5%)
• Missing	5 (6%)
Smoking	
• Yes	18 (22%)
• Quit	24 (30%)
• No	39 (48%)
Diabetes mellitus	
• Type I	10 (12%)
• Type II	48 (60%)
Hypertension	76 (94%)
Hypercholesterolemia	43 (53%)
COPD	17 (21%)
Coronary artery disease	54 (67%)
Congestive heart failure	15 (19%)
Chronic kidney disease	38 (47%)
• eGFR (mL/min per 1.73 m^2)	60.0 [41.5, 78.5]
• Creatinine	97.0 [76.0, 133.0]
Hemodialysis	6 (7%)
Stroke	20 (25%)





Kleiss SF, et al. *J Endovasc Ther*. 2024;31(5):831-839.

Extensive Tibial Artery Calcification

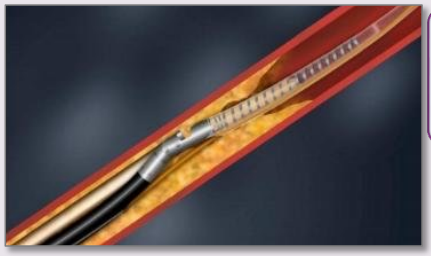


How do we overcome the barriers of tibial calcification to get controlled luminal gain without significant recoil or dissection?

Extensive calcification remained an independent risk factor for technical failure and amputation at 2 yrs (HR=2, *p*=.004)

Ko YG, et al. *J Vasc Surg*, 2016;64(5):1335-1343.

Atherectomy

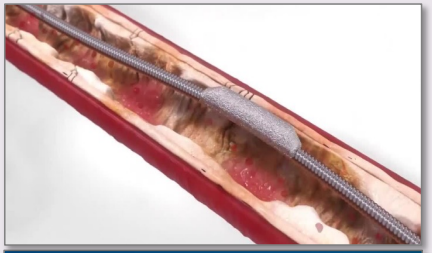


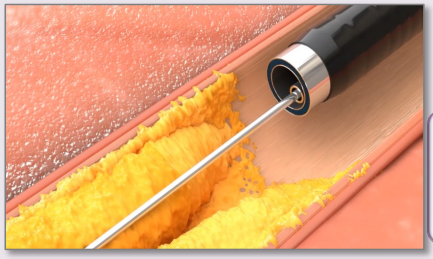
- HawkOne™
- Mild to moderate intimal calcium

Directional Atherectomy

Orbital Atherectomy

- Diamondback®
- Heavy calcification



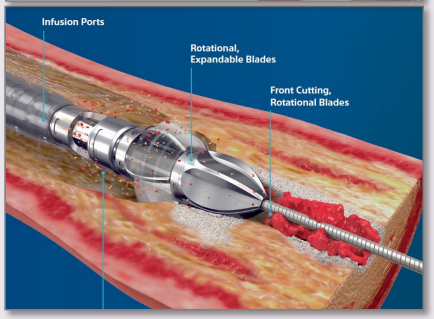


Ablative Atherectomy

- Laser
- Excimer vs Auryon
- ISR

Rotational Atherectomy

- Roto
- JetStream™
- Phoenix
- Rotarex™



ISR = in-stent restenosis.

Shafique S, et al. *J Sem Vasc Surg.* 2007;20(1):29-36.

Atherectomy Downsides

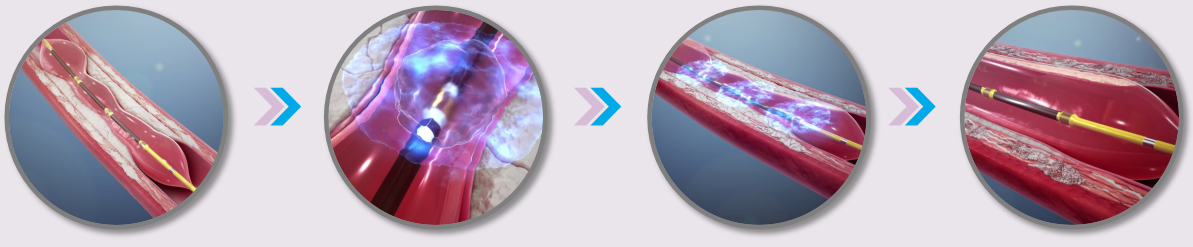
- Distal embolization
- Dissection
- Steep learning curve
- Possible perforation
- Cost

Table 2. Primary Intraoperative Outcomes.

	Femoropopliteal (n=12499)			Tibial (n=6736)		
	POBA (*n*=6304)	A+A (*n*=6195)	p-value	POBA (*n*=5592)	A+A (*n*=1144)	p-value
Composite outcome	174 (2.8%)	366 (5.9%)	**<0.0001**	212 (3.8%)	37 (3.2%)	0.3625
Target lesion dissection	53 (2.6%)	164 (4.5%)	**0.0003**	71 (2.3%)	5 (0.8%)	**0.0111**
Distal embolization	30 (0.7%)	39 (1.5%)	**0.001**	36 (1.4%)	9 (1.8%)	0.5008
Provisional stent placement	0 (0.0%)	95 (1.5%)	**<0.0001**	0 (0.0%)	3 (0.3%)	**0.0001**

A+A = atherectomy and angioplasty.
Sanon O, et al. *J Endovasc Ther*. 2023;30(5):693-702.

Intravascular Lithotripsy

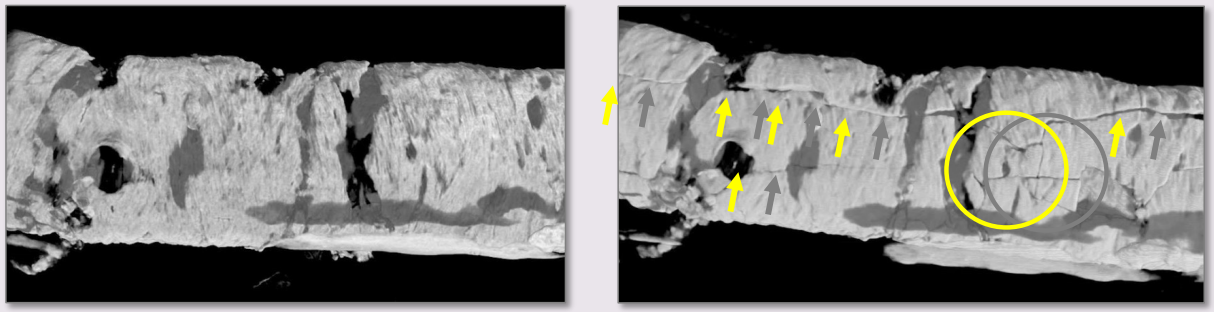


Low Pressure Inflation

Sonic Pressure Waves Using Lithotripsy

Crack Calcium → Change in Compliance

Safely Expand the Vessel



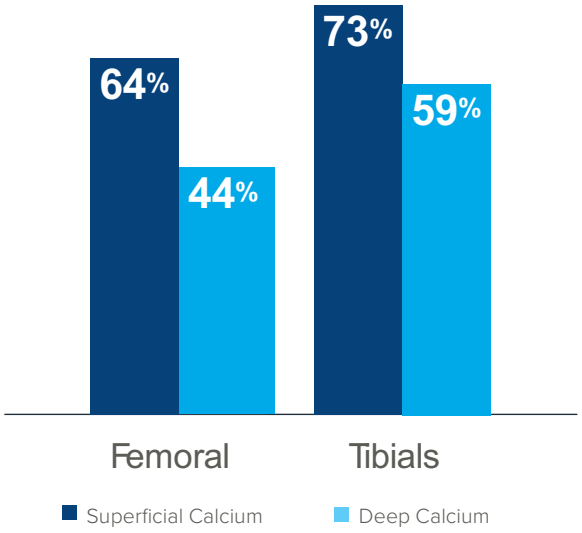
Pre-IVL Treatment*

Post-IVL Treatment*

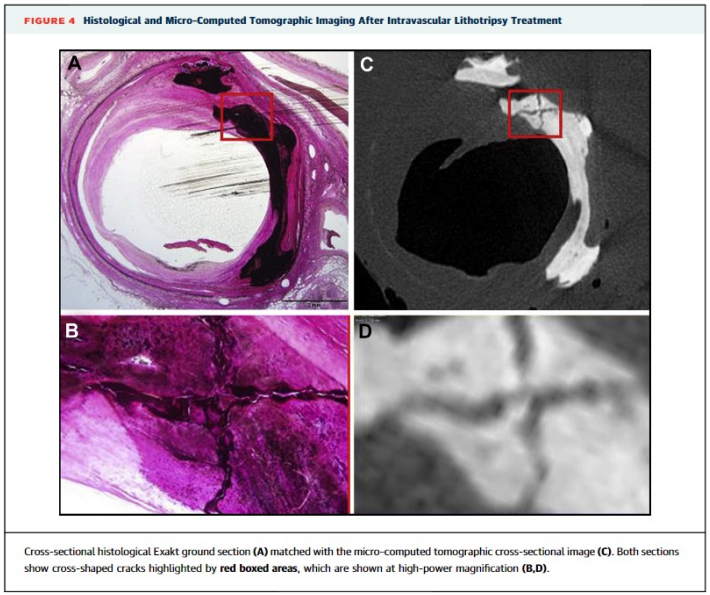
Fractures both superficial and deep calcium

BTK Prevalence and Treatment of Calcium

Superficial and deep calcium are more prevalent in BTK arteries



IVL disrupts superficial and deep calcium demonstrated by histologic images

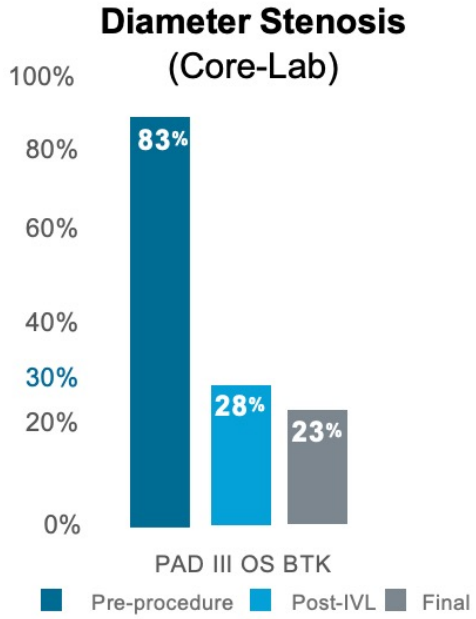


Soor G, et al, *Pathology*. 2008;40(4):385-391. Kereiakes D, et al. *JACC Cardiovasc Interv*. 2021;14(12):1275-1292.

DISRUPT PAD II OS BTK Subgroup

Table 2. Procedural Characteristics.

Characteristics	N=101 procedures
Pre-dilatation	28 (27.7)
Post-dilatation	51 (50.5)
Successful IVL delivery	101 (100.0)
Number of IVL catheters per case	1.1±0.3
IVL pulses	138.5±53.7
Stand-alone IVL therapy[a]	78 (77.2)
Calcium-modifying adjunctive technology[b]	23 (22.7)
Stent	11 (10.9)
DCB	15 (14.8)
Embolic protection	3 (3.0)



Final Angio Complications
(Core-Lab)

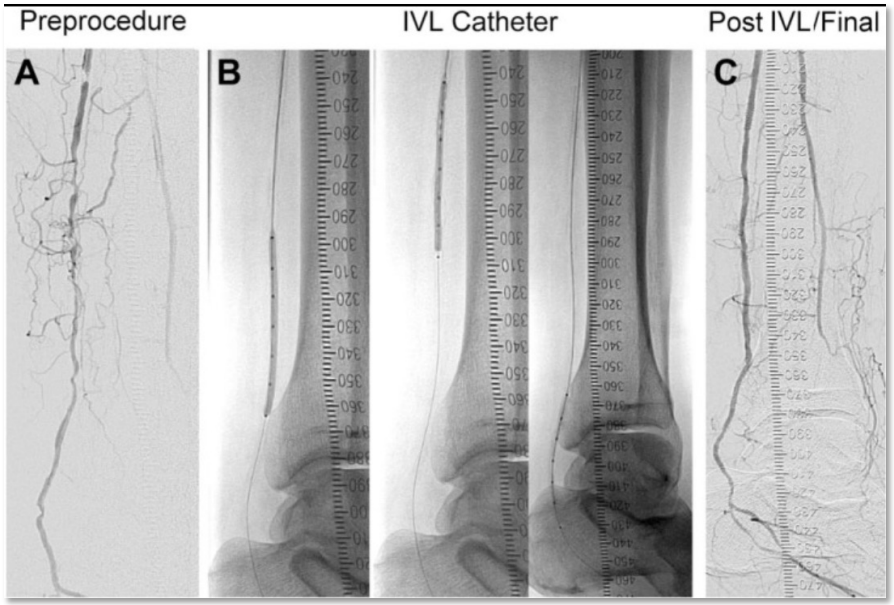
N	101
Vessels	Infrapopliteal
Dissection (Type D-F)	0%
Perforation	0%
Embolization	0%
Thrombus	0%
No reflow	0%
Abrupt closure	0%

Adjunctive atherectomy or specialty balloons used in 24% of cases

Adams G, et al. DISRUPT PAD III OS BTK Interim Results, LINC 2021. Adams G, et al. *J Endovasc Ther.* 2022;29(1):76-83.

Disrupt BTK Trial

- Prospective, non-randomized, multi-center feasibility and safety trial
- 20 patients enrolled (European sites)
- All patients had moderate to severe below-the-knee arterial calcification
- 30 days' follow-up



NIH. Accessed November 5, 2024. https://clinicaltrials.gov/study/NCT02911623. Brodmann M, et al. *J Endovasc Ther*. 2018;25(4):499-503.

Disrupt BTK Results

- 19 patients had successful IVL catheter delivery
- The composite of major adverse events (MAEs) at 30 days was 0%
- 46.5% of patients had acute reduction in percent diameter stenosis of target lesions
- All patients achieved residual diameter stenosis ≤50%
- **Conclusion:** The early results of this pilot study demonstrated that calcified, stenotic infrapopliteal arteries can be safely and successfully treated with intravascular lithotripsy

MAE = major adverse event.
Brodmann M, et al. *J Endovasc Ther*. 2018;25(4):499-503.

DISRUPT BTK II Study Design

Prospective, multi-center, single-arm study of the Shockwave Medical Peripheral IVL System for the treatment of calcified BTK lesions

Principal Investigators
- **Dr. Venita Chandra**, Stanford University Medical Center
- **Dr. Ehrin Armstrong**, Adventist Heart & Vascular Institute

Key Inclusion Criteria
- At least moderate calcification
- Rutherford category (RC) 3 to 5 in the target limb
- Up to 2 BTK lesions ≤200mm in length

Key Exclusion Criteria
- Planned use of cutting/scoring balloons, re-entry or atherectomy devices
- In-stent restenosis
- Acute or chronic renal disease unless on renal replacement therapy

- Independent Clinical Events Committee
- Angiographic Core Lab (Yale Cardiovascular Research Group)
- Duplex Ultrasound Core Lab (VasCore)

Primary safety endpoint

Major adverse limb events (MALE) or post-operative death at 30 days

Primary effectiveness endpoint

Procedural success, defined as ≤50% residual stenosis for all treated target lesions without serious angiographic complications

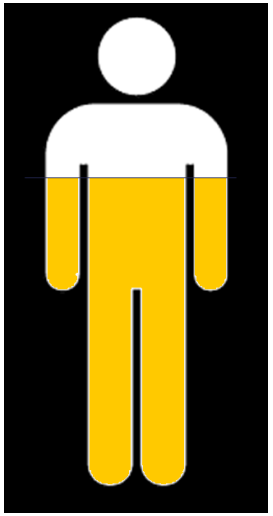
MALE defined as a composite of all-cause death, above-ankle amputation of the index limb, and/or major reintervention to the index limb involving a BTK artery.

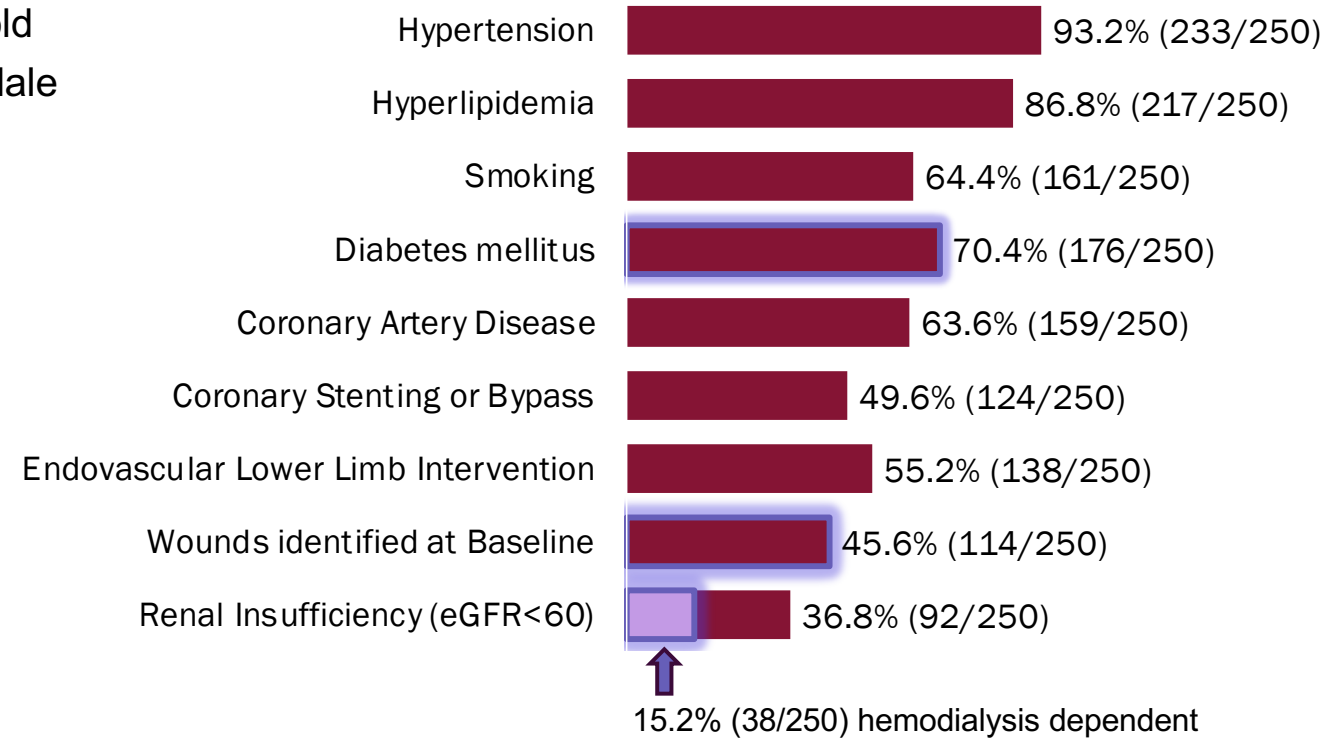
ClinicalTrials. Updated Jan 16, 2024. Accessed Nov 8, 2024. clinicaltrials.gov/study/NCT05007925. Chandra V, et al. Presented at: 22nd Annual Vascular InterVentional Advances (VIVA); Nov 3-6, 2024; Las Vegas, NV.

Baseline Medical History

71.6 ± 11.0 yrs old

72.8% (182/250) Male

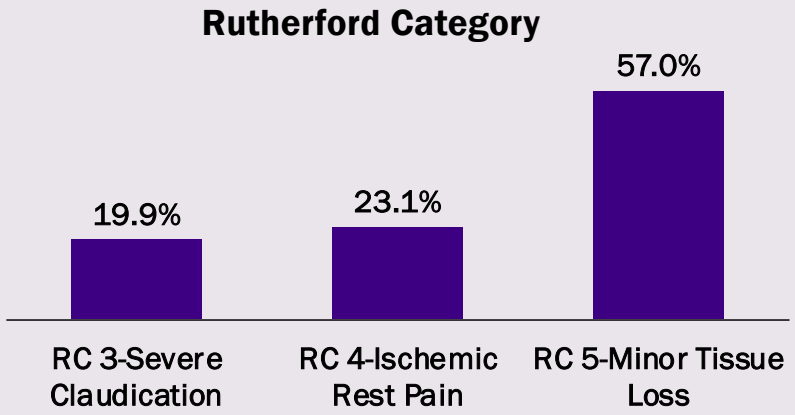


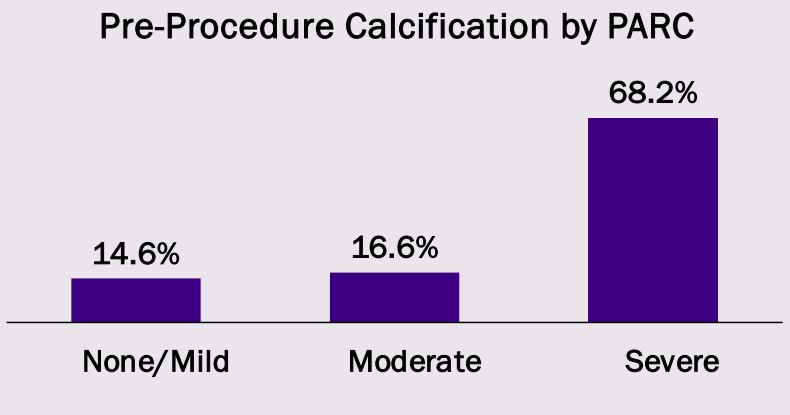


GFR = glomerular filtration rate.

ClinicalTrials. Updated Jan 16, 2024. Accessed Nov 8, 2024. clinicaltrials.gov/study/NCT05007925. Endovascular Today. Updated Nov 4, 2024. Accessed Nov 8, 2024. evtoday.com/news/disrupt-pad-btk-ii-evaluates-shockwave-ivl-system-to-treat-calcified-lesions. Chandra V, et al. Presented at: 22nd Annual Vascular InterVentional Advances (VIVA) Symposium; Nov 3-6, 2024; Las Vegas, NV.

Pre-Procedural Characteristics





Lesion Characteristics (core-lab assessed)	
Total Length of Calcification (mm)	90.7 ± 74.4 (247)
Lesion Length (mm)	76.3 ± 65.2 (301)
Diameter Stenosis	77.7 ± 17.9 (302)
Chronic Total Occlusion	29.5% (89/302)

ClinicalTrials. Updated Jan 16, 2024. Accessed Nov 8, 2024. clinicaltrials.gov/study/NCT05007925. Endovascular Today. Updated Nov 4, 2024. Accessed Nov 8, 2024. evtoday.com/news/disrupt-pad-btk-ii-evaluates-shockwave-ivl-system-to-treat-calcified-lesions. Chandra V, et al. Presented at: 22nd Annual Vascular InterVentional Advances (VIVA) Symposium; Nov 3-6, 2024; Las Vegas, NV.

Procedural Results — Crossing Results

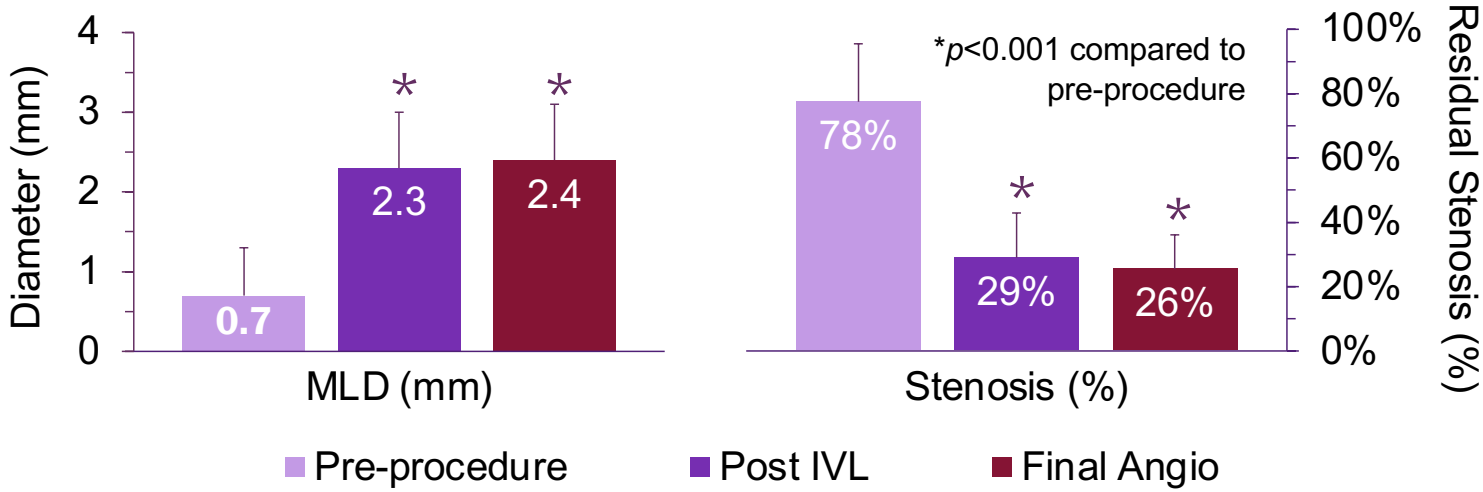
Procedural Results	
Pre-dilatation	34.6% (109/315)
IVL catheters used	
M5+	26.5% (92/347)
S4	73.5% (255/347)
Successful IVL catheter delivery across target lesion	97.5% (307/315)
Number of IVL catheters used in a lesion	
1	82.1% (252/307)
2	15.3% (47/307)
>3	2.6% (8/307)
Maximum IVL balloon pressure used	5.4 ± 1.2 (307)
Total number of pulses (median, Q1, Q3, N)	140.0 (80.0, 180.0, 307)
Post-dilatation performed	34.8% (106/305)
Total number of lesions with stents implanted	4.9% (15/306)

TL = true lumen.

Chandra V, et al. Presented at: 22nd Annual VIVA Symposium; Nov 3-6, 2024; Las Vegas, NV.

Primary Effectiveness and Stenosis Reduction

Final RS of ≤50%** without serious angiographic complications	**97.9%** (232/237, 95% CI 95.1%-99.3%)
Final RS of ≤30%^ without serious angiographic complications	**74.1%** (215/290, 95% CI 68.7%-79.1%)



** Subject-level analysis. ^ Lesion-level analysis.
MLD = minimal lumen diameter.
Chandra V, et al. Presented at: 22nd Annual VIVA Symposium; Nov 3-6, 2024; Las Vegas, NV.

Angiographic Complications

Core Lab Adjudicated Complications	Post-IVL (n=268)	Final (n=290)
Any Serious Angiographic Complications	1.9% (5/268)	1.0% (3/290)
Abrupt Vessel Closure	0.4% (1/268)	0.3% (1/290)
Distal Emboli[1]	0.0% (0/268)	0.0% (0/290)
Perforation	1.5% (4/268)	0.7% (2/290)
Any Serious Flow-Limiting Dissection (D-F)	0.7% (2/268)	0.3% (1/290)
Thrombus, No Reflow[2], Spasm	0.0% (0/268)	0.0% (0/290)

Any serious angiographic complication defined as flow-limiting dissection, perforation, distal embolization, or acute vessel closure. [1]One patient had a distal thromboembolism post-IVL. Transluminal suction thrombectomy was performed, and the event was successfully resolved although imaging was not provided to the core lab for assessment therefore not included in the figure. [2]No reflow defined as reduced antegrade flow without evidence of residual stenosis or dissection at the treatment site.

2 Perforations at Final Angio

.

Chandra V, et al. Presented at: 22nd Annual VIVA Symposium; Nov 3-6, 2024; Las Vegas, NV.

Primary Safety Endpoint at 30 Days

Measure	Rate	95% CI
Major adverse limb events (MALE) or post-operative death (POD)	0.8% (2/242)	0.1% - 3.0%
All-cause death	0.0% (0/242)	0.0% - 1.5%
Above-ankle amputation of the index limb	0.8% (2/242)	0.1% - 3.0%
Major reintervention	0.0% (0/242)	0.0% - 1.5%

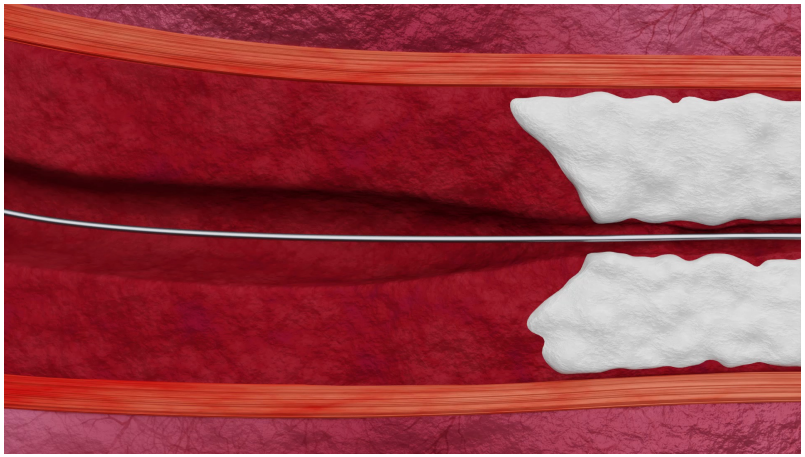
MALE defined as a composite of all-cause death, above-ankle amputation of the index limb, and/or major reintervention to the index limb involving a BTK artery. Both amputation events were reported as not related to the study device or procedure, and the decisions to amputate were made on clinical grounds by the treating physician.

Chandra V, et al. Presented at: 22nd Annual VIVA Symposium; Nov 3-6, 2024; Las Vegas, NV.

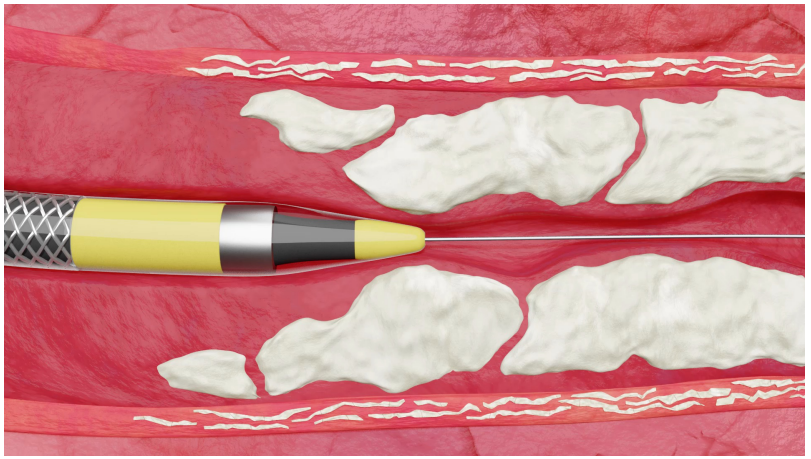
Shockwave Javelin Peripheral IVL Catheter

Modifies calcium and cross sub-total occlusions or extremely narrowed lesions

Tight, difficult-to-cross lesion



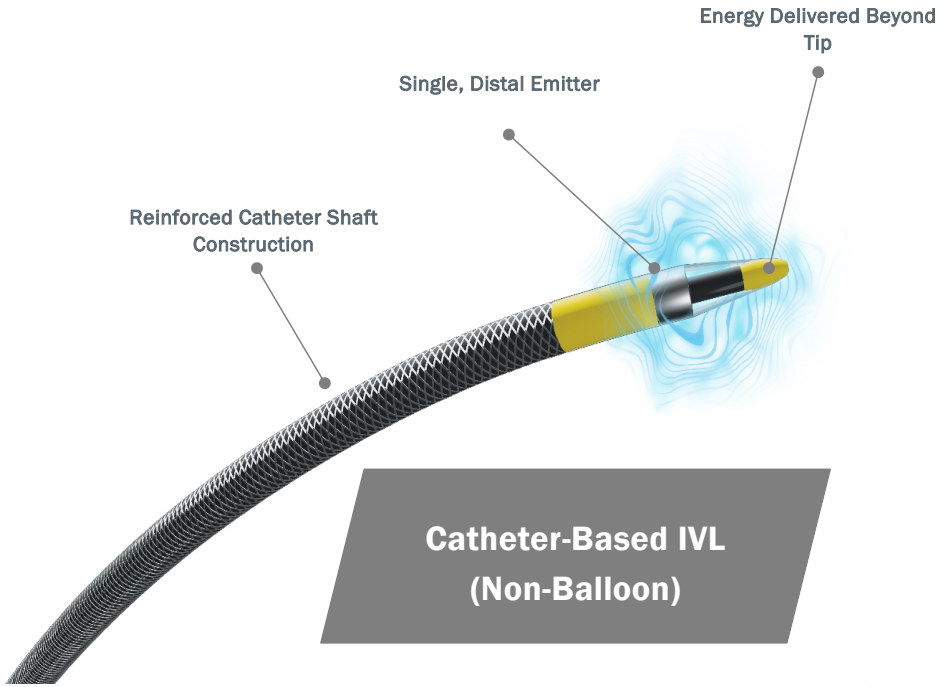
Balloon-based lithotripsy—
emitters in the balloon

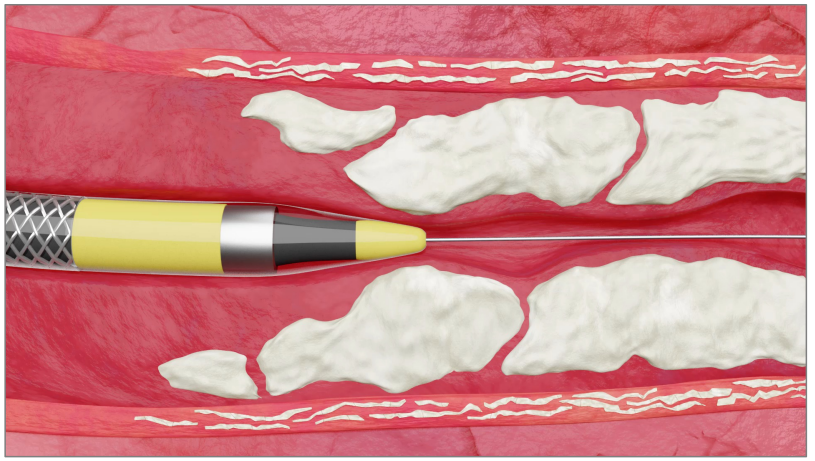


Non-balloon-based lithotripsy—
emitter closer to tip

Shockwave Javelin Peripheral IVL Catheter

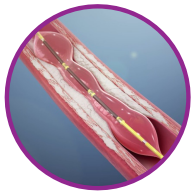
Modifies calcium and cross sub-total occlusions or extremely narrowed lesions



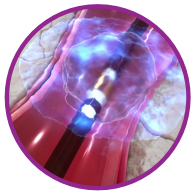


Javelin Leverages the Same IVL MOA

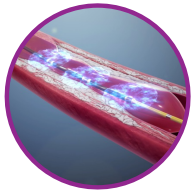
Balloon-Based Shockwave IVL



1. Deliver catheter and inflate to low pressure



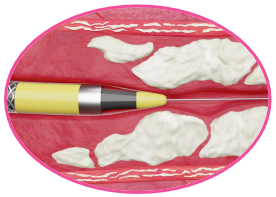
2. Generate sonic pressure waves using lithotripsy



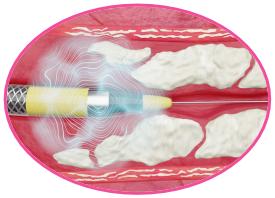
3. Crack both intimal and medial calcium

4. Safely expand the vessel

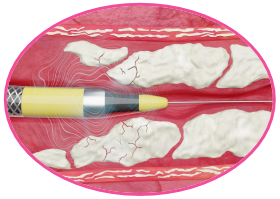
Javelin Non-Balloon-Based Shockwave IVL



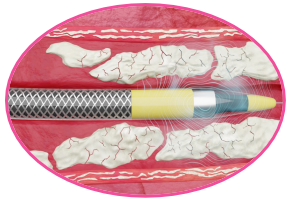
1. Deliver catheter to calcified lesion



2. Generate sonic pressure waves using lithotripsy



3. Modify calcium, create channel

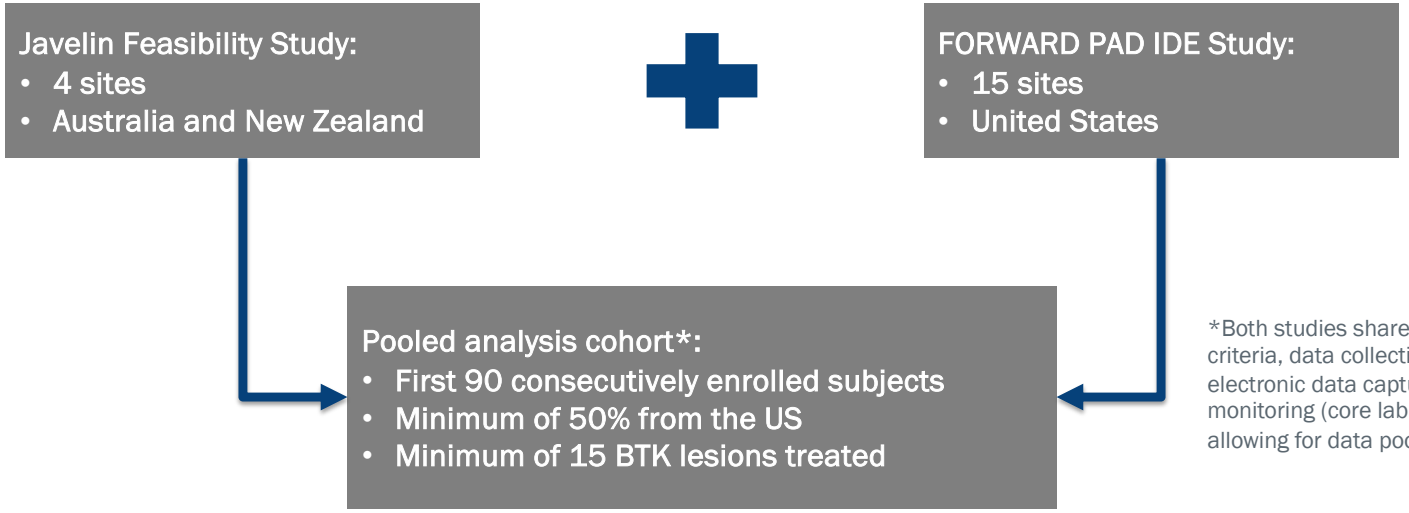


4. Advance catheter, cross lesion

MOA = mechanism of action.

Javelin Feasibility and Forward IDE Studies

Pre-market, prospective, multi-center, single-arm studies* of the Shockwave Medical Javelin Peripheral IVL catheter to treat heavily calcified, stenotic peripheral arteries



*Both studies share the same eligibility criteria, data collection requirements, electronic data capture system, and monitoring (core lab, CEC, data safety) allowing for data pooling

Corl J, VIVA Late Breaking Clinical Trial 2024

Javelin Feasibility Study & Forward PAD IDE Study Analysis

Key Inclusion Criteria:
- At least moderate calcification
- Rutherford Category (RC) 2-5 of target limbs
- Stenosis ≥70% for BTK or ≥90% for ATK lesions
- Lesion length of ≤150 mm

Key Exclusion Criteria:
- Planned use of cutting/scoring balloons, re-entry or atherectomy devices
- In-stent restenosis

Follow-Up Periods:
- 30-days, 6-months, and 12-months

Design

Endpoints

Primary Safety Endpoint
Major Adverse Events (MAE) defined as composite of cardiovascular death, CD-TLR†, or unplanned target limb above the ankle amputation at 30 days

Primary Effectiveness Endpoint
Technical success defined as final residual stenosis of ≤50% without flow-limiting dissection

Secondary Endpoints
Serious angiography complications, IVL Technical Success (post-dilatation), IVL Device Success, and Technical Success (final)

Independent Clinical Events Committee (CEC), Angiographic Core Laboratory, and Duplex Ultrasound Core Laboratory

*Primary analysis was pre-specified to include the first 90 consecutively enrolled subjects across both studies, with a minimum of 50% from the US and a minimum of 15 BTK lesions treated | †CD-TLR = clinically driven target lesion revascularization | Corl J, VIVA Late Breaking Clinical Trial 2024

Patient and Lesion Characteristics

Medical History

- **56.7%** Diabetes Mellitus
- **18.9%** Renal Insufficiency
- **66.7%** Smoking

Rutherford Category

- **43.3%** RC 3 – Severe Claudication
- **12.2%** RC 4 – Ischemic Rest Pain
- **41.1%** RC 5 – Minor Tissue Loss

CLTI

Lesions

- **95.1%** Mod-Severe Ca++[†]
- **0.7 mm** Pre-Procedure MLD
- **42.7%** BTK Lesions
- **38.0%** CTOS

[†]PARC Definition | Corl J, VIVA Late Breaking Clinical Trial 2024

Procedural Details

	90 patients, 105 site reported lesions
Procedure length (min)	96.2 ± 39.3 (90)
Pre-Dilatation	2.9% (3/105)
Number of Javelin catheters per lesion	
1	91.4% (96/105)
2 or more[1]	8.6% (9/105)
Device Success[2]	93.0% (107/115)
Maximum Pressure Used in Javelin IVL	5.1 ± 1.0 (104)
Mean Pulses delivered (N)	89.2 ± 45.7 (104)
Post- Dilatation Performed	98.1% (102/104)
No. of Balloon-based IVL used after Javelin	
None	74.3% (78/105)
1 or more	25.7% (27/105)
Drug-Coated Balloon used	40.0% (42/105)
Embolic protection (no debris found)	6.7% (7/105)
Total Number of Lesions with Stents Implanted	22.9% (24/105)

[1]1.0% (1/105) lesions were treated with 3 Javelin catheters although two had error codes and were not fired | [2]Defined as the ability to deliver, advance across the target lesion, pressurize, pulse, flush and retrieve the Javelin catheter | Corl J, VIVA Late Breaking Clinical Trial 2024

Javelin IVL Shown to Be a Safe Calcium Treatment Option

Core Lab Angiographic Complications

	Post-Javelin IVL	Post-Dilatation	Final
N	85 Lesions	97 Lesions	98 Lesions
Any Serious Angio. Complications (Total)[1]	1.2% (1/85)	4.1% (4/97)	1.0% (1/98)
Dissection (Type D-F)	1.2% (1/85)	4.1% (4/97)	1.0% (1/98)
Perforation	0% (0/85)	0% (0/97)	0% (0/98)
Distal Embolization	0% (0/85)	0% (0/97)	0% (0/98)
Abrupt Vessel Closure	0% (0/85)	0% (0/97)	0% (0/98)
Thrombus	0% (0/85)	0% (0/97)	0% (0/98)
No Reflow	0% (0/85)	0% (0/97)	0% (0/98)
Spasm	0% (0/85)	0% (0/97)	0% (0/98)

Major Adverse Events (MAE)* at 30-Days

Major Adverse Events (MAE)	1.1% (1/90)†
Cardiovascular death	1.1% (1/90)
Clinically-driven target lesion revascularization	0.0% (0/90)
Unplanned target limb major amputation (above the ankle)	0.0% (0/90)

†Cardiovascular death event that was not related to the treated limb, not related to the study procedure, and not related to the study device.

Primary Safety Endpoint Achieved

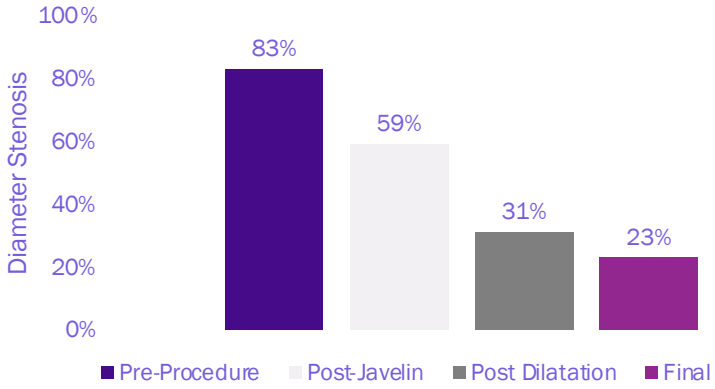
MAE* at 30-days: 1.1%**

- *MAE defined as composite of cardiovascular death, CD-TLR, or unplanned target limb above the ankle amputation at 30 days | **Performance Goal: 11.2%; 95% CI: 0.0%-6.0%, p=0.0012 | Corl J, VIVA Late Breaking Clinical Trial 2024

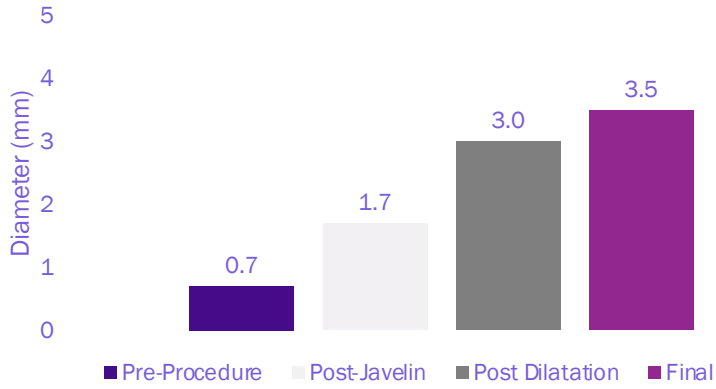
Javelin IVL Shown to Be Effective Calcium Treatment Option

Primary Effectiveness Endpoint Achieved
Final RS ≤ 50% w/o flow-limiting dissection: 99.0%*

Core Lab Measurement	Rate
Lesions with residual stenosis ≤ 30% without flow-limiting dissection	79.6%



Diameter Stenosis – Core Lab

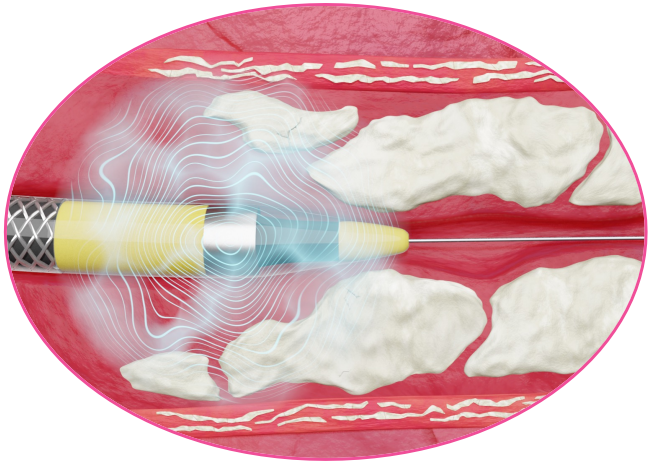


Minimum Lumen Diameter (MLD) – Core Lab

*Performance Goal: 85%; 95%CI: 94.4%-100%, p<0.0001 | Corl J, VIVA Late Breaking Clinical Trial 2024

Conclusions

- Javelin had a crossing success of 93%
- 25% required additional IVL therapies
- 22% required stent implantation
- Excellent safety profile with 1% MAE
- 99% achieved <50% residual stenosis and 79.8% <30% residual stenosis without dissection

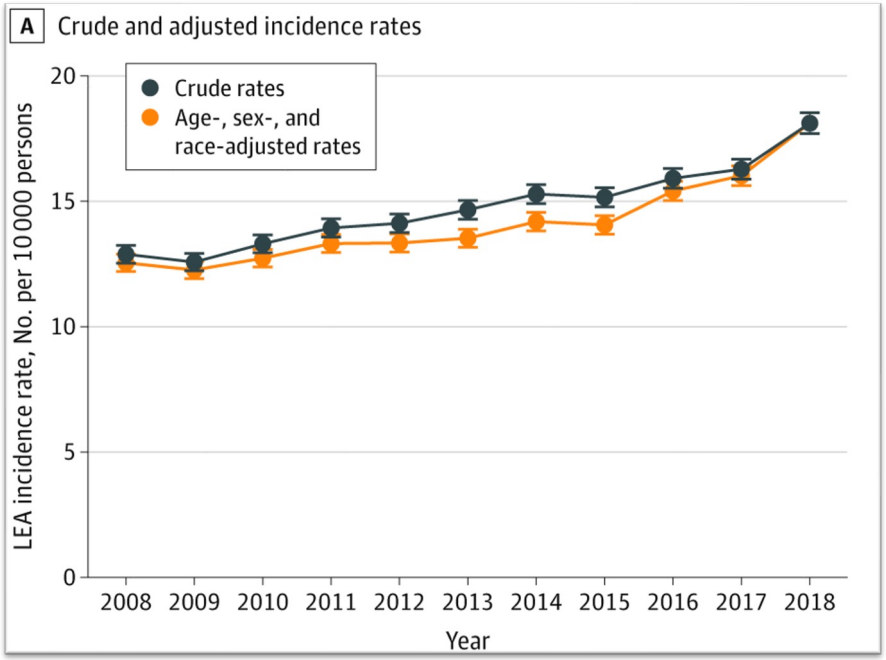


Case 1: How I Do It

Karan Garg, MD

Associate Professor of Surgery, Division of Vascular Surgery,
NYU Langone Medical Center
Bellevue Hospital Center
Manhattan Veterans Affairs Hospital
New York, NY

Increasing Prevalence and Complexity of Peripheral Arterial Disease (PAD)



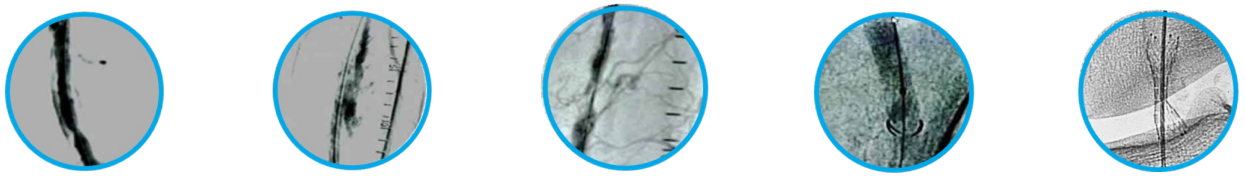
Cai M, et al. *JAMA* Network Open Access 2021.

Why Does Calcium Matter? Difficulty Crossing Lesions

Table 4. Logistic Regression Analysis Identifying Risk Factors for Antegrade Crossing Failure.[a]

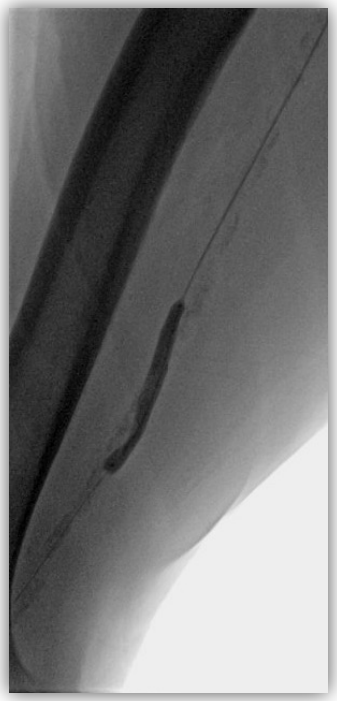
Variable	Odds ratio	95% confidence interval	p-value
Calcification	4.20	1.71–10.29	0.002
Circumferential calcium	2.53	1.32–4.86	0.005
CTO of the proximal SFA	3.52	1.68–7.39	0.0009
CTO of the P3 segment	4.06	1.52–10.84	0.005
CTOP type III or IV	1.91	1.39–2.60	<0.0001

Abbreviations: CTO, chronic total occlusions; SFA, superficial femoral; CTOP, chronic total occlusion crossing approach based on plaque cap morphology.
[a]Variables analyzed in the model not reaching statistical significance: Flush SFA occlusion, lesion length > 25 cm, lesion length > 15 cm, Mid SFA CTO, Distal SFA CTO, P1 CTO, and P2 CTO.

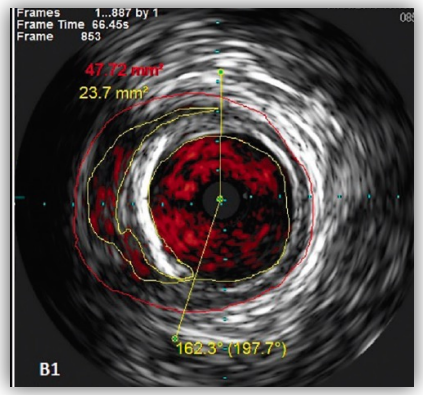


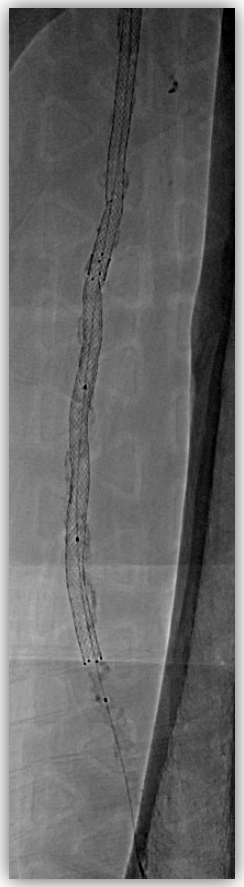
Dissections **Perforations** **Vessel Recoil** **Embolization** **Stent Crush**

How Does Calcific Disease Impact Femoral Popliteal Treatment?

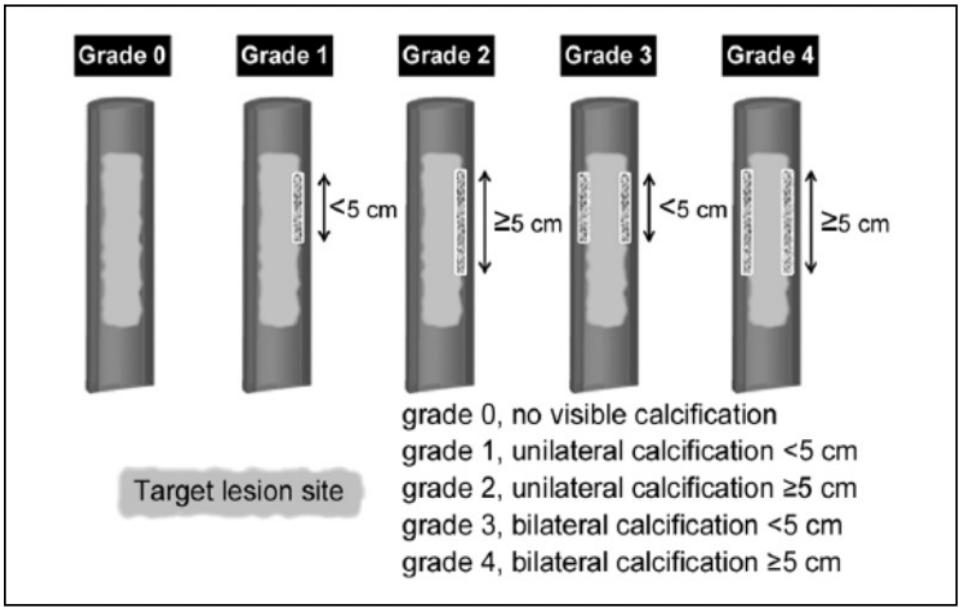


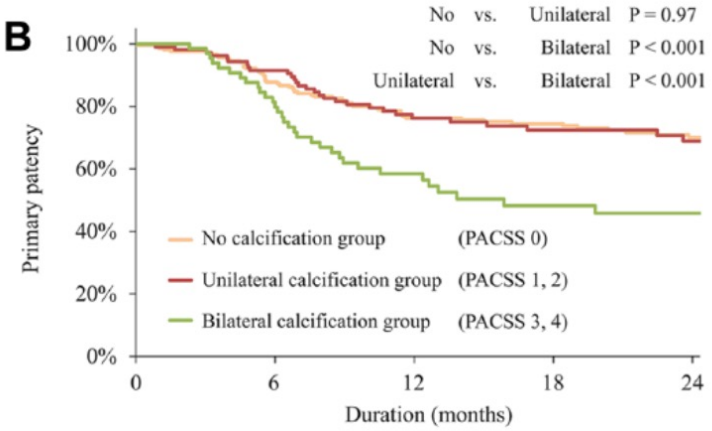
- Difficulty in lesion crossing
- Poor luminal gain with balloon angioplasty
- Increasing rate of dissection
- Increased post-angioplasty recoil
- Perforation
- Poor stent wall apposition





Impact of Peripheral Artery Calcification Scoring System (PACSS) on Outcomes



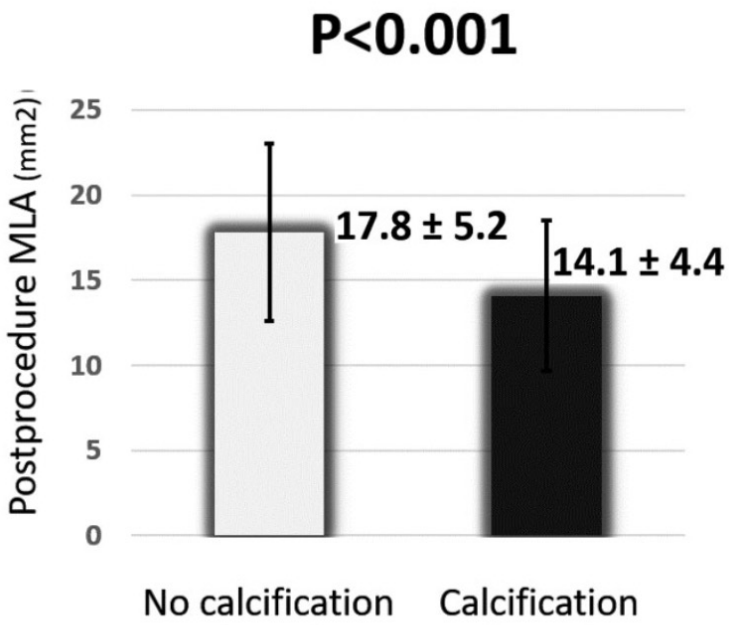


Okuno S, et al. *J Endovasc Ther*. 2016;23(5):731-737.

Why Does Calcium Matter? Luminal Gain

>180-degree calcification = strongest correlation to post-procedure minimal luminal gain on multivariate analysis

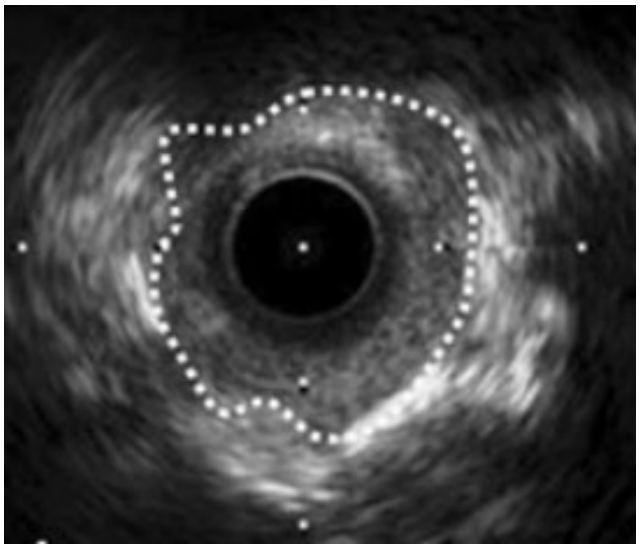
*Remains true on multivariable analysis

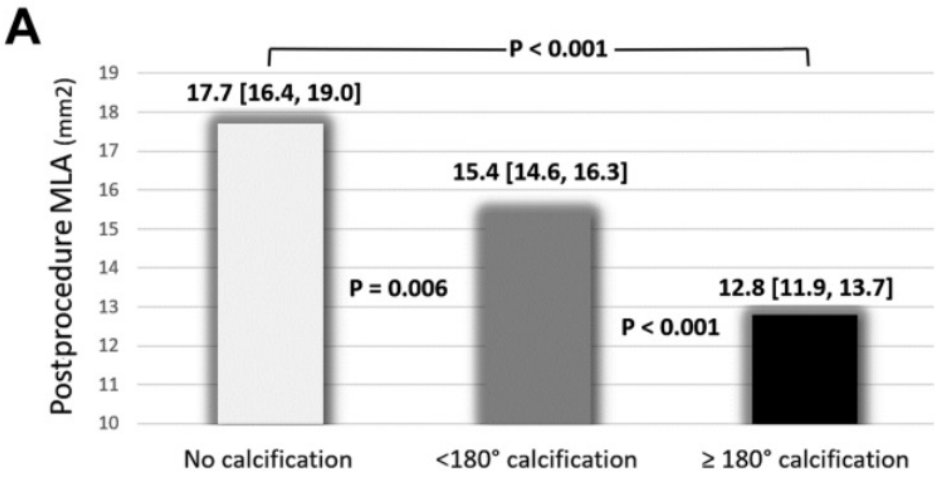


Fujihara M, et al. *J Endovasc Ther*. 2019;26(3):322-330.

Why Does This Matter? Restenosis

- **Restenosis** rate significantly higher in severely calcified group ($p<0.018$)

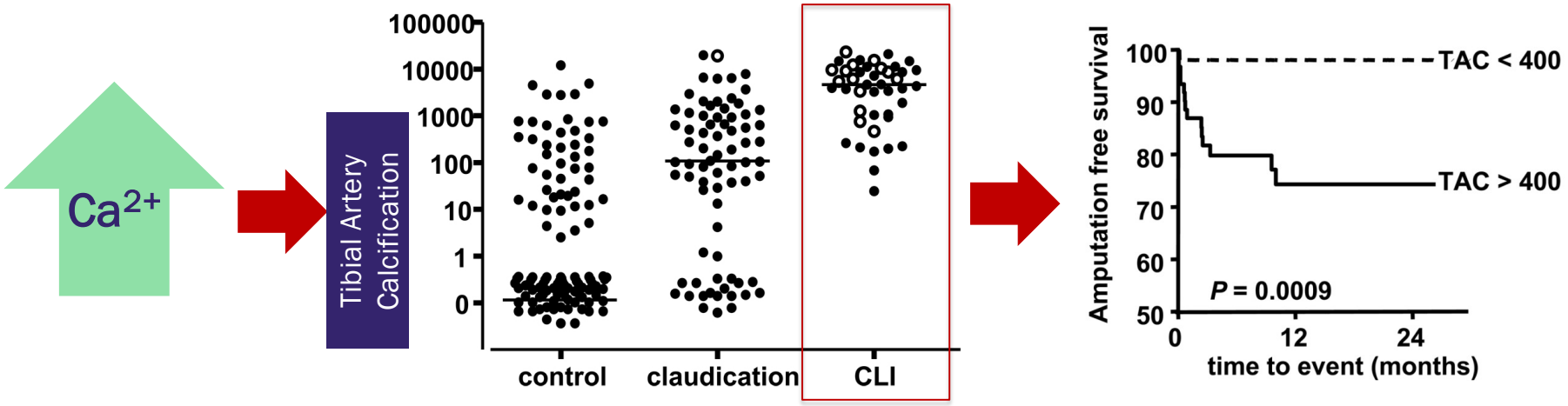




Fujihara M, et al. *J Endovasc Ther*. 2019;26(3):322-330.

Challenges of BTK: The Role of Calcium

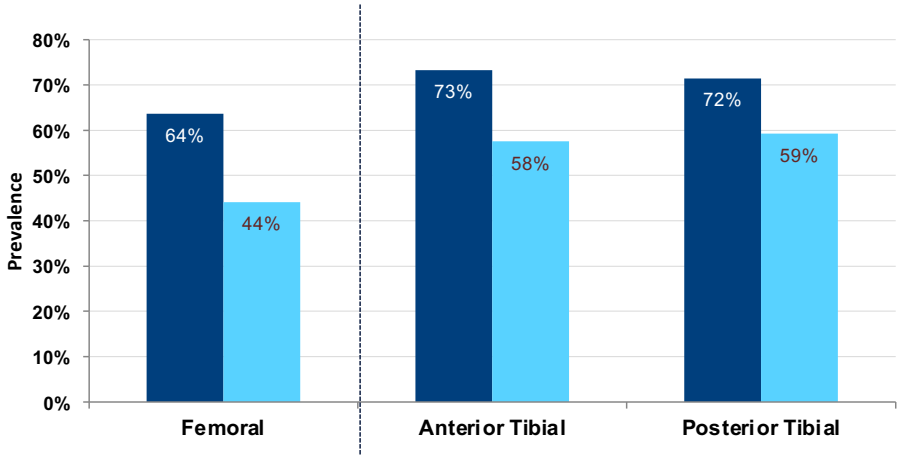
Tibial artery calcification is an independent predictor of ischemia severity, wound healing rate,[1] and amputation risk[2]

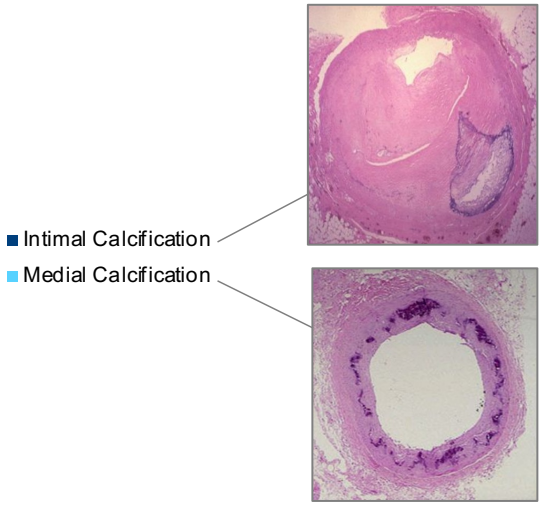


1) Mori et al, Relationship between tibial artery calcification and wound healing in patients with foot tissue loss, LINC 2017
2 Guzman et al, Tibial artery calcification as a marker of amputation risk in patients with PAD, JACC 2008

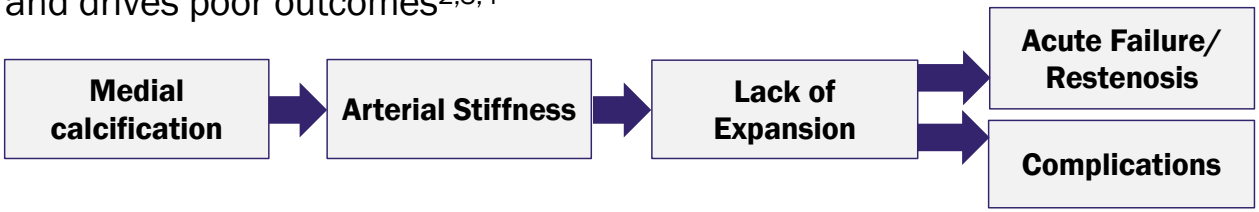
Medial Calcium Is Increasingly Common Below-the-Knee

- Medial calcium is more prevalent in BTK arteries[1]





- Medial calcification produces arterial stiffness and drives poor outcomes[2,3,4]



1) Soor et al, Pathology. 2008. 2) Guzman et al, JACC. 2008. 3) Zettervall et al, 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

Early Recoil Post-PTA Jeopardizes BTK Results; Medial Calcium

- Early recoil (~29% re-narrowing) occurs in ~97% of cases, 15 min. post-PTA

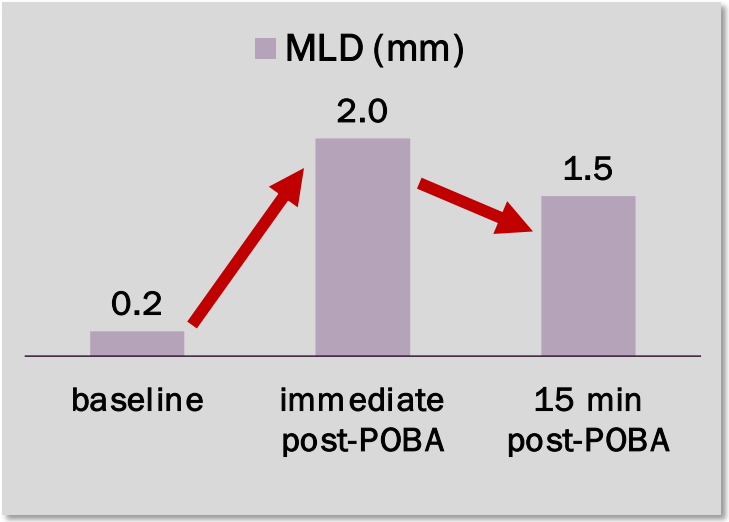
44 J ENDOVASC THER 2014;21:44–51

◆CLINICAL INVESTIGATION ◆

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

Frederic Baumann, MD[1,2]; Jacqueline Fust[3]; Rolf Peter Engelberger, MD[1]; Ulrike Hügel, MD[1]; Do-Dai Do, MD[1]; Torsten Willenberg, MD[1]; Iris Baumgartner, MD[1]; and Nicolas Diehm, MD[1]

[1]Department of Clinical and Interventional Angiology, Swiss Cardiovascular Center, and
[2]Department of Internal Medicine, Inselspital, University Hospital of Bern, Switzerland.
[3]Department of General and Orthopedic Surgery, Hospital of Münsterlingen, Switzerland.



Baumann F, et al. *J Endovasc Ther*. 2014;21(1):44-51.

Role of Plaque Modification in BTK Revascularization

Optimize acute results to improve long-term outcomes

- ✓ Increase lumen gain (size)
- ✓ Increase lumen stability (avoid recoil)
- ✓ Increase vessel compliance (ability to dilate)
- ✓ Reduce potential barrier to drug absorption (increase tissue permeability and prevent restenosis)
- ✓ Avoid flow-limiting dissections (need for stents)

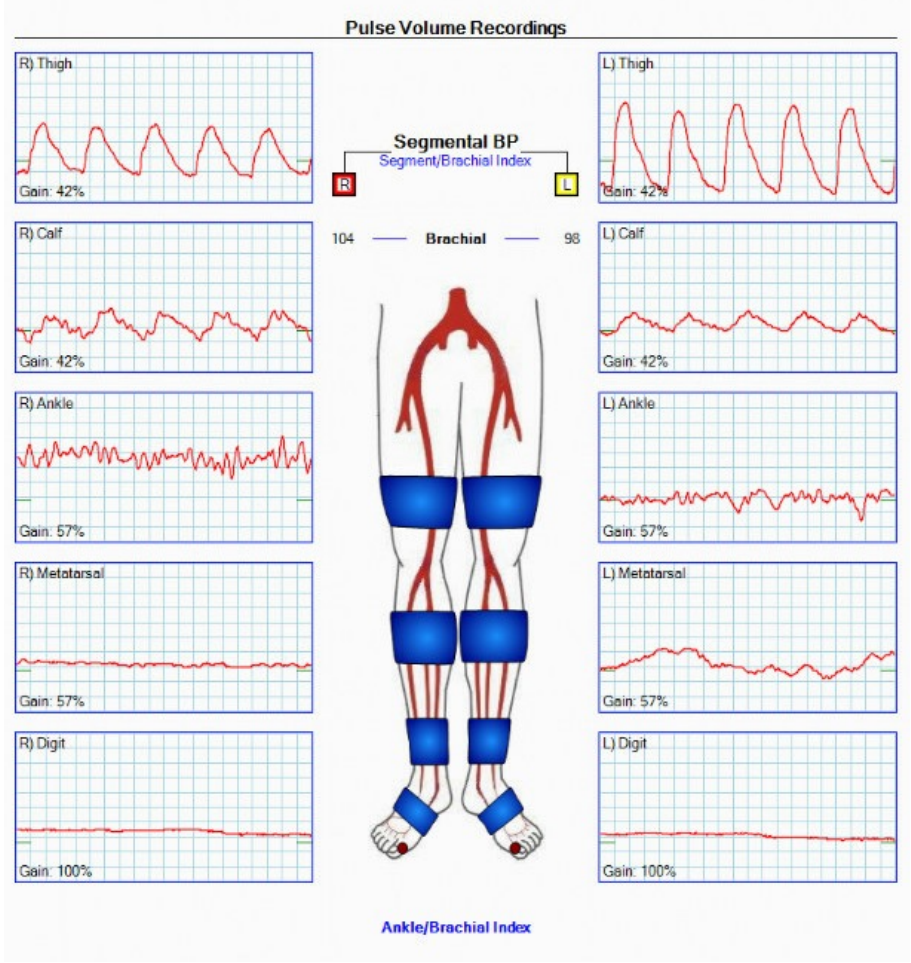
especially important in the small-sized and slow-flow BTK vasculature

In heavily calcified lesions, what tools do we have to optimize success?

- Luminal gain
- Minimize dissection
- Change vessel compliance

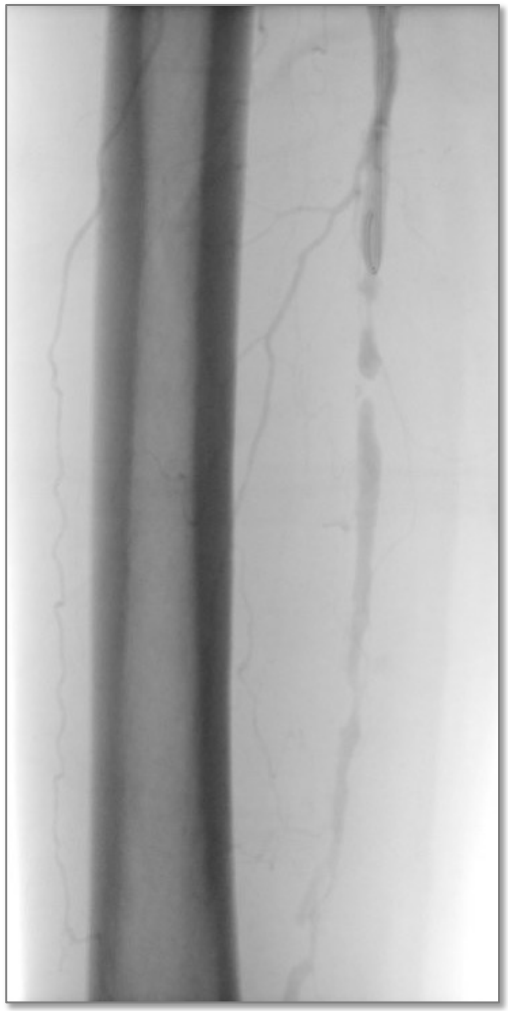
E8 Case

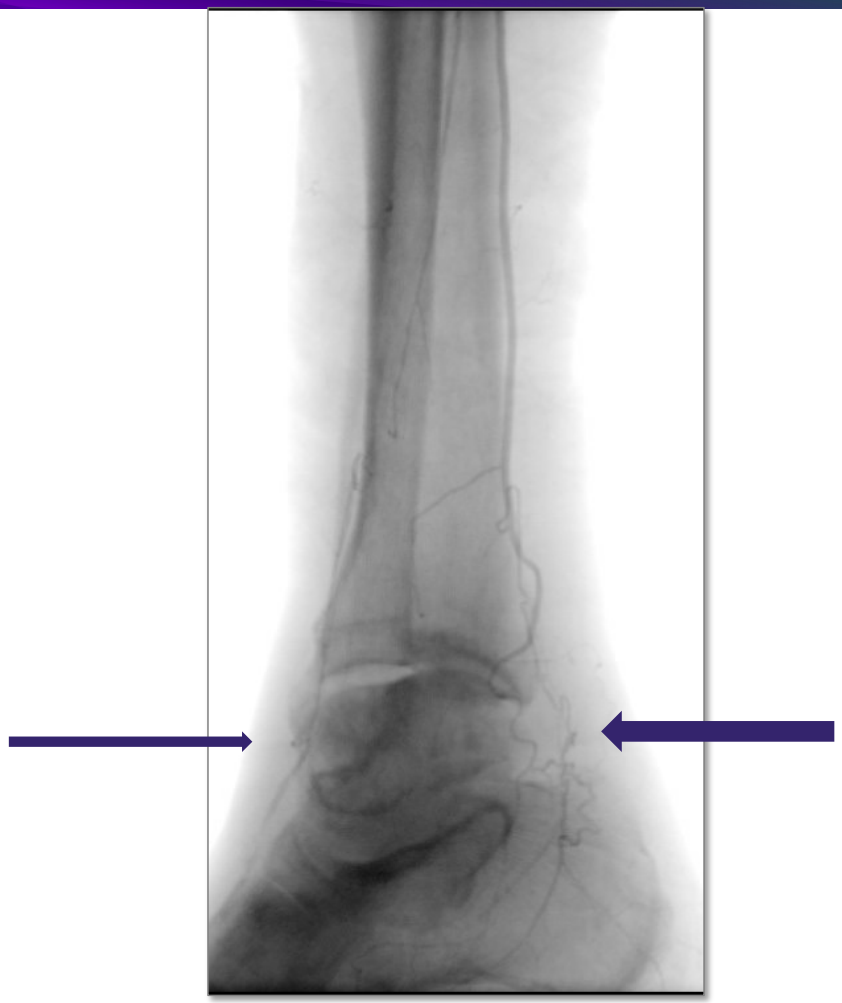
- 78y Male with bilateral gangrene
- PMHx: HTN, CAD
- Smoker
- BMI: 18


Pulse Volume Recordings
R) Thigh
Gain: 42%
L) Thigh
Gain: 42%
Segmental BP
Segment/Brachial Index
R
L
104
Brachial
98
R) Calf
Gain: 42%
L) Calf
Gain: 42%
R) Ankle
Gain: 57%
L) Ankle
Gain: 57%
R) Metatarsal
Gain: 57%
L) Metatarsal
Gain: 57%
R) Digit
Gain: 100%
L) Digit
Gain: 100%
Ankle/Brachial Index

What would you do next?

- CTA/MRA
- Angiogram
- Amputation





What Do You Want to Treat?

- Anterior tibial
- Posterior tibial

Case 2: How I Do It

Sameh Sayfo, MD

Endovascular Fellowship Program Director
Assistant Professor
Baylor Scott & White The Heart Hospital Plano
Plano, TX

Outline

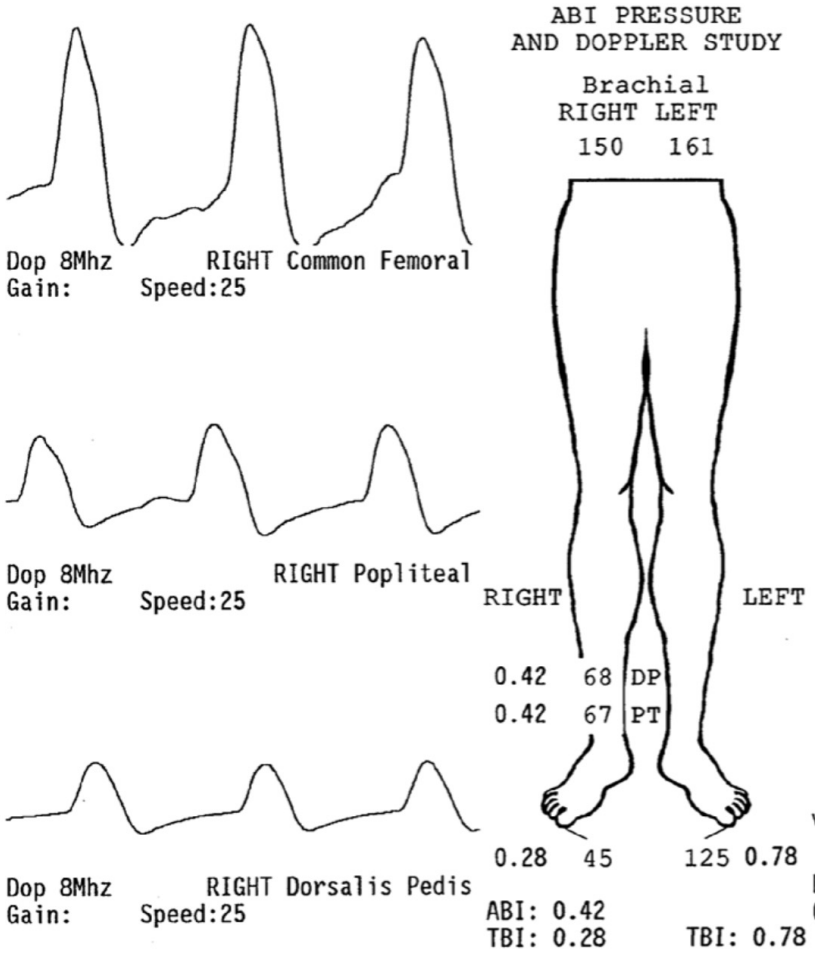
- How to assess calcification (IVUS or not IVUS)
- IVUS role in below-the-knee therapy
- Dual access vs single access
- IVL role and application
- IVL vs specialty balloon vs regular balloon vs atherectomy
- Stent vs no stent in CLTI treatment

Case 1

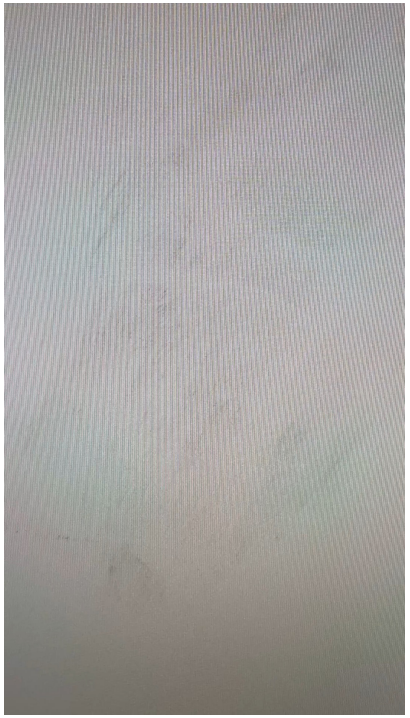
- Patient is a 63y Female
- PMHX: CAD, HLD, DMII, PAD
- Previous procedure
- PTCA of pop and prox ATA with DCB of pop (2 yrs ago)

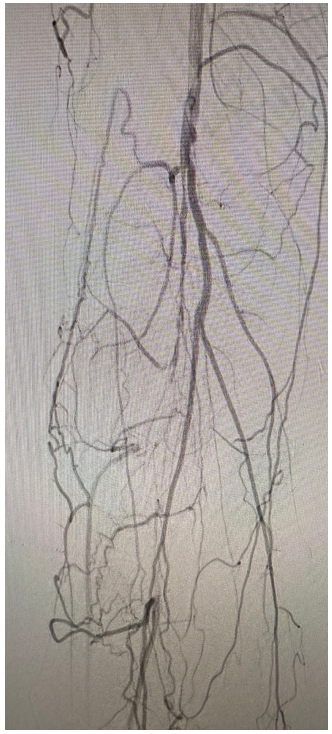
- Worsening claudication over 6 months, then non-healing wound of RLE and resting pain over 6 wks

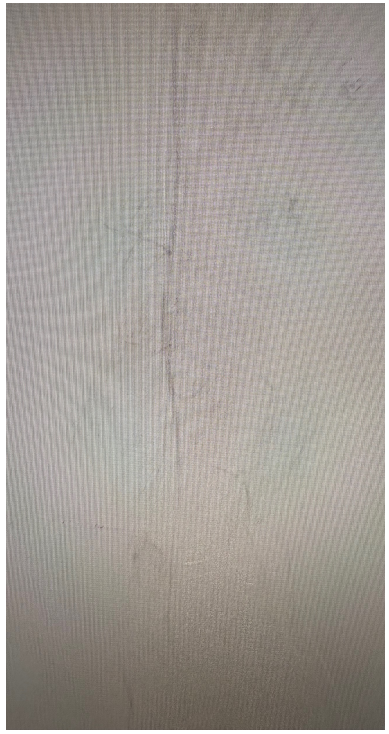
- US showed occluded R popliteal vessel and severe below-the-knee disease



Angiogram



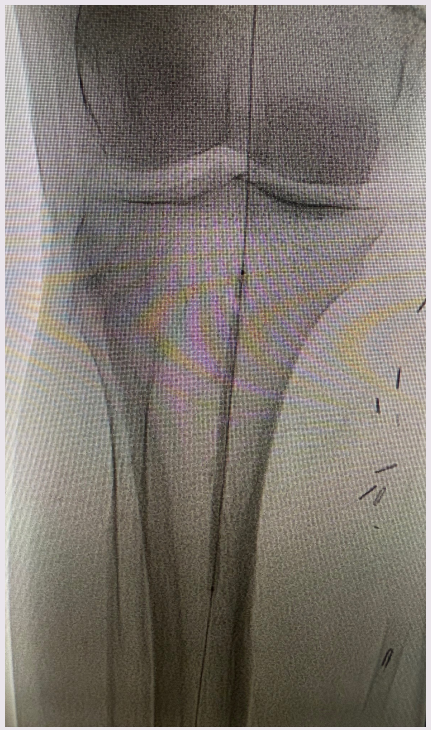




Wire Crossed to Peroneal

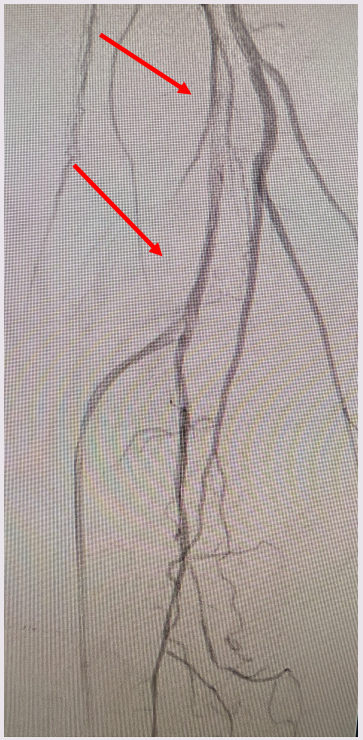
What to do next?

1) Pedal access
2) Dual lumen catheter
3) IVUS guided crossing
4) Other



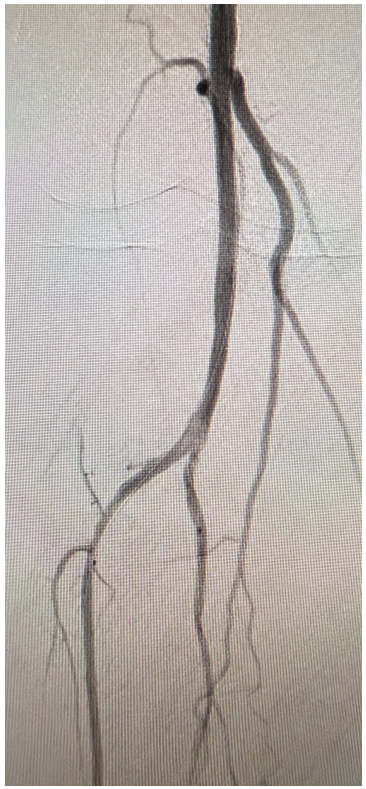
What's Next ?

1) IVUS
2) Atherectomy (Laser, directional atherectomy, etc.)
3) Serration balloon
4) IVL



Zeller T, et al. *J Am Coll Cardiol.* 2014;64(15):1568-1576. Mustapha JA, et al. *J Invasive Cardiol*. 2019;31(8):205-211. Zeller T, et al. *JACC Cardiovasc Interv.* 2015;8(12):1614-1622.

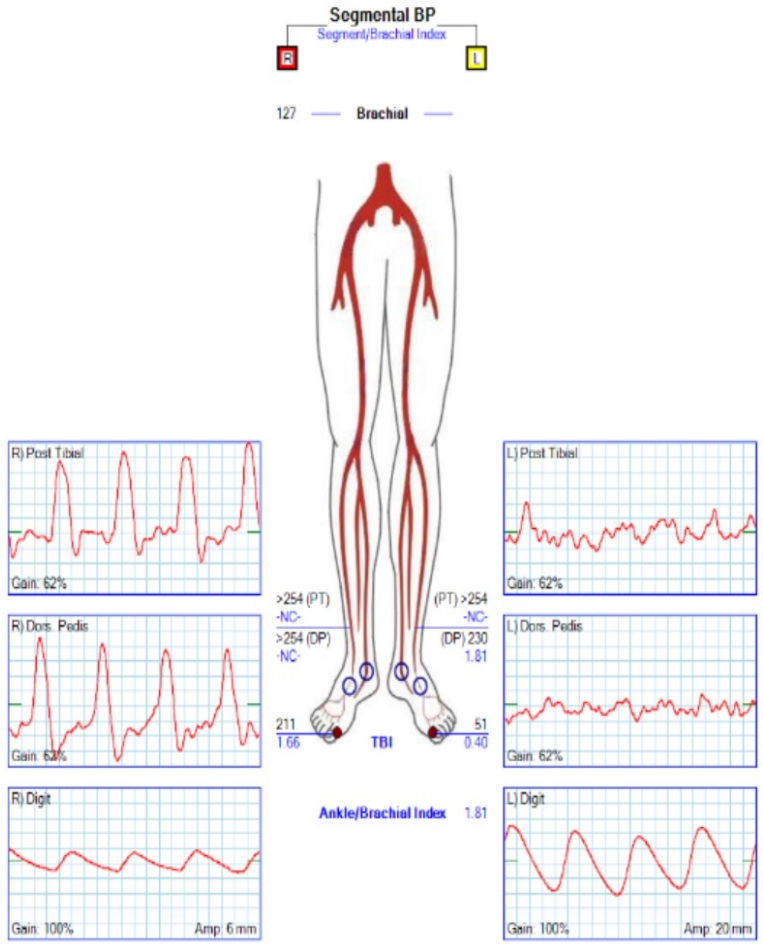
Final Angiogram Post Stent



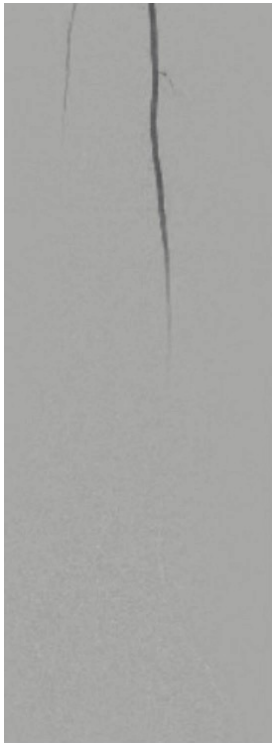
Varcoe RL, et al. *N Engl J Med*. 2024;390(1):9-19.

Case 2: Heavy Calcification

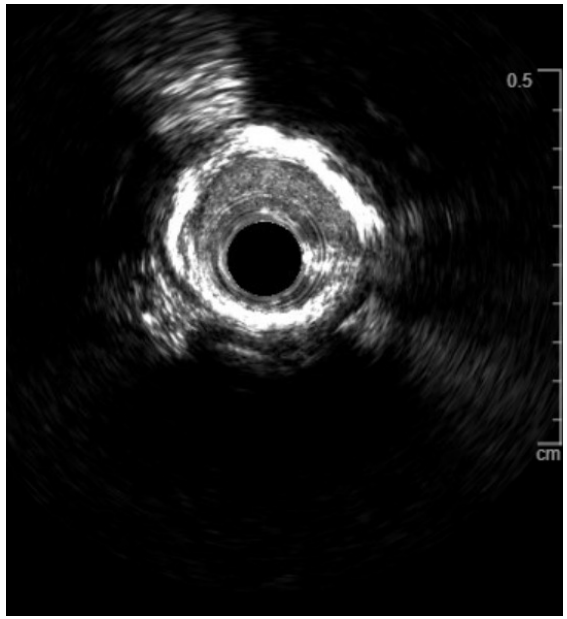
- Patient is an 84y Male with non-healing wound and resting pain
- ABI is 1.8 (NC) with abnormal TBI
- Angiogram shows normal ATK anatomy with two-vessel BTK and one vessel subtotal occluded



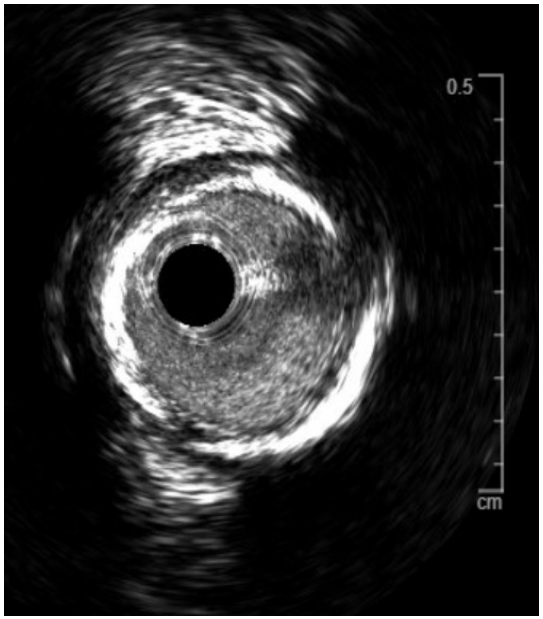
Pre



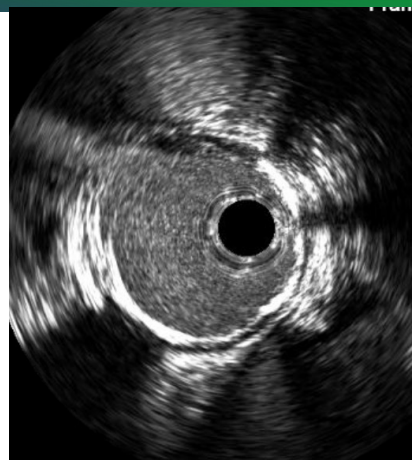
IVUS

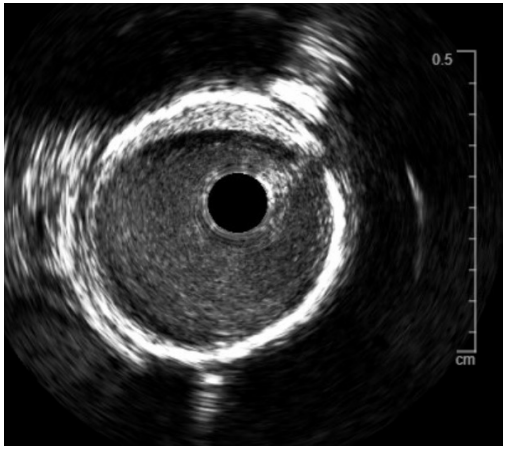


Pre



Post IVL

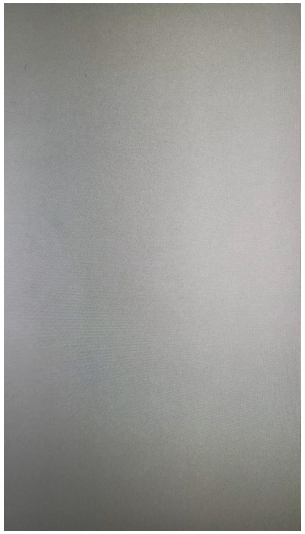


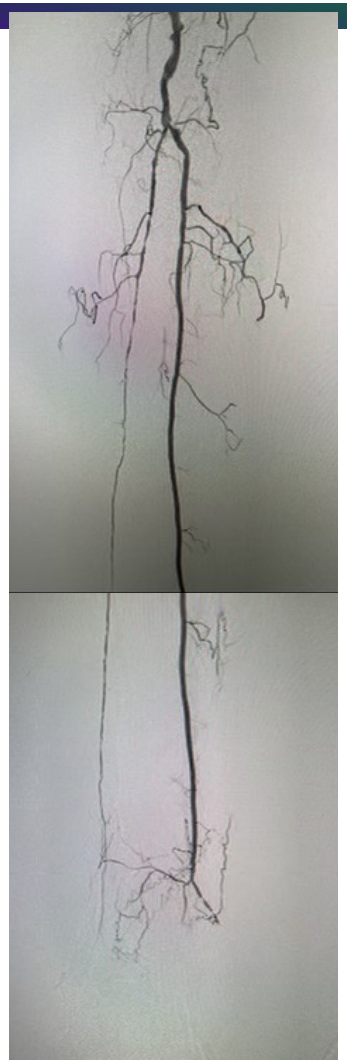


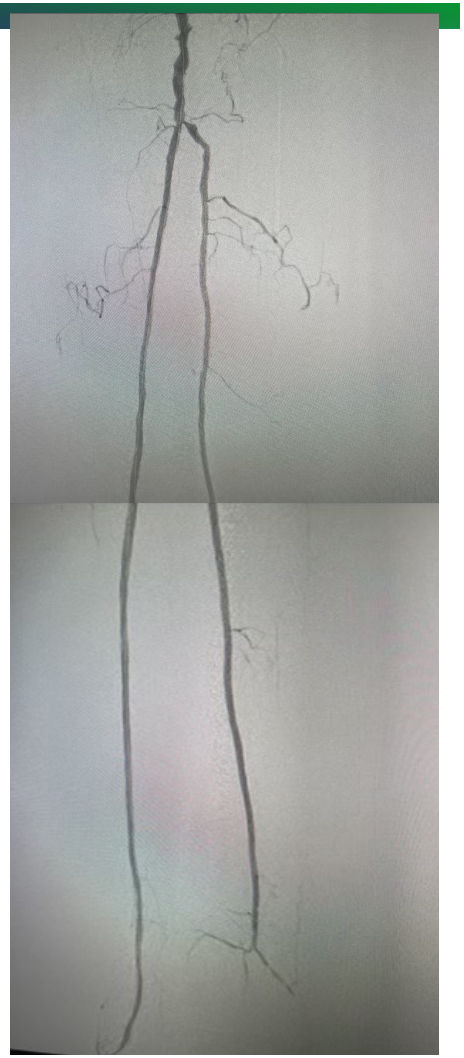
Post Final Therapy

Procedure Details

- Contralateral femoral access
- Lesion was crossed with Command™ 0.018 and NAVICROSS® support catheter
- IVUS showed severe calcification
- E8 3X80 used

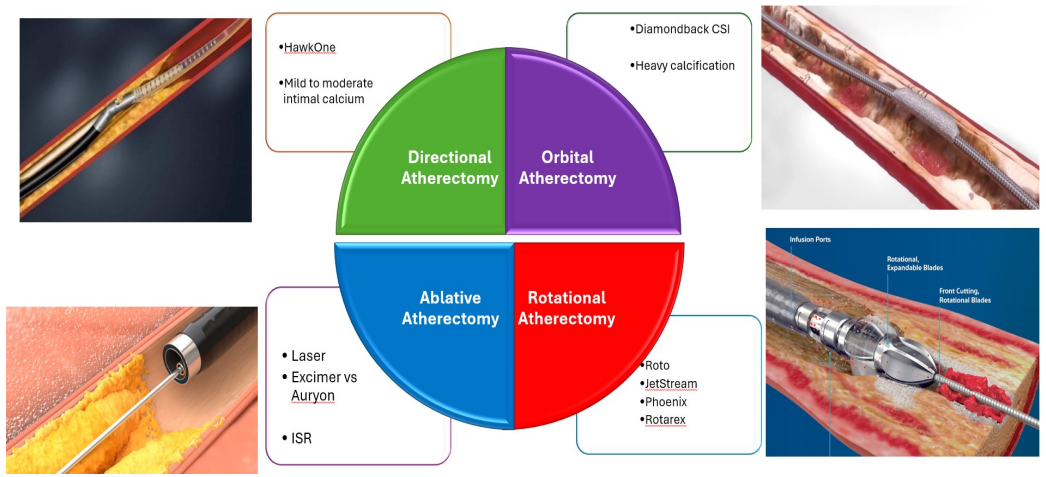






Questions

1) Should we have performed arch reconstruction?
2) Did IVL do the job? IVUS interpretation
3) Role of atherectomy in BTK treatment (+/- IVL)
4) Stent vs no stent?

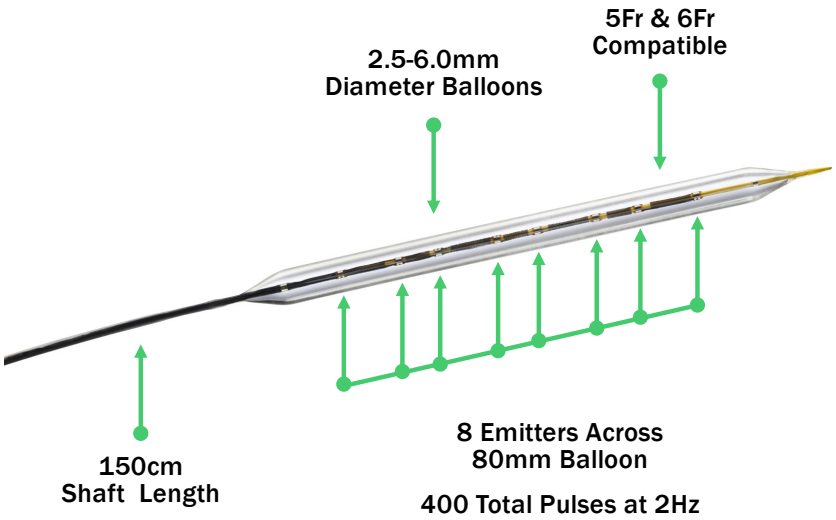


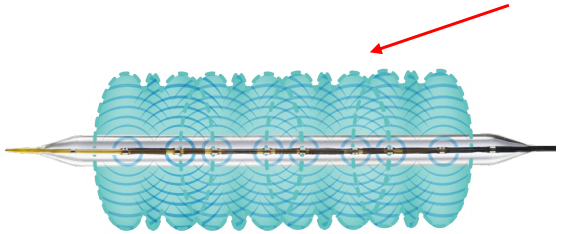
(a) Major disadvantages for all atherectomy devices are the possibility of distal embolization, contraindication following subintimal lesion crossing, and increased overall procedural time.

Katsanos K, et al. *Cardiovasc Intervent Radiol.* 2017;40(7):964-977.

Peripheral IVL Catheters

Treatment of superficial and deep calcium ATK and BTK



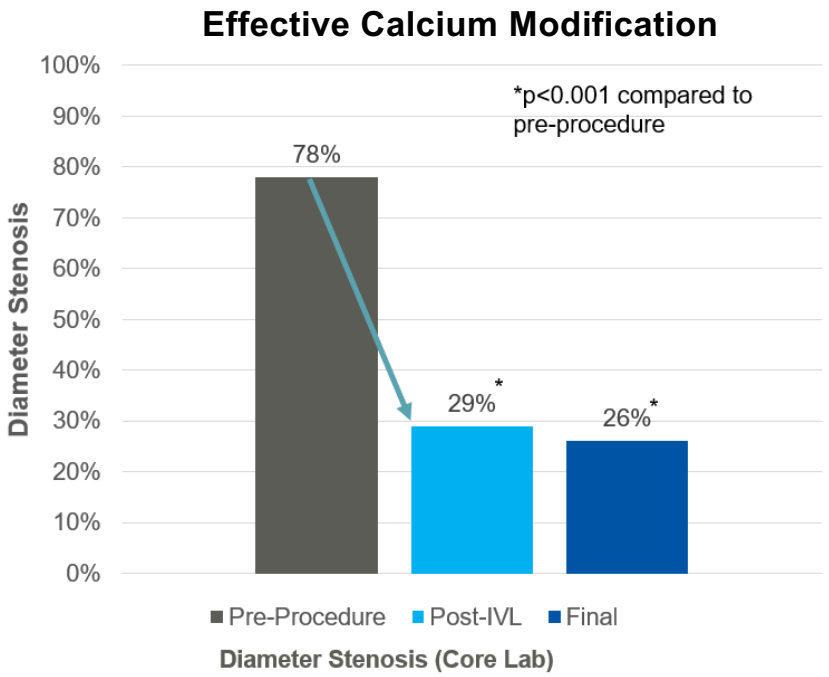


Acoustic Peak Pressure Align with Emitter Location

Balloon Diameter (mm)	Balloon Length (mm)	Guidewire Compatibility (in)	Sheath Compatibility	Catheter Working Length (cm)	Max Pulse Count
2.5 & 4.0	80	0.014	5F	150	400
5.0 & 6.0	80	0.014	6F	150	400

Lesion Stenosis and Calcium Modification

IVL can reduce lesion stenosis with minimal additional treatment therapy

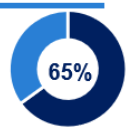


*Remaining Stent/Tack implants were part of physicians' standard algorithm
Holden A, CIRSE Late Breaking Clinical Trial 2024

Core Lab Angiographic Measurements	Post-IVL (n=268)	Final (n=290)
Residual Stenosis ≤ 50%	95.1% (255/268)	99.0% (287/290)
Residual Stenosis ≤ 30%	62.3% (167/268)	74.8% (217/290)

Procedural Information

No pre-dilatation



No post-dilatation

Successful IVL Catheter Delivery Across Target Lesion

Total Stent/Tack Implant

Provisional Stent/Tack Implant*

Armstrong EJ, et al. *J Endovasc Ther*. 2024 Oct 18:15266028241283716.

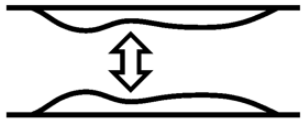
In a patient cohort, IVL was shown to be safe and effective in treating calcific lesions BTK with minimal need for provisional stenting

Safety

1.9% Post-IVL | **1.0%** Final

Total Serious Angiographic Complications

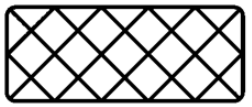
Effectiveness



29% Post-IVL | **26%** Final

Avg. Residual Stenosis

Provisional Stenting



4.9% Total | **2.3%*** Provisional

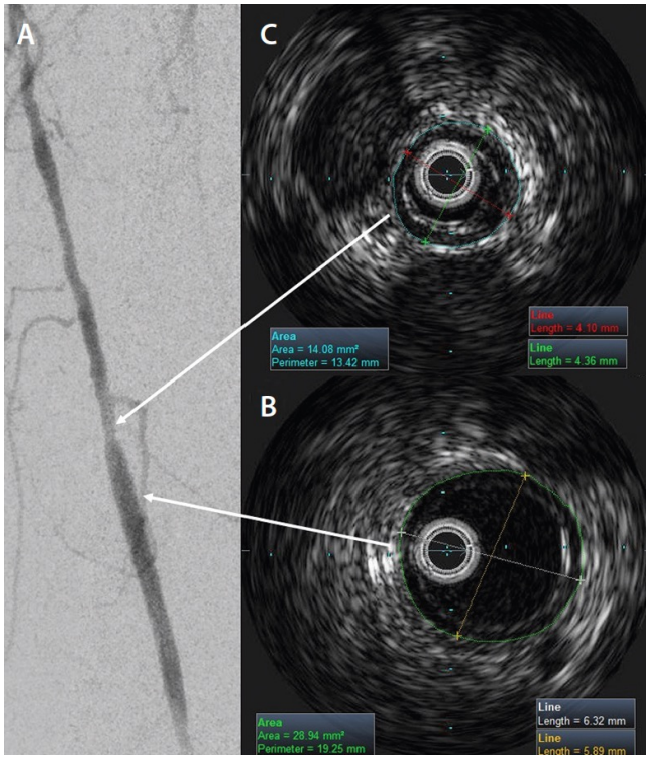
Stent/Tack Implant

*Remaining Stent/Tack implants were part of physicians' standard algorithm
Holden A, CIRSE Late Breaking Clinical Trial 2024

Armstrong EJ, et al. *J Endovasc Ther*. 2024 Oct 18:15266028241283716.

Lesion Assessment

- Use of intravascular imaging is key!
- IVUS associated vessel size 1mm greater than angiographically derived vessel size in one study and .5mm in another
- IVUS leads to use of larger balloons for PTA and 54 days shorter wound healing in Soga, et al cohort
- IVUS permits lesion characterization fibrous, calcified, etc.



Allan RB, et al. *Endovasc Today*. S2022;21(9):46-53. Shammas NW, et al. *J Endovasc Ther*. 2020;27(4):575-580. Soga Y, et al. *Catheter Cardiovasc Interv*. 2021;97(3):E376-E384.

Thank You

X: @samsayfo
317.313.8356
ssayfo83@gmail.com

Case 3: How I Do It

Constantino Peña, MD, FAHA, FSCCT, FSIR
Medical Director of Vascular Imaging,
Miami Cardiac & Vascular Institute
Miami, FL

Endovascular Treatment for Calcified PAD

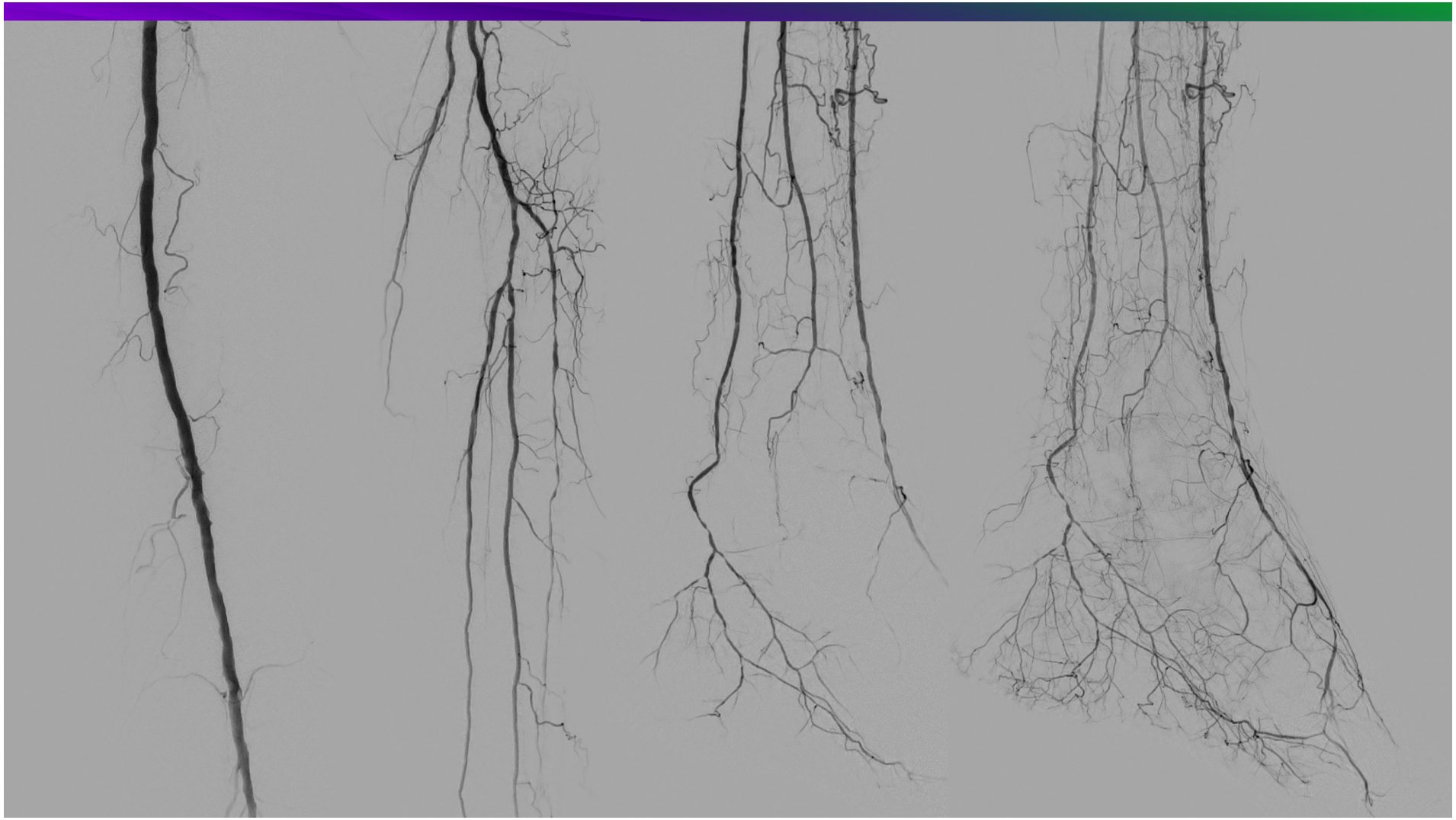
- Known to be the most challenging cases
- Patients with significant calcification usually excluded from trials
- Treatment with PTA, specialty balloons, stents, and atherectomy are of higher cost and more possible complications
- Distal embolization, dissection, and perforation remain a concern with atherectomy treatment

Creating an Algorithm for BTK Lesions

- Lesion factors
  - Location, length, outflow of that vessel, and outflow of other vessels important
- Indication
  - Gangrene or tissue loss
- Expectation prior to treatment
- Patient factors
  - DM, ESRD
- Prior treatments
  - Successful?
  - Duration?

Case

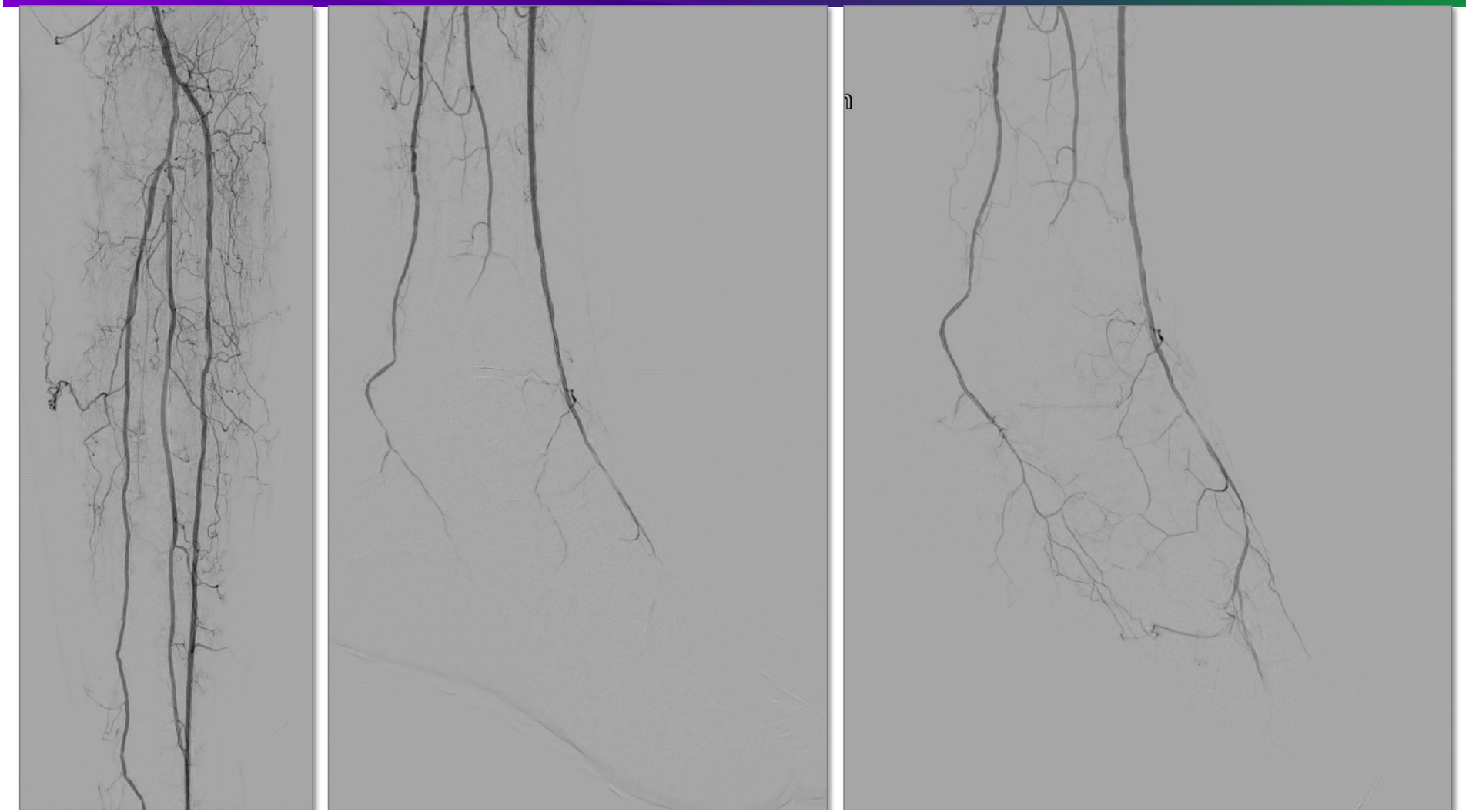
- 68y Male with left toe ulceration, ESRD, s/p right TMA



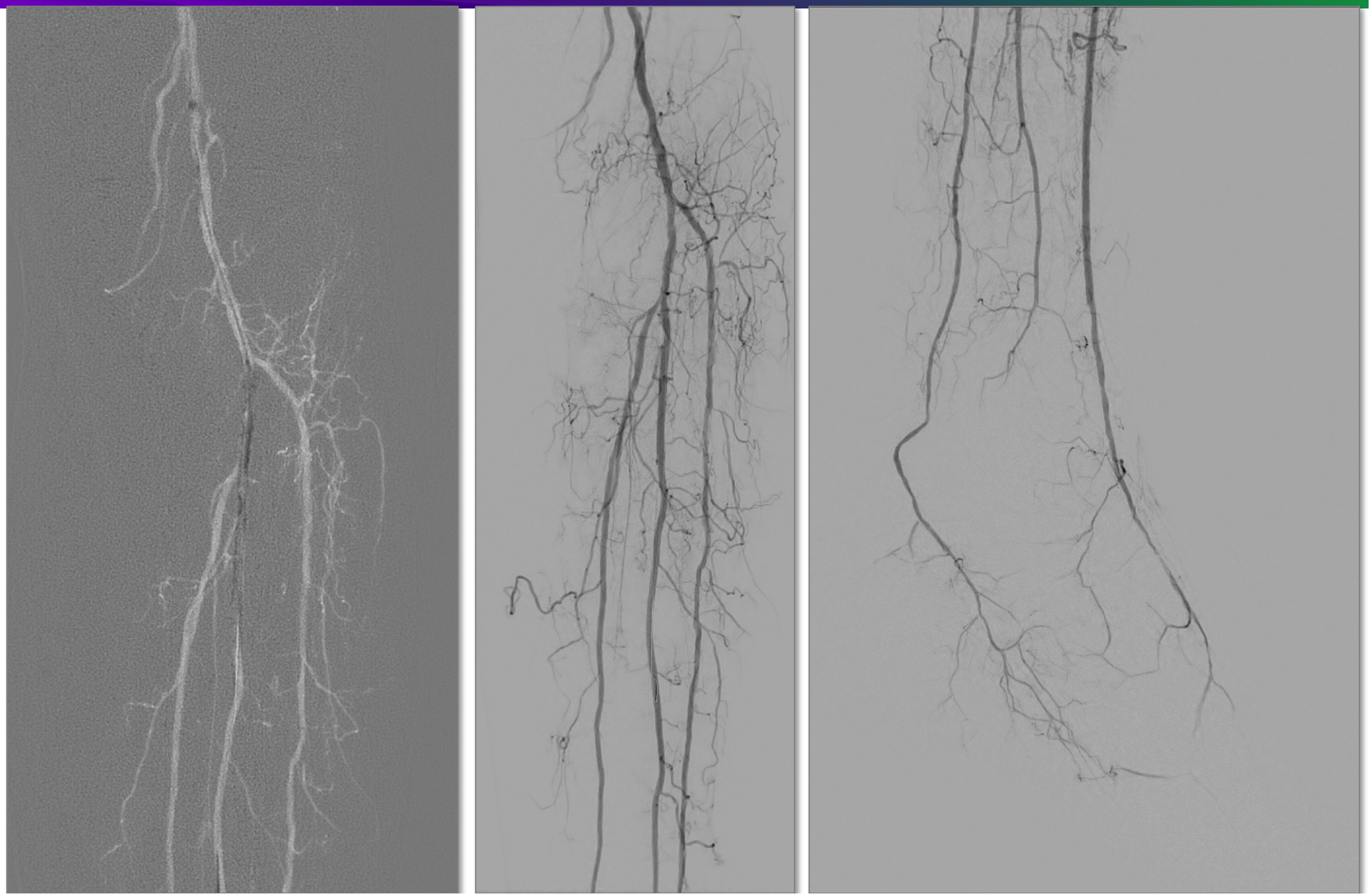
What to Do?

Non-healing toe ulcer

3mm E8 AT



3mm E8
Peroneal



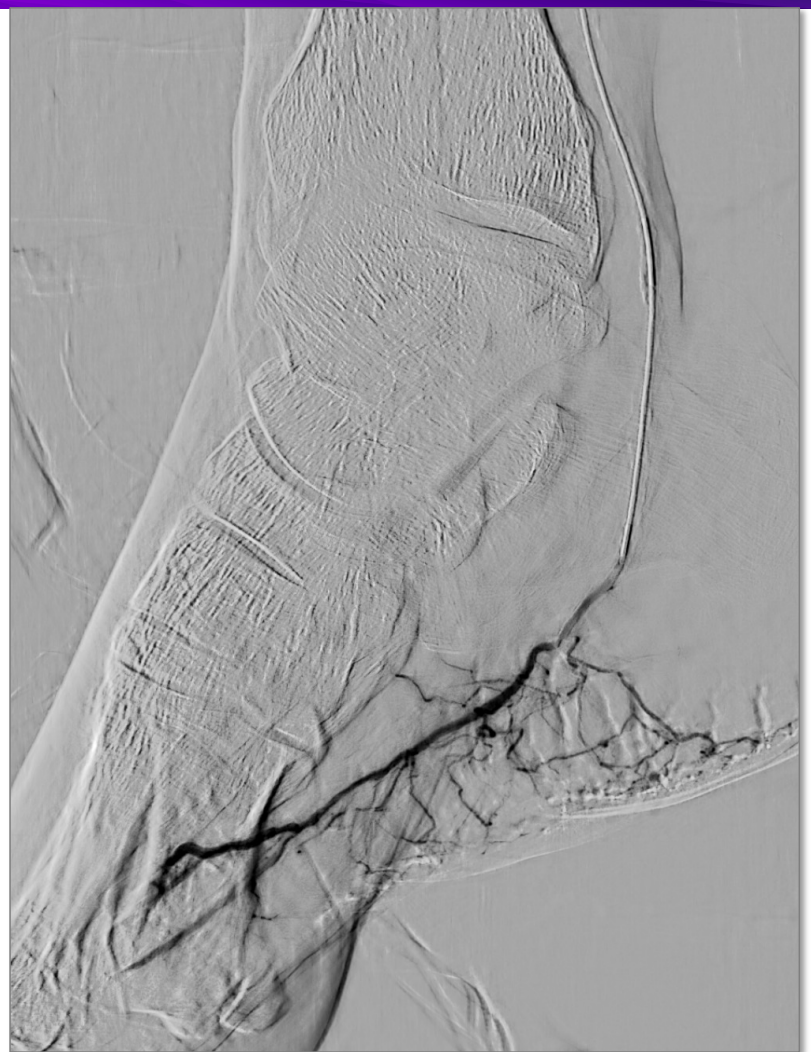
Case

- 85y with non-healing first hallux amputation
- Nail avulsion complicated to amputation
- Initially treated with PTA with short term-recoil

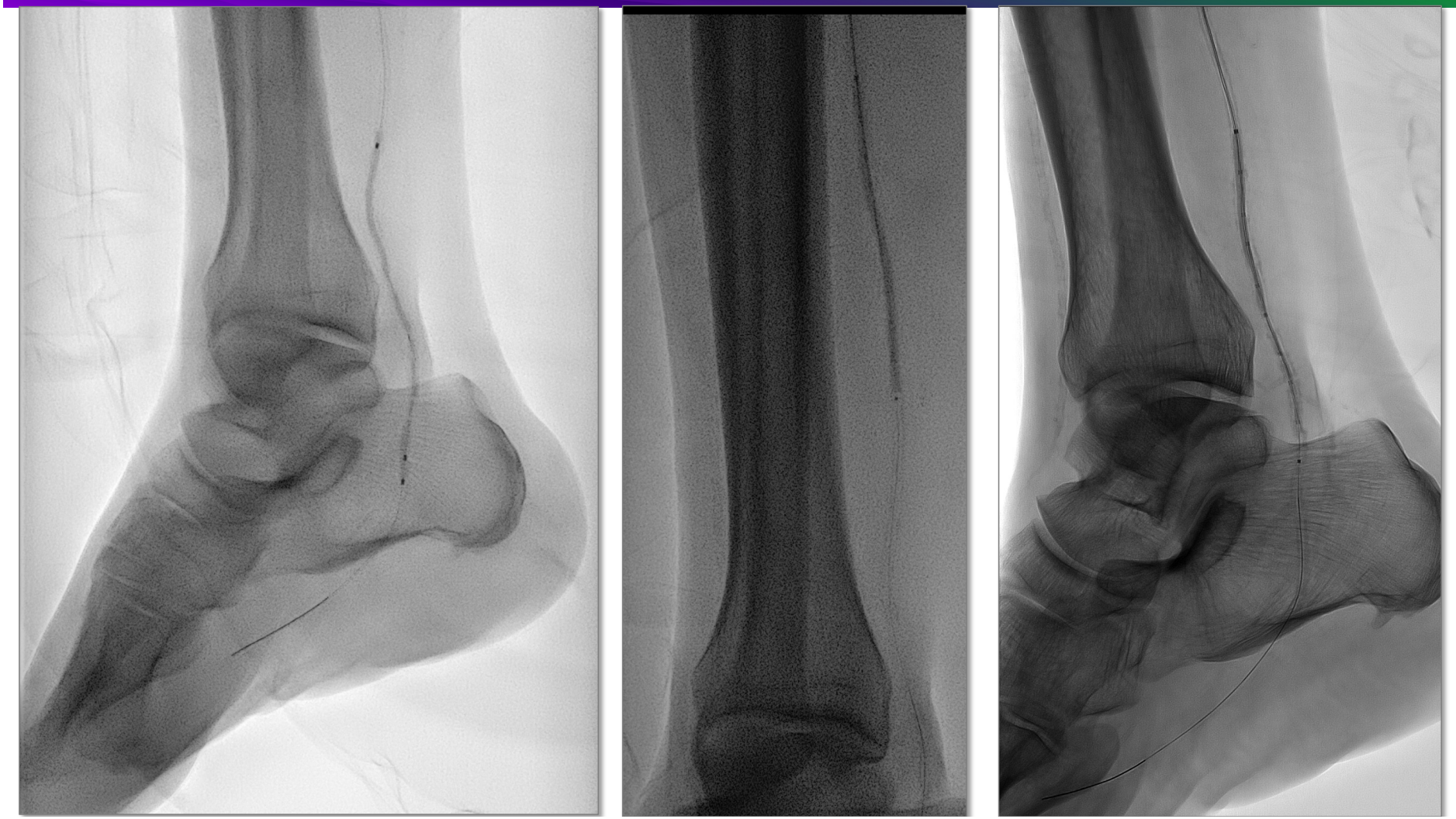
Thoughts?

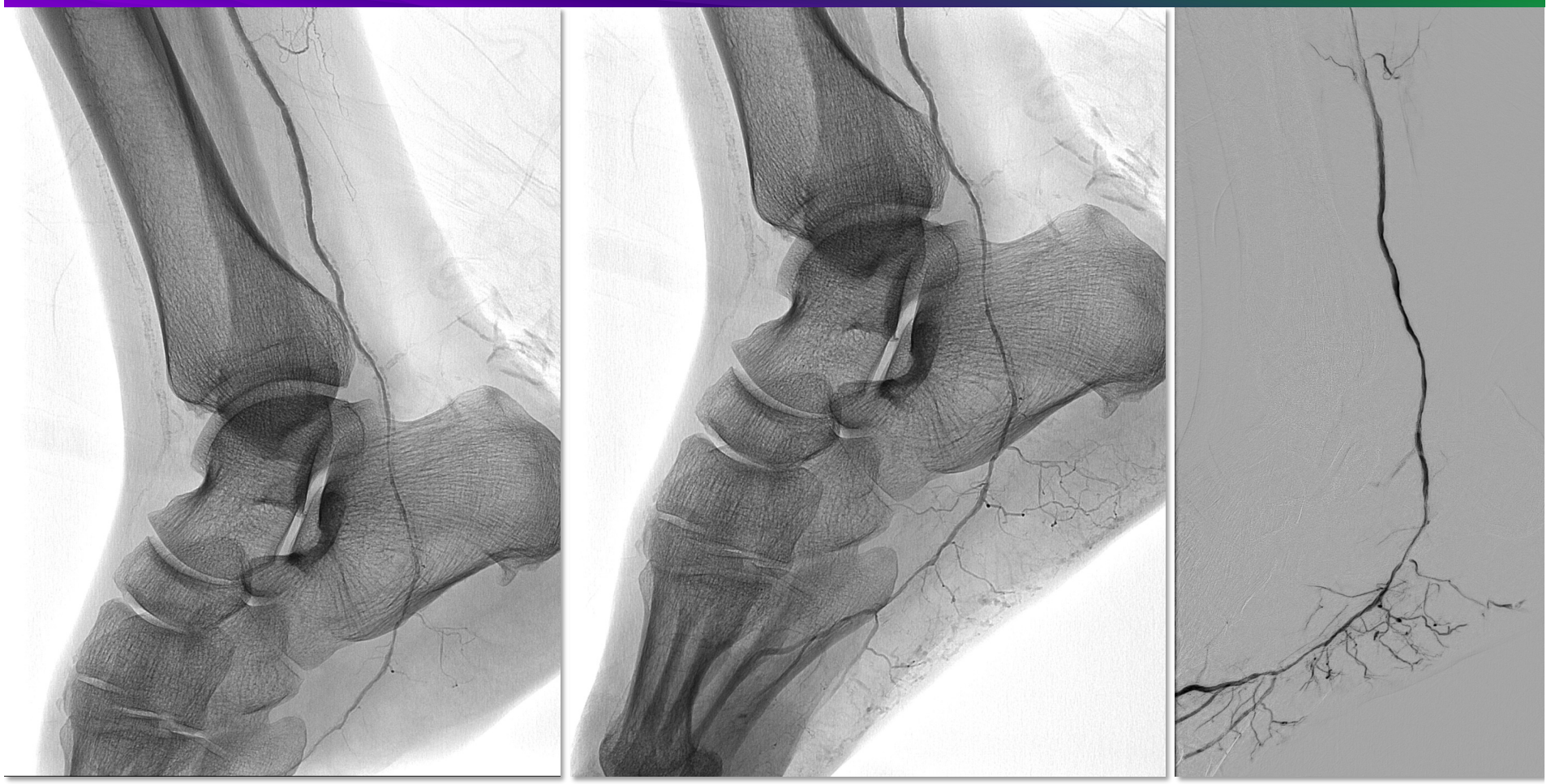
Can I get the PT open?

What about AT?



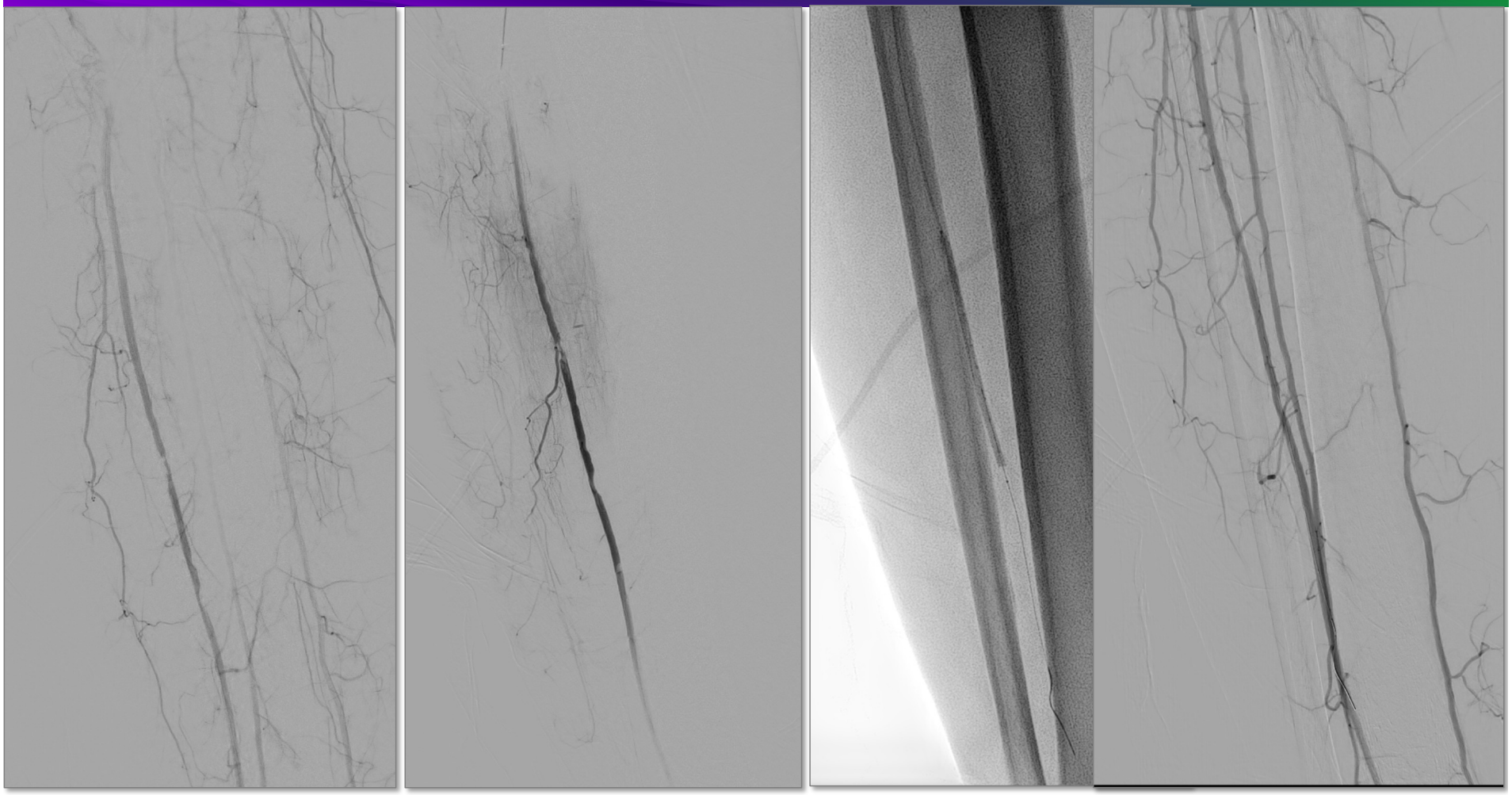
2.5mm E8

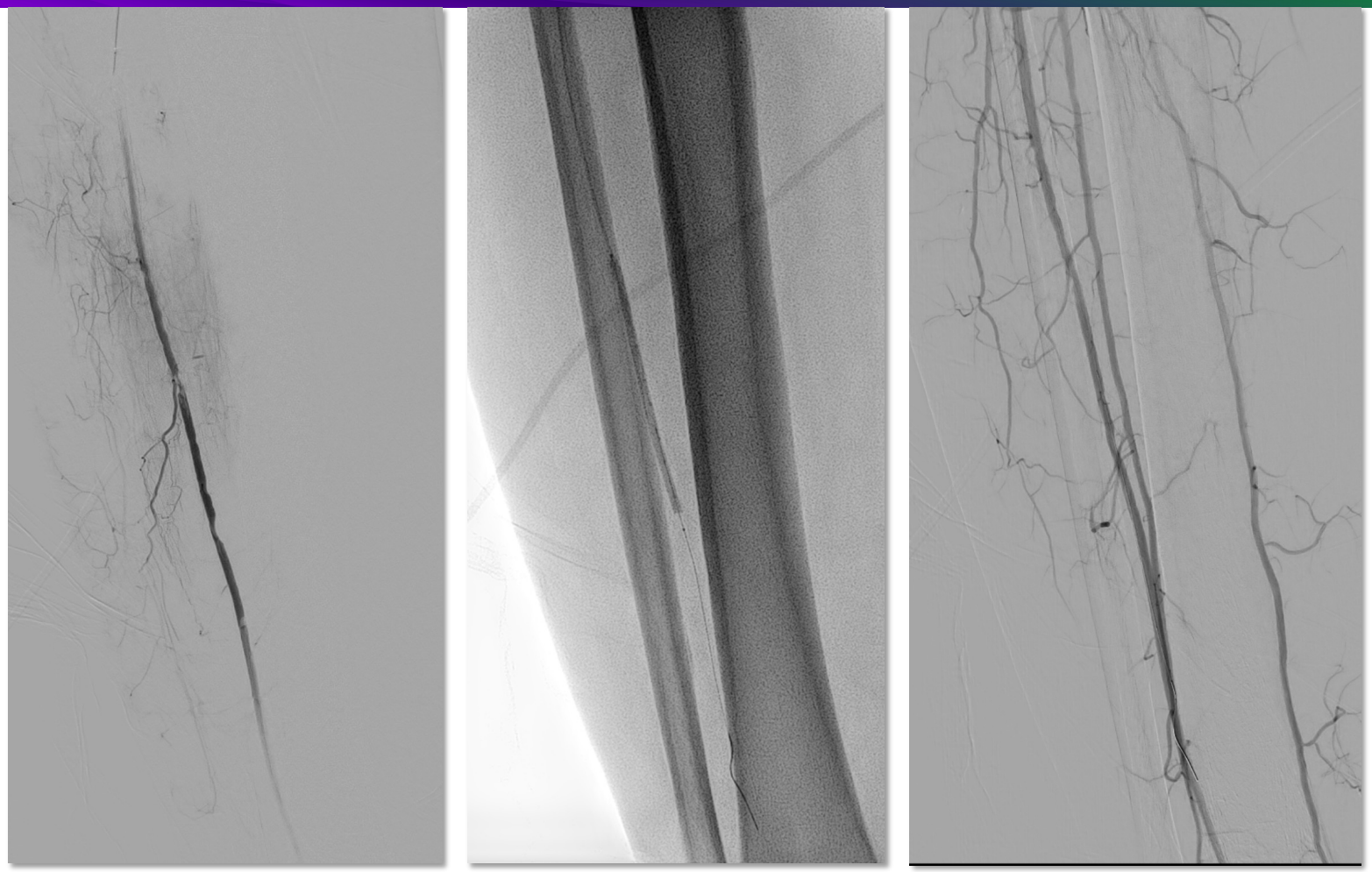




Case

- 70y with DM, ESRD
- 5th metatarsal osteomyelitis s/p resection and non-healing
- Arterial studies with monophasic tibial waveforms





3mm E8 IVL

Maximizing Results

1. Importance of crossing the lesion
2. Prolonged low atmosphere dilatation with IVL
3. Sizing of the balloon to lesion (1.1 to 1)
4. Once treated with IVL can further angioplasty
5. What will be the role for drug delivery?

What are the risks of PTA of calcified BTK vessels?

1. Recoil
2. Dissection
3. Embolization
4. All of the above

How can one assess amount of calcification in a vessel?

1. MRI
2. IVUS
3. Pulse examination
4. Serum calcium level

What is the best way to size tibial vessels?

1. CTA
2. MRA
3. Doppler examination
4. IVUS

Panel Discussion
and
Audience Q&A

Thank You

How I Do It:

Treating Complex, Below-the-Knee Disease

Supported by an educational grant from Shockwave Medical