BTK Interventions in 2025:

What is going to help make BTK procedures more effective?

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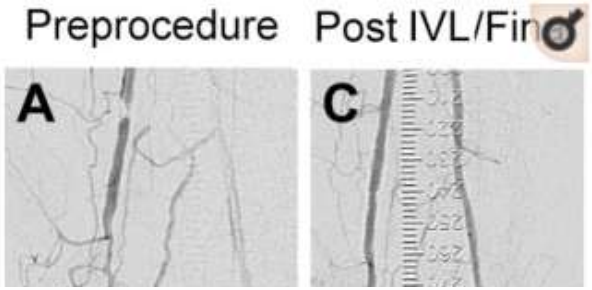
2025 is not that far in the future!

- Realistically…only devices either already approved/available, or currently in or soon to be starting clinical trials are relevant for inclusion in this discussion
- In the US today, only PTA, atherectomy, lithoplasty and Tack system are approved for BTK intervention. No ani-proliferative therapy is available
- So there is much to look forward to…

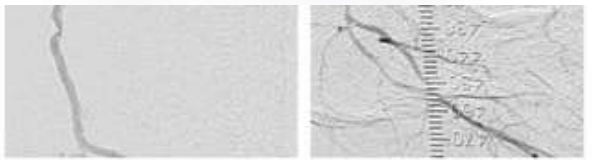
What are some of the incompletely addressed issues?

- Maintenance of vessel patency
  - Acute recoil
  - “Classic” restenosis (intimal hyperplasia consisting of fibroblast proliferation and extracellular matrix production resulting in vessel contraction and lumen loss)
- Assessment of tissue perfusion deficits pre-procedure, intra-procedural effectiveness of intervention, and post-procedure surveillance
- Better understanding and treatment of the “no option” patient

Maintenance of vessel patency



- Acute recoil
  - Since PTA is currently ed today, we must reconcile its well-known shortcc vessel contraction, and neointimal hyperpl
  - Specialty balloons a signed to address some of these issues
  - Intravascular Lithop nt promise in the most heavily calcified les
  - The Tack system, in nc ls, achieves high-rates of long-term patency likely in f dissection and in part due to anti-recoil action, all while seemingly without provoking excessive hyperplasia with 6 month primary patency of 87% and freedom form TLR of 92%

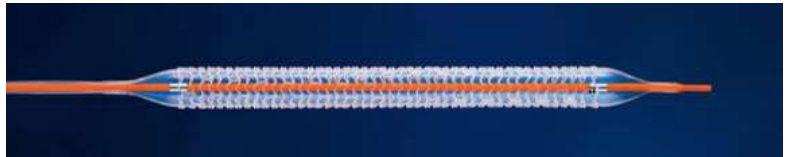


Maintenance of vessel patency

- Restenosis avoidance
  - Paclitaxel DCB has been underwhelming
  - Current data is strongest for sirolimus analogue DES in the proximal vessels, but not well-tested/suited to more distal locations
  - SAVAL PTX coated self-expanding stent trial in progress

  - Adventitial injection of temsirolimus using the Mercator Bullfrog device in a small Phase 2 trial showed marked reductions in TVAL (19% vs. 38%)

  - Bioabsobable scaffolds are currently in testing: Abbott LIFE-BTK study



Real-time assessment of tissue perfusion

- The adequacy of an interventional result is generally perfusion of the affected angiosome
- Currently judged primarily by angiogram-determined flow of the macroscopic vessel, but this may not reflect the tissue-level perfusion

Angiosome-driven BTK is helpful, but…

…only if the metric for success is clear

- By comparison, the ability to assess completeness of *procedural* revascularization in the coronary artery beyond angiography is reasonably established
  - Anatomic
    - IVUS
    - OCT (ILLUMIEN)
  - Physiologic
    - FFR/iFR

In infrapopliteal intervention…

- …the challenge is even greater
  - Longer segments of disease
  - Calcification
  - Bony background interference
  - Outflow/pedal circulation is smaller than coronaries
  - There are 3 of them!

What are the options?

- Improve the ascertainment of procedural adequate/optimal distal perfusion (physiologic)
- Once determined, would guide not only intra-procedural decisions but also augment pre- and post- decision clinical assessment

Assessment of global perfusion

Table 1 – Overview of global perfusion studies.

Modality	Description	Benefits	Limitations
Doppler (physiological)	Continuous wave Doppler transmits and receives sound waves to evaluate rate of blood flow in vessels	Fast, noninvasive, cost effective Office/clinic application	Limited by user skill and patient body habitus Cannot localize location of obstruction
ABI/segmental pressure (physiological)	Measuring the difference in blood pressure between the brachial and ankle arteries with Segment pressures displaying a gradient if there is PAD	Fast, noninvasive, cost effective Office/clinic application	Can be false elevated secondary to arterial calcinosis in DM and renal disease
Plethysmography/ PVR (physiological)	Evaluates and records variations in the volume or blood flow through an extremity as well as arterial pulsatility	Fast, noninvasive, cost effective Office/clinic application	Must be combined with PVR and Segmental pressures to provide a relevant and significant clinical information
Ultrasound (anatomical)	Sonography to visualize vessel caliber, obstruction, flow, and characterize plaque lesions	Fast, noninvasive, cost effective Office/clinic application	Limited by user skill Difficulty assessing perfusion in distal and smaller size vessels in lower leg and foot
CTA (anatomical)	CT–cross-sectional imaging to provide 360 reconstruction of vasculature	Fast and noninvasive More cost effective vs traditional angiography	Iodinated contrast is nephrotoxic Imaging obscured by vessel calcification
MRA (anatomical)	MR–cross-sectional imaging to provide 360 reconstruction of vasculature	Noninvasive Not obscured by vessel calcification	Length and cost of study Gadolinium is nephrotoxic Imaging obscured by venous artifact

Assessment of regional perfusion

Modality	Description	Benefits	Limitations
$TcPO_2$	Physiologic testing to evaluate potential wound healing by measuring the partial pressure of O_2 in tissue	Fast, noninvasive, cost effective Office/clinic application	The accepted level of $TcPO_2$ that indicates tissue healing remains controversial.
his	Scanning spectroscopy to display tissue perfusion on a microvascular level. Measures oxyhemoglobin and deoxyhemoglobin, along with surface temperature	Noninvasive Can be used for surveillance imaging post revascularization procedure	No large-scale studies have been undertaken to verify the reliability of measurements in patient with PAD
ICGA	Traditional angiography with injection of intravascular contrast agents to visualize the vasculature and areas of tissue perfusion	Can be used to monitor perfusion closely Can perform on the spot interventions	Nephrotoxic contrast agents Costly and time consuming Invasive study requiring direct arterial puncture for access
SPECT	Employ small amounts of radioactive substances that are injected into a vein and used with special cameras to produce images of the lower-extremity vasculature and angiogenesis	Noninvasive Can be used for surveillance imaging post revascularization procedure	No large-scale studies have been undertaken to verify the reliability of measurements in patient with PAD
Laser Doppler	Uses light penetration and absorption to evaluate microcirculatory perfusion	Fast, noninvasive, cost effective	Cannot provide absolute perfusion values, must combine with other modalities

HSI, hyperspectral imaging; ICGA, indocyanine green angiography; PAD, peripheral arterial disease; SPECT, single photon emission tomography; $TcPO^2$, transcutaneous partial pressure of oxygen.

Better understanding and treatment for the no-option patient

A Review and Proposed Classification System for the No-Option Patient With Chronic Limb-Threatening Ischemia

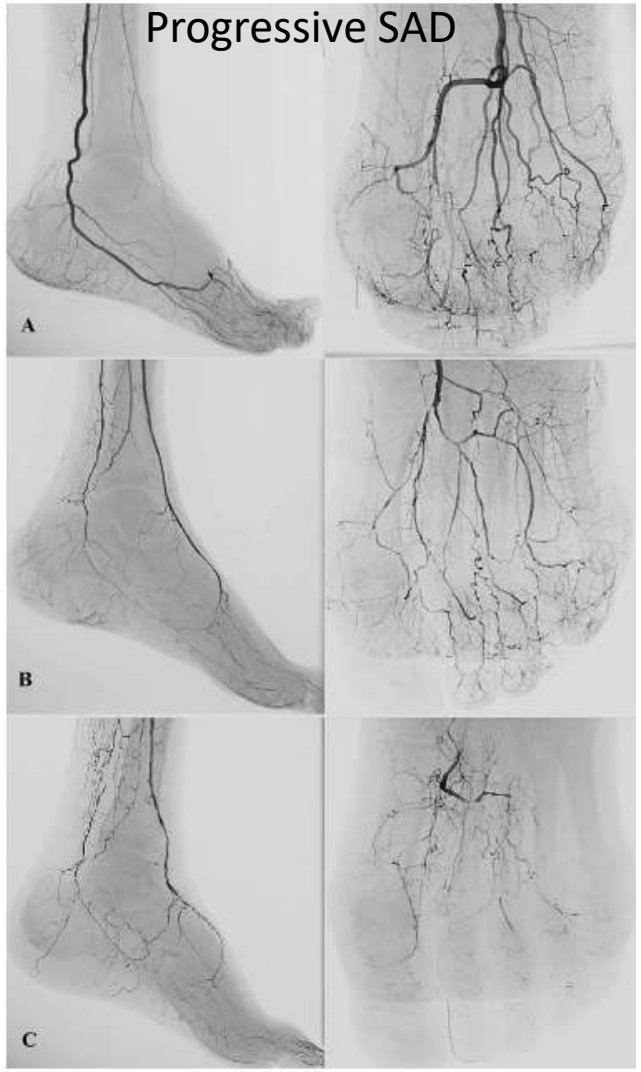
Tanner I. Kim, MD[1], Shant S. Vartanian, MD[2], and Peter A. Schneider, MD[2]

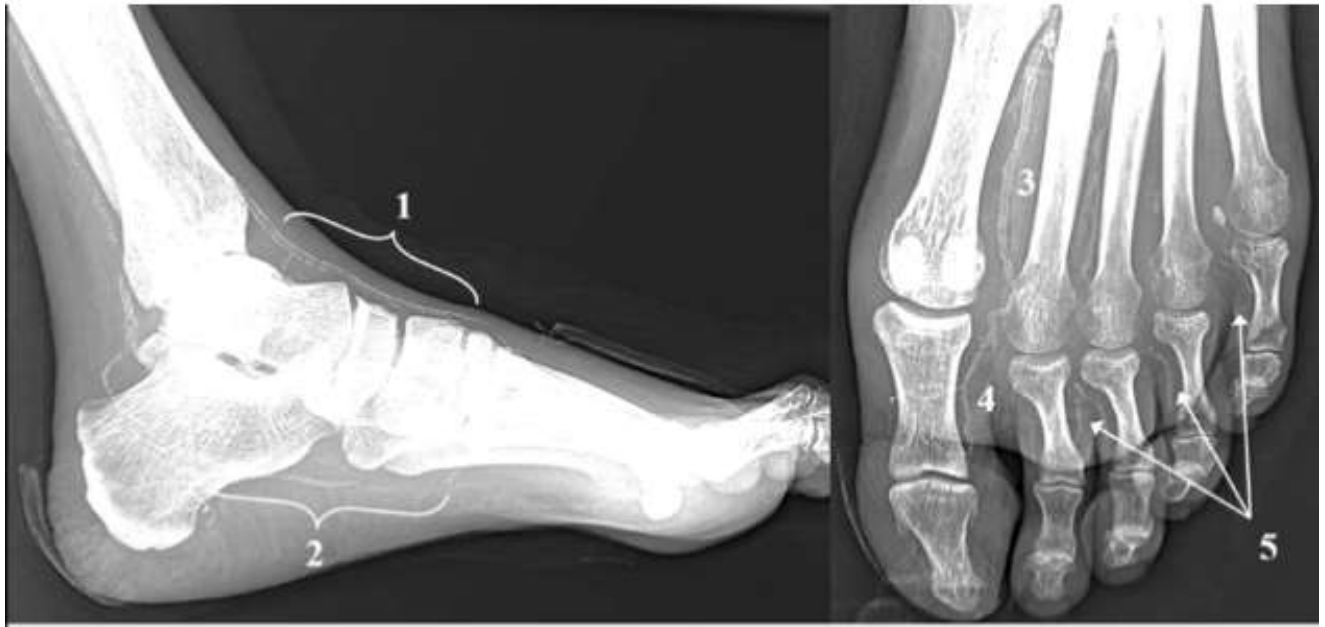
Table 3. Classification of the No-Option and Poor-Option Patient.

Type	Category	Conventional Revascularization Options	No or Poor Option	Description
I: Desert foot pedal anatomy	Anatomic	No	No option	• No patent pedal vessels or desert foot anatomy • Should be staged with the WIfI and GLASS staging classifications (including pedal modifier)
II: Inadequate venous conduit	Anatomic	No	No option	• Patent pedal target without adequate venous conduit for bypass • No endovascular options
III: Extensive tissue loss	Anatomic	Yes	Poor option	• Tissue loss with exposure of vital structures precluding limb salvage of a functional foot
IV: Prohibitive risk for procedure	Medical-comorbid	Yes	Poor option	• Excessive or prohibitive risk for revascularization due to advanced medical comorbid conditions
V: Nonfunctional limb	Medical-comorbid	Yes	Poor option	• Nonfunctional limb due to conditions, such as contractures, paralysis, or chronic nonambulatory status

Abbreviations: GLASS, Global Limb Anatomic Staging System; WIfI, wound, ischemia, and foot infection.

High SAD (small artery disease)and MAC (medial artery calcification) score patients





1	≥ 2 cm?	yes = 1 or no = 0
2		yes = 1 or no = 0
3		yes = 1 or no = 0
4	≥ 1 cm?	yes = 1 or no = 0
5		yes = 1 or no = 0

Sum all points →

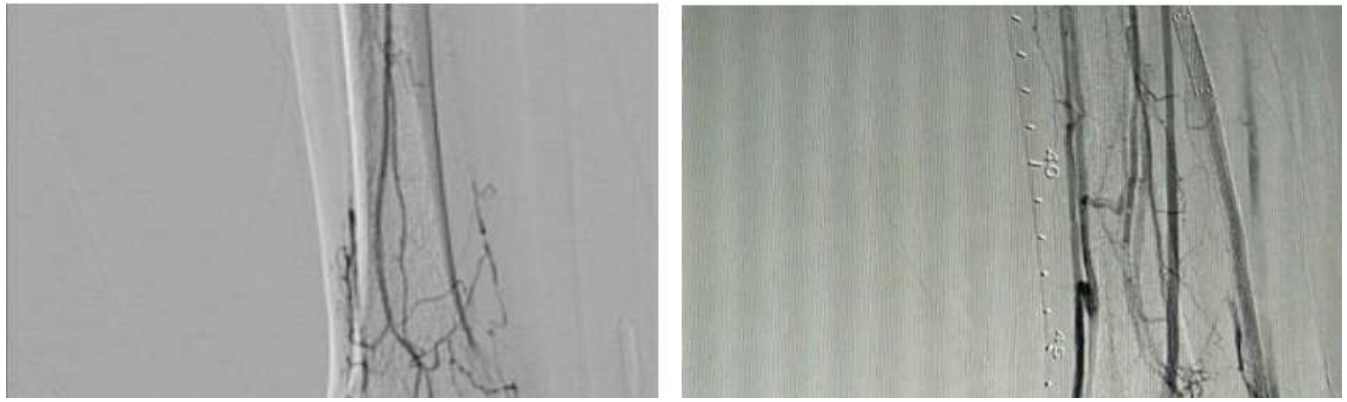
0-1 = no MAC

2-3 = moderate MAC

4-5 = severe MAC

Ferraresi R et al JEVT 2020

Deep venous arterialization (DVA) LimFlow



	AFS	Wound Healing	Demographics
PROMISE I[18] 32 No-Option Patients	70%	75%	87% Rutherford 5 13% Rutherford 6 69% Diabetes 34% Renal insufficiency
ALPS Registry[19] 32 No-Option Patients	71%	86%	72% Rutherford 5 28% Rutherford 6 66% Diabetes 16% Dialysis dependent

Summary

- 2025 is just around the corner

- Anticipated BTK interventional strategies intended to augment our current approaches will address, and hopefully improve:
  - Maintenance of vessel patency
  - Real-time, and reliable, assessment of tissue perfusion
  - Therapy for the no-option patient