Advancements in Peripheral Vascular Disease

(Peripheral Artery Disease and Venous Disease)

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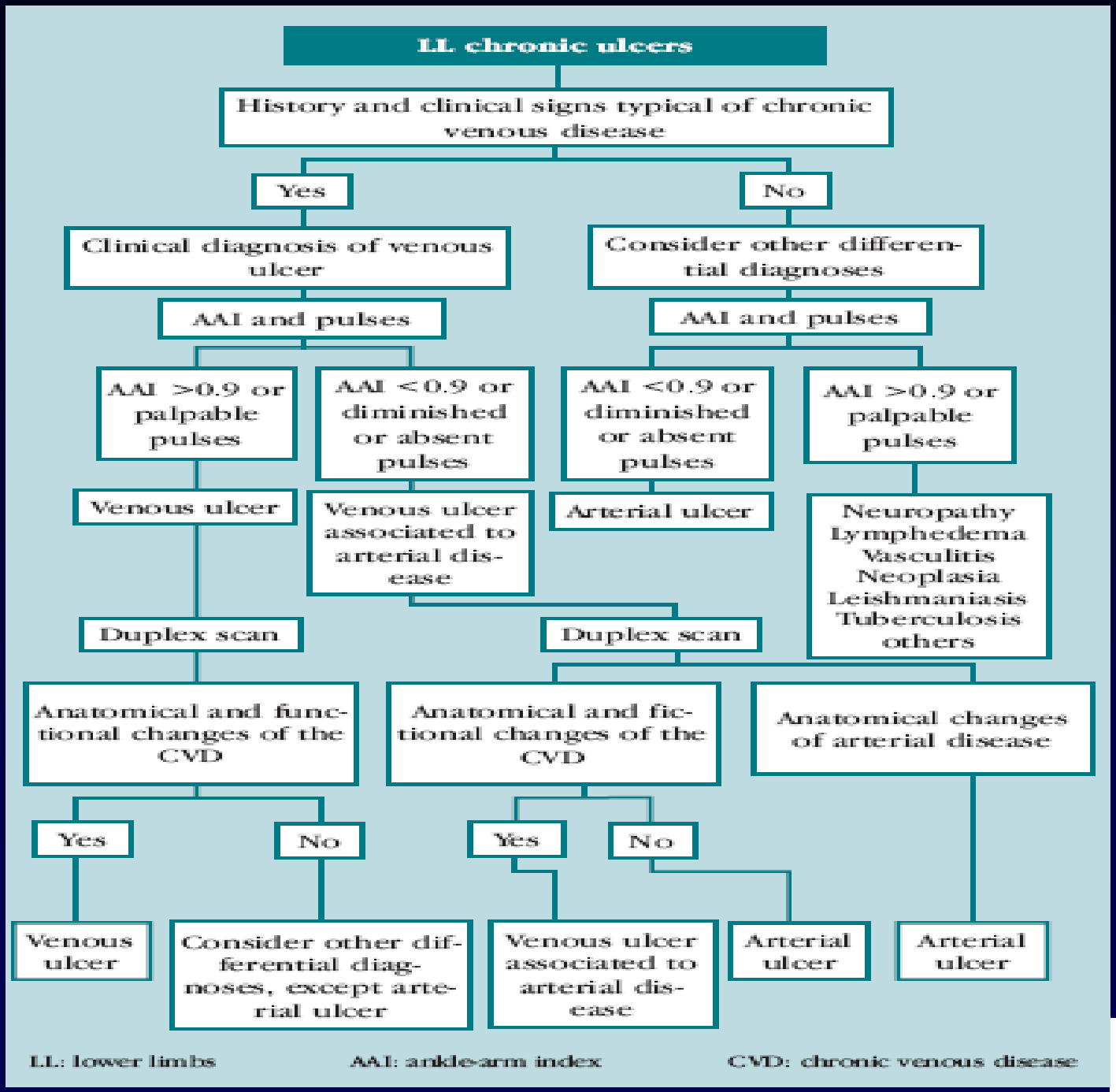
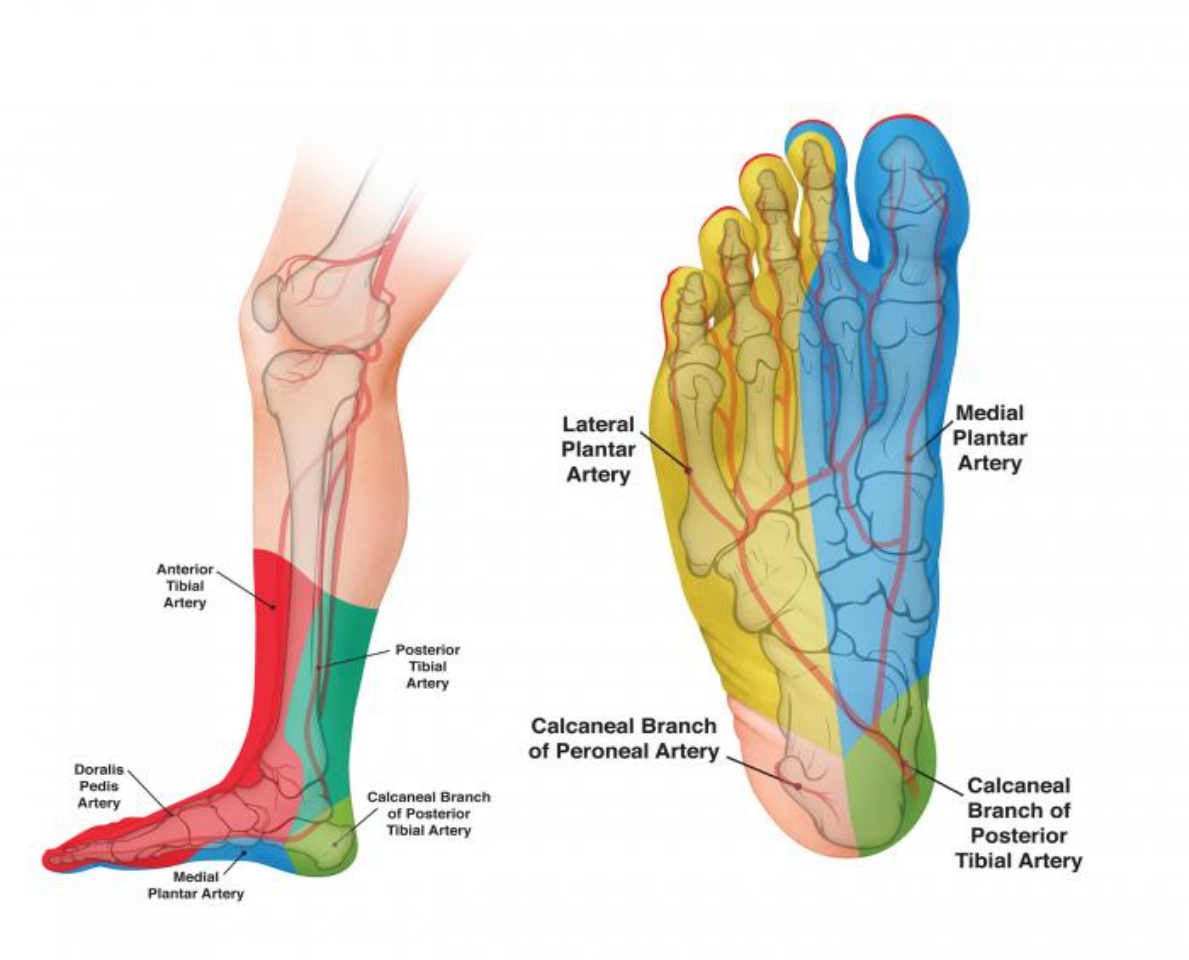

LL chronic ulcers
History and clinical signs typical of chronic venous disease
Yes
No
Clinical diagnosis of venous ulcer
Consider other differential diagnoses
AAI and pulses
AAI and pulses
AAI >0.9 or palpable pulses
AAI <0.9 or diminished or absent pulses
AAI <0.9 or diminished or absent pulses
AAI >0.9 or palpable pulses
Venous ulcer
Venous ulcer associated to arterial disease
Arterial ulcer
Neuropathy
Lymphedema
Vasculitis
Neoplasia
Leishmaniasis
Tuberculosis
others
Duplex scan
Duplex scan
Anatomical and functional changes of the CVD
Anatomical and fictional changes of the CVD
Anatomical changes of arterial disease
Yes
No
Yes
No
Venous ulcer
Consider other differential diagnoses, except arterial ulcer
Venous ulcer associated to arterial disease
Arterial ulcer
Arterial ulcer
LL: lower limbs
AAI: ankle-arm index
CVD: chronic venous disease

Angiosome Theory

Six angiosomes of the foot and ankle originate from the three arteries.



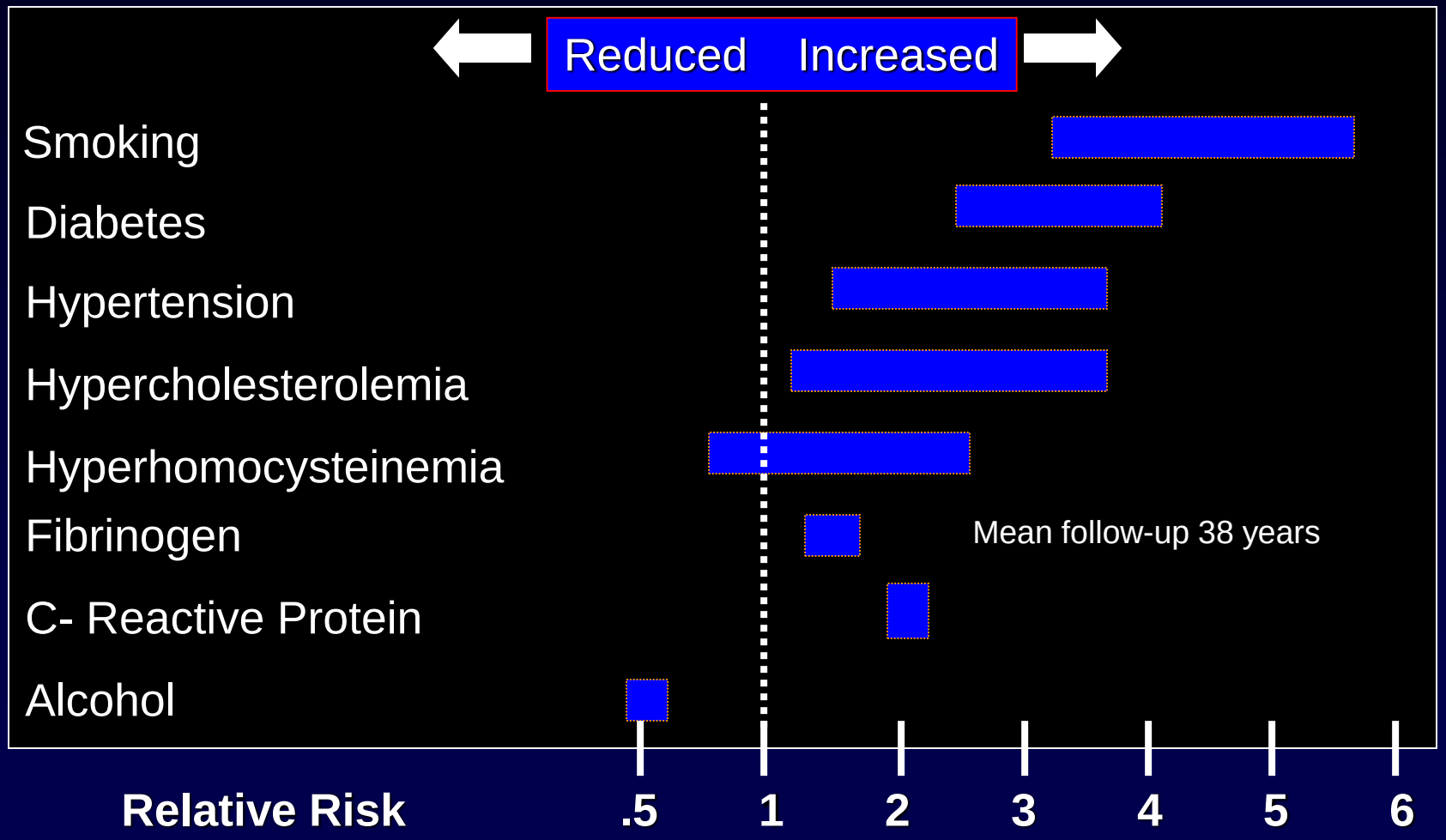
Strategy for BTK Angioplasty based on Angiosome Concept

Method of Revasc	Appropriate Angiosome Treated	Boundary Angiosome Treated
PTA Alexandrescu et al. J Endovasc Ther 2010;15:580	94% healed	59% healed
Bypass Neville et al. Ann Vasc Surg 2009;23:367	91% healed	62% healed

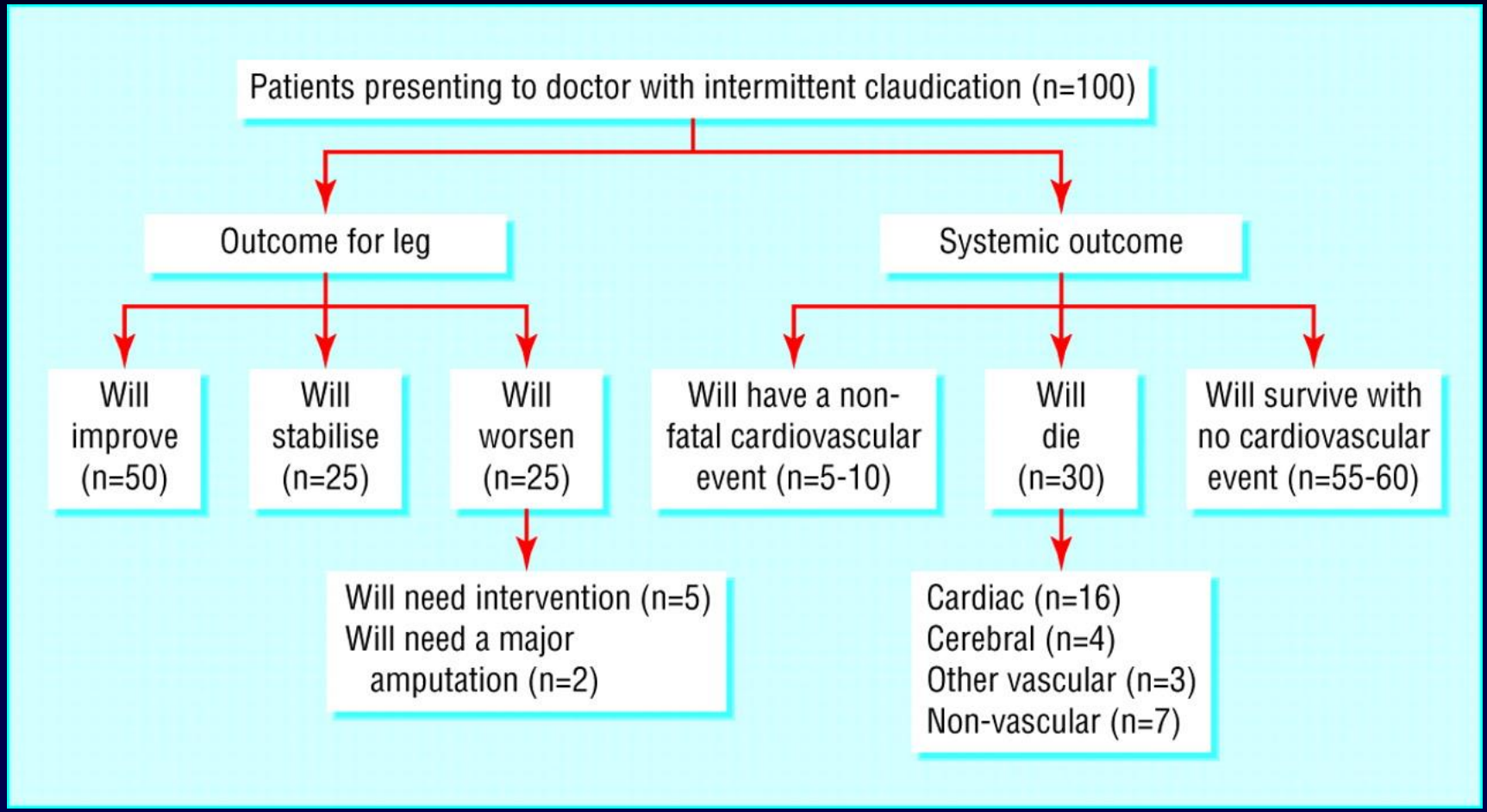
PAD : Background

- Occurs in approximately 1/3 of patients
  - ✓ Over age 70
  - ✓ Over age 50 who smoke or have DM
- Strong association with CAD
  - ✓ Obvious associated risk of stroke, MI, cardiovascular death
- Progressive disease in 25% with progressive intermittent claudication/limb threatening ischemia
- Outcomes
  - ✓ Impaired QoL
  - ✓ Limb Loss
  - ✓ Premature Mortality

Risk Factors for PVD: Framingham Heart Study



Outcomes in PVD Patients



Clinical Care of the Diabetic Foot, 2005

Diabetics:Tragic "Rule of 15"

- 15% of diabetes → Foot ulcer in lifetime patients
- 15% of foot ulcers → Osteomyelitis
- 15% of foot ulcers → Amputation

Diabetics: Tragic "Rule of 50"

- 50% of amputations → Transfemoral/ transtibial level
- 50% of patients → 2nd amputation in ≤ 5 years
- 50% of patients → Die in ≤ 5 years

Clinical Care of the Diabetic Foot, 2005

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The Most Important Aspect of the Diagnostic Evaluation of PAD

- History
  - Location of Symptoms
  - Description of Discomfort
  - Exacerbating/Ameliorating Characteristics
  - Reproducible Symptoms

Fontaine Classification

I Asymptomatic

II Intermittent claudication

a. > 200 meters

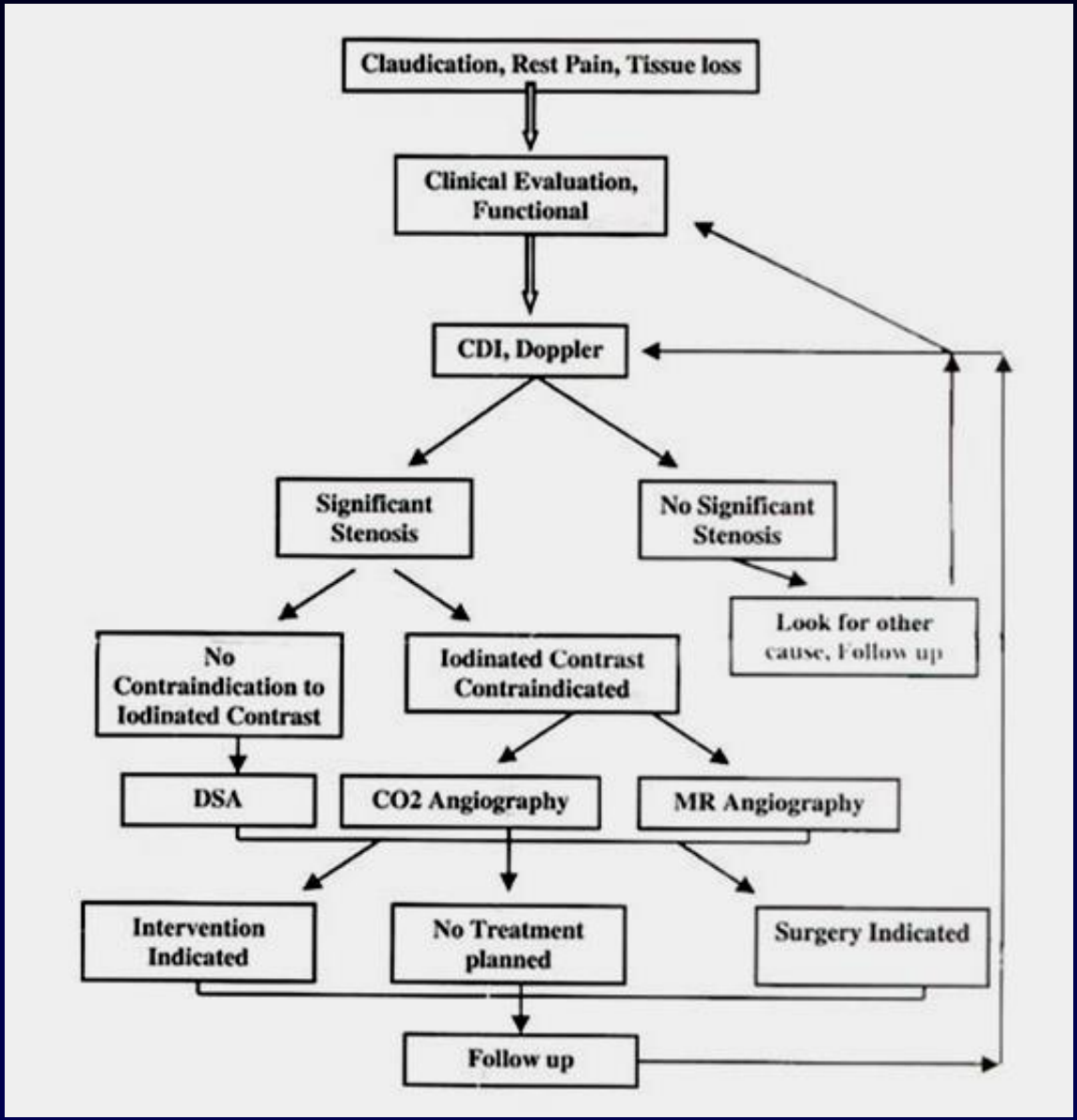
b. ≤ 200 meters

III Rest pain

IV Necrosis, gangrene, or non-healing wounds

Pentecost MJ, Circulation 89:51, 1994

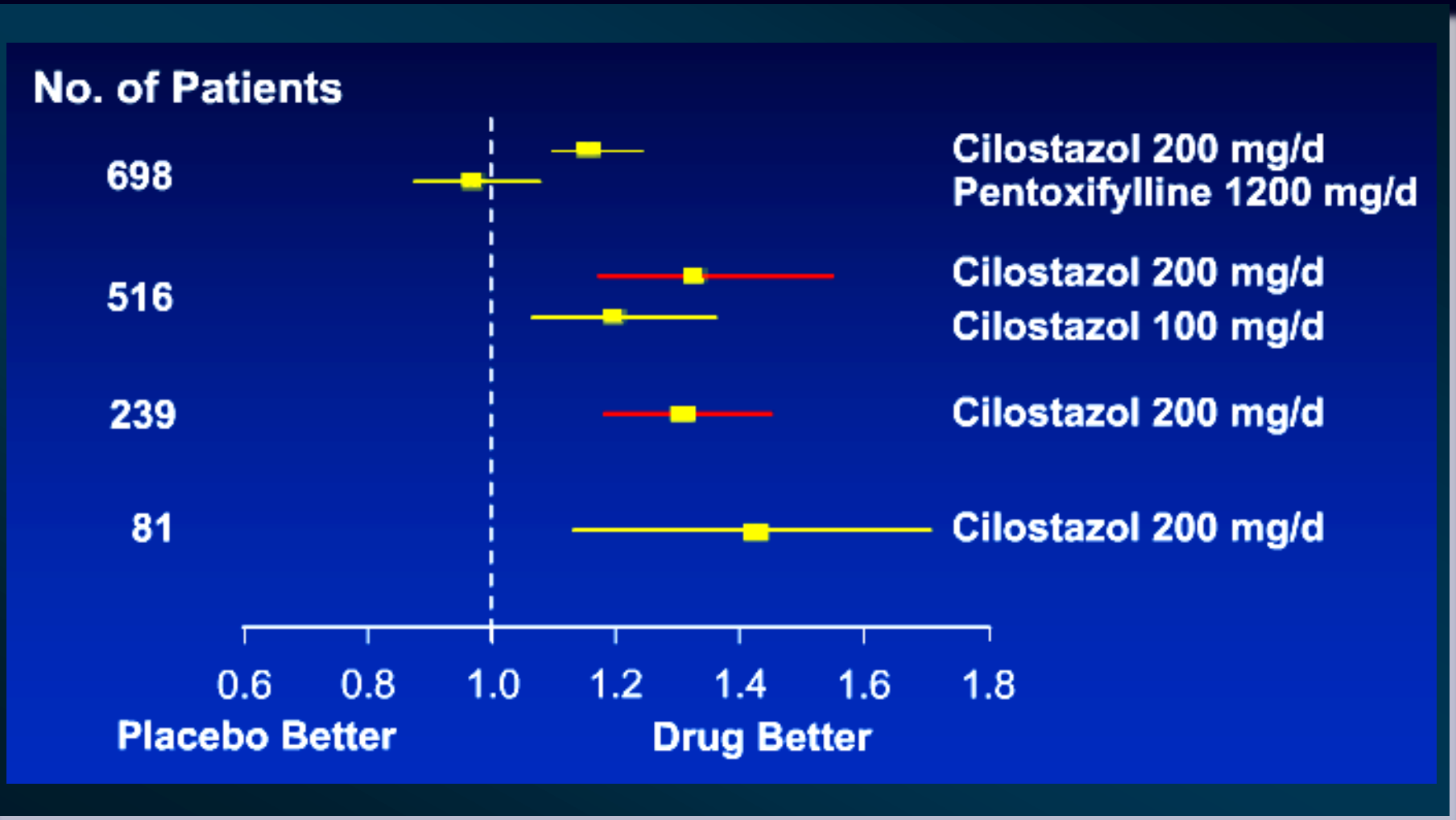
Suggested Algorithm for Work-up



Interpretation of ABI

- ≥0.90 Normal
- ≥1.30 Calcified Arteries
- ≥0.70-<0.90 Mild PAD
- ≥0.40-<0.70 Moderate PAD
- <-.40 Severe PAD

Effect of Cilostazol on walking distance in patients with intermittent Claudication



Hiatt WR N Engl J Med 2001; 344: 1608 - 1621

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Infrainguinal Surgical Revascularization

Results of Autogenous Infrainguinal Reconstruction

		Five-Year Cumulative Rates			
		Graft Patency			
No. of Limbs	Operative Mortality (%)	Primary (%)	Secondary (%)	Limb Salvage (%)	Survival (%)
3005	2	70	81	90	54

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Infrainguinal Arterial Surgical Revascularization

Infrainguinal Revascularization with PTFE

F-P AK and BK		F-P AK		F-P AK Claudication		Infrapop	
No.	Patency (%)	No.	Patency (%)	No.	Patency (%)	No.	Patency (%)
1067	40	984	50	400	63	202	14

Infrainguinal Surgical Revascularization

- **Complications**
  - ✓Mortality 2-5%
  - ✓Hemorrhage <2%
  - ✓Graft Thrombosis 2-7%
  - ✓Wound Infection 8-19%

Basil Trial even concluded Endo better first..

- 452 patients with CLI to strategy of bypass first or angioplasty first
- Attempted allocated treatment
  - 86% (195/228) bypass vs 96% (216/224) angioplasty
- No difference in amputation-free survival at 6 months
  - Unadjusted hazard ratio 1.07 95% CI [0.72-1.6]
  - Adjusted hazard ratio 0.73 95% CI [0.49-1.07]
- No difference in health-related QOL
- Hospital costs one-third higher with bypass first
- Later (after 2 years) results favored bypass
- Conclusion: endovascular first strategy for CLI
- 7-year f/u: no cost benefit

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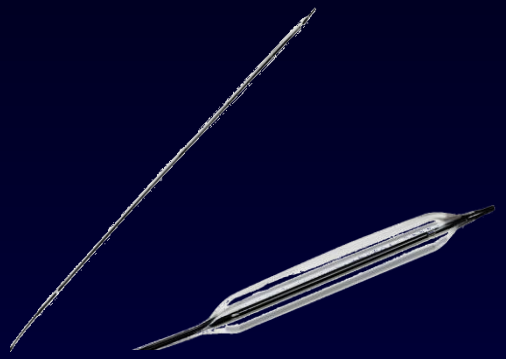
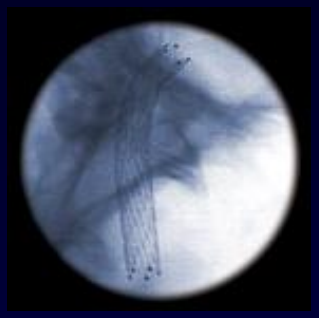
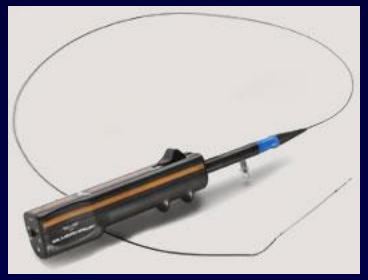
Endovascular Management of Limb Ischemia

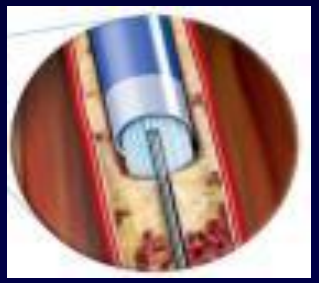
Endovascular Procedures

- Percutaneous Transluminal Angioplasty (PTA)
- Stenting
- Atherectomy
  - ✓ Directional
  - ✓ Laser
- "Specialized" Angioplasty Devices
  - ✓ Cutting Balloon
  - ✓ Cryoplasty









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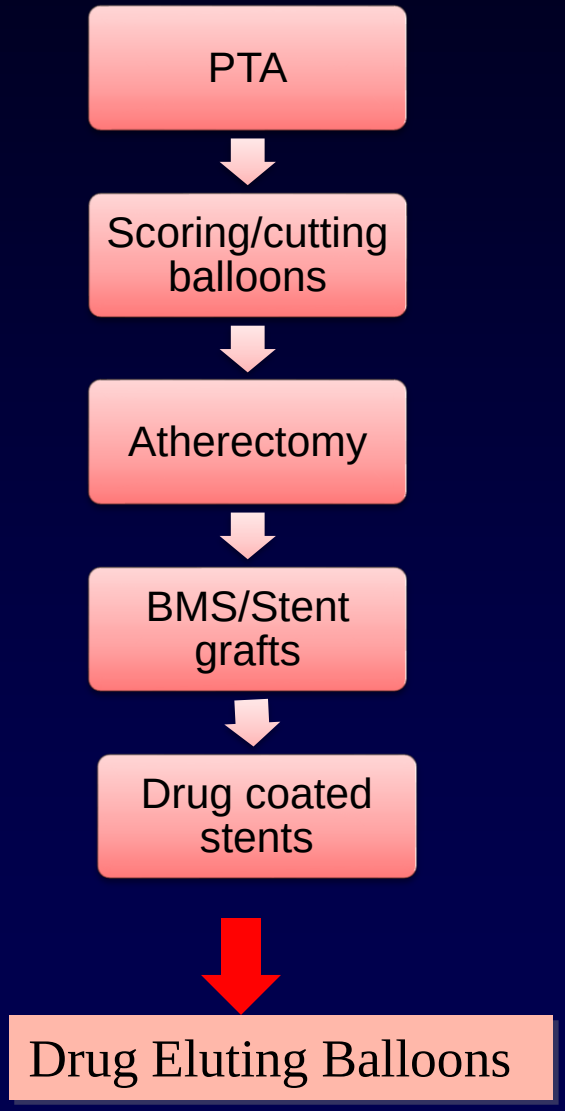
Current SFA Endovascular Intervention Options in the US



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Percutaneous Transluminal Angioplasty (PTA)

Efficacy

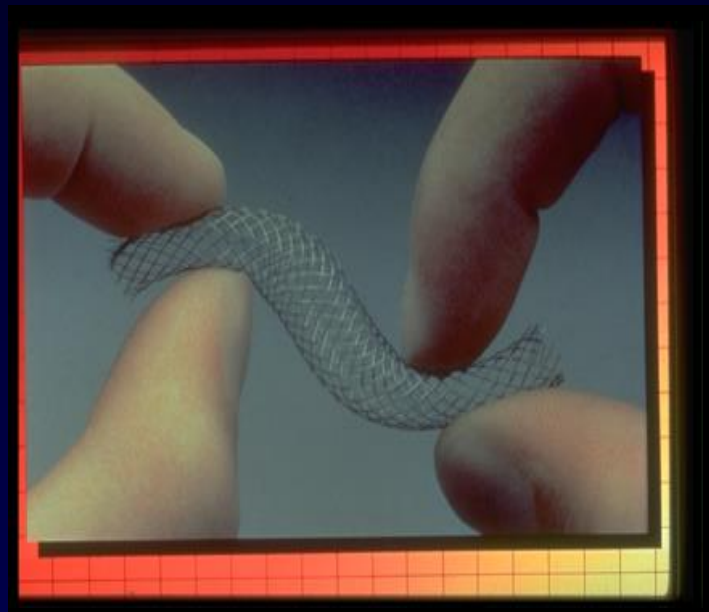
	Technical Success Rate	Clinical Success Rate	Primary 1- Year Patency	Assisted 5-Year Patency	Limb Salvage Rate	Major Comp. Rate	Patients /Mean Follow
Faglia, Grazziani, et al (2005)	99%			88%	97%	3%	993/26 months
Kudo, Ahn (2004)	96%	93%		76%	89%	2%	111/15 months
Mousa, Rhee, et al (2005)	98%		89%		97%	9%	66/6 months

9. Faglia, Paolo, Clerci, Cleressi, Graziani, et al. Peripheral Angioplasty as the First-choice Revascularization Procedure in Diabetic Patients with Critical Limb Ischemia: Prospective Study of 993 Consecutive Patients Hospitalized and Followed Between 1999 and 2003. *Eur J Vasc Endovasc Surg*. 2005;29:620-627.
10. Kudo, Ahn, Chandra. The effectiveness of percutaneous transluminal angioplasty for the treatment of critical limb ischemia: A 10-year experience. *The Western* ascular Soci 2005;Sep 11-14, 2004.
11. Mousa, Rhee, Trocciola, Dayal, et al. Percutaneous Endovascular Treatment for Chronic Limb Ischemia. *Ann Vasc Surg*. 2005;19: 186-191.

Stents

- Nitinol Self Expanding Stents
- Covered stents
- Zilver PTX Drug Eluting Stents
- Supera stents

Endovascular Stent



Flexible
Delivery safely
Non-compressible.

Stenting

Treatment

- Placement of metallic tube in damaged artery to support and maintain lumen
- May be bare metallic, PTFE, or drug-eluting

Best Use

- Primary therapy for focal Iliac and diffuse SFA lesions
- “Bail-out” for infrapopliteal PTA interventions

Efficacy

- 95% technical success rate[12]
- 88% 1 and 3 year primary patency rate[12]

12. Wolosker, Nakano. Primary Utilization of Stents in Angioplasty of SFA. Vasc Endovasc Surg Jul-Aug; 37(4): 271-7. 2003

Pre Intervention: Total Occlusion

SFA CTO

Post Intervention

SFA Revascularized

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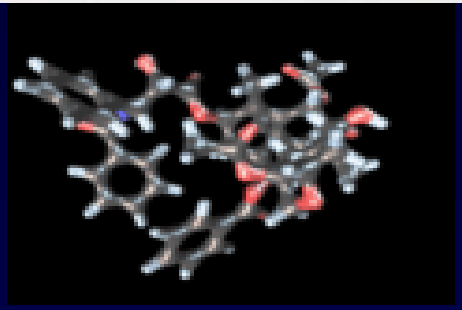
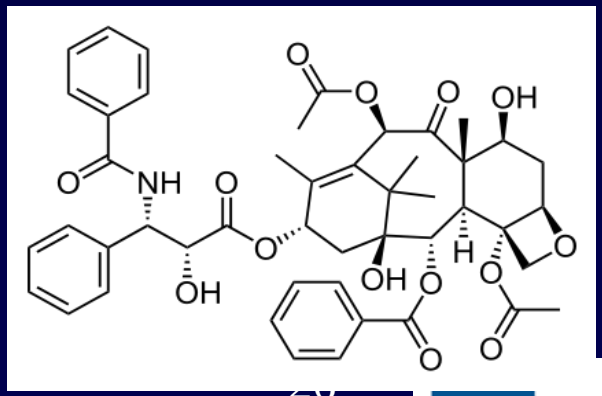
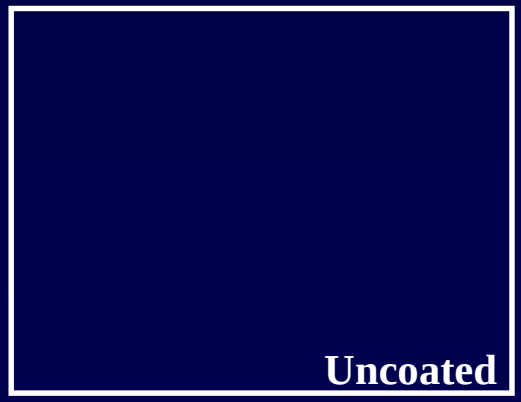
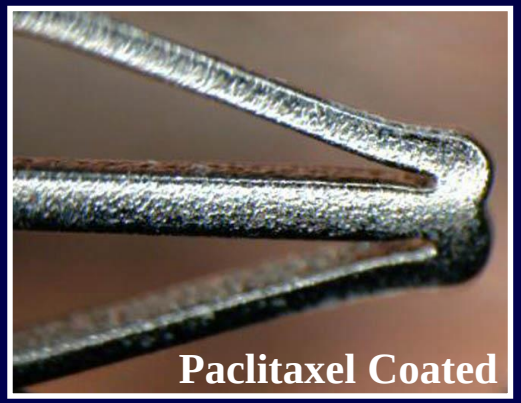
Zilver PTX Device Description

- Zilver Flex® Stent Platform
  - ✓ Nitinol stent
  - ✓ Designed for the superficial femoral artery (SFA)
- Outer surface coated with paclitaxel
  - ✓ 3 μg/mm^2 dose density
  - ✓ No polymer or binder
  - ✓ Same active ingredient as Taxus coronary DES









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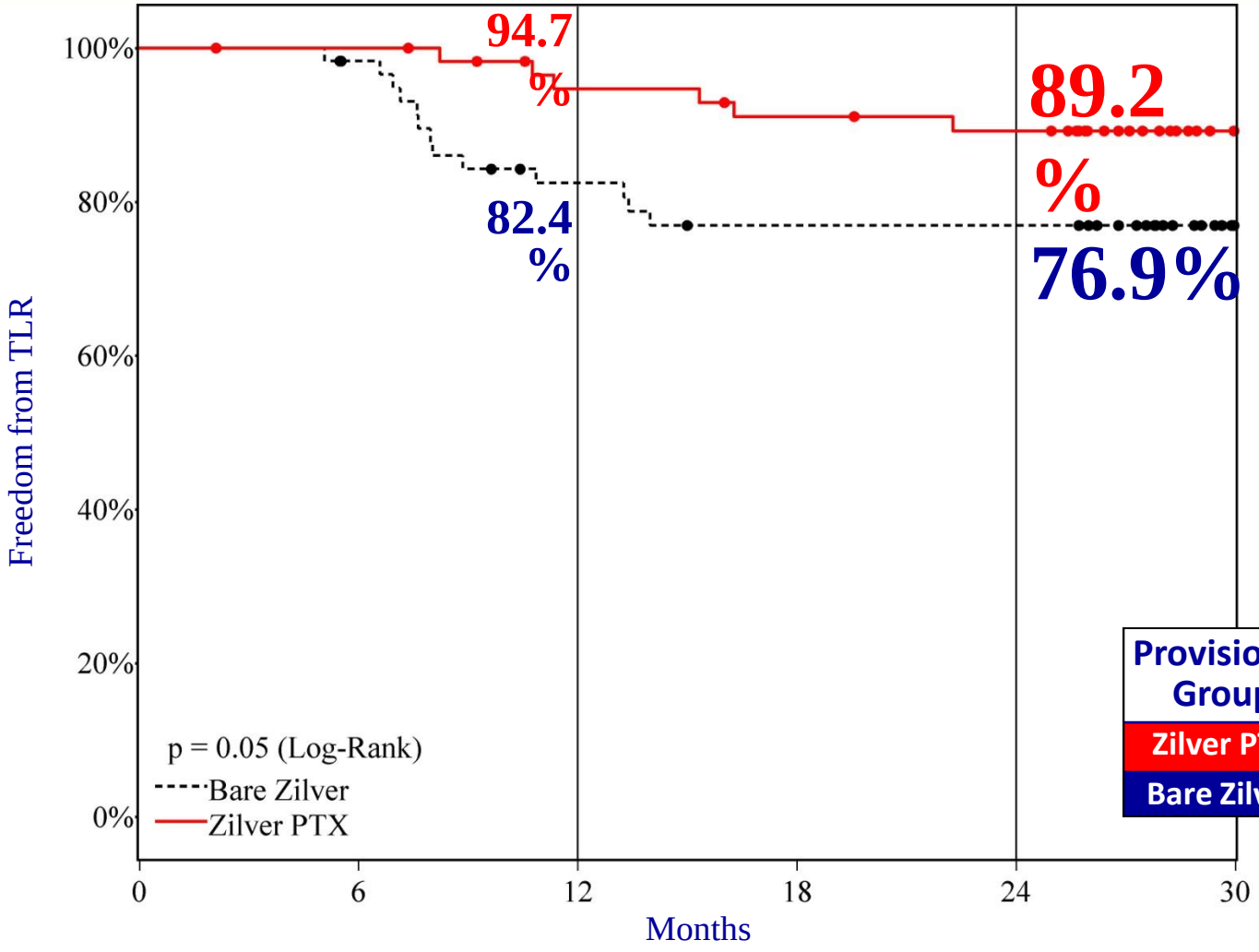
24-Month Freedom From TLR
Provisional **Zilver PTX vs. BMS**



Provisional
Zilver PTX
54 Lesions

p = 0.05

Provisional
Bare Zilver
54 Lesions

Provisional Group	24-month TLR	
	Rate	Reduction
Zilver PTX	10.8%	53%
Bare Zilver	23.1%	

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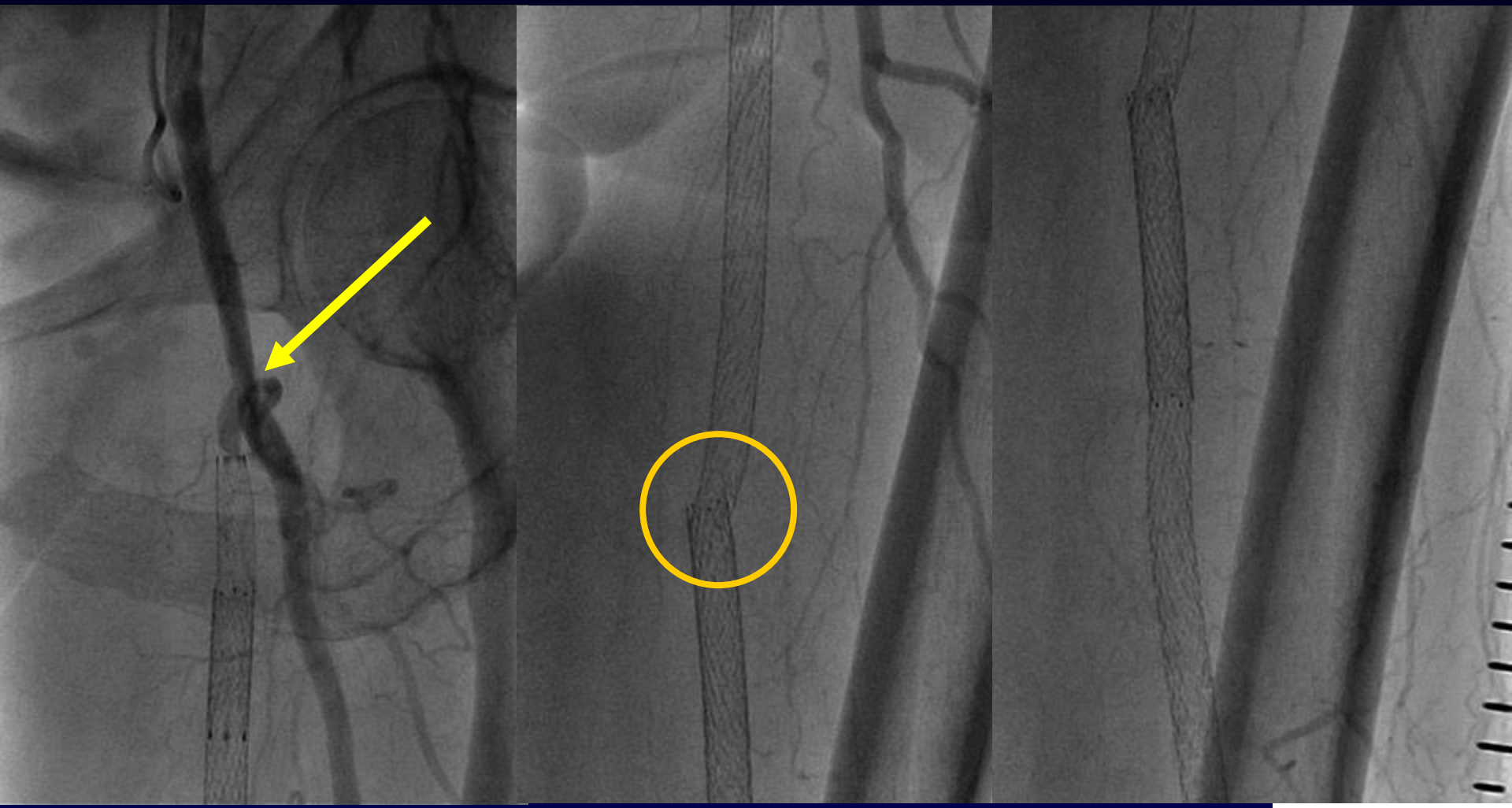
Long InStent Occlusion FemPop



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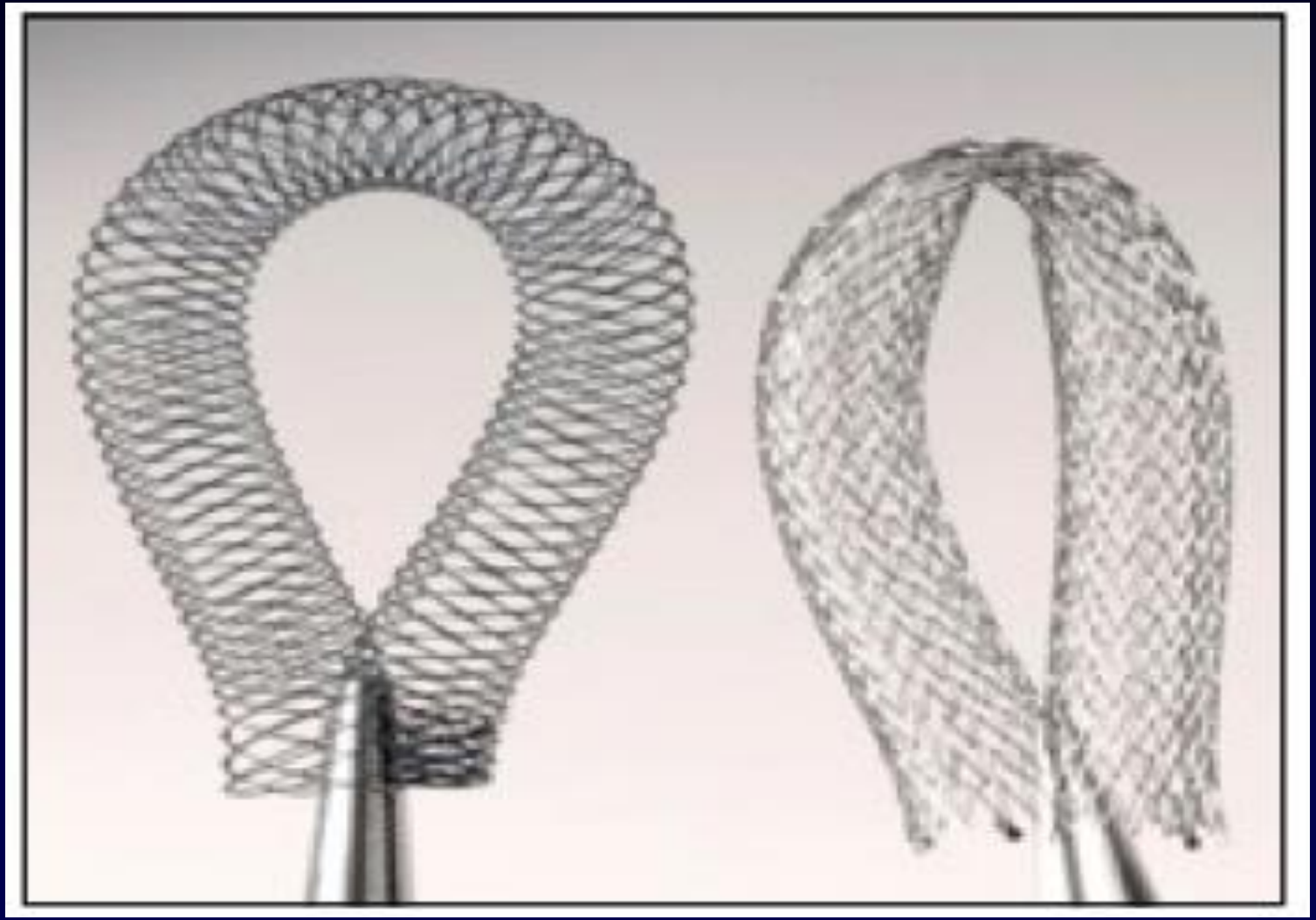
SUPERA stent

- Interwoven self-expanding nitinol stent
- Six pairs of super-elastic nitinol wires which are interwoven in a helical pattern in a closed cell geometry

1) Radial strength
2) Flexibility and Durability
3) Conformability
4) Kink, Crush and Fracture resistant

Supera vs. Other



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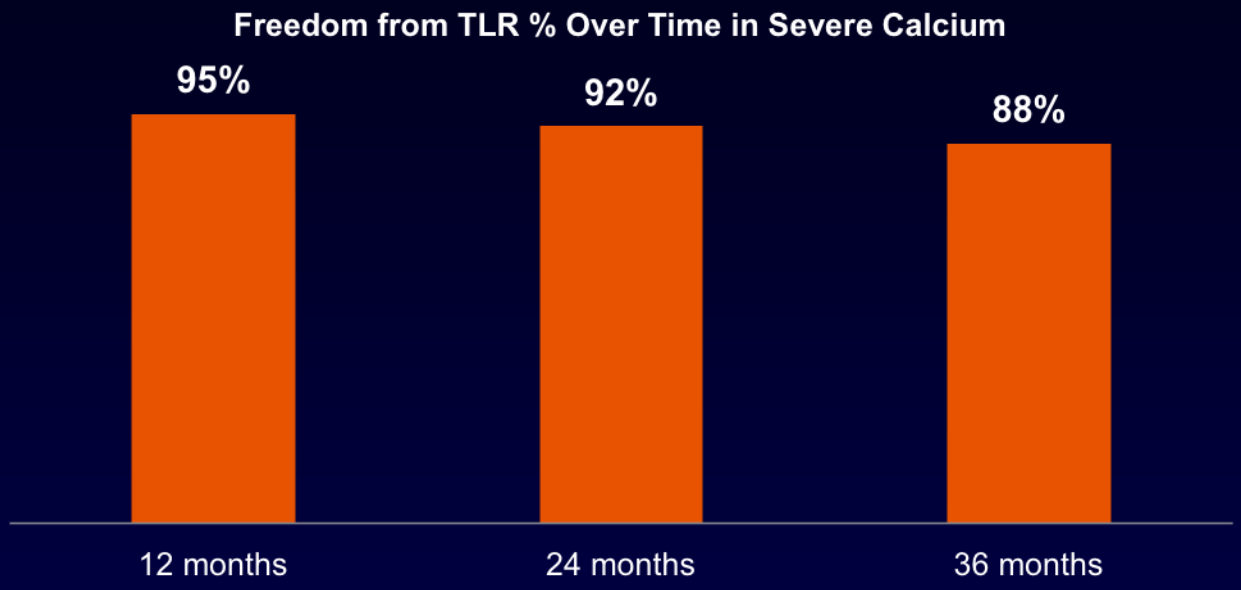
Clinical Outcomes in Calcification at 3 yrs



SUPERB Data – Severe Calcification

% of Lesions with Severe Calcification (SUPERB Trial)	45% (n=118)
Patency (VIVA 12 months)	

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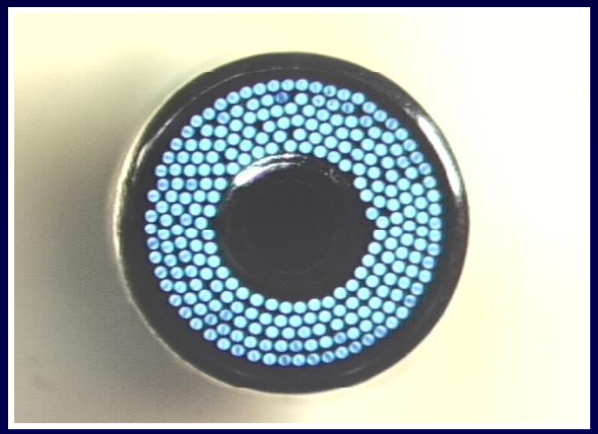
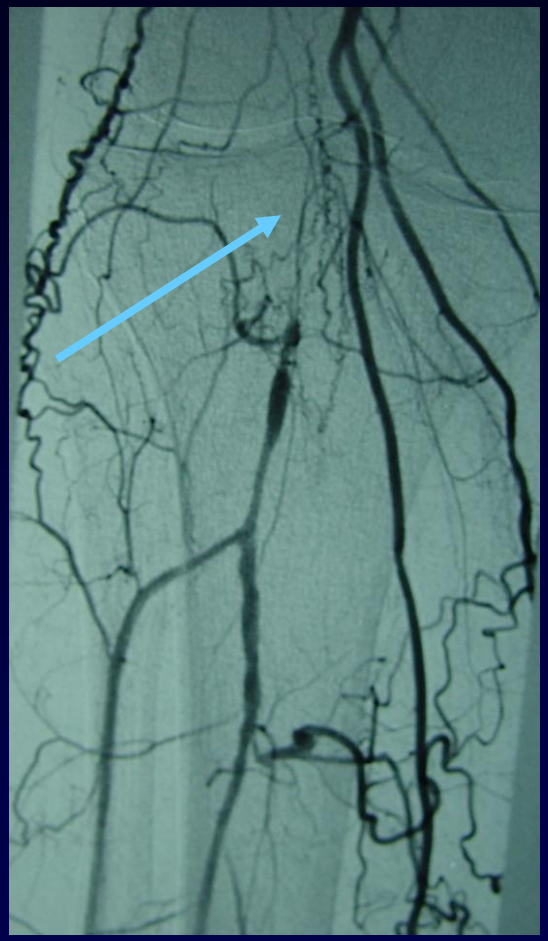
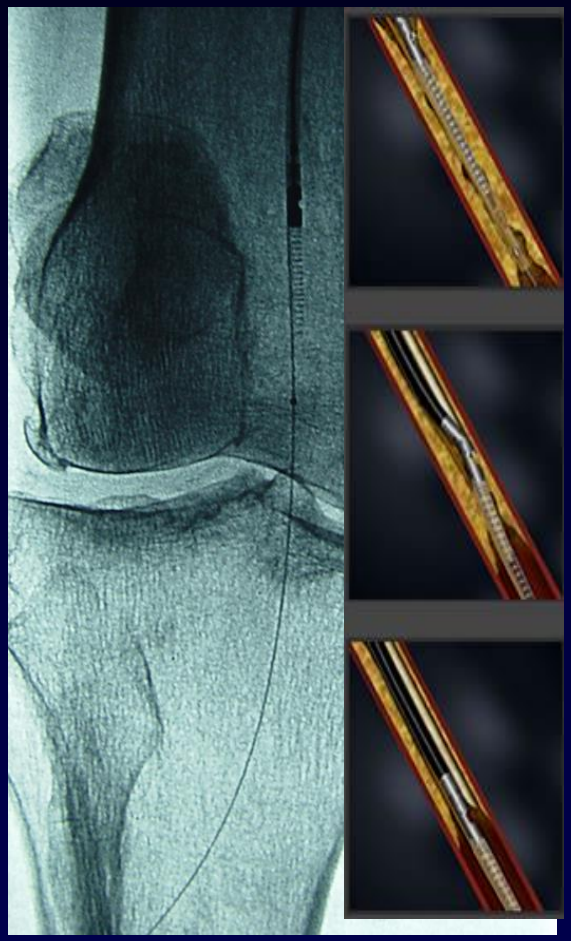
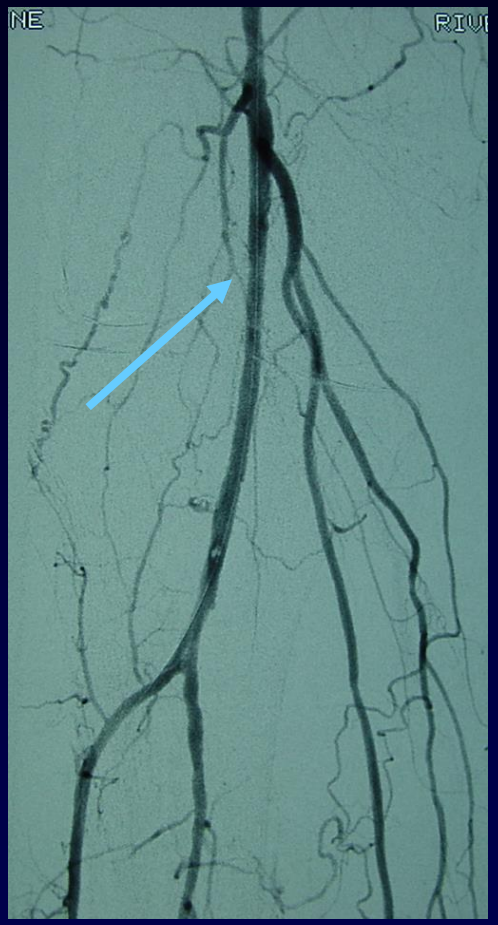
Atherectomy

- **More data but still** none randomized



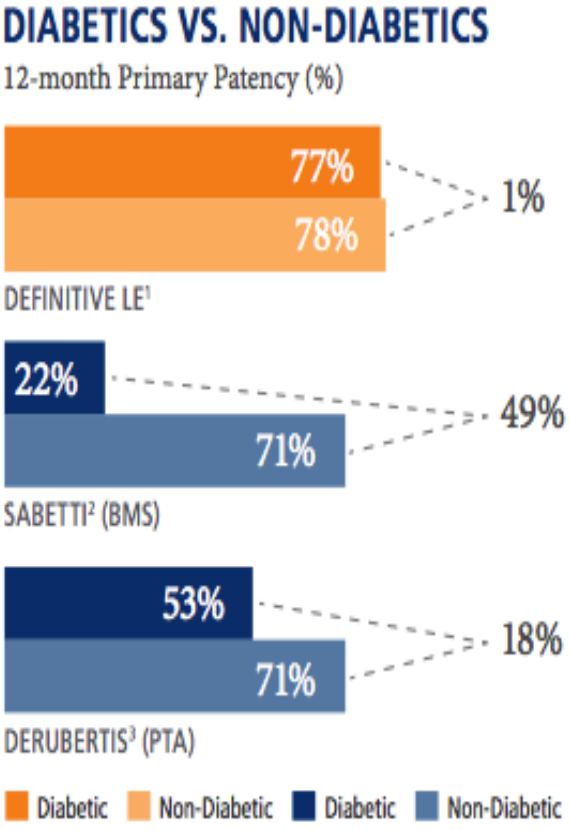




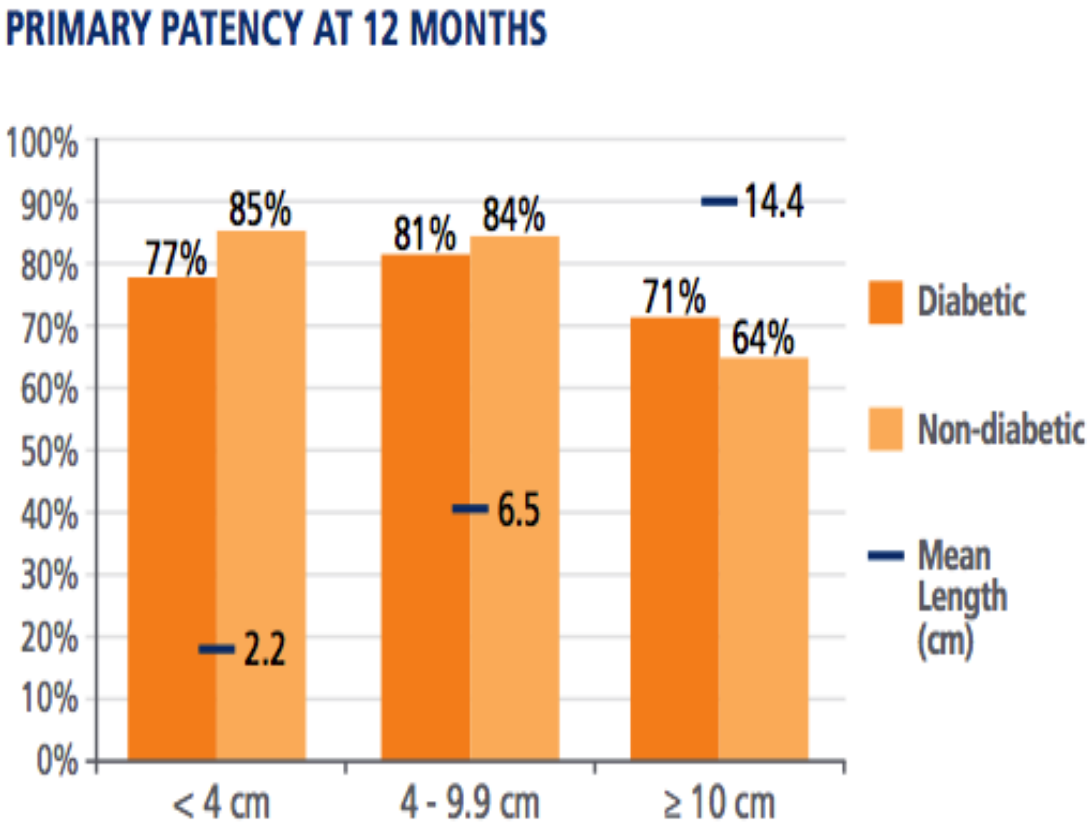


Still Ooh and aah factor for physician and patients
‘Nothing left behind”

DEFINITIVE LE Results



Diabetic patients show a more positive response to directional atherectomy than to other therapies.

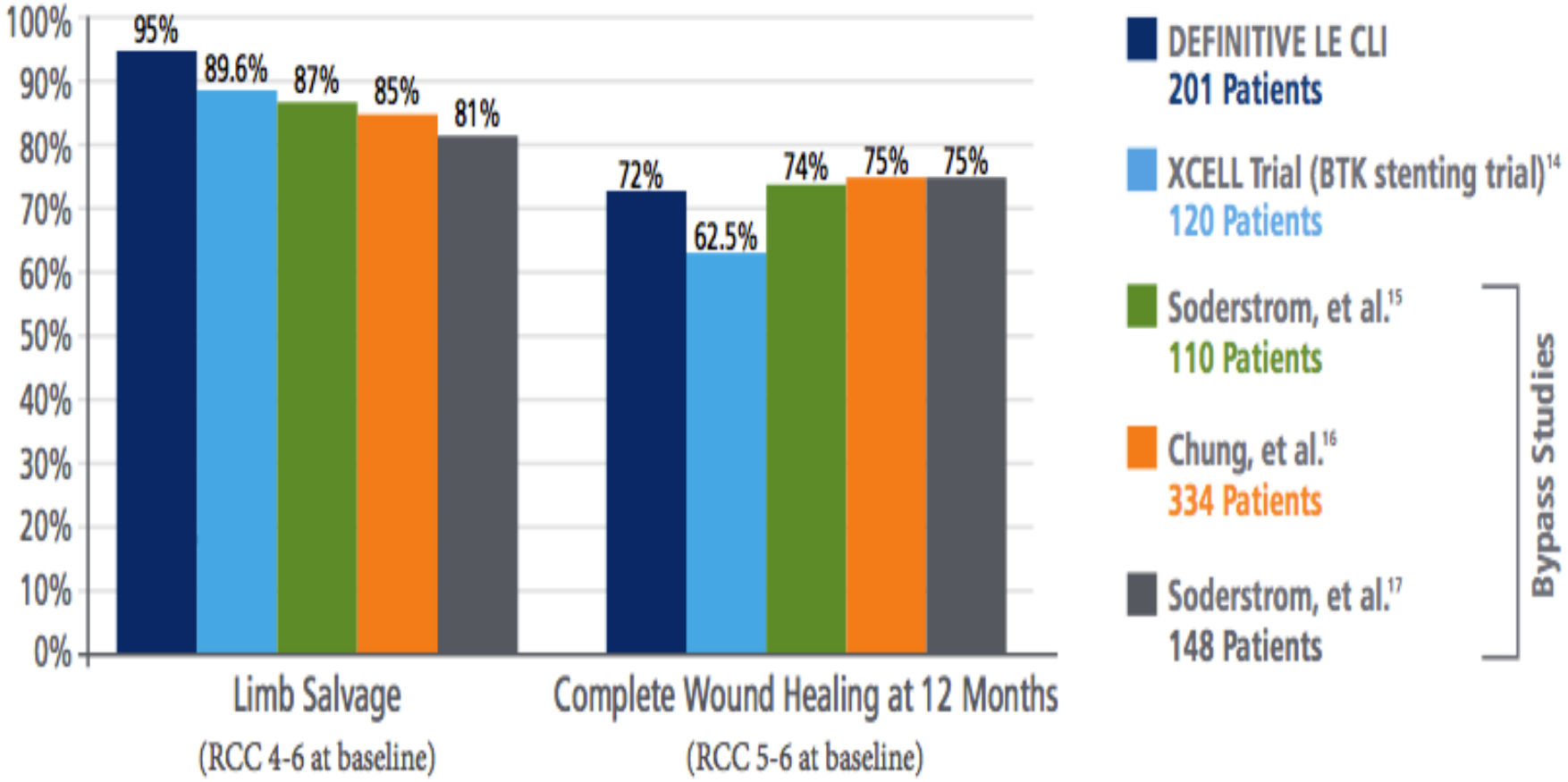


Overall, primary patency results are comparable in diabetics vs. non-diabetics when treating short, medium, and long lesions.

Results Across Different Segments

SFA	Subjects	Lesions	Baseline Stenosis	Mean Lesion Length (cm)	Primary Patency (PSVR ≤ 2.4)
< 4 cm	130	145	66.2	2.3	77.9%
4 - 9 cm	194	206	69.4	6.5	83.0%
10+ cm	182	184	79.8	14.6	65.4%
Popliteal					
< 4 cm	51	41	66.8	2.2	84.4%
4 - 9 cm	54	54	78.9	6.5	75.4%
10+ cm	18	18	89.6	13.1	64.9%
Infrapopliteal					
< 4 cm	29	34	65.1	1.8	89.6%
4 - 9 cm	42	47	74.8	6.2	89.4%
10+ cm	12	12	80.9	13.4	90.9%

Impact on CLI



IN.PACT SFA Trial Overview

IN.PACT SFA I
150 subjects enrolled at 13 EU sites
Sep 2010 - Apr 2011

IN.PACT SFA II
181 subjects enrolled at 44 US sites
Apr 2012 - Jan 2013

- Prospective
- Multicenter
- Randomized (2:1)
- Single-blinded
- Subjects followed up to 5 years

- Independent and blinded Duplex Ultrasound Core Lab,[1] Angiographic Core Lab,[2] and Clinical Events Committee[3]
- Independent Data Safety Monitoring Board[3]
- External monitoring with 100% source data verification

1. VasCore DUS Core Laboratory, Boston, MA, US
2. SynvaCor Angiographic Core Laboratory, Springfield, IL, US
3. CEC and DSMB services provided by HCRI, Boston, MA, US

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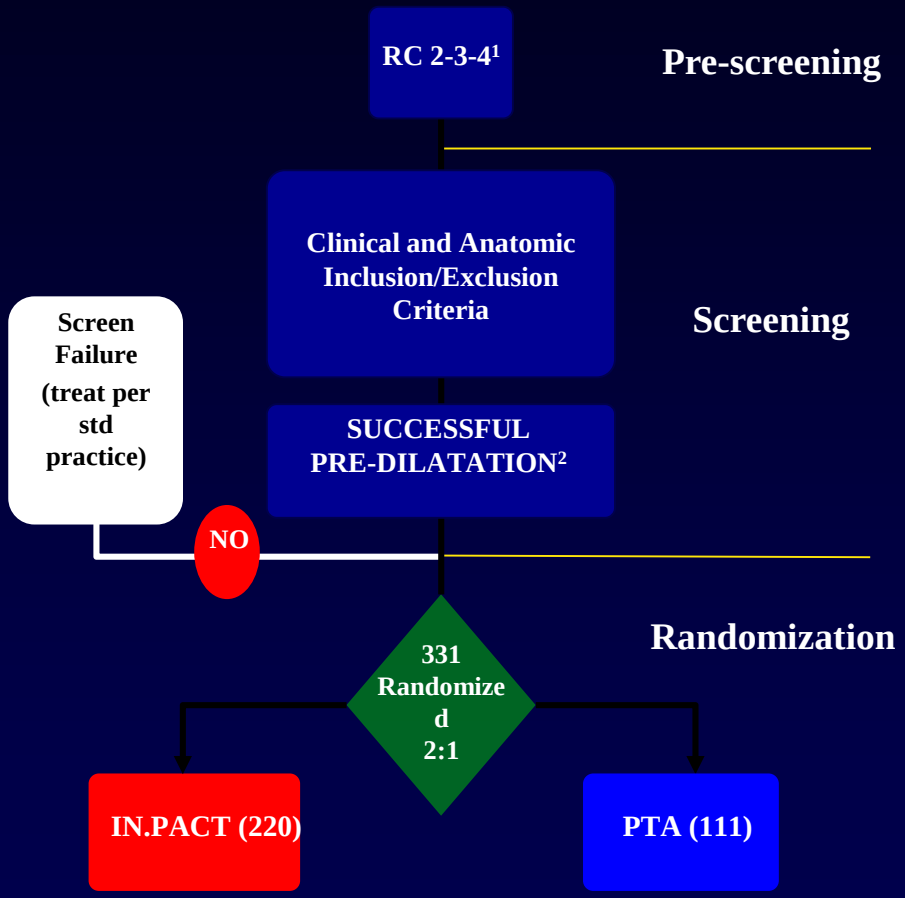
IN.PACT SFA Trial Design



IN.PACT SFA

Aggregate dataset from Phase I and II

Primary Endpoints:

- **Efficacy**[3]: 12-month Primary Patency
- Freedom from clinically-driven TLR and duplex ultrasound derived restenosis (PSVR ≤2.4)
- **Safety**[4]: 30-day device/procedure death, 12-month amputation, 12-month clinically-driven TVR

Key Inclusion Criteria:

- Rutherford 2-3-4
- SFA and proximal popliteal
- Lesion length 4-18 cm
- Total occlusion ≤10 cm

1. With symptoms of claudication and/or rest pain and angiographic evidence of SFA/PPA stenosis
2. Pre-dilatation mandatory for all subjects in IN.PACT SFA II phase only
3. Primary Efficacy Analysis on all ITT non-stented subjects based on superiority assumption of DCB vs. PTA
4. Primary Safety Analysis on all ITT non-stented subjects based on non-inferiority of DCB vs. PTA

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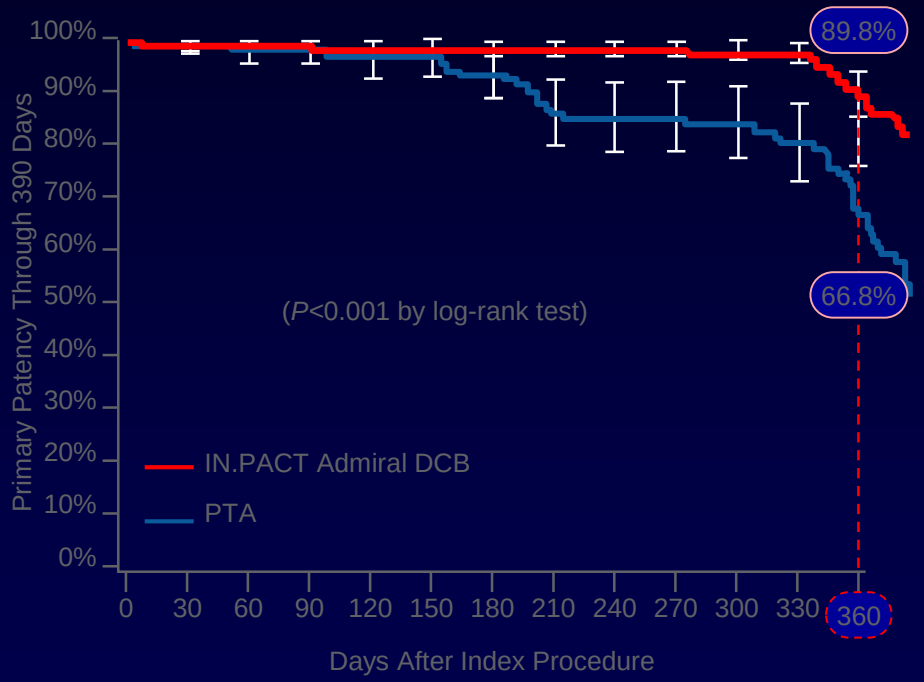
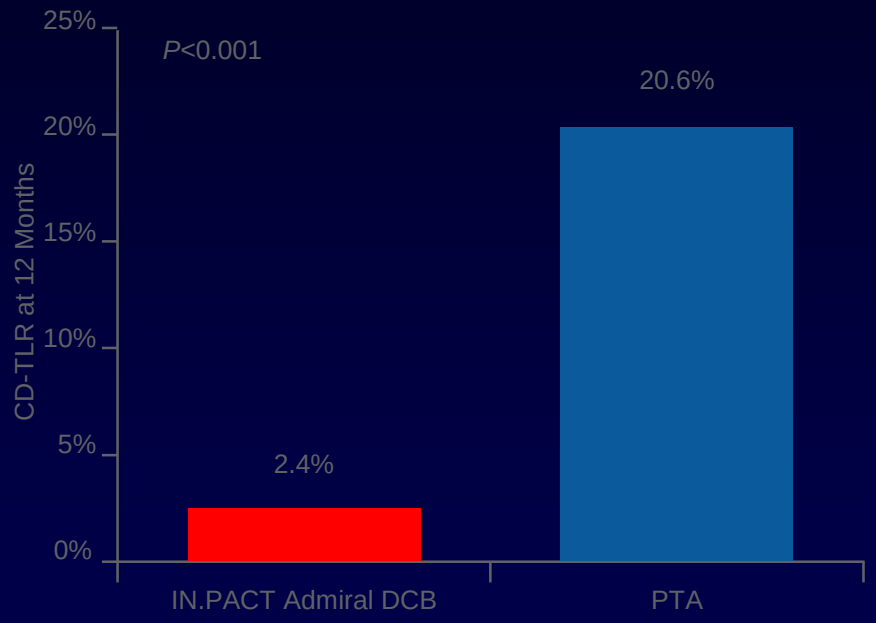
IN.PACT SFA 12-Month Efficacy Outcomes

Primary Patency Kaplan Meier (All ITT)[1]



Clinically-Driven Target Lesion Revascularization (CD-TLR)[2]



1. Primary patency is defined as freedom from clinically-driven TLR and freedom from restenosis as determined by DUS PSVR ≤2.4
2. Clinically-driven TLR defined as any re-intervention due to symptoms or drop of ABI/TBI of >20% or >0.15 compared to post-procedure ABI/TBI

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Potential advantages of DEB c/w DES

- Greater/more uniform drug delivery per mm^2 of surface area=greater efficacy?
- Lack of ongoing drug and polymer
  - ✓ Less/shorter inflammation
  - ✓ More rapid endothelialization
  - ✓ Less late thrombosis
  - ✓ Shorter/less intense DAPT
- Lack of permanent stent prosthesis
  - ✓ Less provocation of neointimal formation
- Use in "stent-disadvantaged" zones
  - ✓ Small vessels, bifurcations, ISR, infra-inguinal
- Ease of use

Summary of Management of Non-CTO SFA Disease

Treatment Strategies	Focal Lesions	Calcified Lesions	Diffuse Lesions
Standard Balloon PTA	Can be used as Primary therapy	Can be used to prime the lesion or after Atherectomy (Avoid before Directional, Orbital or Rotational Atherectomy)	
Cutting Balloon PTA			
Atherectomy	Directional (SilverHawk)	Directional, Orbital & Rotational	Directional, Orbital, Rotational & Laser
Stenting	For residual stenosis or flow limiting dissection	Supera stents should be considered in moderate to heavy calcified lesions	Focal stenting vs. Zilver PTX vs. Supera. Ostial lesions should be st
Drug Coated Balloon Angioplasty	Can be considered in lesions longer than 30mm	Better results with directional atherectomy	Should be strongly considered

Critical Limb Ischemia/ Limb Salvage

71 yo female

- HTN
- ↑Cholesterol
- Prior stroke
- Atrial fibrillation
- Non-diabetic

Recommended treatment: lower limb amputation

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Critical Limb Ischemia/ Limb Salvage

Silverhawk

3 mos post plaque excision with no skin graft, no prosthesis and no pain meds

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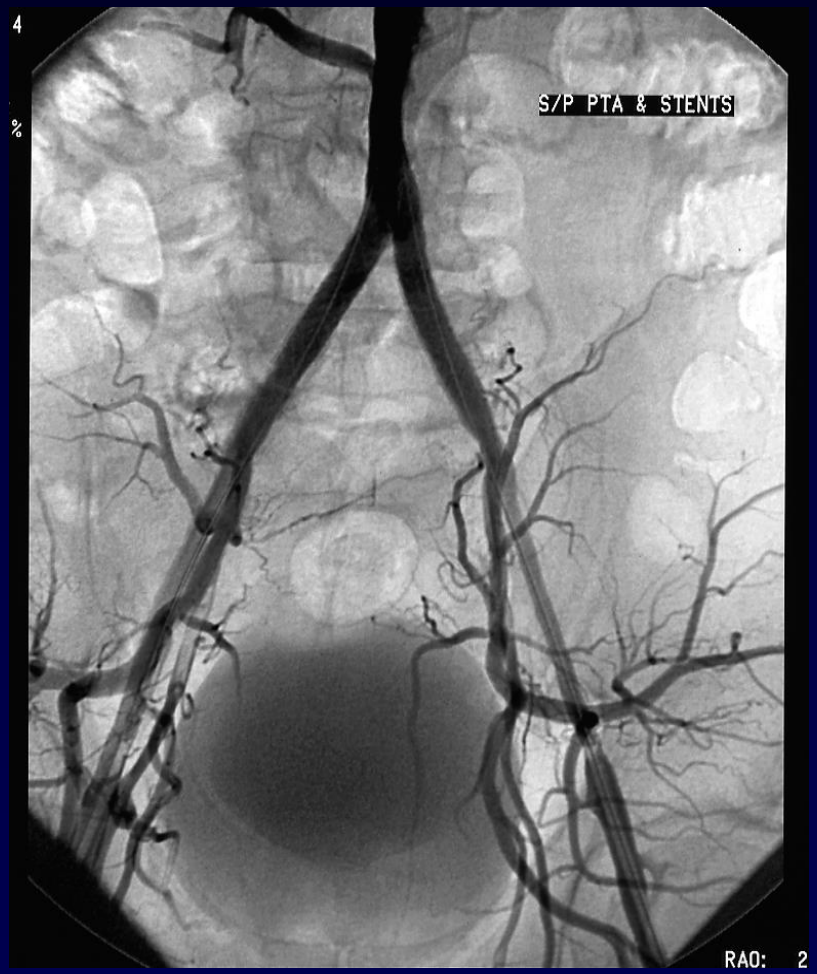
Endovascular Repair of Aortoiliac Disease



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Tibial CTO with PTA

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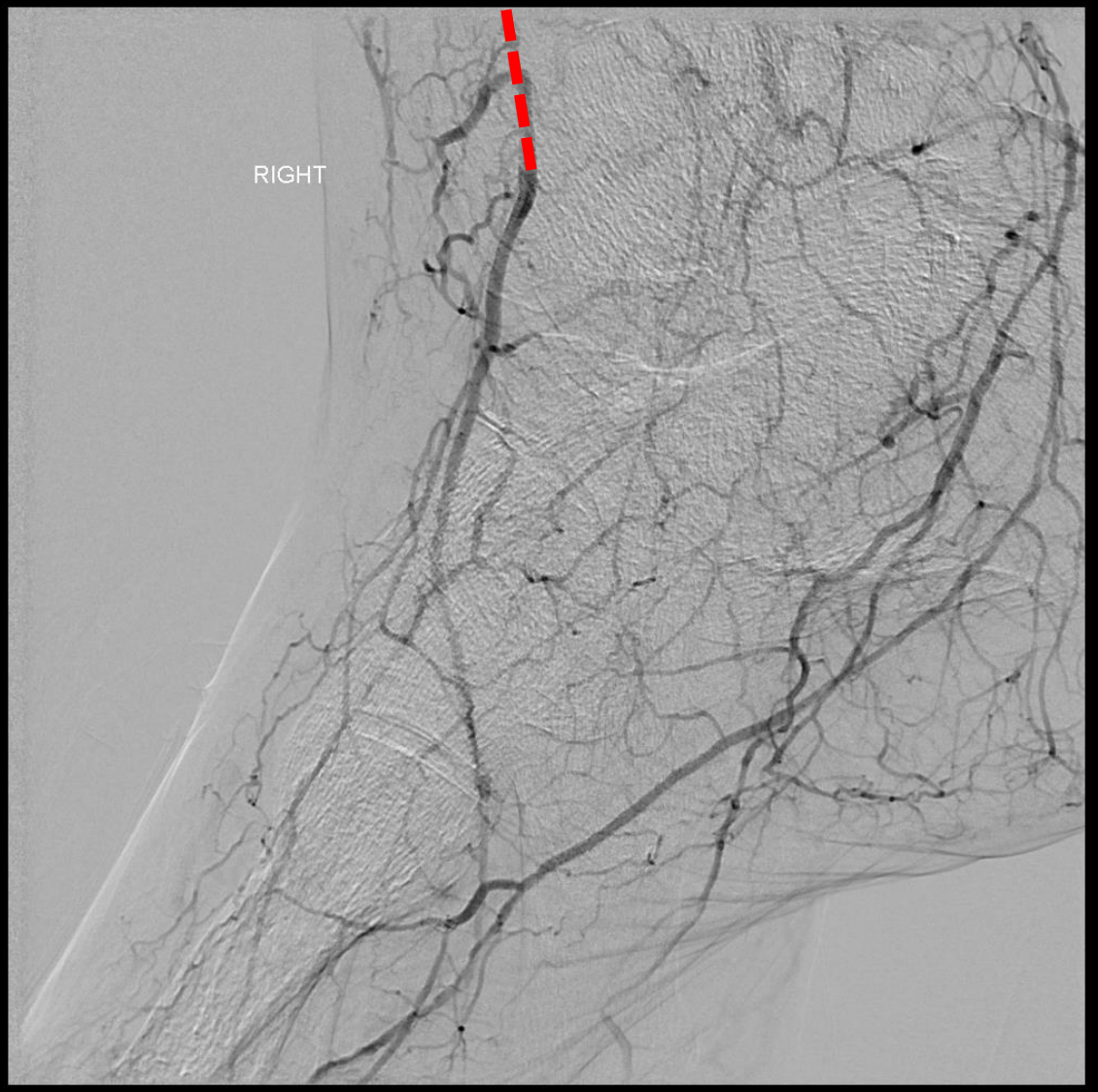
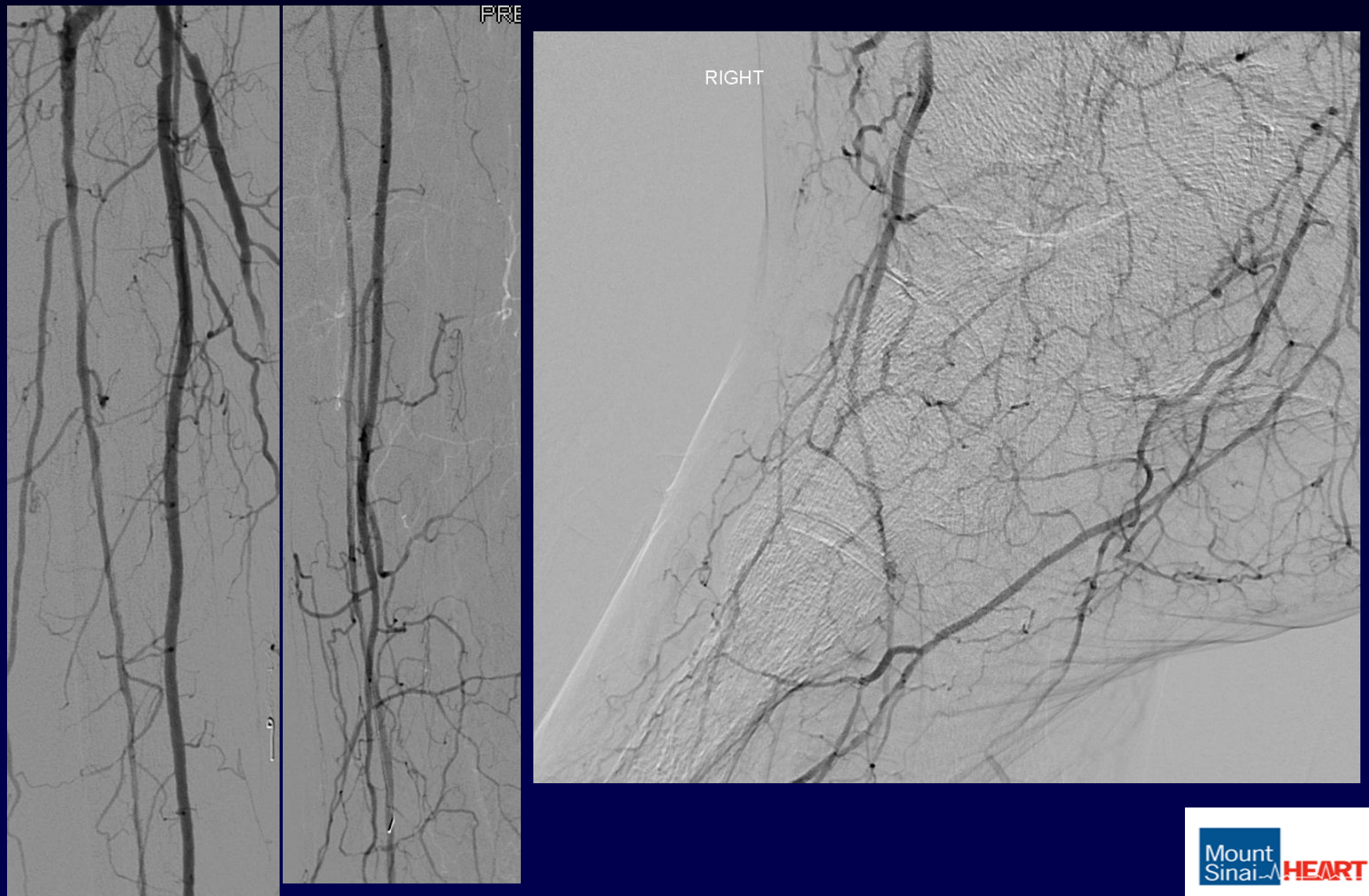
Angiogram
Patent Peroneal/Occluded AT



Direct Access to DP at foot

Retrograde Recanalization

Final Result



So you decide….

- Limb salvage rates for PTA, Laser, Cryoplasty, Silverhawk, DES, DEB are ALL greater than 85%, many 95%
- And the RIGHT artery and MORE than one artery can be treated to the correct angiosome

You Are Never Too Old To Walk!

Peripheral Angioplasty

Summary

- PAD progresses in severity
- Surgery has been the "Old Standard"
- Advantages of using interventional procedures over surgery to treat PAD
  - ✓ Avoids complications of general anesthesia
  - ✓ Avoids wound healing complications
  - ✓ Less systemic stress
  - ✓ Early recovery and ambulation
  - ✓ Procedure may be repeated more readily than surgery
  - ✓ Preserves future surgical intervention options
- Generally, all a patient needs is a few months of good flow – for foot survival or salvage

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25 Million people suffer from venous reflux disease, the underlying cause for most varicose veins




Images courtesy of Paul McNeill, MD and Rajabrata Sarkar, MD

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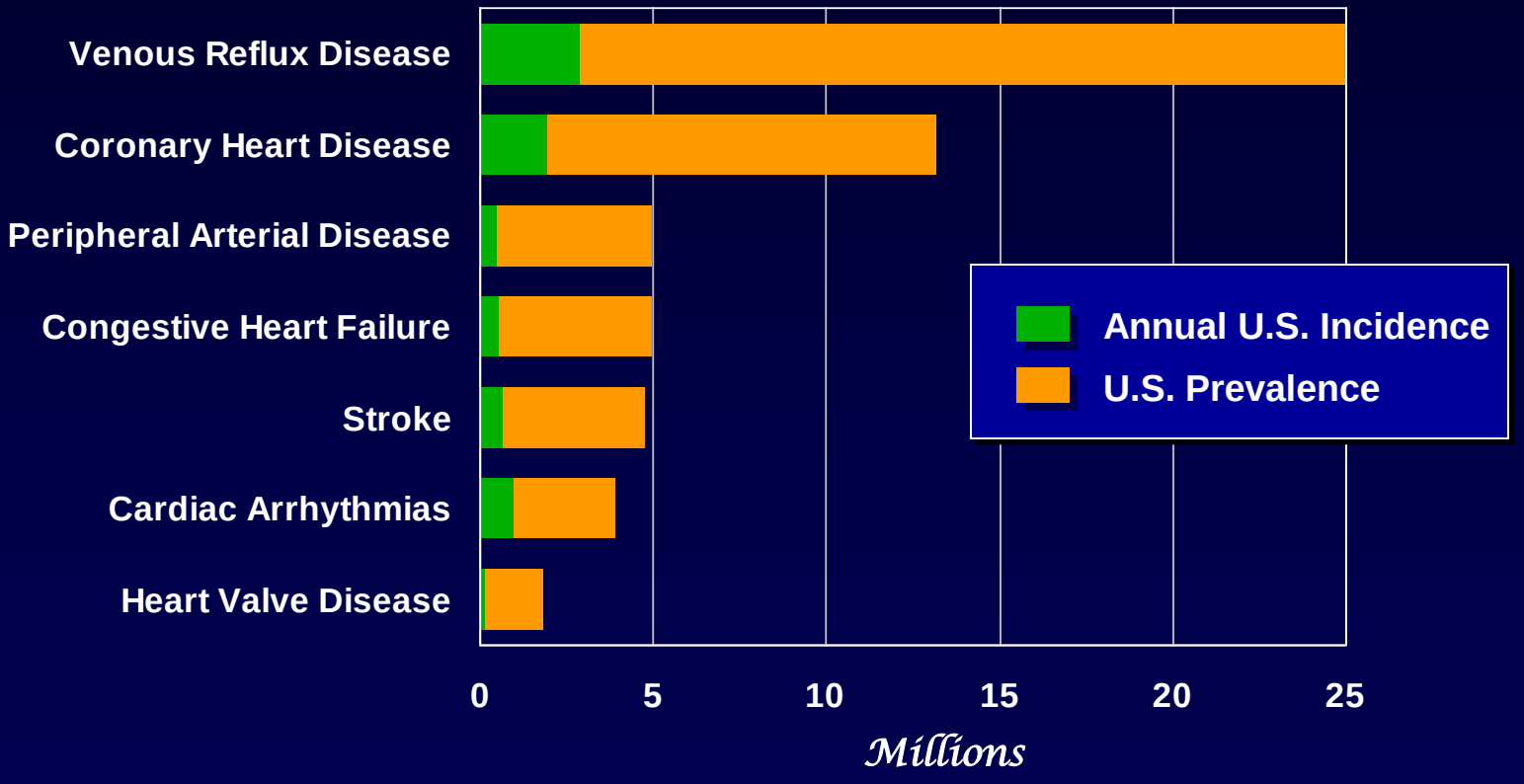
Prevalence and Etiology of Venous Insufficiency

Venous reflux disease is 2x more prevalent than coronary heart disease (CHD) and 5x more prevalent than peripheral arterial disease (PAD)[1]



Prevalence and Etiology of Venous Insufficiency

Of the estimated 25 million people with symptomatic superficial venous reflux[1] :

- *Only 1.7 million seek treatment annually[2]*
- *Over 23 million go untreated*

Prevalence by Age and Gender[3,4]

Age	Female	Male
20 - 29	8%	1%
40 - 49	41%	24%
60 - 69	72%	43%

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Systemic Reflux in Venous Ulceration

Photos courtesy of Steven A. Kaufman, MD.

Sources of Reflux in Venous Ulcer Patients[8]		
Superficial	**Perforating**	**Deep**
79%	**63%**	**50%**

Incompetent perforators found in 63% of venous ulcer patients

Comprehensive care treats all sources of reflux

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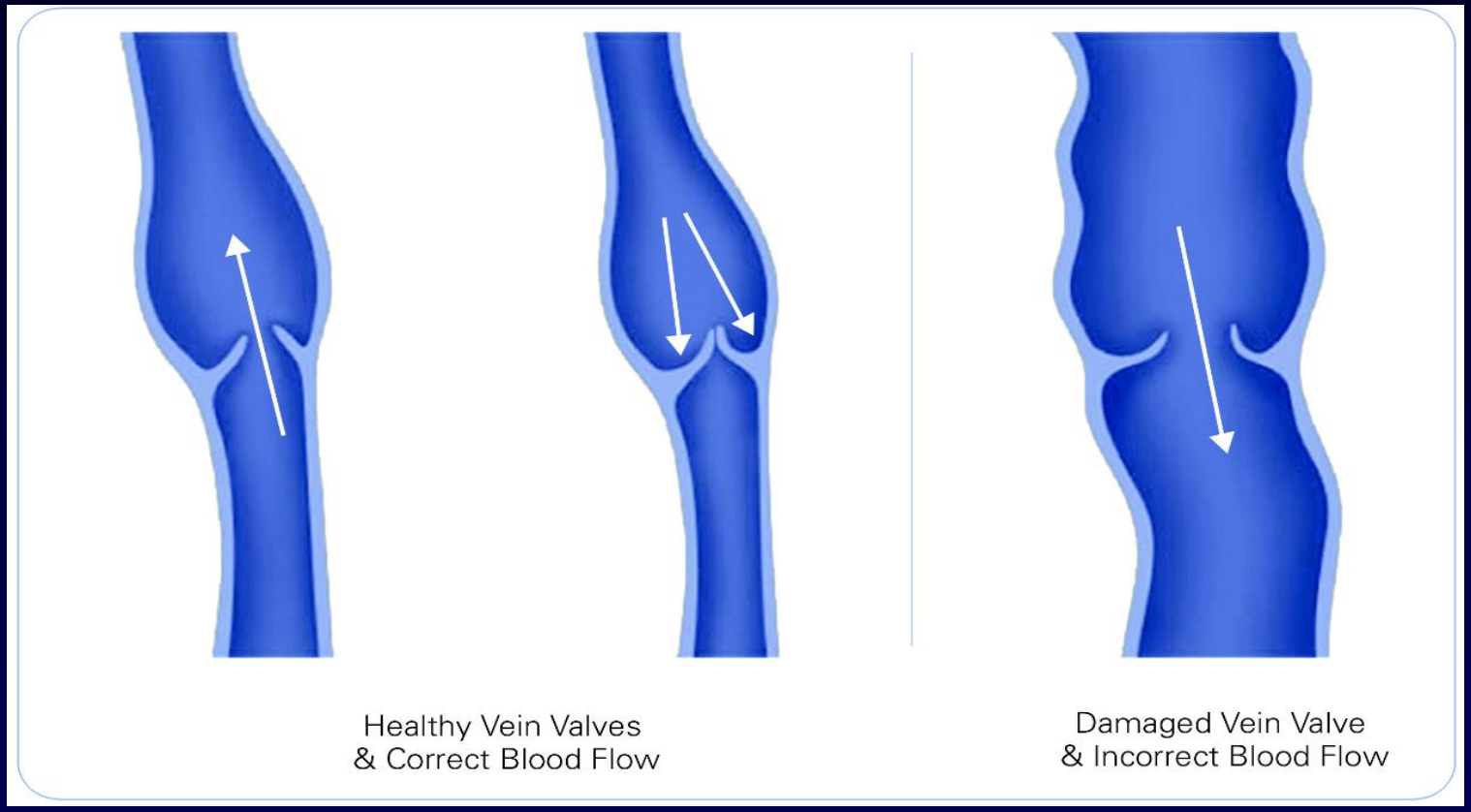
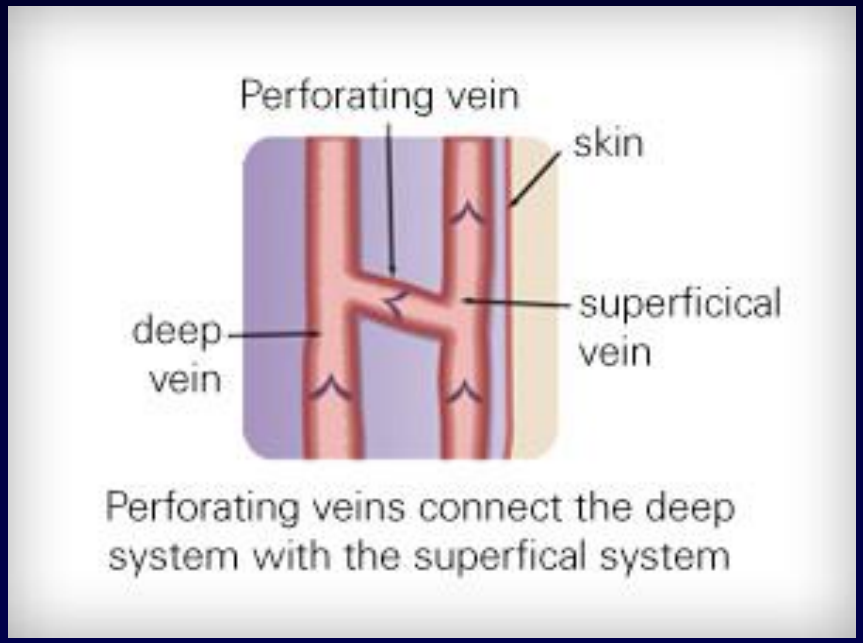
Pathophysiology of Venous Insufficiency



Perforating Veins and Reflux

- Perforator valves maintain one-way flow from superficial to deep veins
- Perforator valve failure causes:
  - ✓ Higher venous pressure and GSV/branch dilation
  - ✓ Increasing pressure results in GSV valve failure
  - ✓ Additional vein branches become varicose
  - ✓ Further GSV incompetence and dilation

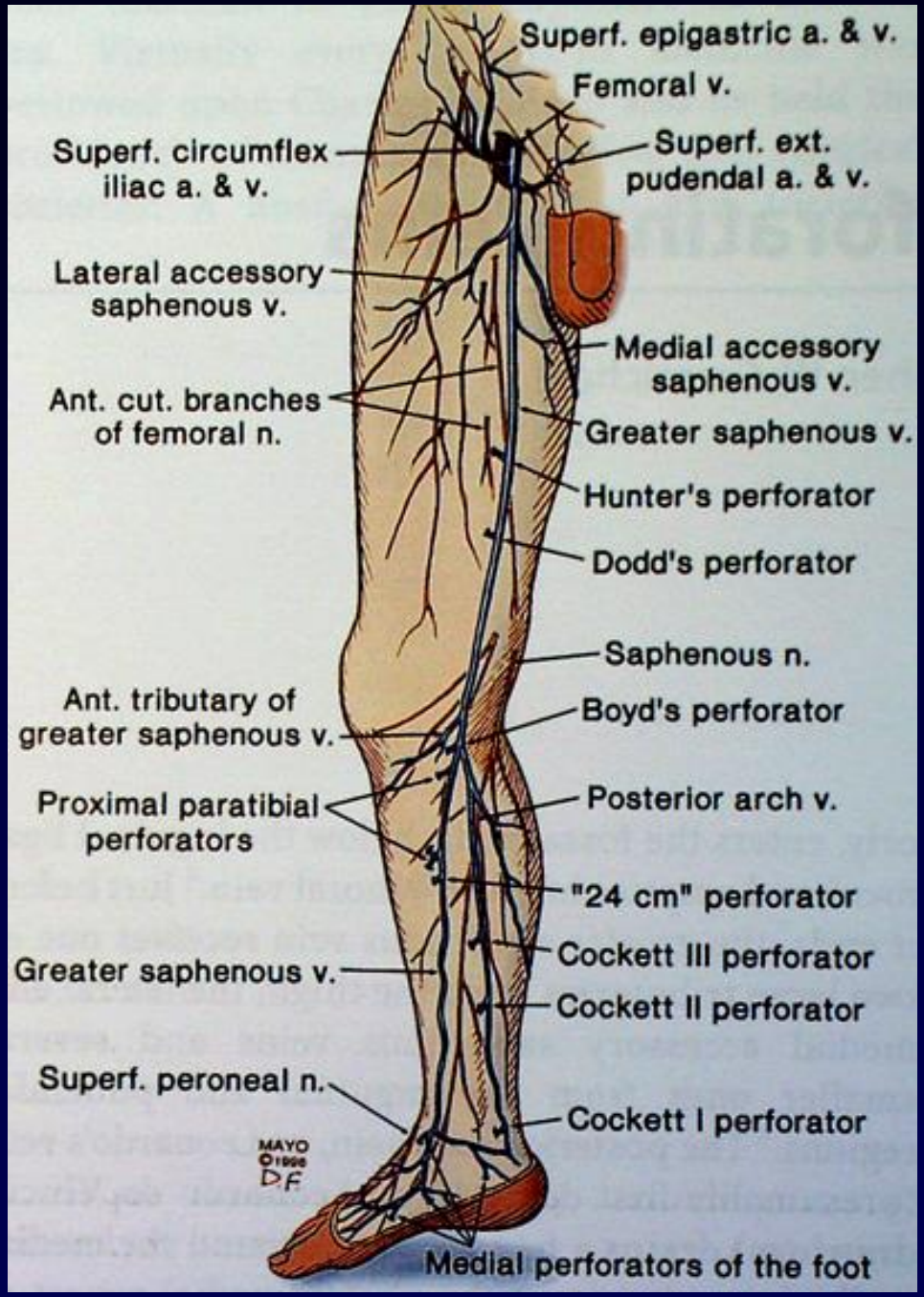


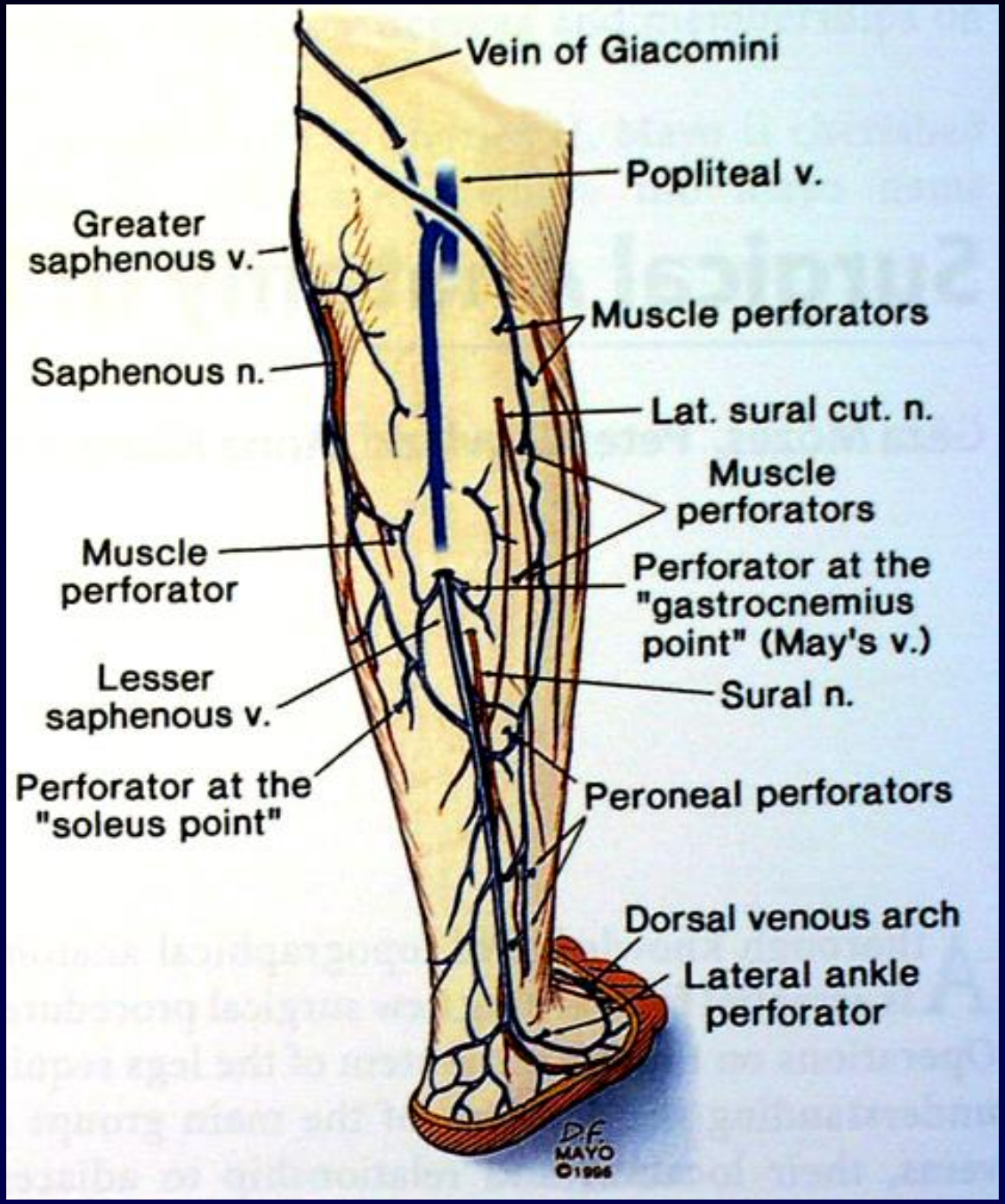
Perforating veins connect the deep system with the superfical system

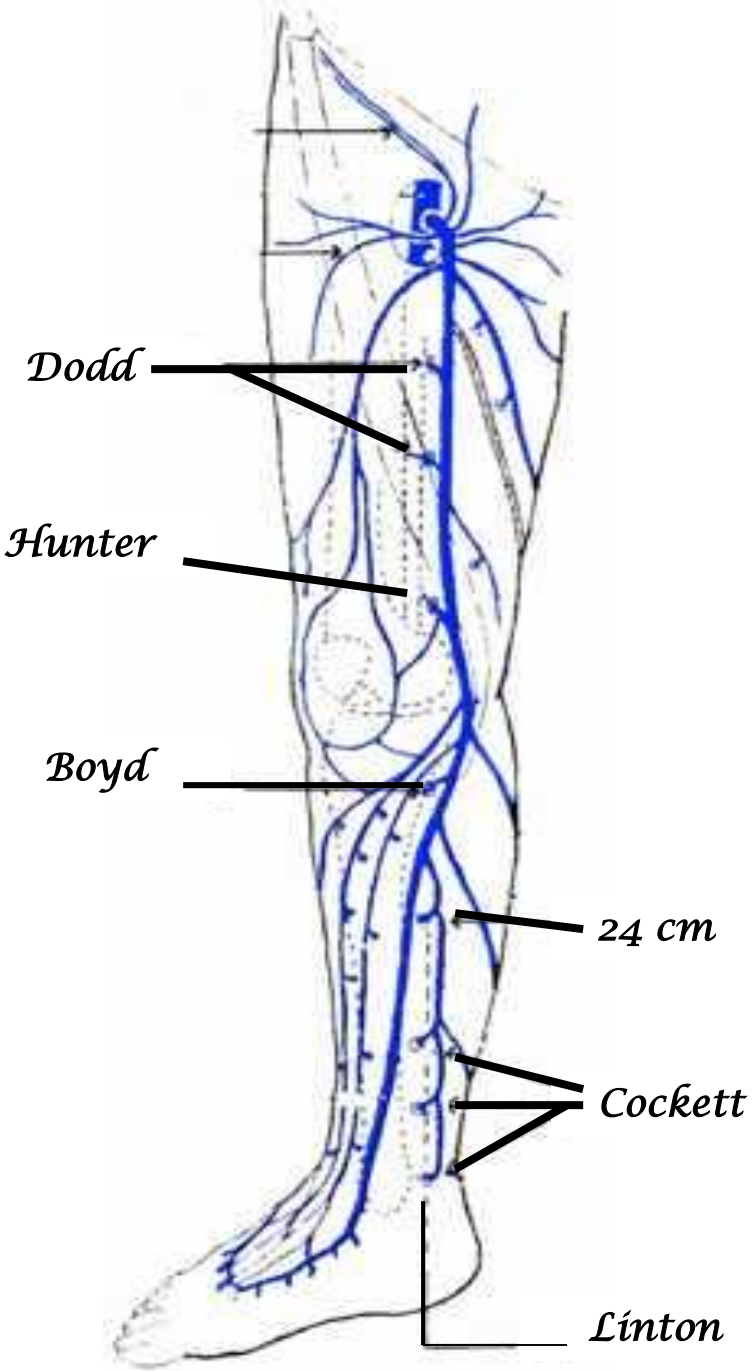
Risk Factors and Symptoms of Venous Insufficiency

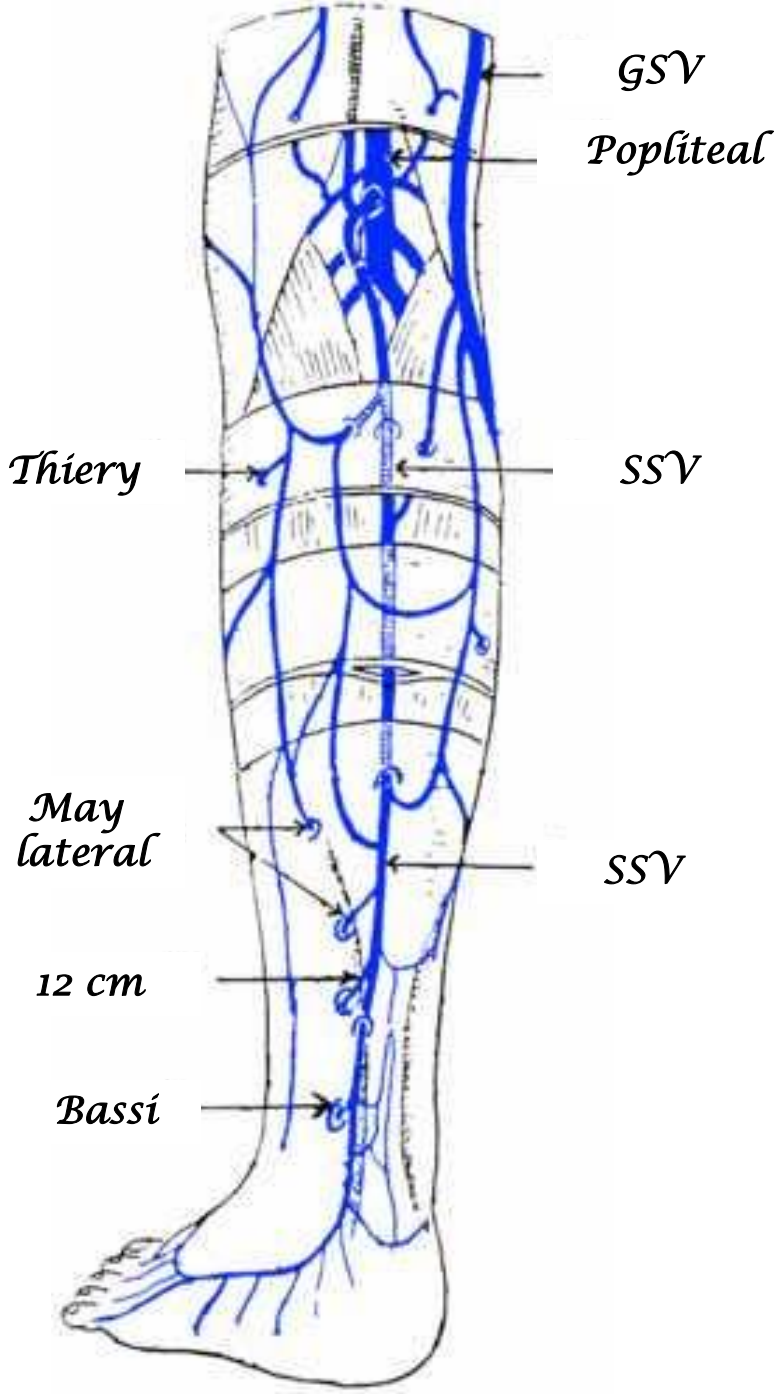
Risk factors of venous insufficiency:
• Gender
• Age
• Heredity
• Pregnancy
• Standing occupation
• Obesity
• Prior injury or surgery
• Sedentary lifestyle

Symptoms of venous insufficiency:
• Leg pain, aching, or cramping
• Burning or itching of the skin
• Leg or ankle swelling
• “Heavy” feeling in legs
• Skin discoloration or texture changes
• Open wounds or sores
• Restless legs
• Varicose Veins


Superf. epigastric a. & v.
Femoral v.
Superf. circumflex iliac a. & v.
Superf. ext. pudendal a. & v.
Lateral accessory saphenous v.
Medial accessory saphenous v.
Ant. cut. branches of femoral n.
Greater saphenous v.
Hunter's perforator
Dodd's perforator
Saphenous n.
Ant. tributary of greater saphenous v.
Boyd's perforator
Proximal paratibial perforators
Posterior arch v.
"24 cm" perforator
Greater saphenous v.
Cockett III perforator
Cockett II perforator
Superf. peroneal n.
Cockett I perforator
MAYO ©1996 DF
Medial perforators of the foot

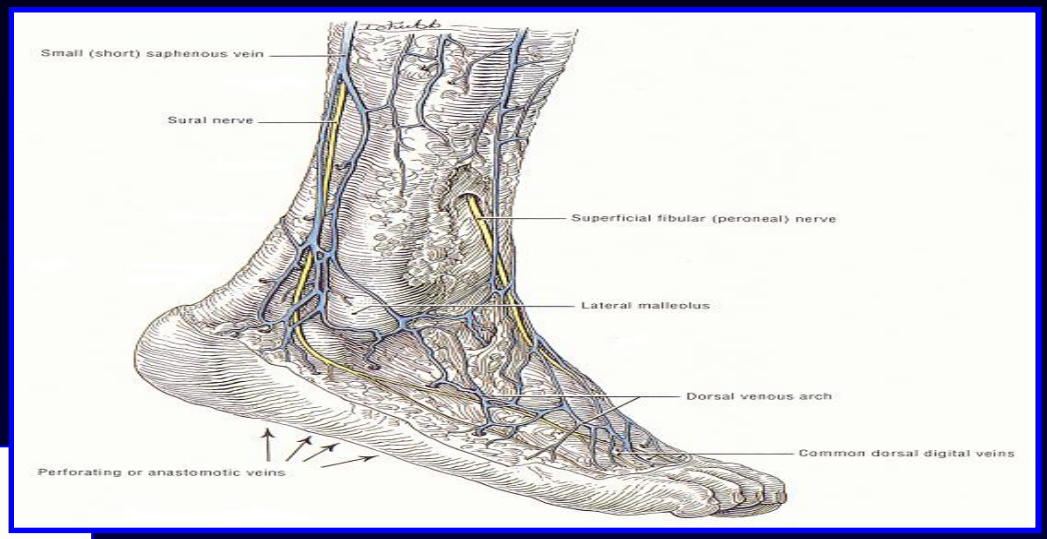


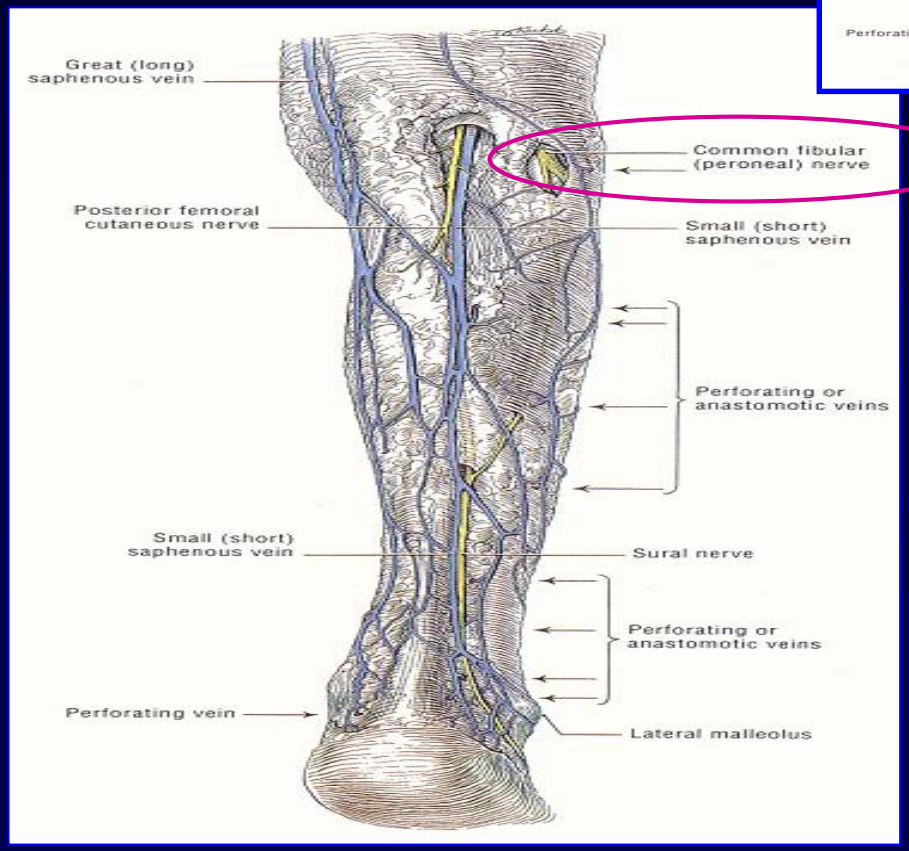

Dodd
Hunter
Boyd
24 cm
Cockett
Linton


GSV
Popliteal
Thiery
SSV
May lateral
SSV
12 cm
Bassi

SMALL SAPHENOUS VEIN ANATOMY

- **Anterolateral View**
  - The SSV originates at the lateral heel/ankle
  - Distally, the SSV lies superficial to the fascial planes
  - The sural nerve lies very close to the SSV from the lateral ankle to mid-calf





- **Posterior View**
  - From its origin, the SSV continues up the posterior calf
  - At its mid-1/3 segment, the SSV lies between the superficial and deep fascial planes
  - Proximally, the SSV and sural nerve dive beneath the deep fascia
  - The SSV empties into the popliteal vein in the region of the popliteal fossa

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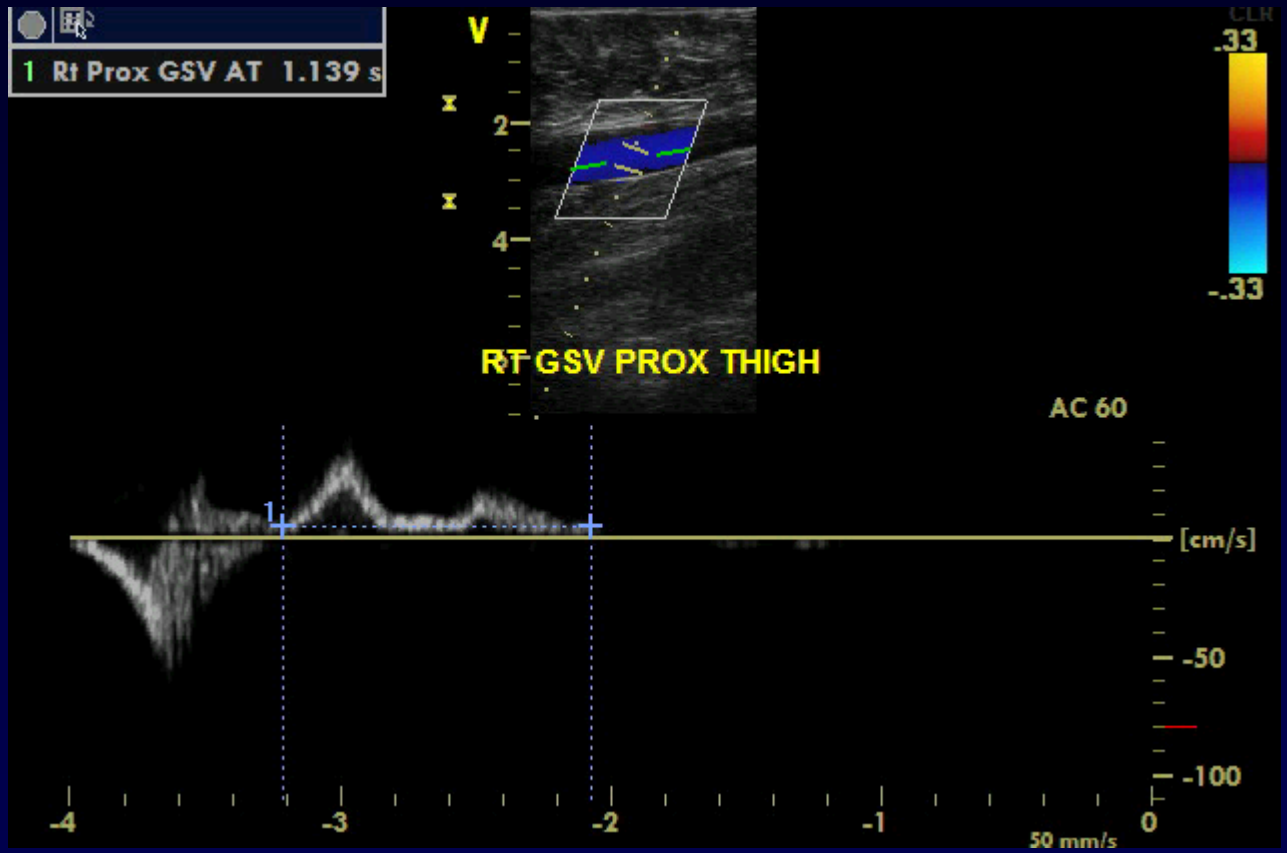
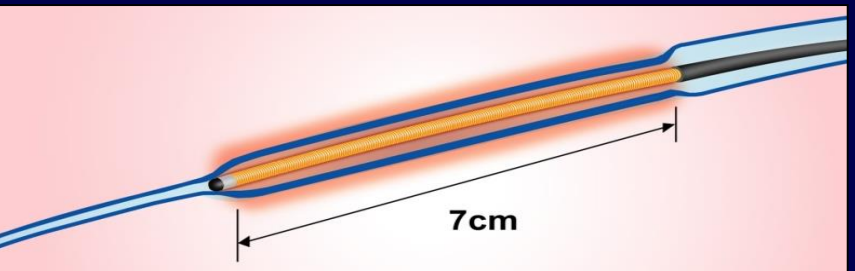
Rt. GSV Reflux study



RFA
Design and Mode of Action

- RF Energy heats Catheter tip (7cm heating element) to 120˚ C
- **Conductive Heat Transfer** from heating element to vein wall achieves temperatures of 85-120˚ C
  - ✓ Vein wall heating causes collagen vein wall contraction and thrombosis



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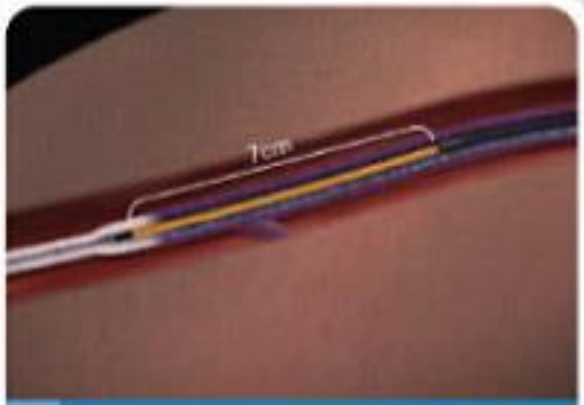
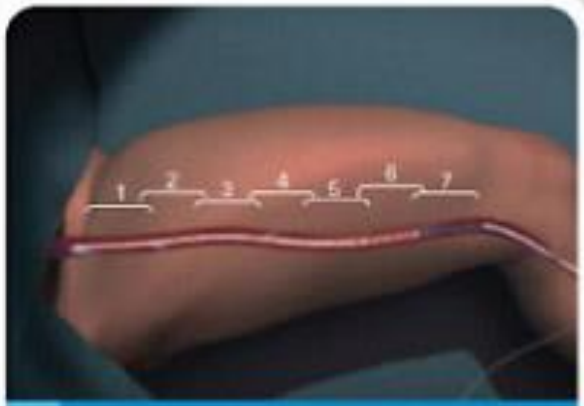
1. Catheter tip positioned 2cm distal to the saphenofemoral junction. Tumescent infiltration is administered.



2. 7 cm vein segment treated all at once during 20-second treatment cycle. Additional vein segments treated serially.

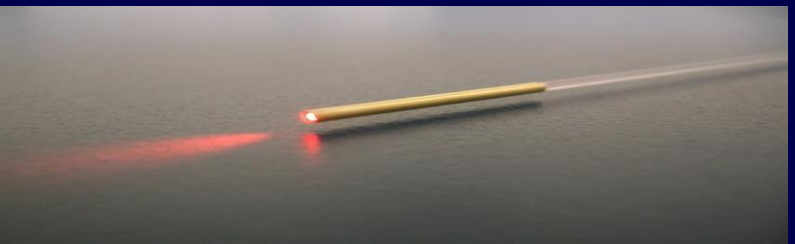
3. Catheter shaft markings allow fast and accurate catheter re-positioning between treatment cycles. No energy is delivered during re-positioning.



4. Treatment of 45 cm vein length takes 3 to 5 minutes (seven treatment segments).

ELA
Design and Mode of Action

- ELA Energy steam bubbles within vessel (blood) or vessel wall (water) depending on laser wave length
- **Steam bubbles** from laser tip can achieve temperatures as high as 1200˚ C at the tip to 48˚ C to the exterior of the vein wall
  - ✓ Steam bubbles causes collagen vein wall contraction and thrombosis



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RECOVERY Trial: Conclusions

- ClosureFAST proved to be significantly superior to endovenous laser ablation when evaluating post-procedural recovery and patient QOL parameters
- Compared to laser ablation, treatment with ClosureFAST produced significantly

✓ Less pain	**p < 0.0001**
✓ Less bruising	**p < 0.0001**
✓ Less tenderness	**p = 0.0008**
✓ Fewer adverse events	**p = 0.021**
✓ Greater improvement in VCSS scores*	**p = 0.0035**
✓ Better quality of life*	**p = 0.045**

** Out to 14 days*

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Endovascular Treatment (EVT) of Chronic Iliac Vein Obstruction

Objectives

- ✓ Compare stent-related and clinical outcomes, results and complications of EVT in limbs with nonthrombotic iliac vein lesions (NIVL) and post-thrombotic syndrome (PTS)

NIVL = Nonthrombotic iliac vein lesion (NIVL/MTS)

PTS = Post-thrombotic syndrome

Neglen et al., J Vasc Surg, 2007: 979-990

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EVT of Chronic Iliac Vein Obstruction

Materials/Methods

- 870 patients / 982 limbs
- Chronic symptoms (mean = 60 mos)
- NIVL = 518, PTS = 464 limbs
- Follow-up (mean = 22 mos), 1-107 mos
- IVUS
- PTA / stenting

Neglan, et al., J Vasc Surg, 2007:979-990

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EVT of Chronic Iliac Vein Obstruction
Technical Results

- Technical success = 97%
- Post-op stent thrombosis (<30 d) = 1.5%
- Primary, primary-assisted and secondary patency rates (6-years)
  - 79%, 100%, 100% (NIVL)
  - 57%, 80%, 86% (PTS)
  - ISR (>50%) = 5%

    - 10% (PTS), 1% (NIVL)

Neglan et al., J Vasc Surg, 2007:979 -990

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Technique: Endovascular Treatment of Chronic Iliac Vein Obstruction

- Access via CFV if isolated iliac/caval dz
- Popliteal vein if thrombosed femoral V
- PTA / stent w / *IVUS guidance* !!
- Pressure gradient if equivocal lesion
- Wallstents or nitinol (14 mm - 18 mm)
- Wallstents preferred if CIV confluence (MTS)

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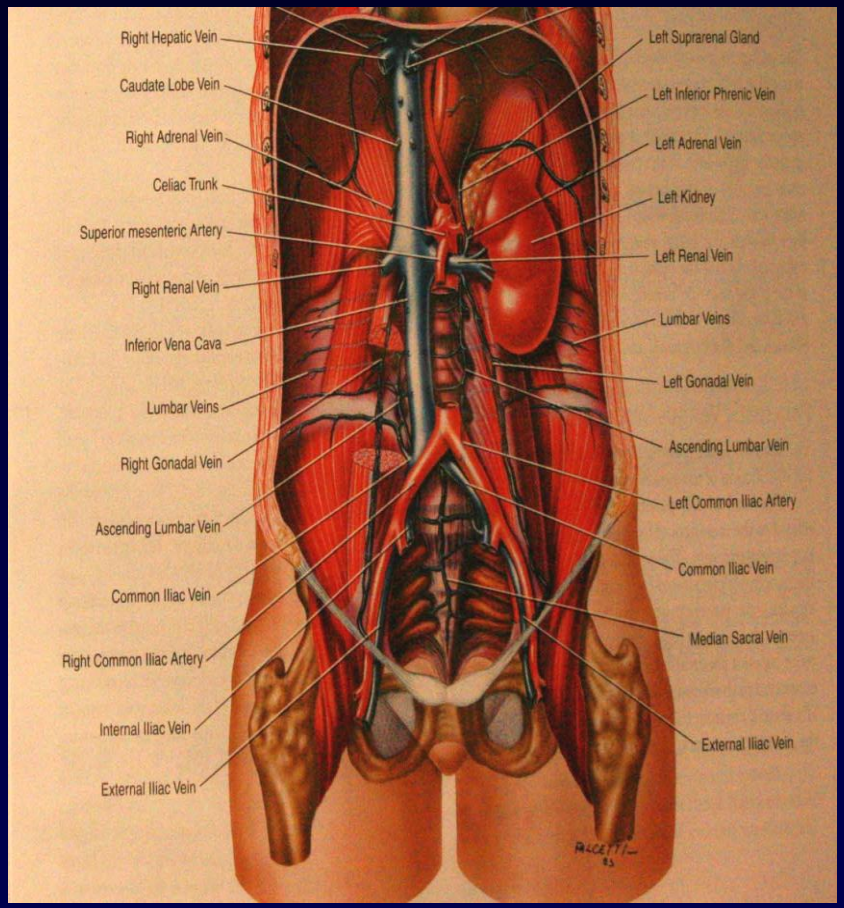
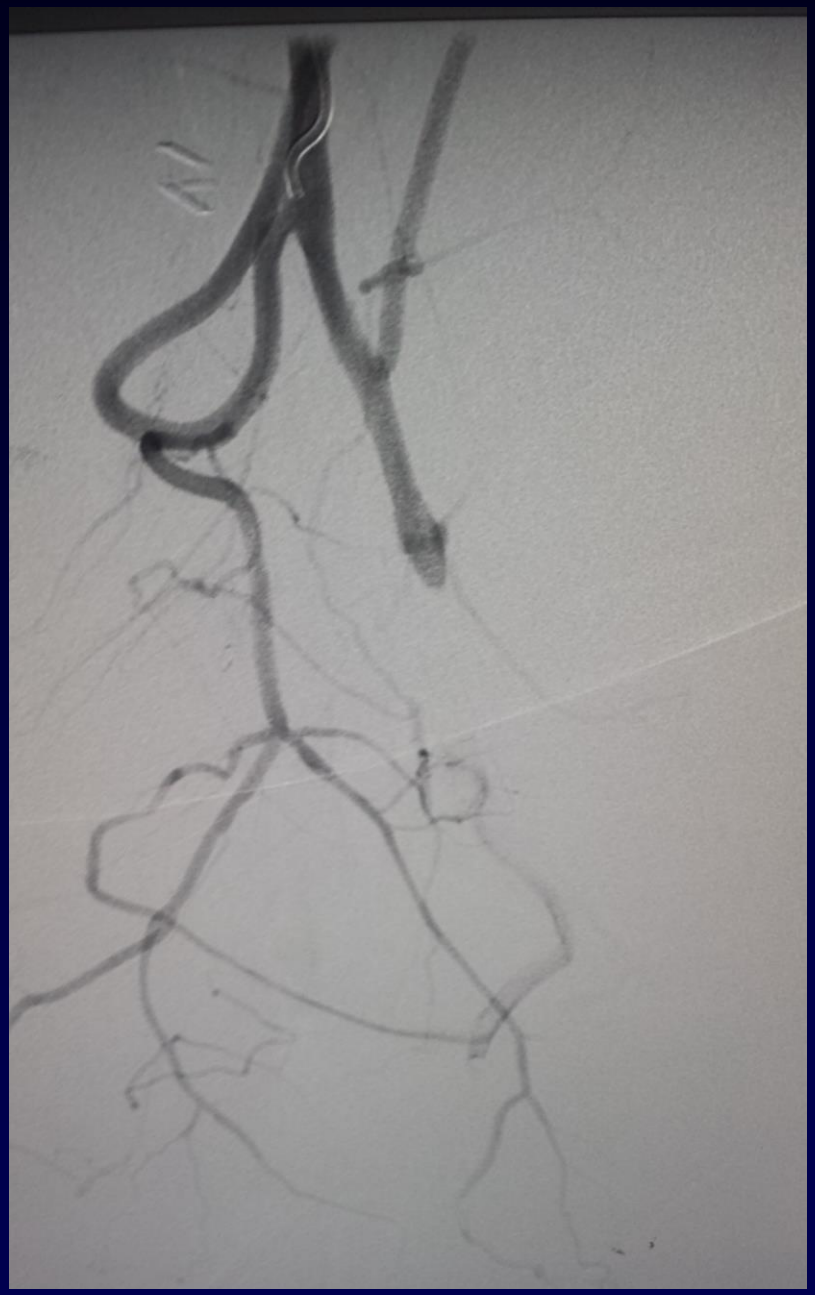
May-Thurner (MTS) or Cockett's Syndrome

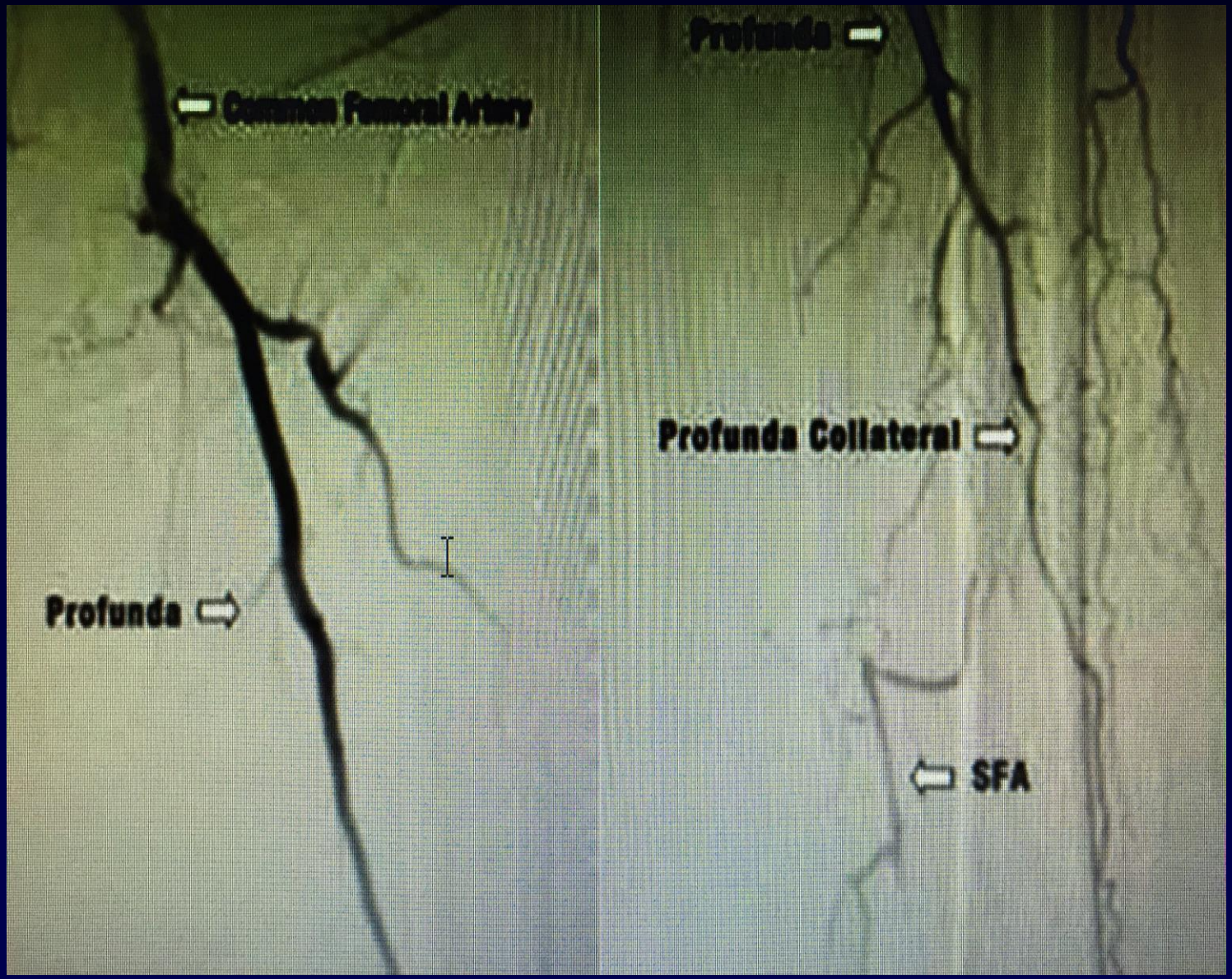
- 1851- Virchow sinistral (left-sided) DVT
- Dx in 2%-5% of pts w/ venous dz
- Right CIA/compresses the left CIV against the lumbar vertebrae
- 25% of asymptomatic pts > 50% stenosis
- 3rd – 5th decade of life / women

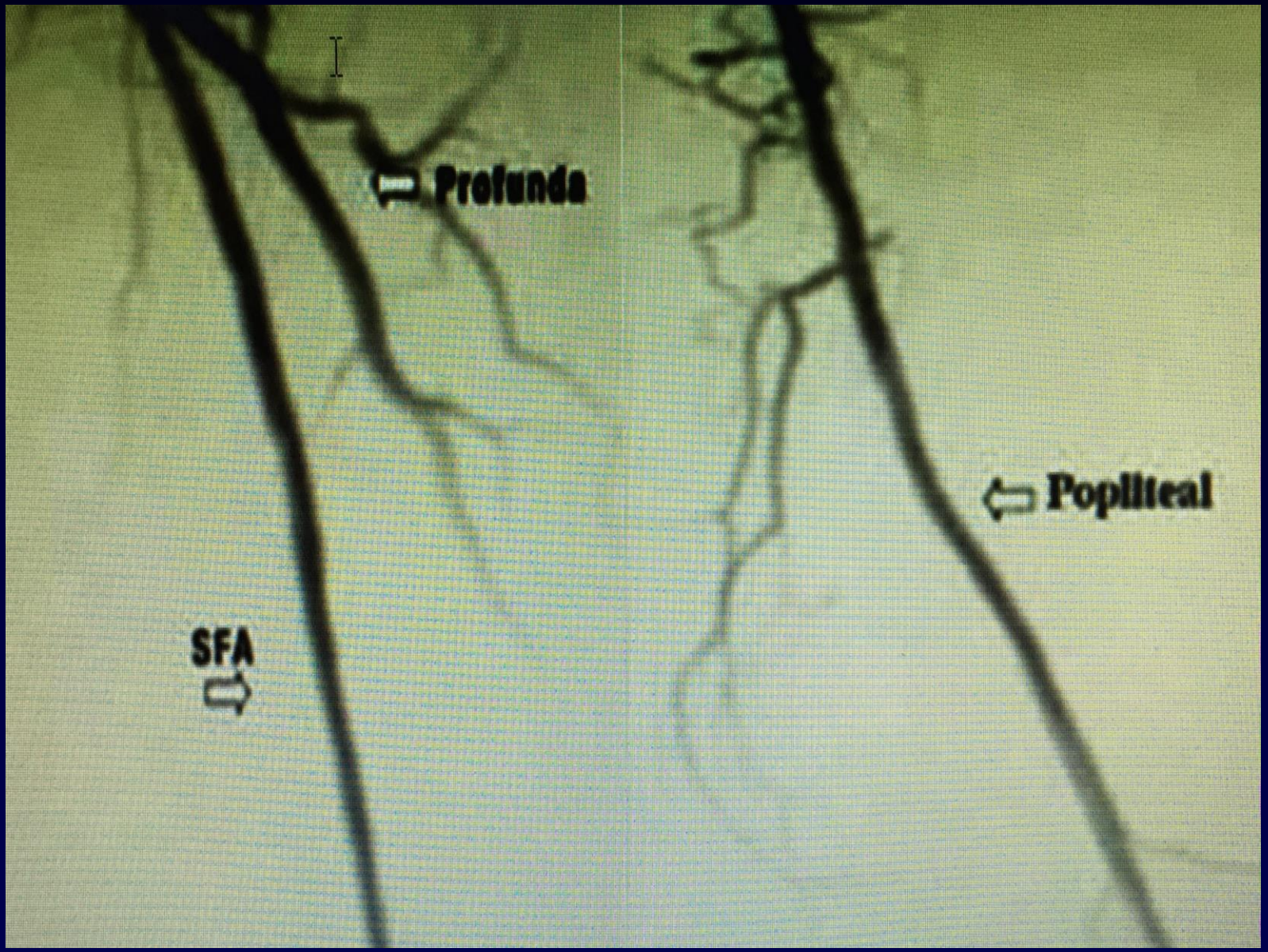
May-Thurner Syndrome



What Can be Done by Endovascular Approach




Common Femoral Artery
Profunda
Profunda
Profunda Collateral
SFA


Profunda
Popliteal
SFA