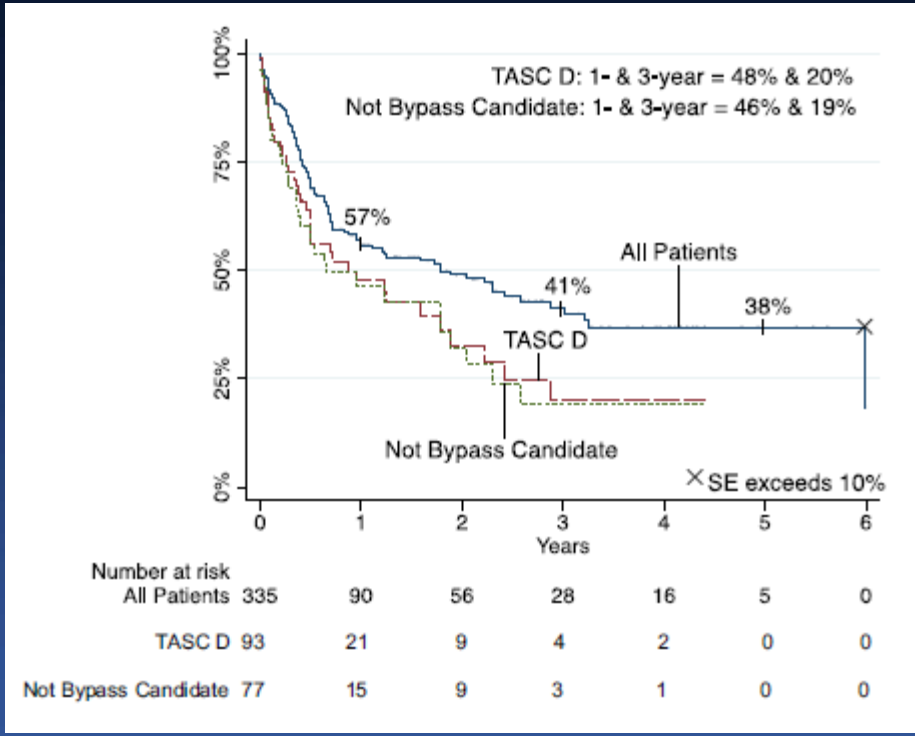
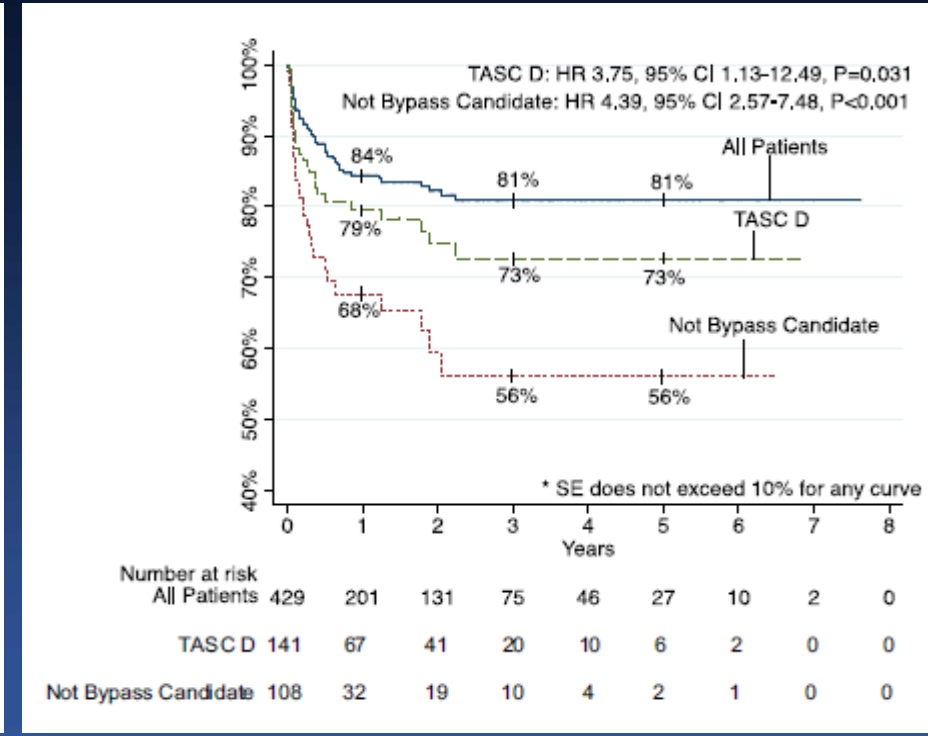
Below The Knee

Long-term Outcomes Following Infrapopliteal Angioplasty for Critical Limb Ischemia

413 patients with CLI in 459 limbs; lesions classified according to TransAtlantic Inter-Society Consensus (TASC) by severity.

- **Technical success was achieved in 93% (n = 427 limbs) with all failures in TASC D lesions**





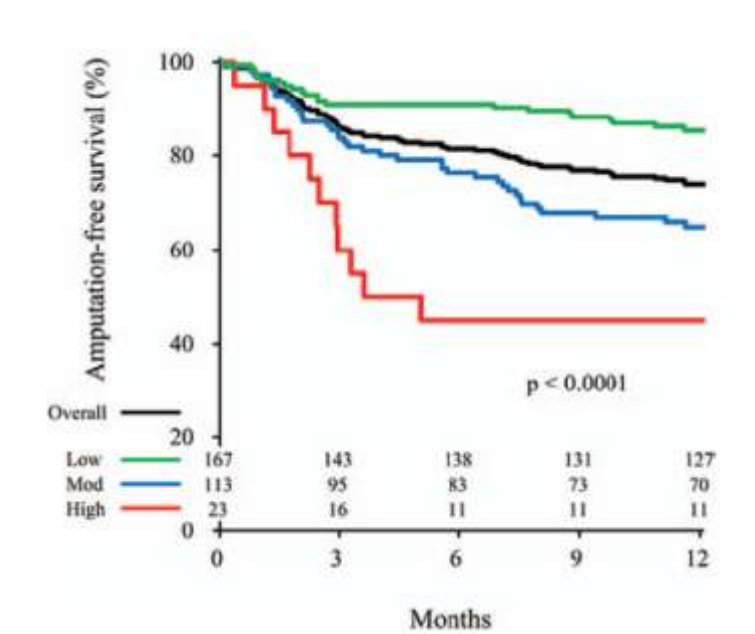
Infrapopliteal PTA is effective primary therapy for TASC A, B, and C lesions. Surgical bypass should be offered to patients with TASC D disease who are suitable candidates

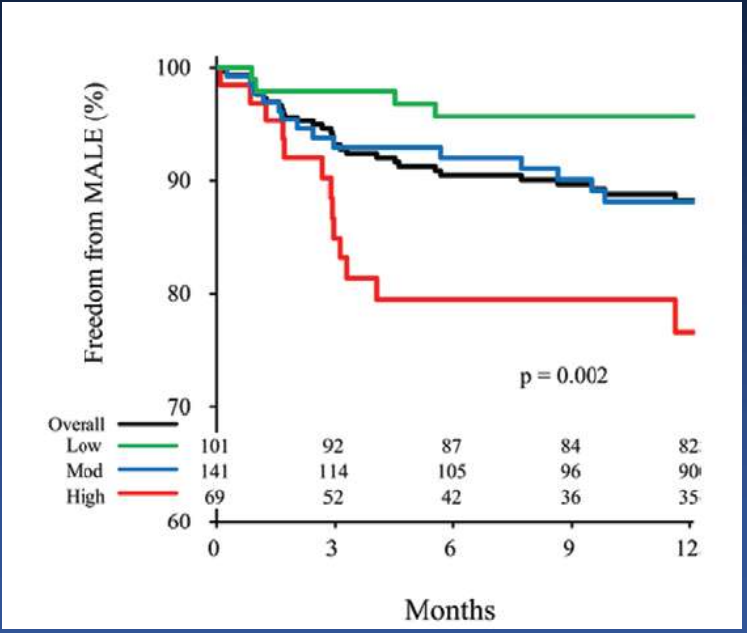
Lo RC, et al. *J Vasc Surg*. 2013;Epub ahead of print.

Endovascular Treatment for Infrainguinal Vessels in Patients with CLI: OLIVE Registry

Prospective, multicenter Japanese study of 312 patients.

- Major adverse cardiovascular event and major adverse event rates were 17% and 27% at 1 year, respectively
- Reintervention was required in 34% of patients by 1 year to achieve freedom from ischemic symptoms



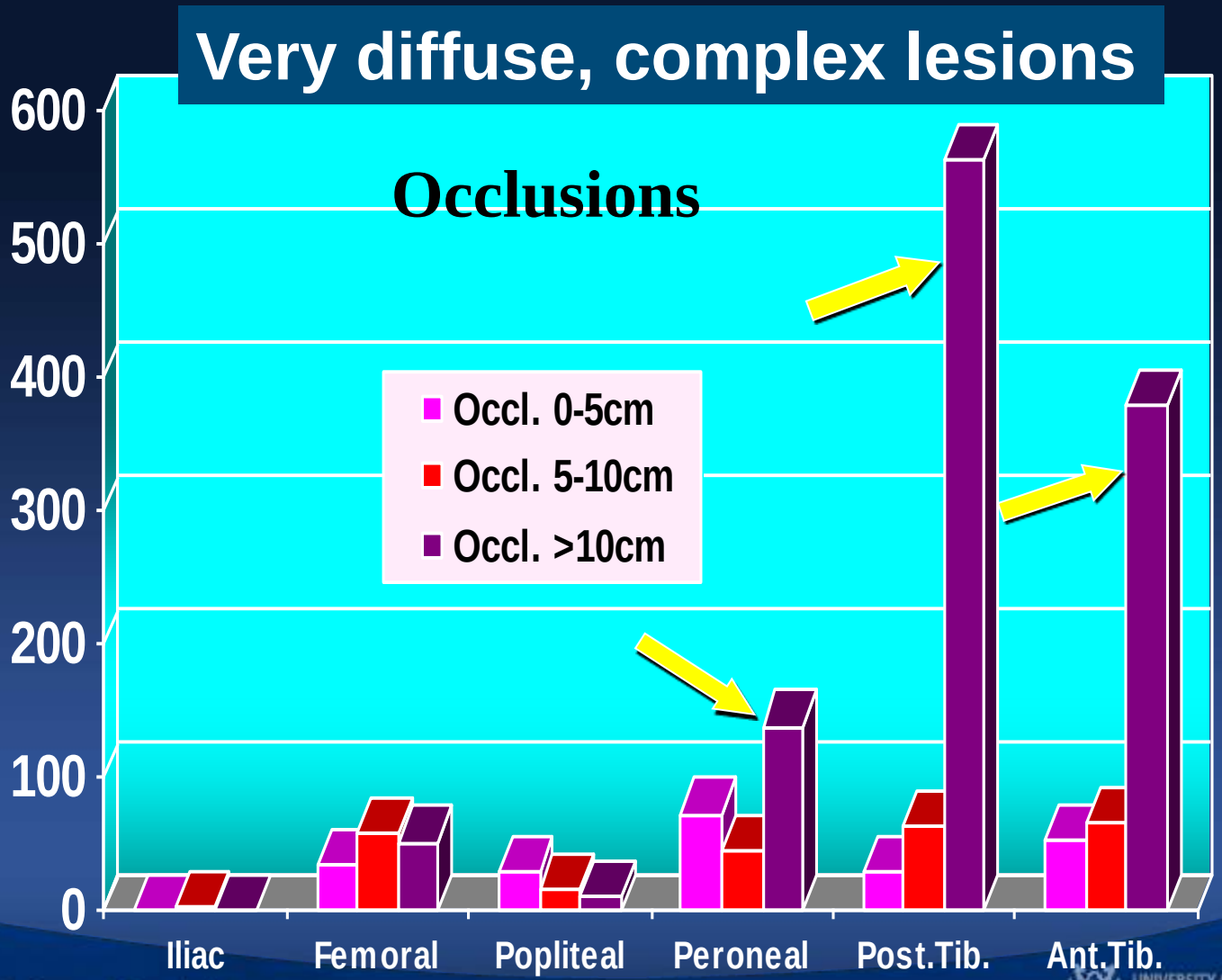


Iida O, et al. *Circ Cardiovasc Interv*. 2013;Epub ahead of print.

Wagner (wound) classification

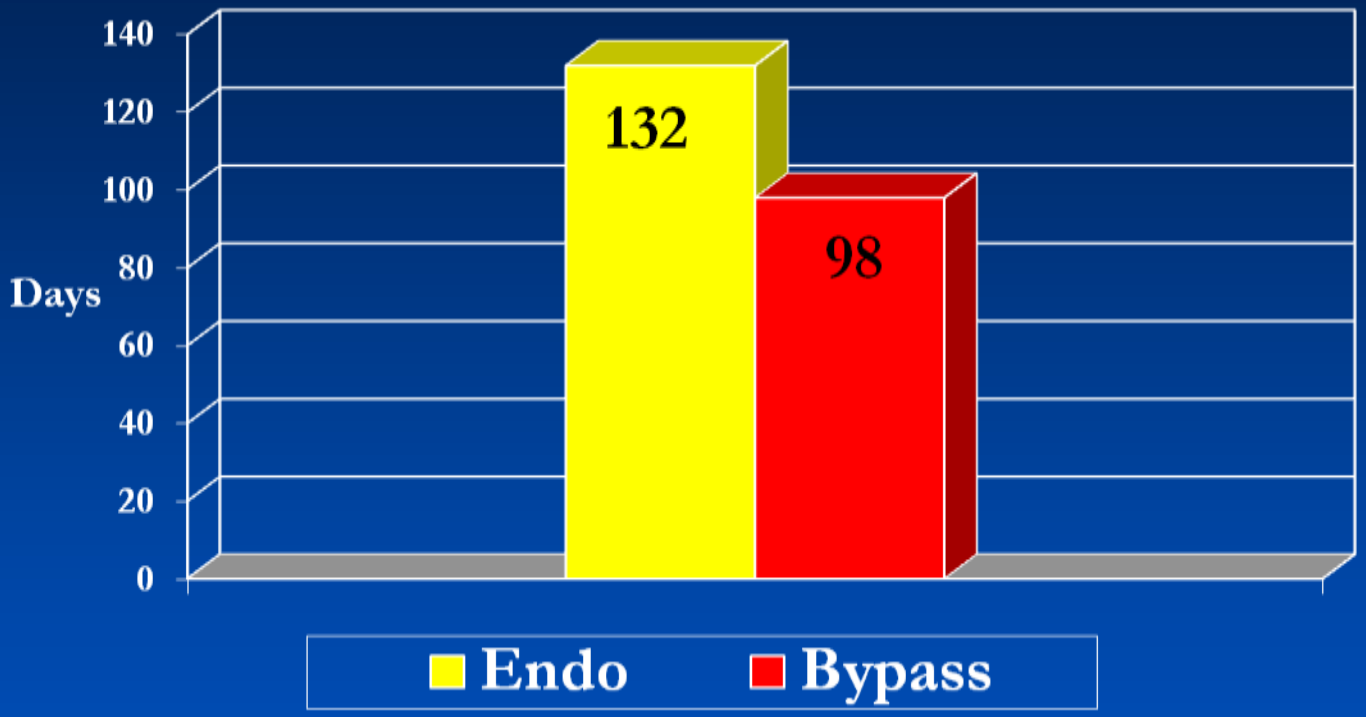
Grade 0 - no ulcer in a high-risk foot
Grade 1 - Superficial ulcer involving the full skin thickness but not underlying tissue
Grade 2 - Deep ulcer, penetrating down to ligaments and muscle, but no bone involvement or abscess formation
Grade 3 - Deep ulcer with cellulitis or abscess formation, often with osteomyelitis
Grade 4 - Localized gangrene
Grade 5 - Extensive gangrene involving the whole foot

TYPE AND DISTRIBUTION OF 2,893 LESIONS in 417 Consecutive Diabetic with Ischaemic Foot Ulcer:



Time to complete healing

3 ~ 4 months

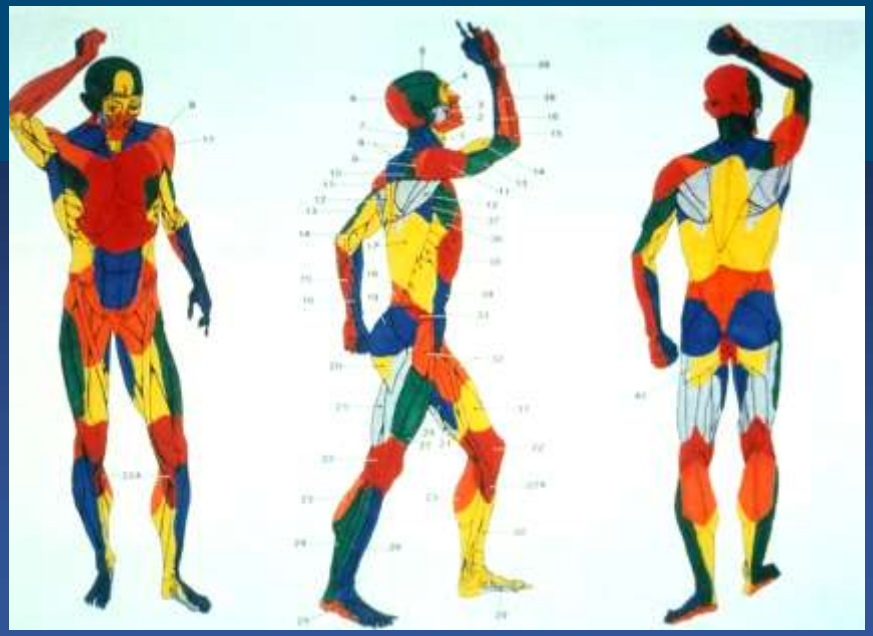


Group	Bypass	Endovascular	P value
Wound size	142	148	
A (0 – 5mm)	84 days	105 days	P = NS
B (5mm – 20mm)	102 days	128 days	P = NS
C (>20mm)	115 days	164 days	P = 0.01

Angiosome Concept

Angiosome – 3D anatomic unit fed by a source artery

(skin, subcutaneous tissue, fascia, muscle and bone)

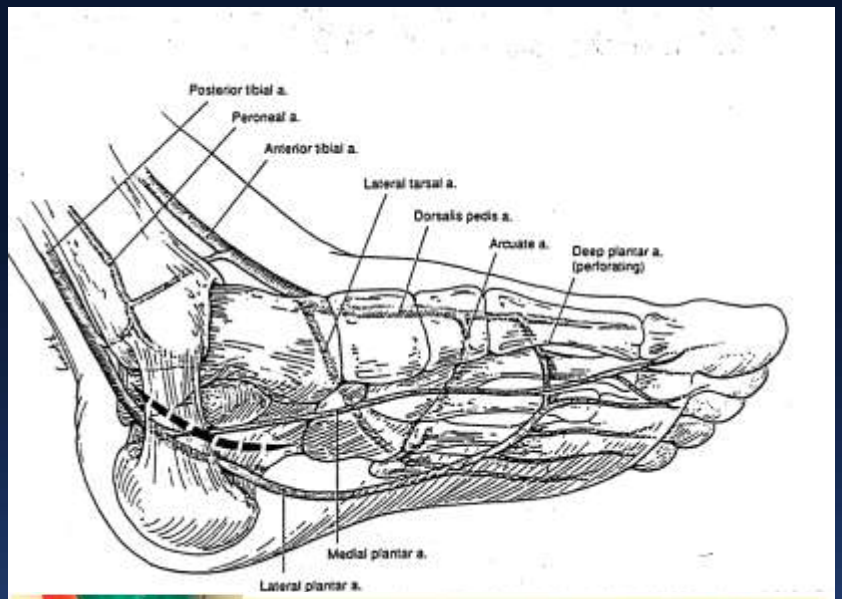


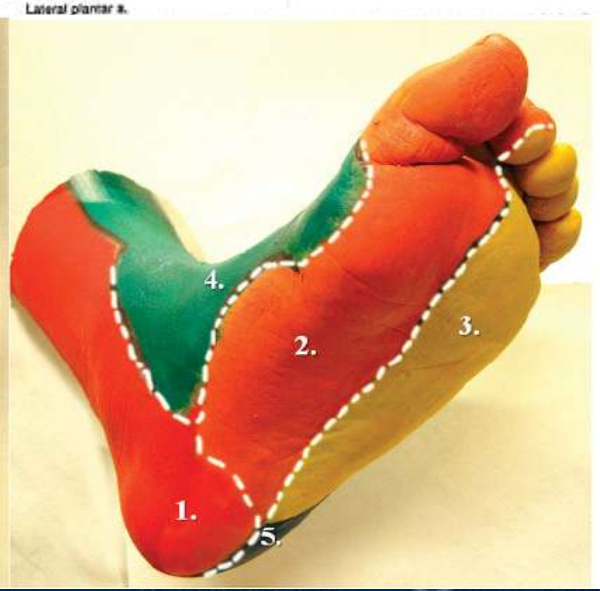
Taylor, et al. Br J Plastic Surger

Angiosome concept

Six distinct angiosomes:

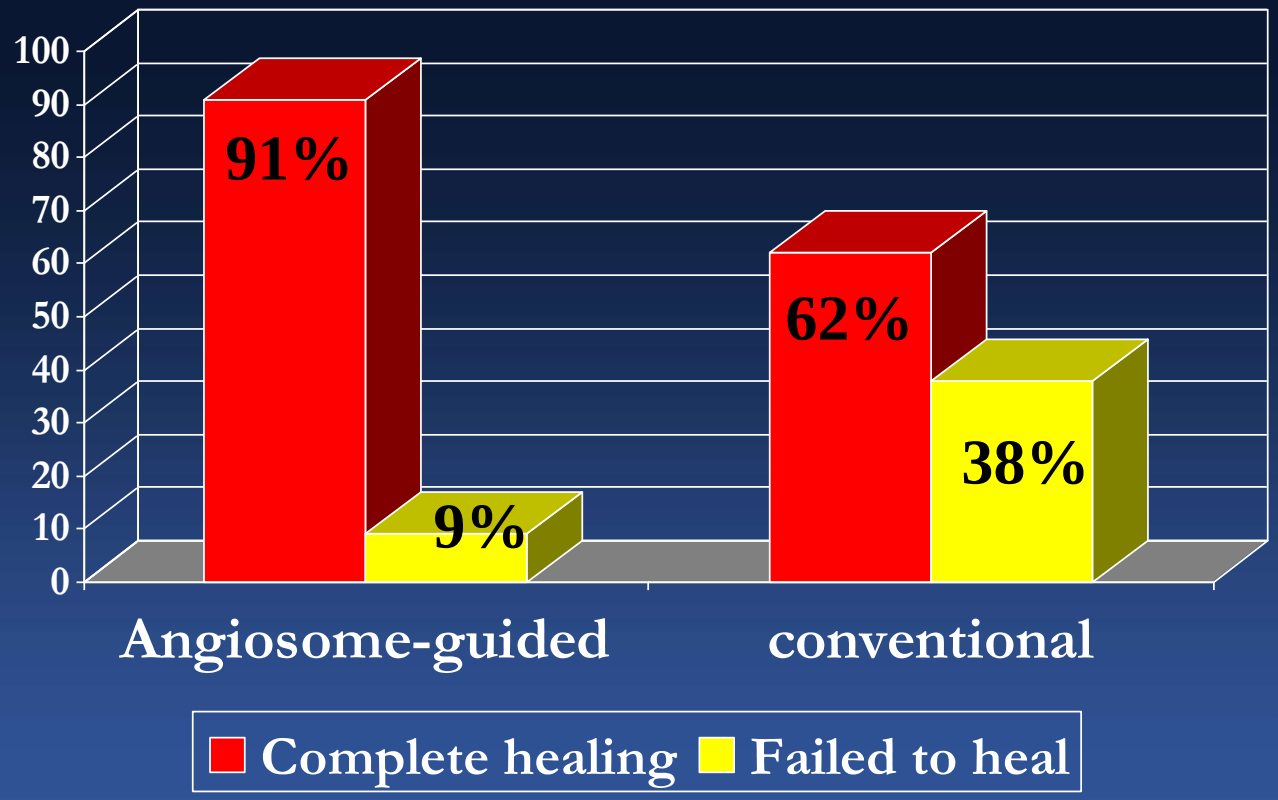
- Posterior tibial artery (3)
  - Calcaneal
  - Medical plantar
  - Lateral plantar
- Anterior tibial artery (1)
  - Dorsalis pedis
- Peroneal artery (2)
  - Lateral calcaneal
  - Anterior perforator





Angiosome-targeted Intervention

P = 0.03



Neville RF, et al. Ann Vasc Surg 2009; 23(3):367-373

Angiosome-based Recanalization

- Tibial angioplasty:
  - Appropriate angiosome treated — 83% healed
  - Boundary artery treated — 59% healed

Alexandrescu et al. JEVT 2008

- Tibial bypass:
  - Appropriate angiosome bypassed — 91% healed
  - Boundary artery bypassed — 62% healed

Neville et al. Ann Vasc Surg 2009

PTA following the Angiosome-Concept

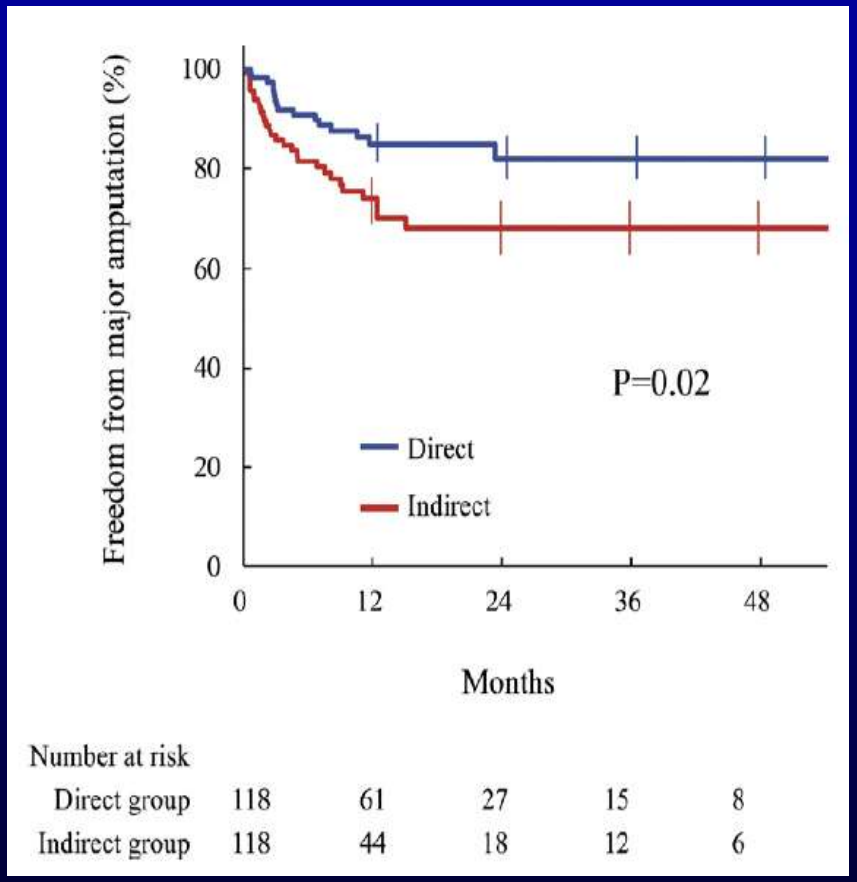
- 369 limbs with ischemic ulcerations
- Rutherford 5 73 %
- Rutherford 6 27 %

If treatment of the angiosome-based target lesion was unsuccessful, a non-angiosome-based lesion was treate

- DIRECT revascularization 54 %
- INDIRECT revascularization 46 %

Iida et al. JVS 2012

PTA following the Angiosome-Concept



- 369 limbs with ischemic ulcerations
- Rutherford 5 73 %
- Rutherford 6 27 %
- DIRECT revascularization 54 %
- INDIRECT revascularization 46 %

An unsuccessful intervention indicates more complex and extensive disease, which is usually linked to a less favourable clinical outcome.

Iida et al. JVS 2012

PTA following the Angiosome-Concept or as many Arteries as Possible ?

- Retrospective analysis of 1268 CLI-patients and PTA BTK

- Most important factor influencing limb salvage was the number of patent arteries post PTA.

Authors-conclusion: every effort should be made to open up as many arteries as possible BTK.

Angisome-concept was not mentioned in this paper.

Peregrin et al., *Cardiovasc Intervent* Radiol 2010;33:720-725

Classification of disease
*T*ransatl*A*ntic inter*S*ociety *C*onsensus document

Preferred Treatment

- Group A consists of single stenoses shorter than 1 cm. **PTA**

- Group B consists of multiple focal (<1 cm) stenoses of the tibial or peroneal arteries (including up to two focal stenoses at the tibial trifurcation) and short tibial or peroneal stenoses in conjunction with femoropopliteal disease. **PTA**

- Group C consists of longer stenoses 1–4 cm and **Surgery**

However, due to the improvements in equipment and technique, endovascular therapy is now considered a feasible option in groups C–D. In addition the presence of co-morbid conditions and operator skills should be considered when making the final decision.

diffusely diseased tibial vessels

Classification of disease
*T*ransatl*A*ntic inter*S*ociety *C*onsensus document

However, due to the improvements in equipment and technique, endovascular therapy is now considered a feasible option in groups C–D. In addition the presence of co-morbid conditions and operator skills should be considered when making the final decision.

Recommendations	Class[a]	Level[b]
When revascularization in the infrapopliteal segment is indicated, the endovascular-first strategy should be considered.	IIa	C
For infrapopliteal lesions, angioplasty is the preferred technique, and stent implantation should be considered only in the case of insufficient PTA.	IIa	C

Indication

PTA for intrapopliteal lesions

- Critical limb ischemia
- Moderate to severe claudication (debate)
- Prevention of proximal PTA or bypass failure

Critical limb ischemia

Clinical description	Fontaine class	Rutherford category	ABI	Symptom
Asymptomatic	I	0	0.85-1	none
Mild claudication	IIa	1	0.5-0.8	Walking distance>200m
Moderate claudication	IIb	2	0.5-0.8	Walking distance=100-200m
Severe claudication	IIb	3	0.5-0.8	Walking distance<100m
Ischemic rest pain	III	4	<0.5	Resting pain
Minor tissue loss	IV	5	<0.5	Minor tissue loss (ulceration)
Major tissue loss	IV	6	<0.5	Major tissue loss (gangrene)

RESULTS of PTA

Technical success

- The technical success rates of infrapopliteal angioplasty range between 78% and 100%.
- Occlusion length >10 cm is an adverse factor both for technical success and patency.

Discrepancy between primary patency and clinical success

- Primary patency rates for PTA vary widely
  - 13% to 81% at 1 year
  - 48% to 78% at 2 years.

- The limb salvage rate for PTA
  - 77% to 89% at 1 year
  - 94% at 3 years (one report).

- The limb salvage rate for surgery
  - 81% to 88% at 1 year
  - 88 at 2 years.
  - 80 at 3 years.

Discrepancy between primary patency and clinical success

- This feature is more prominent in patients with tissue loss, especially with ulcers, than in those with rest pain.

- Ulcer healing reduces the oxygen demand and as a consequence less blood flow is generally required to maintain tissue integrity compared with the amount required for initial ulcer healing.

- Collaterals may therefore be sufficient to preserve tissue integrity if there is no further injury.

Factors Influencing the Patency of Infrapopliteal Artery after PTA

- Diabetes: lower rate of limb salvage & ulcer healing.
- Renal insufficiency
- Elevated lipoprotein (a)
- Presence of ulcer or gangrene
- Lack of angiographic improvement
- Extensive atherosclerotic disease

Complications of PTA

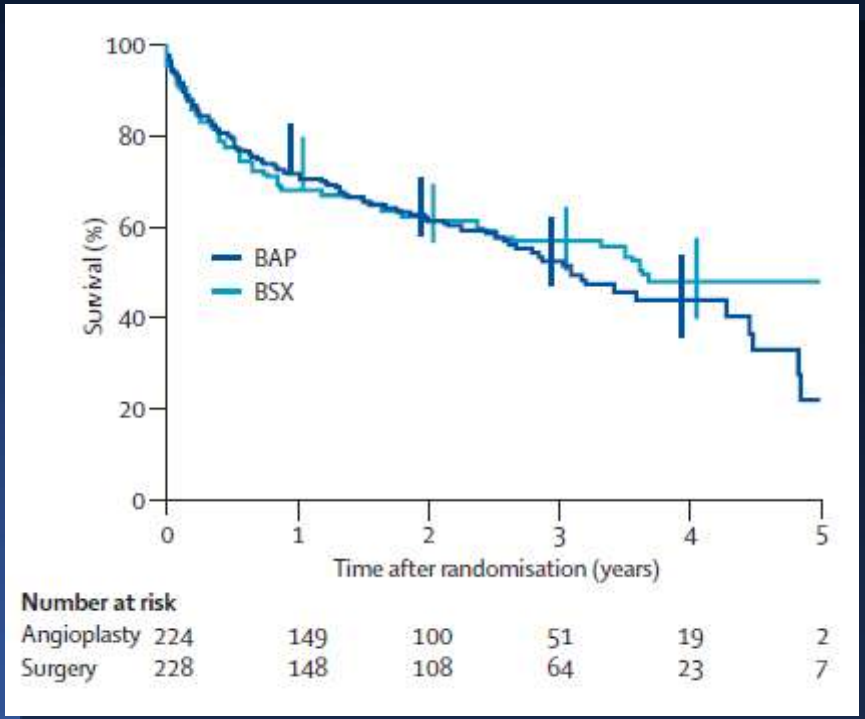
- Complication rate : 2-6%
- Puncture site hematoma
- Acute arterial occlusions by spasm or dissection: (stent or liberal use of antispasmodics)
- Embolic occlusion: thrombolysis or thrombectomy
- Arterial perforations (3.7%): rarely require intervention
- 30-day mortality : 1.7% vs. bypass surgery :1.8-6%

BASIL trial

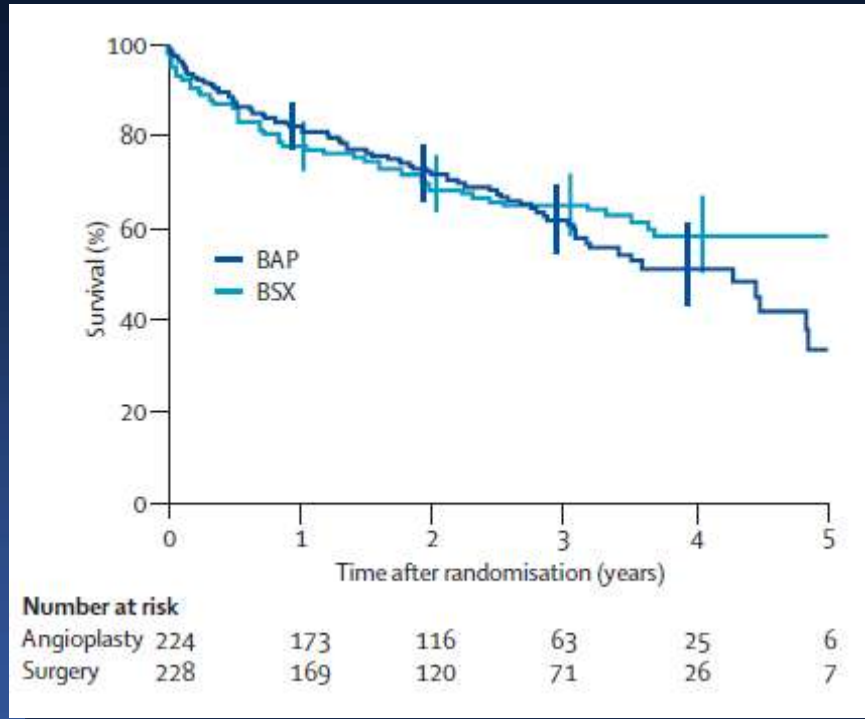
(Multicenter randomized trial for infrainguinal severe ischemia)

Surgery vs. Balloon angioplsty

Amputation-free survival



Mortality-free survival



Lancet. 2005;366:1925-34

New approach

- Laser angioplasty
- Cutting balloon.
- Coated stent
- Drug-eluting stents
- Absorbable metal stent

SiroBTK study with SES

30 patients, 62 arteries, 106 SES

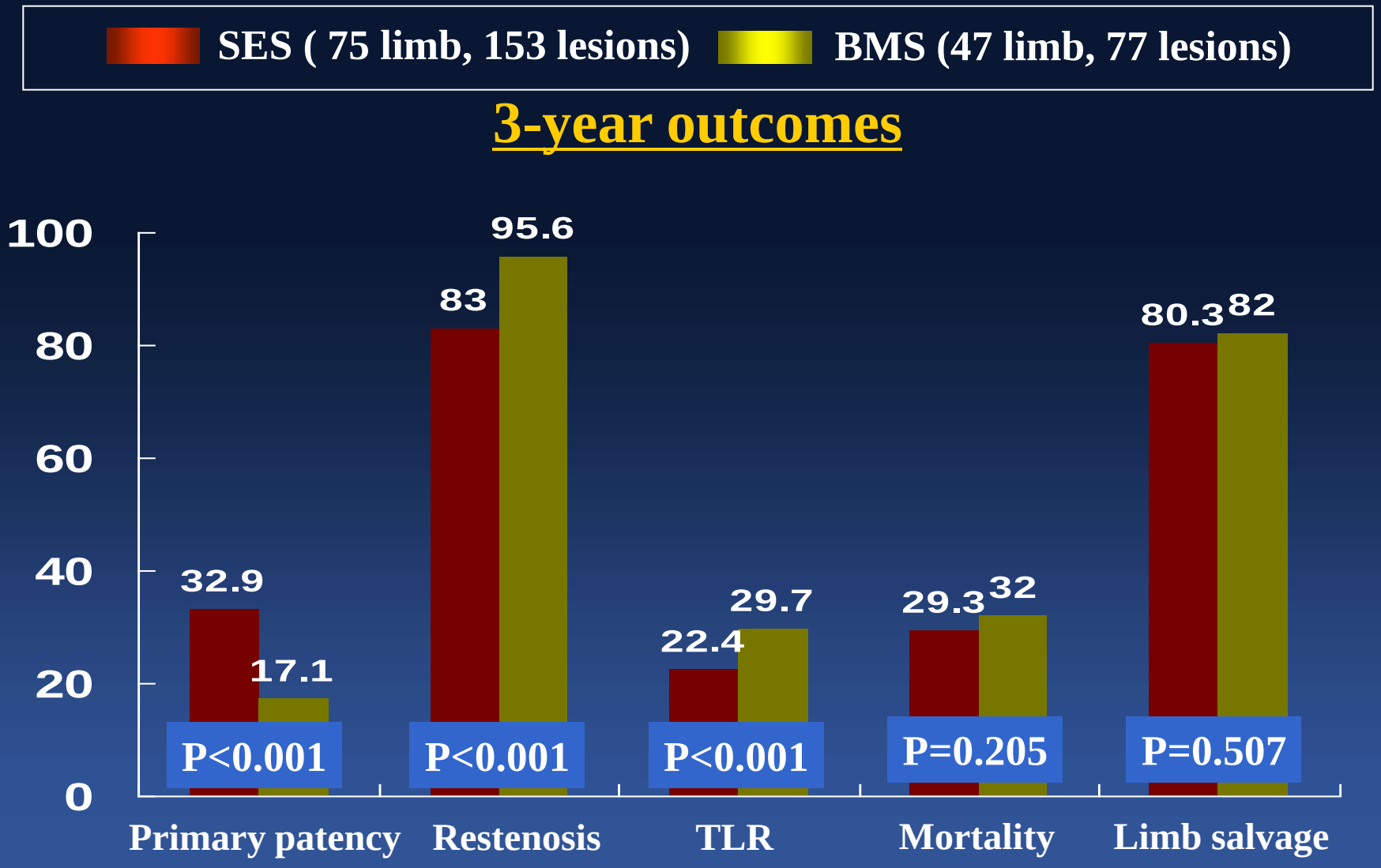
Primary endpoint: clinical improvement and healing of ulcer @ 1 & 7.7 months

- Angiographic and procedural success : 100%.
- 7 months outcomes

- Amputatiton 1 toe in one patient and 1 mid-foot in another.
- **Limb salvage : 100% of patients.**
- Death : two cardiac deaths unrelated to CLI
- Three recurrent homolateral claudication.
- **Mid-term clinical improvement : 100%**
- **Primary patency: 97% (56 patent arteries on 58 arteries).**

J Endovasc Ther. 2007;14:241-50.

SES vs. BMS

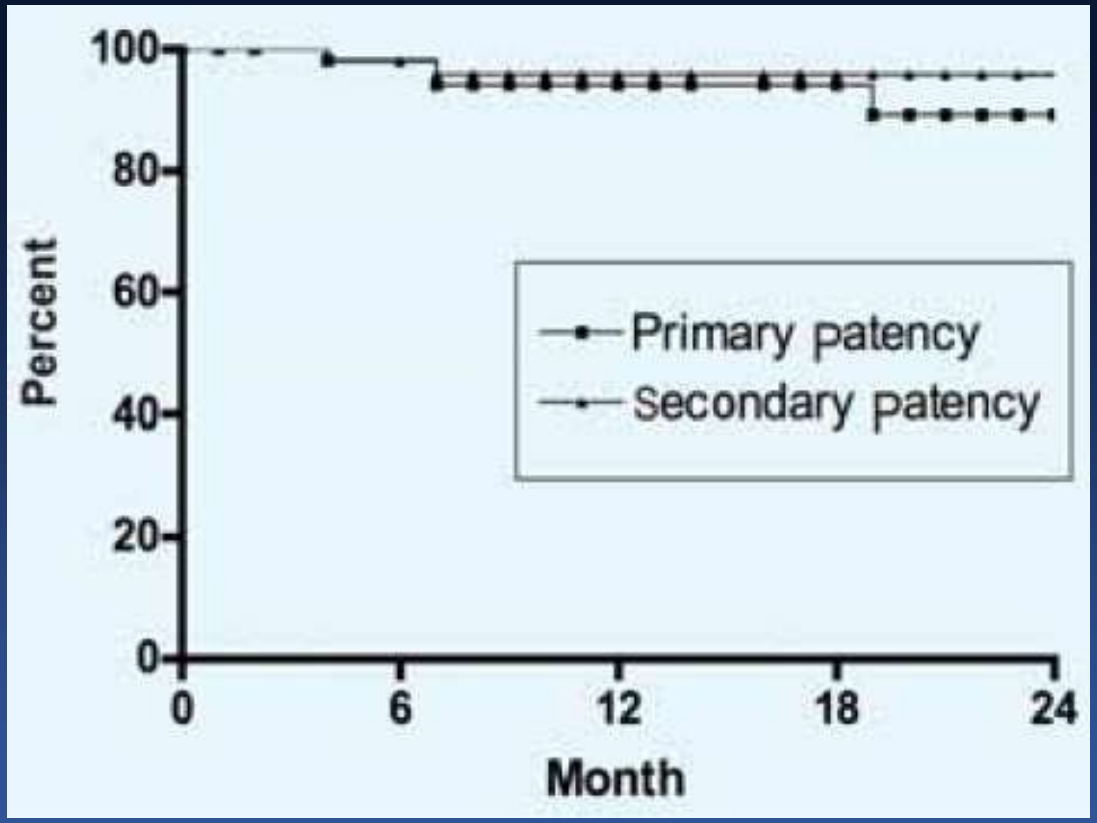


Siablis D et al. J Vasc Interv Radiol 2009; 20:1141–1150

BTK SES registry

Prospective nonrandomized single center registry

SES for Sxmatic focal infrepopliteal obstruction (n=74 pts)



Patency at 24 months

Primary: 89.2%

Secondary: 95.9%

Endovascular today 2007;August.71-74

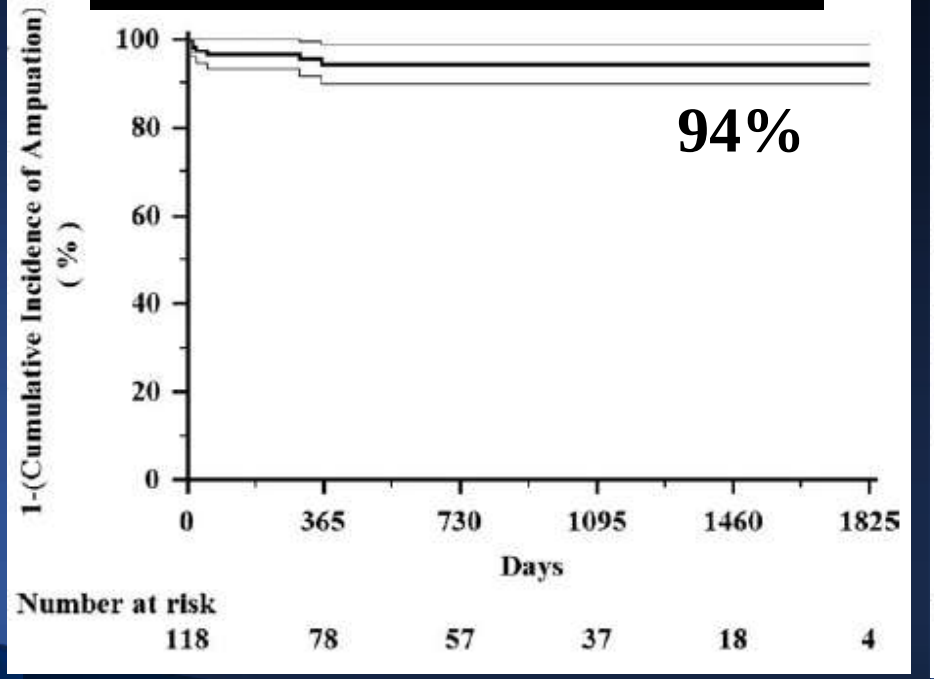
PaRADISE trial

(PReventing Amputation using Drug-elutIng StEnt)

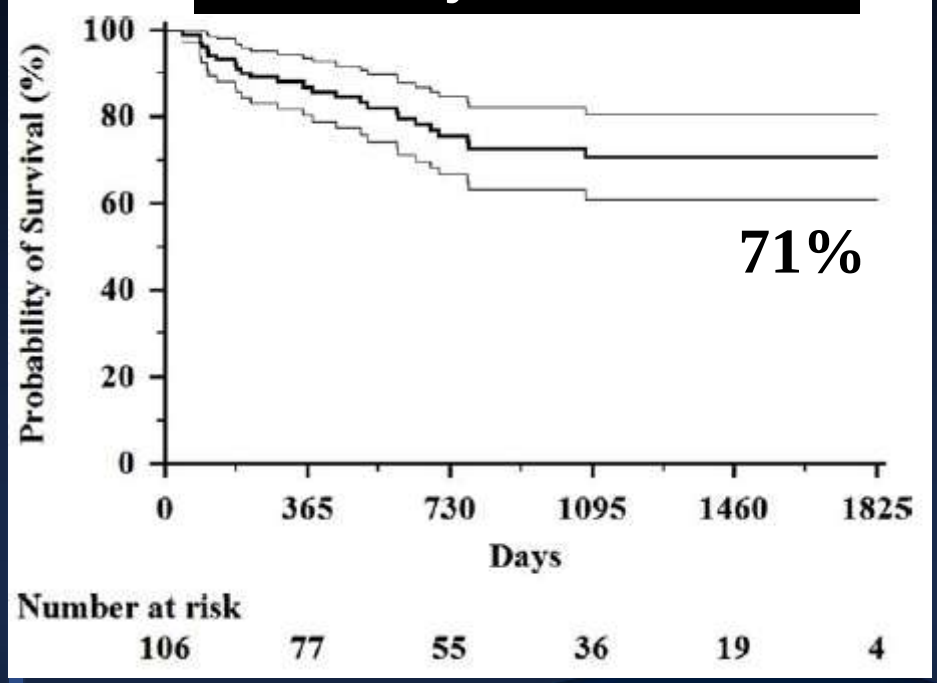
Critical limb ischemia (106 pts, 108 limbs, SES 83%, PES 17%)

- Stent number/limb: 1.9±0.9, Stent length : 60±13 mm
- Target limb revascularization: 15%
- Angiographic restenosis: 12% (follow-up rate 35%)

Amputation-free survival

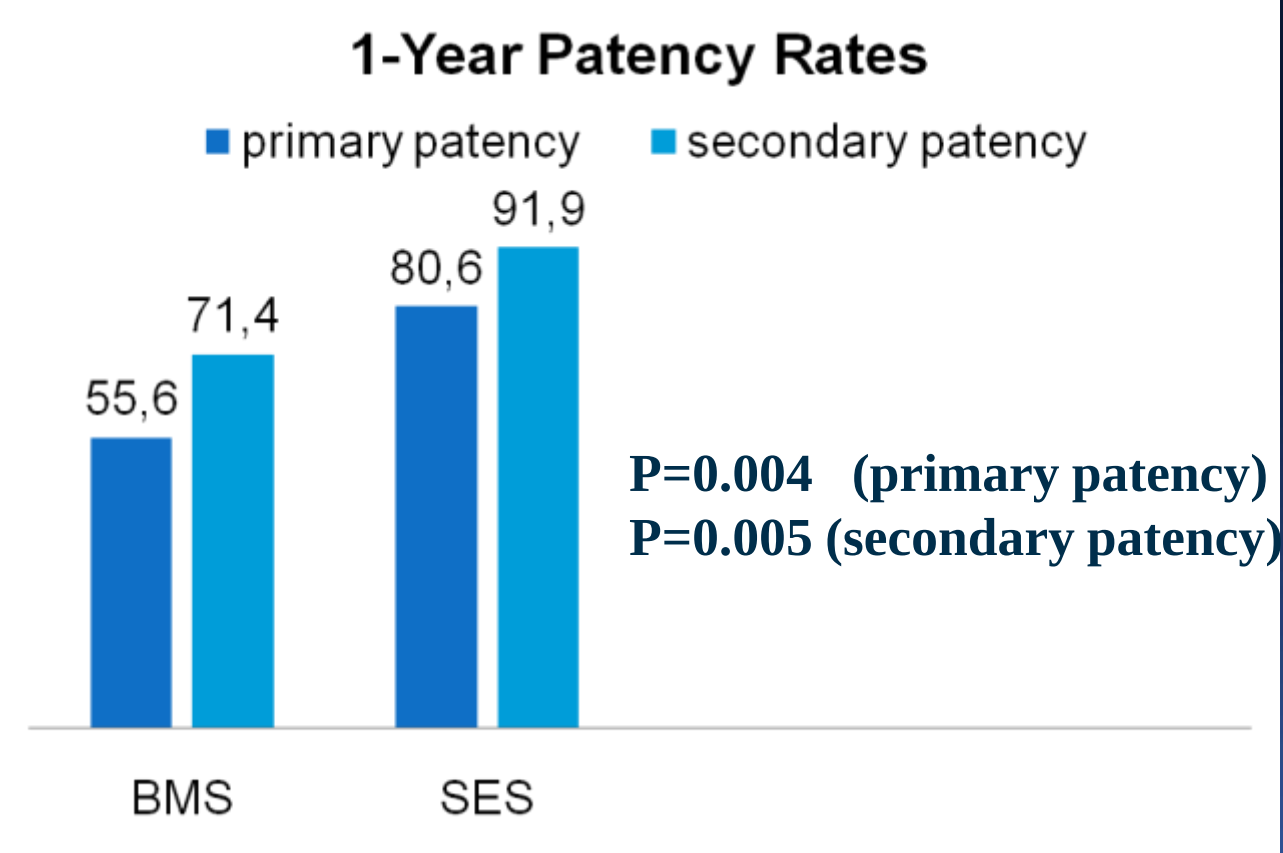


Mortality-free survival



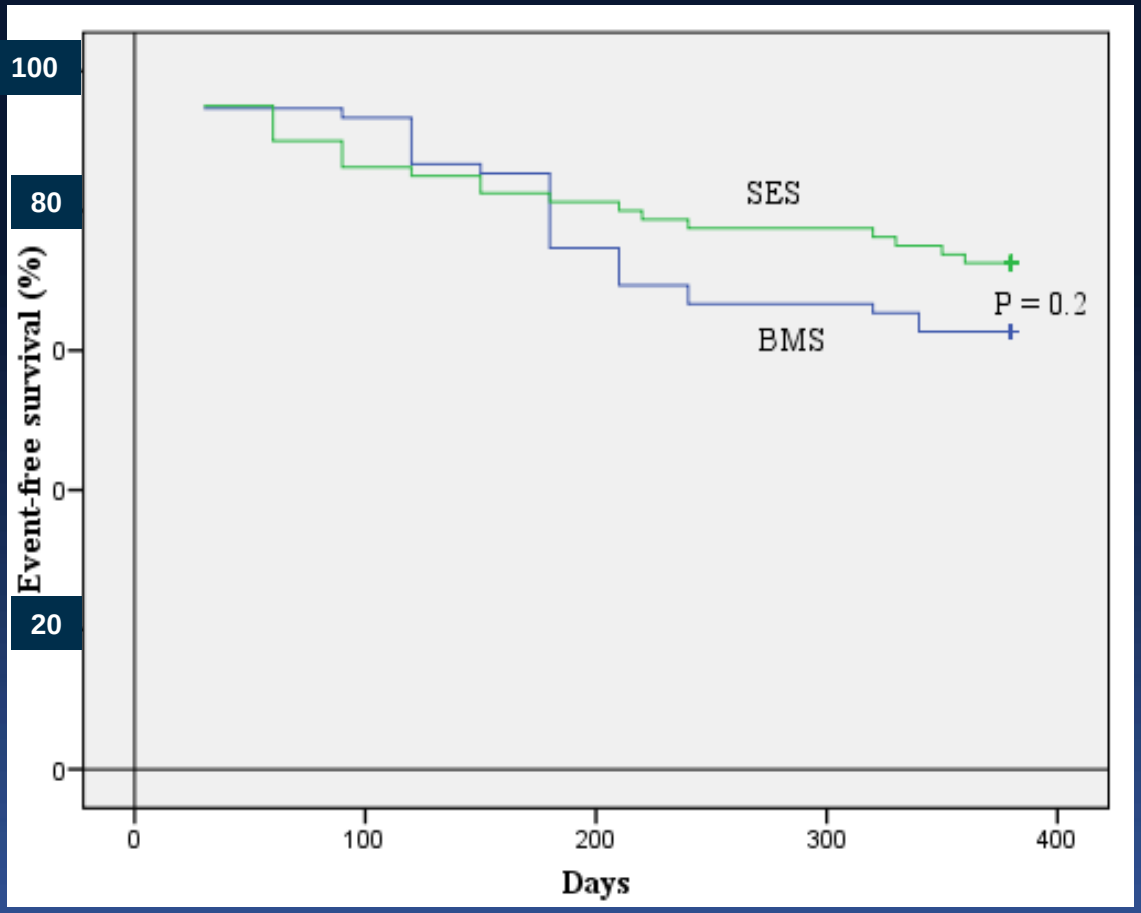
Feiring AJ et al. J Am Coll Cardiol. 2010;55:1580-9

YUKON-BTK Trial
Primary & Secondary Patency



Event-free Survival at 12 months

Survival free from target lesion revascularisation, major and minor amputation, myocardial infarction and death was compared by Kaplan-Meier analysis with the use of the Mantel-Cox log-rank test.



No. at risk					
Sirolimus Stent	82	71	64	63	62
Bare-metal Stent	79	72	67	64	63

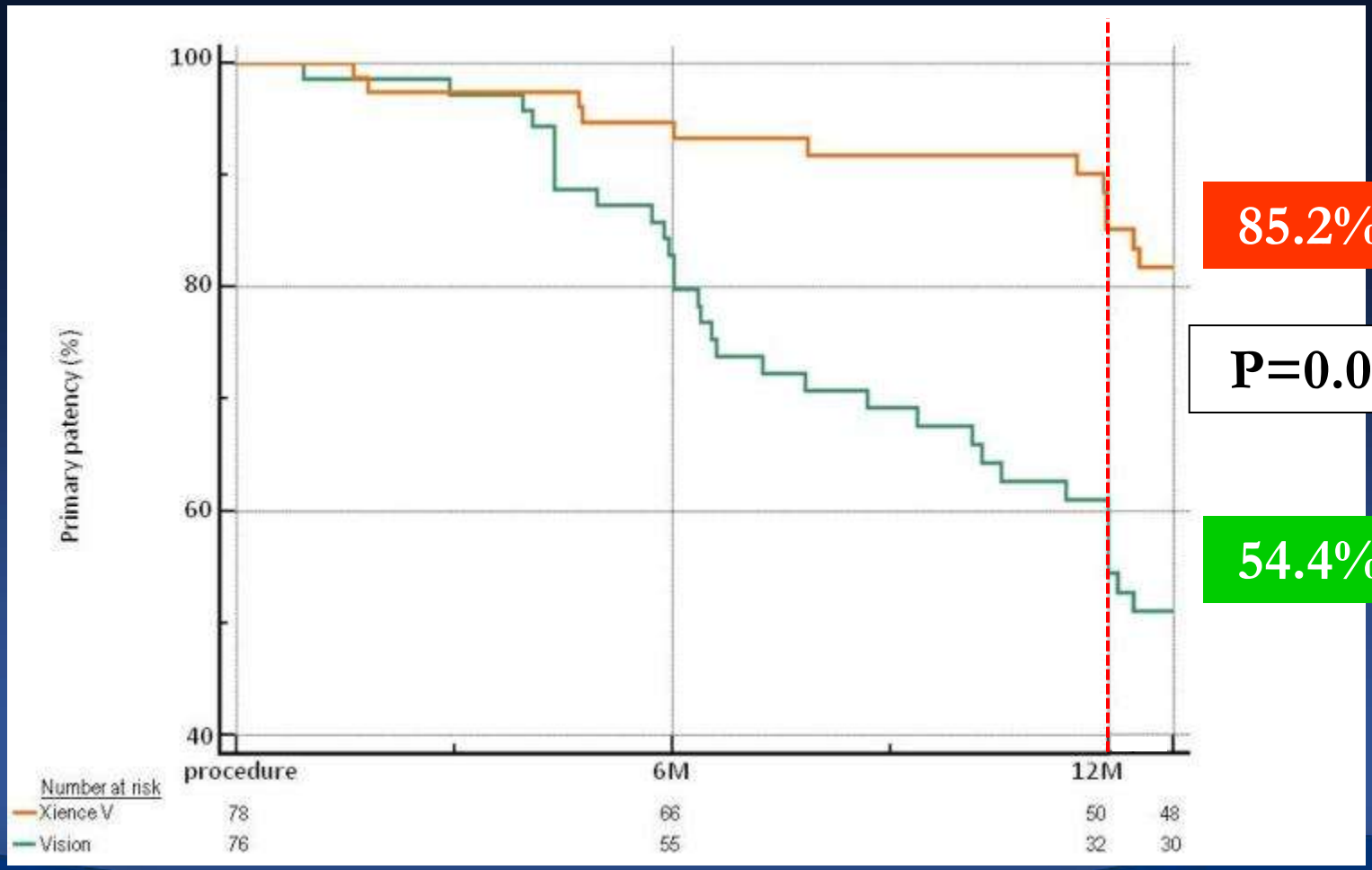
Rastan et al. EHJ 2011 in revision

MAE and Limb salvage at 2-year FU in patients with CLI DES vs. BMS
(YUKON Trial, Rastan A. et al. JACC 2012)

CLI cohort	Sirolimus Stent (N=38)	Bare Metal Stent (N=31)	P
Death	10 (26.3%)	10 (30.3%)	0.60
Major-/Minor Amputation	1/1 (5.3%)	4/3 (22.6%)	0.04
TVR	4 (10.5%)	4 (12.9%)	0.70
Myocardial infraction	0 (0%)	2 (6.4%)	0.20
Limb salvage	37 (97.4%)	27 (87.1%)	0.10

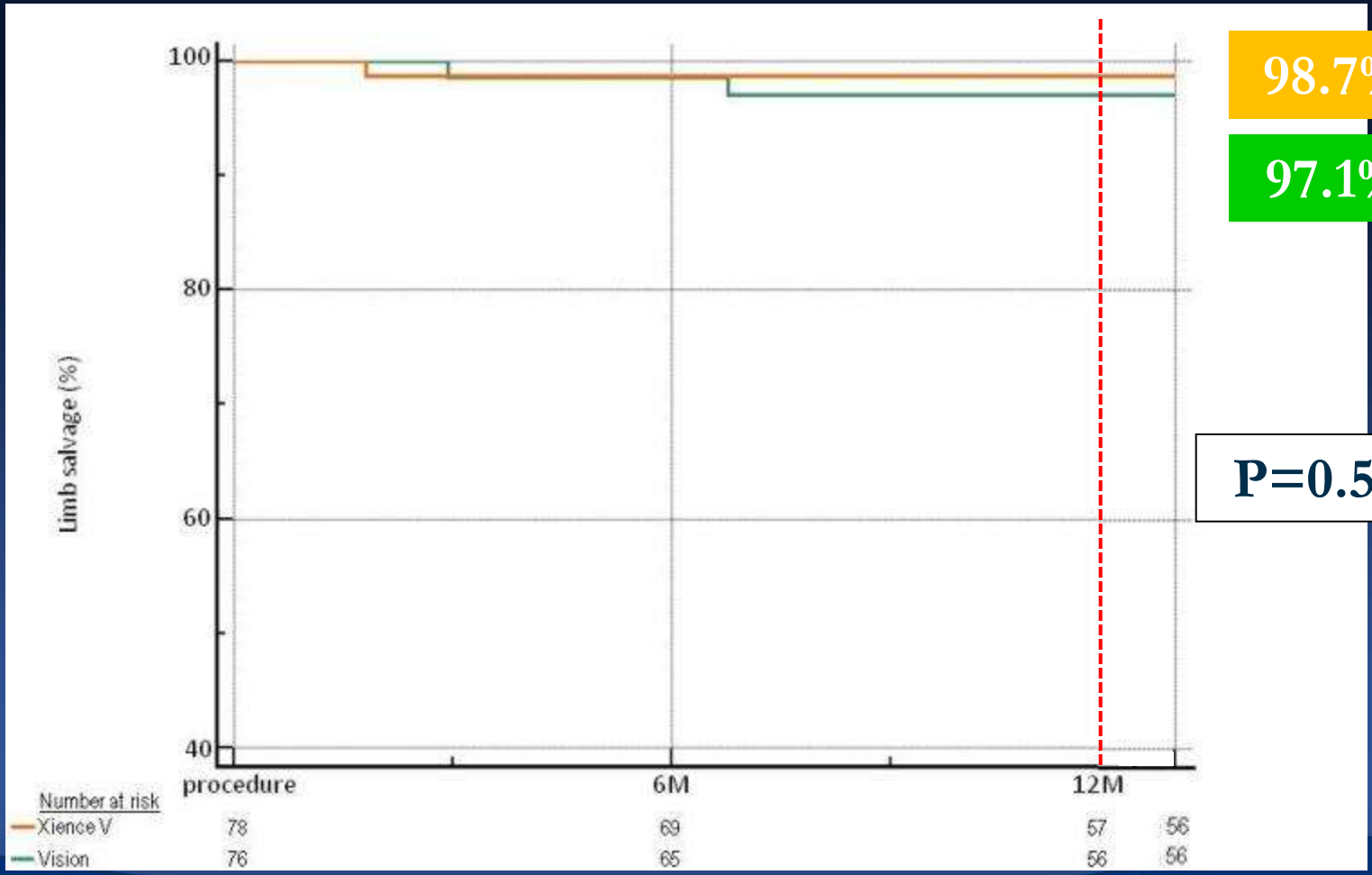
DESTINY - 12-month primary patency

MultiLink Vision vs Xience V



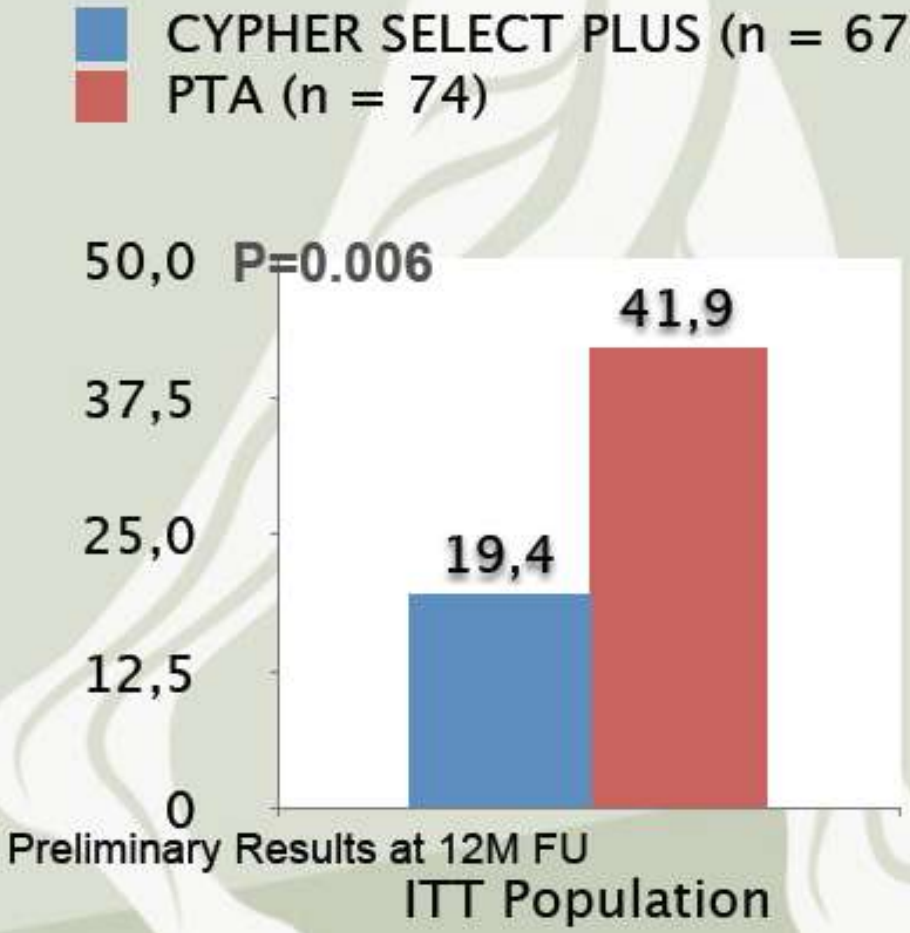
12-month limb salvage

MultiLink Vision vs Xience V



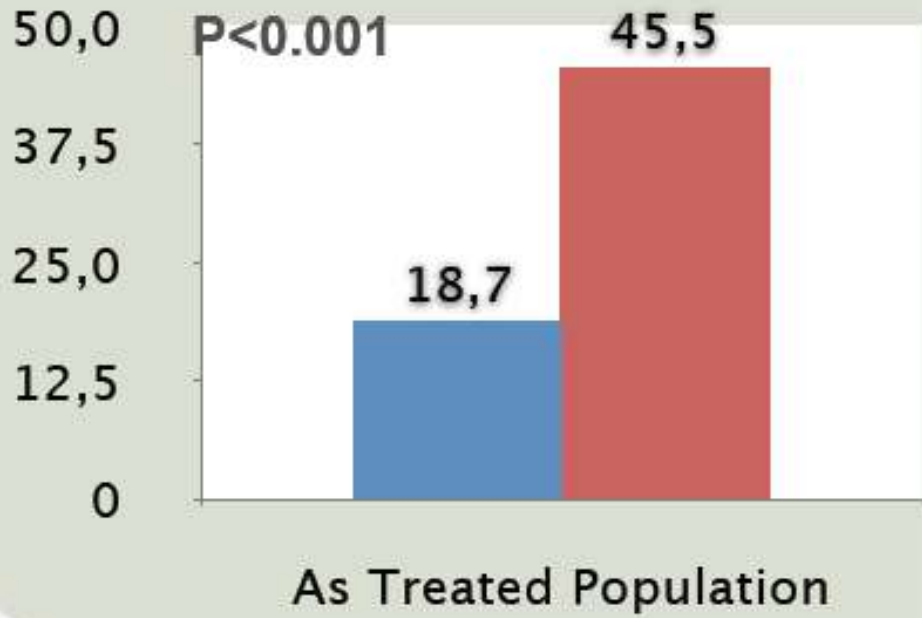
The ACHILLES Study

Primary Endpoint
12M In-Segment Binary Restenosis by QA



Preliminary Results at 12M FU

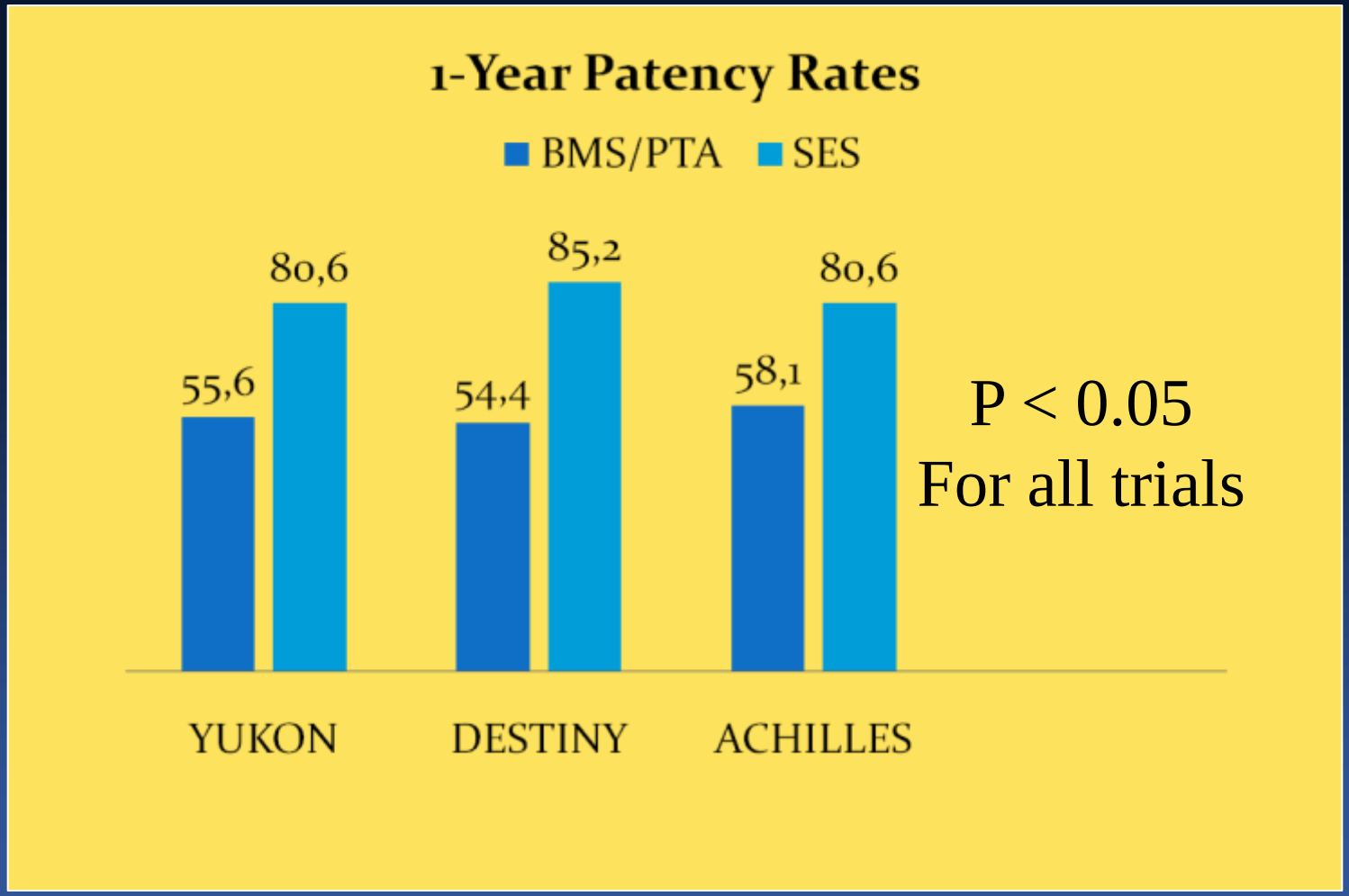
ITT Population



As Treated Population

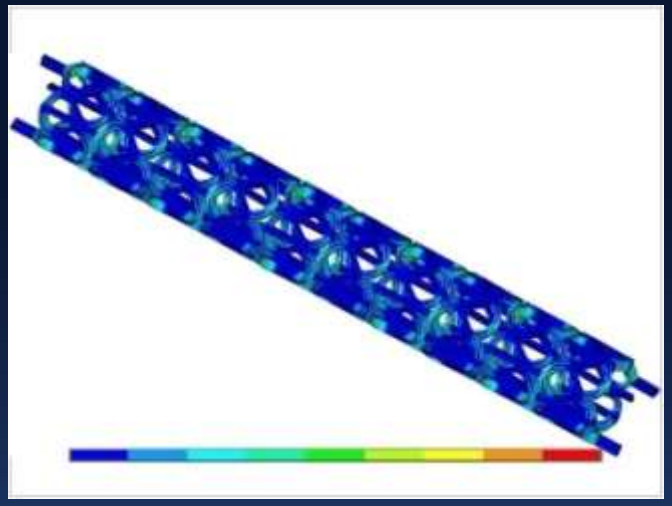
YUKON, DESTINY & ACHILLES Trials

Primary Patency



Rastan et al. EHJ 2011
Scheinert et al. JACC 2012
Bosiers et al. JVS 2012

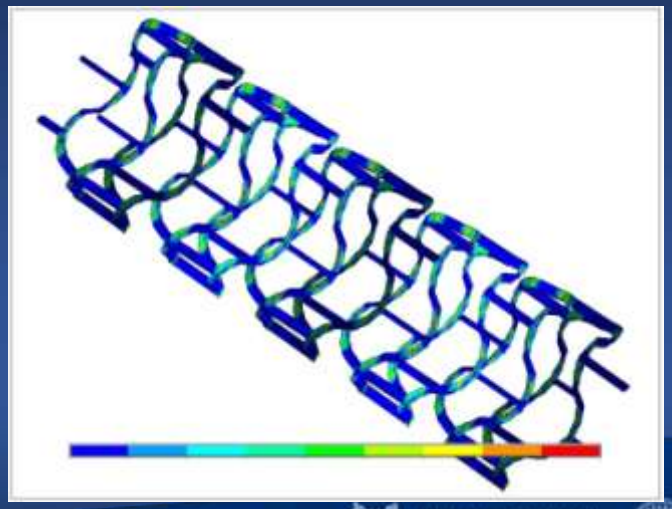
Absorbable Magnesium Stent



FEA: Crimped state

Recoil	~ 5%
Foreshortening	< 5%

* Investigational device only - not for sale -



FEA: Fully expanded state

Clinical Results

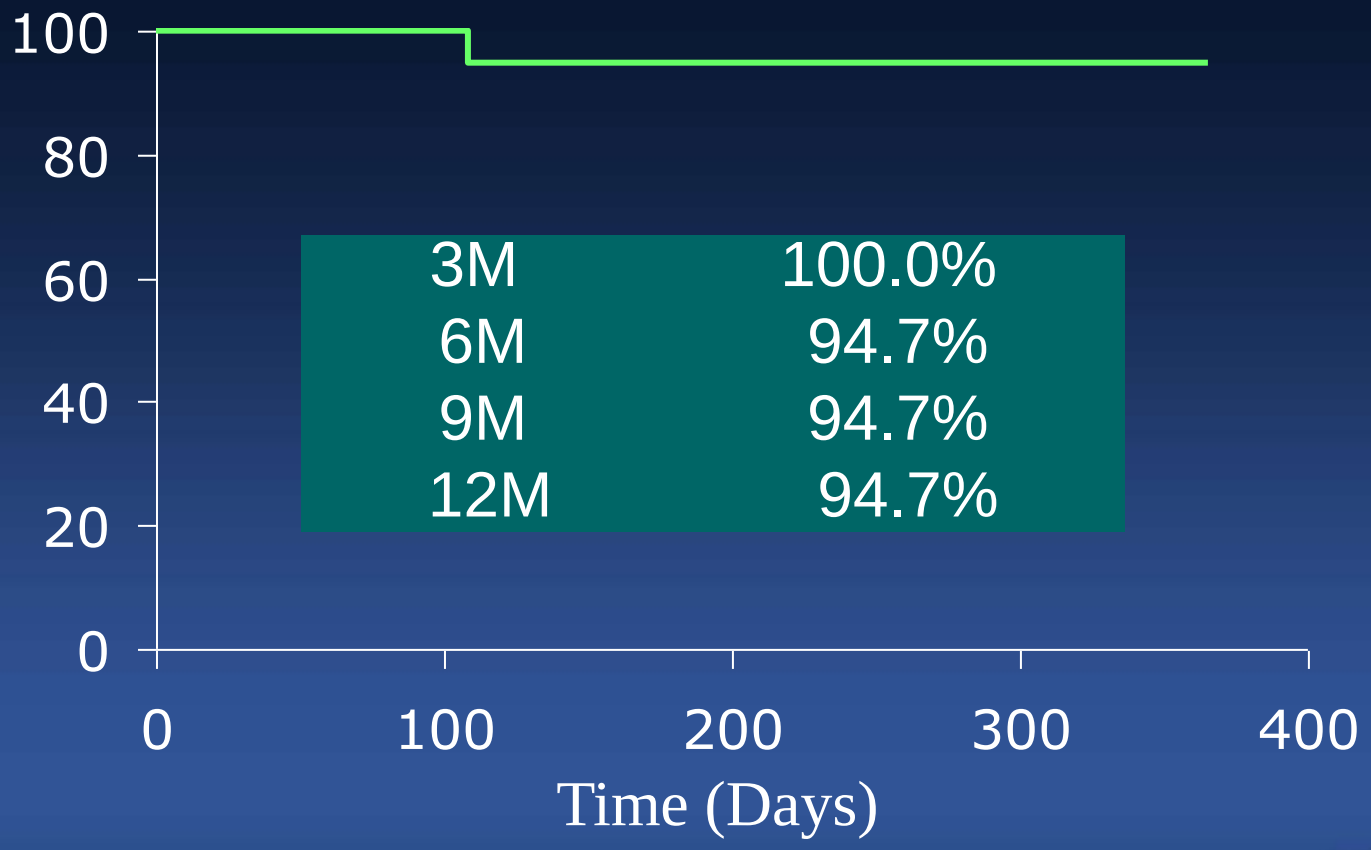
BEST-BTK

First in Man experience with the Biotronik absorbablE metal StenT Below The Knee

- 20 CLI patients (Rutherford 4-5) with BTK pathology
- Implants performed between December ‘03 – January ‘04

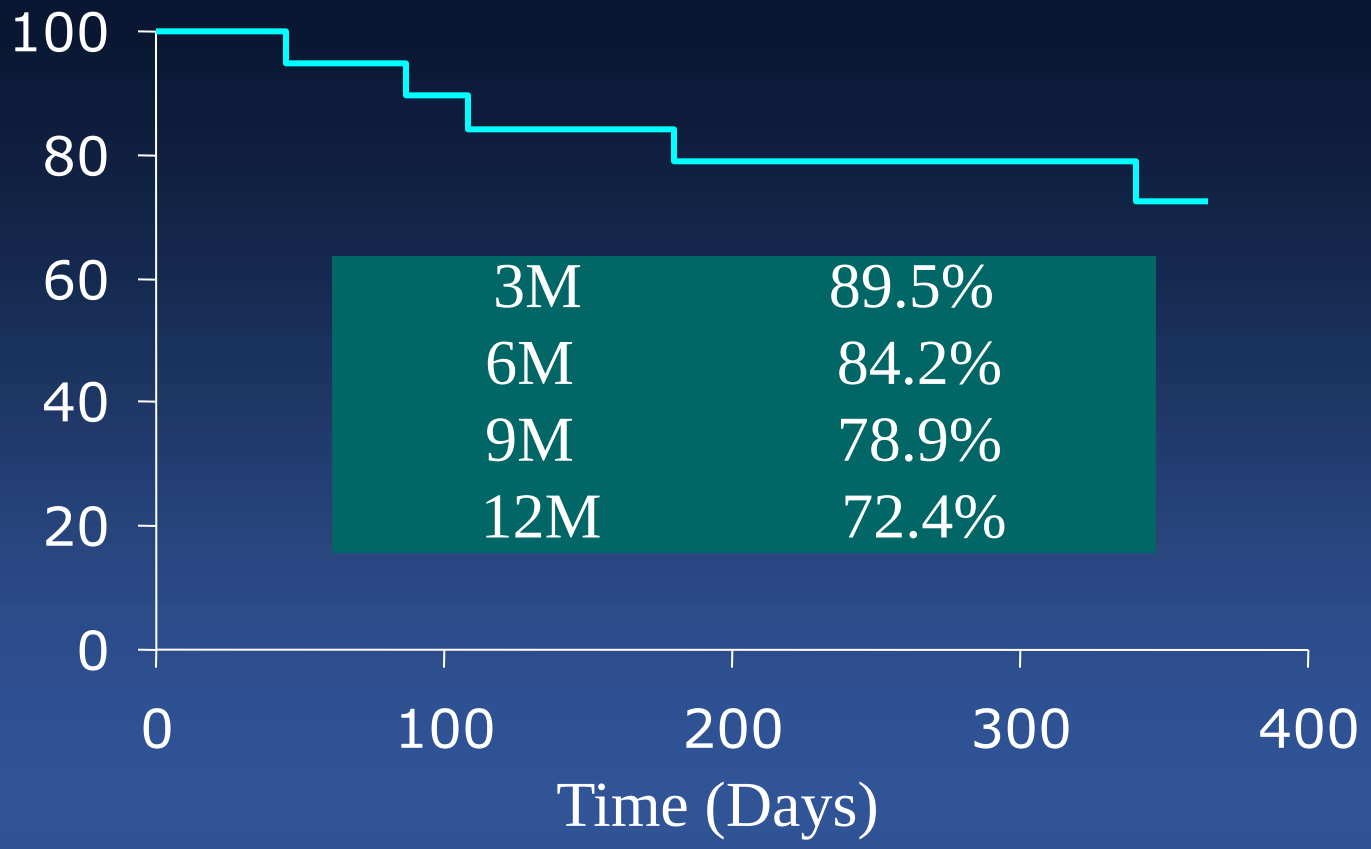
Limb Salvage After One Year

Limb Salvage Rate



High Patency Rate

Primary Clinical Patency



DEB in BTK

DEB BTK Registry

104 patients
(angio subgroup 84 arteries)
RC 3-4-5-6

IN.PACT

Primary EP:
3m (angio) Rest. Rate

CLINICAL RESEARCH — Interventional Cardiology

First Experience With Drug-Eluting Balloons in Infrapopliteal Arteries

Andrej Schmidt, MD,* Michael Piorkowski, MD,* Martin Werner, MD,* Matthias Ulrich, MD,* Yvonne Baudack, MD,* Sven Brändich, MD,* Henrik Ick, MD,* Johannes Schuster, MD,* Spiridon Botsios, MD,* Hans-Joachim Krause, MD,† Ramon L. Varcoe, MD,‡ Dirk Scheinert, MD*

Leipzig and Zschopau, Germany; and Sydney, Australia

Low restenosis rates at 3 months in long BTK lesions and occlusions

Key Baseline characteristics

- CLI = 82.6%; Diabetics = 73%
- Avg Lesion length = 173 ± 87 mm
- Tot Occlusions = 61.9%

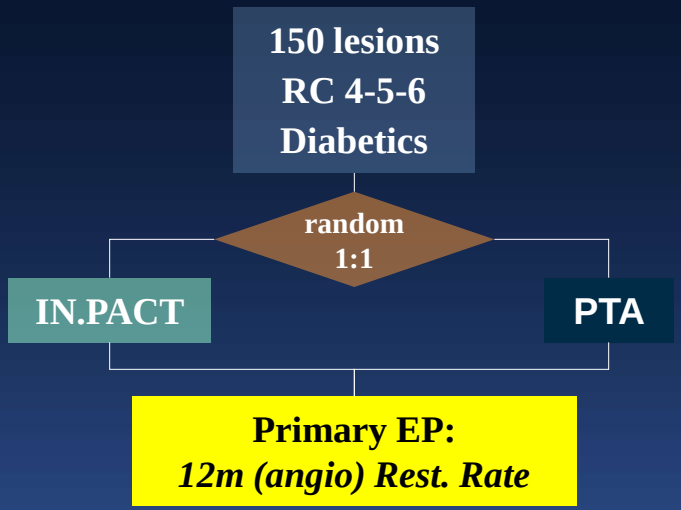
Angiographic FU	DEB 3-month	PTA* 3-month
Restenosis (>50%)	27.4%	69%
Full-segment Resten.	10%	56%
Restenosis Length	64 mm	155 mm
Clinical FU	**12-month**	**15-month**
Deaths	16.3%	10.5%
Limb Salvage	95.6%	100%
Clinic. Improvem.	91.2%	76.5%
Compl. wound healing	74.2%	78.6%
TLR	17.3%	50%

* *PTA* historical cohort (*A.Schmidt et al. CCI 2010*)

(A.Schmidt JACC 2011)

DEB in BTK

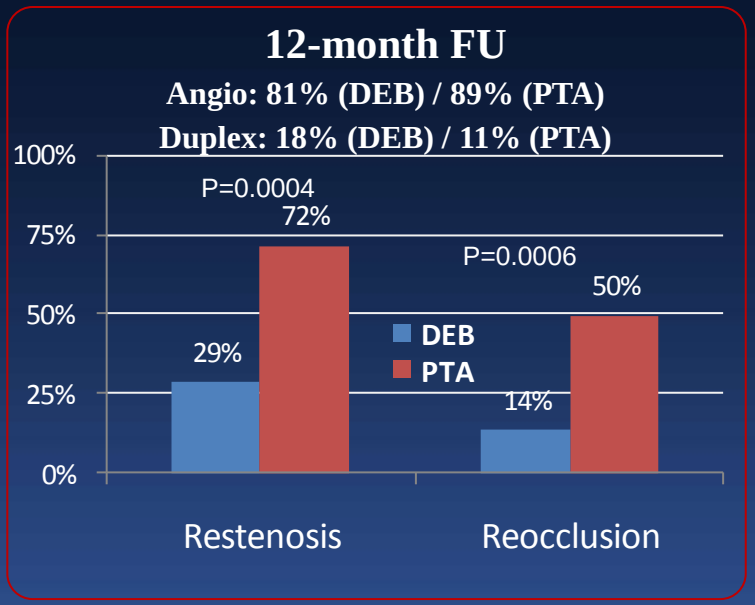
DEBATE BTK RCT



Key Baseline characteristics (DEB vs. PTA):

- CLI = 100%
- Diabetics = 100%
- Mean lesion length = 121 ± 83 vs. 123 ± 68 (p=ns)
- Tot Occlusions = 80% vs. 82% (p=ns)
- Pre-dilat. = 100%

Significant reduction in 12-m Rest. Rate vs. PTA in BTK / CLI / Diabetics



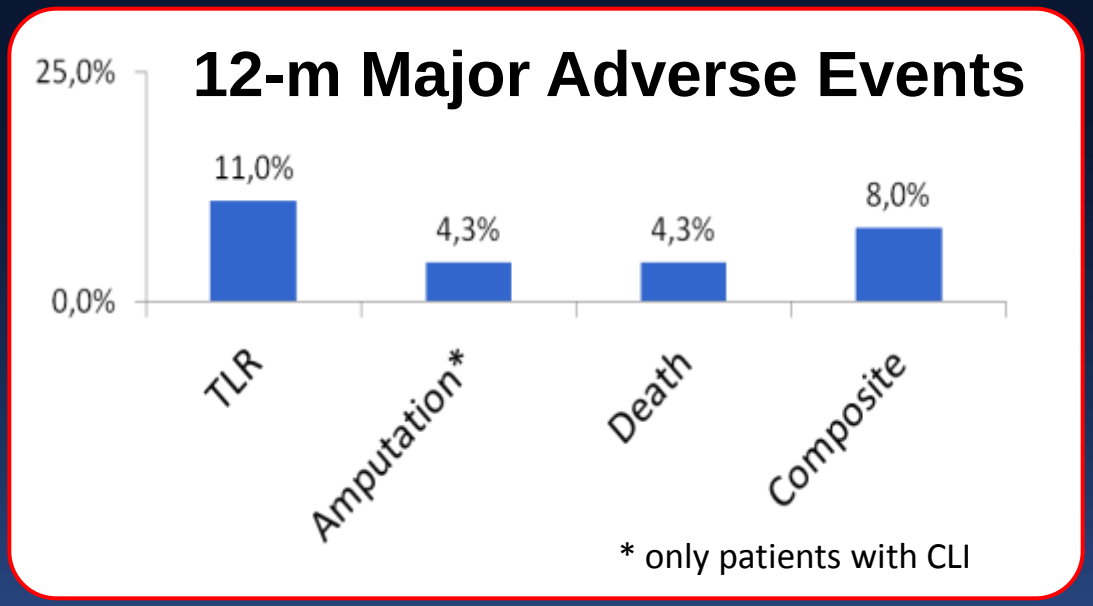
	PTA	DEB	
Death	3(4%)	4(6%)	0.2
Major Amputation	1	0	
CVA	3(4)	2(3)	0.7
AMI	3(4)	3(4)	0.7

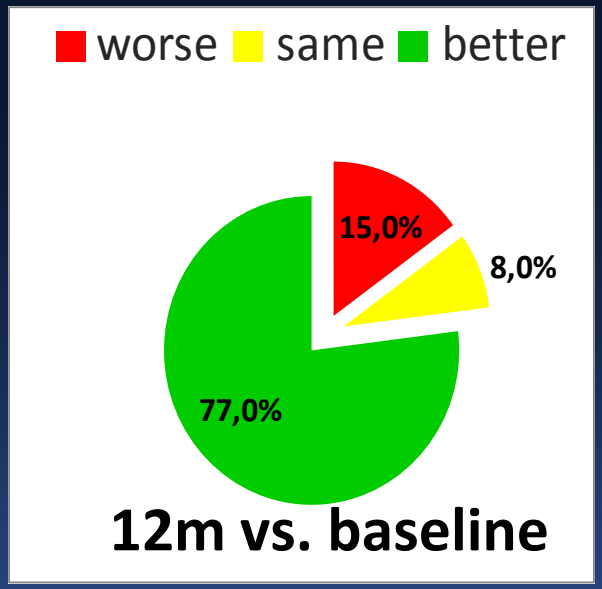
(F.Liistro LINC 2012)

Montevegine DEB-BTK Registry

12-month Clinical Outcome

Patients n = 70 **Lesions = 90**





Twelve-Month Target Lesion Revascularization was 11%.

8 symptomatic (RC≥ 3) patients (10 lesions) were referred to revascularization (7 re-PTA and 1 Surgery) with Secondary Patency of 94%.

Limb Salvage in patients was 96% (3 Major Amputation)

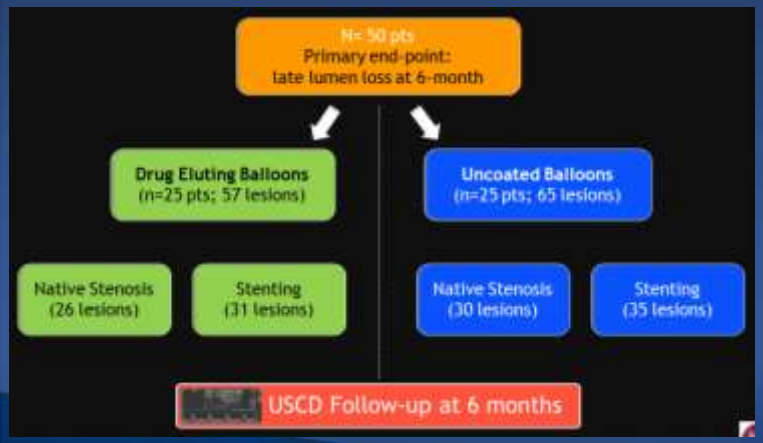
DEBELLUM Randomized Trial

Drug **E**luting **B**alloon **E**valuation for **L**ower **L**imb m**U**ltilevel treat**M**ent

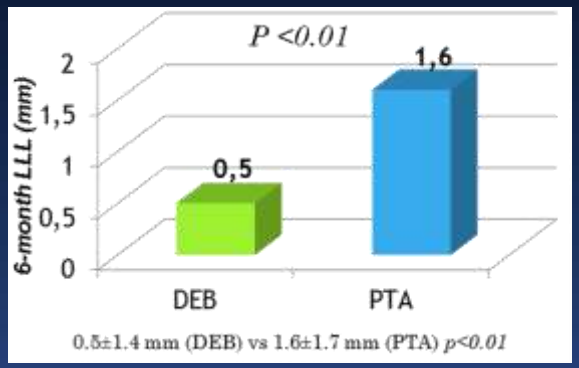
Single center RCT of DCB vs. PTA in MULTILEVEL lower limb disease

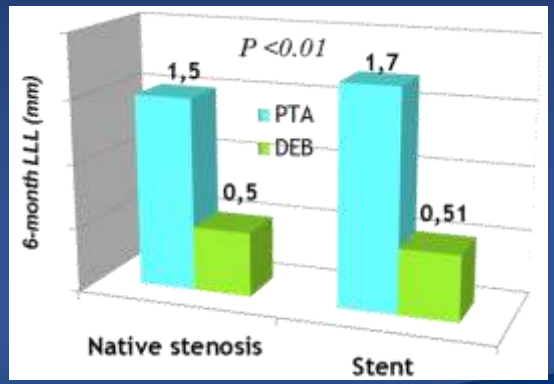
(Fabrizio Fanelli MD - Roma, Italy)

- **Prim. Endpoint: 6m LLL**
- **50 patients**
- **Fempop / BTK: 76% / 24%**
- **LLC / CLI: 62% / 38%**



DCB shows reduction of restenosis vs. PTA in multilevel (SFA + BTK) disease with and without Stent





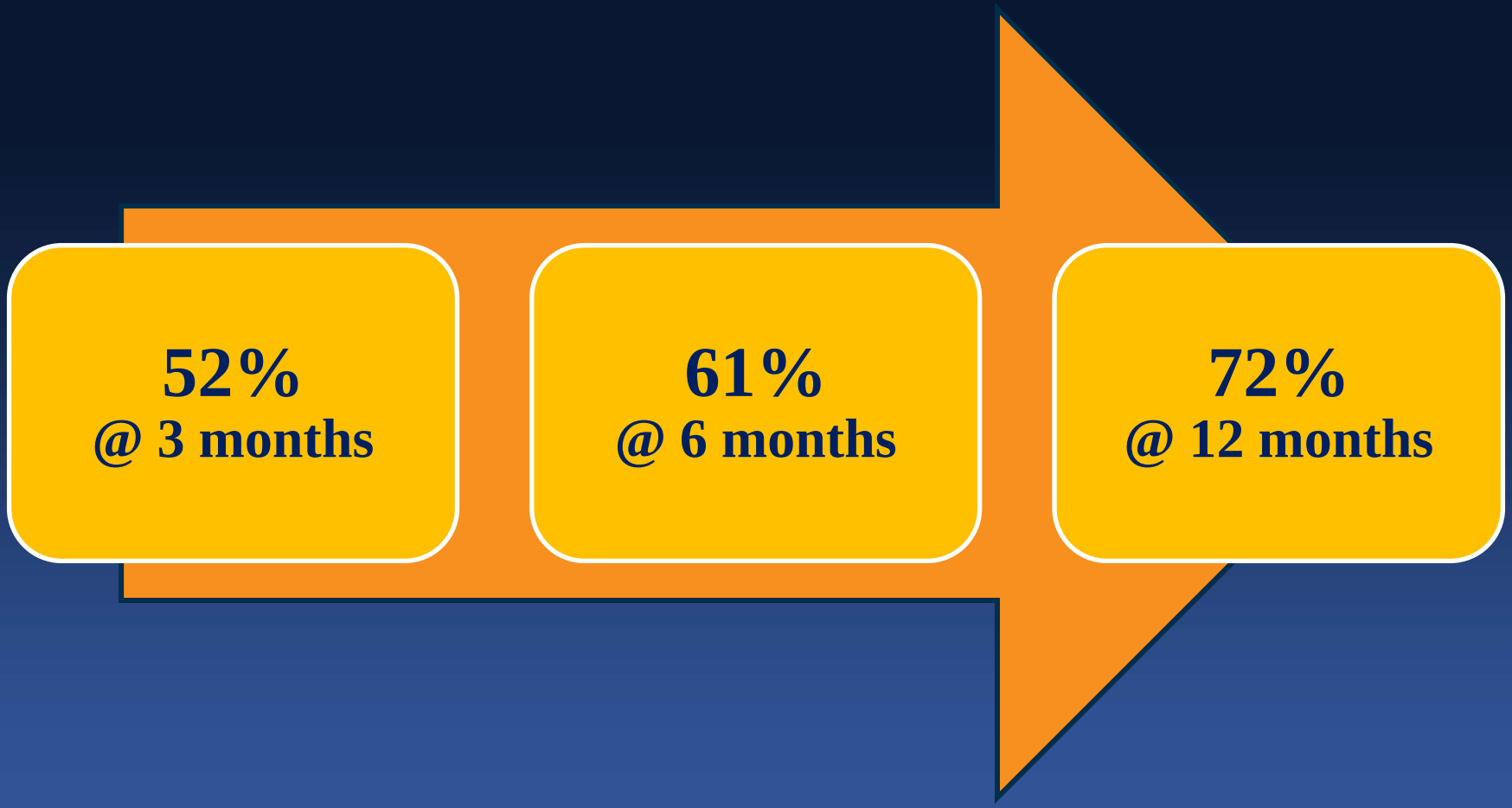
DEFINITIVE LE (Atherectomy)
Primary Patency by Vessel - CLI Cohort

	Patency (PSVR ≤ 2.4)	Lesion Length (cm)
All (n= 279)	**71%**	**7.2**
Lesion Location (proximal edge)		
SFA (n=135)	68%	8.6
Popliteal (n=48)	66%	5.4
Infrapopliteal (n=96)	78%	6.0

DEF LE CLI Cohort Primary Endpoint:
Freedom from Major Amputation at 1 Year

95%

DEFINITIVE LE
Wound Healing in CLI (RCC 5 & 6)



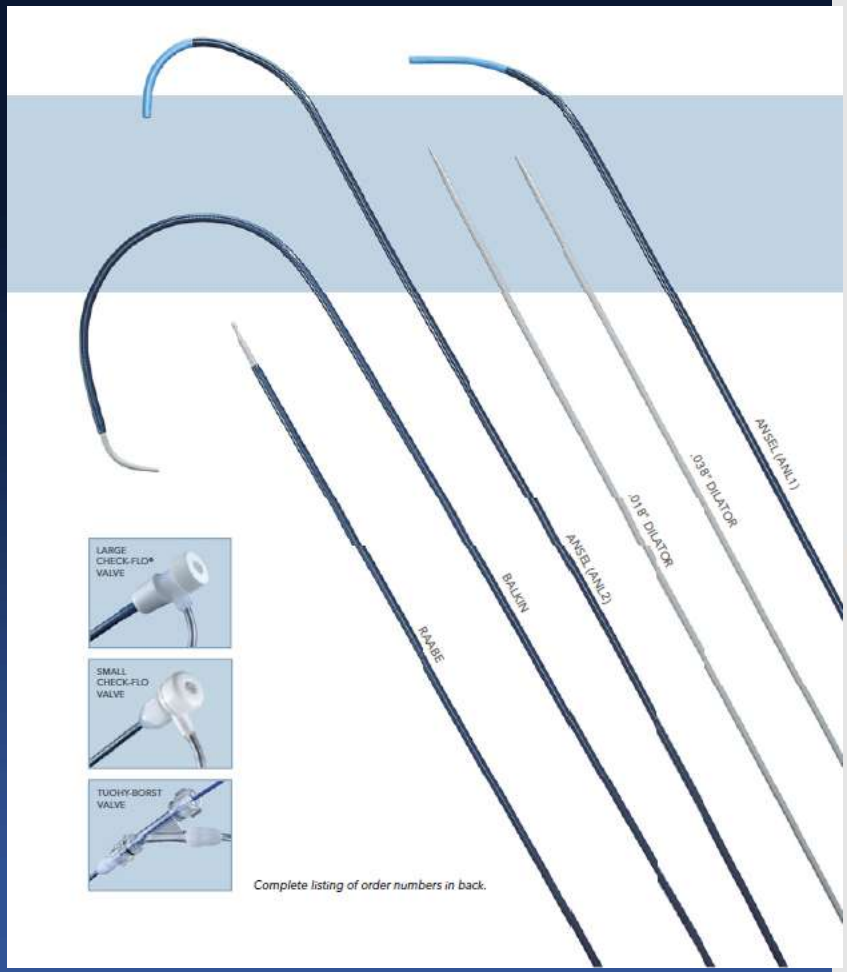
Transpedal Approach

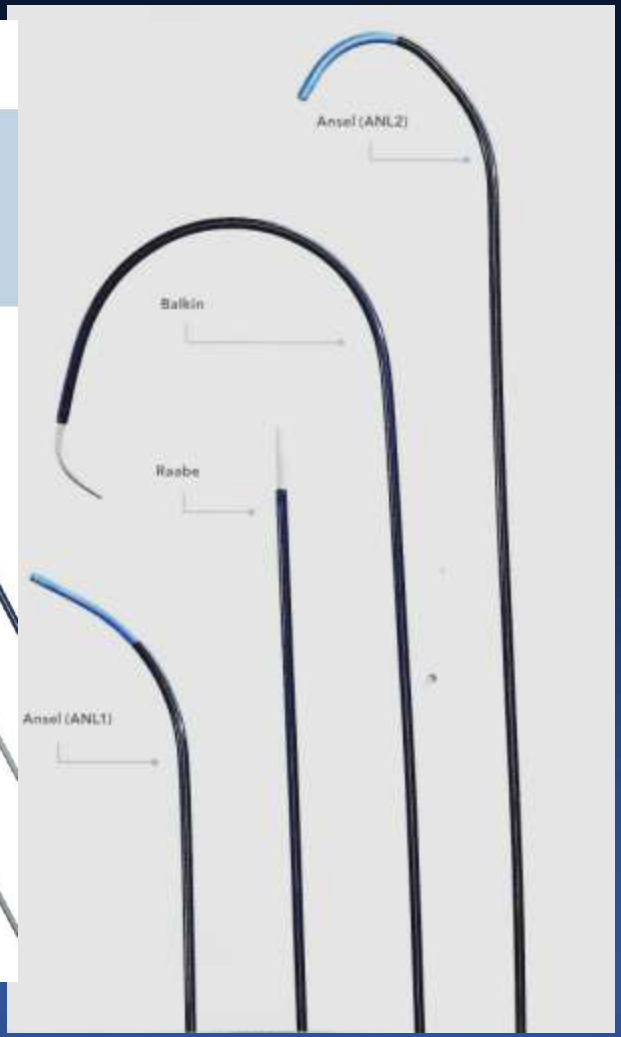
- The interventional therapy of critical limb ischemia requires crossing lesions. Often total occlusions that can't be crossed from above can easily be traversed intraluminally from below.
  - Collaterals
  - Operator can't discern where true lumen should be
  - Distal cap of occlusion may be softer than the proximal cap
  - "Hibernating vessel"

- Micro puncture .014 wire access under direct visualization (Angiographic or US)

- If pedal access is to cross only (vast majority of cases) then a .014 or .018 microcatheter is placed over the wire (to lessen risk of vessel occlusion)
- If pedal access is to cross and deliver therapy a sheath is introduced

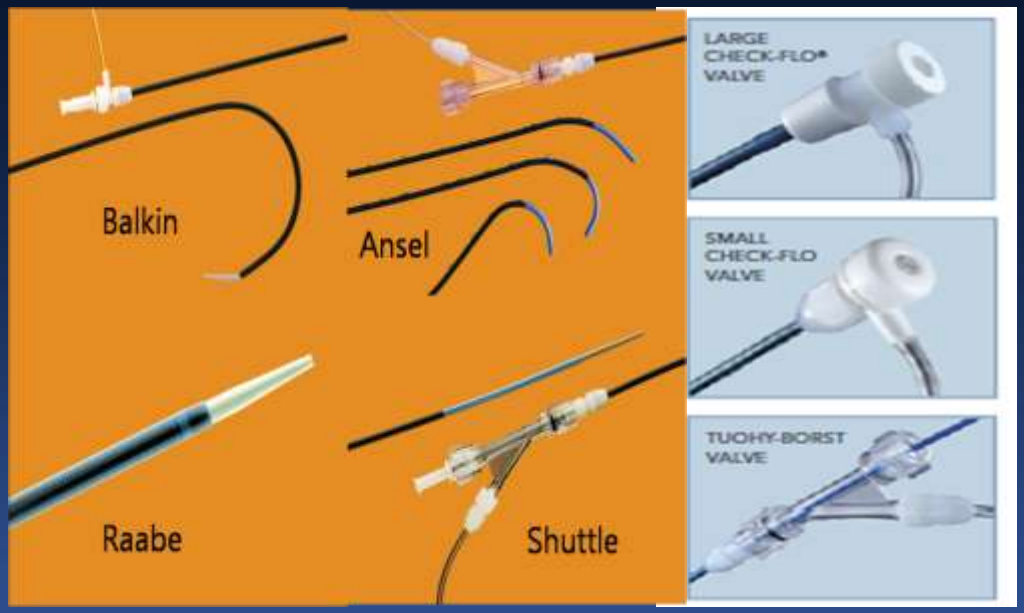
Shuttle System





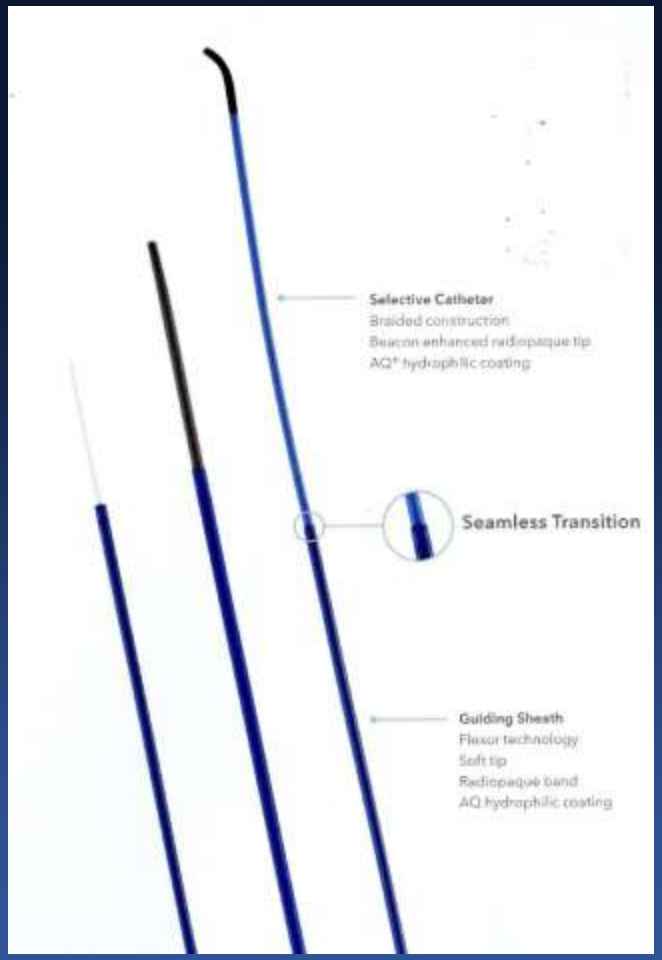
Shuttle System

Trackability and Choice
: 0.018 and 0.038 inch
Versability
Dependable



Shuttle Tibial System

Infra-popliteal Targeting
Compatible For Coaxial Use
Flexor Technology



Wire

- Standard-guide wire
  - Hydrophilic tipped guidewire
    0.014 inch Choice PT & PT2 (Boston Scientific)
    0.014 inch Shinobi (Cordis)
    0.018 inch V18-Control (Boston Scientific)
    0.035 inch Terumo (Terumo)

  - Specialized coronary CTO wire
    Miracle guidewire (Asahi, ABBOTT)
    Confienza guidewire (Asahi, ABBOTT
    Fielder XT, Fielder FC (Asahi)

Wire

- Peripheral Wire

  - 0.018 inch 480 cm Roadrunner Extra Support Wire Guide (Cook)
  - Approach Hydro ST & Approach CTO wire (Cook)

Balloon

- Monorail coronary balloon

Long, low-profile balloons

- Tracking over 0.018 inch guidewire

Pacific (Invatec), Savvy (Cordis), Fox SV (Abbott), Sterling (BS), Passeo 18 (Biotronik), Symmetry (Boston Scientific)

- Tracking over 0.014 inch guidewire

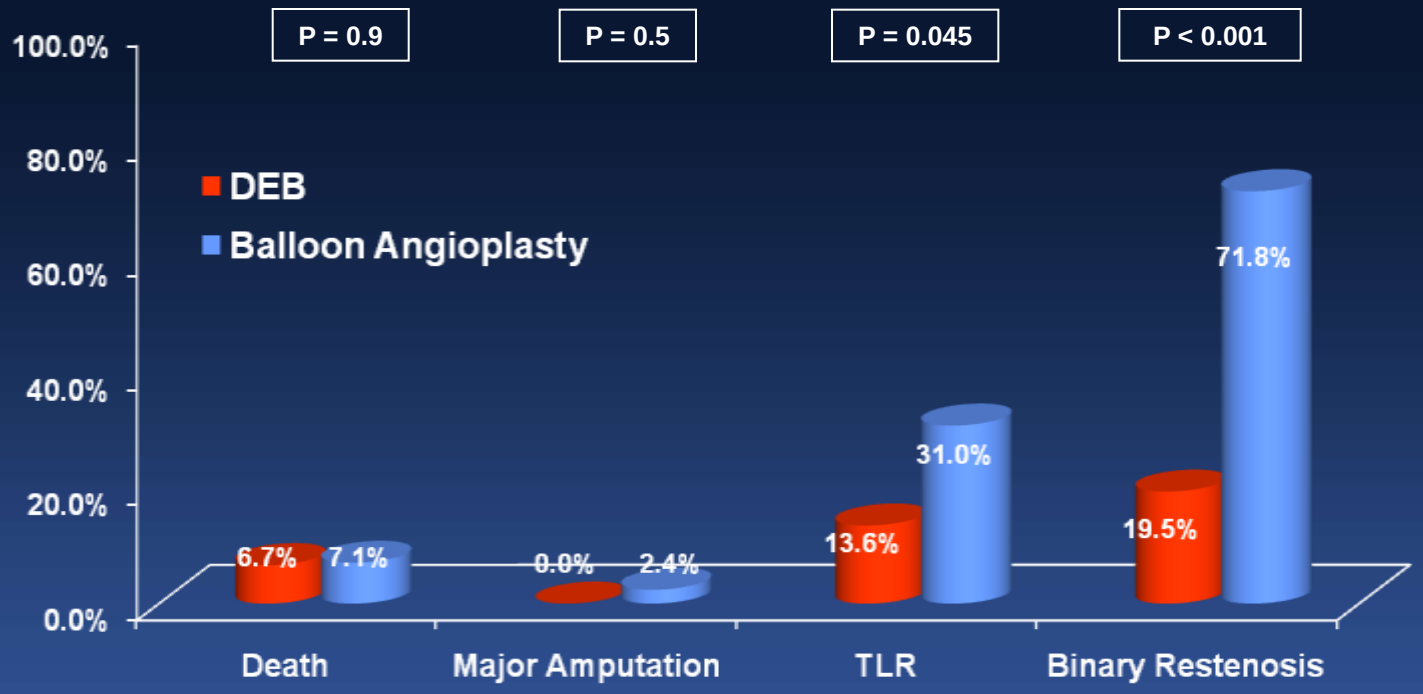
Amphirion Deep, OTW + RW (Invatec)
Sleek RX (Cordis) - 150 cm
Advanced 14 LP (Cook)

Micro-catheter

- JAMIRO microcatheter
  (2.9-French microcatheter, Kaneka)
- Corsair microcatheter (Asahi)
- FineCross microcatheter (Terumo)
- Tornus catheter (Asahi)
- CXI support catheter (Cook)

DEBATE-ISR (DEB vs Standard Angioplasty to Reduce Recurrent Restenosis in Diabetics with Femoropopliteal ISR)

44 patients with claudication or CLI treated with paclitaxel eluting balloon, 2010-2011 are compated with historical control



Conclusion: Use of DEBs to treat diabetic patients with femoropopliteal in -stent restenosis appears to reduce recurrent restenosis and repeat angioplasty at 1 year.

Liistro F, et al. J Endovasc Ther. 2014;21:1-8.