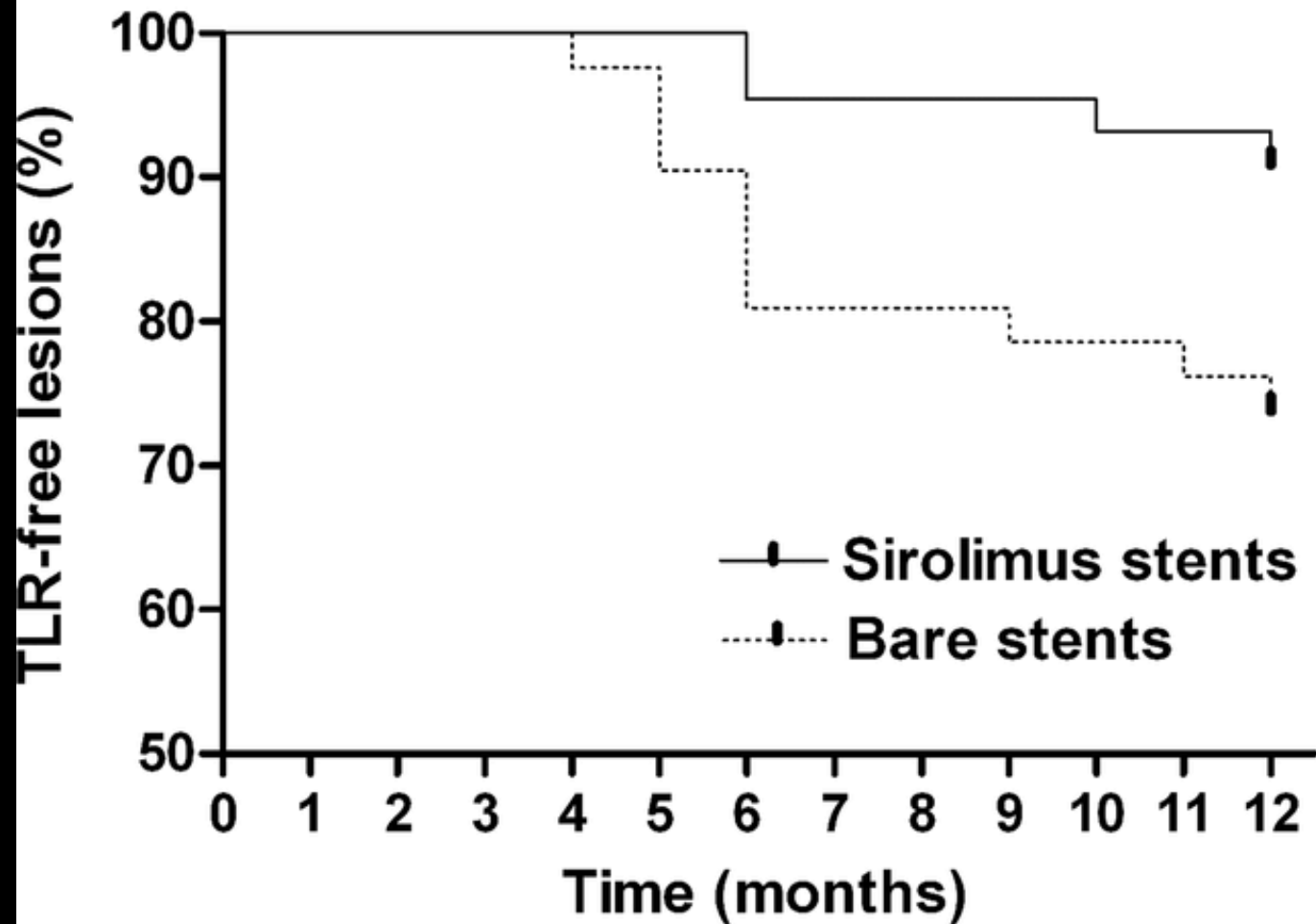


Target Lesion Reintervention (TLR)



Lesions at risk

Months	0	1	2	3	4	5	6	7	8	9	10	11	12
Sirolimus	44	44	44	44	44	44	44	44	44	44	42	42	41
Bare	42	42	42	42	42	41	38	38	38	34	34	33	32





Infrapopliteal Limb Salvage Data

<u>Modality</u>	<u>Pts</u>	<u>Lesion Length</u>	<u>Primary Patency</u>	<u>Secondary Patency</u>	<u>TLR</u>	<u>Amp free survival</u>
Laser Atherectomy	145	162mm				93 % 6month
Directional atherectomy	49	48 mm	67% at 1 yr 60% at 2 yr	91% at 1 yr 80% at 2 yr	24% at 1 yr 33% at 2 yr	
Cutting Balloon	73	25 mm				90 % 12month
Balloon Ex Stent	49	13 mm	40% at 1 yr		26% at 1 yr	87 % 12month
Self Ex Stent	47	51 mm	76% at 12 months	90% at 6 months		96% 12month
Cryoplasty	123	41 mm				85% 12month
Drug Eluting Stents	44	14 mm	86% at 1yr		9.1% at 1 yr	96 % 12month

Infrapopliteal Limb Salvage Data

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Infrapopliteal Stents: Balloon Expandable and Self Expanding

- Numerous coronary stents exist
- DES has already received CE mark in Europe for below the knee application
- Numerous single center series from Europe
- Large coronary literature showing efficacy compared to bare metal balloon expandable stents
- Dedicated nitinol stents are relatively new, little data currently available



Balloon Expandable Stent: Multilink Vision

**Bare metal: Multilink Vision
(Abbott)**

**Single Center experience:
12M duplex**

–Feb -Oct 2005

–50 CLI patients

•Rutherford 4 68%

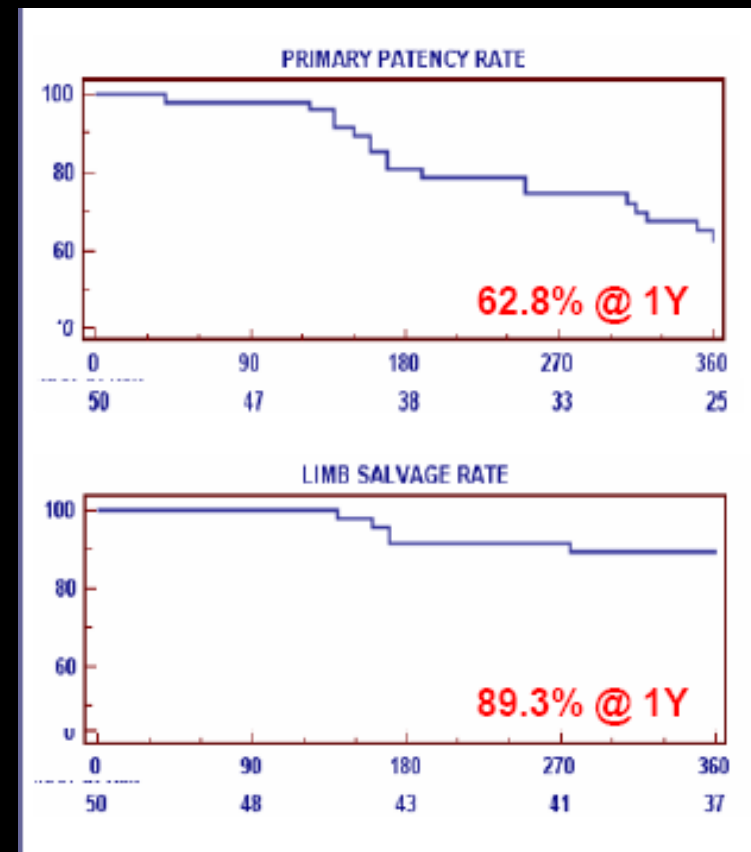
•Rutherford 5 32%

–62 BTK-lesions

–68 Vision stents

•Endpoint

–12-month duplex patency



Balloon Expandable Stent: CHROMIS Deep



- -Stent-diameter: 2.0 –4.0 mm
- -Stent-length:10 –80 mm
- -Introducer-compatibility:4 Fr
- Infrapopliteal Balloon-Expandable Stent



Chromis-Deep Registry

- Single center prospective registry
- -29 patients (31 limbs) included (05/2006-12/2007)
- -Patients with CLI or severe claudication
- -Stenting in case of unsatisfactory result after balloon or of restenoses
- -Lesions to be covered with 1 –3 78mm-stents
- -6 months angiographical follow-up



Chromis-Deep Registry

Baseline-Data Chromis-Deep Registry

Limbs	31	
Stenosis	8 (26%)	
Occlusion	23 (74%)	
Mean lesion length		100 ±54.9 mm
Mean stent length		106 ±54.0 mm
Stents / limb		limbs
1 stent		22
2 stents		6
3 stents		3



Chromis-Deep Registry

Angiographic follow-up after 5.4 ± 2.2 mo.

31 Limbs

No restenosis 10 (32.2%)

Restenosis > 50% 10 (32.2%) focal diffuse
4 6

Reocclusion 11 (35.6 %)

No Stent-fractures or -compressions



Chromis-Deep Registry



- One year follow up
 - Primary patency 52.9%
 - Limb salvage 91.5%
 - Survival 79.8%

Deloose K, Bosiers M, Peeters P. One year outcome after primary stenting of infrapopliteal lesions with the Chromis Deep stent in the management of critical limb ischaemia. *EuroIntervention*. 2009 Aug;5(3):318-24..

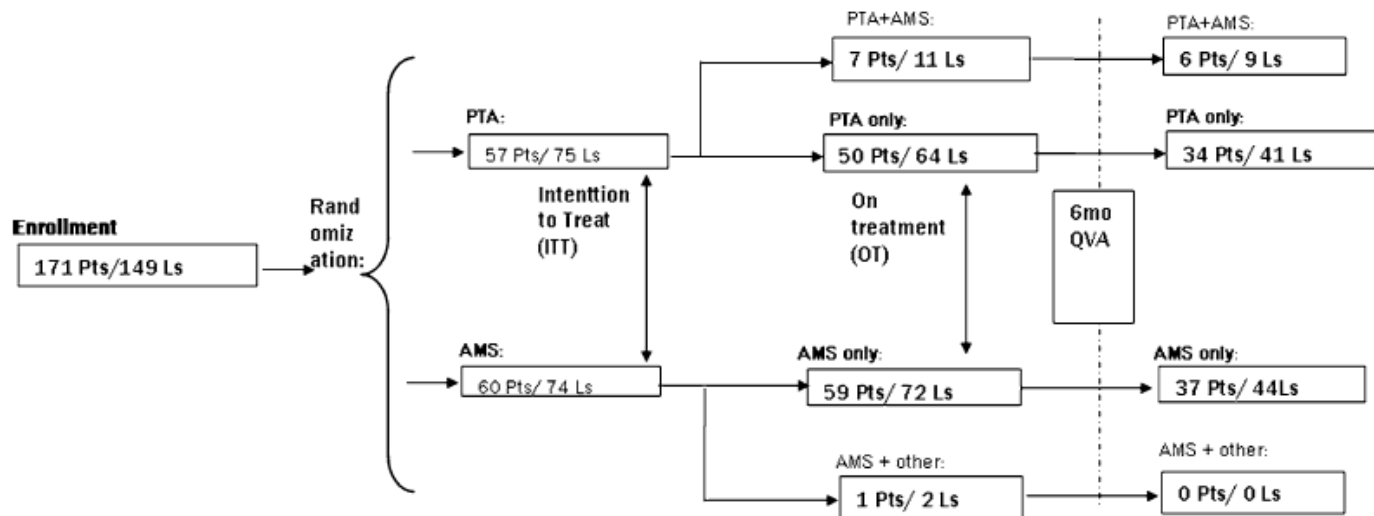


Balloon Expandable Stents: Bioabsorbable stents

CLINICAL INVESTIGATION

AMS INSIGHT—Absorbable Metal Stent Implantation for Treatment of Below-the-Knee Critical Limb Ischemia: 6-Month Analysis

Marc Bosiers · On Behalf of the AMS INSIGHT Investigators



Bosiers M; On Behalf of the AMS INSIGHT Investigators.

AMS INSIGHT-Absorbable Metal Stent Implantation for Treatment of Below-the-Knee Critical Limb Ischemia: 6-Month Analysis
Cardiovasc Intervent Radiol. 2008 Dec 18.



	PTA preproc	AMS preproc	PTA postproc	AMS postproc	6-mo QVA: PTA	6-mo QVA: AMS
No. patients	57	59	57	59	40	37
No. lesions	74	72	74	72	50	44
Patency	na	na	na	na	29/50 (58%) <i>p</i> = 0.0134	14/44 (31.8%)
Non patency	na	na	na	na	21/50 (42%) <i>p</i> = 0.0134	30/44 (68.2%)
Binary restenosis, mm						
Lesion length	12.0 ± 5.0	10.6 ± 4.9				
Min-max	3.5-30.4	3.1-27.6				
Stenosis diameter, mm Mean ± SD	68.7 ± 11.5	69.0 ± 10.7	21.9 ± 12.4	15.1 ± 10.2	47.8 ± 22.7	66.4 ± 27.1
(Min-max)	(51.4-100)	(51.3-100)	(-7.2-53.6)	(-18.4-38.9)	(3.8-100)	(2.5-100)
MLD, mm Mean	0.8 ± 0.3	0.8 ± 0.3	2.1 ± 0.5	2.2 ± 0.4	1.4 ± 0.7	0.9 ± 0.7
(Min-max)	(0.0-1.6)	(0.0-1.5)	(1.0-3.2)	(1.4-3.4)	(0.0-2.9)	(0.0-2.9)
					<i>p</i> = 0.0009	
RVD, mm Mean	2.7 ± 0.5	2.6 ± 0.5	2.7 ± 0.5	2.6 ± 0.5	2.7 ± 0.5	2.6 ± 0.5
(Min-max)	(1.4-4.4)	(1.5-4.4)	(1.5-4.6)	(1.5-4.6)	(1.8-4.5)	(1.9-3.9)
Late lumen loss, mm Mean ± SD	na	na	na	na	0.7 ± 0.7	1.4 ± 0.8
(Min-max)					(-0.3-2.9)	(-0.4-2.9)
					<i>p</i> = 0.0001	

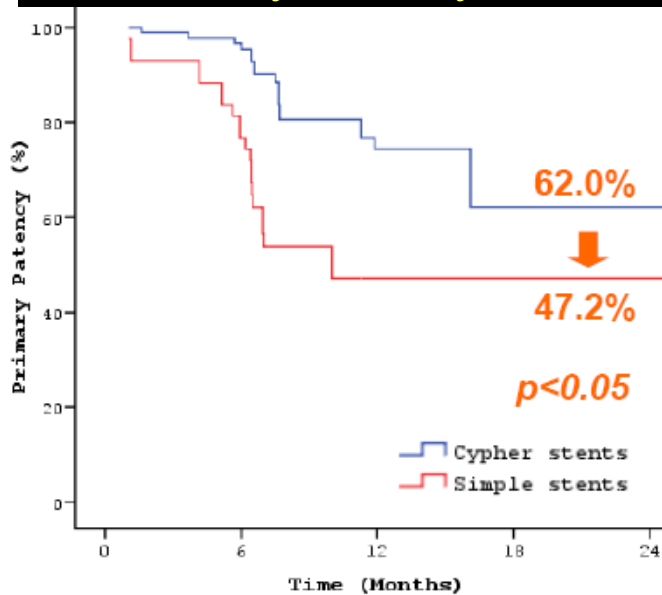
Bosiers M; On Behalf of the AMS INSIGHT Investigators.
AMS INSIGHT-Absorbable Metal Stent Implantation for Treatment of Below-the-Knee Critical Limb Ischemia: 6-Month Analysis.
Cardiovasc Intervent Radiol. 2008 Dec 18.



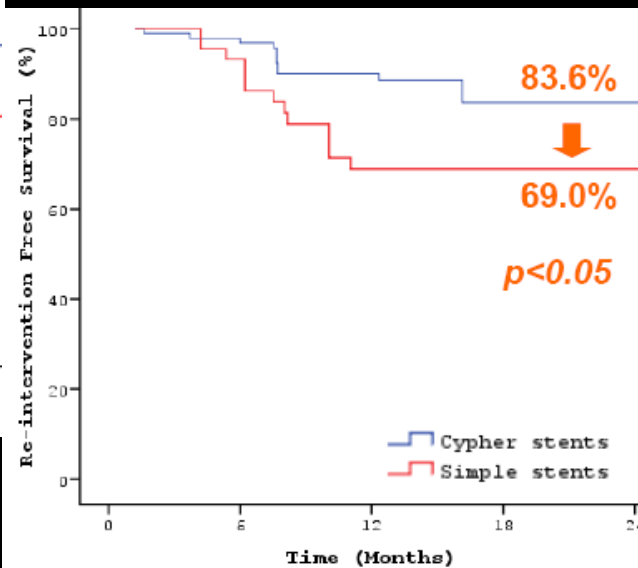
Balloon Expandable Stent: Sirolimus Eluting Stents

Siablis et al.

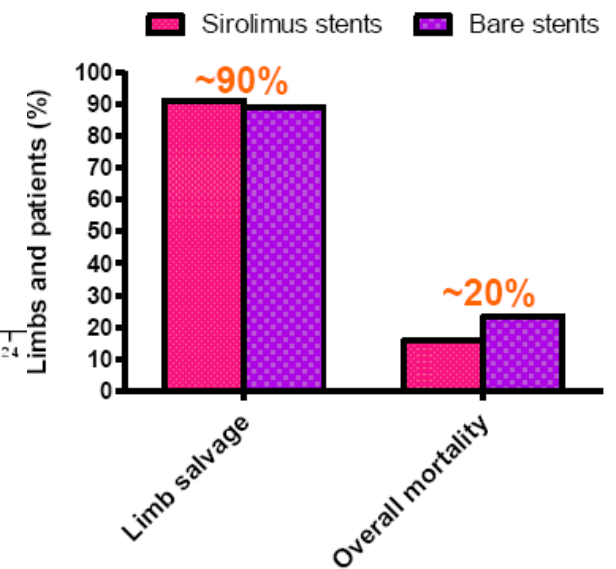
Primary Patency



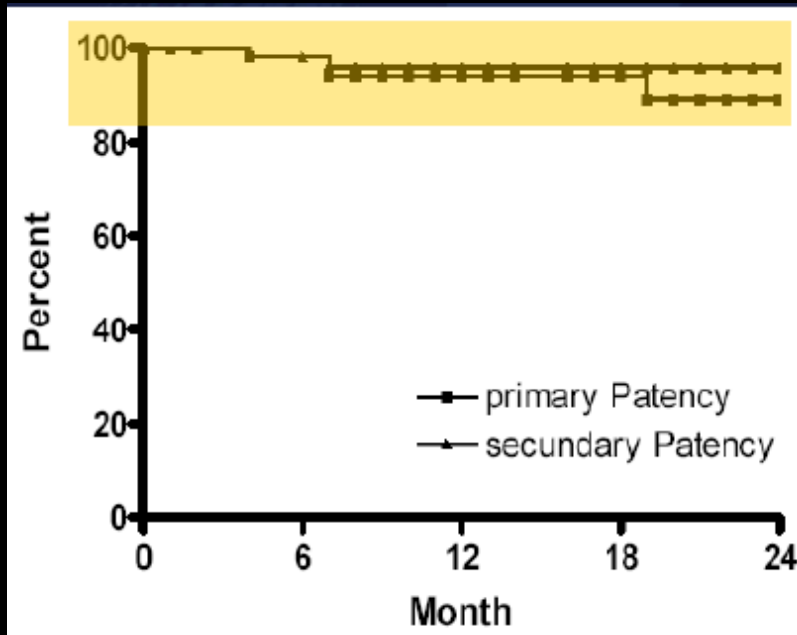
Freedom from TLR



Limb Salvage and Mortality



Balloon Expandable Stent: Sirolimus Eluting Stents



Patients (n) 74
Alive at 2 yrs (n) 59
DSA FUP (n) 47
DSA FUP time ~1 year

	Primary	Secondary
6 months	98.2%	98.2%
12 months	94.1%	95.9%
24 months	89.2%	95.9%

Balloon Expandable Stents: Paclitaxel Eluting Stents

Infrapopliteal Application of Paclitaxel-eluting Stents for Critical Limb Ischemia: Midterm Angiographic and Clinical Results

Dimitris Siablis, PhD, Dimitris Karnabatidis, PhD, Konstantinos Katsanos, MD,
Athanasios Diamantopoulos, MD, Nikolaos Christeas, MD, and George C. Kagadis, PhD

J Vasc Interv Radiol 2007; 18:1351-1361

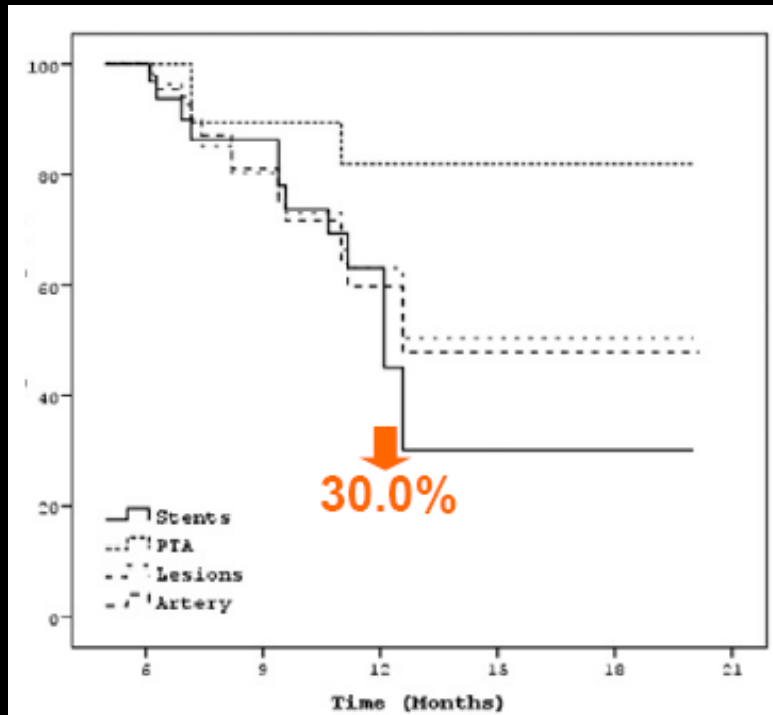
PACLITAXEL STENTS	
Limbs (n)	32
Diabetes Mellitus	79.3%
Lesions (n)	79
PTA length	4.5 ± 5 cm
Stents (n)	62
Stented length	2.5 ± 1 cm

Siablis D, Karnabatidis D, Katsanos K, Diamantopoulos A, Christeas N, Kagadis GC.
Infrapopliteal application of paclitaxel-eluting stents for critical limb ischemia:
midterm angiographic and clinical results. J Vasc Interv Radiol. 2007 Nov;18(11):1351-61.

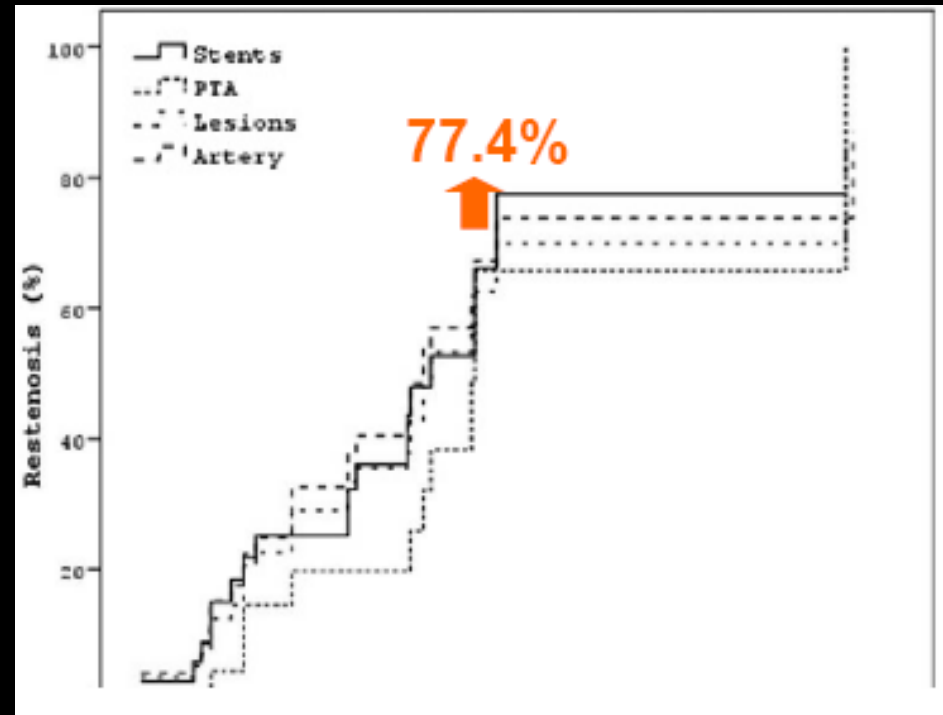


Balloon Expandable Stents: Paclitaxol Eluting Stents

Primary Patency



Restenosis



Siablis D, Karnabatidis D, Katsanos K, Diamantopoulos A, Christeas N, Kagadis GC.
Intrapopliteal application of paclitaxel-eluting stents for critical limb ischemia:
midterm angiographic and clinical results. J Vasc Interv Radiol. 2007 Nov;18(11):1351-61.



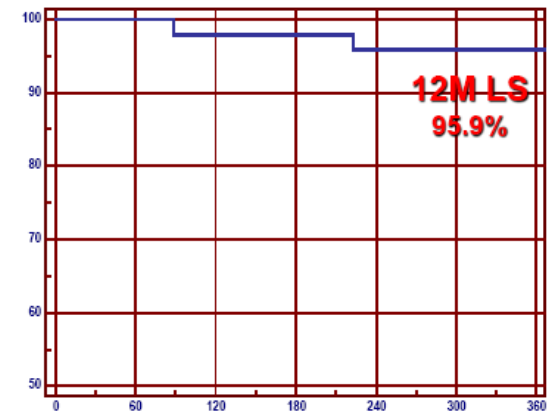
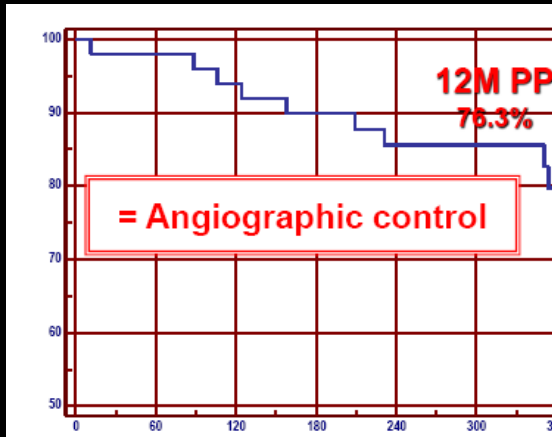
Self Expanding Stents



- Xpert self-expanding nitinol stent
- 3-8mm diameters
- 4 Fr shaft diameter
- Biliary indication

Self Expanding Stents: Xpert

- Belgian single center series
- 67 stents in 47 patients
- Rutherford category 4 and 5 disease
- 12 month Angiographic follow up
- Primary patency at 12 months 76%
- Limb salvage was 96%
- Proximal calf disease had better prognosis for limb salvage



Infrapopliteal Stent Data

<u>Modality</u>	<u>Pts</u>	<u>Lesion Length</u>	<u>Primary Patency</u>	<u>Secondary Patency</u>	<u>TLR</u>	<u>Amp free survival</u>
Multilink Vision Cobalt Cr BMS	50		63% at 12 months			89% 12month
Chromis Deep Cobalt Cr BMS	29	100mm	74% at 6 months			93% 6 month
Biotronik Absorbable Mg Alloy BMS	37	10.6mm	32% at 6 months			88 % 6 month
Paclitaxel Eluting Stents	49	26 mm	30% at 12 months		30% at 1 yr	87 % 12month
Self Ex Stent/ Xpert	47	51 mm	76% at 12 months	90% at 6 months		96% 12month
Carbostent	23	24 mm	83% at 6 months			85% 12month
Sirolimus Eluting Stents	44	14 mm	86% at 12 months		9.1% at 1 yr	96 % 12month

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Preventing Leg Amputations in Critical Limb Ischemia With Below-the-Knee Drug-Eluting Stents

The PaRADISE (PREventing Amputations using Drug eluting StEnts) Trial

Andrew J. Feiring, MD,* Mari Krahn, RN,* Lori Nelson, NP,* Amy Wesolowski, RN,* Daniel Eastwood, MS,† Aniko Szabo, PhD†

Milwaukee, Wisconsin

Infrapopliteal Drug-Eluting Stents for Chronic Limb Ischemia

A.G. Grant, MD, C.J. White,* MD, T.J. Collins, MD, J.S. Jenkins, MD, J.P. Reilly, MD, and S.R. Ramee, MD

Sirolimus for Below the Knee Lesions: Mid-Term Results of SiroBTK Study

Philippe Commeau,* MD, FSCAI, Paul Barragan, MD, and Pierre O. Roquebert,

J CARDIOVASC SURG 2010;51:183-91

Percutaneous interventions below the knee in patients with critical limb ischemia using drug eluting stents

J. O. BALZER¹, T. ZELLER², A. RASTAN², S. SIXT², T. J. VOGL³, T. LEHNERT³, V. KHAN⁴

Original Studies

Drug Eluting Stents for Below the Knee Lesions in Patients With Critical Limb Ischemia: Long-Term Follow-Up

Oscar R. Rosales,^{1*} MD, Shiny Mathewkutty,² MD, and Charlie Gnaim,³ MD

Infrapopliteal Application of Sirolimus-eluting versus Bare Metal Stents for Critical Limb Ischemia: Analysis of Long-term Angiographic and Clinical Outcome

Dimitris Siablis, MD, PhD, Dimitris Karnabatidis, MD, PhD, Konstantinos Katsanos, MD, Athanasios Diamantopoulos, MD, Stavros Spiliopoulos, MD, George C. Kagadis, BSc, MSc, PhD, and John Tsolakis, MD, PhD

◆ CLINICAL INVESTIGATION ◆

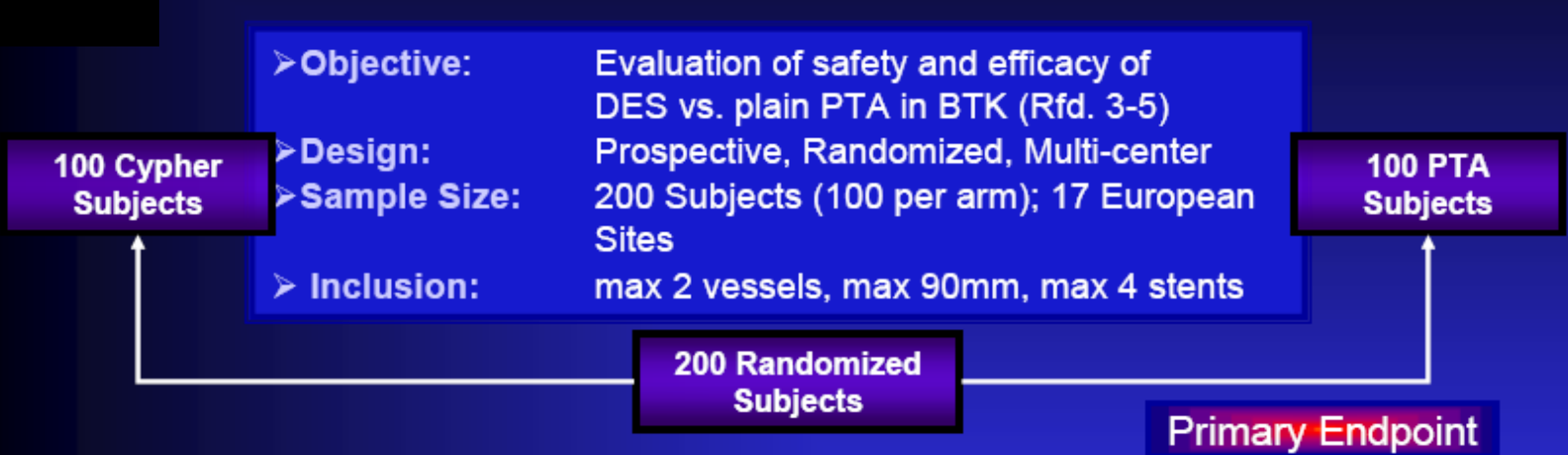
Sirolimus-Eluting Versus Bare Stents After Suboptimal Infrapopliteal Angioplasty for Critical Limb Ischemia: Enduring 1-Year Angiographic and Clinical Benefit

Dimitris Siablis, PhD¹; Dimitris Karnabatidis, PhD¹; Konstantinos Katsanos, MD¹; George C. Kagadis, PhD²; Pantelis Kraniotis, MD¹; Athanassios Diamantopoulos, MD¹; and John Tsolakis, PhD³

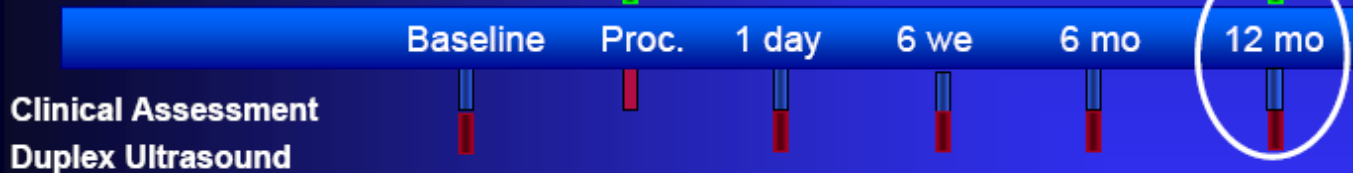


Study Design: Achilles (Cypher)

PI: Scheinert



Angiographic Assessment



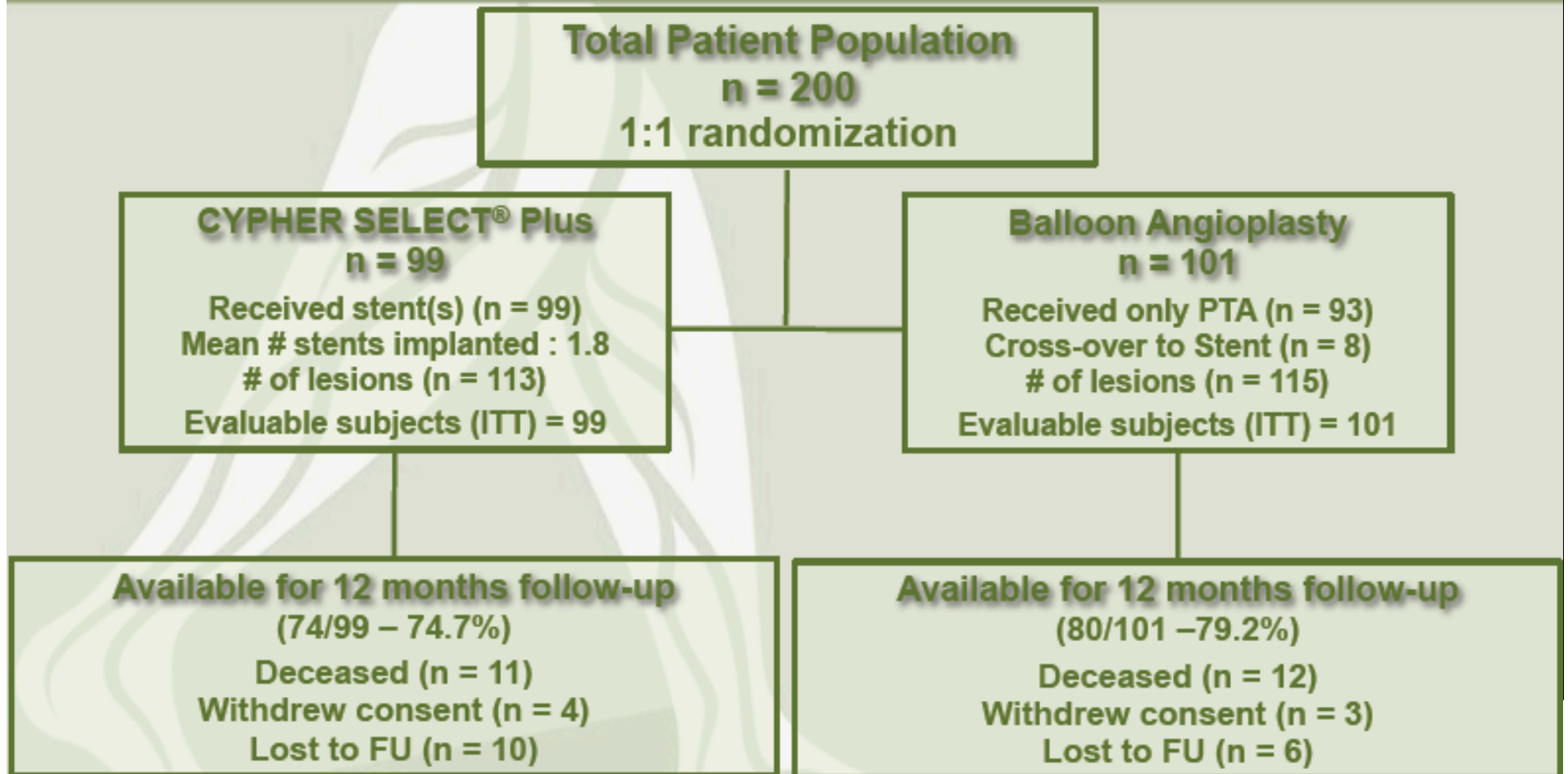
Primary endpoint: Angiographic in-stent restenosis (>50% stenosis) at 12 months.

Secondary endpoints: Device success (< 30% residual stenosis), limb salvage, SAE + clinical success at all time points, QoL, stent fracture

Current status: 17 centres (A,G,F,GR,B,CH,P) enrolling

The ACHILLES Study

Patient Enrollment



The ACHILLES Study

Lesion Characteristics – ITT

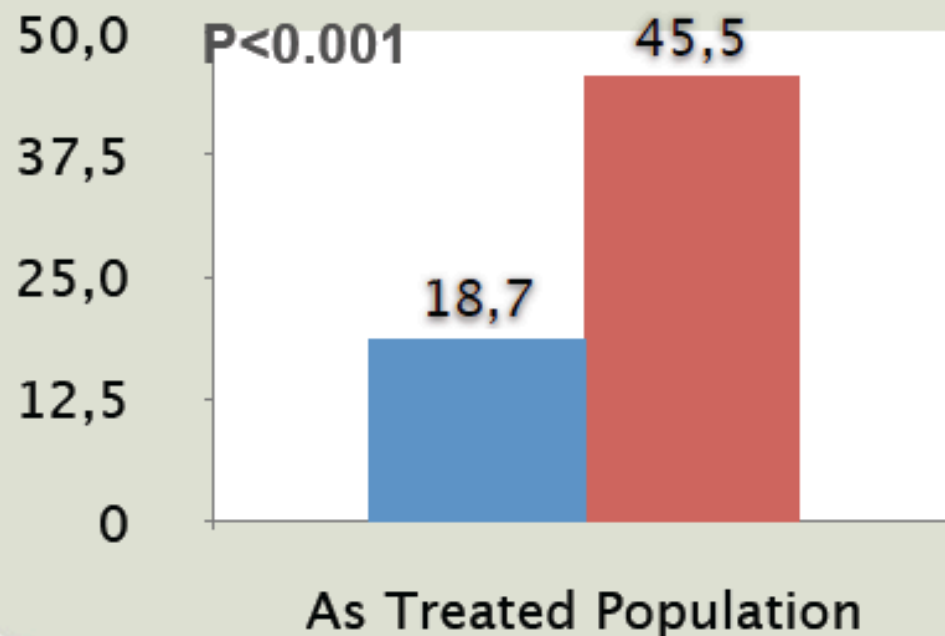
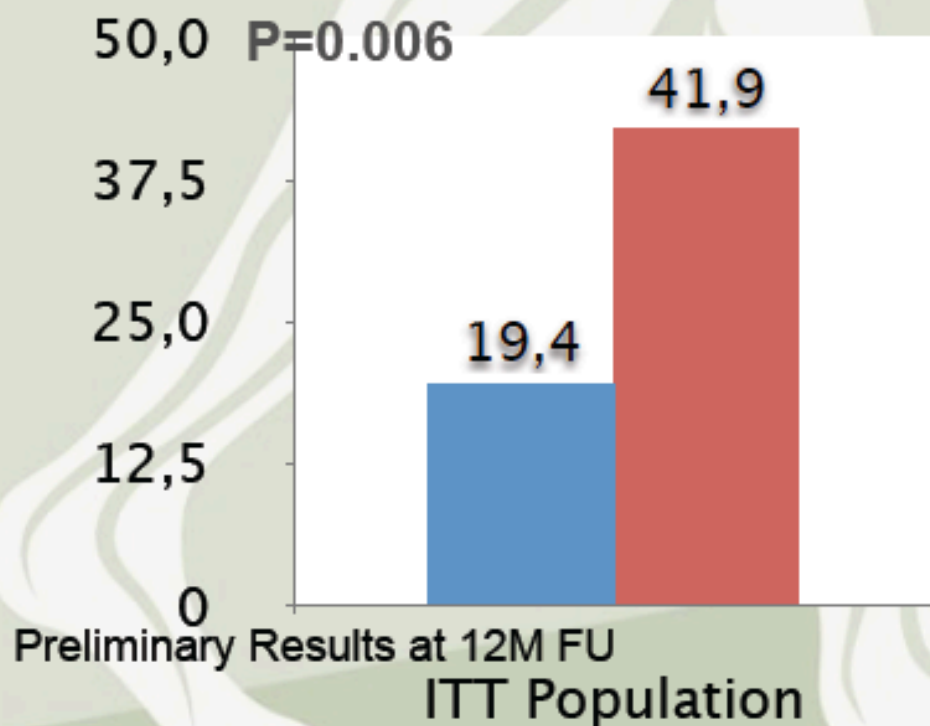
	CYPHER SELECT® Plus (n = 113)	PTA (n =115)	p-value
Total Lesion Length, mm	26.9 ± 20.9	27.5 ± 21.9	0.864
Total Occlusion, %	81.3	75.4	0.334
Total Length of Occlusion, mm	6.7 ± 19.3	11.0 ± 22.4	0.135
Reference Vessel Diameter, mm	2.6 ± 0.5	2.8 ± 1.3	0.402
De novo lesion, %	94.7	98.2	0.171
Restenotic, %	5.3	1.8	
Calcification (moderate, severe), %	15.1	15.2	1.000
Rutherford Classification, %			0.650
3	38.4	38.6	
4	15.2	17.8	
-	

The ACHILLES Study

Primary Endpoint 12M In-Segment Binary Restenosis by QA

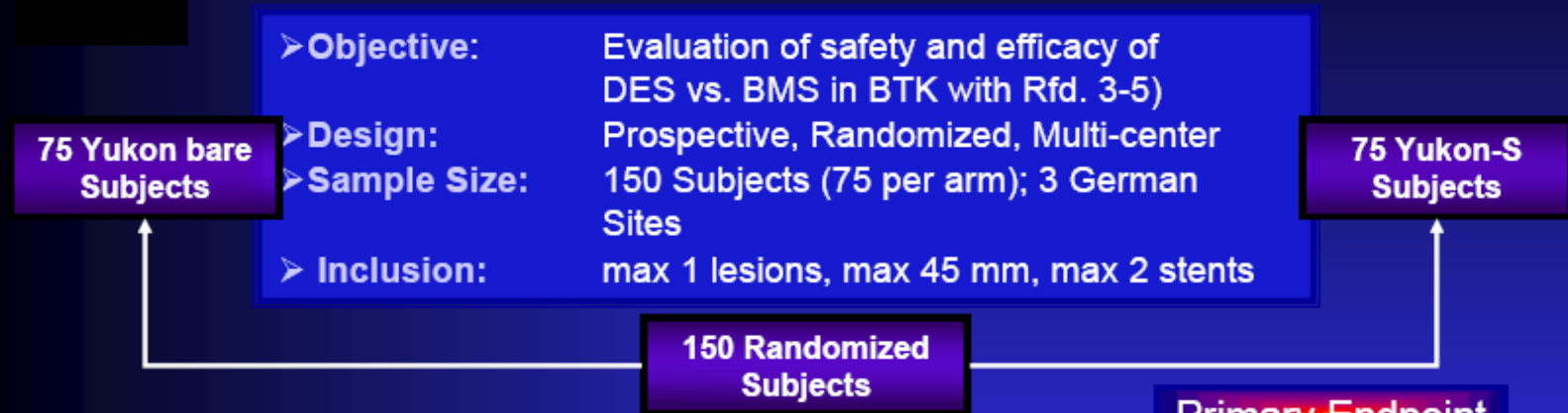
■ CYPHER SELECT PLUS (n = 67)
■ PTA (n = 74)

■ CYPHER SELECT PLUS (n = 75)
■ PTA (n = 66)



Study Design: Yukon (Yukon-S)

PI: Zeller



Angiographic Assessment



Primary endpoint: In-stent restenosis (>50% stenosis) at 12 months.

Secondary endpoints: Restenosis at 6 months, limb salvage, SAEs and clinical success at 6 and 12 months

Current status: 3 centres (G – completed)

Sirolimus-eluting stents vs. bare-metal stents for treatment of focal lesions in infrapopliteal arteries: a double-blind, multi-centre, randomized clinical trial

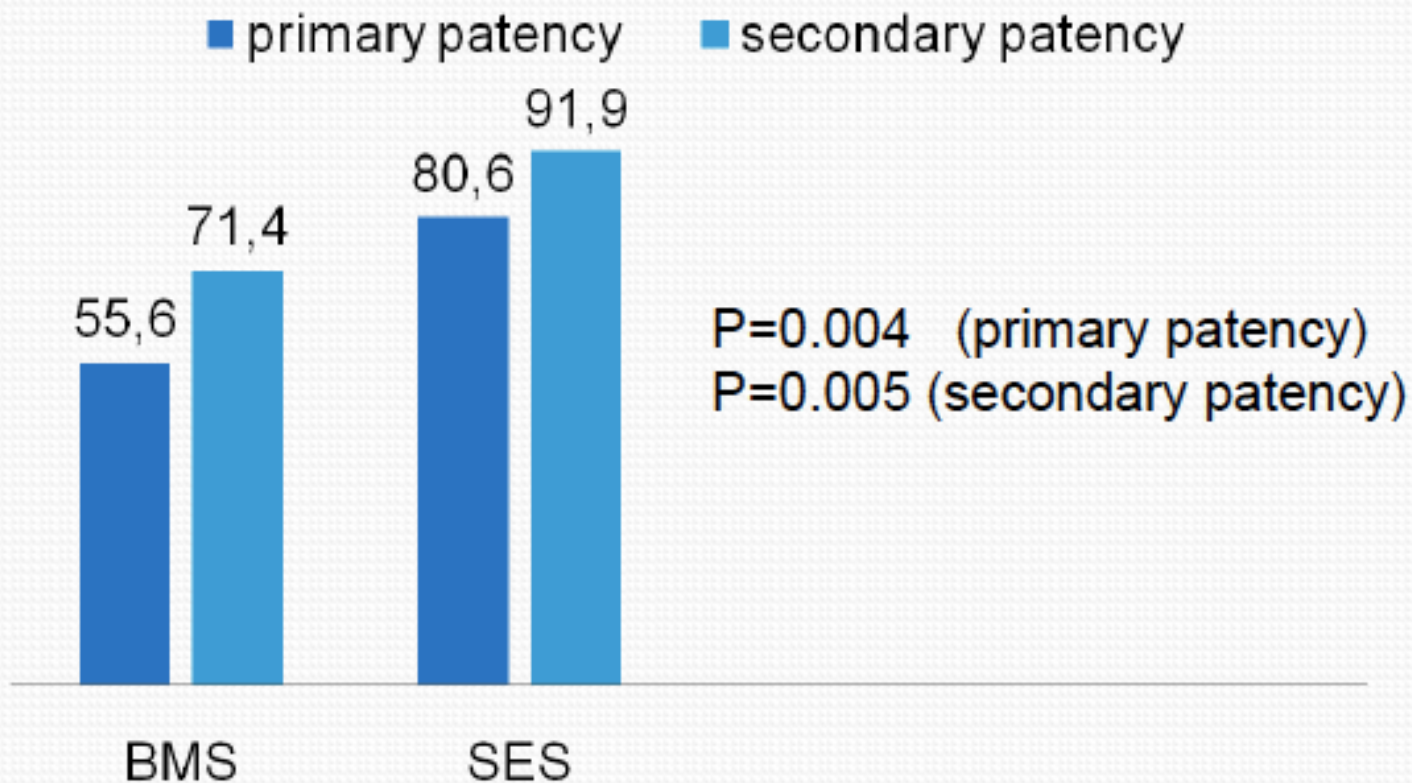
**Aljoscha Rastan^{1*}, Gunnar Tepe², Hans Krankenberg³, Rainer Zahorsky⁴,
Ullrich Beschorner¹, Elias Noory¹, Sebastian Sixt¹, Thomas Schwarz¹,
Klaus Brechtel², Catherine Böhme¹, Franz-Josef Neumann¹, and Thomas Zeller¹**

¹Abteilung Angiologie, Herz-Zentrum Bad Krozingen, Südring 15, D-79189 Bad Krozingen, Germany; ²Radiologische Klinik, Diagnostische und Interventionelle Radiologie, Eberhard-Karls-Universität, Tübingen, Germany; ³Universitäres Herz- und Gefäßzentrum Hamburg, Hamburg, Germany; and ⁴Cardiologicum Hamburg, Hamburg, Germany

Received 10 January 2011; revised 23 March 2011; accepted 4 April 2011; online publish-ahead-of-print 26 May 2011

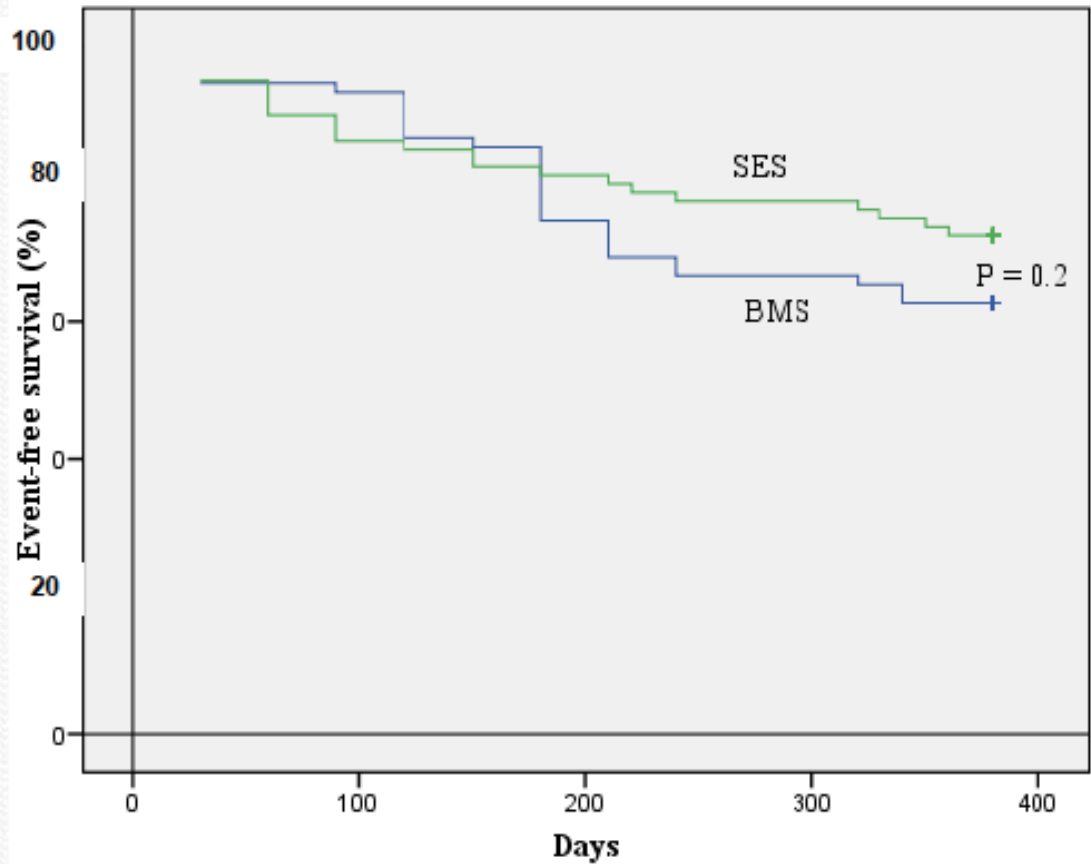
Primary Endpoint Primary & Secondary 1-Year Patency

1-Year Patency Rates



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.

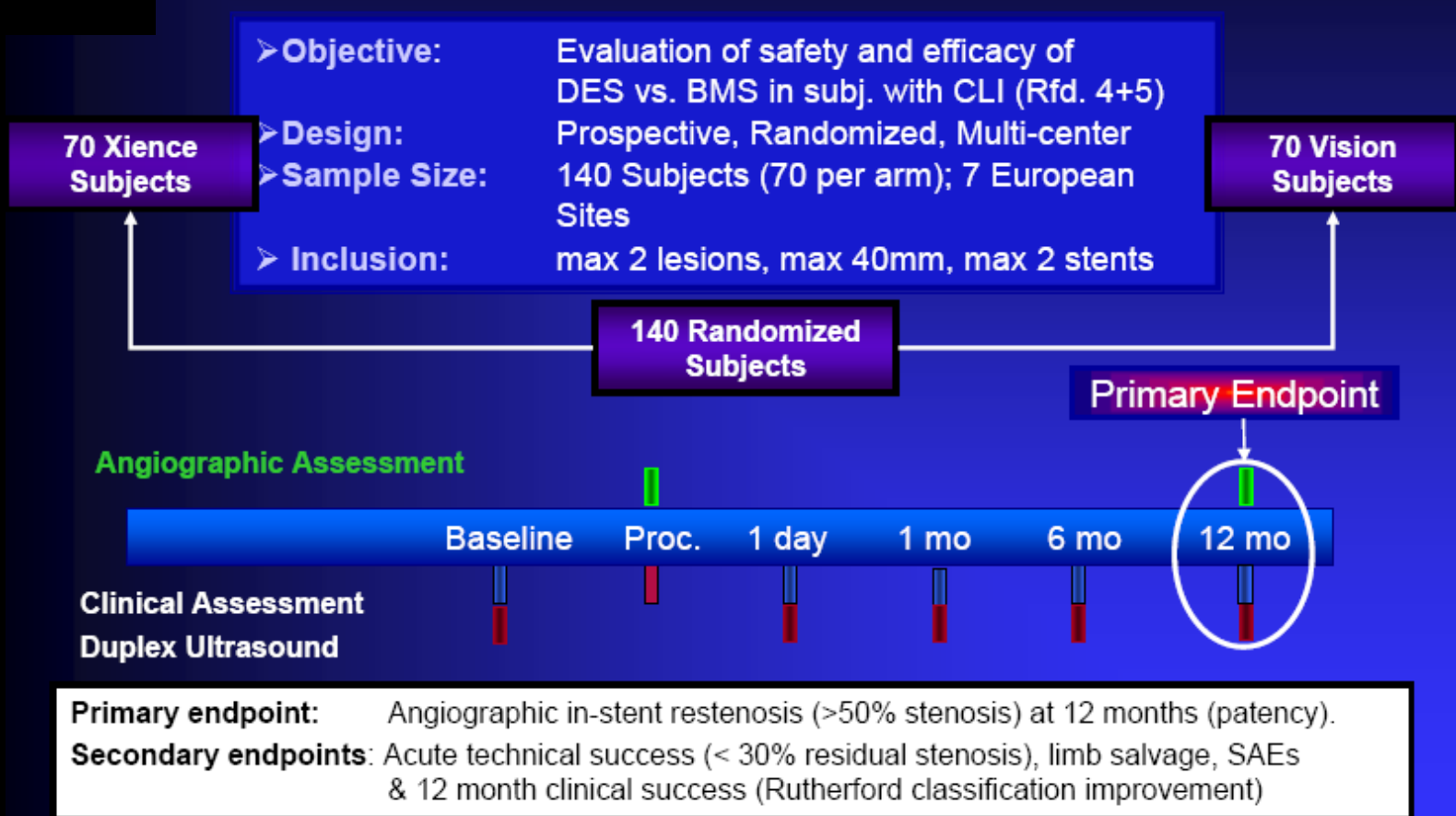


No. at risk

	0	100	200	300	400
Sirolimus Stent	82	71	64	63	62
Bare-metal Stent	79	72	67	64	63

Study Design: DESTINY (Xience BTK)

PI: Bosiers, Scheinert

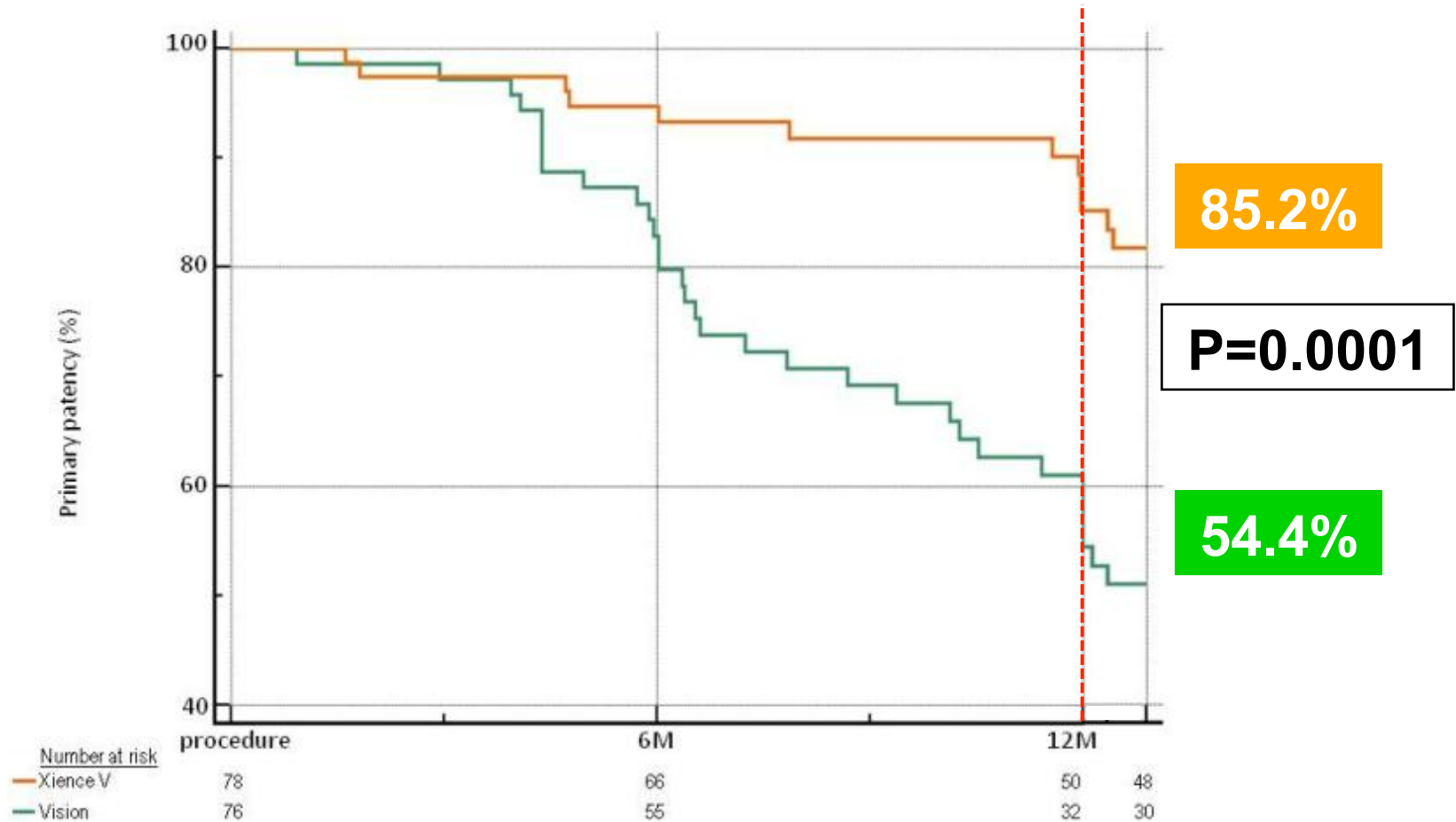


Current status: 7 centres (B,G,F – enrolling)



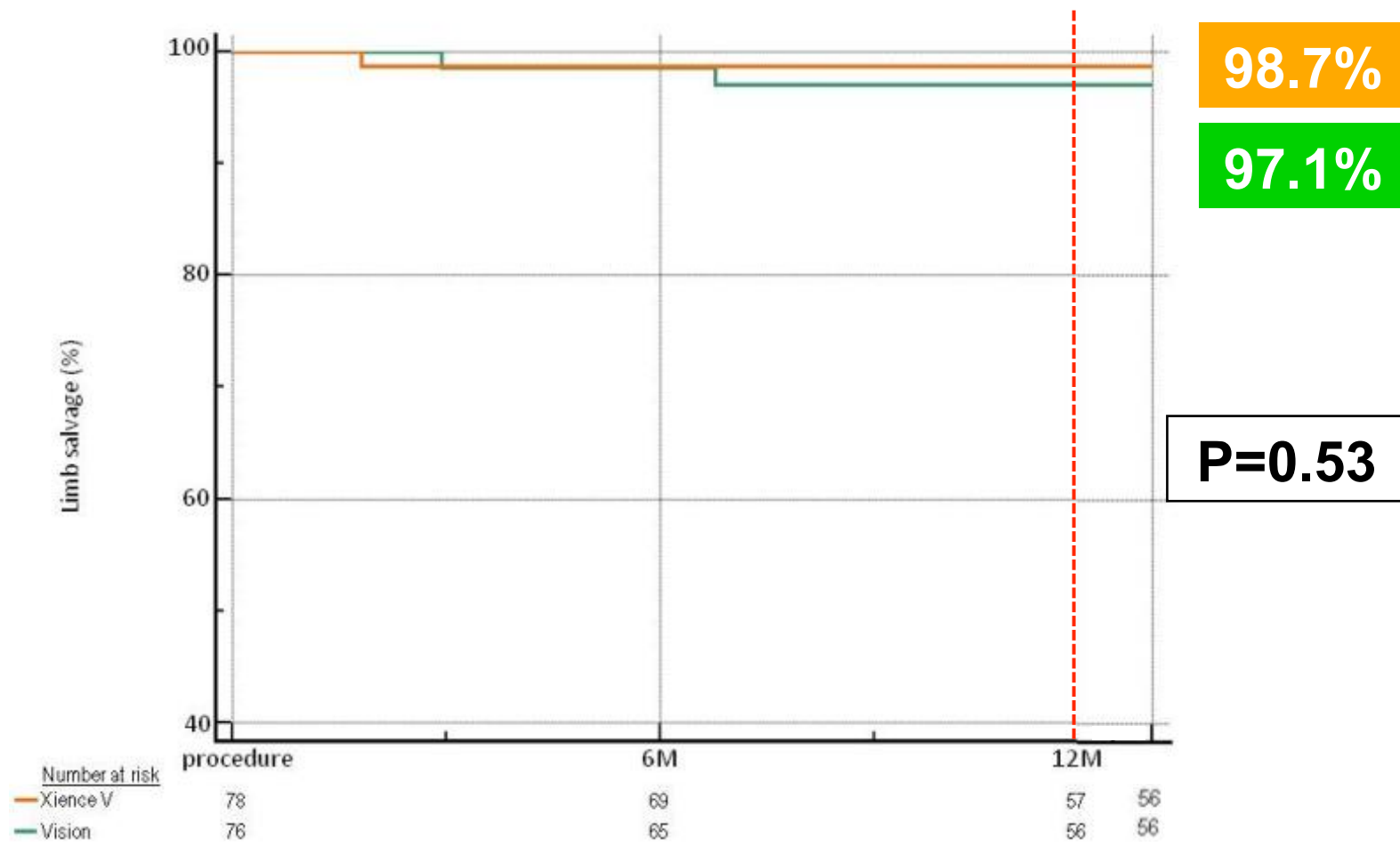
12-month primary patency

MultiLink Vision vs *Xience V*



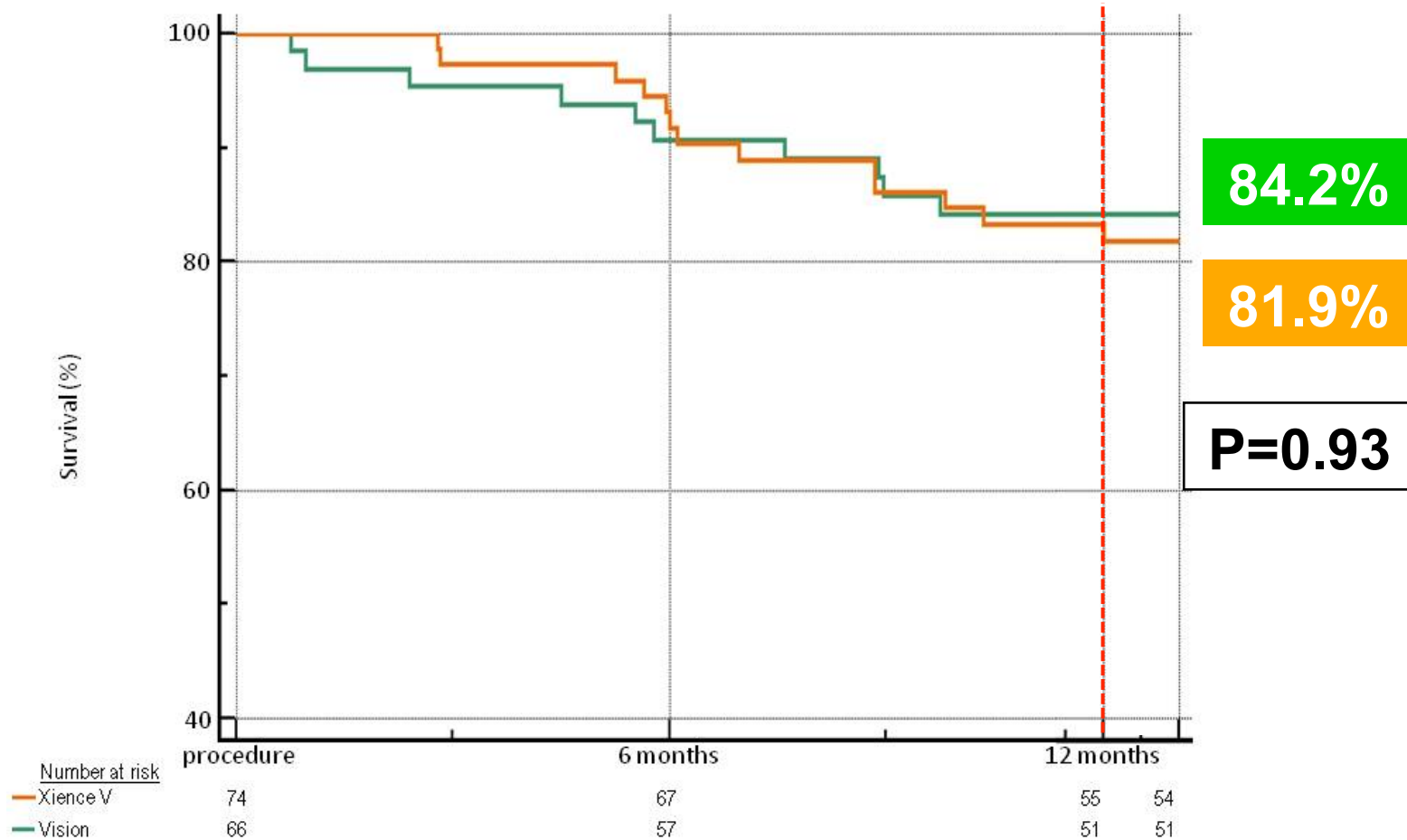
12-month limb salvage

MultiLink Vision vs *Xience V*



12-month survival

MultiLink Vision vs *Xience V*



Value of drug-eluting stents after failed percutaneous transluminal angioplasty in the infrapopliteal vessels for the treatment of critical limb ischemia: favorable mid-term patency and limb salvage results

R. A-LOOKSTEIN¹, T. J. WARD¹, E. KIM¹, A. M. FISCHMAN¹, F. S. NOWAKOWSKI¹,
S. ELLOZY², V. TEODORESCU², A. G. VOYOUKA², P. L. FARIÉS², J. L. WEINTRAUB¹

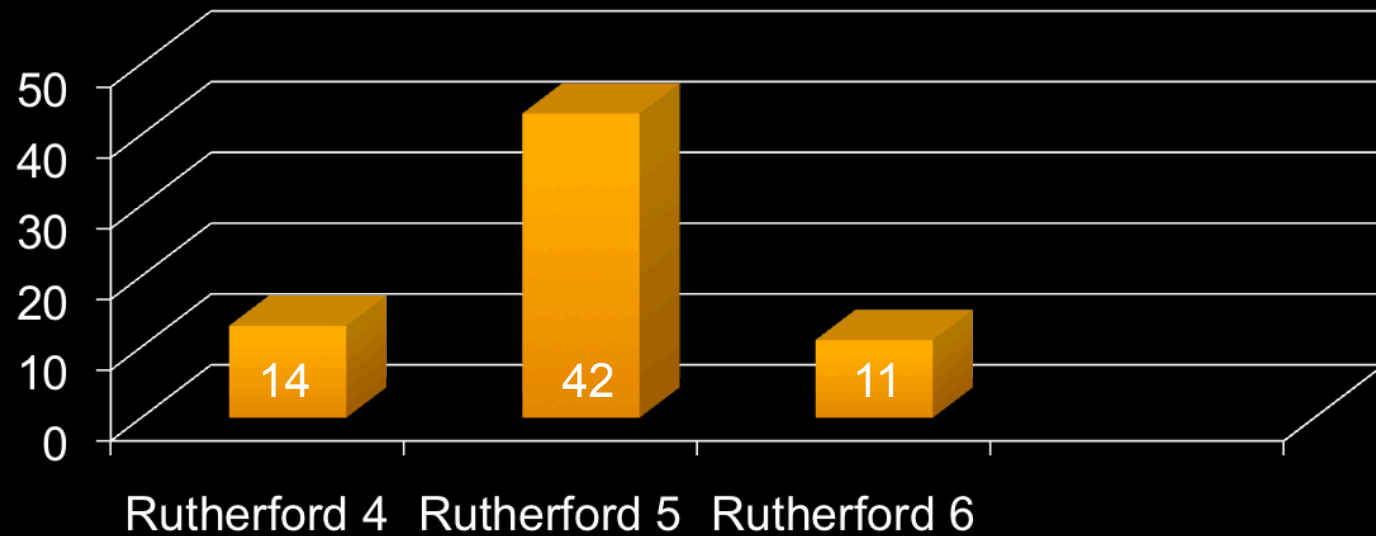


Materials and Methods

- October 2005 to February 2010
- 67 patients 36 male, 31 female
 - mean age 71, range 43-93
 - ALL patients had symptoms of critical limb ischemia at presentation prior to treatment
 - All patients were considered poor surgical candidates due to poor conduit or severe medical comorbidities
 - All stents were placed following a suboptimal balloon angioplasty result



Materials and Methods



Fontaine			Rutherford		
Stage	Clinical	Grade	Category	Clinical	Objective criteria
I	Asymptomatic	0	0	Asymptomatic	Normal treadmill or reactive hyperemia test
IIa	Mild claudication	I	1	Mild claudication	AP after exercise > 50 mmHg but ≥ 20 mmHg lower than resting value
IIb	Moderate-severe claudication	I	2	Moderate claudication	
III	Ischemic rest pain	II	3	Severe claudication	Resting AP < 60 mmHg, ankle or metatarsal PVR flat or barely pulsatile; TP < 40 mmHg
		II	4	Ischemic rest pain	
IV	Ulceration or gangrene	III	5	Minor tissue loss	Resting AP < 60 mmHg, ankle or metatarsal PVR flat or barely pulsatile; TP < 40 mmHg
		IV	6	Ulceration or gangrene	



Demographics

CAD	DM	Chronic Renal Disease
82%	72%	43%
(55/67)	(48/67)	(29/67)



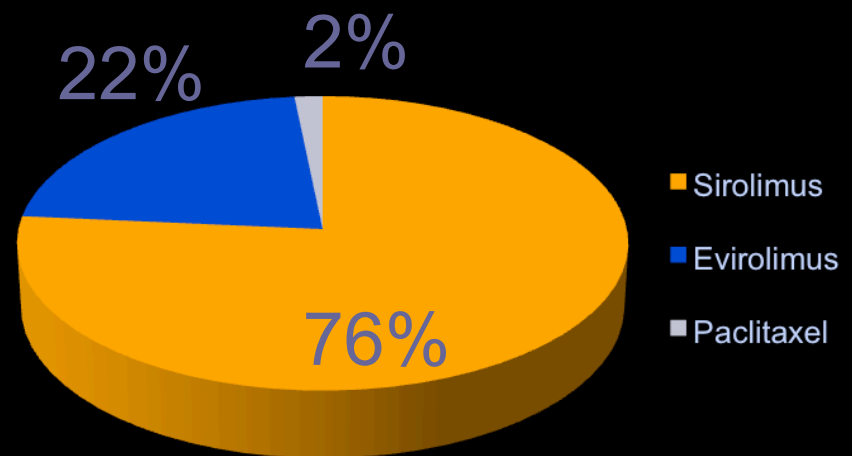
Materials and Methods

- **Clinical endpoints**
 - technical success of the revascularization procedure
 - primary patency as assessed by duplex ultrasound at 1,3,6,12,18,24 months
 - freedom from major amputation
 - survival at follow up
- All patients were placed on clopidigrel and aspirin peri-procedurally and continued indefinitely

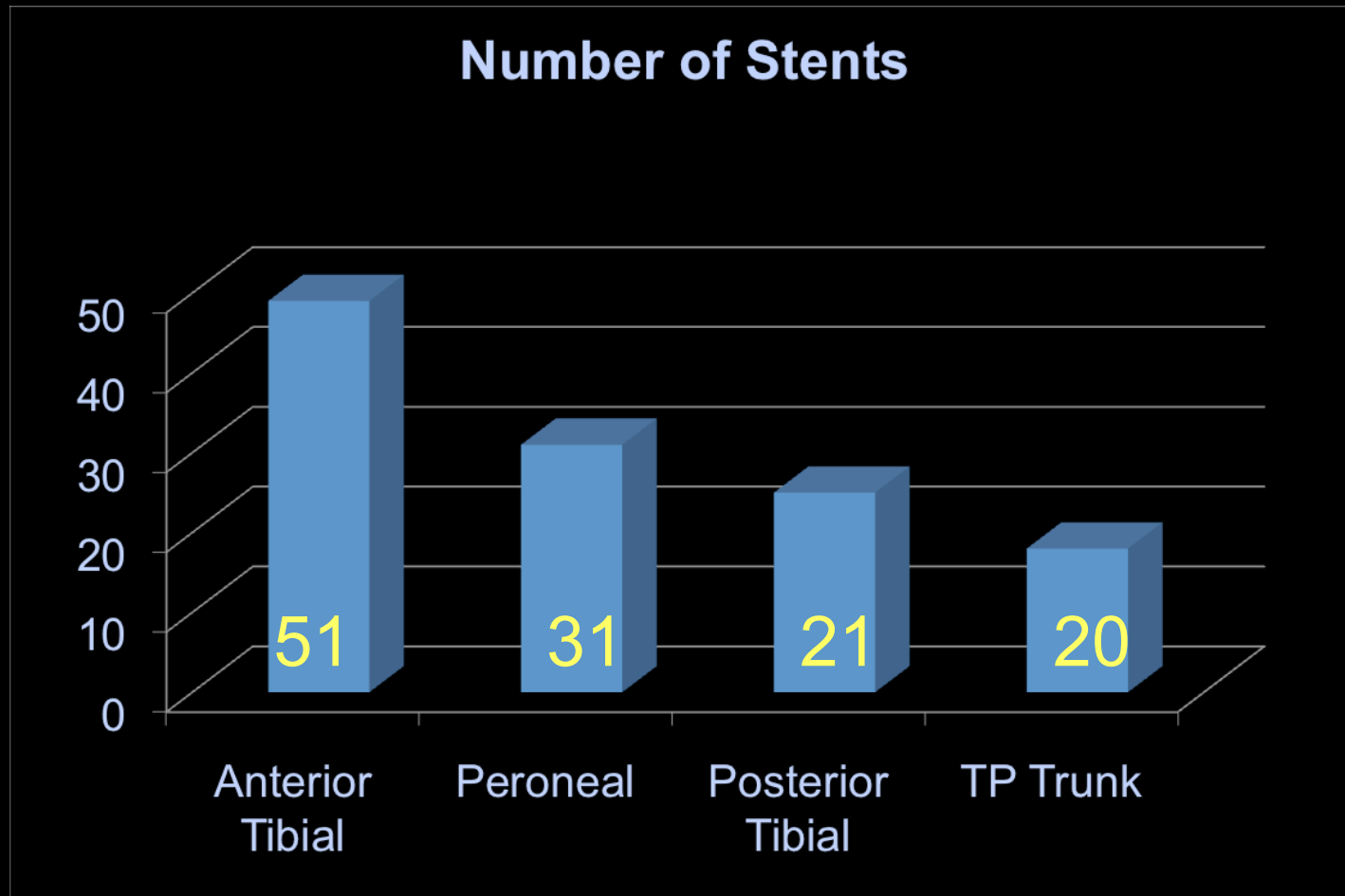


Results

- 67 patients (37 men, 30 women)
(mean age 71, range 43-93)
84 angiographic lesions
- 123 infrapopliteal drug eluting stents
- 94 sirolimus, 27 evirolimus, 2 paclitaxel



Vessel Distribution



Results:

Technical Details

Technical Success	Mean Lesion length	Mean number of stents per patient	Stent Diameter	Simultaneous Fem-Pop Intervention	Total Occlusions
100%	49.7mm (17-142mm)	1.83 (1-5)	2.5 – 4 mm	66% (45/67)	45% (38/84)

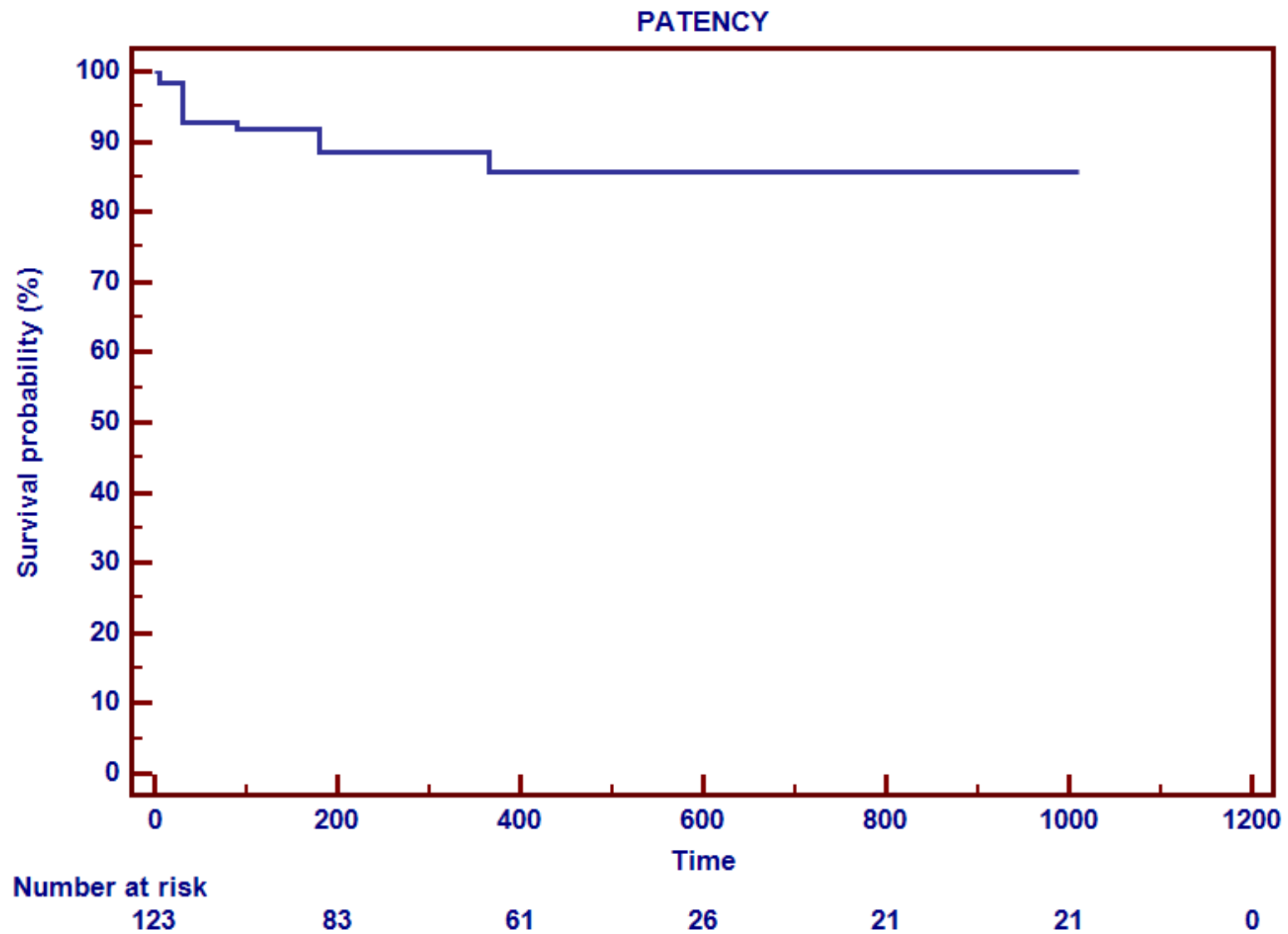


Follow-up

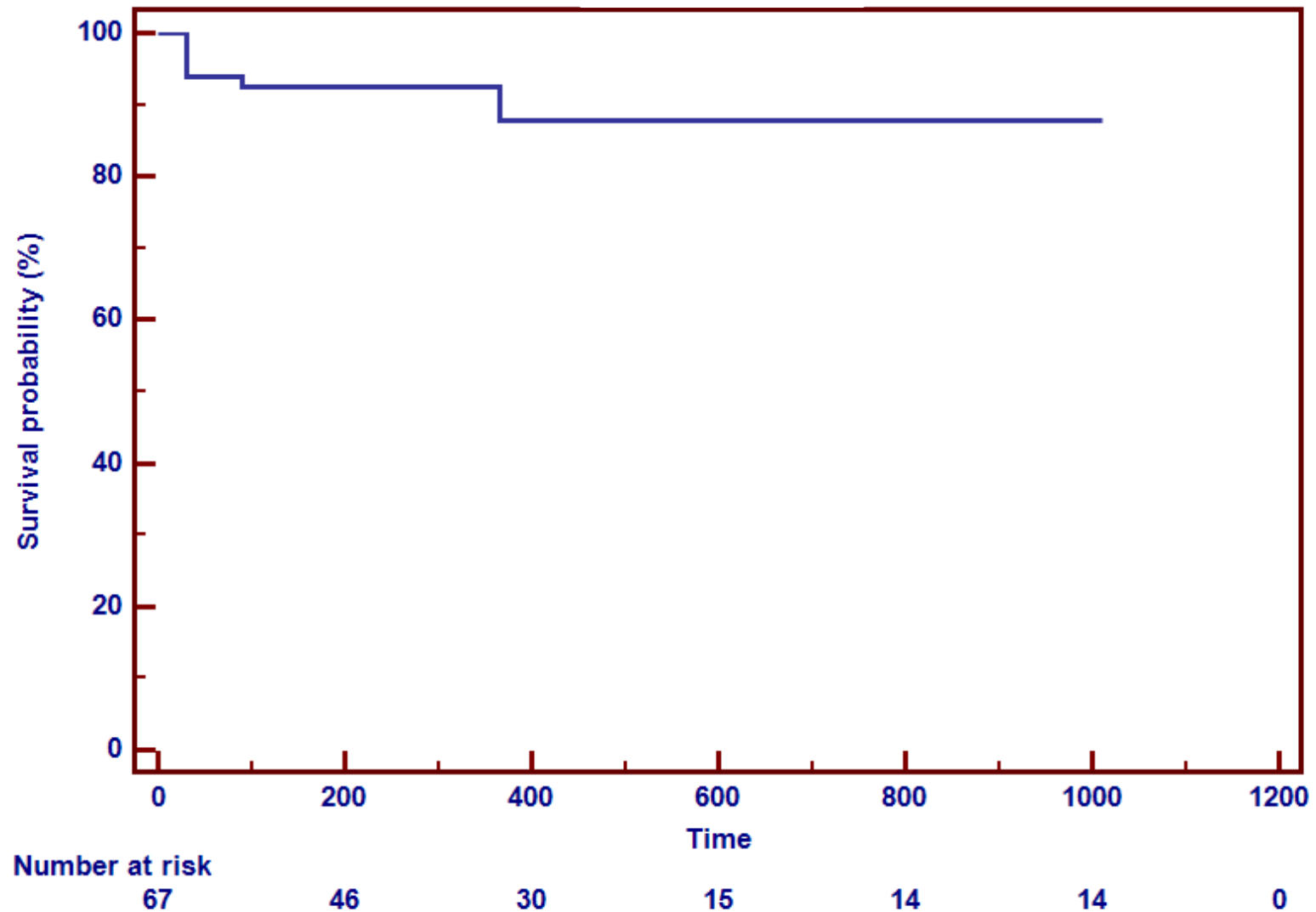
- Mean follow up was 20 months (1-42 months)
- Primary patency at 6 months was 90/100 stents **(90%)**
- Primary patency at 12 months was 76/88 **(86%)**
- Primary patency at 24 months was 32/45 **(72%)**
- Freedom from major amputation was **91.1%** (61/67) for the entire cohort
 - **100%** (56/56) for patients with Rutherford 4 and 5 disease.
- 30 day mortality rate was 1.4% (1/67)
- Overall mortality rate was 19.0% (13/67)



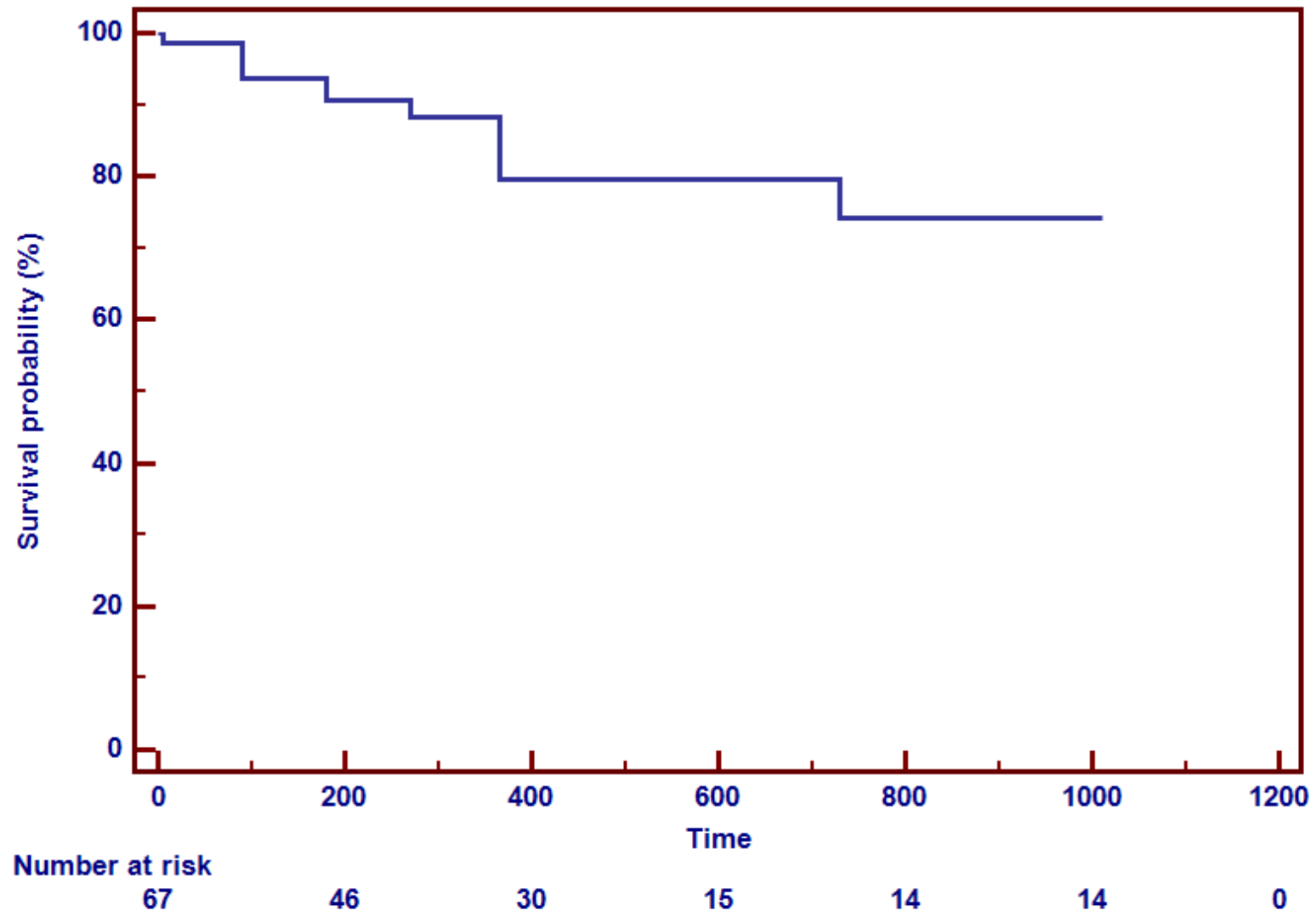
Primary Patency



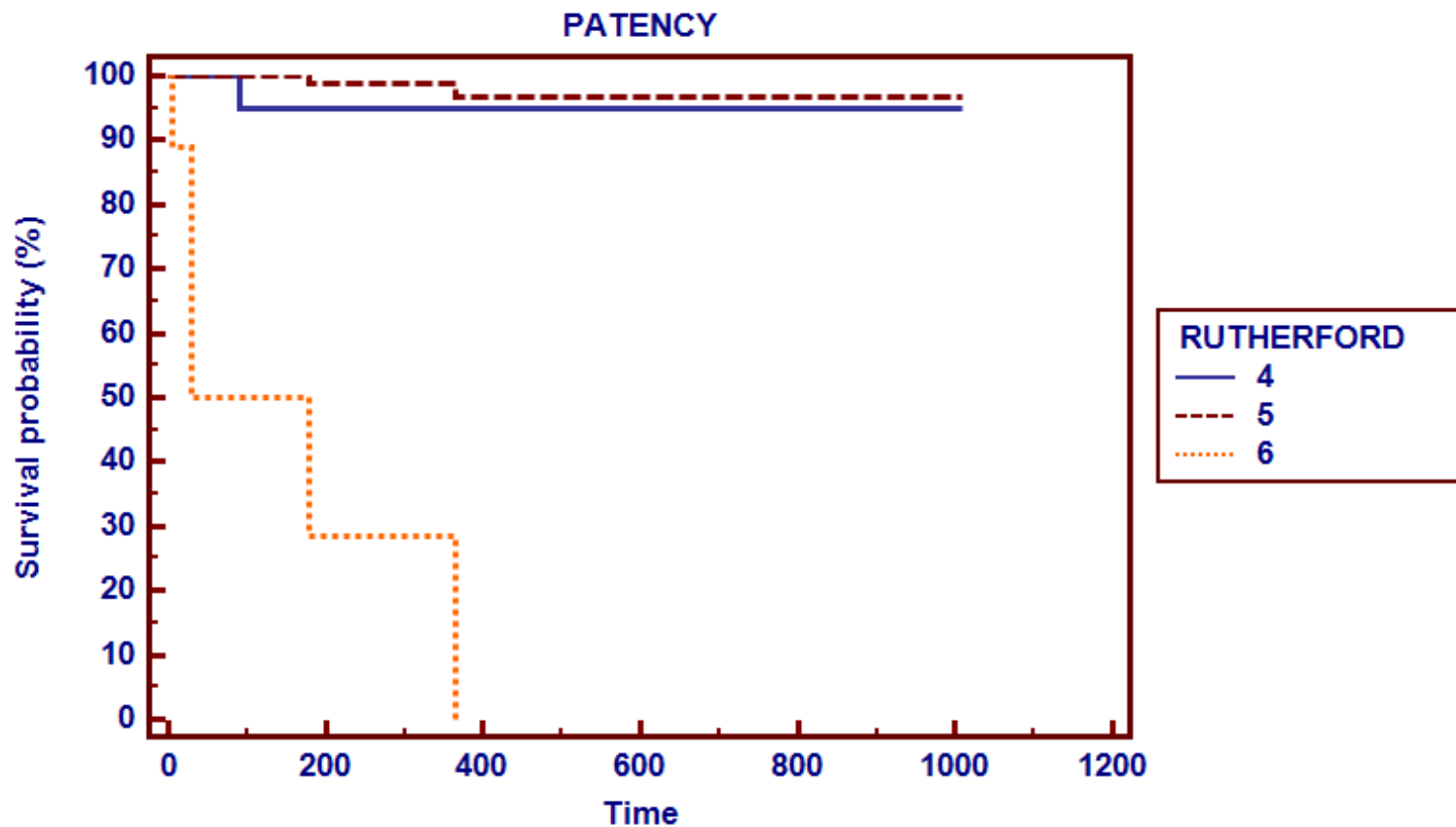
Freedom from Major Amputation



Survival



Primary Patency



Number at risk

Group: 4

20	19	13	5	5	5	0
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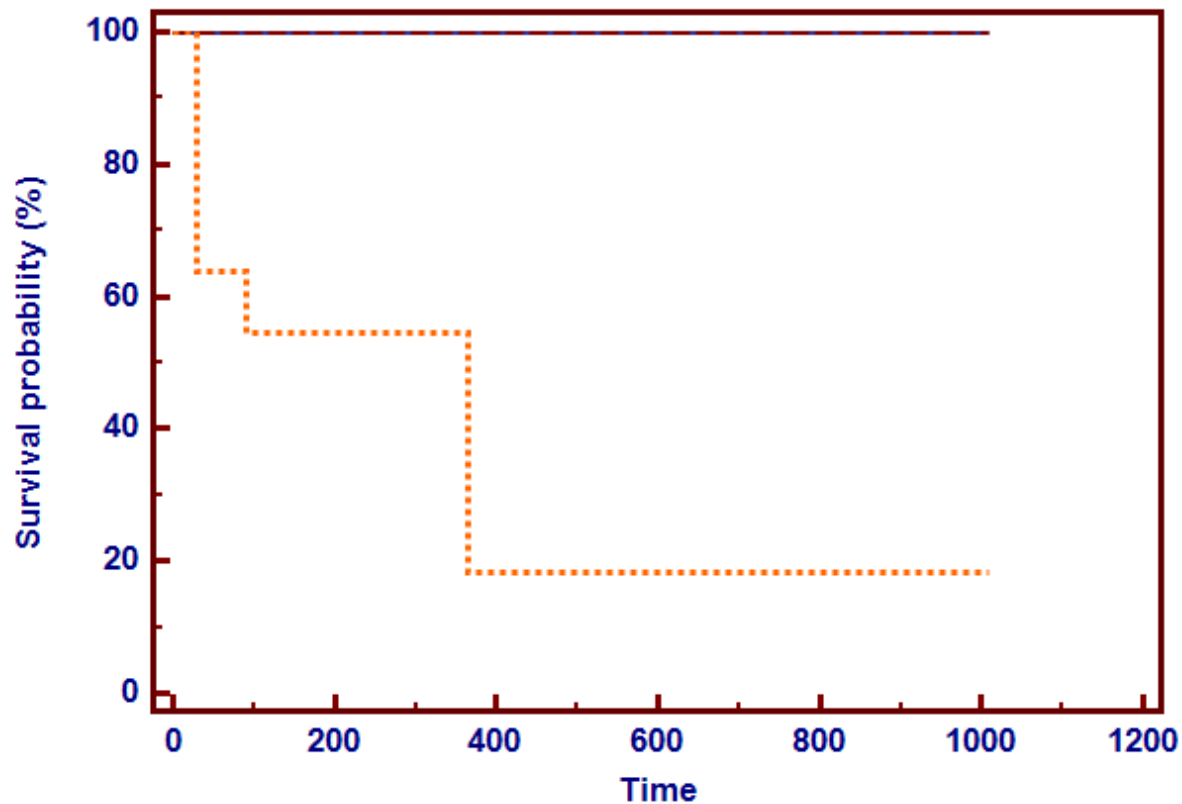
Group: 5

85	63	48	21	16	16	0
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Group: 6

18	1	0	0	0	0	0
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Freedom from Major Amputation



Number at risk

Group: 4

13	12	7	4	4	4	0
----	----	---	---	---	---	---

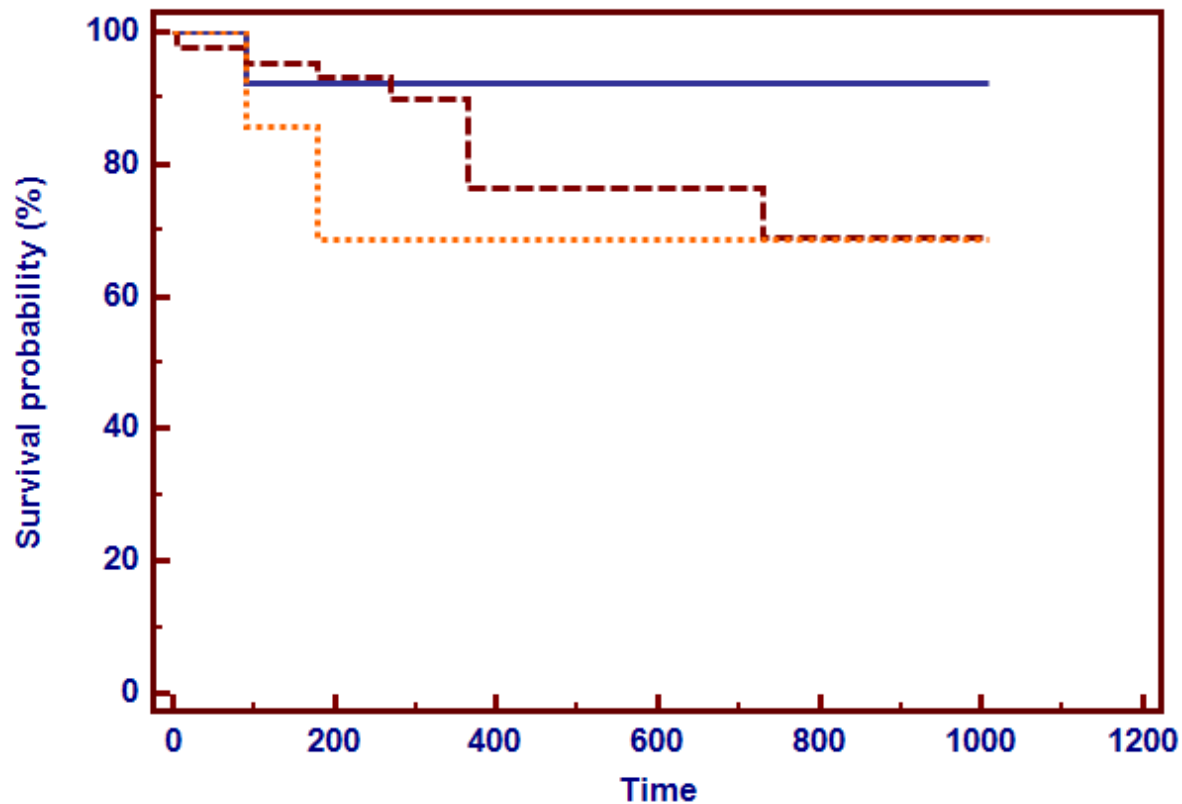
Group: 5

43	31	22	10	9	9	0
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Group: 6

11	3	1	1	1	1	0
----	---	---	---	---	---	---

Survival



Number at risk

Group: 4

13	12	7	4	4	4	0
----	----	---	---	---	---	---

Group: 5

43	31	22	10	9	9	0
----	----	----	----	---	---	---

Group: 6

11	3	1	1	1	1	0
----	---	---	---	---	---	---

CASE

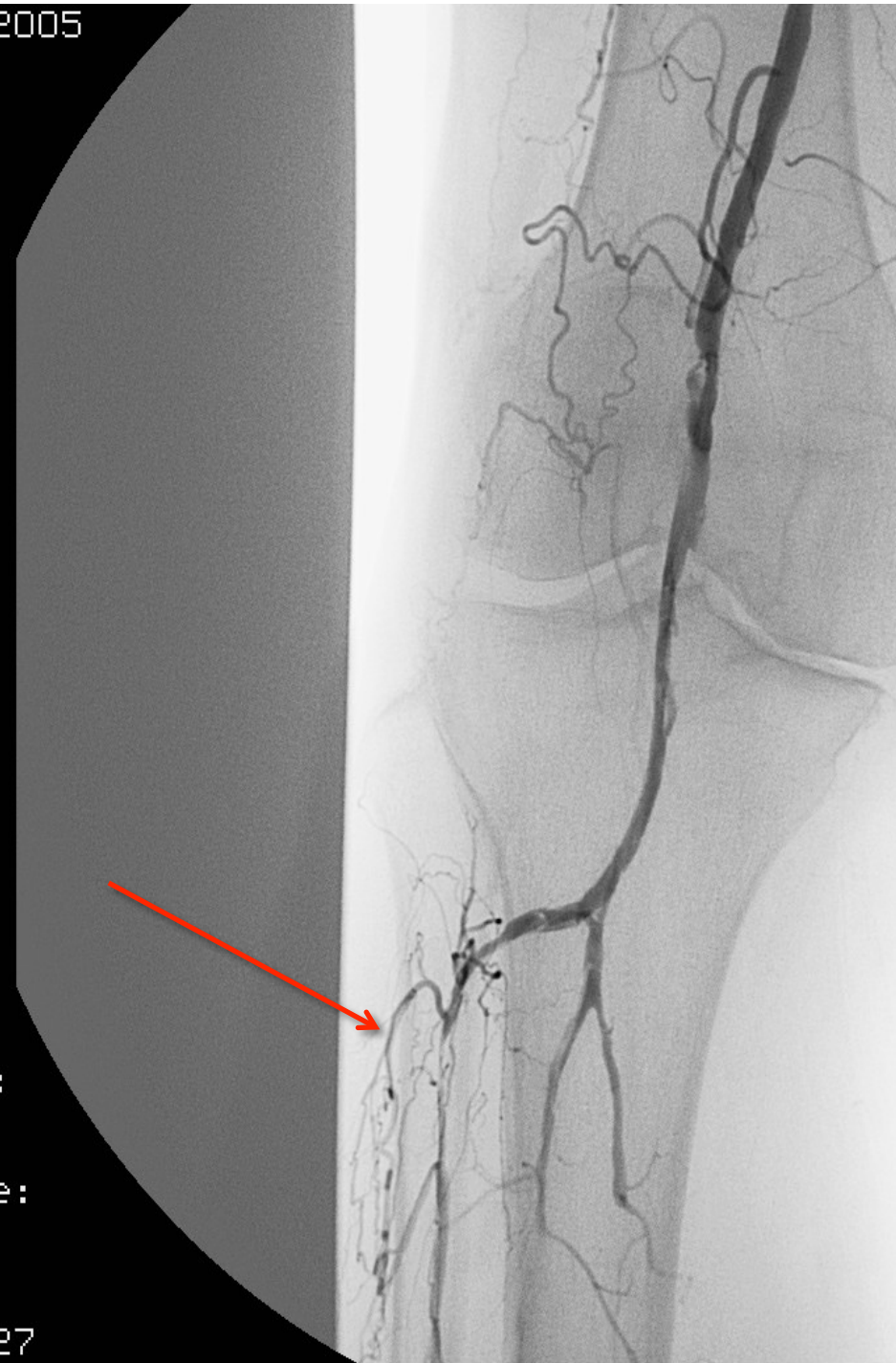
- 77 yr old female hypertension, coronary artery disease, renal insufficiency with great toe ulcer



06-29-2005

CASE

Following balloon angioplasty of the
popliteal and anterior tibial artery



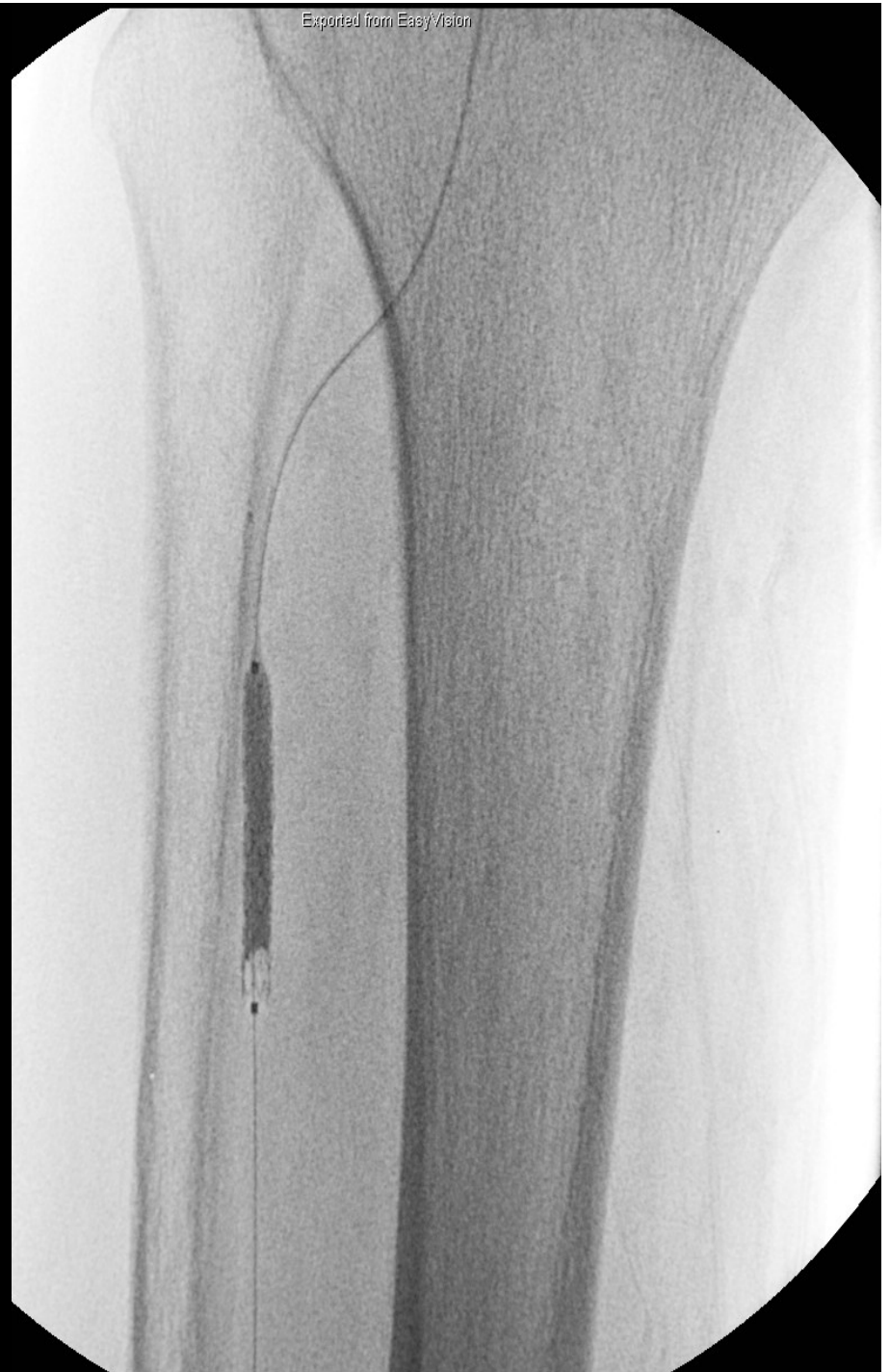
T-mask:
1.00

T-image:
7.00

T-run:
13:00:27

CASE

- Following placement of a 3.5mm X 33mm CYPHER stent



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