Trends in Endovascular Procedures for the Lower Extremity

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Conflicts of Interest

- **Consultant**
  - Cordis Endovascular (Modest)
  - Boston Scientific (Modest)
  - Pathway Medical (Modest)
  - Paragon IP (Modest)
  - Proteon Therapeutics (Modest)
  - X-Tent, Inc (Modest)
  - Harvard Clinical Research Institute (Modest)
  - Bacchus Vascular, Inc (Modest)
- **Equity**
  - Access Closure, Inc (Modest)
  - Square One, Inc (Modest)
  - Vascular Therapies, Inc (Modest)
  - Icon Interventional, Inc (Modest)
  - Setagon (Modest)
- **Speaker's Bureau**
  - Bristol-Myers/Sanofi-Aventis Pharmaceuticals Partnership (Modest)
- **Research Support**
  - Pfizer, Inc.
  - Abbott Vascular
  - Genzyme
  - ActivBiotics

April, 2007

Published November 2005!

ACC/AHA Guidelines for the Management of Patients With Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic)

http://www.acc.org/clinical/guidelines/pad/index.pdf

PAD Guidelines: Therapy of PAD

- Supervised Exercise Training (A)
- Tobacco Cessation (B)
- Control of Hypertension (A)
- Control of Hyperlipidemia (B)
- Glycemic Control (B)
- Antiplatelet Therapy (A)
  - ASA (A)
  - Clopidogrel (B)
- Cilostazol 100 mg po BID (A)

http://www.acc.org/clinical/guidelines/pad/index.pdf

PAD Guidelines: Surgical Intervention

Table 24. Vascular Surgical Procedures for Outflow Improvement

Outflow Procedure	Operative Mortality (%)	Expected Patency Rate (%)
Fem-AK popliteal vein	1.3 to 6.3	66 (5 years)
Fem-AK popliteal prosthetic	1.3 to 6.3	47 (5 years)
Fem-BK popliteal vein	1.3 to 6.3	66 (5 years)
Fem-BK popliteal prosthetic	1.3 to 6.3	33 (5 years)
Fem-Tib vein	1.3 to 6.3	74 to 80 (5 years)
Fem-Tib prosthetic	1.3 to 6.3	25 (3 years)
Composite sequential bypass	0 to 4	28 to 40 (5 years)
Fem-Tib blind segment bypass	2.7 to 3.2	64 to 67 (2 years)
Profundaplasty	0 to 3	49 to 50 (3 years)

http://www.acc.org/clinical/guidelines/index.pdf

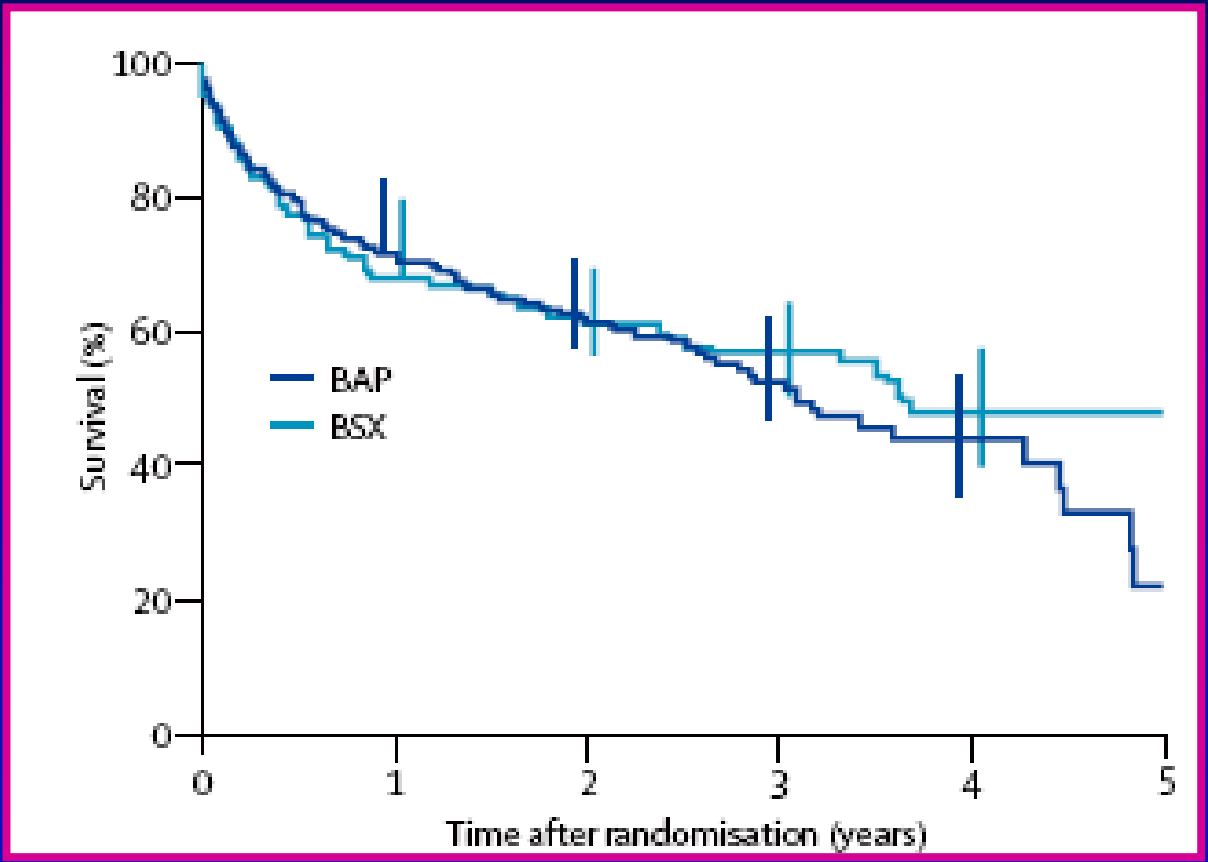
Surgical Morbidity/Mortality

Parameter	*Short term (first year)*	*Long term (3–5 years)*
Mean time to pedal wound healing	15–20 weeks	–
Incisional wound complications*	15%–25%	–
Persistent severe ipsilateral lymphedema§	10%–20%	Unknown
Graft stenosis**	20%	20%–30%
Graft occlusion	10%–20%	20%–40%
Graft surveillance studies	100%	100%
Major amputation	5%–10%	10%–20%
Ischemic neuropathy	Unknown	Unknown
Graft infection†	1%–3%	–
Perioperative death (primarily cardiovascular)	1%–2%	–
All death (primarily cardiovascular)	10%	30%–50%

TASC 2. J Vasc Surg 2007

The BASIL Trial

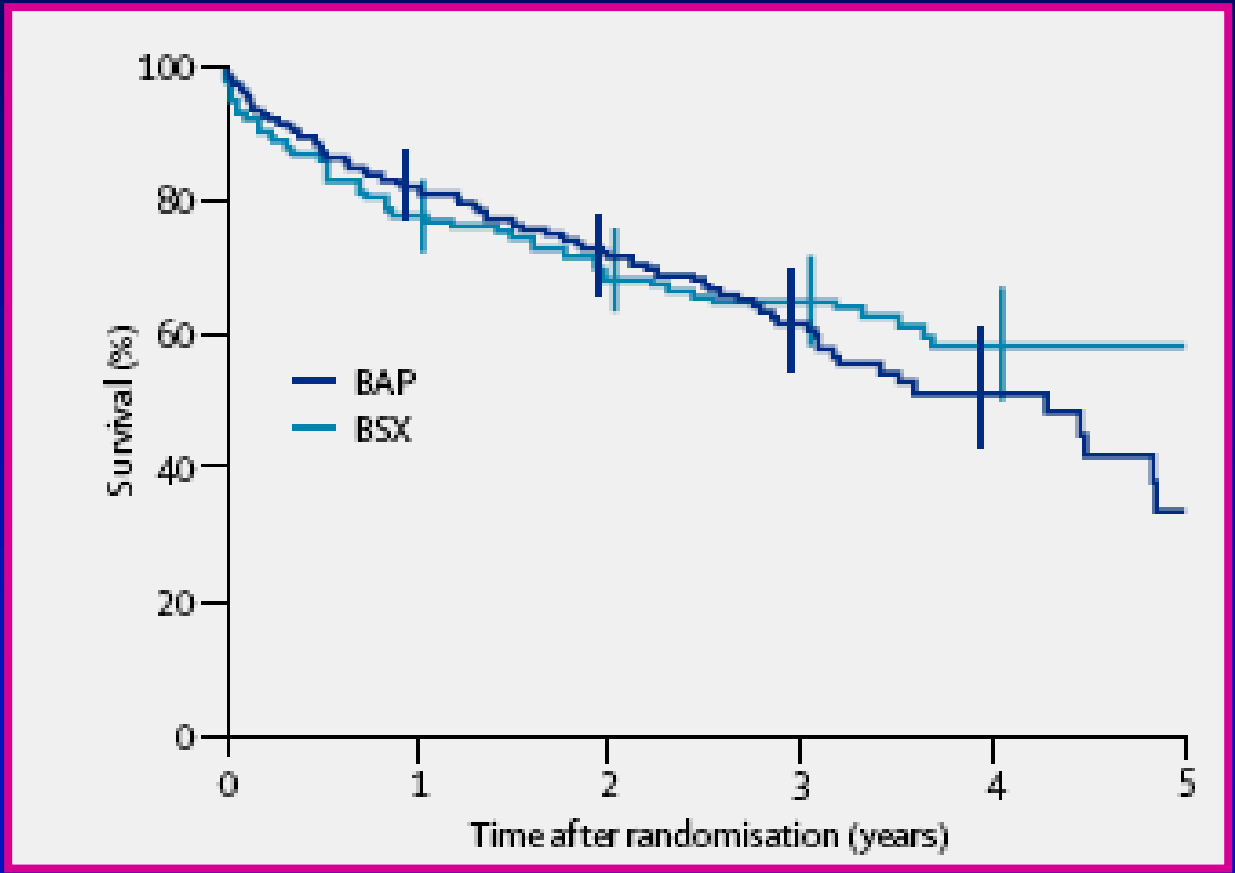
Amputation-Free Survival of Index Limb



Lancet 2005;366:1925-1934

The BASIL Trial

All-Cause Mortality



Lancet 2005;366:1925-1934

TASC 2 Classification of Infrainguinal PAD

Type A lesions	■ Single stenosis ≤10 cm in length ■ Single occlusion ≤5 cm in length
Type B lesions	■ Multiple lesions (stenoses or occlusions), each ≤5 cm ■ Single stenosis or occlusion ≤15 cm not involving the infra geniculate popliteal artery ■ Single or multiple lesions in the absence of continuous tibial vessels to improve inflow for a distal bypass ■ Heavily calcified occlusion ≤5 cm in length ■ Single popliteal stenosis
Type C lesions	■ Multiple stenoses or occlusions totaling >15 cm with or without heavy calcification ■ Recurrent stenoses or occlusions that need treatment after two endovascular interventions
Type D lesions	■ Chronic total occlusions of CFA or SFA (>20 cm, involving the popliteal artery) ■ Chronic total occlusion of popliteal artery and proximal trifurcation vessels

TASC 2. J Vasc Surg 2007.

PAD Guidelines: Endovascular Therapy?

- Vocational or lifestyle disabling symptoms
- Failed exercise/pharmacotherapy
- Risk:benefit ratio favorable
  - Focal CIA stenosis

PAD Guidelines:
Stents, Atherectomy, Thermal Devices, Laser

- Infrainguinal Arteries: only as "salvage therapy" after failed PTA
  - Persistent gradient
  - Residual >50% stenosis
  - Flow-limiting dissection
- "Primary stent placement is not recommended in the femoral, popliteal, tibial arteries"

Current PTA Results

	Restenosis Rate (9mo)
• ≤ 7 cm	
▪ Intracoil cntrl (3.3cm)	34%
▪ Paris cntrl (5.6cm)	28%
• ≥ 7cm	
▪ Vienna cntrl (8.3cm)	64%
▪ PELA cntrl (20.2cm)	85%

Cryoplasty

Cryoplasty for the Treatment of Femoropopliteal Arterial Disease: Results of a Prospective, Multicenter Registry

Baseline Lesion Characteristics (N = 102)

Characteristic	Value
Target lesion location (%)	
Superficial femoral artery	84.3
Popliteal artery	13.7
Combined	2.0
Angiographic measurements	
Reference vessel diameter (mm)	5.5 ± 0.5
Diameter stenosis (%)	87 ± 10
Total occlusions (%)	14.7
Lesion length (cm)	4.7 ± 2.6
Runoff vessels	1.7 ± 0.4
TASC Distribution (%)	
A (n = 35)	34.3
B (n = 26)	25.5
C (n = 41)	40.2

JVIR 2005;16:1067-73

Cryoplasty for the Treatment of Femoropopliteal Arterial Disease: Results of a Prospective, Multicenter Registry

Acute and Midterm Cryoplasty Results

Outcome	Value (%)
Procedural success	94.1
Technical success	85.3
Dissection rate	6.9
Bail-out stent rate	8.8
Residual diameter stenosis	11 ± 11*
Target lesion revascularization	17.8
TASC A (n = 35)	11.4
TASC B (n = 26)	15.4
TASC C (n = 41)	19.5
9-Month clinical patency	82.2
9-Month primary patency	70.1

* $P < .05$ versus baseline.

JVIR 2005;16:1067-73

Directional Atherectomy

- Potential Appeal
  - No stent required in most
    - Flexion Points
    - Long SFA Lesions
    - CLI (infrapopliteal disease)
  - Excellent immediate post-angiographic appearance
  - Many vocal enthusiasts

The TALON Registry

- 220 consecutive patients undergoing directional atherectomy with SilverHawk catheter
  - 73% above knee interventions
    - 47% SFA
  - 66% with moderate-severe calcification
  - No adjuvant intervention in 74% of lesions
- *No reported cases of emboli*

Presented at the Society for Vascular Surgery Annual Scientific Session, 2005

Silverhawk Data

- N = 52
- No total occlusions or dense calcification
- Mean lesion length 4.8 cm
- 20% for instent restenosis

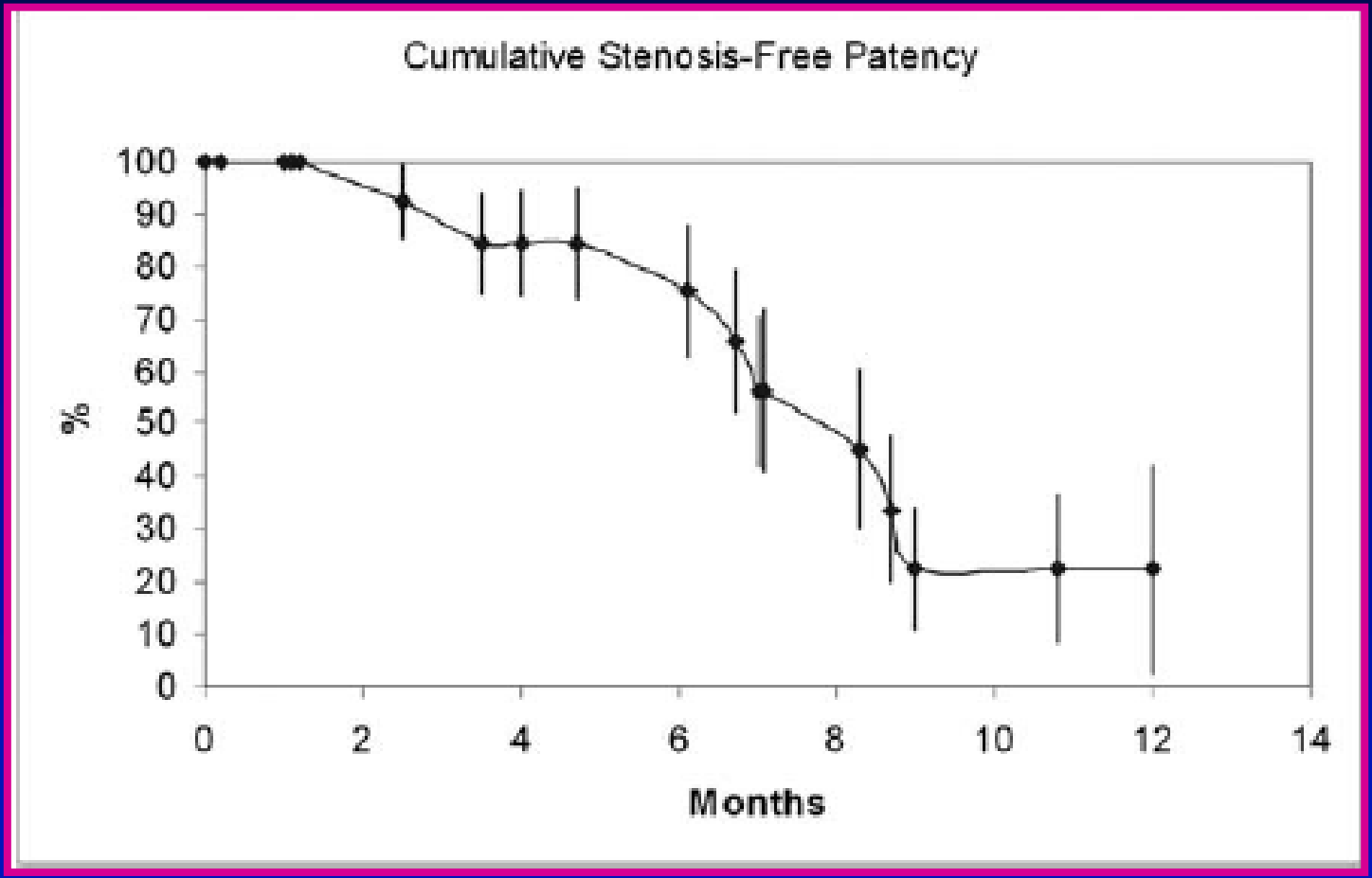
Zeller et al. J Endovasc Ther 2004;11:676-685

Silverhawk Data

- 6 month follow-up data
- Restenosis 27 – 41% by duplex ultrasound
- ABI data
  - Pre 0.62
  - Post 0.84
  - 6 mo 0.72
- Clinical patency 80%

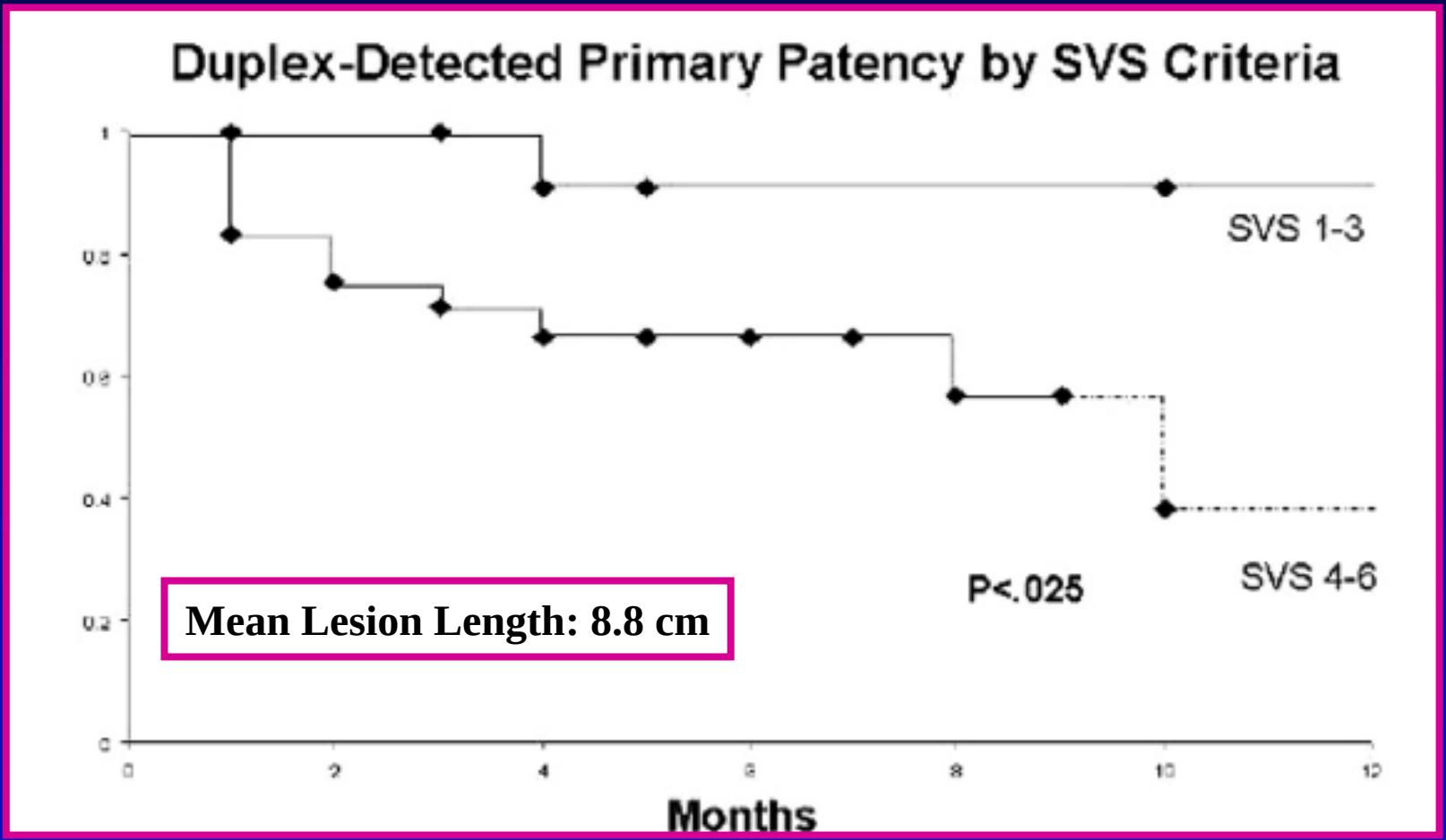
Zeller et al. J Endovasc ther 2004;11:676-685

Results of Femoropopliteal Atherectomy for TASC C Lesions



J Vasc Surg 2006;44:503-9

Outcomes of Atherectomy in 66 Limbs



Mean Lesion Length: 8.8 cm

J Vasc Surg 2007;45:25-31

Are There Risks with Atherectomy?

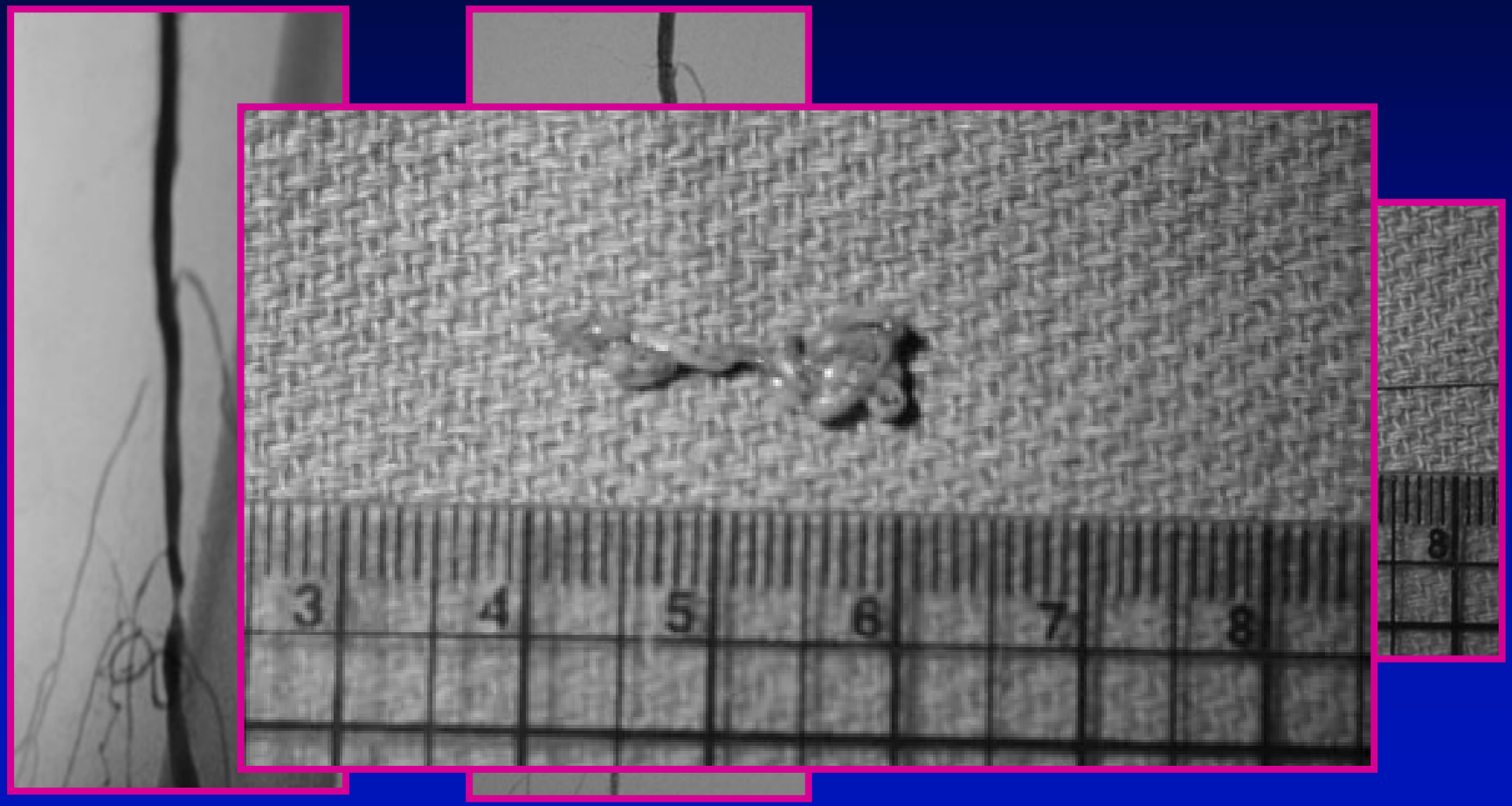
Distal Embolic Protection During Femoropopliteal Atherectomy

Rajeev Suri,[1] MD, Michael H. Wholey,[1] MD, Darren Postoak,[1] MD, Ryan T. Hagino,[2] MD, and Boulos Toursarkissian,[2*] MD

- 10 consecutive cases of directional atherectomy in SFA/popliteal arteries
- All cases used distal embolic protection

Cath Cardiovasc Intervent 2006;67:417-422

Embolic Protection in Atherectomy

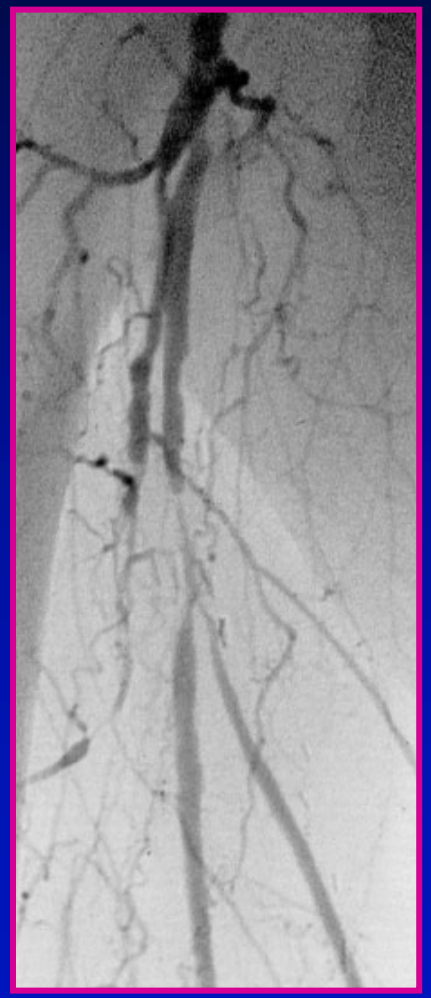


Pre-DA **Post-DA**

Cath Cardiovasc Intervent 2006;67:417-422

Embolic Protection in Atherectomy

- Macroscopic debris found in all filters
- No adverse clinical sequelae

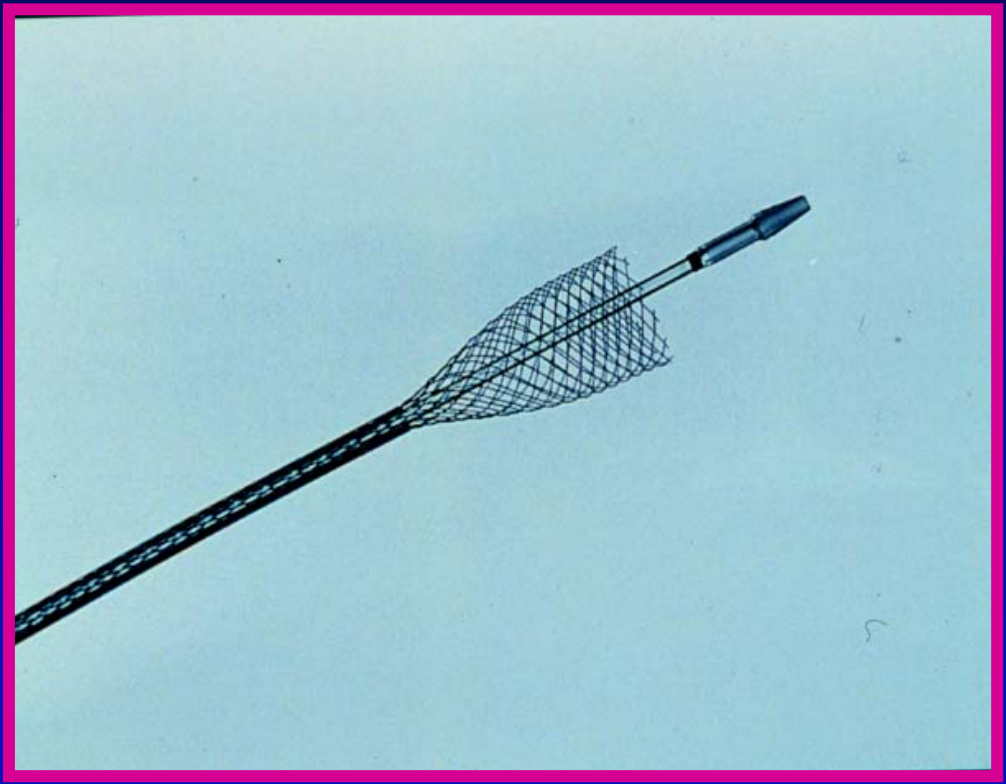


Pre-DA

DA

Cath Cardiovasc Intervent 2006;67:417-422

What About Stents?



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 4, 2006 VOL. 354 NO. 18

Balloon Angioplasty versus Implantation of Nitinol Stents in the Superficial Femoral Artery

Stent vs PTA in SFA Disease

- 104 patients with Rutherford 3-5 PAD
- SFA stenosis/occlusion >3 cm
- Primary Endpoint
  - Binary Restenosis >50% at 6-months as determined by CTA or DSA
- Secondary Endpoints
  - DUS-derived restenosis >50% at 3, 6, 12 months or finding of stent fracture
  - Clinical: Deterioration in Rutherford Class, amputation, death at 12-months
  - Hemodynamic: Resting ABI

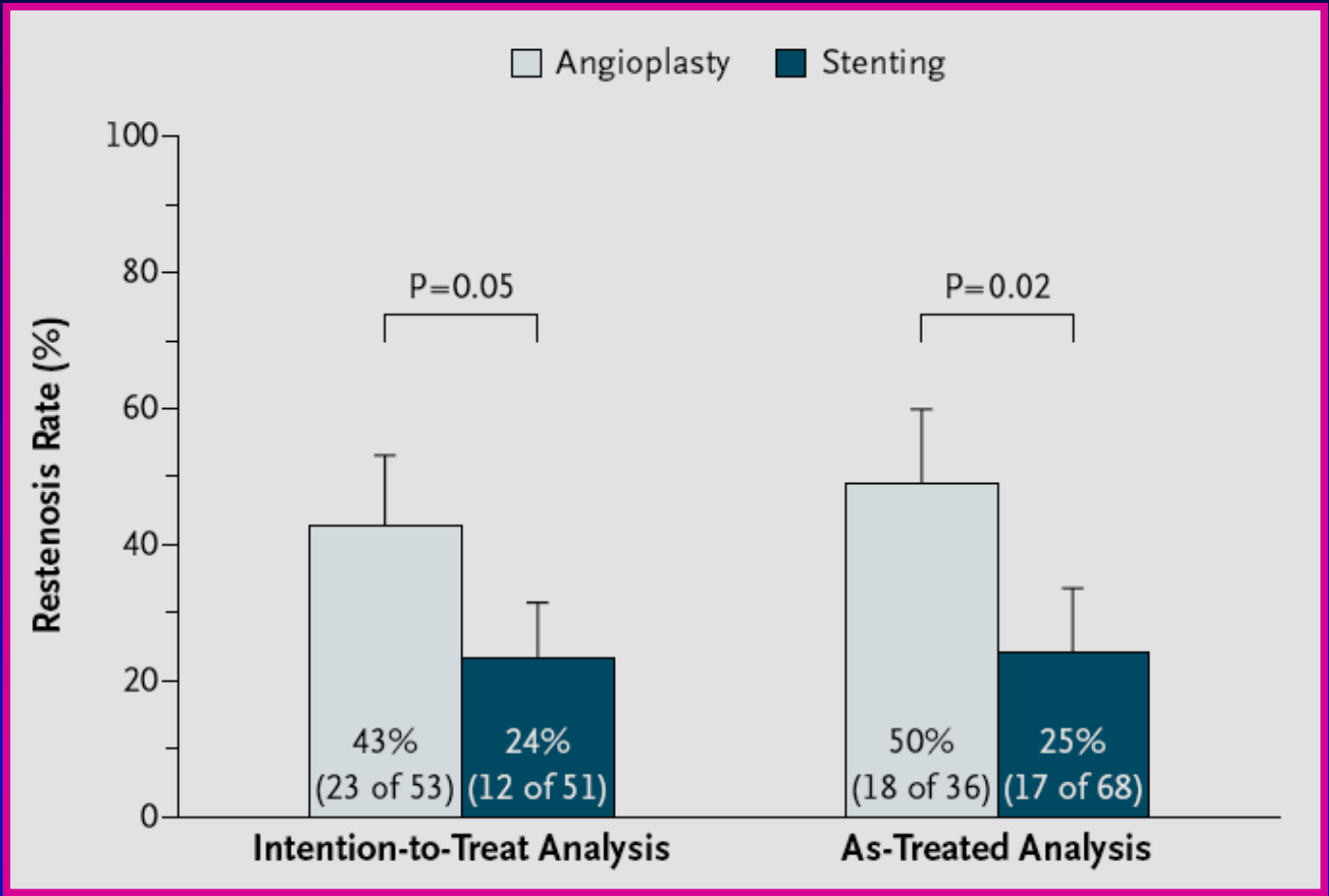
N Engl J Med 2006;354:1879-88

Stent vs PTA in SFA Disease

Rutherford stage of peripheral-artery disease — no. (%)‡	Stent (N=51)	PTA (N=53)
3	45 (88)	46 (87)
4	1 (2)	2 (4)
5	5 (10)	5 (9)
Treated side — no.		
Left	25	26
Right	26	27
Maximal distance walked on a treadmill — m§		
Median	92	87
Interquartile range	45–113	44–118
Baseline ankle–brachial index	0.57±0.19	0.54±0.20

N Engl J Med 2006;354:1879-88

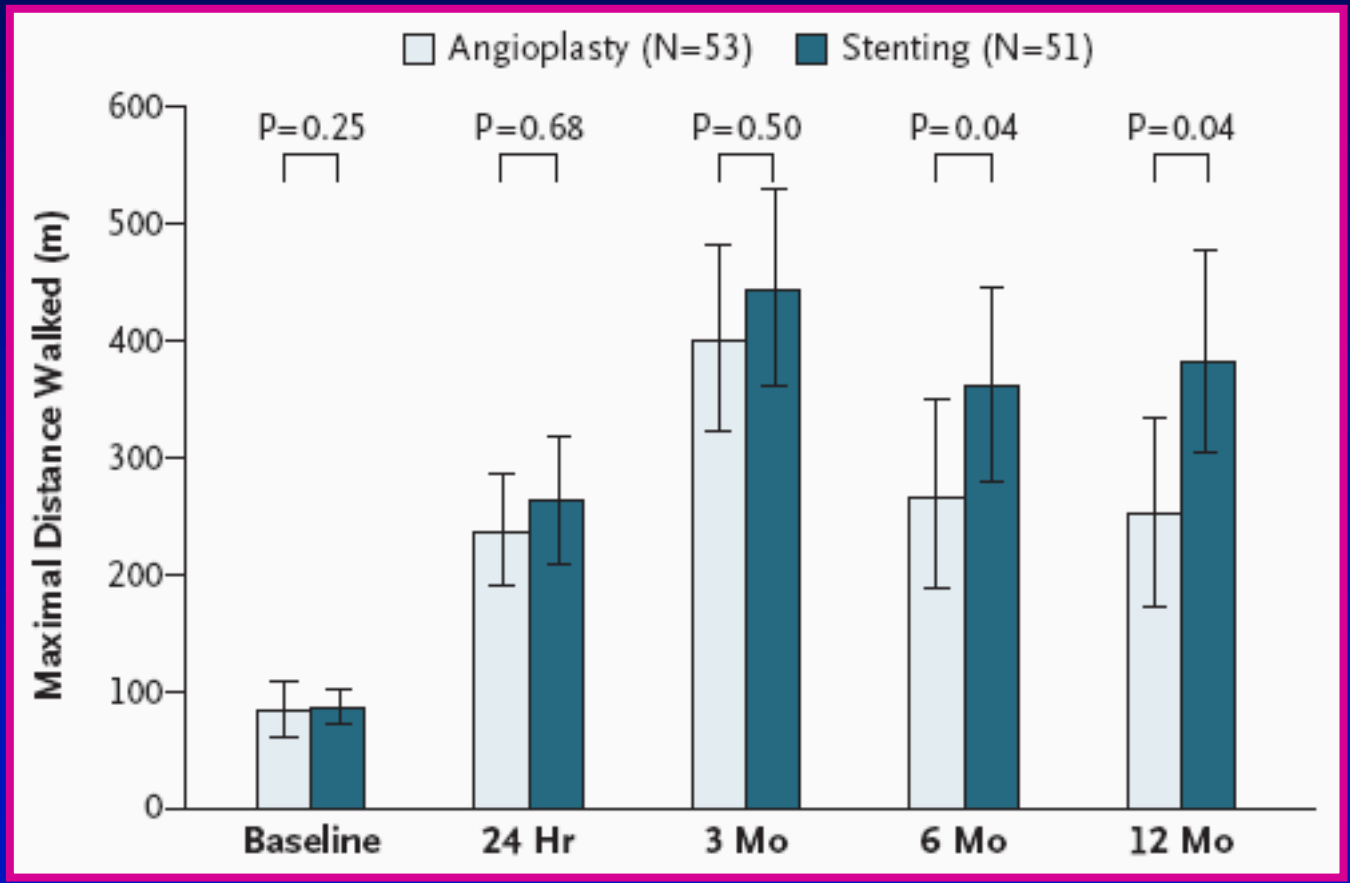
Stent vs PTA in SFA Disease



N Engl J Med 2006;354:1879-88

Stent vs PTA in SFA Disease

Treadmill-Measured Absolute Claudication Distance (m)



N Engl J Med 2006;354:1879-88

What About DES in the Infrainguinal Arteries? SIROCCO Strategy

- Design:
  - Double-blind, Randomized Prospective studies (sirolimus vs. bare stent) in patients with Superficial Femoral Artery (SFA) disease (>70%)
- Primary endpoints:
  - Stent mean diameter via quantitative angiography determined within six months after stent placement.

Phase I	Phase II
36 patients	57 patients
>70% stenosis	> 70% stenosis
>7 to <20 cm	> 7 to < 14.5 cm
or total occlusion >4 to <20 cm	or total occlusion > 4 to < 14.5 cm
max of 3 S.M.A.R.T.™ stents	max of 2 S.M.A.R.T.™ stents

Sirolimus-Eluting Stents for the Treatment of Obstructive Superficial Femoral Artery Disease

Six-Month Results

	DES (N=18)	BMS (N=18)	p
Restenosis rate, %			
In lesion	0	23.5 (n=4)	0.1026
In stent	0	17.6 (n=3)	0.2273

Circulation 2002;106:1505-1509

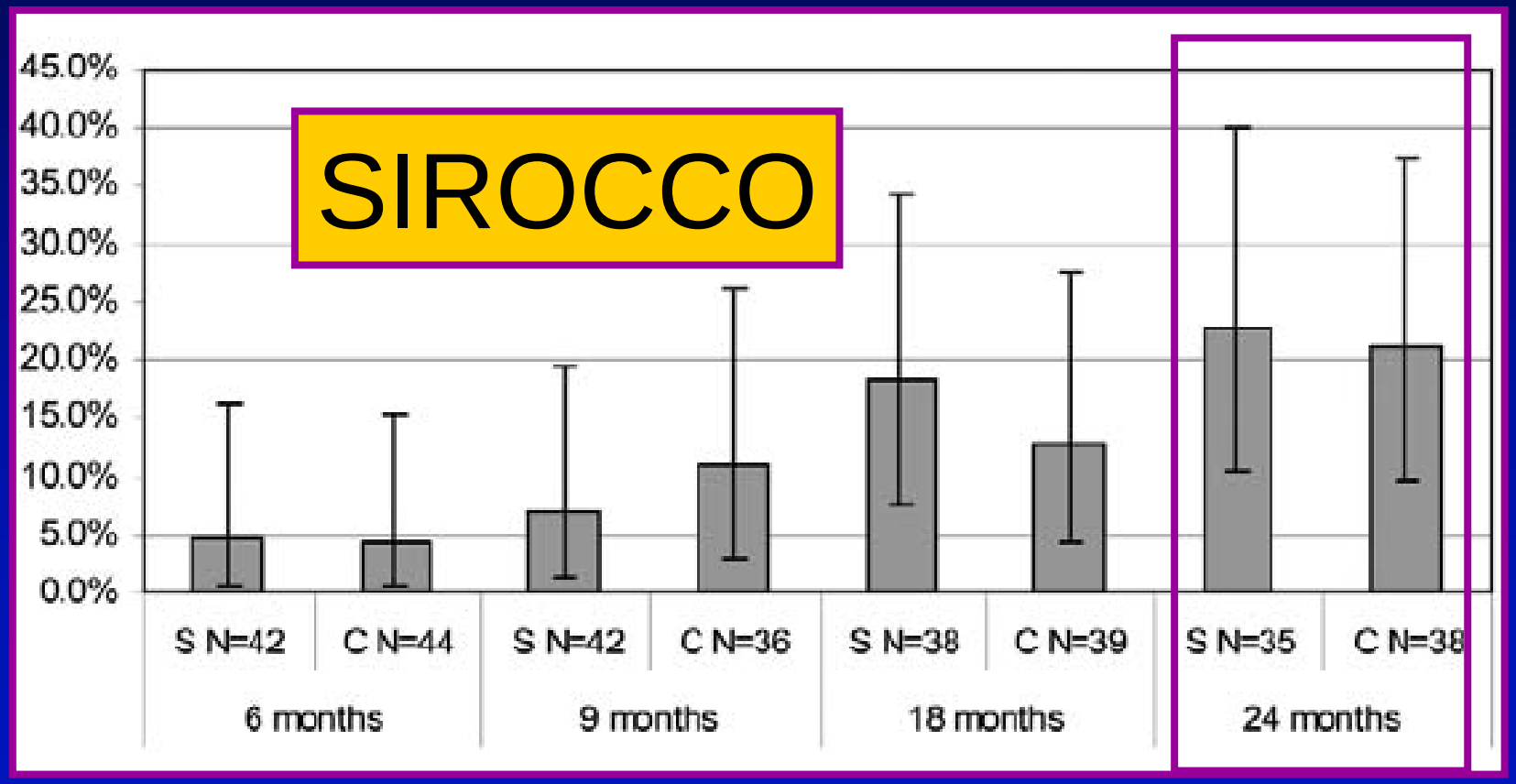
Sirolimus-Eluting versus Bare Nitinol Stent for Obstructive Superficial Femoral Artery Disease: The SIROCCO II Trial

In-Stent	DES (n=24)	BMS (n=26)	P-value
MLD (mm)	3.91 ± 0.72	3.62 ± 0.91	0.22
Mean Lumen Diameter (mm)	4.94 ± 0.69	4.76 ± 0.54	0.31
Late Loss (mm)	0.38 ± 0.64	0.68 ± 0.97	0.20
Binary Restenosis Rate (%)	0 (0%)	2 (7.7%)	0.49

J Vasc Interv Radiol 2005;16:331-338

Restenosis by Duplex Ultrasonography

J Endovasc Ther 2006;13:701-10



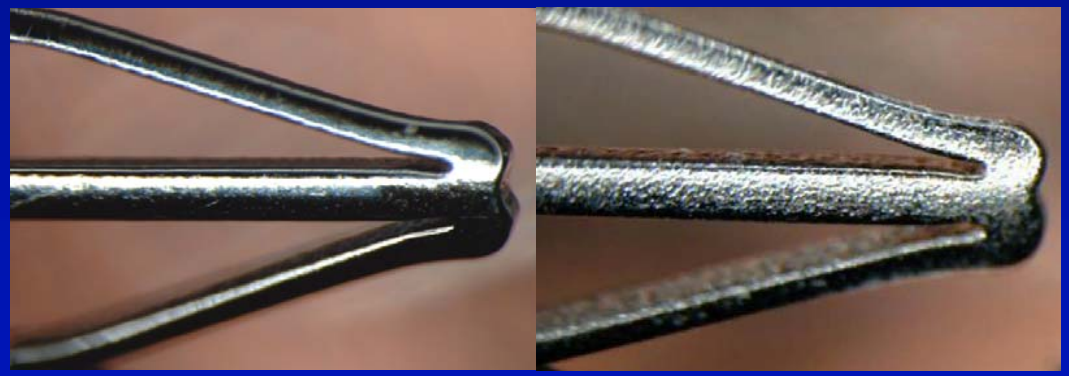
Zilver® PTX™ Clinical Trial

- First U.S. trial of DES in the SFA
- Sponsor: Cook® Incorporated
- Steering Committee:
  - Michael Dake, M.D., Study P.I.
  - Gary Ansel, M.D. Study Co-P.I.
  - Lindsay Machan, M.D.
  - Michael R. Jaff, D.O.
  - Richard Saxon, M.D.
  - H. Bob Smouse, M.D.

Zilver® PTX™ Coating

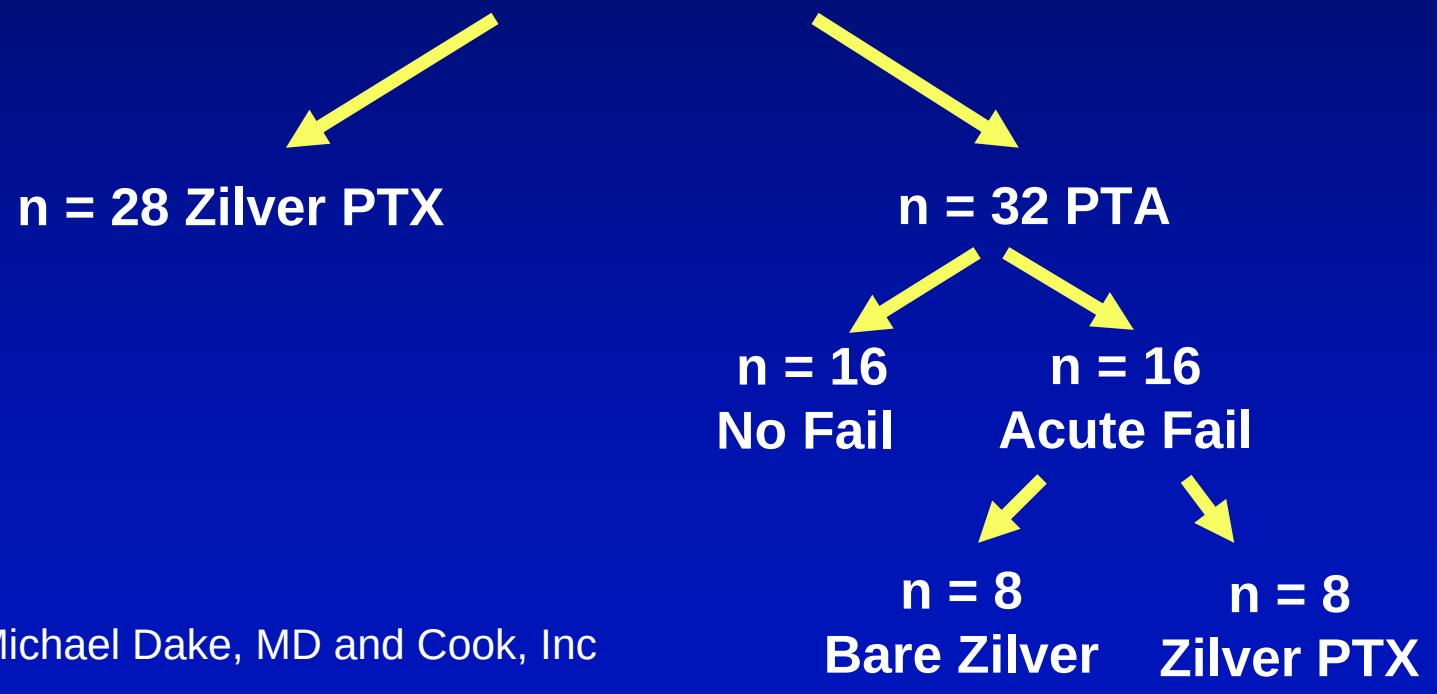
- Paclitaxel only (no polymer or binder)
- Thin coating (less than 5 µm)
- 3 µg/mm^2 dose density

  (maximum 880 µg total dose, largest stent)



Enrollment

- Phase 1: 60 patients enrolled (U.S.)
  - Data available as of Nov. 30, 2006 (6-18 month follow-up range, 9 month mean)



Courtesy Michael Dake, MD and Cook, Inc

Patency

- Patency rates for patients experiencing acute PTA failure and subsequently receiving stents (9 mo mean f/u) were:
  - 75% for Bare Zilver ®
  - 100% for Zilver® PTX ™
- Primary patency rates were dependent on lesion length in the Control Group but *not* in the Treatment Group

Lesion Length (mm)	Primary Patency Rate	
	Control Group	**Treatment Group**
< 40 mm	64%	88%
> 40 mm	27%	92%

Courtesy Michael Dake, MD and Cook, Inc

RESILIENT Trial

A Randomized Study Comparing the Edwards Self-Expanding LifeStent vs. Angioplasty-alone In LEsions INvolving The SFA &/or Proximal Popliteal Artery

Courtesy of John Laird, MD

RESILIENT Trial Interim Results (Intent to Treat)
30-Day Results

Measure	PTA Patients	LifeStent Patients
Death, % (#)	0.0% (0)	0.0% (0)
Stroke, % (#)	0.0% (0)	0.0% (0)
Myocardial Infarction, % (#)	0.0% (0)	0.0% (0)
Significant Distal Embolization, %(#)	1.4% (1)	0.0% (0)
Emergent Surgical Revascularization, % (#)	0.0% (0)	0.0% (0)
Thrombosis, % (#)	0.0% (0)	0.0% (0)

Courtesy of John Laird, MD

RESILIENT Trial Interim Results (Intent to Treat)
6-Month Results

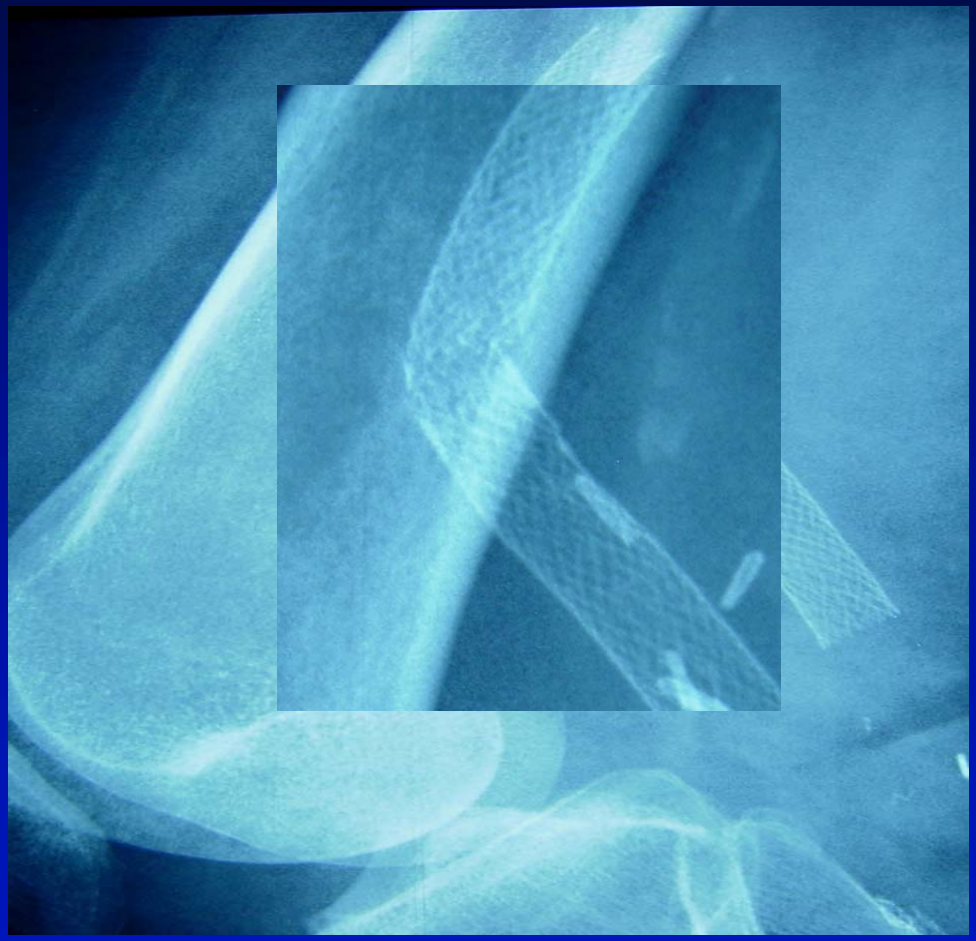
Measure	PTA Patients	LifeStent Patients
Target Limb ABI (mmHg), μ ± S.D. (#)	0.9 ± 0.2 (58)	0.9 ± 0.2 (102)
Clinical Success, % (#)	56.8% (42)	67.4% (89)
Primary Patency (duplex), % (#)	41.2%	89.7%
Freedom from Re-Intervention, %	56.5%	94.6%

Clinical Success: Sustained one Rutherford category improvemen from baseline.

Primary Patency: Duplex velocity increase greater than 2.5 over normal and no prior intervention

Courtesy of John Laird, MD

Stent Fractures and Mechanical Stress

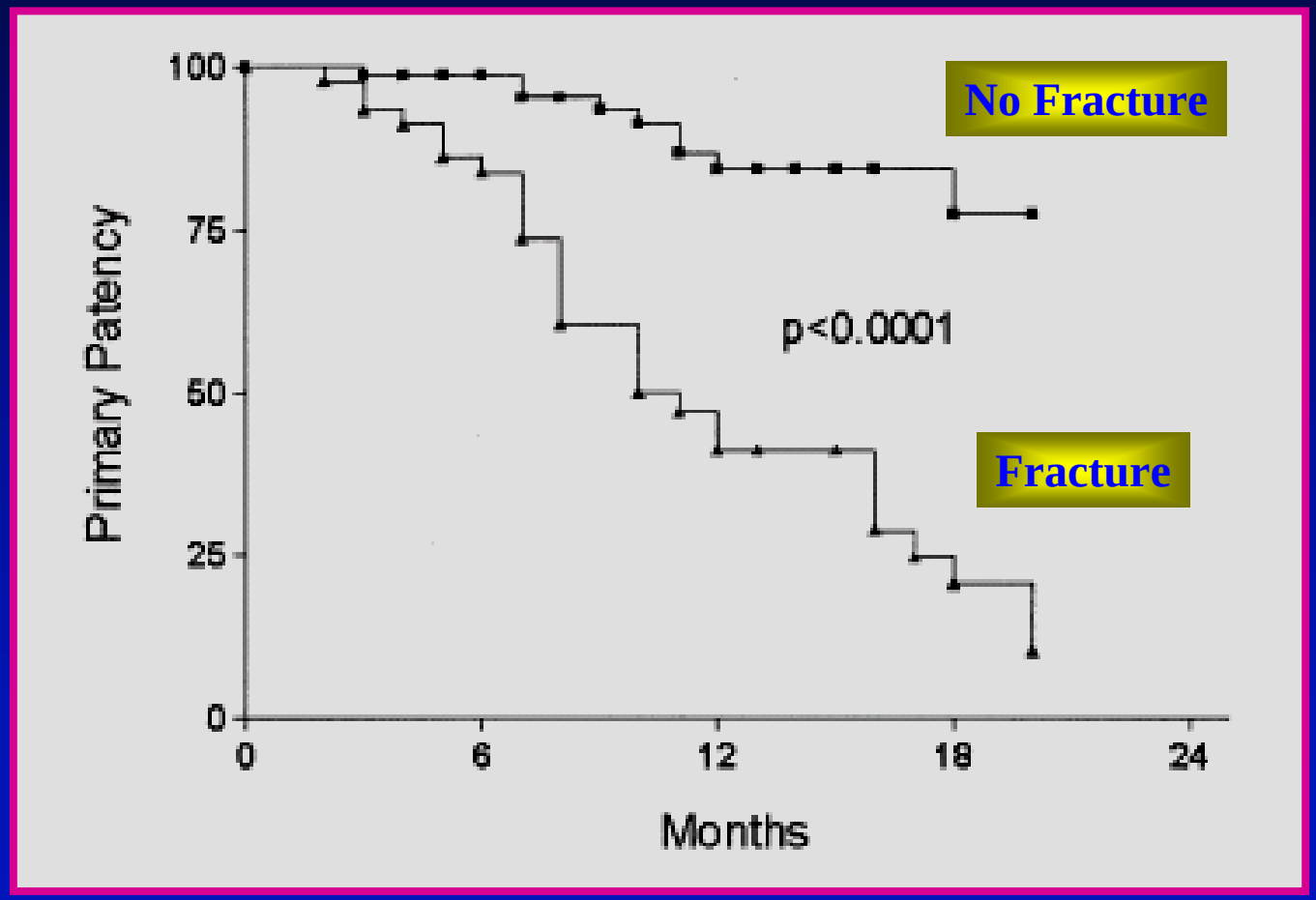


The Clinical Impact of Stent Fractures

- 93 patients/121 limbs underwent systematic investigation for stent fracture
- All stents were Nitinol
- Mean follow-up 10.7 months
- Mean length of treated segment: 15.7 cm
- 45/121 limbs with fracture (37.2%)
- 64/261 stents with fracture (24.5%)

J Am Coll Cardiol 2005; 45:312-5

The Clinical Impact of Stent Fractures



J Am Coll Cardiol 2005; 45:312-5

ABI, >50% Restenosis, and Fracture Rates

SIROCCO

	Sirolimus Stent	Bare Stent	p
ABI at 24 months	0.90±0.17/0.96 (n=35)	0.84±0.20/0.87 (n=37)	0.127*
Binary in-stent restenosis by DUS at 24 months	22.9% (8/35) 95% CI 10.4 to 40.1	21.1% (8/38) 95% CI 13.4 to 43.1	1.000†
Stent fracture rate up to 18 months by radiography	36% (9/25)	20% (8/40)	0.245†

J Endovasc Ther 2006;13:701-10

RESILIENT Trial Interim Results (Intent to Treat)
12-Month Results

Stent Fracture

Measure	12-months
No. of Stented Subjects	81
No. of Implanted Stents	136
No. of Fracture Stents	5*
Fracture Rate (per evaluable stents)	3.7%

*No clinical symptoms,
all treated vessels patent at last follow-up

Courtesy of John Laird, MD

Secondary Endpoints –

Stent Fractures

Fracture rate @ 6 mo (biplane X ray)

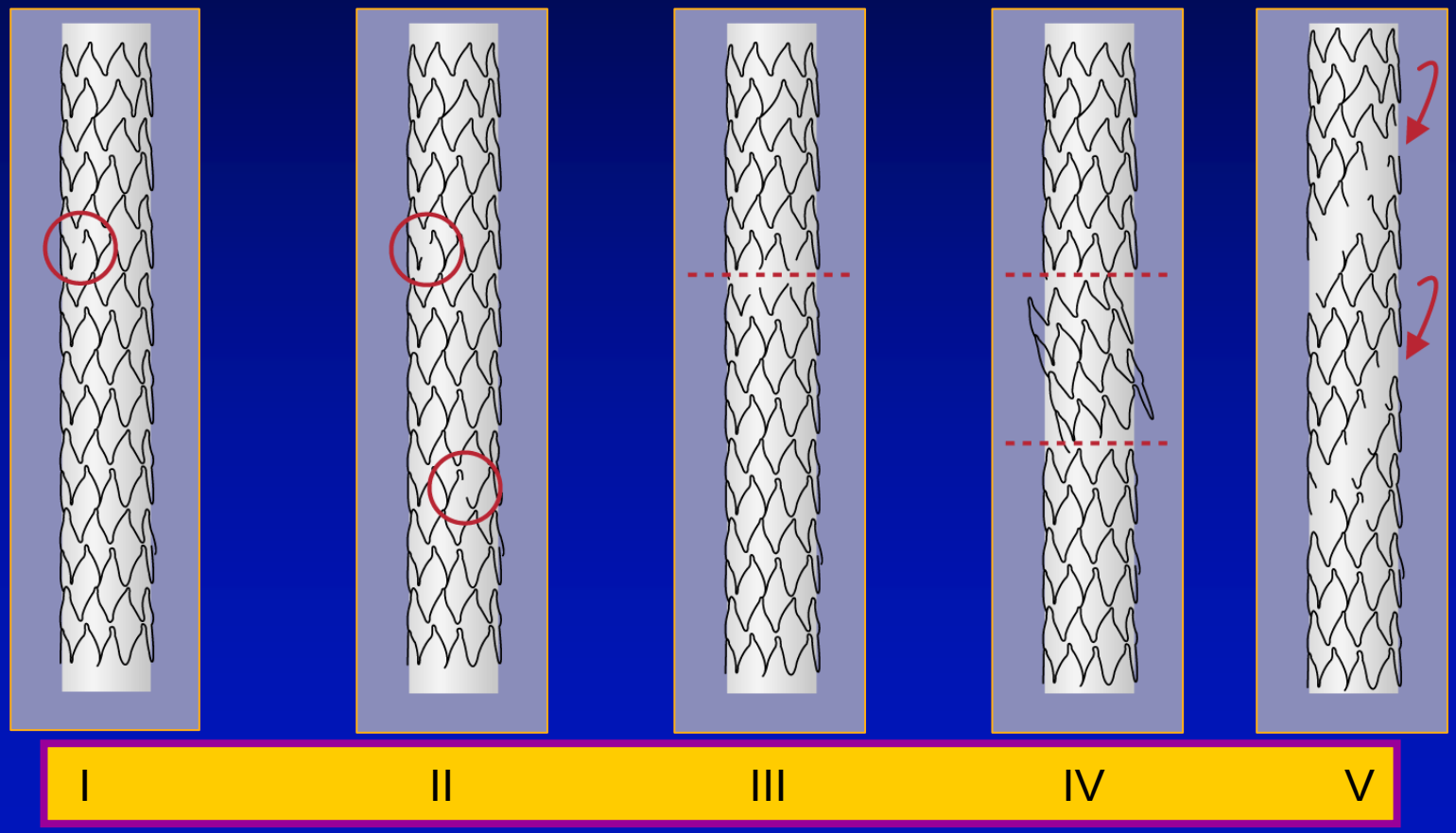
1 / 68 stented limbs	**1.5%**
1 / 115 stents	**0.9%**

Fracture rate @ 12 mo (biplane X ray)

1 / 66 stented limbs	**1.5%**
1 / 113 stents	**0.9%**

N Engl J Med 2006;354

Stent Fracture Classification



Rocha-Singh K, Jaff MR, Ansel G et.al. Accepted for publication, CCI, 2007

Patency of Nitinol Stents in Femoropopliteal Segment

- Emerging data suggests significant improvement in 9-12 month patency compared to PTA alone
  - ~80%
- Fracture rates are variable
  - Increased scrutiny
  - Surveillance required at 12 months
- Clinical impact of fracture remains uncertain

FDA Suggested Reading…

http://www.sri.com/psd/fracture/

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- Fracture Sciences
- Failure Analysis
- Aircraft Engine Fragment Barriers
- Finite Element Analysis
- Poulter Lab
- Material Research Lab
- Physical Sciences Division

Center for Fracture Physics

At SRI we have a passion for fracture physics. We love understanding how and why things break, and finding ways to keep them from breaking. (Or in cases like rock quarrying or frozen food grinding, how to break them more efficiently).

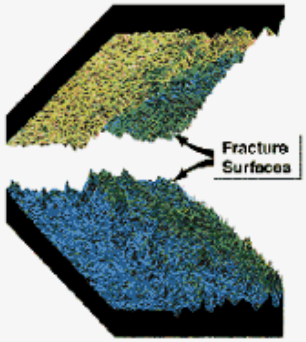
For example, we are advancing the state of practice in failure analysis by developing new methods to quantify and analyze fracture surface topography. These methods will allow the history of a crack to be reconstructed and the loading conditions to be retroactively determined.

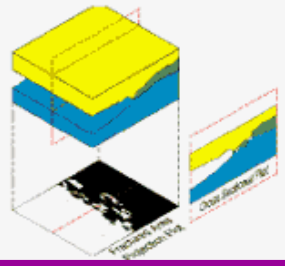
We are extending the lifetime of aging systems, such as aircraft, power plants, and electronics.

We are inventing ballistic fabrics like Zylon and designing protective structures for commercial aircraft against engine fragments— and police and soldiers against hostile fire.

And when a structure fails, we sleuth out the cause to ensure the failure doesn't happen again.

We are materials scientists, mechanical engineers, computational physicists, and corrosion experts combining our knowledge and experience to advance fracture science and solve failure problems.





Positive Trends in Endovascular Therapy for Infrainguinal PAD

- Increasing prospective data
- Improved technology
- Advancing combination strategies
  - DES
  - Atherectomy/Stent
- Emerging Options
  - Antirestenosis without stent
    - ie Drug coated balloon, drug alone
- Future clinical trials must be prospective, multicenter