SFA Stenting and the Promise of DES in the Peripheral Circulation

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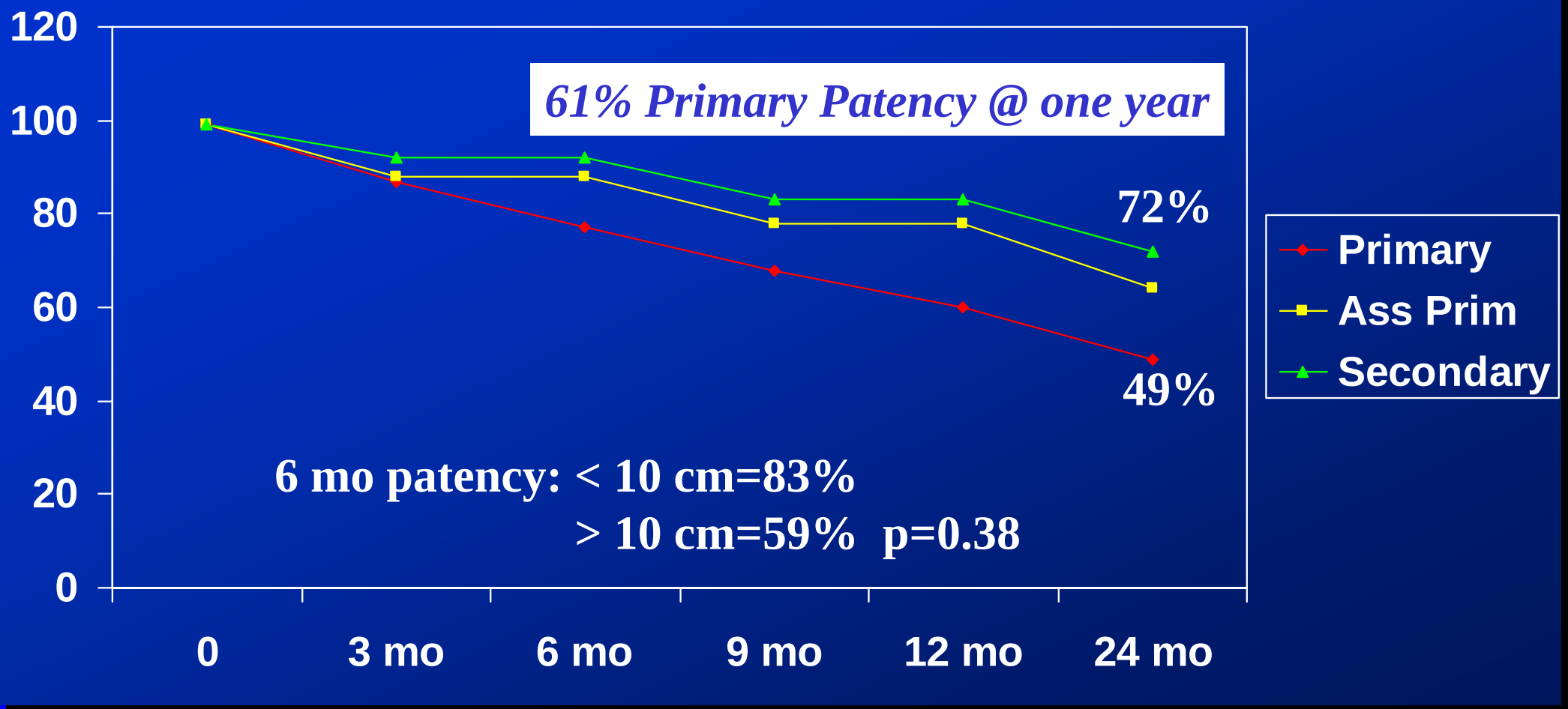
Disclosures

- Consultant: Spectranetics
- Advisory Board:
  - Cordis
  - Boston Scientific
  - Medtronic Vascular
  - Edwards Lifesciences
  - eV3

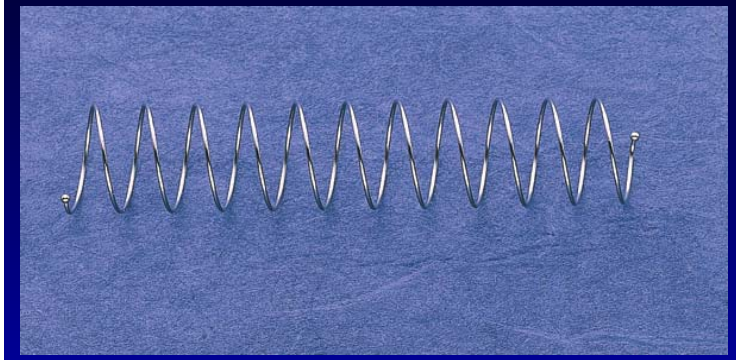
Do Stents Improve the Results of Femoropopliteal Intervention?

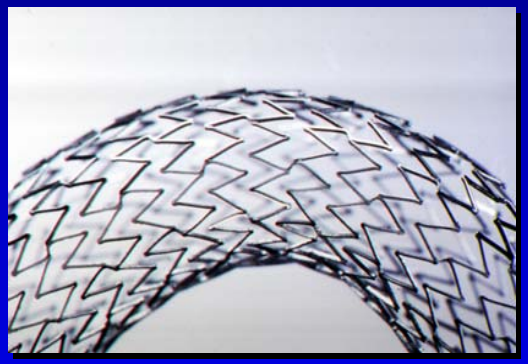
SFA Wallstents

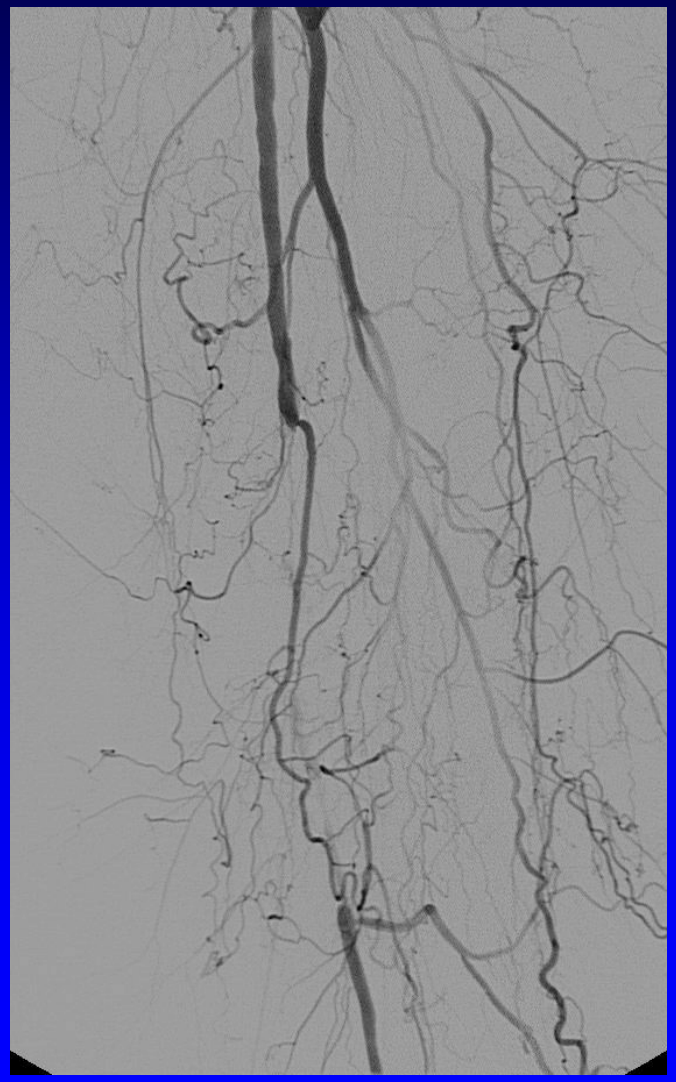


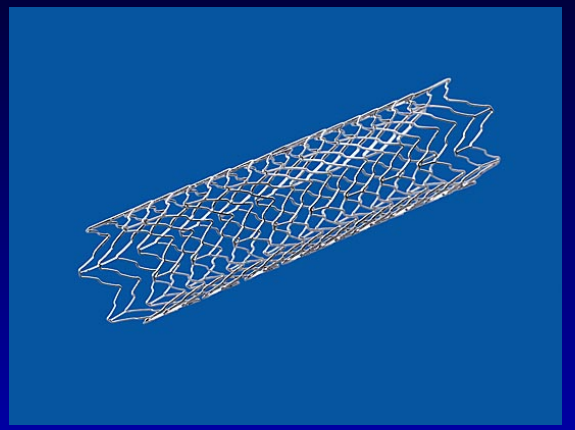
Martin, etal., JVIR 1995;6:843-849

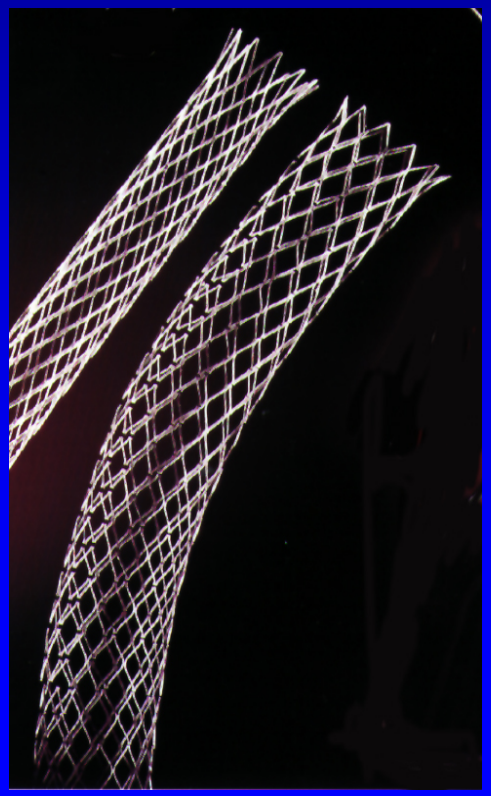
Nitinol Stents for the SFA



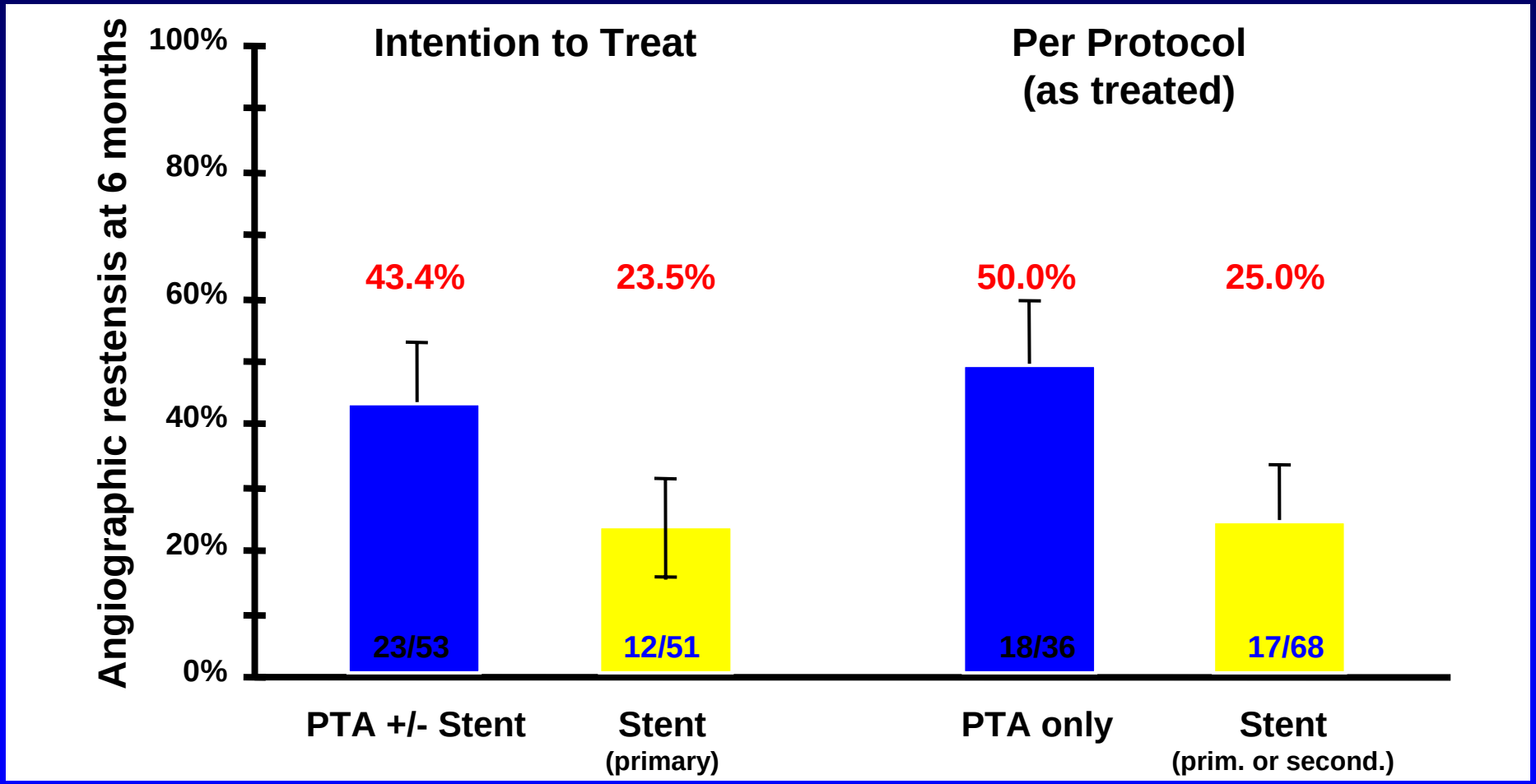








ABSOLUTE TRIAL
6 Mo Angiographic Restenosis



Schillinger M et al. N Engl J Med 2006;354:1879-1888

ABSOLUTE TRIAL
Restenosis Rates by DUS

	Stent (n=51)	PTA +/- Stent (n=53)	p-value
Duplex sonographic restenosis @ 3 mo	7/51 (13.7%)	12/53 (22.6%)	0.24
Duplex sonographic restenosis @ 6 mo	13/51 (25.5%)	24/53 (45.3%)	0.035
Duplex sonographic restenosis @ 12 mo	18/49 (36.7%)	33/52 (63.5%)	0.007

MEDIZINISCHE UNIVERSITÄT WIEN

DEPARTMENT OF ANGIOLOGY – GENERAL HOSPITAL VIENNA

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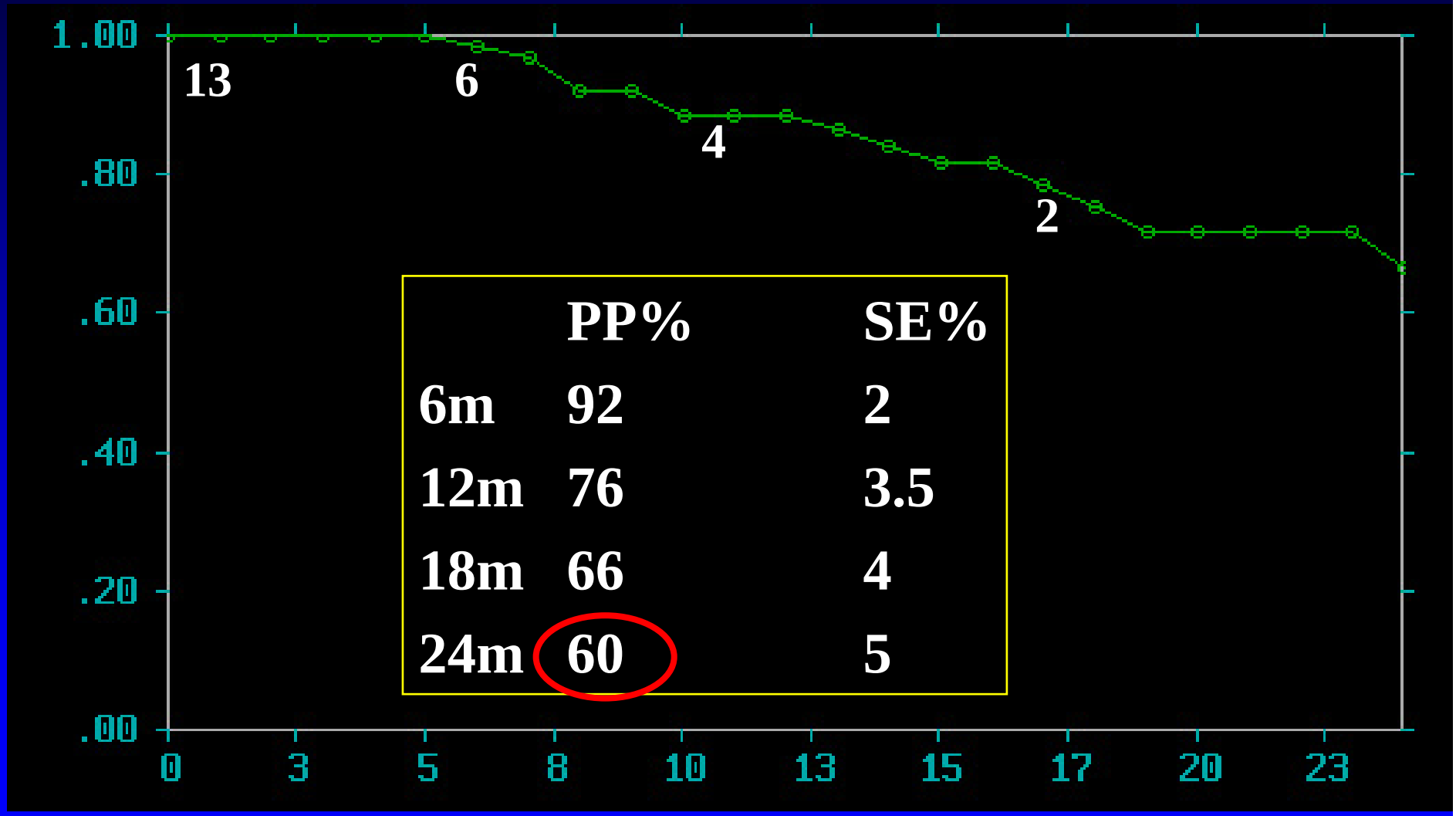
The Dark Side of SFA Stenting

FP Primary Stenting

The Problem of Late Restenosis



50-99% Stenosis Free Survival

Months

Results of X-Ray Screening – FESTO Trial 10.7 Month Follow-up

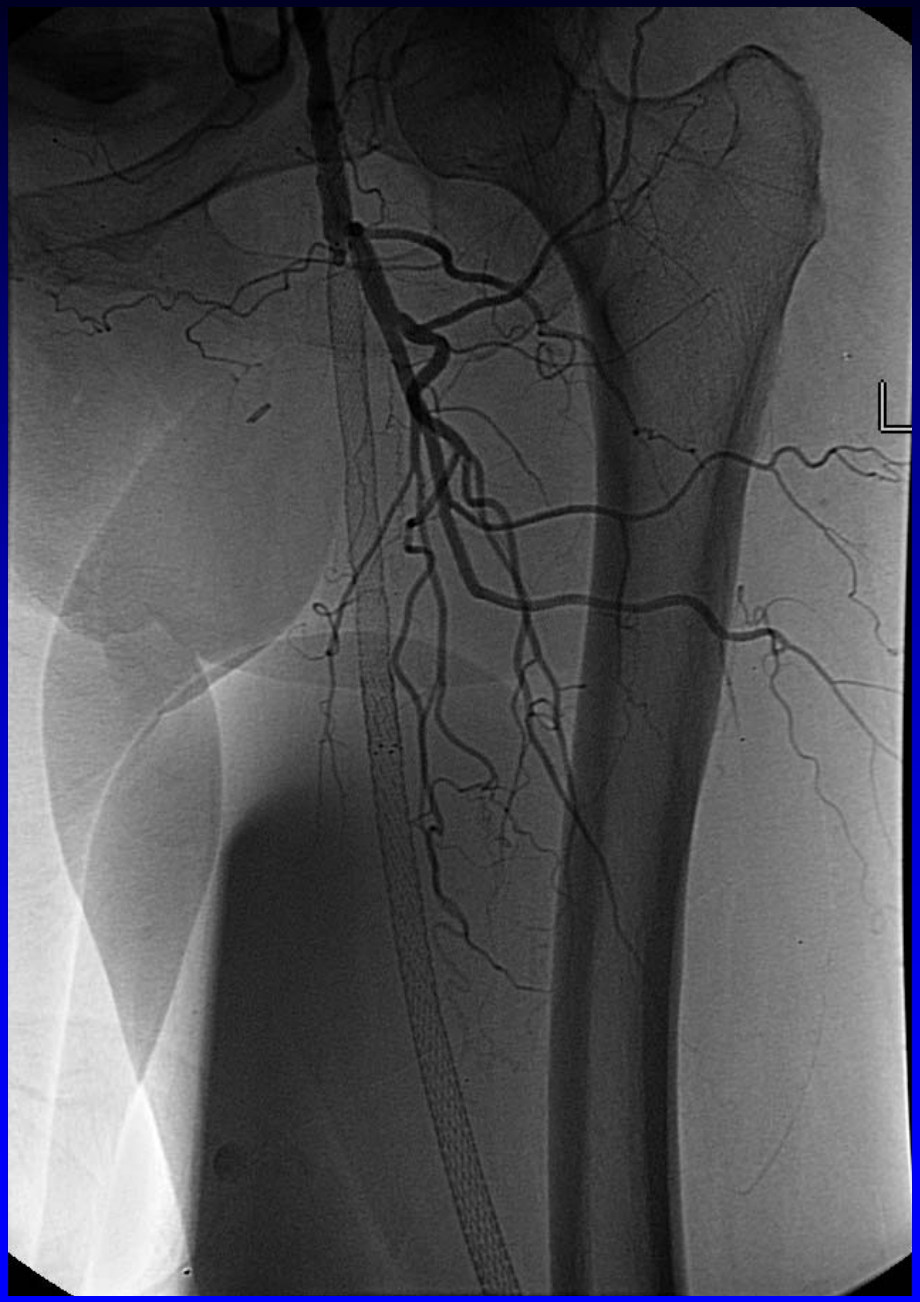
- Fractures in 45 of 121 treated legs:

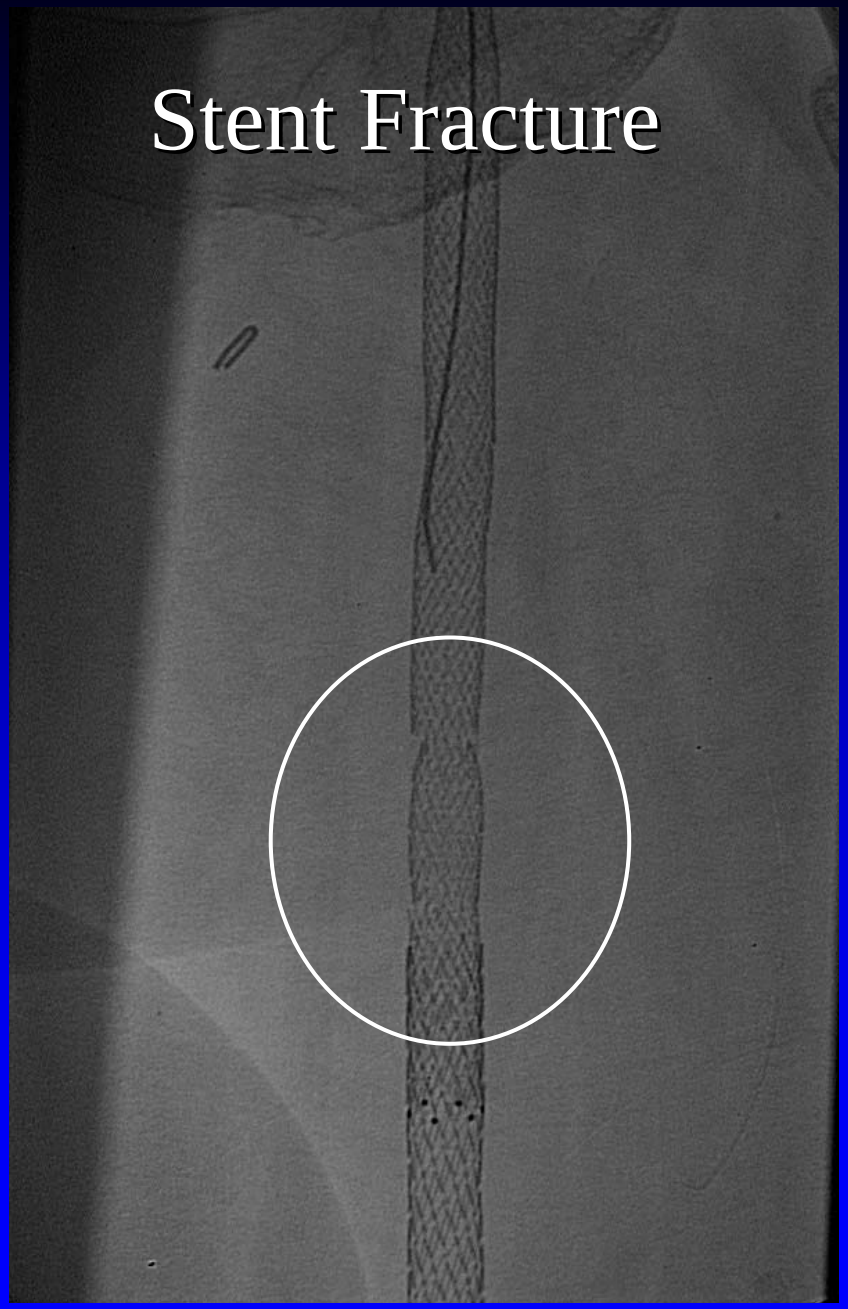
37.2%

- Fractures in 64 of 261 implanted stents:

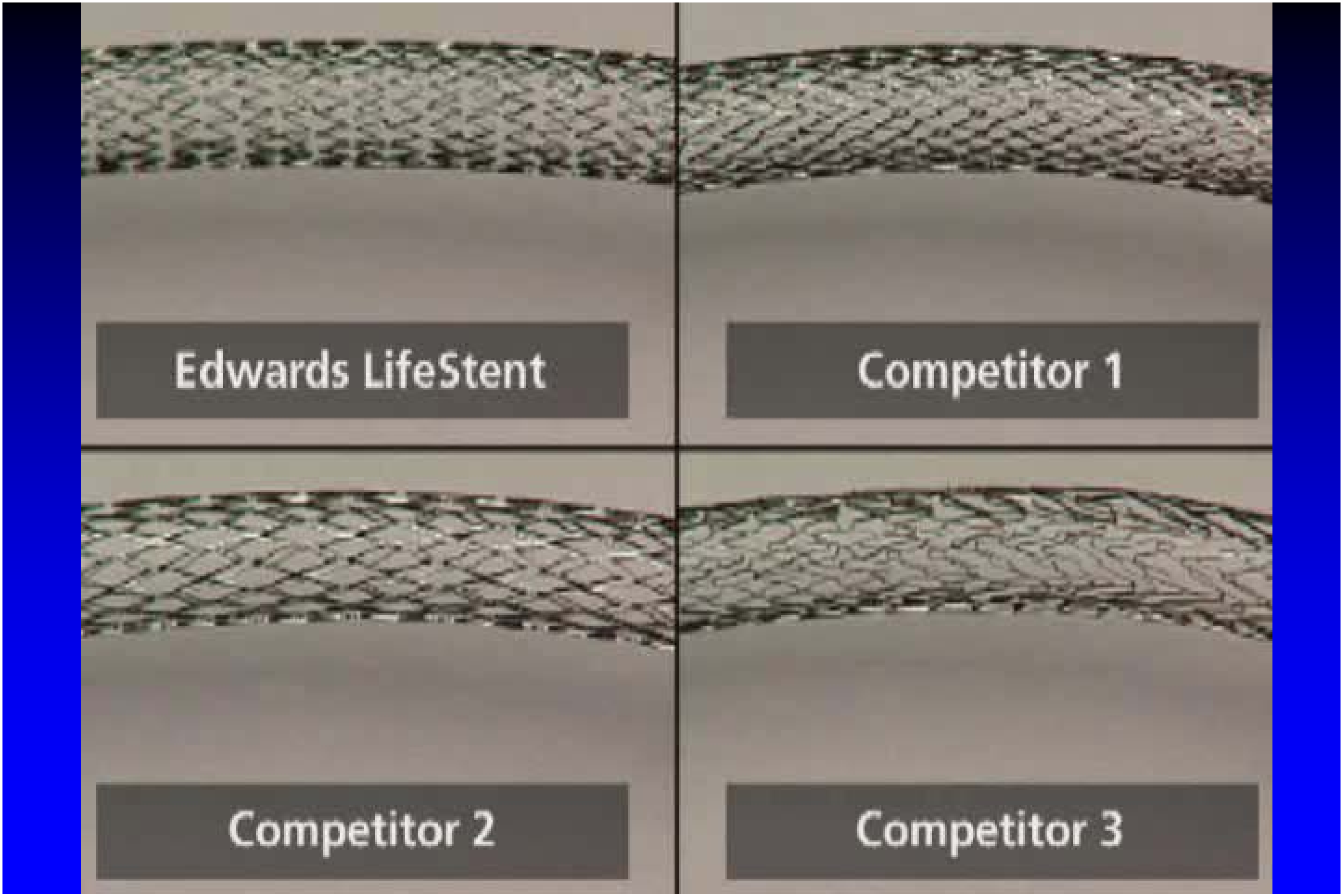
24.5%

D. Scheinert




Stent Fracture

Does Stent Design Matter?


Edwards LifeStent
Competitor 1
Competitor 2
Competitor 3

Edwards LifeStent Stent System

- Unique helical pattern enables multi-dimensional flexibility
  - Bending up to 180° or twisting without kinking
  - High radial strength

RESILIENT Trial

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

RESILIENT TRIAL

- Multi-center, prospective, randomized trial comparing balloon angioplasty to stenting for SFA disease (LifeStent)
- 20 patient feasibility trial
- 206 patient randomized trial
- 2:1 randomization

RESILIENT 30-Day Results

Measure	All PTA Patients	All Stent Patients
Target Limb ABI (mmHg), μ ± S.D. (#)	0.9 ± 0.1 (58)	1.0 ± 0.1 (143)
Rutherford Category		
Category 0, % (#)	61.3% (30/58)	62.8% (91/145)
Category 1, % (#)	27.0% (18/58)	25.5% (37/145)
Category 2, % (#)	9.0% (6/58)	9.7% (14/145)
Category 3, % (#)	2.7% (2/58)	2.1% (3/145)
Category 4, % (#)	1.7% (1/58)	0.0% (0/145)
Category 5, % (#)	1.7% (1/58)	0.0% (0/145)
Clinical Success, % (#)	87.9% (51/58)	95.8% (138/144)
Primary Patency (duplex), % (#)	57.4% (27/47)	99.2% (118/119)
Freedom from Re-Intervention, % (#)	58.0% (40/69)	99.4% (160/161)

RESILIENT Trial Interim Results
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 improvement from baseline.

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

RESILIENT Trial Interim Results
12-Month Results

Measure	PTA Patients	LifeStent Patients
Target Limb ABI (mmHg), μ ± S.D. (#)	0.9 ± 0.2 (31)	0.9 ± 0.2 (61)
Freedom from Re-Intervention, %	44.1%	81.5%

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%

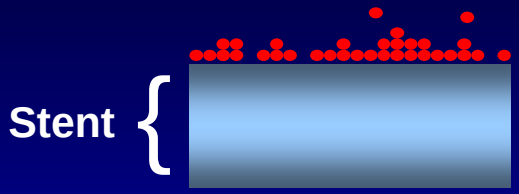
*No clinical symptoms,
all treated vessels patent at last follow-up

DES in the Peripheral Circulation: *Promise Yet Unfulfilled*

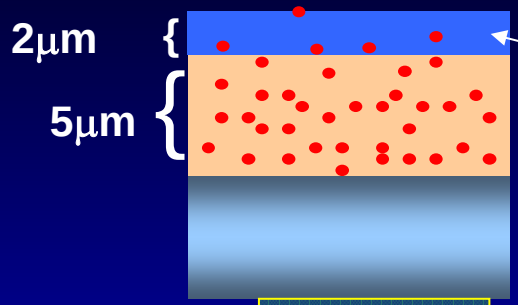
SFA Drug Eluting Stents
Issues to be Resolved

- Best drug?
- Proper dose?
- Ideal release kinetics?
- Type of polymer vs no polymer?
- Impact of stent fracture?
- Is diffusion an adequate mechanism for drug delivery?

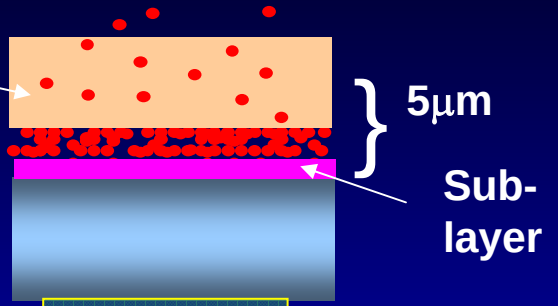
METHODS OF STENT-MEDIATED DELIVERY



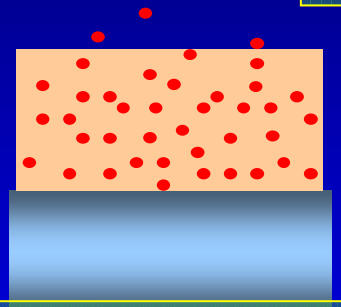
COOK



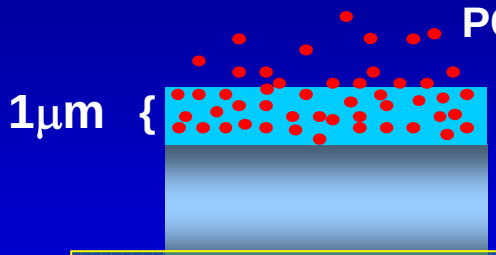
CORDIS



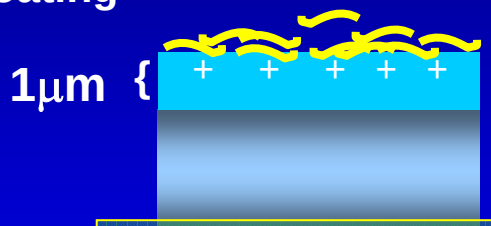
GUIDANT



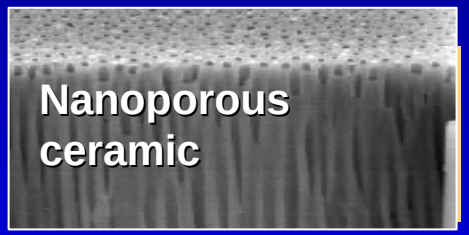
Boston Scientific



Bio*divYsio* Matrix LO



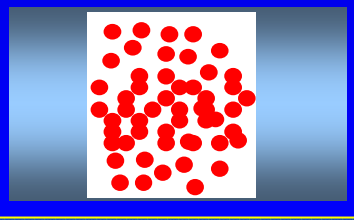
Bio*divYsio* Matrix HI



JOMED

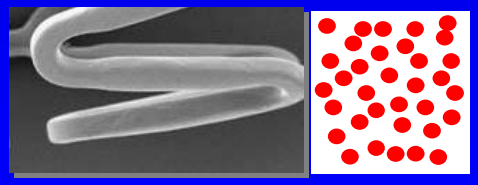
SORIN

Degradable inlays



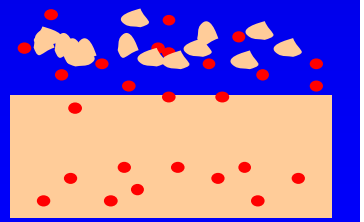
CONOR-Medsystems

Degradable polymer



Biosensor

Degradable stent



Igaki-Tamai

Polymeric slow-release sirolimus eluting stents: Comparison of Coronary and SFA Designs

Component	Coronary	SFA
Stent Material/Type	316L Stainless steel Balloon expandable	Nitinol Self-expanding
Polymer Drug/polymer ratio Physical properties Coating methods	EVA:BMA 33:67 Non-absorbable Elastomeric Spray-coat	PVDF-HFP 30:70 Non-absorbable Elastomeric Spin-coat
Sirolimus surface dose/stent area	140 ug/cm^2 3.5x18mm = 180ug	52 ug/cm^2 6x80mm=1000ug
Sirolimus surface dose/vessel area	90 ug/cm^2	66 ug/cm^2

Courtesy of Andy Carter

What is the Proper Dose?

Dose of Sirolimus in SIROCCO Trial:

1 mg per 6 x 80 cm SMART stent

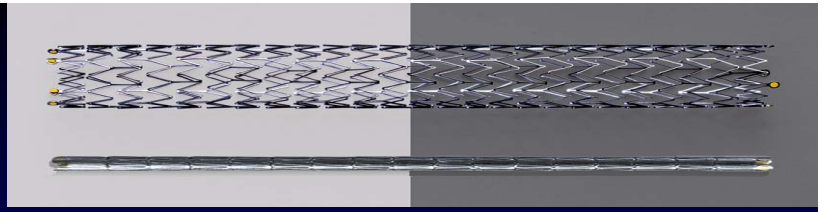
SIROCCO I
Six Month Angiographic Results

	Slower eluting N=5	Fast eluting N=11	Control N=17
MLD (mm)	4.31	3.47	3.28
Late Loss (mm)	0.39	0.72	1.03
Restenosis Rate	0%	0%	17.6%

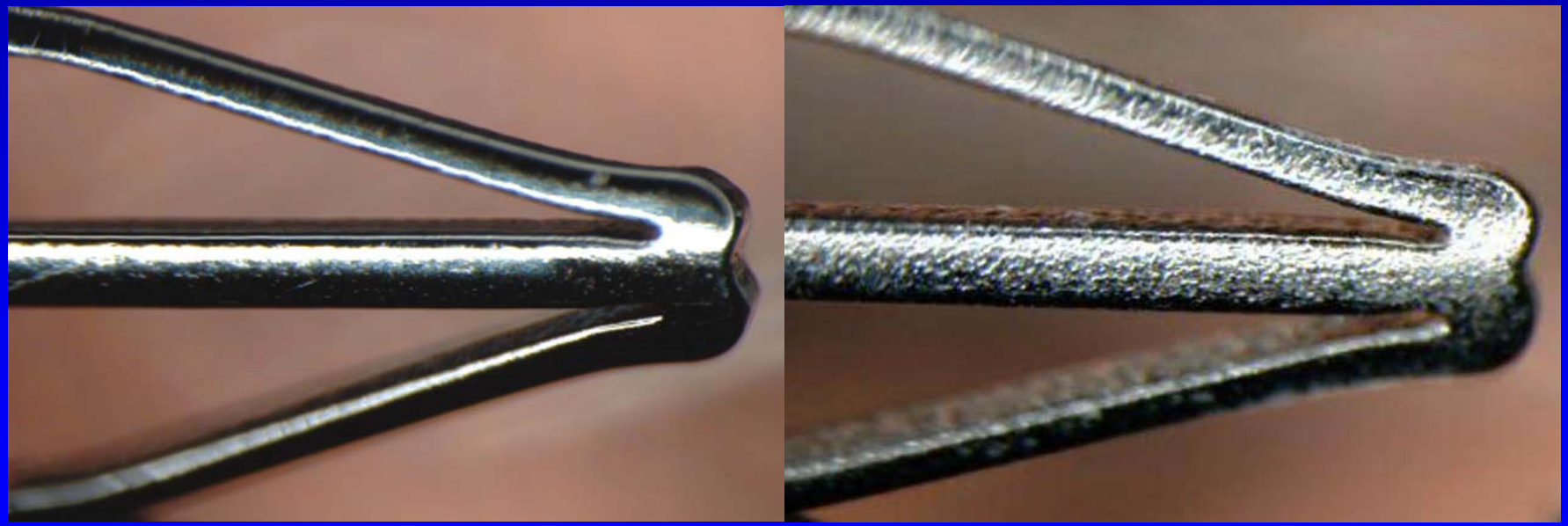
SIROCCO II
Six Month Angiographic Results

	Sirolimus N=24	Control N=26
MLD (mm)	3.91±0.72	3.62±0.91
Late Loss (mm)	0.38±0.64	0.68±0.97
Restenosis Rate	0%	7.7%

Zilver® PTX™ Coating



- Paclitaxel only (no polymer or binder)
- Thin coating (less than 5 microns)
- 3 microgm/mm^2 dose density
  (maximum 880 microgm total dose, largest stent)



What are the Optimal Release Kinetics?

Is the time course of restenosis the same in the SFA?

Late Failures in SIROCCO I
18 Month Follow-up

	Slower Eluting n=5	Fast Eluting n=9
Binary Restenosis	0	33%
Total Occlusion	0	0
TLR	0	11% (1)

Late Failures in SIROCCO I
24 Month Follow-up

	Slower Eluting n=5	Fast Eluting n=9
Binary Restenosis	40% (2)	44% (4)
Total Occlusion	0	0
TLR	0	11% (1)

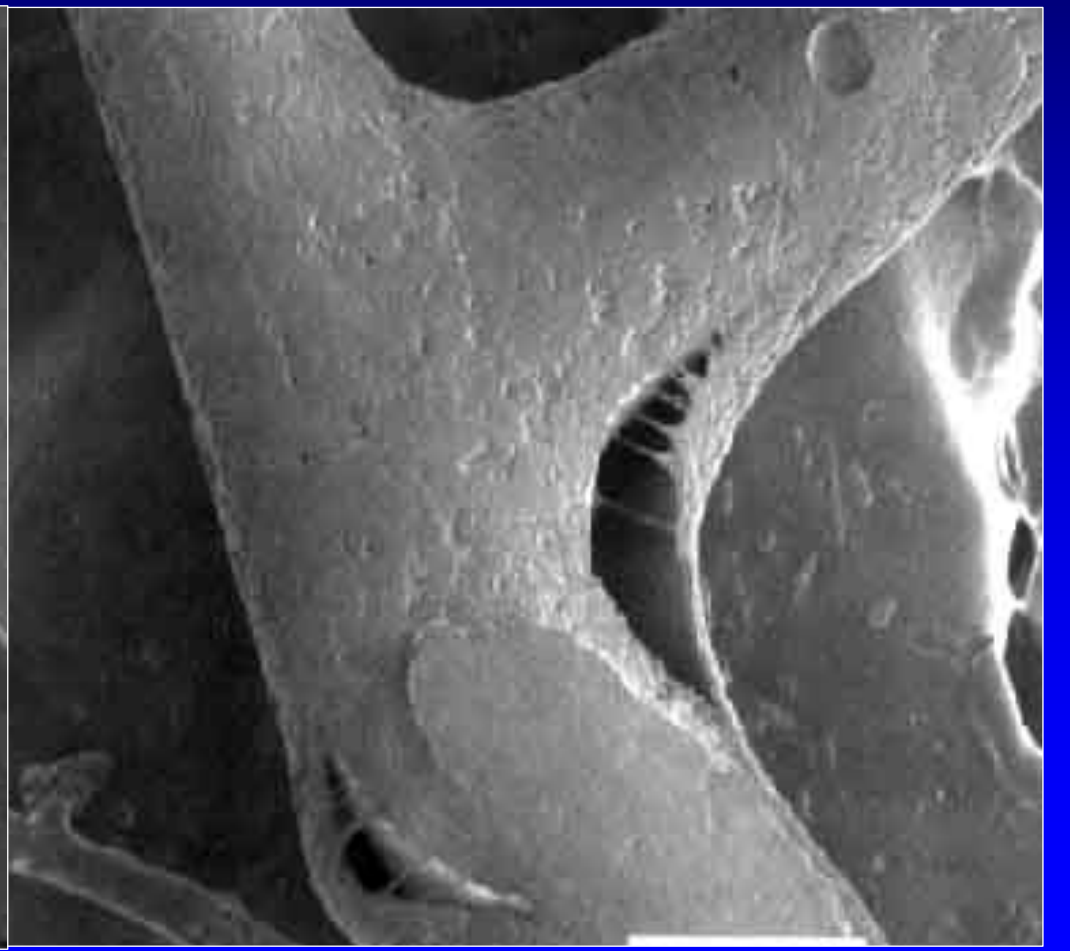
SIROCCO II – 24 Months
Duplex Restenosis/Reocclusion
N=57

	6 Months	9 Months	18 Months	24 Months
Sirolimus Coated N=29	0%	10.3%	20.7%	24.1%
Bare Metal N=28	7.7%	14.3%	17.9%	25.0%

Polymer vs. No Polymer?

What Will Happen to the Polymer?

Drug-Eluting Stent



SFA DES – Where do we Stand?

- **SIROCCO II confirmed the short term efficacy of the slower release formulation identified in SIROCCO I.**
- **Slower eluting data pooled from SIROCCO I and II resulted in an early statistically significant difference in the primary endpoint (mean stent diameter) , however, this advantage was lost by 18 months.**
- **The DESTINY trial using the Cook Zilver PTX devices with Paclitaxel recently completed Phase 1 - enrolling 60 patients with SFA disease <7cm long.**

Conclusions

- Recent trials have shown that Nitinol stents appear superior to balloon angioplasty in the SFA (lesion lengths less than 15 cm)
- There are important limitations of SFA stenting: late restenosis, stent fracture, increased restenosis for diabetics and long lesions
- Given these limitations, there is hope that DES will improve outcomes in the SFA
- Many unanswered questions, and no proof yet that DES will be more effective than BMS in the SFA