

Endovascular Therapy for Femoropopliteal Disease

Clinical Outcomes, Challenges and
Potential for Disease Management

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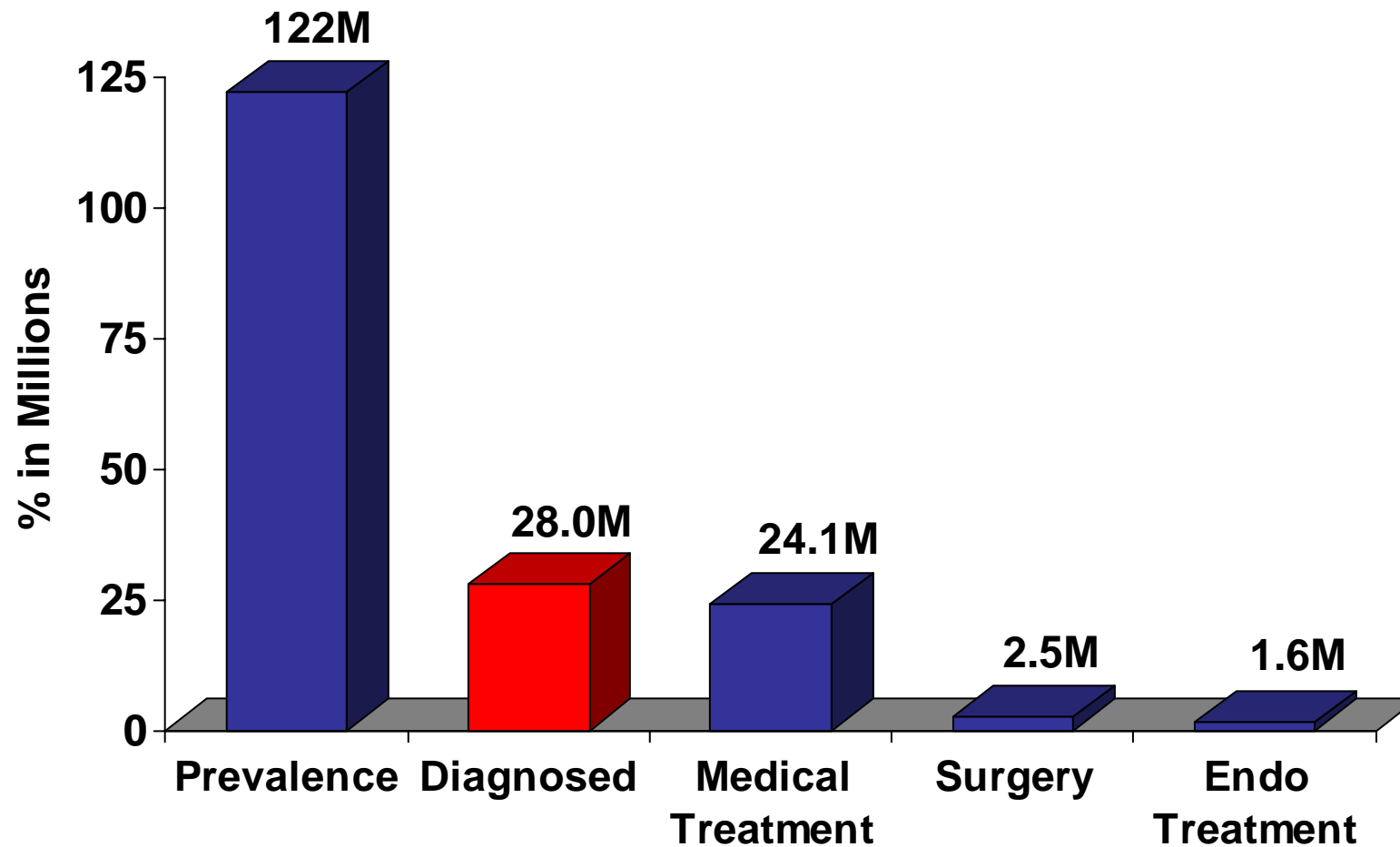
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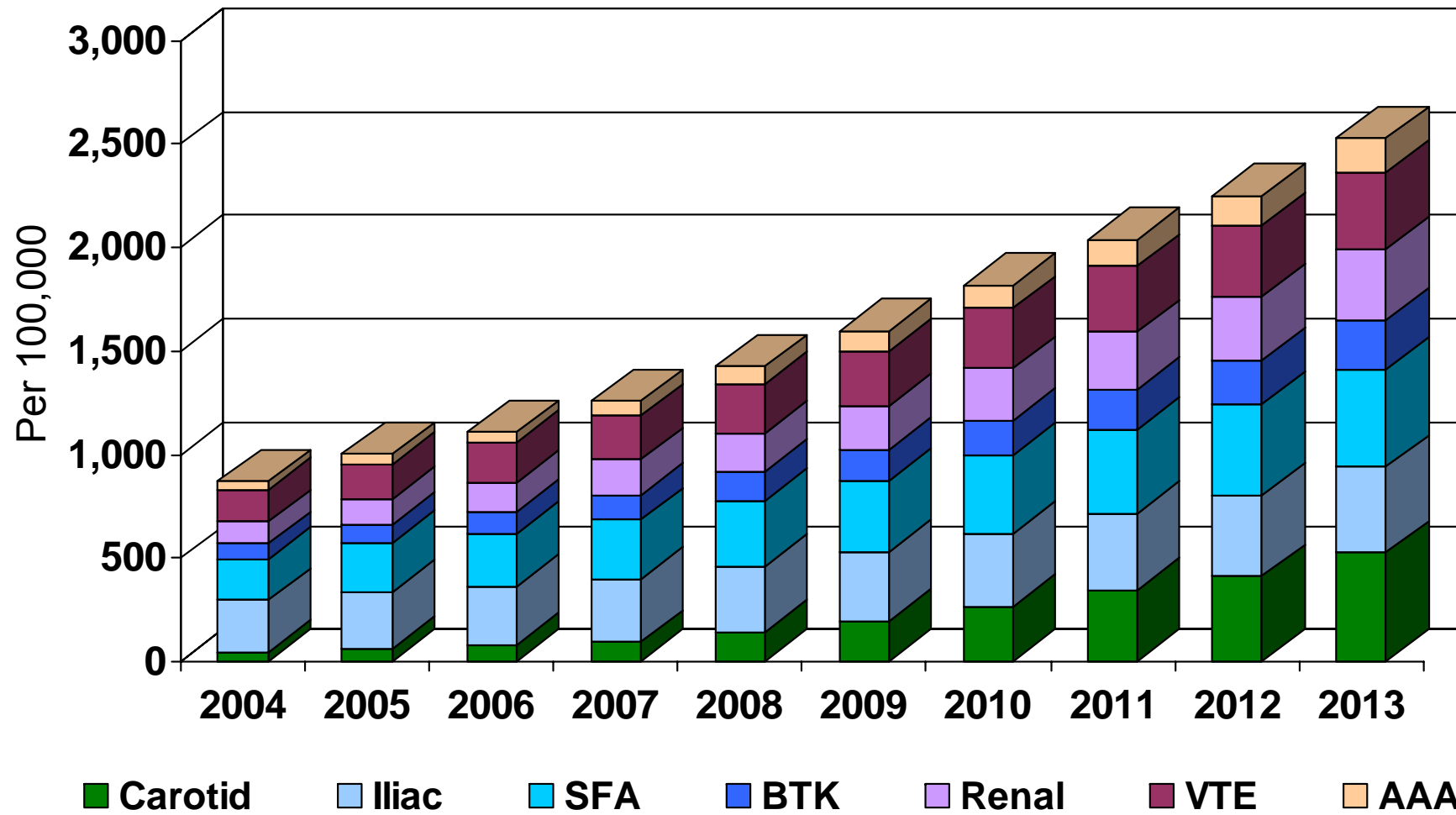
*Disclosure: Research/grant support, Medtronic
vascular; consultant, Cordis/Johnson & Johnson*

Peripheral Arterial Disease Statistics Worldwide: 2008



Based on Millennium Research Group Data

Estimated Number of Endovascular Procedures Worldwide



Based on Millennium Research Group Data, 2008

Current Challenges for Endovascular Therapy for Symptomatic PAD

- › Many trials, few approved indications
 - *Potential for indication-specific reimbursement*
 - *Inability to promote products/educate clinicians regarding 'off-label' use*
- › Evolving regulatory process to raise threshold requirements for approval
- › Variability in trial endpoints and design permits broad interpretation of safety and efficacy
 - Anatomic vs clinical endpoints
 - Quantifying restenosis (duplex, angiography, CTA, IVUS)
 - Consistent and standardized endpoint reporting
- › Technologies, technique and outcomes are specific to vascular territory

Endovascular Stent Treatment of Lower Extremities

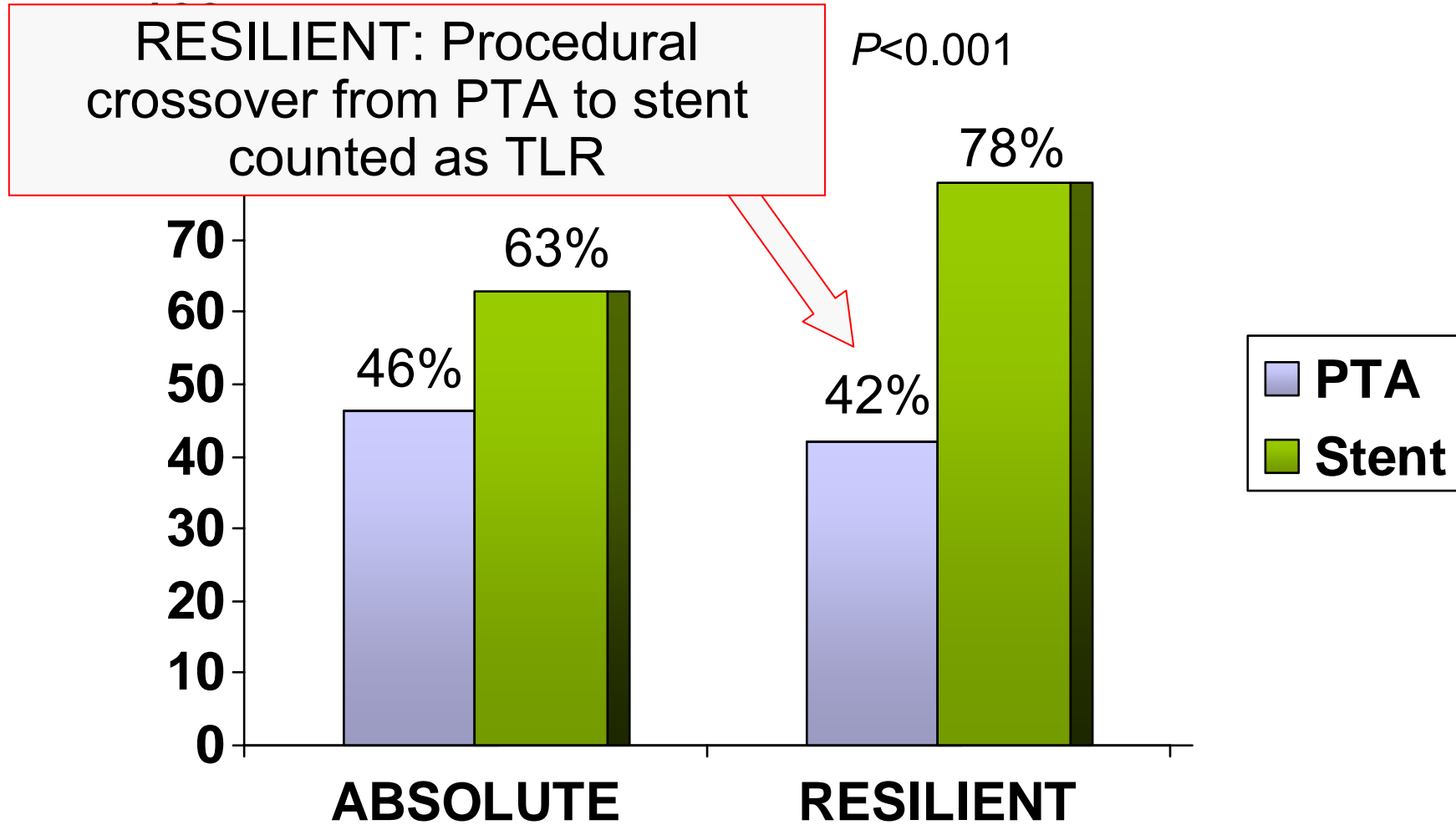
Randomized Trials: PTA vs. Stenting in the SFA

	FAST ¹		VIENNA ²		RESILIENT ³		PREVENT III ⁴
	PTA n=121	Stent n=123	PTA n=53	Stent n=51	PTA n=72	Stent n=134	FP Bypass n=697
Lesion length (cm)	4.5	4.5	9.3	12.2	5.7	6.2	–
Occlusions (%)	25	37	31	41	19	17	–
Crossover (%)	11	–	32	–	40	–	–
12-month Primary Patency (%)	61	68	37	63	38	80	59.5
No. of Fractured Stents (n)	–	10	–	4	–	9	–

¹H. Krankenberg, *Circulation* 2007; 116. ²Schillinger M, *Circulation* 2007; 115:2745-9.

³B. Katzen et al., Oral Presentation TCT 2007. ⁴Conte, *J Vasc Surg* 2006;43:742-51.

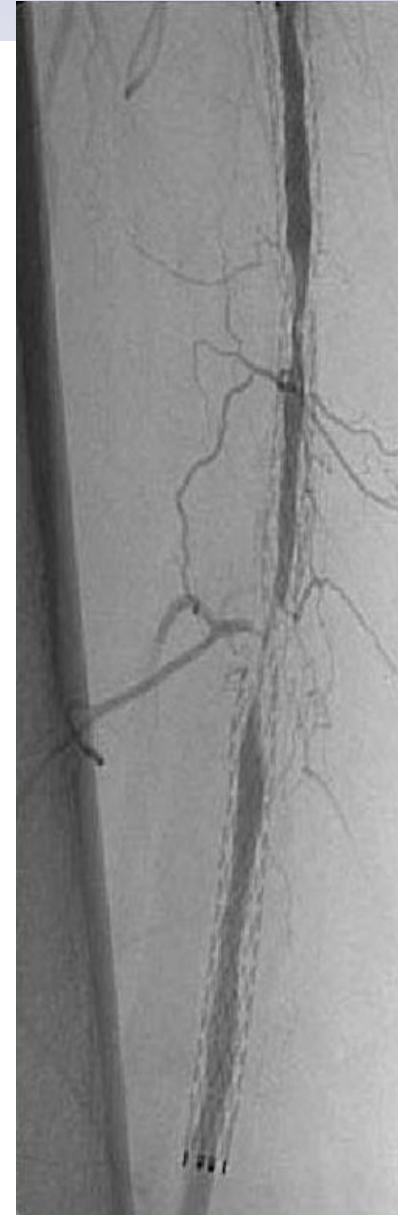
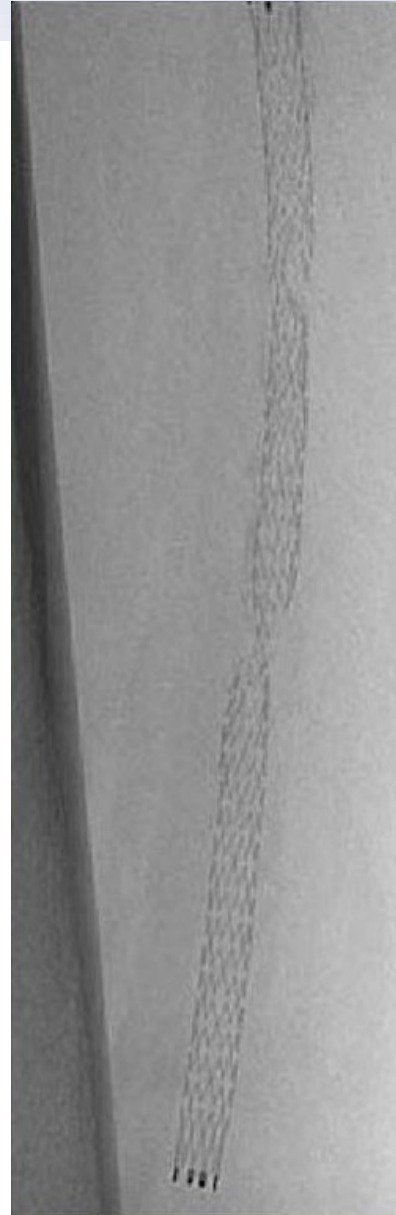
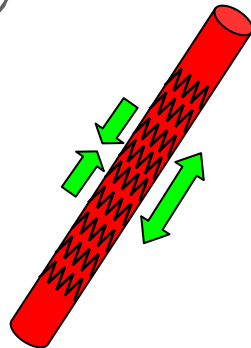
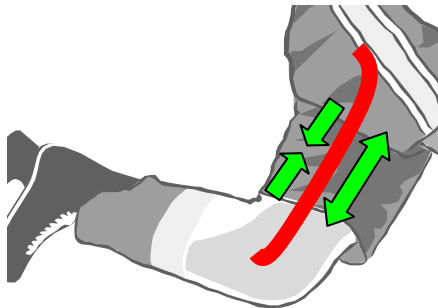
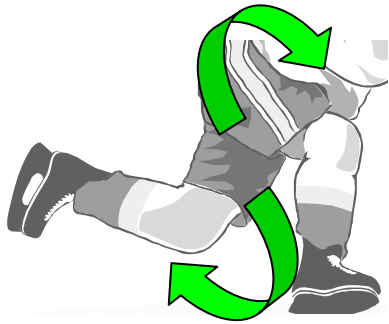
Randomized Trials: PTA vs. Stenting in the SFA 2 Year Follow Up



¹Schillinger M, *Circulation* 2007; 115:2745-9.

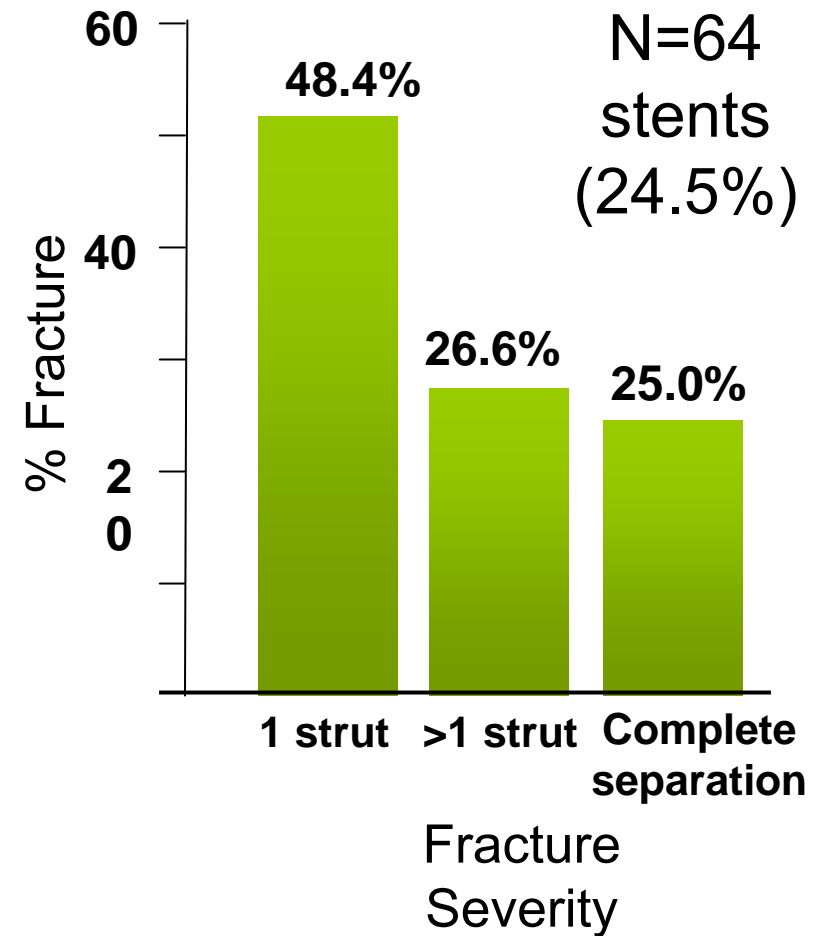
²B. Katzen et al., Oral Presentation ISET 2009

SFA Stenting: Strut Fractures



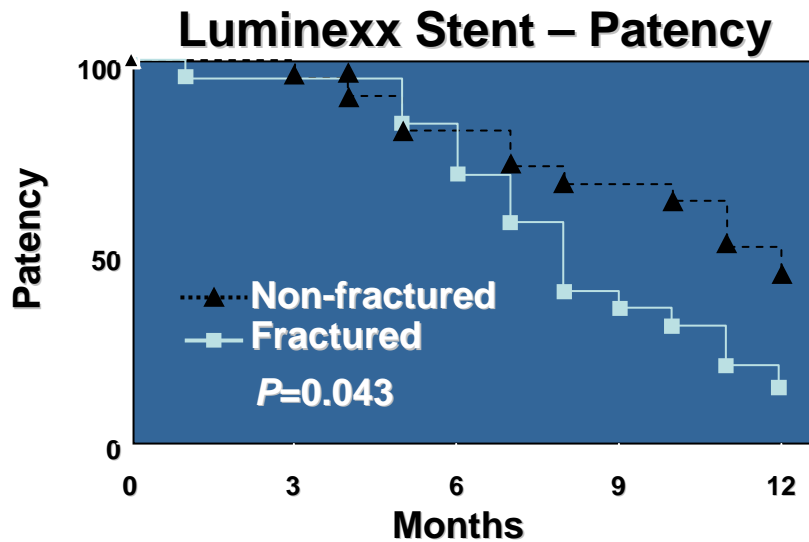
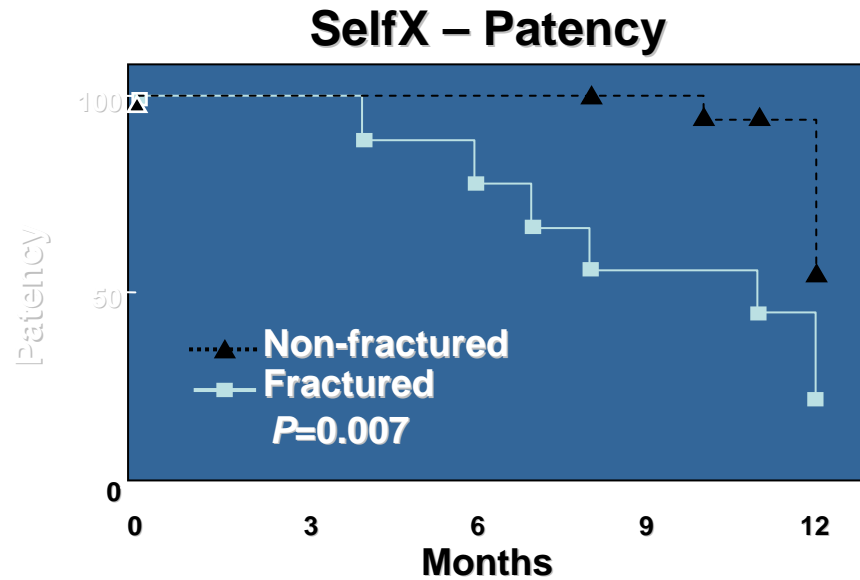
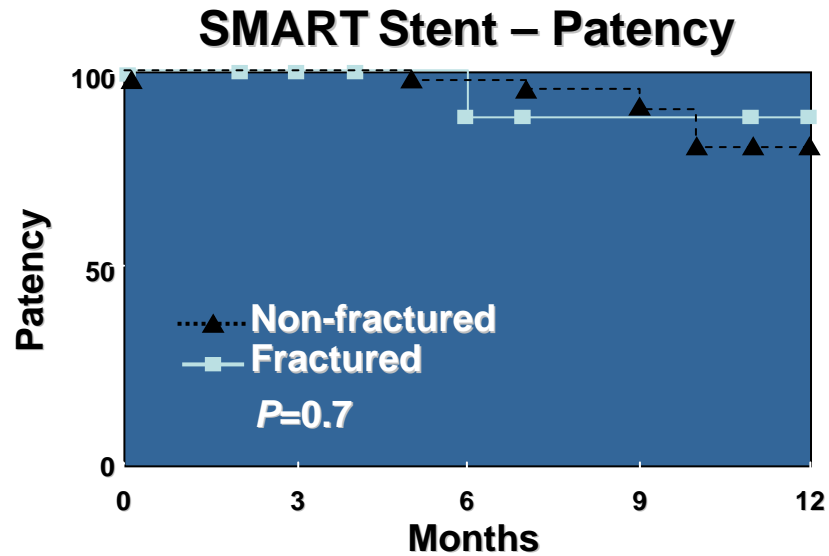
Prevalence and Implications of Stent Fracture in Femoropopliteal Stenting

- 91 pts, 121 limbs treated with 261 nitinol stents
- Mean stent length 157 mm
- Mean follow-up 10.7 months
- Strut fractures observed in 24.5%



Impact of Stent Fracture on Stent Patency

FESTO Trial



Alternative Therapies for Lower Limb Ischemia

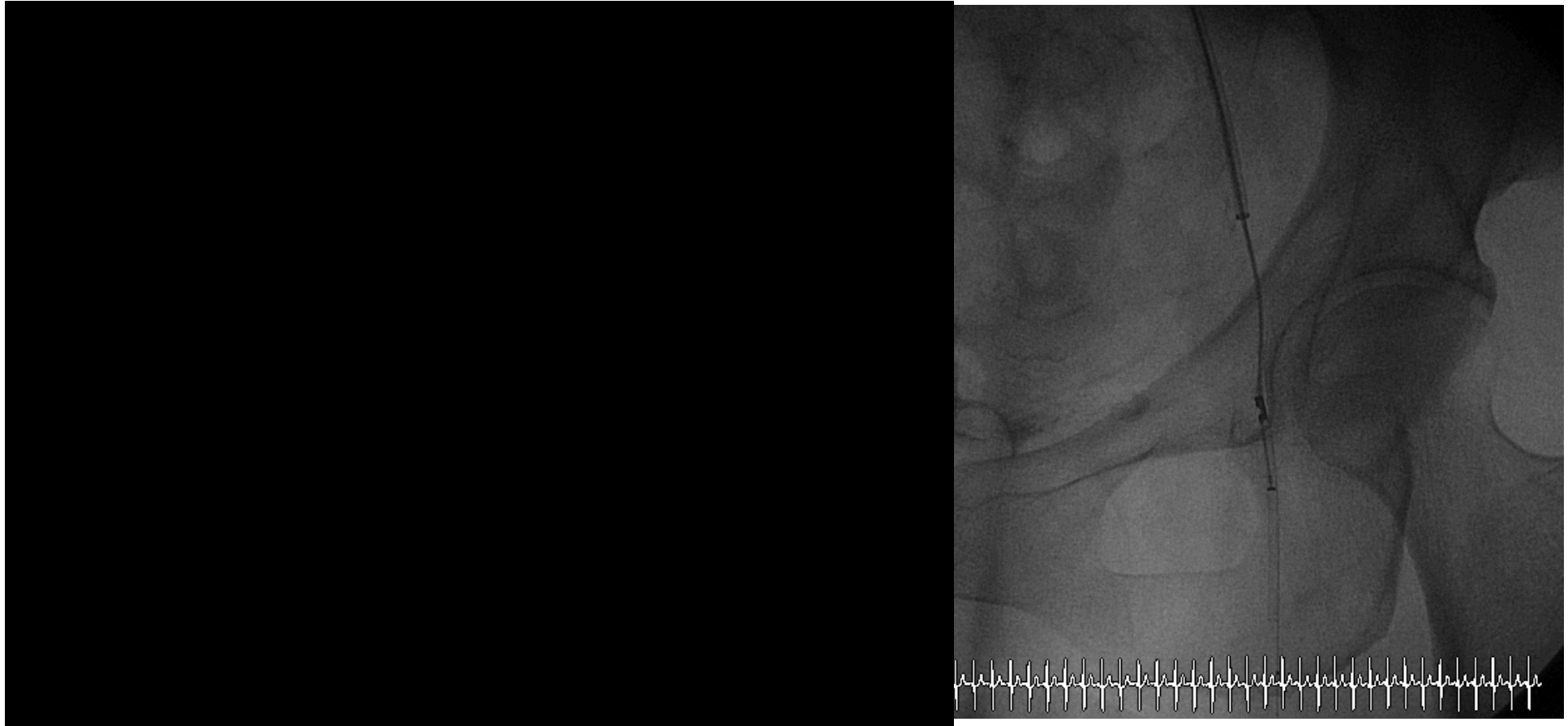
	Claudication			CLI		
	Atherectomy	Laser	Cryo	Atherectomy	Laser	Cryo
Study	Zeller¹	CELLO²	CHILL³	Zeller⁴	LACI⁵	BTK CHILL⁶
Centers	Single	20	16	Single	14	Multicenter
Patients	84	85	102	36	145	108
Occlusions (%)	N/A	16.0	14.7	N/A	91.0	33.9
Lesion length (cm)	9.0 ± 10.6	5.6 ± 4.7	4.7 ± 2.6	4.8 ± 2.8	4.0	4.1 ± 3.0
Adjunctive therapy (%)	>60%	N/A	8.8	~40%	>95%	N/A
Follow-up time	12 mo.	6 mo.	9 mo.	12 mo.	6 mo.	12 mo.
Clinical Patency (%)	84.0	84.0	82.2	76.0	N/A	84.3
Primary Patency (%)	84.0	63.0	70.1	67.0	N/A	N/A


¹T. Zeller, *JACC* 2006; 48:1573-8. ²R. Dave, TCT 2007. ³J.R. Laird, *J Vasc Interv Radiol* 2005; 16:1067-73.

⁴T. Zeller, *J Vasc Interv Radiol* 2004; 15:1391-97. ⁵J.R. Laird, *J Endo Ther* 2004; 3:1-11.

⁶B. Gray, TCT 2006.

Silverhawk Plaque Excision Catheter *EV3/ Foxhollow Technologies*





High-grade stenoses of SFA/profunda bifurcation

The image is a grayscale angiogram of a lower extremity artery. It shows a main vessel (likely the superficial femoral artery) that bifurcates into two branches (likely the profunda femoris artery and its branches). There are significant, dark, irregular narrowing of the vessel lumen at the bifurcation point and in the proximal segments of both branches, indicating high-grade stenoses. The background shows a network of smaller, less distinct vessels.

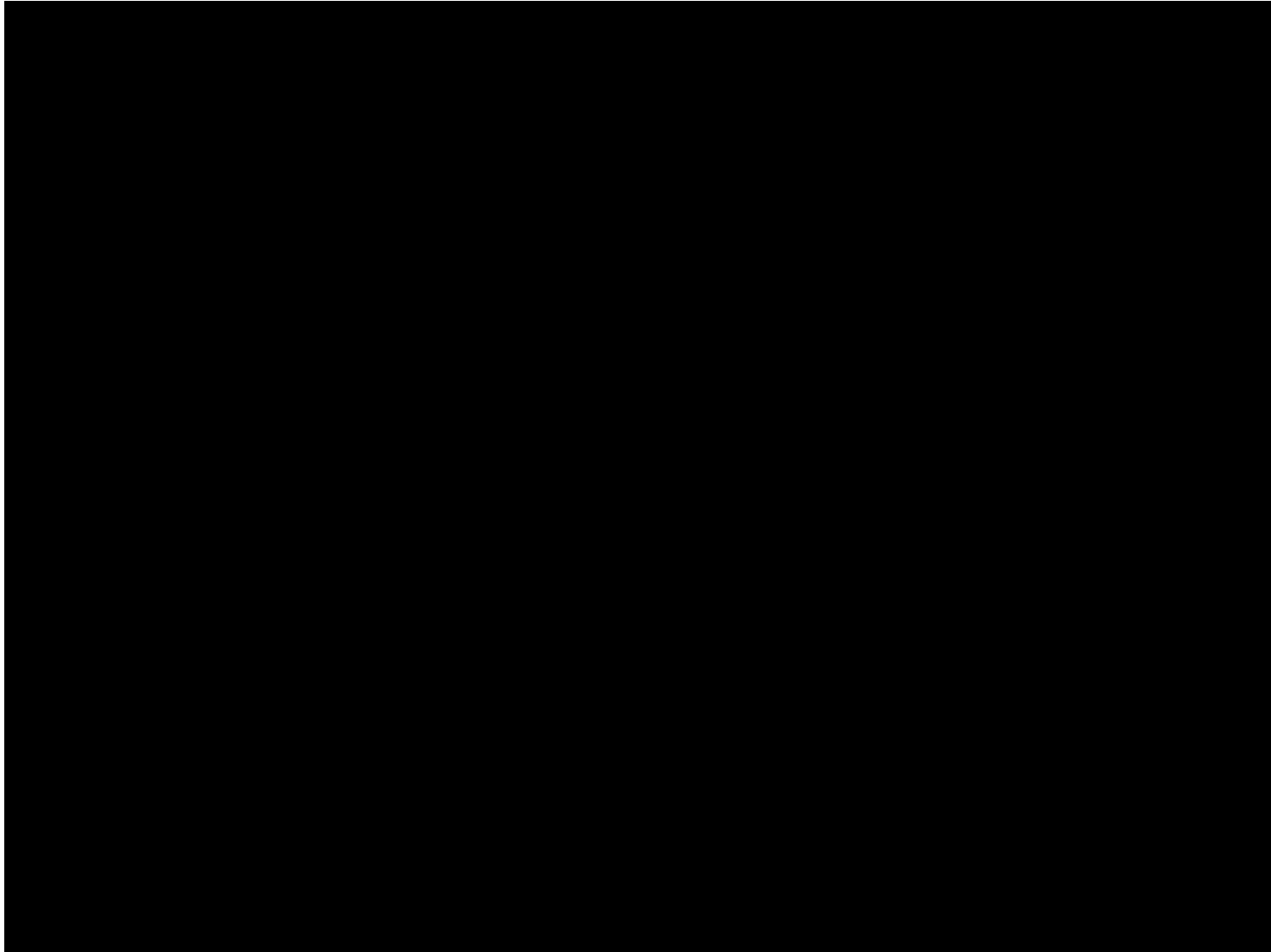


Silverhawk in both branches



Final result

Elliptical Atherectomy for Femoropopliteal Disease

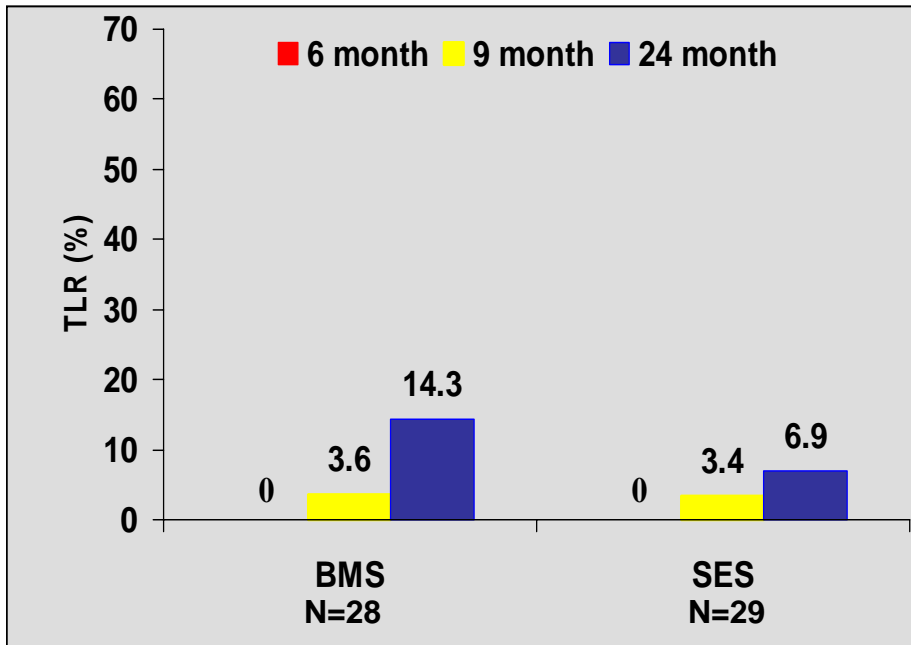


Elliptical Atherectomy for Femoropopliteal Disease

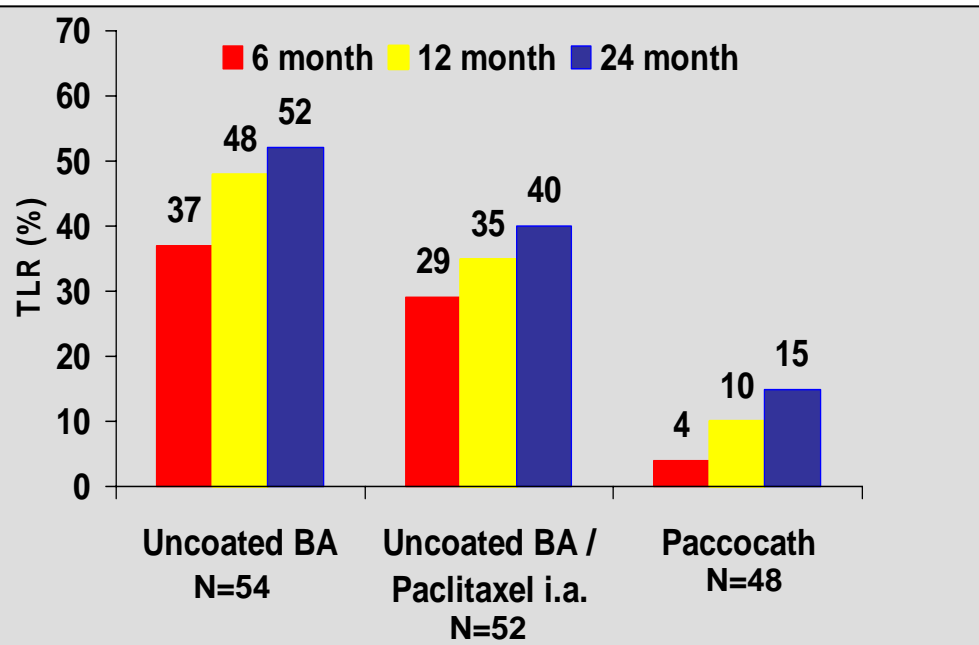


Drug-Eluting Stents & Drug-Coated Balloons in SFA Disease

SIROCCO II: TLR to 2-Years¹



THUNDER: TLR to 2-Years²



SIROCCO II:
Bare SMART Nitinol Stent vs. Sirolimus-Eluting SMART Nitinol Stent

Sirolimus 90 µg/cm² (total 1mg/stent)
 Co-polymer matrix (sirolimus 30:70 co-polymer)

THUNDER Trial:
Uncoated Balloon vs. Uncoated Balloon Iopromid-Paclitaxel* vs. Paclitaxel-Coated Balloon**

* ~17 mg Paclitaxel/100 ml KM
 ** ~3 µg/mm² Paclitaxel

Drug-Eluting Stents in SFA Disease Cook Zilver Paclitaxel Program

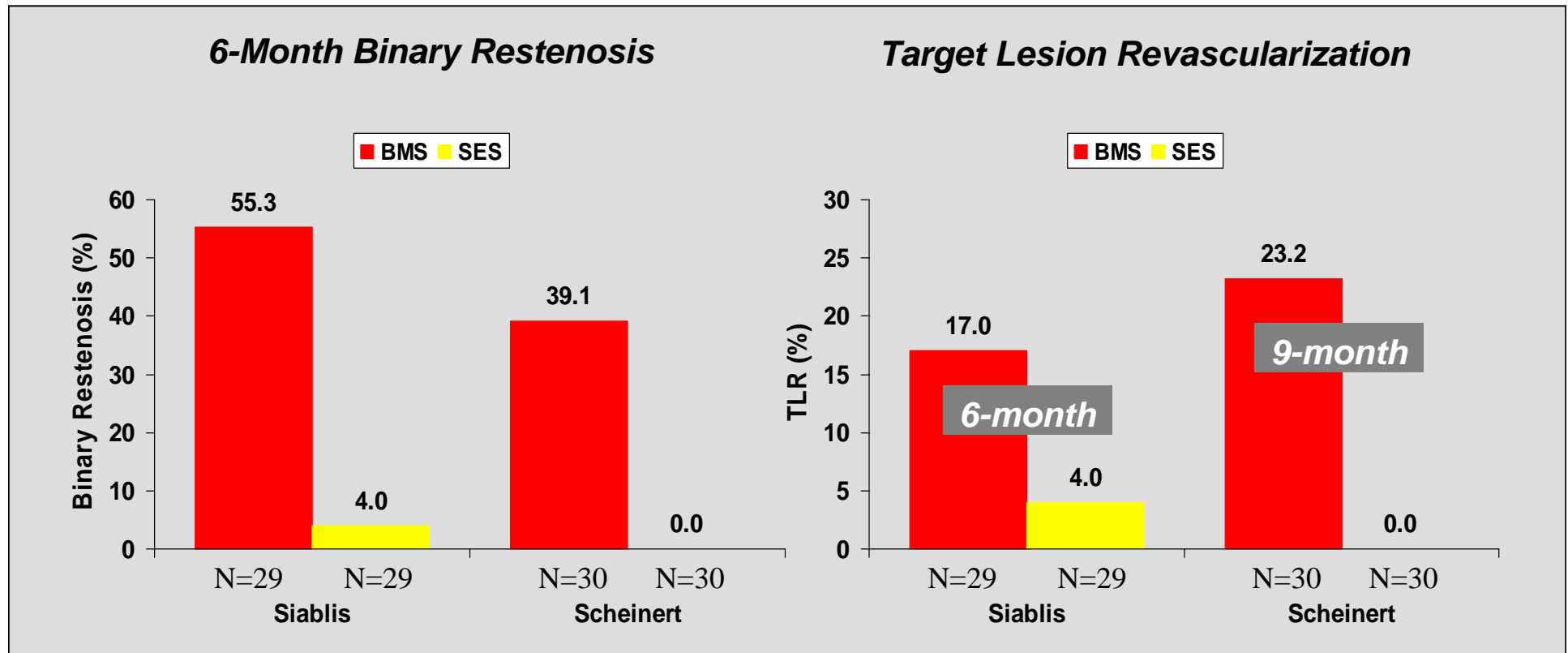
- Randomized Study (480 pts)
 - Phase 1: 60 patients*
 - Lesions <7 cm, up to 1 stent per limb
 - Enrollment complete
 - Phase 2: 420 patients*
 - Lesions <14 cm, up to 2 stents per limb
 - Currently enrolling
- Registry Study (760 pts)
 - Up to 4 Zilver[®]PTX[™] stents per patient
 - Currently enrolling:
 - more than 700 patients
 - enrolled/approximately 2500 stents implanted

Drug-Eluting Stents in SFA Disease

Cook Zilver Paclitaxel Program

	6-month Freedom From TLR
Phase 1 of Randomized Trial	
PTA	52% (17/33)
No PTA Failure	100% (17/17)
PTA acute failure → BMS Zilver	75% (6/8)
PTA acute failure → PTX Zilver	100% (8/8)
Zilver PTX	90% (26/29)
Registry Zilver PX	90% (82/91)

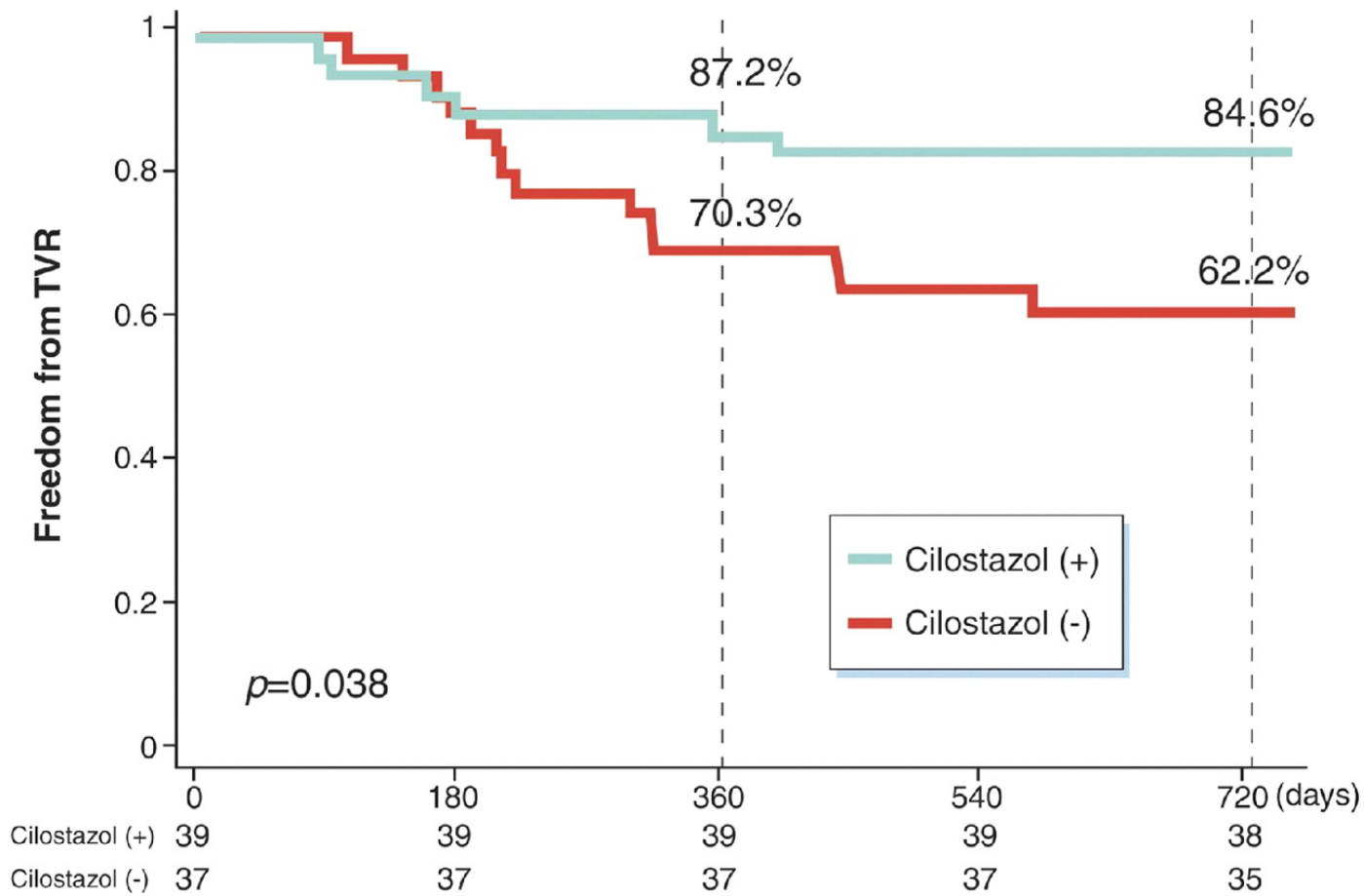
CYPHER Sirolimus-eluting Coronary Stent Below the Knee



¹D. Siablis et al., *J Endovasc Ther* 2005; 12:685-95. ²D. Scheinert et al., *EuroIntervention* 2006; 2:169-74

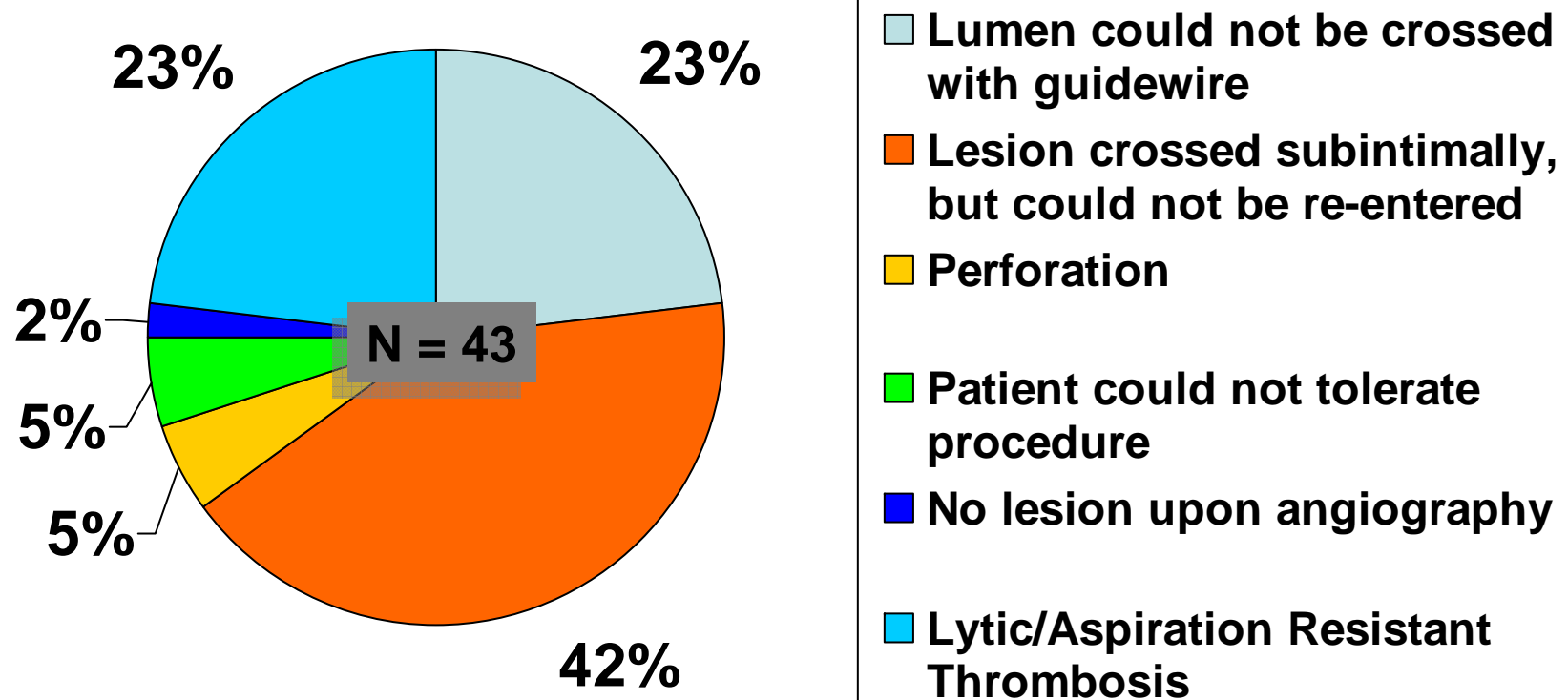
Pharmacologic Prevention of Restenosis

Cilostazol



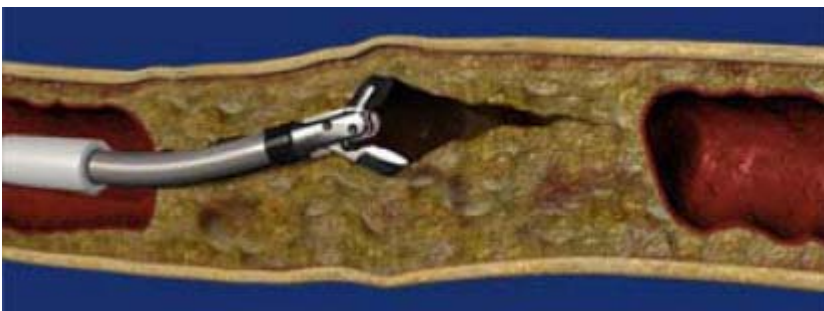
Angioplasty Attempts/Immediate Failures

- Of the 224 patients allocated to angioplasty, 216 underwent attempted angioplasty
- Of these, 43 (20%) were considered immediate failures:



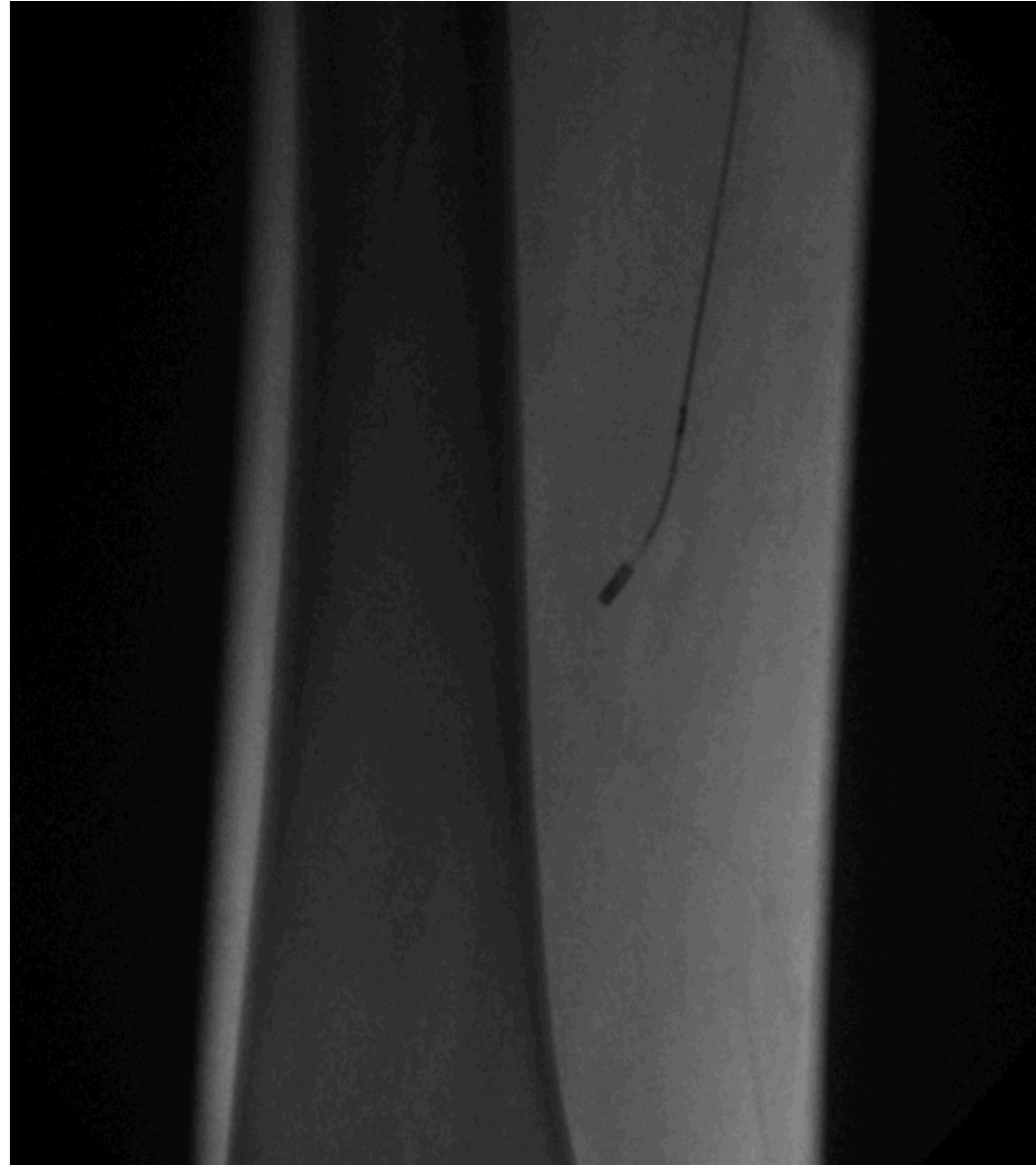
Novel 'Enabling' Technologies

Chronic Total Occlusions



Enabling Technologies

Chronic Total Occlusion Re-entry



Enabling Technologies

Chronic Total Occlusion Re-entry





Novel Endovascular Therapies for PAD

› Stents

- Fracture resistant self-expanding

- Drug-eluting stents

- Bioresorbable stents

› Alternative anti-restenotic therapies

- Drug-eluting balloons

- Adventitial injection

- Nanoparticle delivery

› Plaque excision/atherectomy

› Chronic total occlusion and re-entry technologies

› Critical limb ischemia

- Angiogenesis and stem cell therapies

Endovascular Therapy for PAD

Summary

- › Large patient population with PAD but multiple challenges to establishing a standard of care
- › Strategies developing to establish endovascular treatments as first line therapy for revascularization
 - More trials are being conducted to pursue indications specific to PAD
 - Advanced therapies such as a DEB and DES are now being evaluated
- › Evolution of novel endovascular therapies has broadened treatment to pts previously without options
 - Improvements in procedural safety and efficacy have lowered interventional threshold for complex PAD, CLI
 - ‘Enabling’ technologies and techniques have revolutionized treatment paradigm of PAD
- › Issue is to focus on not what can be done, but what should be done, with emphasis on modifying cardiovascular risk