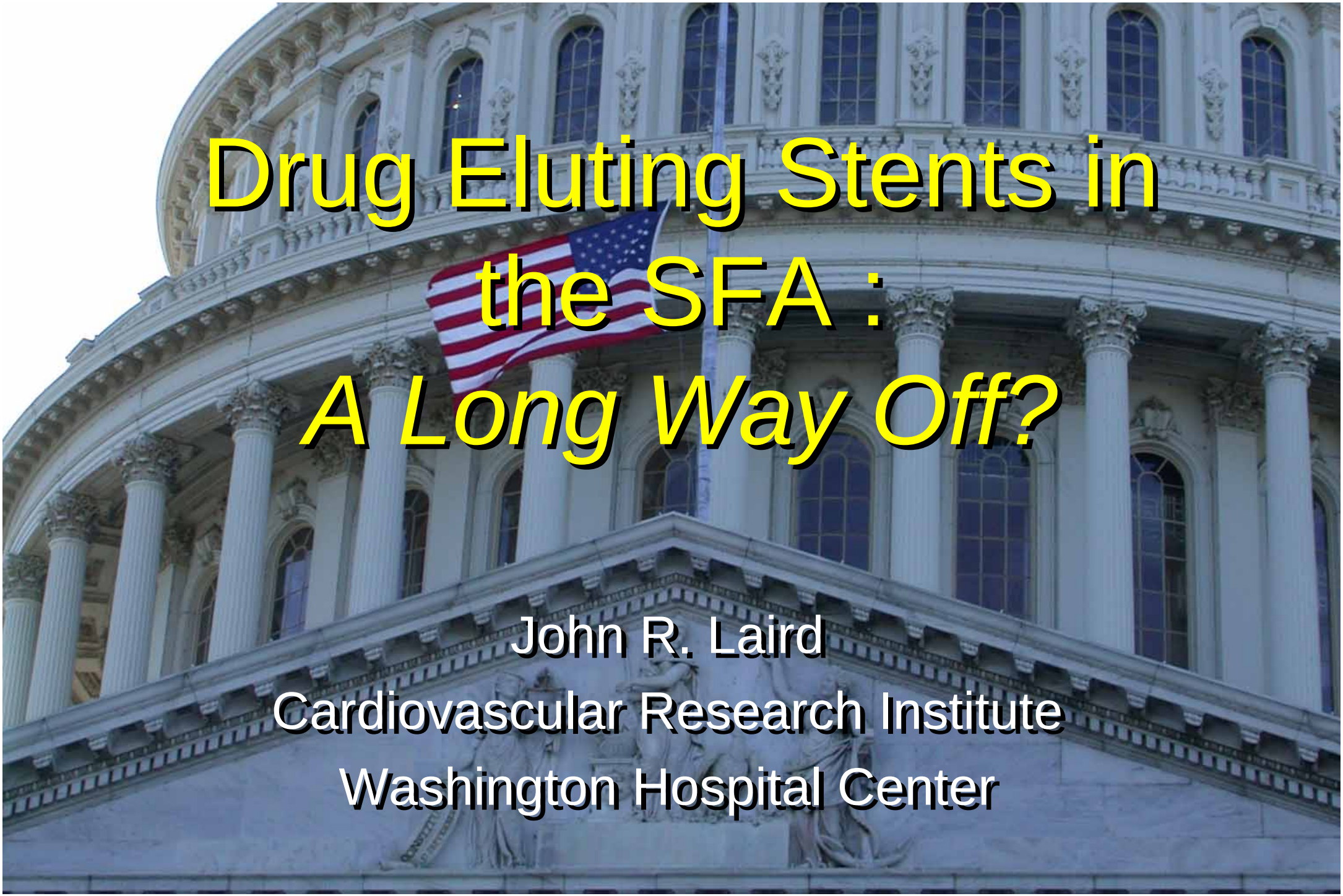
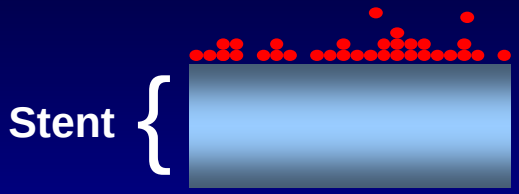


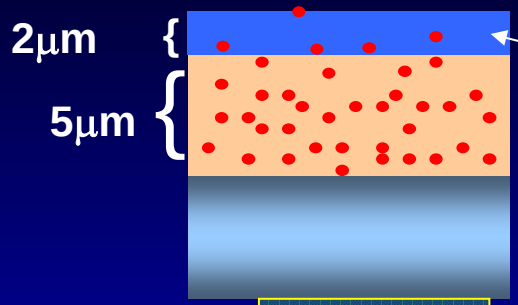
Drug Eluting Stents in the SFA : *A Long Way Off?*

John R. Laird
Cardiovascular Research Institute
Washington Hospital Center

METHODS OF STENT-MEDIATED DELIVERY



COOK



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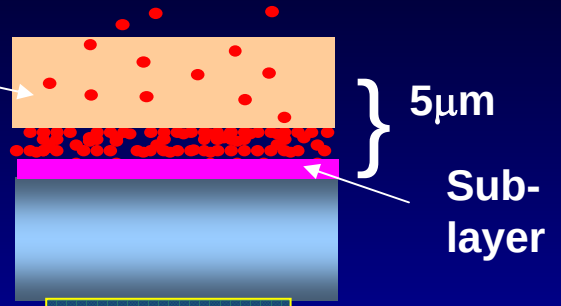
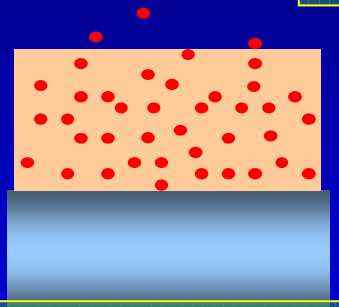
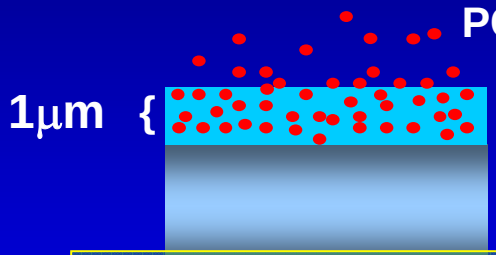


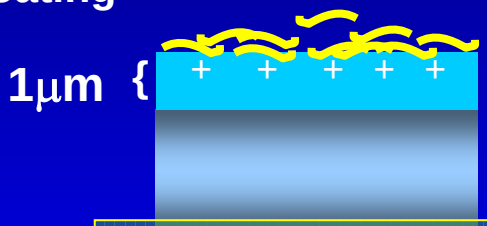
GUIDANT



Boston Scientific



Bio*divYsio* Matrix LO



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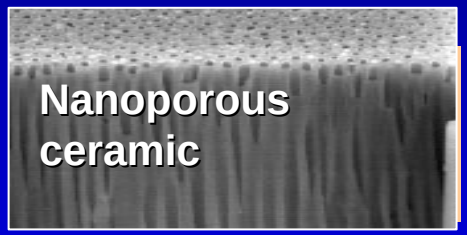
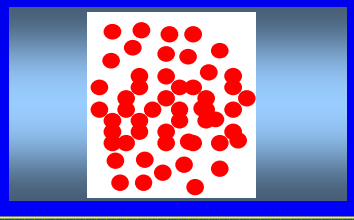


JOMED

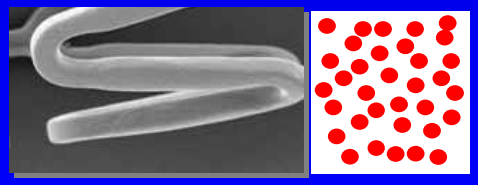
SORIN

Degradable inlays



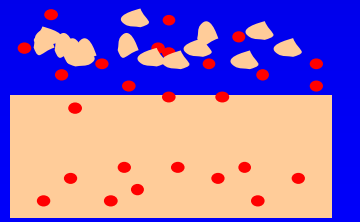
CONOR-Medsystems

Degradable polymer



Biosensor

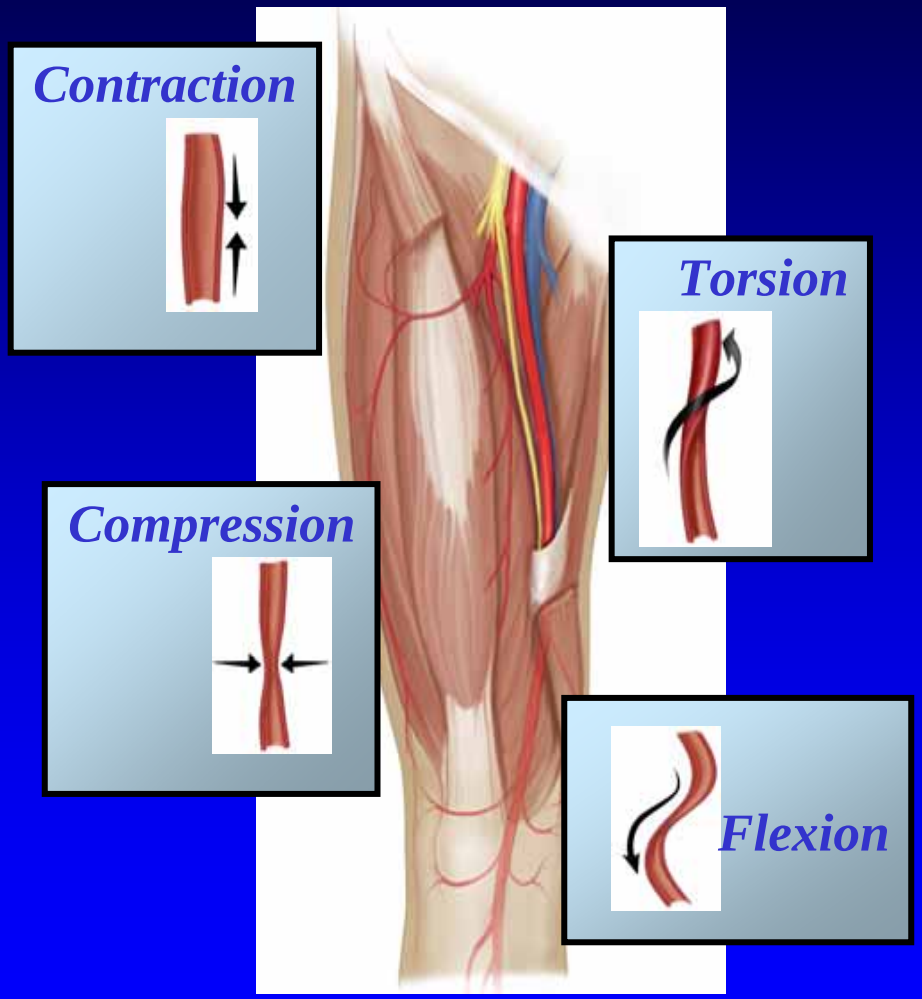
Degradable stent



Igaki-Tamai

SFA Intervention - Nature of the Problem

- Occlusion predominates over stenosis
- Diffuse disease common
- Adductor canal
- Low flow/high resistance
- Coexistant disease of distal run-off vessels



SFA Drug Eluting Stents
Issues to be Resolved

- Proper dose
- Ideal release kinetics
- Applying drug with or without a polymer to self-expanding stents that are implanted in a dynamic environment
- Stent fractures
- Cost

What is the Proper Dose?

Dose of Sirolimus in SIROCCO Trial:

1 mg per 6 x 80 cm SMART stent

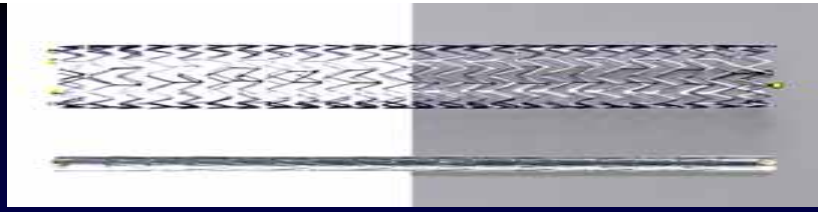
SIROCCO I
Six Month Angiographic Results

	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%

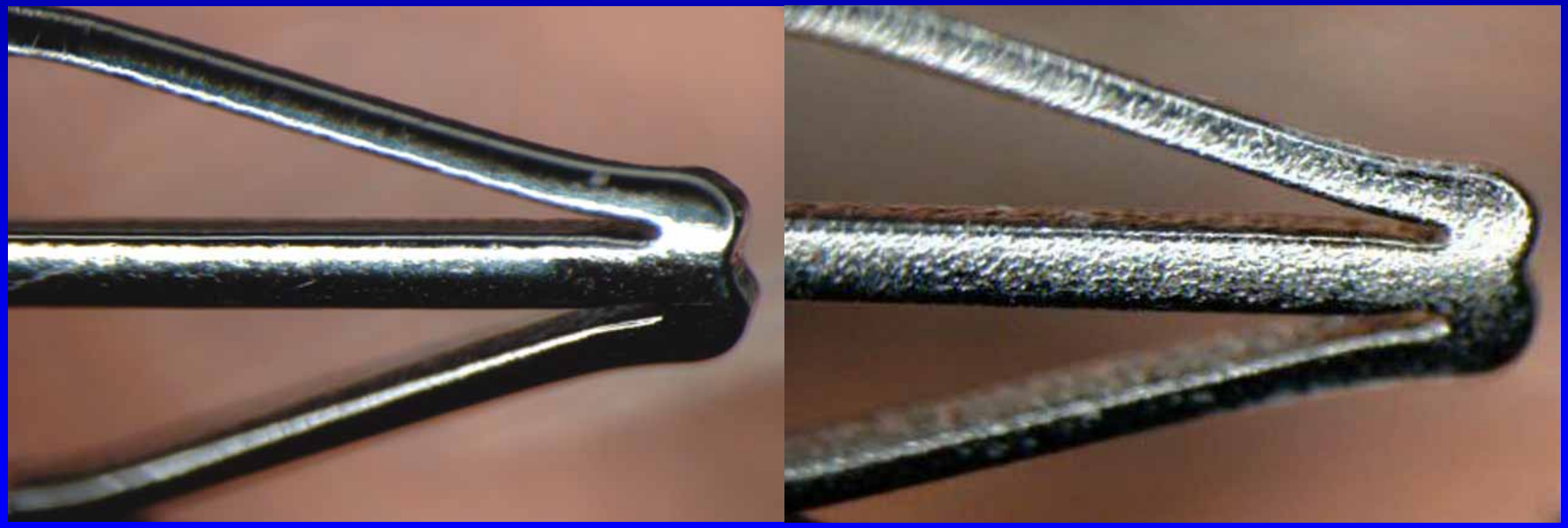
SIROCCO II
Six Month Angiographic Results

	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



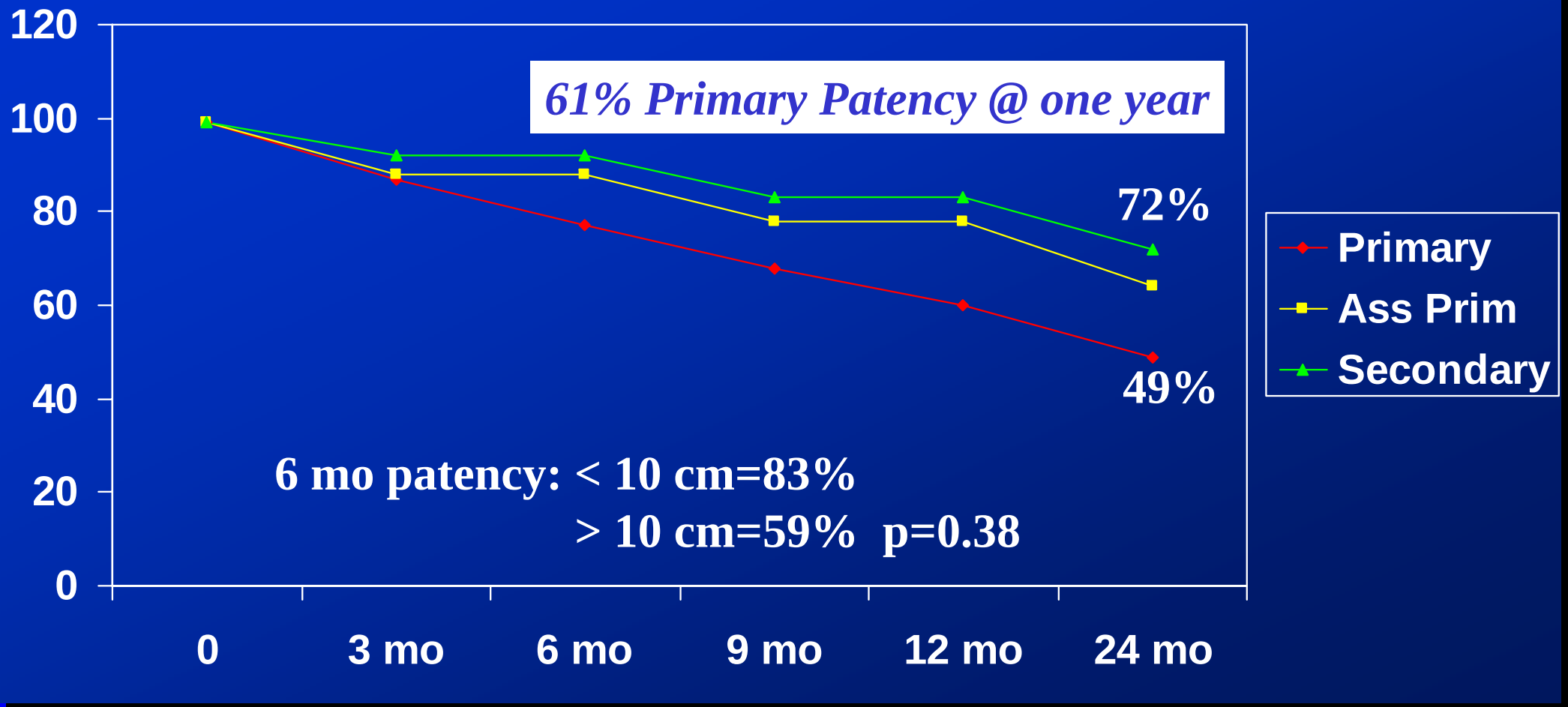
- Paclitaxel only (no polymer or binder)
- Thin coating (less than 5 microns)
- 3 microgm/mm^2 dose density
  (maximum 880 microgm total dose, largest stent)



What are the Optimal Release Kinetics?

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

SFA Wallstents



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

SFA Stenting – Nitinol Stents

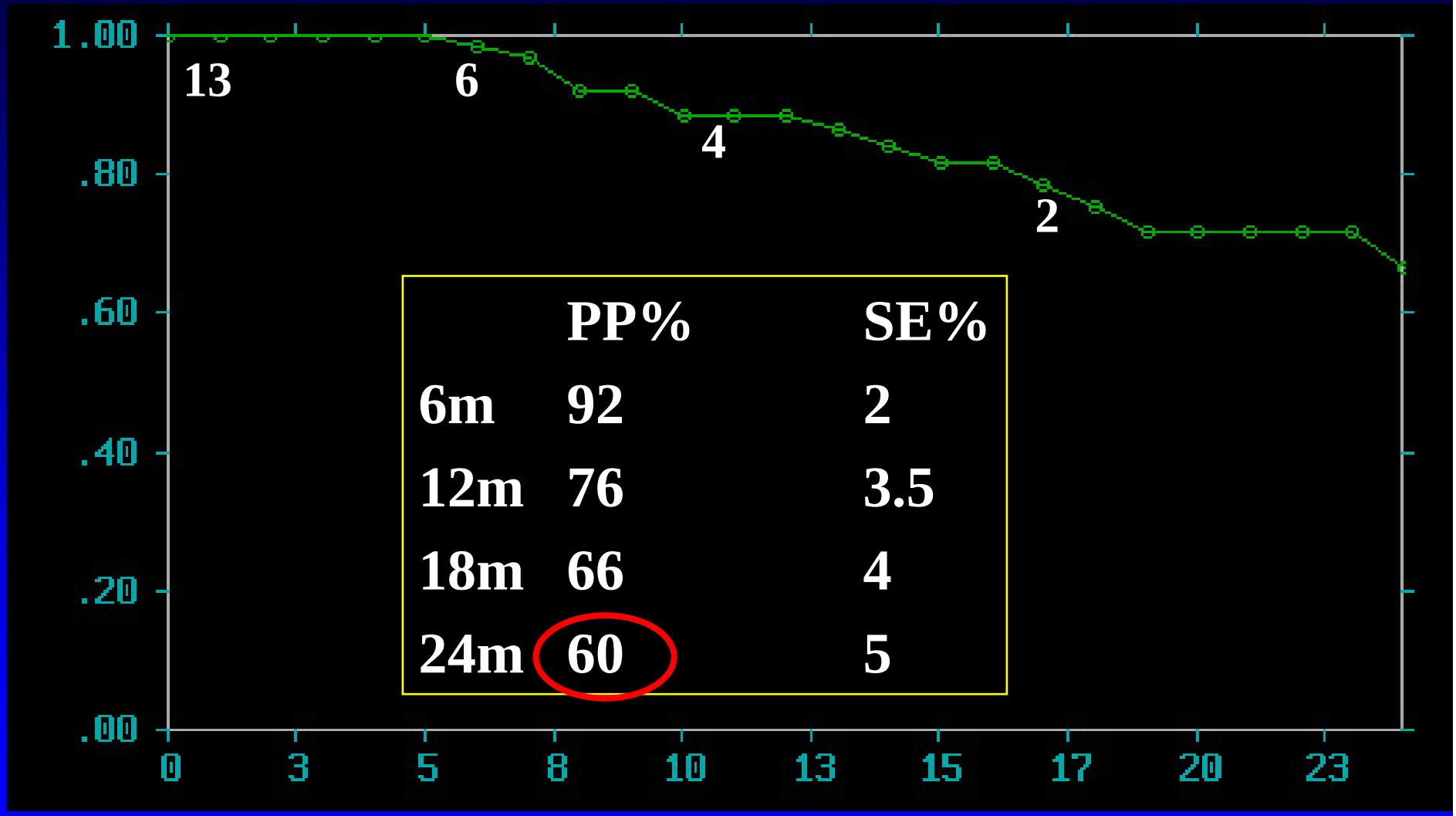
- 137 limbs in 122 patients
- Cordis SMART stent (n=246, 1.8 stents/limb)
- Mean lesion length: 12.6 cm
- Technical Success 98%
- No acute (<30 day) occlusion
- Mean follow-up 302 days
- Primary Patency:
  - 6 month: 92%
  - 12 months: 76%

Mewissen, Endovascular Today 2003

FP Primary Stenting

Results

50-99% Stenosis Free Survival



	PP%	SE%
6m	92	2
12m	76	3.5
18m	66	4
24m	60	5

The SIROCCO Studies: Stent Binary Restenosis Rates

	6 months	18 months	24 months
Follow up	**Angiographic**	**Duplex Ultrasound**	**Duplex Ultrasound**
SIROCCO I Lesion Length (mm) 88.6mm	**17.6%** (n=17)	**24%** (n=17)	**47.1%** (n=17)
SIROCCO II Lesion length (mm) 76.3 ± 45.7	**7.7%** (n=26)		
SIROCCO I & II (Pooled data)	**11.6%** (n=43)		

Are the Current DES Release Kinetics Going to Work?

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)

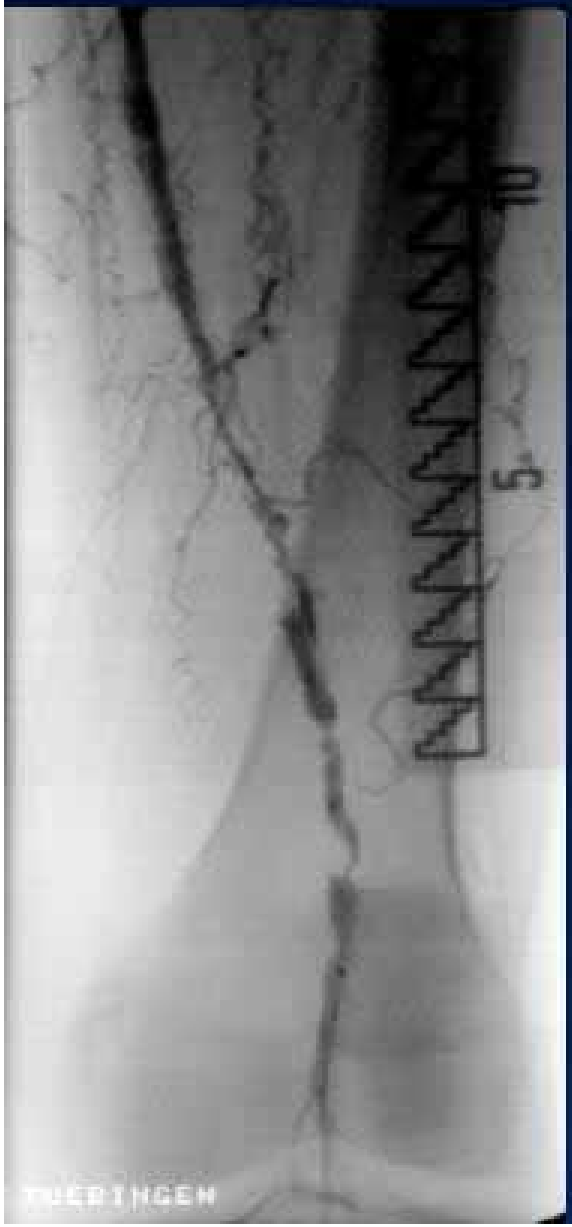
Late Failures in SIROCCO I
24 Month Follow-up

	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%

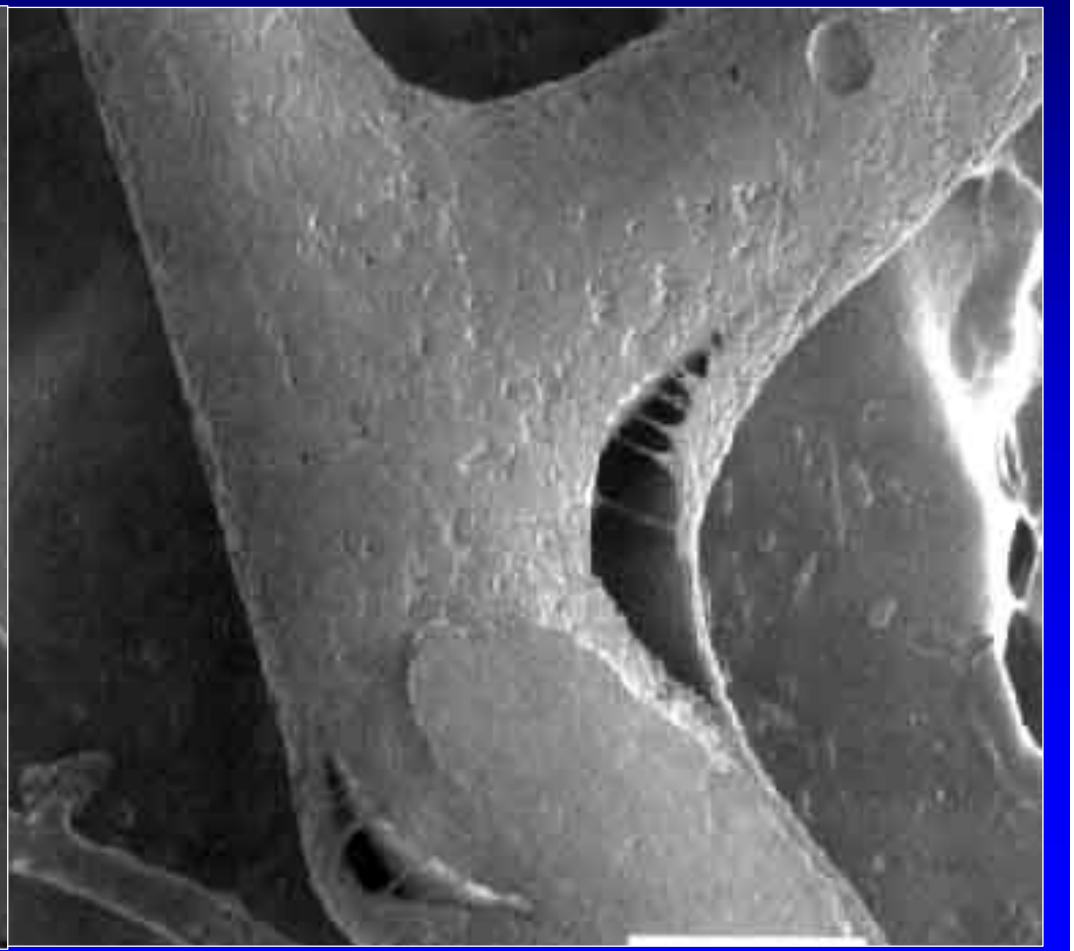
SIROCCO Cases (Pt. #11, sirolimus)



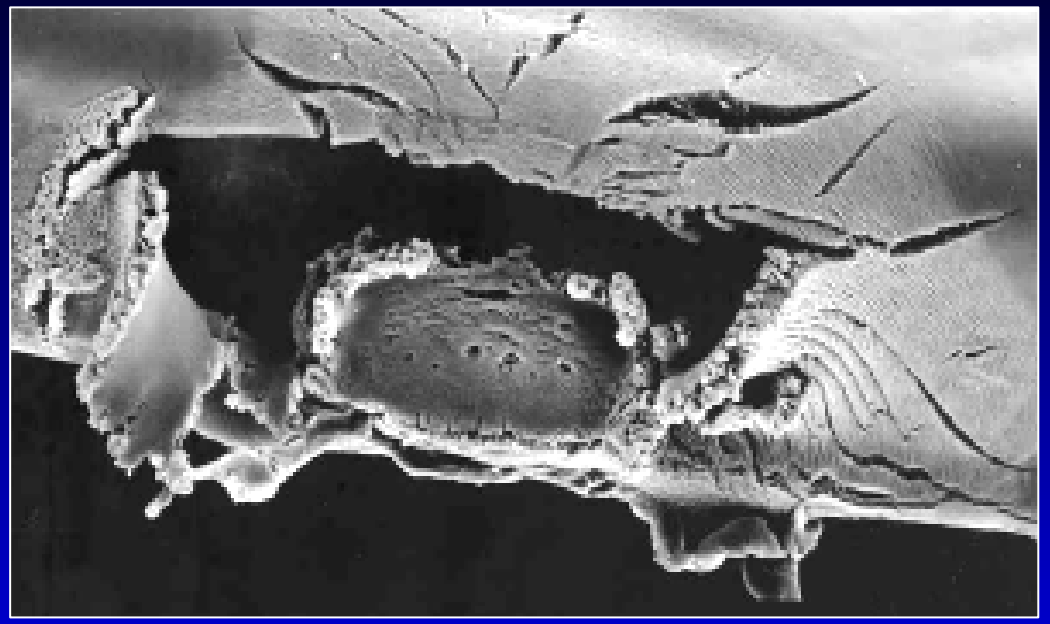
Polymer vs. No Polymer?

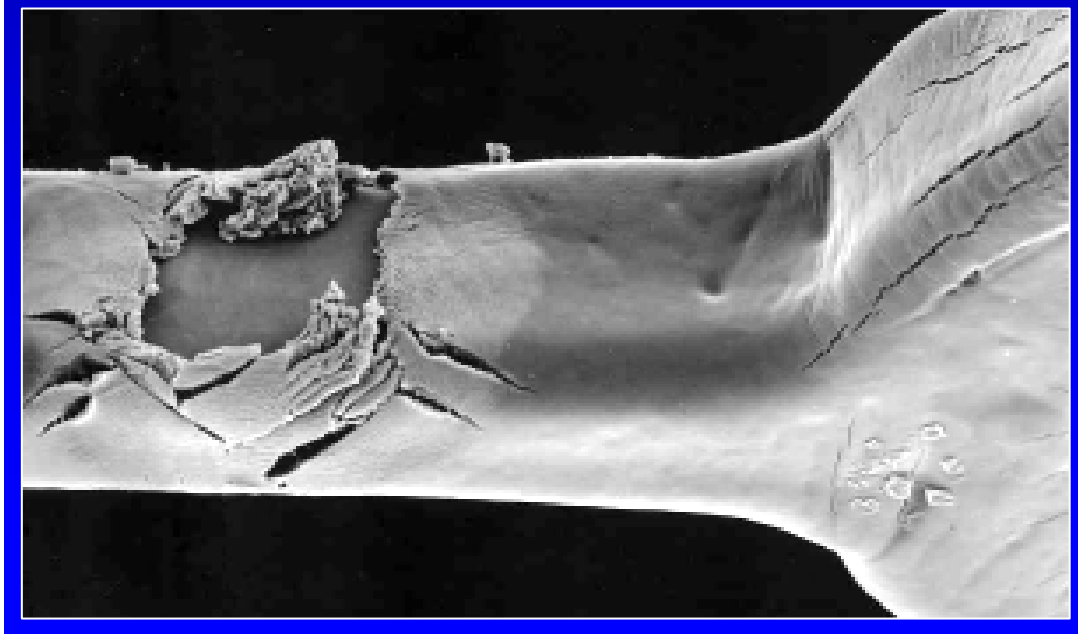
What Happens to the Polymer?

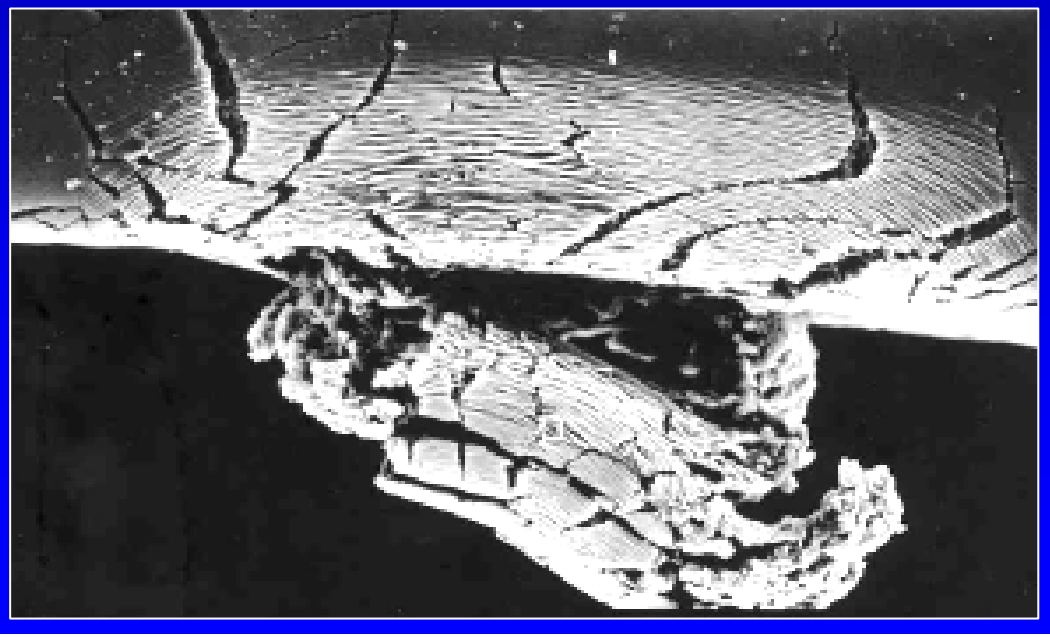
Drug-Eluting Stent



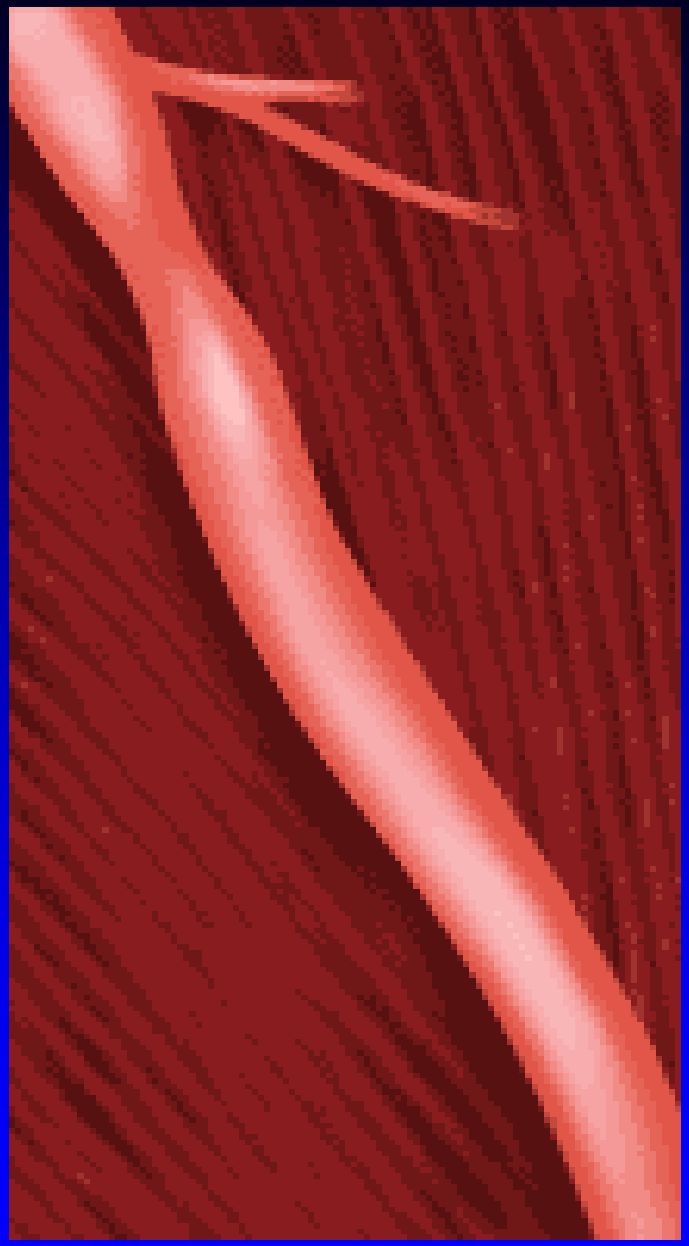
U.S. Approved Coronary DES (Ormiston, et al., TCT2004)







Mechanical Forces Applied to the SFA



Polymer-free Coating Rationale

- Paclitaxel is hydrophobic, lipophilic and highly protein bound
  - Minimal washout during stent delivery (also protected within sheath)
  - Long tissue residence time (>2 months)
- All known stent coatings have imperfections

What is the impact of stent fracture in the SFA?

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

Results of X-Ray Screening

- Minor (single strut fracture)

  In 31 cases — 48.4%

- Moderate (>one strut fracture)

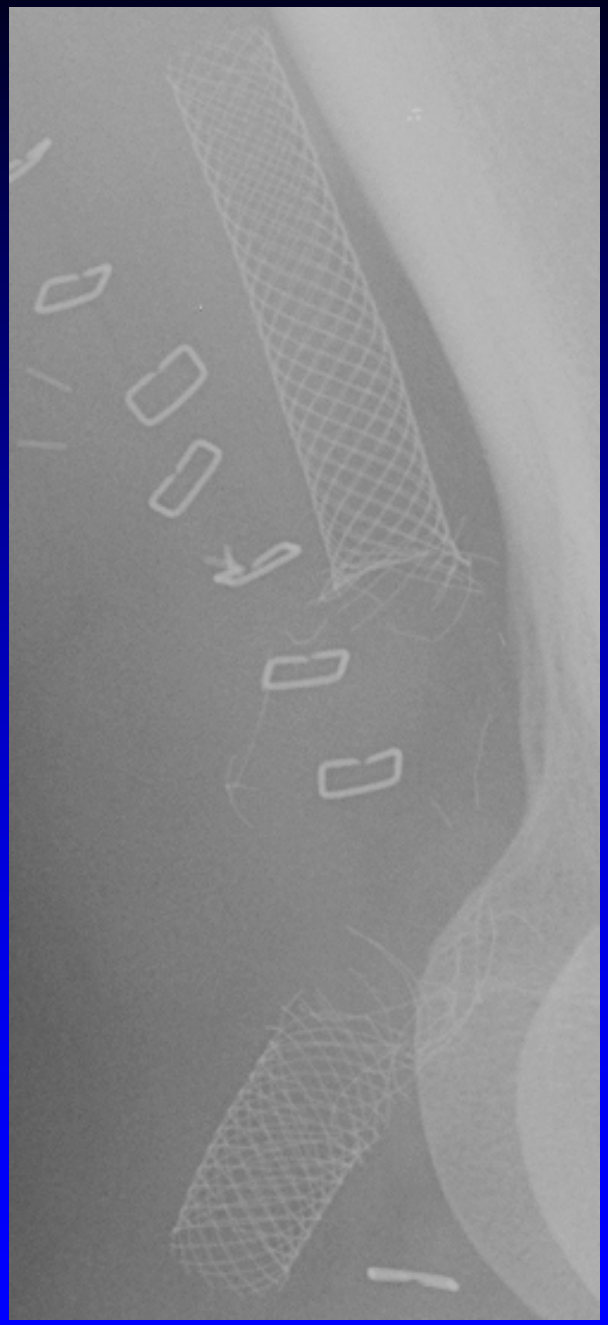
  In 17 cases — 26.6%

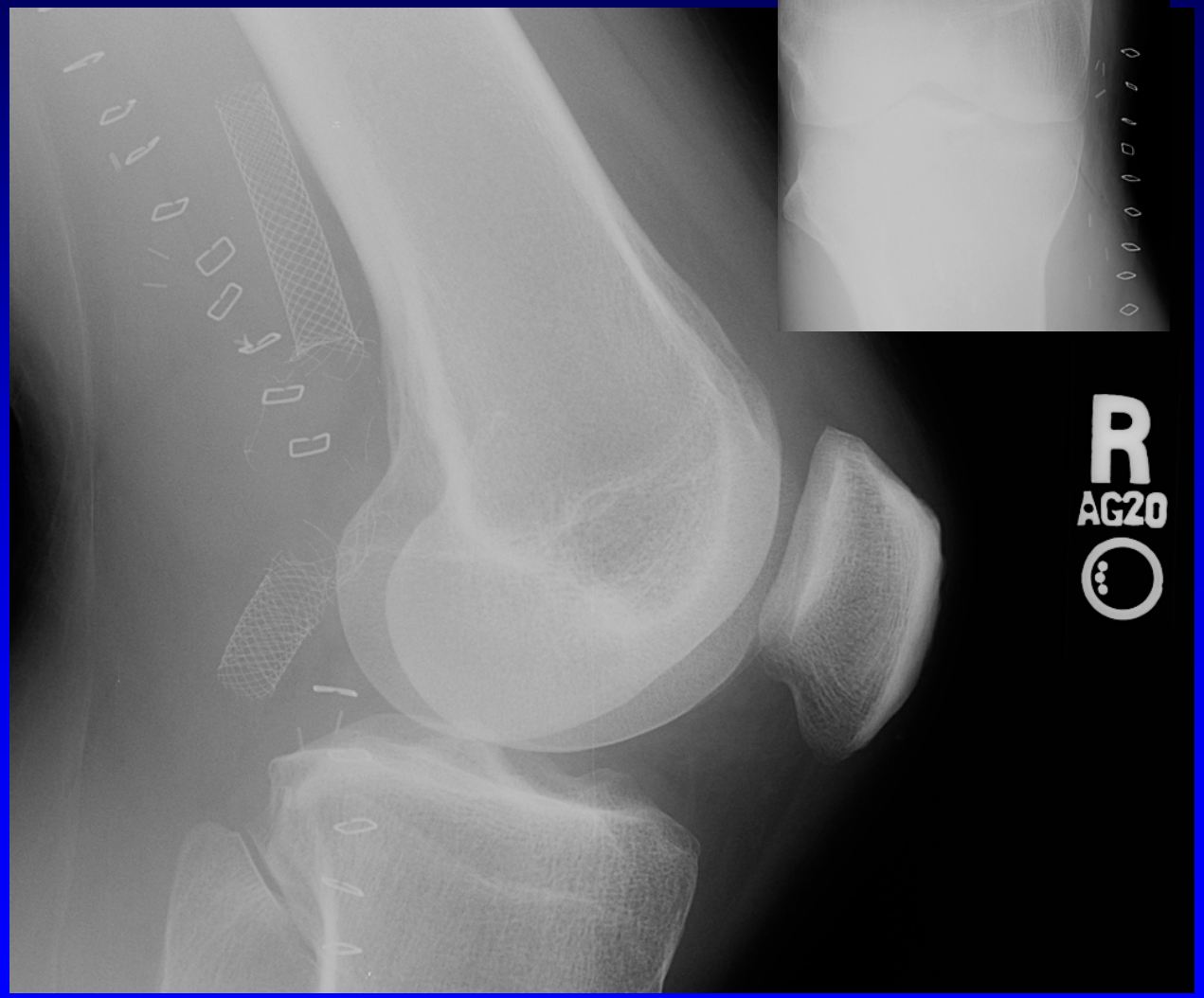
- Severe (separation of segments)

  In 16 cases — 25.0%

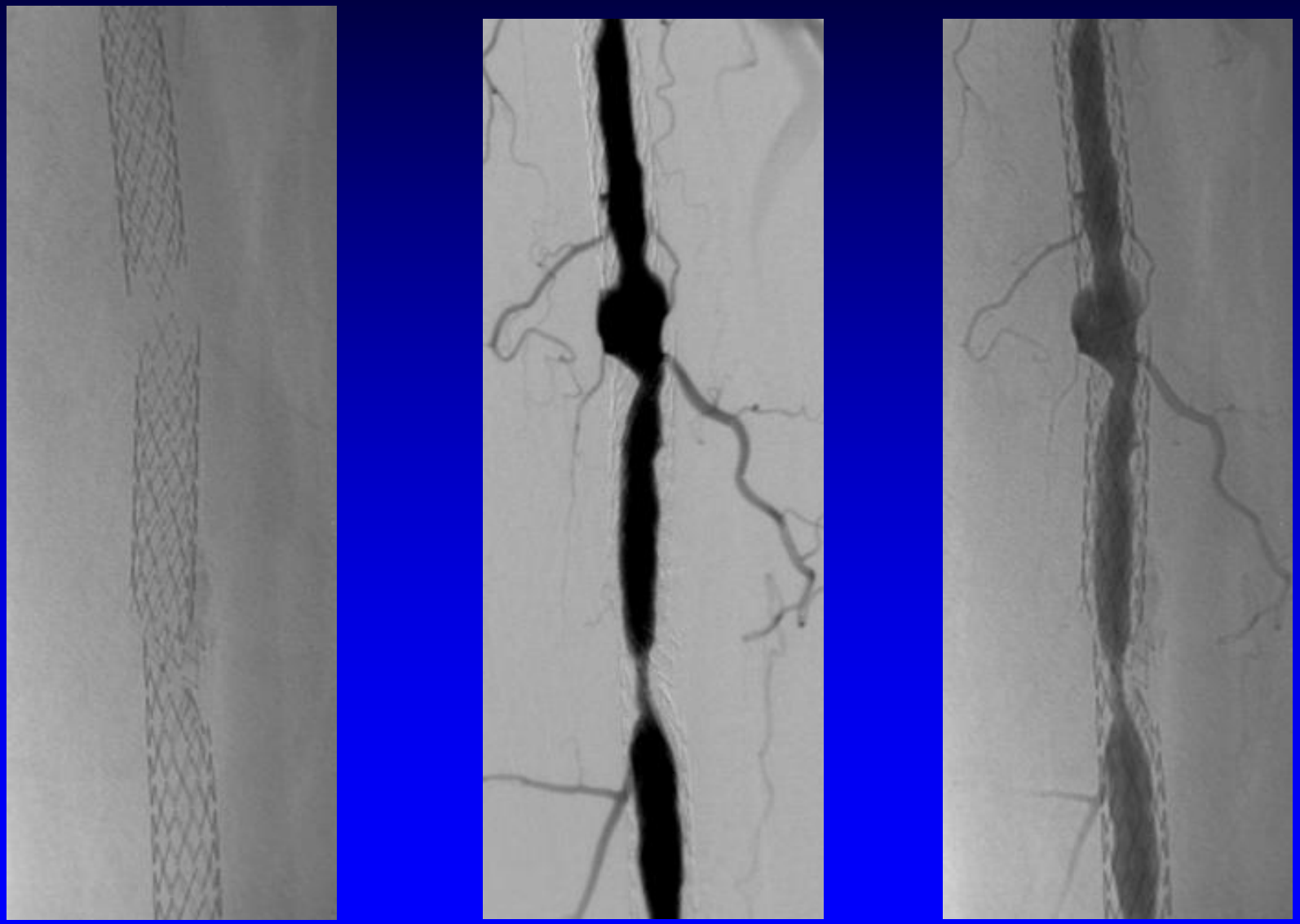
D. Scheinert

Stent Fracture



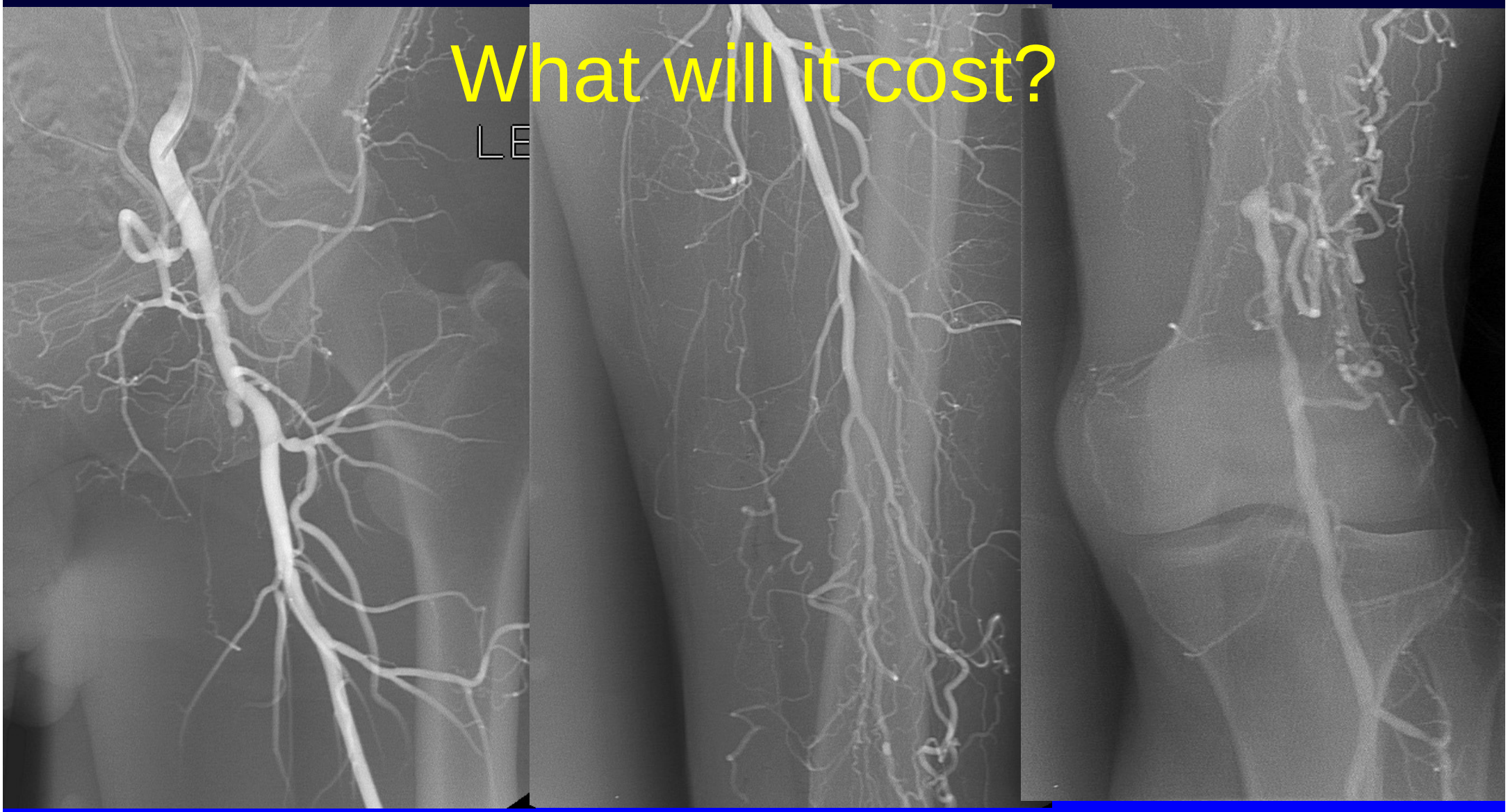


Femoropopliteal Stent-Fracture



D. Scheinert

What will it cost?

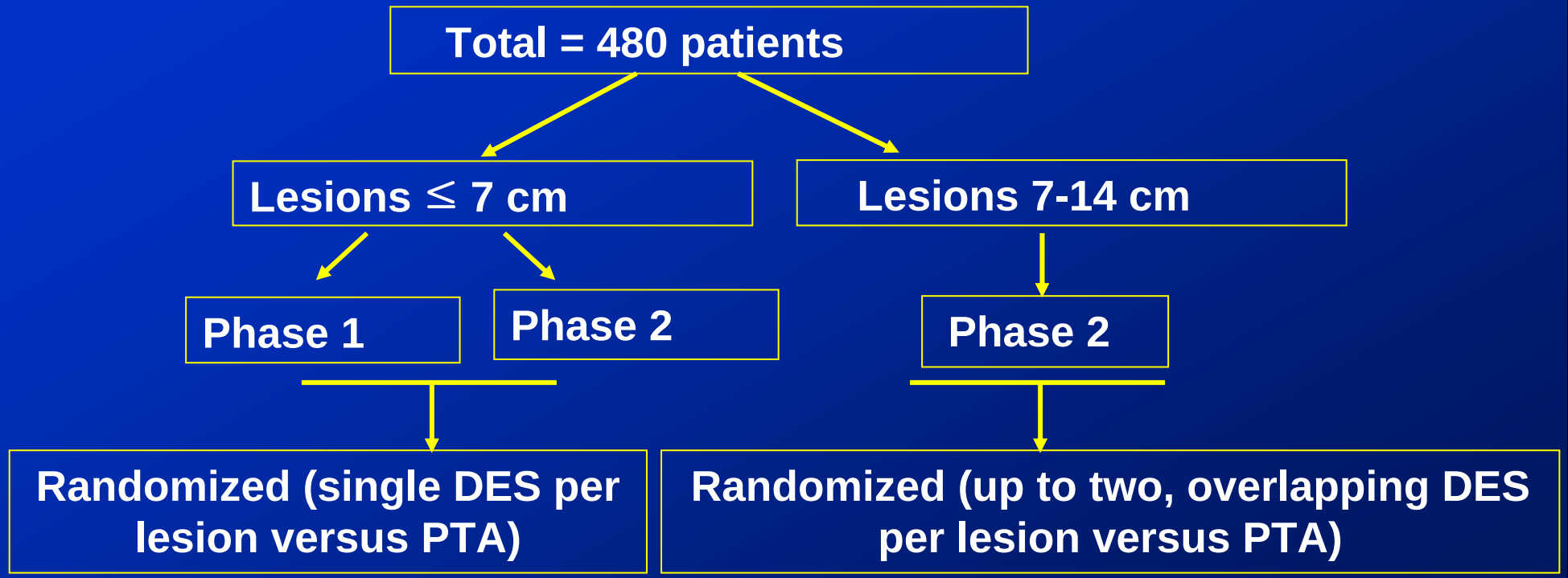


SFA DES – Where do we Stand?

- **SIROCCO II confirmed the short term efficacy of the slower release formulation identified in SIROCCO I.**
- **Good outcomes in the bare SMART stent arm of the trial with an overall 6 month angiographic pooled restenosis rate of 11.6% (n=43) and an 18 month rate of 22.2% (n=45)**
- **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.**

Study Design – Phase 2

- Controlled, randomized, multicenter study
- Up to two lesions, one in each limb, may be treated and up to two stents (one stent in Phase 1) may be used per lesion



Substudies

- Angiographic Substudy
  - 6 months in Phase 1 (plus IVUS)
  - 12 months in Phase 2
- Long-term Duplex Ultrasound Substudy
  - 2, 3, 4, and 5 years
  - All DES patients
  - Subgroup of PTA patients
- Pharmacokinetic Substudy (DES group)

Summary

- Still many reasons for optimism given the excellent results with DES in the coronary arteries
- No guarantee that DES will work in the SFA
- Many unanswered questions
- Given the current pace of investigation, commercially available DES for the SFA is several years away (at least!)