Eberhard-Karls-University of Tubingen
Department of Diagnostic Radiology

Neuestes aus der Therapie der pAVK – beschichtete Stents + Ballons

Gunnar Tepe

Berlin Dezember 08

Local Drug Delivery
Basic Principles

To be modified

Stent based

A

Stent design (homogenoius delivery)
Delivery kinetic
„Coating/Adsorption“
Drug

Short time contact

B

Mode of delivery (with a balloon, fluid)
Adjuncts
Drug

DES in the AFS

SIROCCO Study Design

A1

- blinded, randomized, prospektiv
- 36 patients (Sirocco I) + 57 patients (Sirocco II)
- primary endpoint: Restenosis in stent after 6 months

Duda et al.: Circulation. 2002; 106: 1505-1509
Tepe et al: J Cardiovasc Surg. 2005; 46: 249-259
Duda et al: J Endovasc Ther. 2006; 13: 701-710

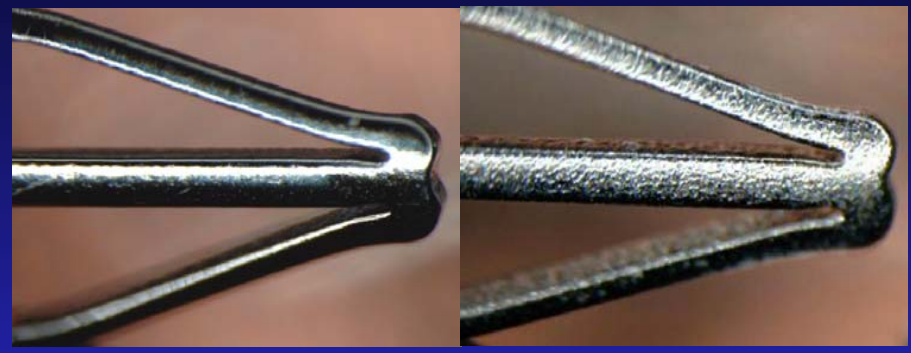
A1

SIROCCO II
Restenosis Rate

	6m	9m	18m	24m	36m	48m
Sirolimus Restenosis Rate	3.8% (1/26)	7.7% (2/26)	15.4% (4/26)	29.2% (7/24)	31.8% (7/22)	42.1% (8/19)
"Bare metal" Restenosis Rate	0% (0/26)	11.5% (3/26)	20.0% (5/25)	20.0% (5/25)	33.3% (7/21)	41.2% (7/17)
Total Restenosis Rate	**1.9%** (1/52)	**9.6%** (5/52)	**17.6%** (9/51)	**24.5%** (12/49)	**32.6%** (14/43)	**41.7%** (15/36)

More Drug Eluting Stent Trials

A2



Zilver PTX Trial (Cook Inc.)

a. PTX adsorbed

b. Studies: 1000 patients

Prim. Endpoints

USA: 240 patients Stent vs. PTA

12 months effictiveness
Freedom from TLR
- a. Interv.: Reststenosis >30%
- b. Clin. driven Reintervention

12 months safety

Europe: 760 patients (Safety DES)

6 months event-free survival
- a. serious adverse event,
- b. worsening Rutherford by 2 classes

Lesion Characteristics

A2

Characteristic	Randomized Study (Phase 1)		Registry Study
	PTA	ZPTX	ZPTX
Number of lesions	33	29	91
TASC class: A	13 (39%)	13 (45%)	12 (13%)
B	9 (27%)	3 (10%)	26 (29%)
C	6 (18%)	9 (31%)	36 (40%)
D	1 (3%)	1 (3%)	17 (19%)
Calcification	23 (70%)	24 (83%)	66 (72%)
Total occlusion	5 (15%)	4 (14%)	37 (40%)
In-stent restenosis	0 (0%)	0 (0%)	24 (26%)
Other stenosis in artery > 50%	1 (3%)	6 (21%)	22 (24%)
Average stents per lesion	1.0	1.0	2.2

Baseline Angiographic Data

A2

	Randomized Study (Phase 1)		Registry Study
	PTA (N = 33 lesions)	ZPTX (N = 29 lesions)	ZPTX (N = 91 lesions)
Lesion Length (cm)	3.6 ± 2.0 (range 1 to 7)	4.1± 3.1 (range 1 to 10)	10 ± 8.1 (range 1 to 33)
Proximal RVD (mm)	5.2 ± 1.0	5.0 ± 1.1	5.3 ± 0.8
Distal RVD (mm)	5.3 ± 1.0	4.9 ± 1.1	5.1 ± 0.8
MLD in lesion (mm)	1.3 ± 0.8	1.1 ± 0.7	0.6 ± 0.7
% Diameter Stenosis	76 ± 15	78 ± 14	89 ± 12

A2

6-Month Effectiveness

Study	Freedom from TLR
Randomized Study (Phase 1)	
PTA Group	52% (17/33 lesions)
No PTA failure	100% (17/17)
Acute PTA failure → Bare Zilver®	75% (6/8)
Acute PTA failure → Zilver® PTX™	100% (8/8)
ZPTX Group	90% (26/29 lesions)
Registry Study	90% (82/91 lesions)

Registry Study Effectiveness

A2

TASC A and B	92% (of 38 lesions)
TASC C and D	89% (of 53 lesions)
De novo	91% (of 57 lesions)
Restenotic	88% (of 34 lesions)
In-stent Restenosis	92% (of 24 lesions)
≤ 7cm lesions	91% (of 43 lesions)
> 7 cm lesions	90% (of 48 lesions)

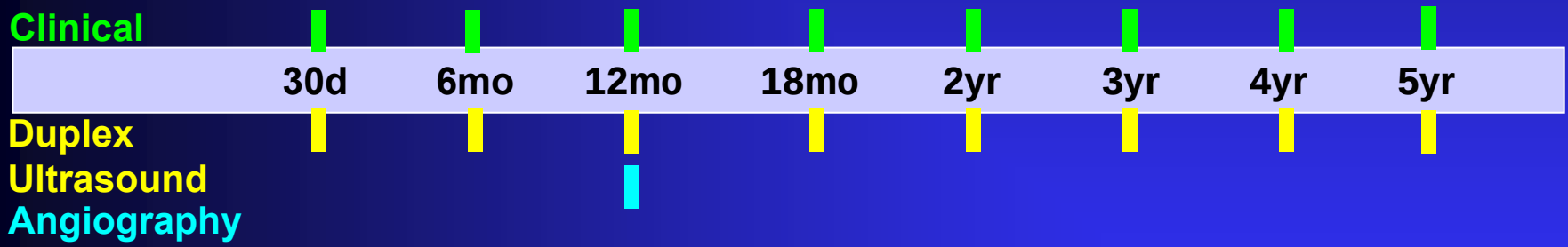
More Drug Eluting Stent Trials

A3

Strides Trial (Abbott Vascular)

a. Everolimus coating

b. Study: 100 patients



Short time local drug contact:

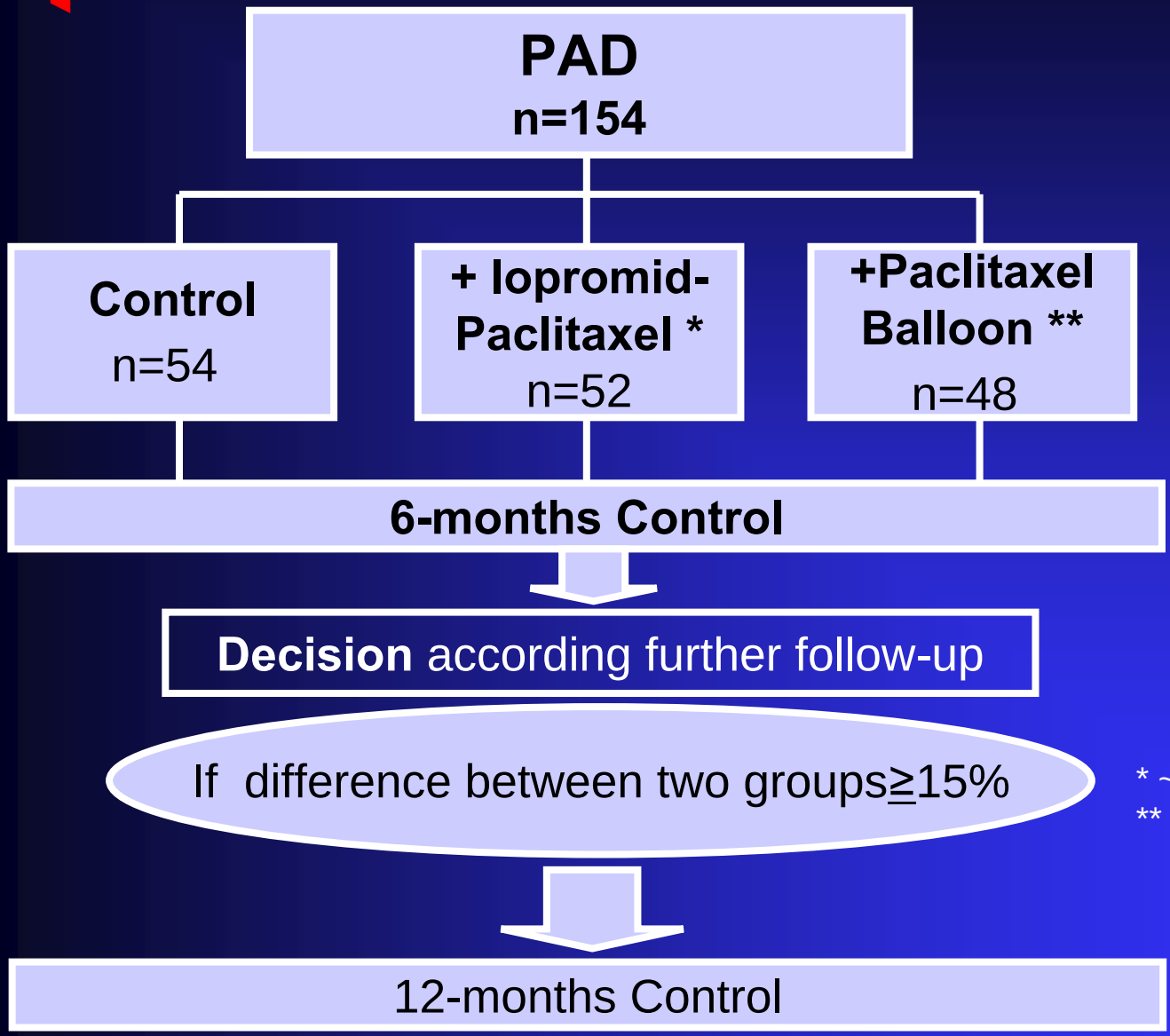
…the alternative approach

DES vs. Short Time Drug Contact

- DES dramatically improve interventional cardiology
- Potential disadvantages
  - DES require stent implantatio
  - Long-term effects of th eric matrix
  - Drug concentrat highest at the stent struts where heal ost important
  - SEA fractures? SIROCCO?

Do we need sustained drug release?

Thunder trial – study design



Design
- prospective
- randomized
- blinded
- multi-center

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

Inclusion criteria

- Occlusion or stenosis ≥ 2 cm
  (mean grade of stenosis ≥ 70%)
- SFA, APOP
- History > 6 weeks (no thrombolysis)
- Successful guide wire passage
- Rutherford 1 - 5
- Age: 18 - 95 years
- Informed consent, agreement for f/u

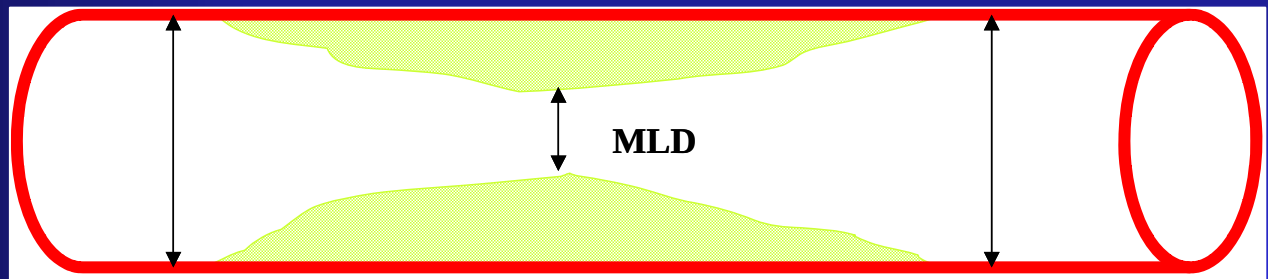
Exclusion criteria

- Distal run-off less than one artery
- Known allergy: Aspirin, Clopidogrel, Heparin, Paclitaxel, Contrast media
- Creatinine > 2.0 mg%
- PTA directly at the proximal origin of the SFA

Primary endpoint

Late Lumen Loss (LLL)

Quantitative Angiography



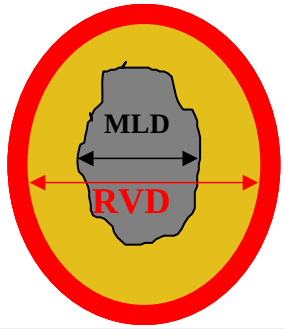
RVD (prox)

RVD (distal)

Minimal Lumen Diameter = MLD

Reference Vessel Diameter (RVD) = average of vessel diameter proximal and distal to the lesion

Percent Diameter Stenosis (%DS) = ratio of MLD to RVD



Patient characteristics

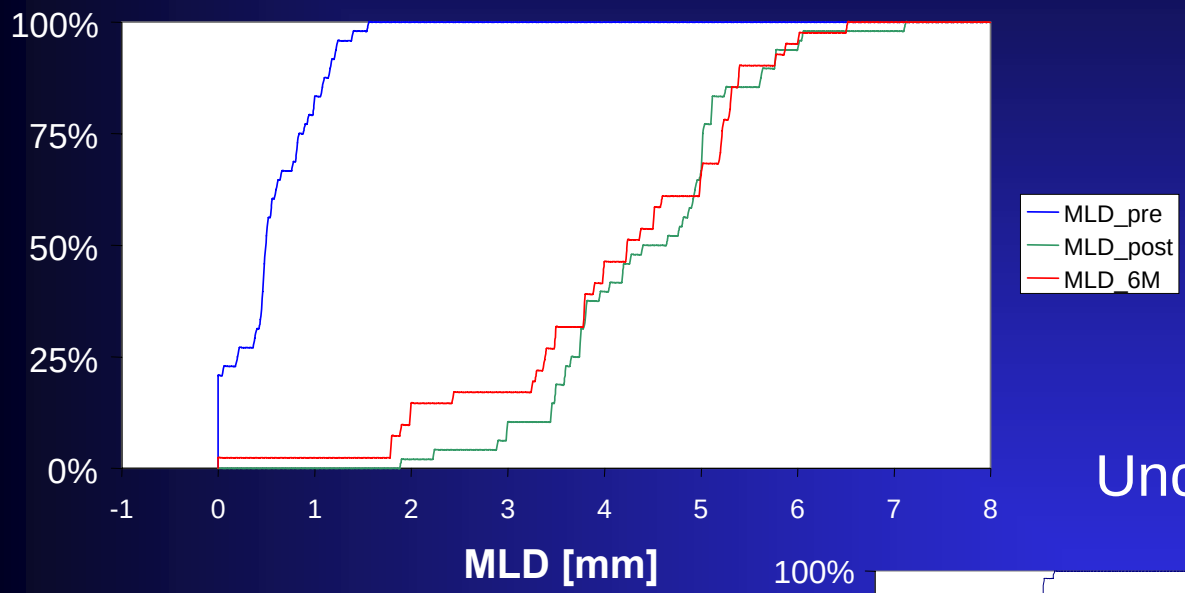
Characteristics	Uncoated BA n = 54	Uncoated BA + Paclitaxel i.a. n = 52	Paccocath n = 48
Mean age	68 ± 9	68 ± 8	69 ± 8
Gender m/f	1.8	2.3	1.8
Smoker [%]	22	27	23
Diabetes [%]	46	52	50
Hypertension [%]	83	87	79
Hypercholesteremia [%]	63	65	69

Lesion characteristics

Characteristics	Uncoated BA n = 54	Uncoated BA + Paclitaxel i.a. n = 52	Paccocath n = 48
Lesion lengths [cm] pre-procedure	7.4 ± 6.7	7.4 ± 6.5	7.5 ± 6.2
Mean degree of stenosis [%]	91	88	89
Occlusion [%]	26	27	27
Mean number of lesions treated	1.6	1.7	1.8
De-novo lesion [%]	70	58	62

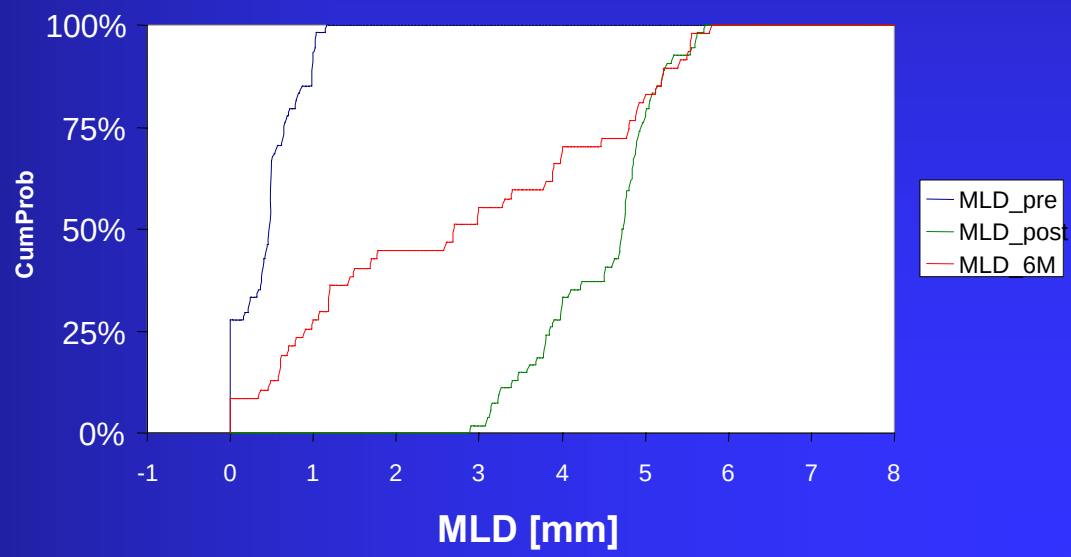
Cumulative MLD at month 6

Paccocath

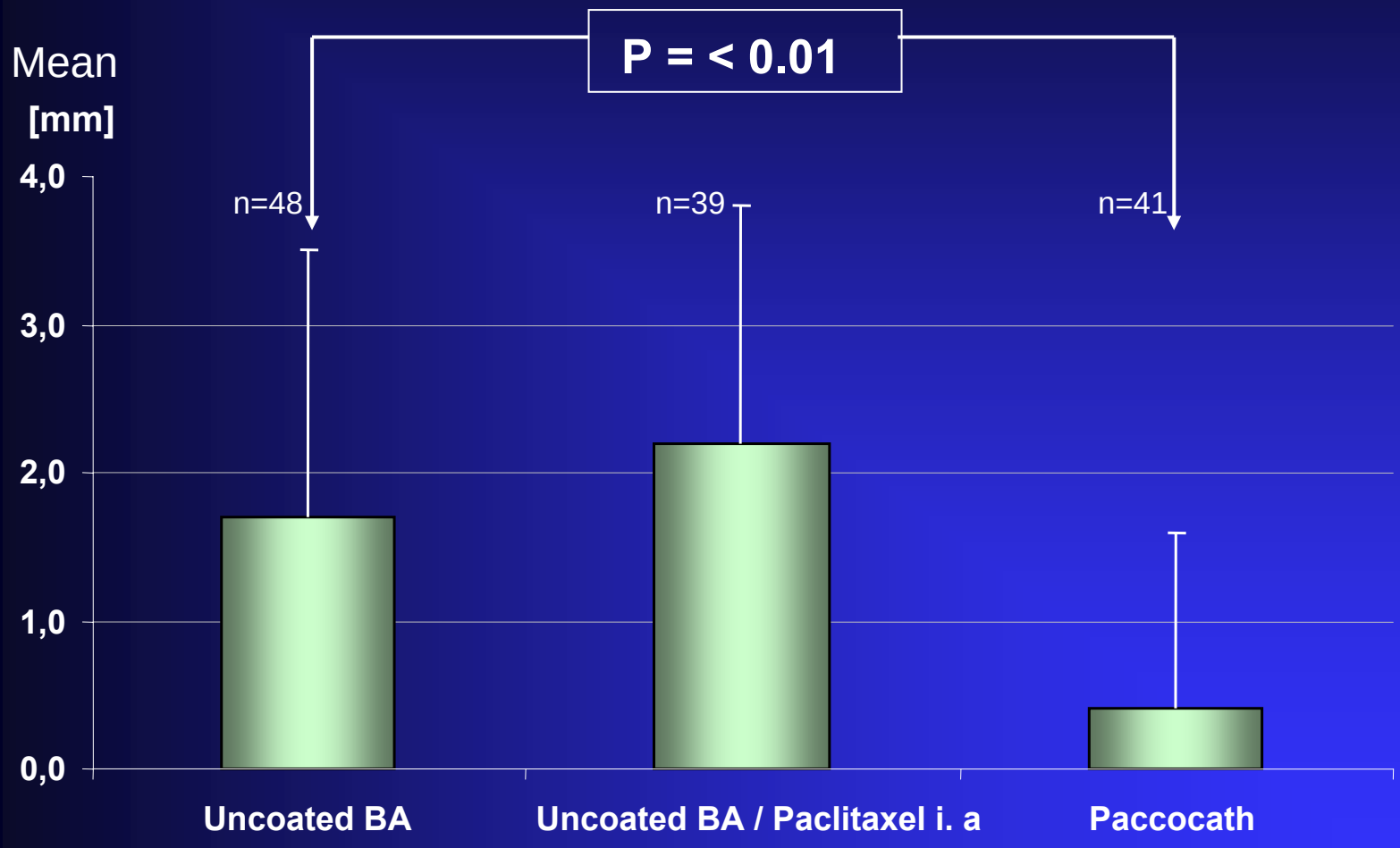


$P < 0.01$

Uncoated BA



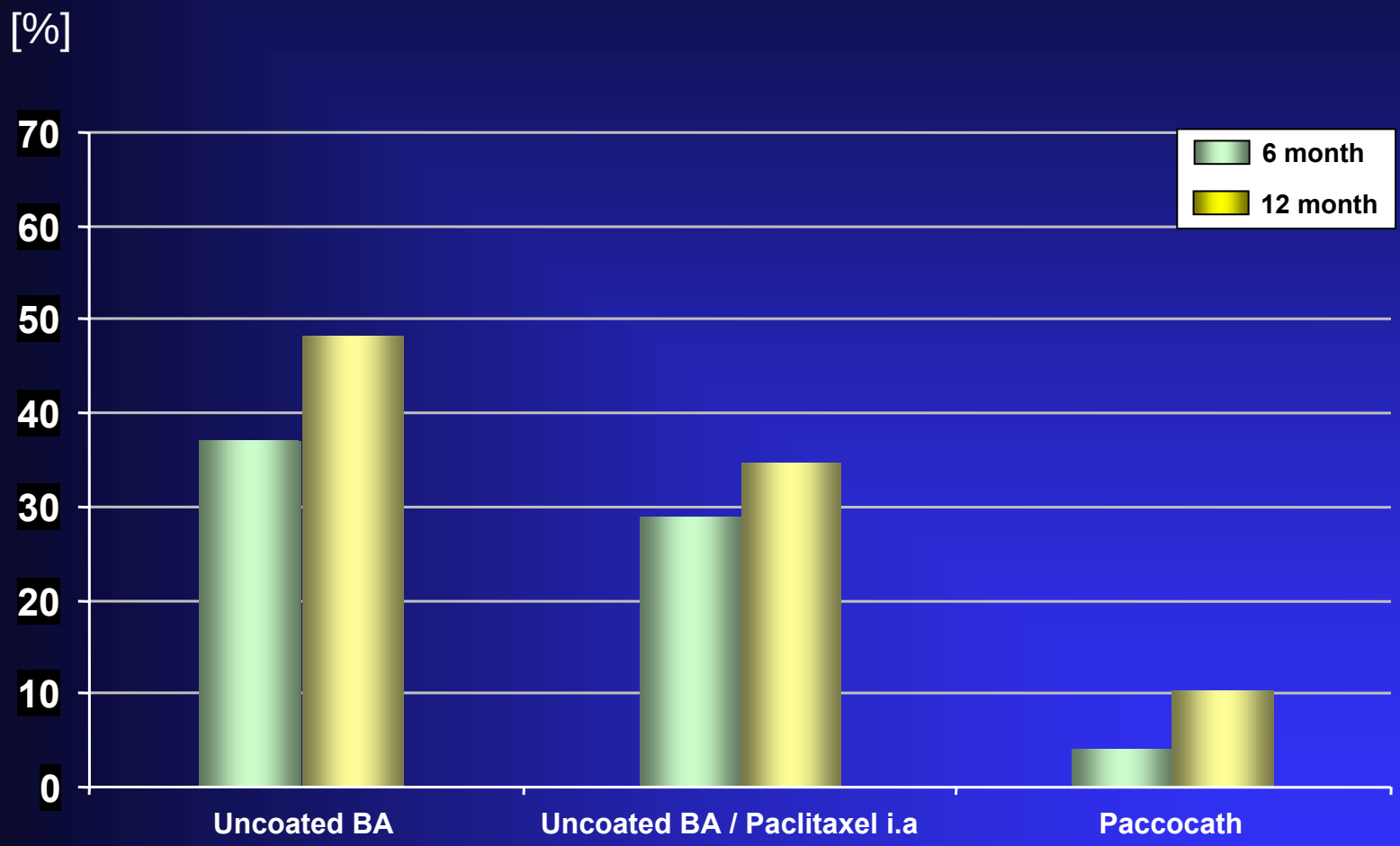
Late lumen loss at month 6*



* for available patients

Wilcoxon test

Target lesion revascularization*

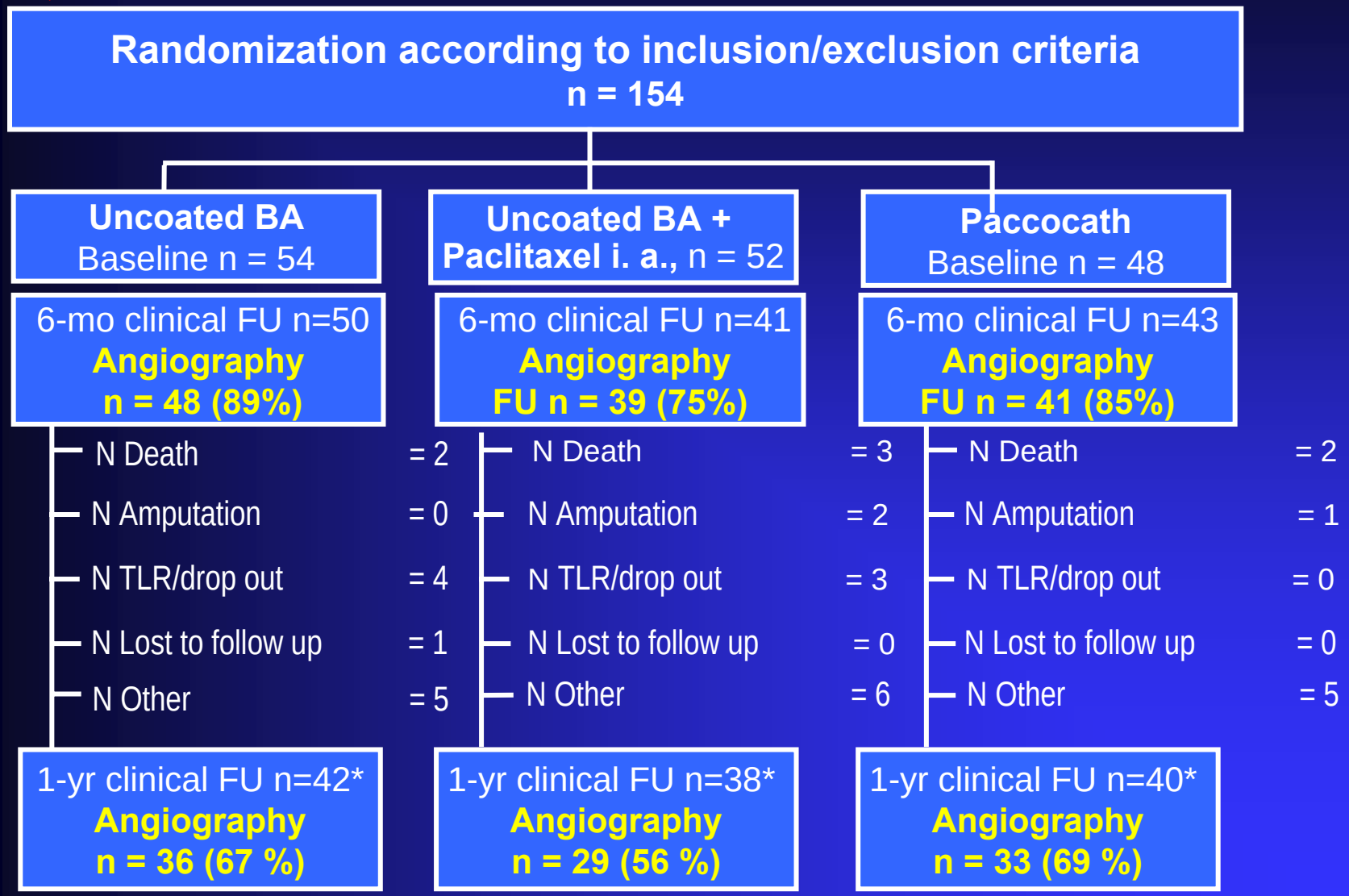


BA = Balloon angioplasty

* Including 12 months re-intervention

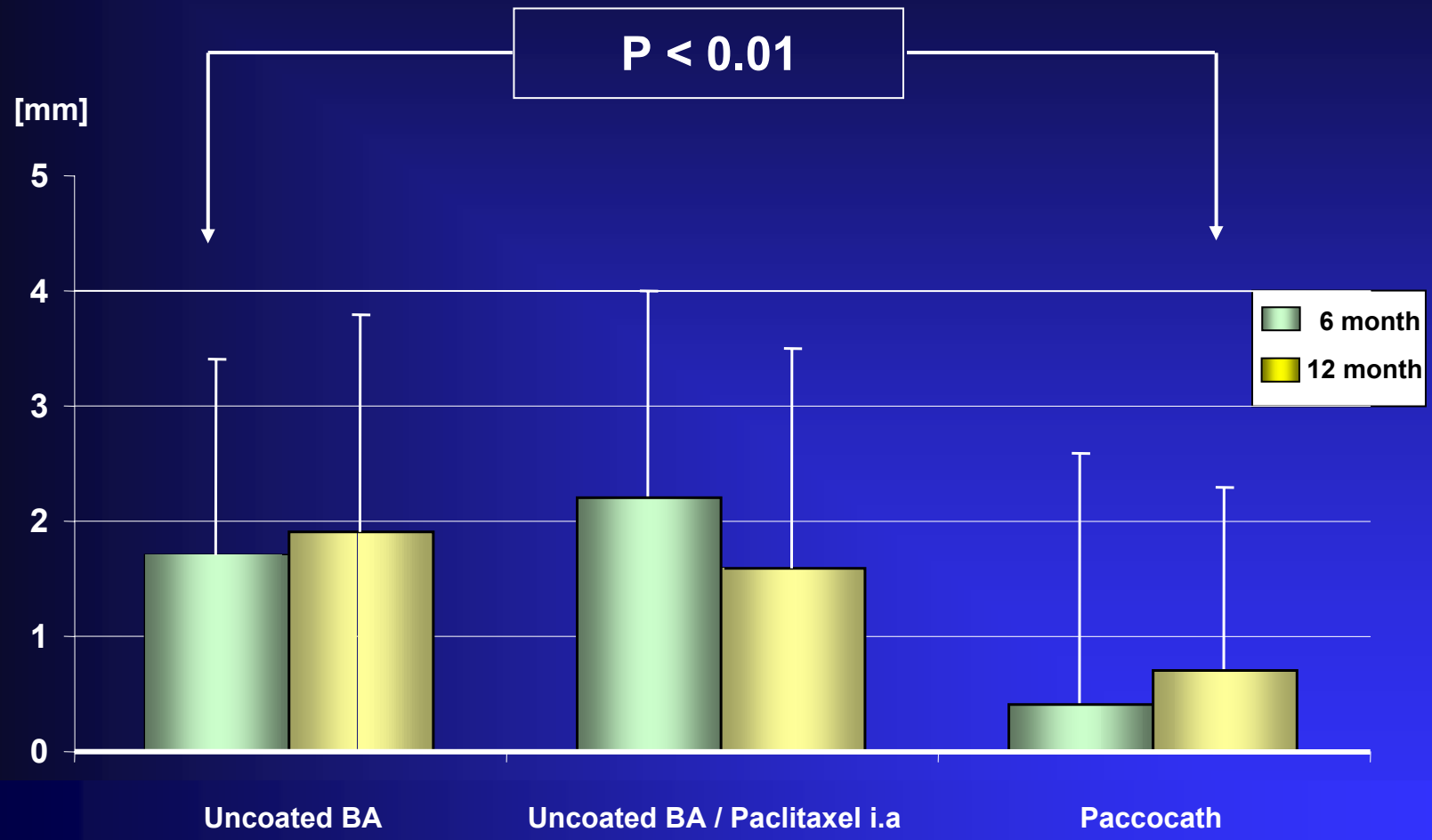
Disposition of patients at month 12

Reasons for not having a 12 month follow up



* Including patients with telephone contact

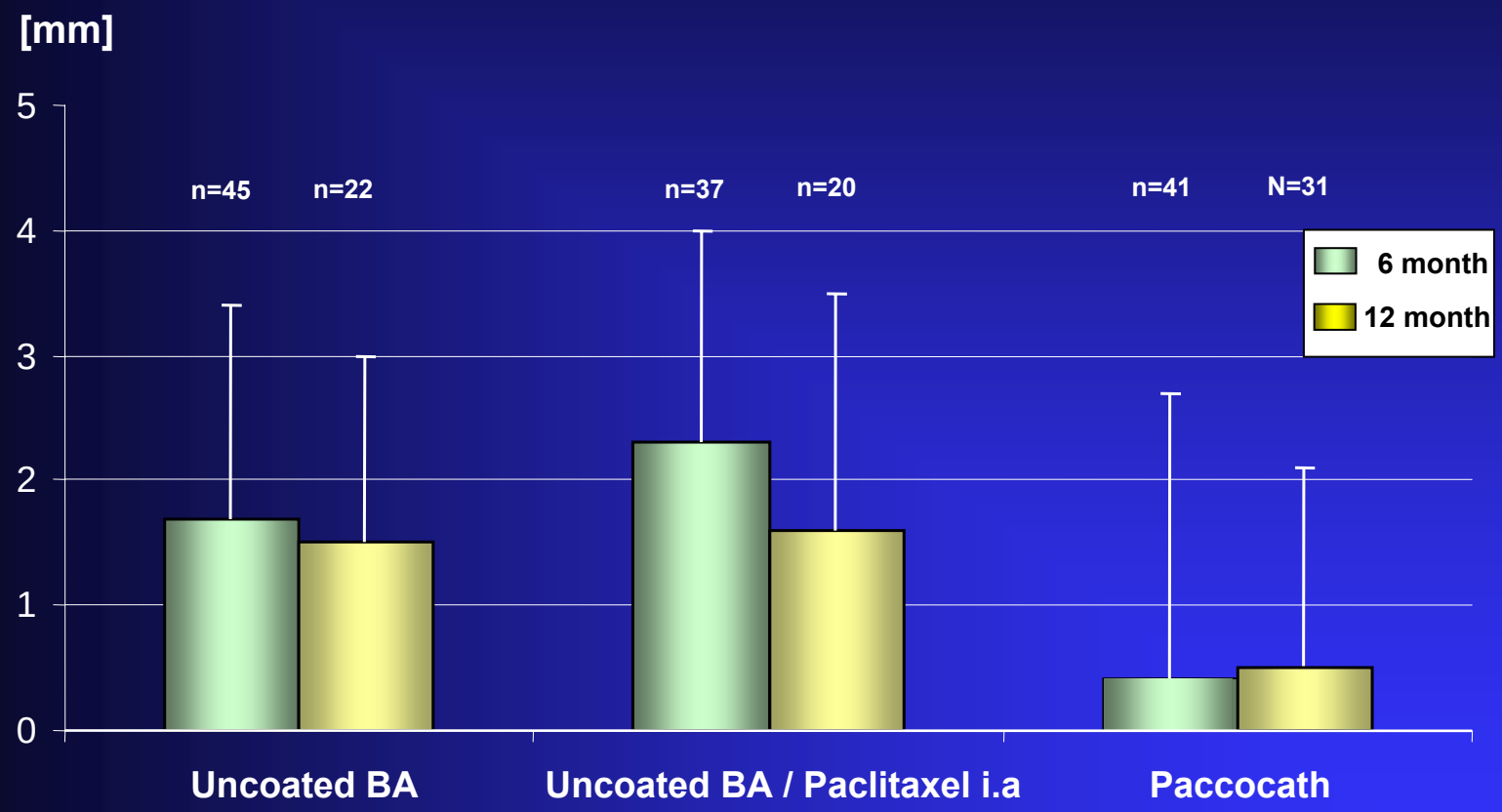
Primary Endpoint: Late Lumen Loss*



BA = Balloon angioplasty

* Available patients

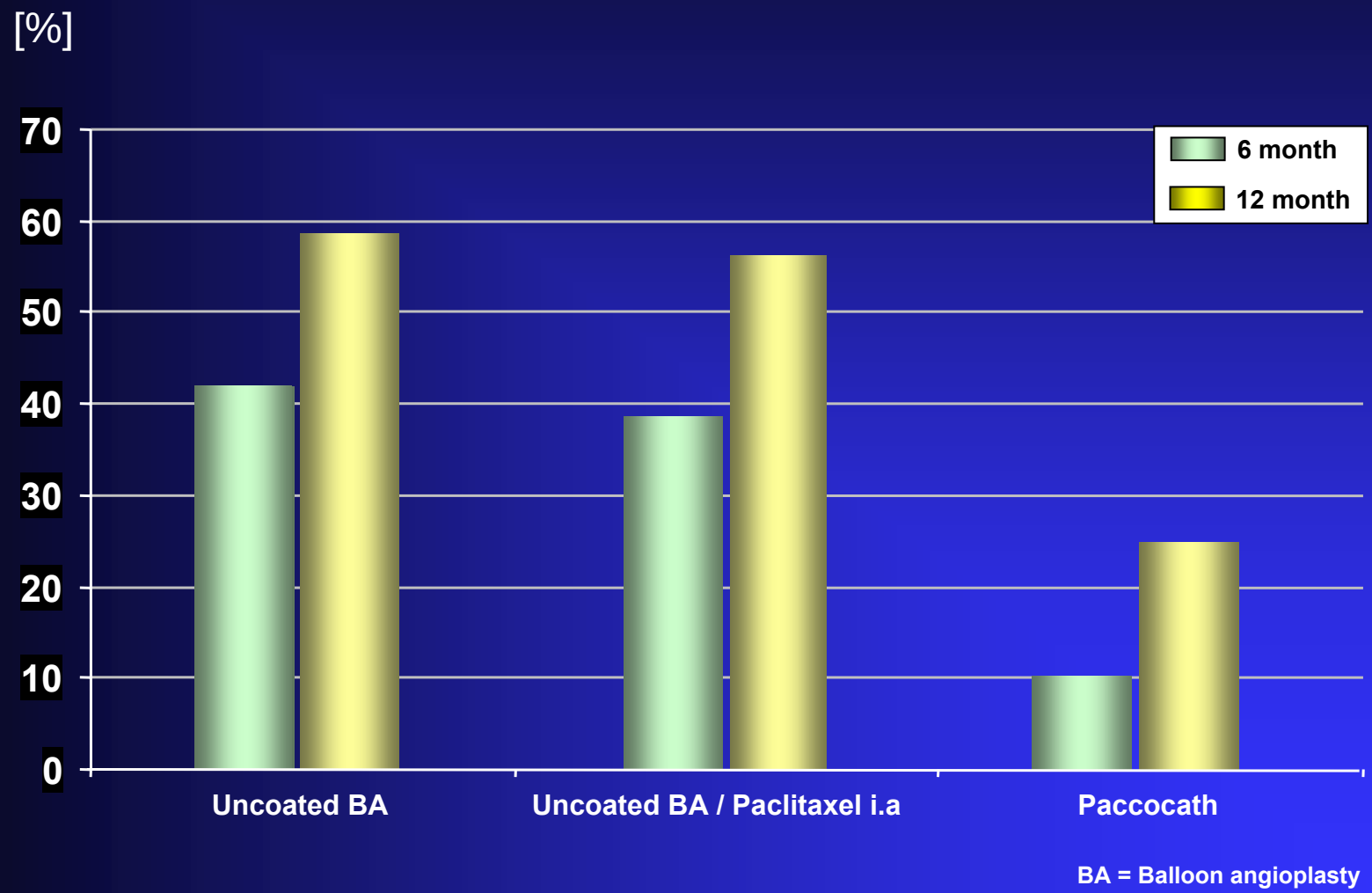
Late lumen loss
in patients WITHOUT previous TLR



BA = Balloon angioplasty

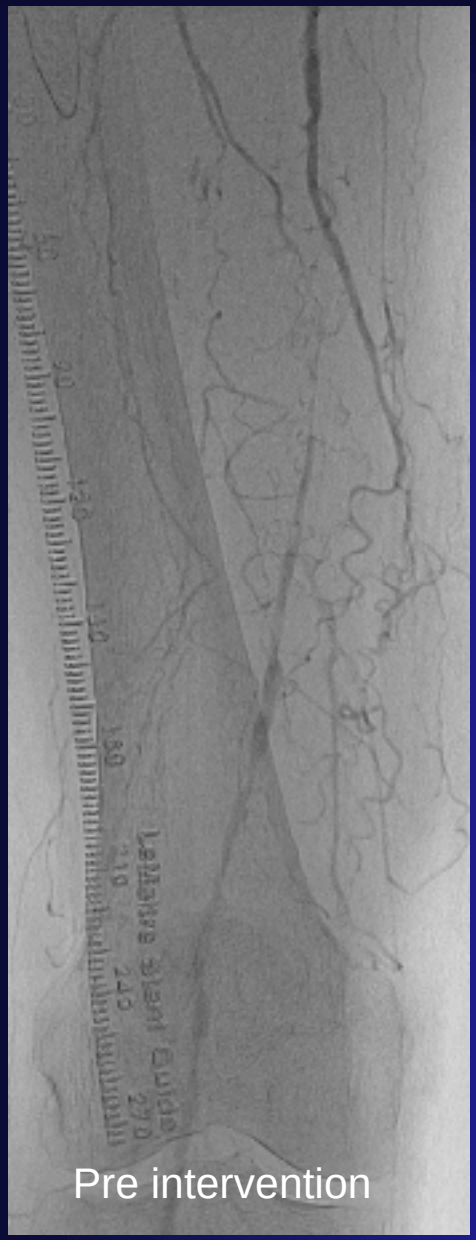
Binary Restenosis Rate

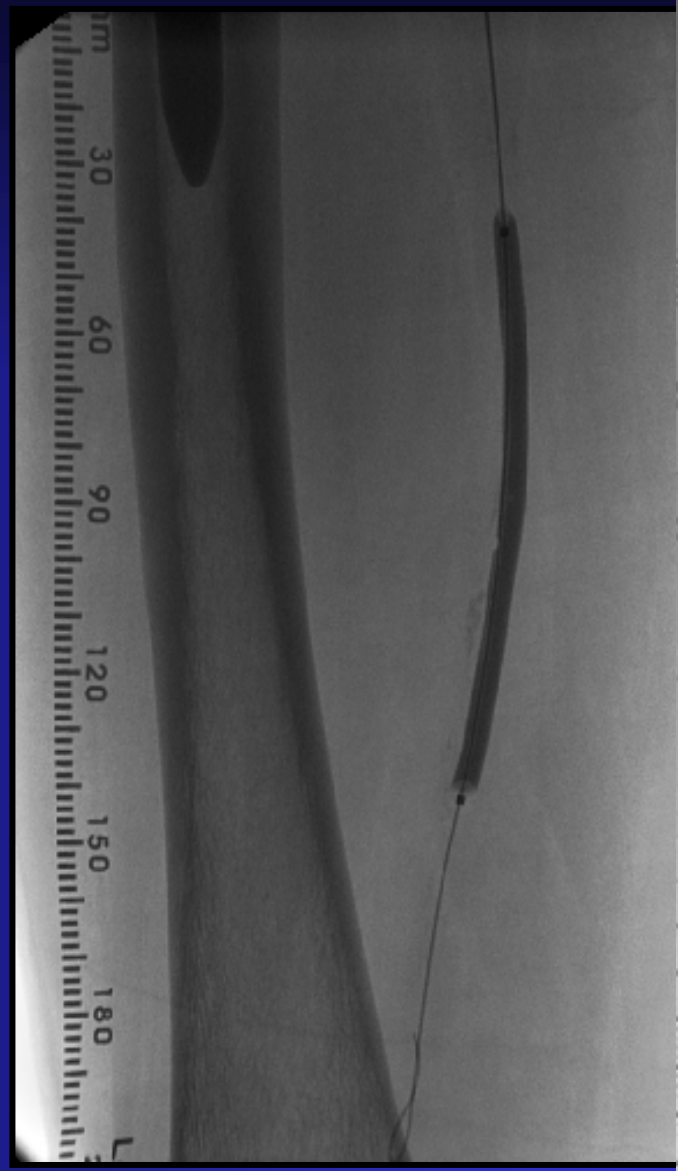
% of patients reaching ≥ 50% stenosis in target lesion after initial PTA

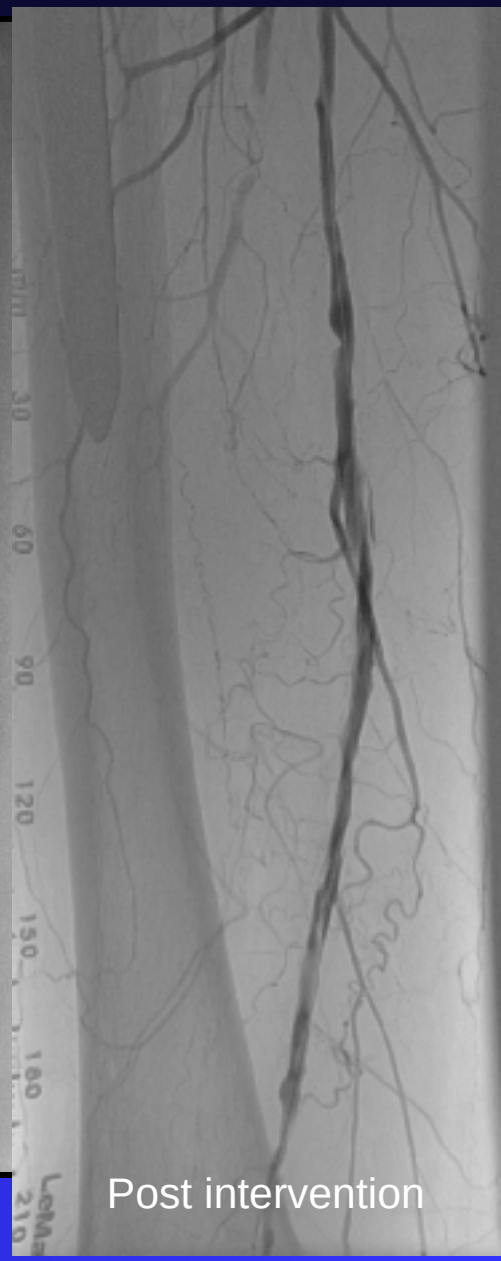


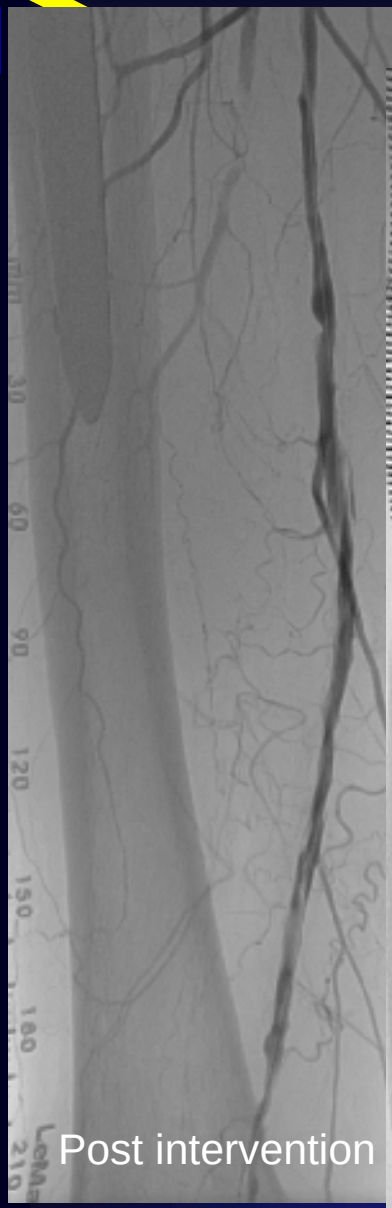
BA = Balloon angioplasty

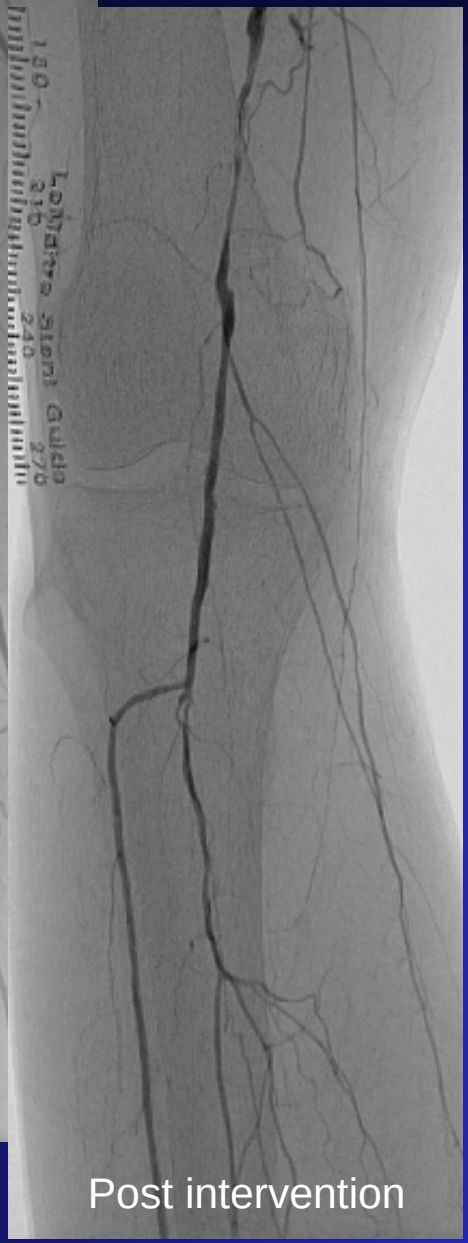
Patient treated with Paccocath

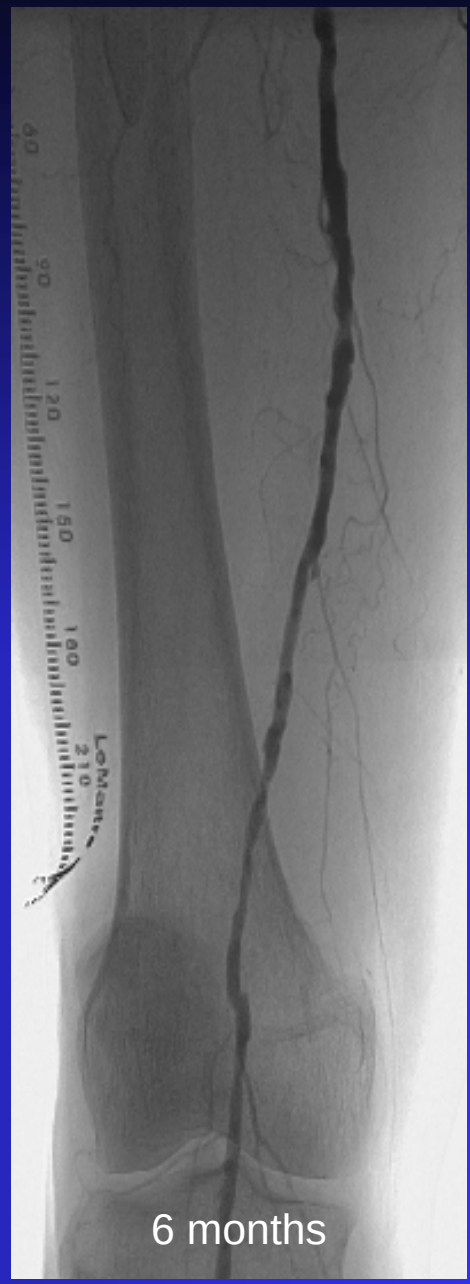

Pre intervention

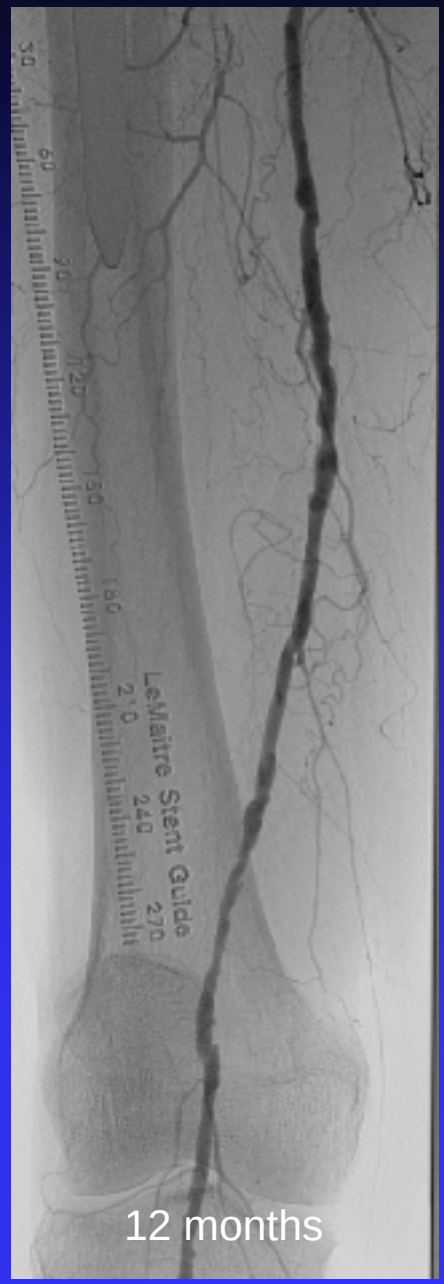

30
60
90
120
150
180


Post intervention


Post intervention


Post intervention


6 months


12 months

Conclusions

On DES

- Currently NO data that DES in the SFA work
- 2 ongoing trials
- With ((D)ES?) high risk lesions treated effectively

On short time contact with PTX

- DEB safe and effective
- Sustainded results after 12 months
- Local delivery with CM does not work