

Freeway, the coated peripheral balloon, first experiences in PAD (femoro-popliteal intervention)

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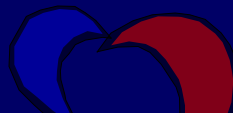


Potential conflicts of interest

Speaker's name: K-L Schulte

I have the following potential conflicts of interest to report:

- X Research contracts
 - X Consulting
 - Employment in industry
 - X Stockholder of a healthcare company
 - Owner of a healthcare company
 - Other(s)
- I do not have any potential conflict of interest**



Endovascular intervention, bypass surgery and major amputation rates in the U.S. (1996-2006)

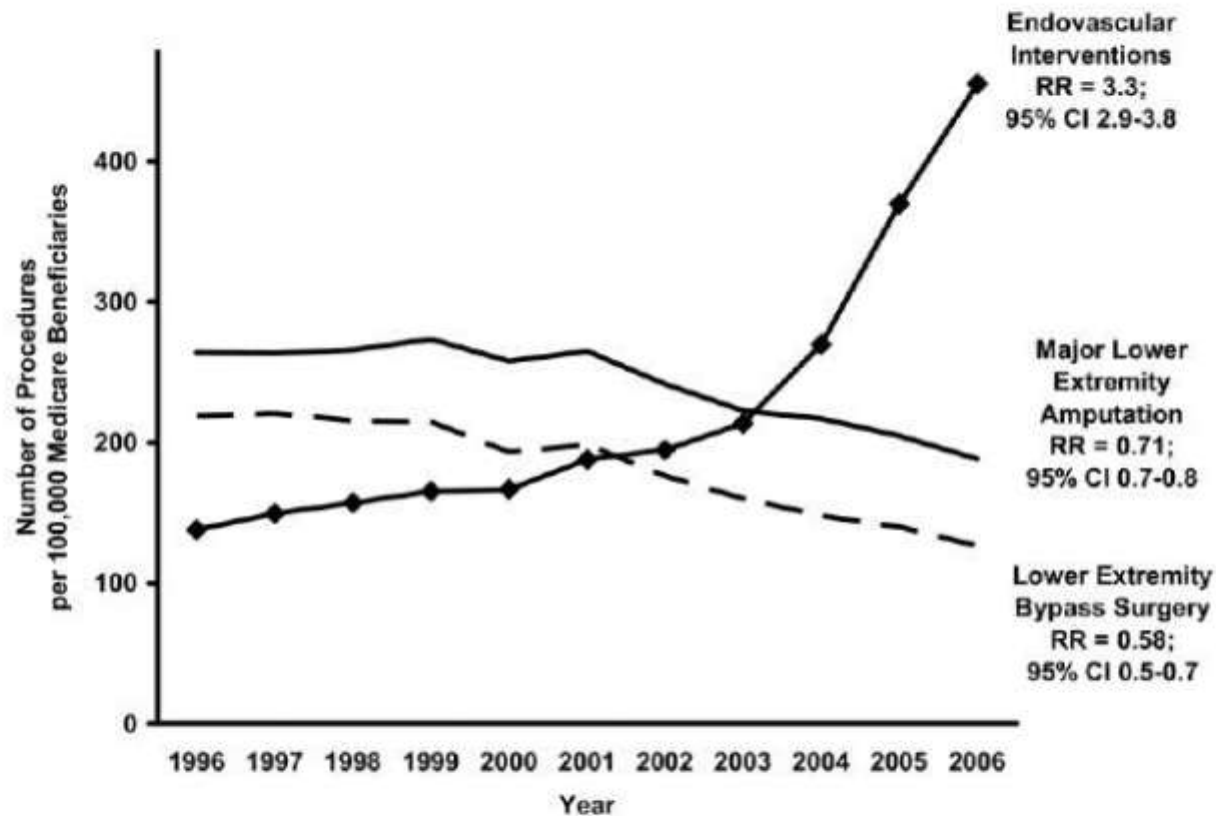
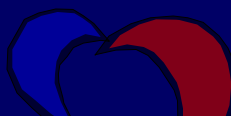


Fig 1. Trends in endovascular interventions, major amputation, and lower extremity bypass surgery, 1996-2006. RR, Risk ratio; CI, confidence interval.

Problems with SFA PTA and Stenting

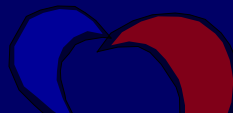
Restenosis



Results of Balloon Angioplasty

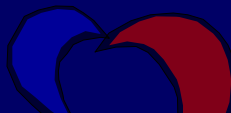
	Patients (n)	Lesion Length	F/U	Primary Patency
Matsi PJ et al., 1995	107	7.2 cm	2 years	51%
Stanley B et al., 1996	176	>10 cm	2 years	46%
Krankenbergh H et al., 2001	58	22 cm	1 year	44%
Jämsén TS et al., 2002	173	5.2 cm	1 year	46%

Weighted average: 47 %



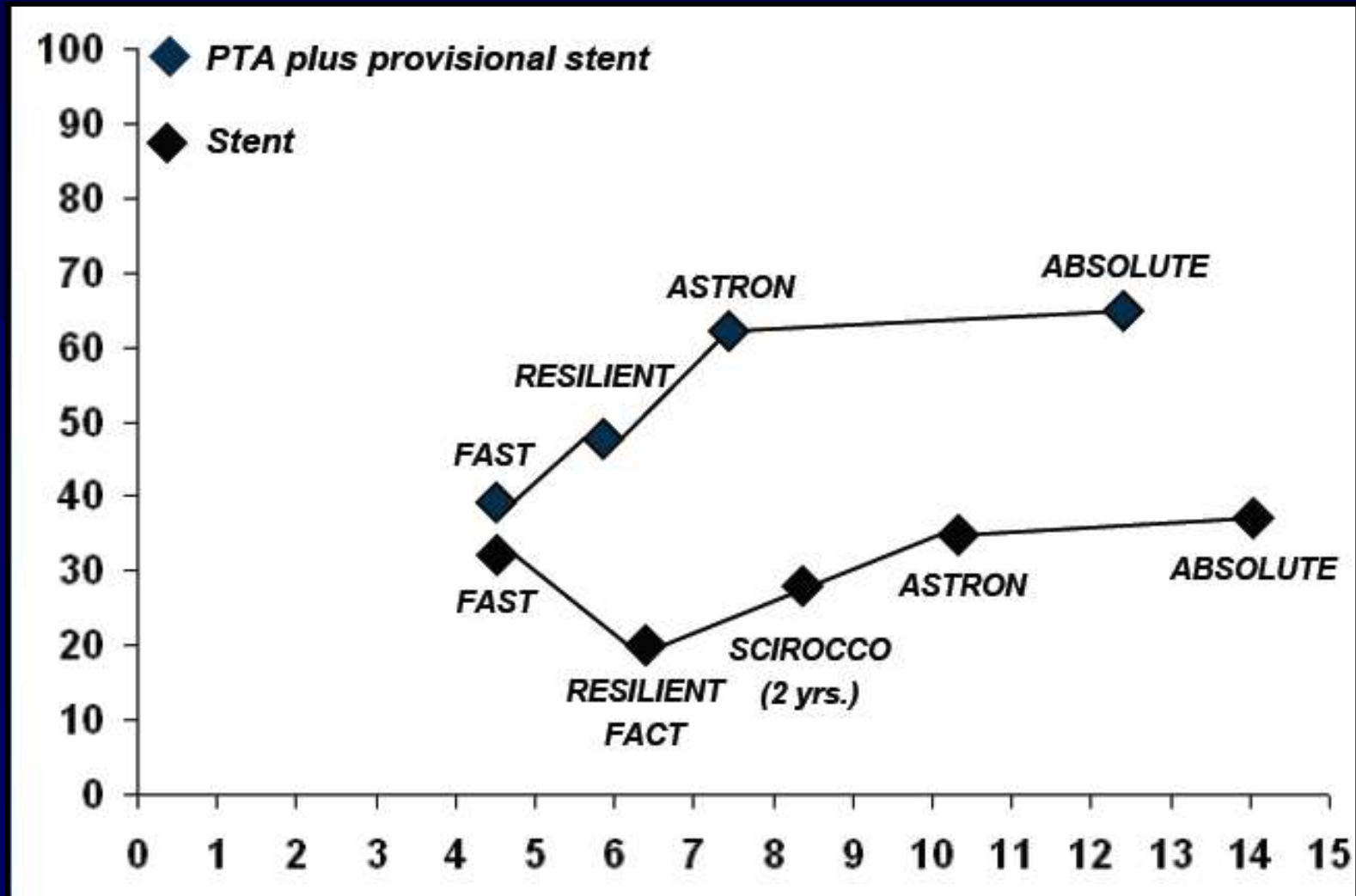
Restenosis rates (%) PTA vs. Stent (Duplex)

Studie	Lesion (cm)	PTA	Stent	P<
ABSOLUTE	ca. 10	63 (33/52)	37 (18/49)	0.01
FAST	ca. 4.5	35 (29/82)	32 (31/97)	n.s.

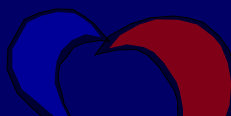


12 Months Restenosis vs. Lesion Length: Data from Controlled Trials

Binary Restenosis @ 12 Months (%)

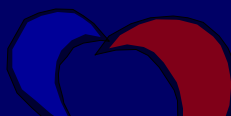


Length of the Lesion (cm)



Improvement of patency in SFA

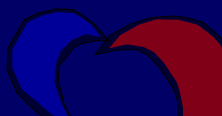
- Drugs
- Subintimal Angioplasty
- Bare Stents
- Covered stents
- Drug Eluting Stents
- Drug eluting balloon
- Bioabsorbable Stents
- Brachytherapy
- Cryoplasty
- Cutting balloon
- Photodynamic therapy
- Debulking



How Well Does DES Work ?

SIROCCO II Restenosis Rate

	6m	9m	18m	24m	36m	48m
Sirolimus Restenosis	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	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	1.9% (1/52)	9.6% (5/52)	17.6% (9/51)	24.5% (12/49)	32.6% (14/43)	41.7% (15/36)

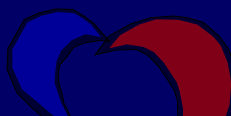


Zilver PTX stent (paclitaxel): Registry

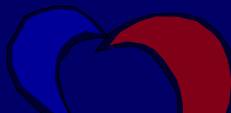
Lesion Characteristics

Patients	718
Lesions	818
TASC Class*: A	26%
B	29%
C	26%
D	14%
Lesion > 7 cm	47%
Lesion > 15 cm	22%
Total Occlusion	38%
Restenosis (all)	24%
In-stent Restenosis (ISR)	15%

*TASC 2000



Drug-Eluting Balloons in the SFA: Promising, Proven, or Placebo?

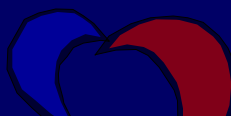


THUNDER Trial

Local Delivery of Paclitaxel to Inhibit Restenosis during Angioplasty of the Leg

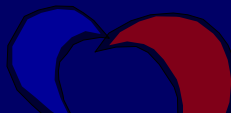
Gunnar Tepe, M.D., Thomas Zeller, M.D., Thomas Albrecht, M.D.,
Stephan Heller, M.D., Uwe Schwarzwälder, M.D., Jean-Paul Beregi, M.D.,
Claus D. Claussen, M.D., Anja Oldenburg, M.D., Bruno Scheller, M.D.,
and Ulrich Speck, Ph.D.

NEJM, 2008



DEB Clinical Trials: Femoral-Popliteal **THUNDER**

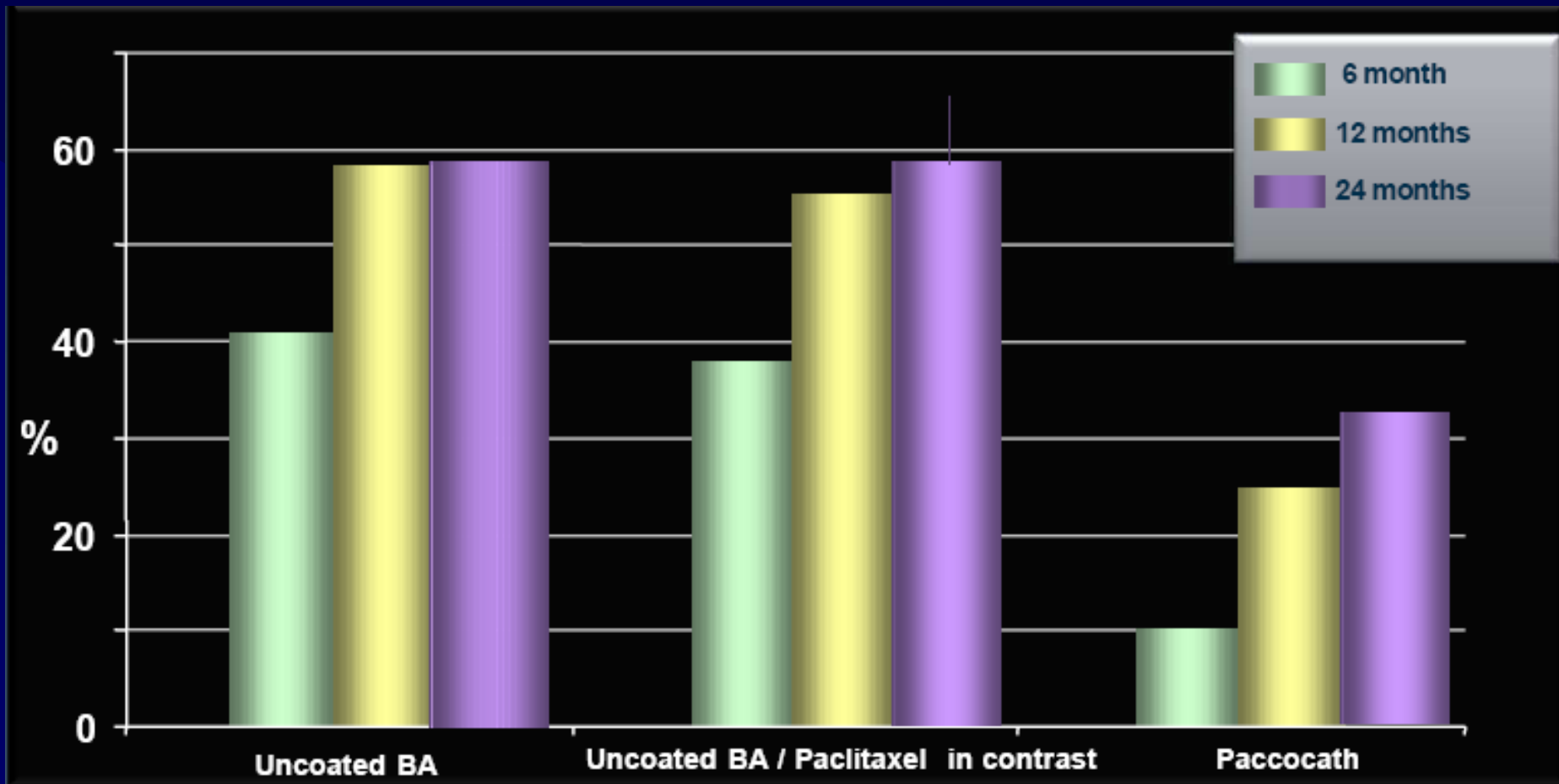
- 3 arm randomized multicenter trial
 - Rutherford 1-5
 - SFA and/or popliteal lesion >2cm (mean 7.5 cm)
 - *De novo*/restenotic lesions (~20%) including ISR (~15%)
 - Randomized 1:1:1
 - Conventional balloon
 - Conventional balloon with 17.1 mg paclitaxel/100 ml contrast
 - Paclitaxel-coated balloon 3 $\mu\text{g}/\text{mm}^2$
 - 1 minute inflation



DEB Clinical Trials: Femoral-Popliteal

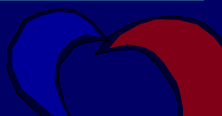
THUNDER

Long-Term Follow-Up



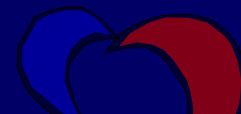
Binary Restenosis Rate

Late Lumen Loss at 6, 12 or 24 Months or Before 1st TLR (Primary Endpoint)



THUNDER: Late Lumen Loss Subgroups

Subgroup	n control/ n DCB	LLL (mm) Control minus DCB	LLL (%) DCB/ Control
Diabetes	21/14	1.2	33
Restenotic lesion	14/12	1.5	21
Calcification	18/16	1.2	25
> 10 cm	5 / 8	1.3	50
Pop. involvement	13/11	1.5	29



Inhibition of Restenosis in Femoropopliteal Arteries

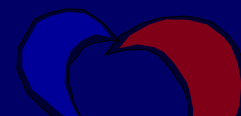
Paclitaxel-Coated Versus Uncoated Balloon: Femoral Paclitaxel Randomized Pilot Trial

Michael Werk, MD; Soenke Langner, MD; Bianka Reinkensmeier, MS; Hans-Frank Boettcher, MD; Gunnar Tepe, MD; Ulrich Dietz, MD; Norbert Hosten, MD; Bernd Hamm, MD; Ulrich Speck, PhD; Jens Rieke, MD

Background—The success of percutaneous intervention in peripheral arterial disease is limited by restenosis. The aim of the present pilot study was to evaluate a novel method of local drug delivery.

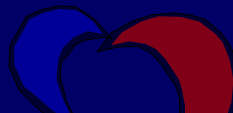
Methods and Results—This randomized multicenter study with blinded reading enrolled 87 patients in Rutherford class 1 to 4 with occlusion or hemodynamically relevant stenosis, restenosis, or in-stent restenosis of femoropopliteal arteries. Treatment was performed by either conventional uncoated or paclitaxel-coated balloon catheters. The primary end point was late lumen loss at 6 months. Secondary end points included restenosis rate, ankle brachial index, Rutherford class, target lesion revascularization, and tolerance up to >18 months. Before intervention, there were no significant differences in lesion characteristics such as reference diameter (5.3 ± 1.1 versus 5.2 ± 1.0 mm), degree of stenosis ($84 \pm 11\%$ versus $84 \pm 16\%$), proportion of restenotic lesions (36% versus 33%), and mean lesion length (5.7 cm [0.8 to 22.6 cm] versus 6.1 cm [0.9 to 19.3 cm]) between treatment groups. The 6-month follow-up angiography performed in 31 of 45 and 34 of 42 patients showed less late lumen loss in the coated balloon group (0.5 ± 1.1 versus 1.0 ± 1.1 mm; $P=0.031$). The number of target lesion revascularizations was lower in the paclitaxel-coated balloon group than in control subjects (3 of 45 versus 14 of 42 patients; $P=0.002$). Improvement in Rutherford class was greater in the coated balloon group ($P=0.045$), whereas the improvement in ankle brachial index was not different. The difference in target lesion revascularizations between treatment groups was maintained up to >18 months. No adverse events were assessed as related to balloon coating.

Conclusions—In this pilot trial, paclitaxel balloon coating caused no obvious adverse events and reduced restenosis in patients undergoing angioplasty of femoropopliteal arteries. (*Circulation*. 2008;118:1358-1365.)

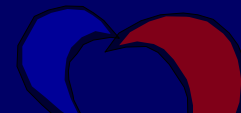


Restenosis rates (%) PTA vs. Stent (Duplex)

Studie	Lesion (cm)	PTA	Stent	P<
ABSOLUTE	ca. 10	63 (33/52)	37 (18/49)	0.01
FAST	ca. 4.5	35 (29/82)	32 (31/97)	n.s.
		<i>PTA</i>	<i>DEB</i>	
THUNDER	ca. 7.5	49 (18/37)	21 (7/34)	0.01



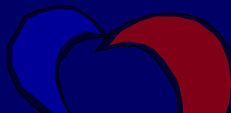
Company	DCB Name
Aachen Resonance GmbH (distributed by Biotronik AG)	ELUTAX®
B. Braun Melsungen AG	SeQuent® Please
Bayer AG (MEDRAD, Inc.)	Cotavance™ with Paccocath® coating technology
Caliber Therapeutics, Inc.	TADD (Targeted Angioplasty Drug Delivery)
Cook Group, Inc.	Advance® 18PTX®
Eurocor AG	DIOR®, Freeway
Invatec s.r.l. ABBOTT	IN.PACT™ Amphirion
Lutonix, Inc.	Unknown



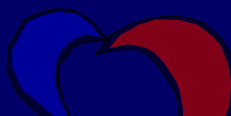
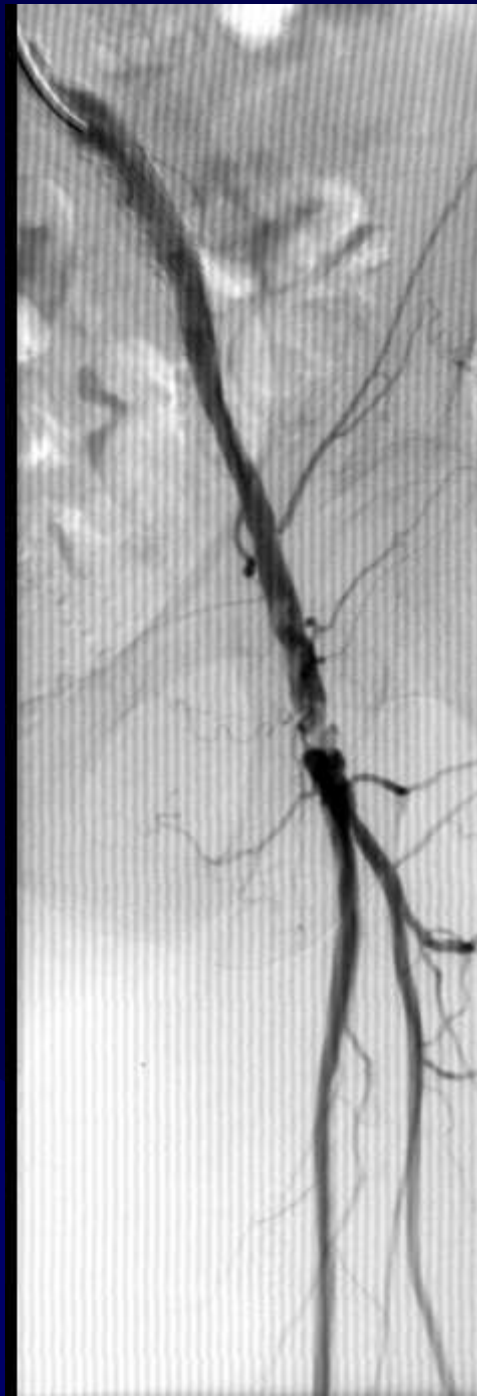
First Experiences

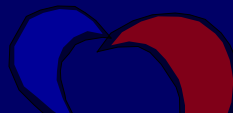
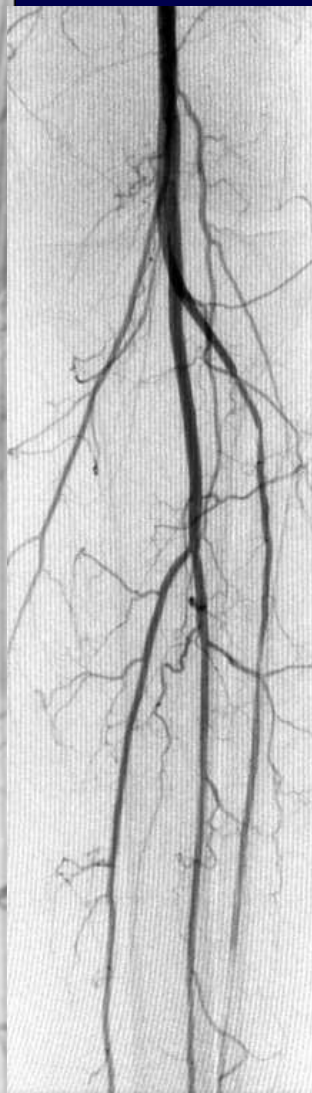
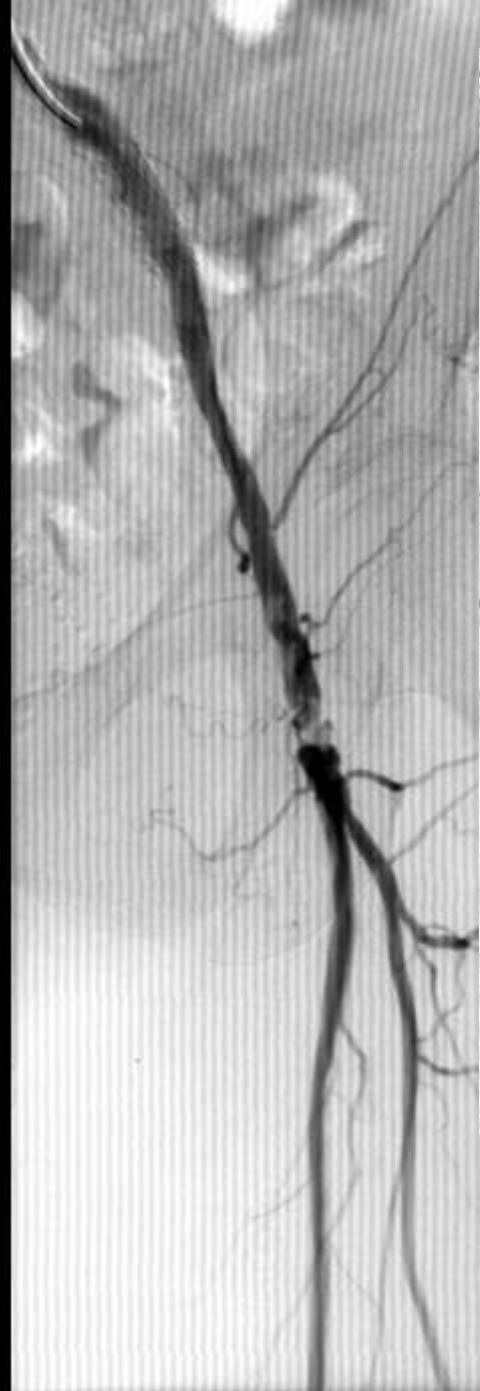


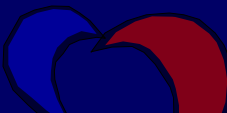
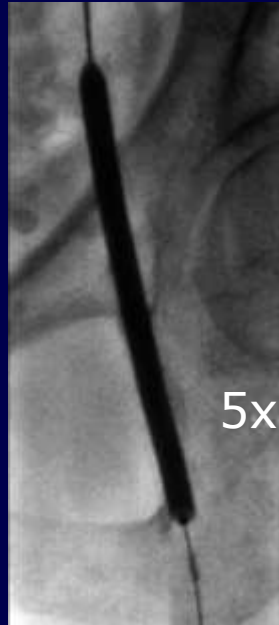
FREEWAY 035, femoropopliteal PTA balloon 0.035" OTW

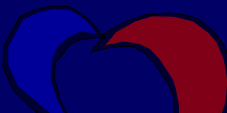
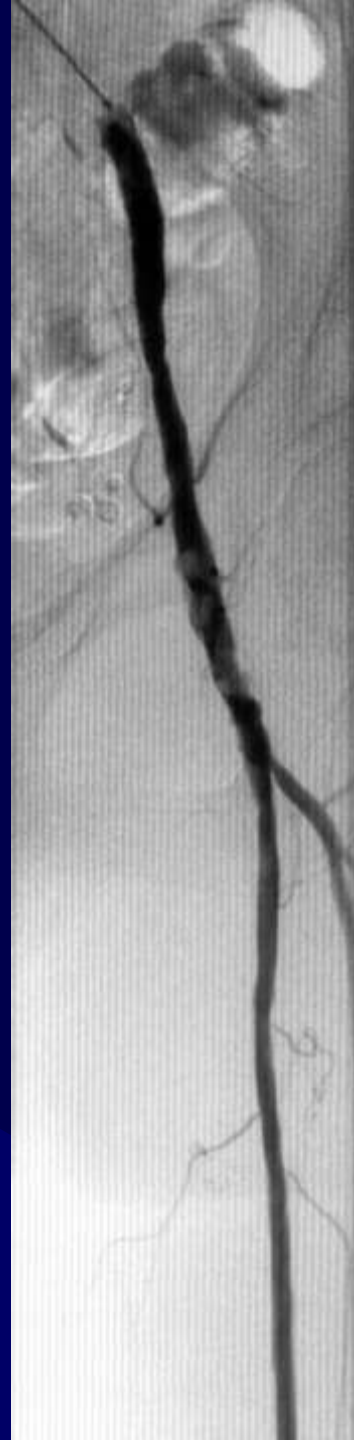
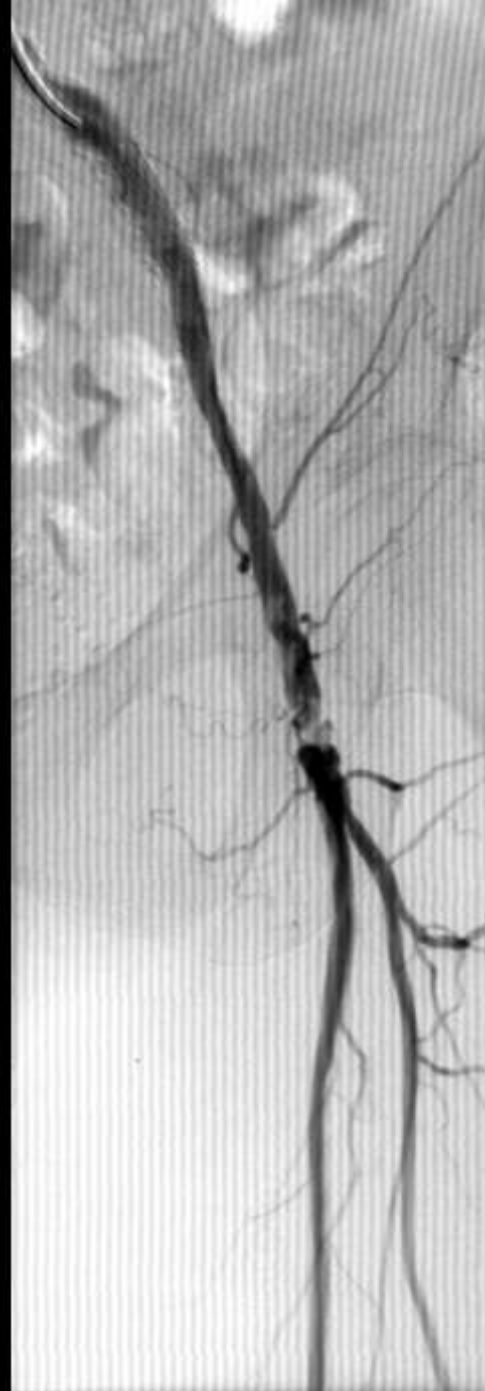


1. Left AFC, bending zone

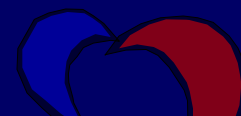
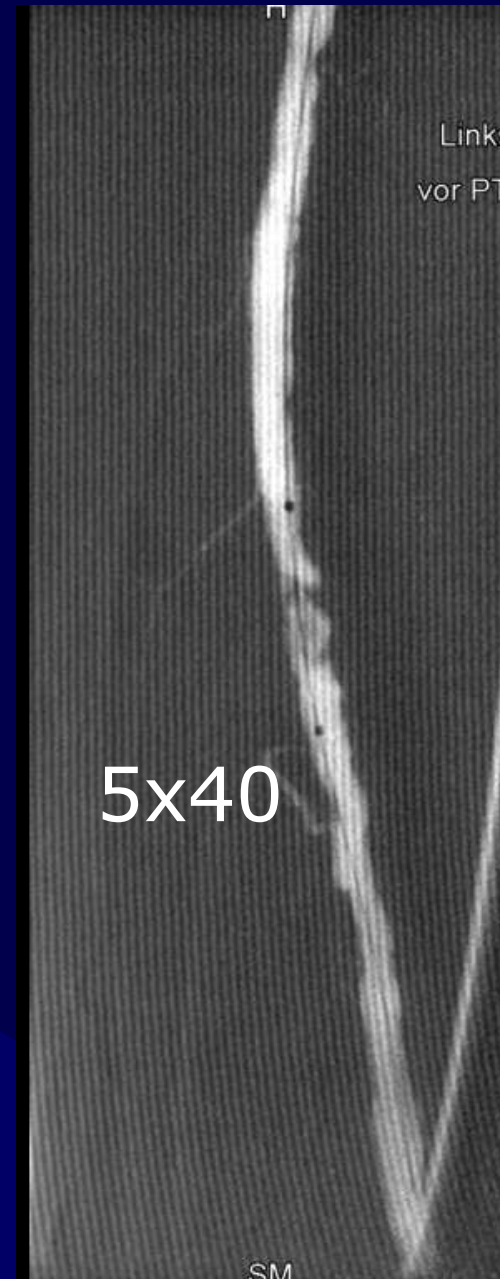
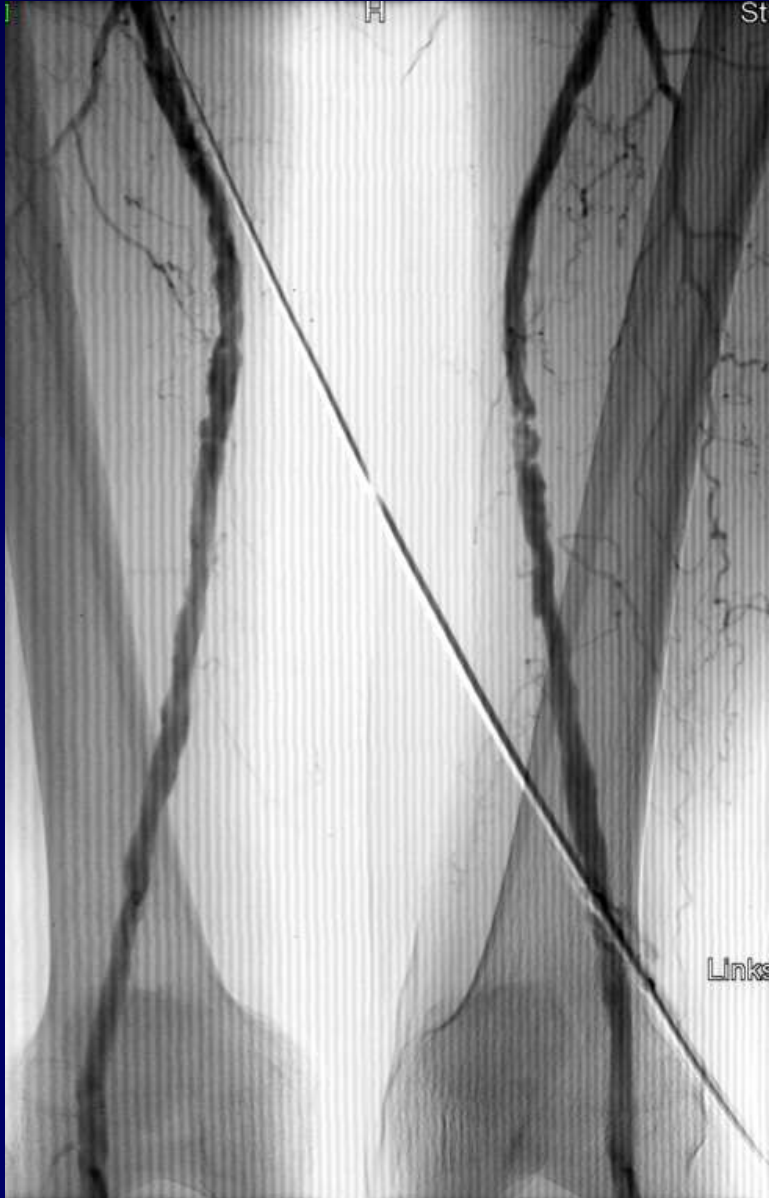


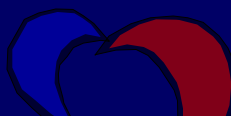
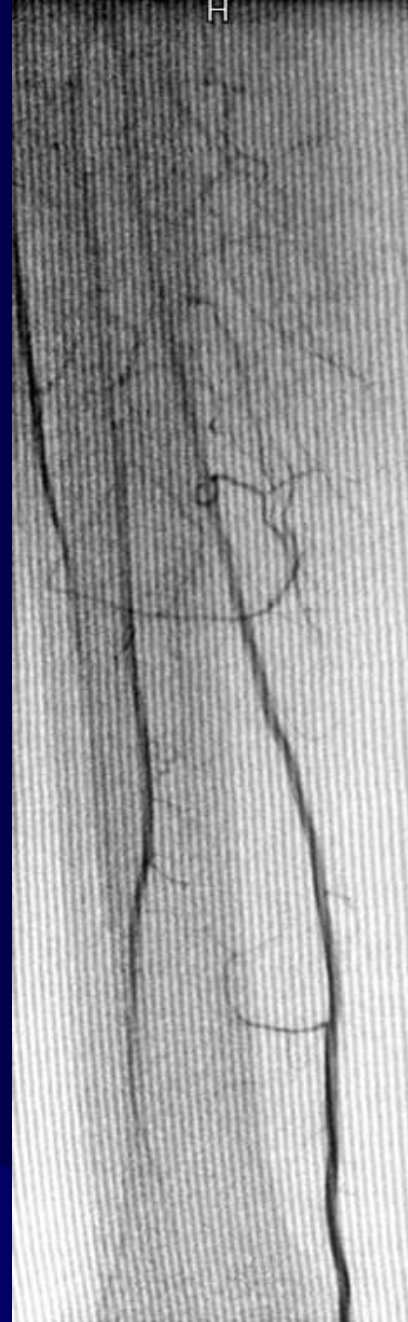
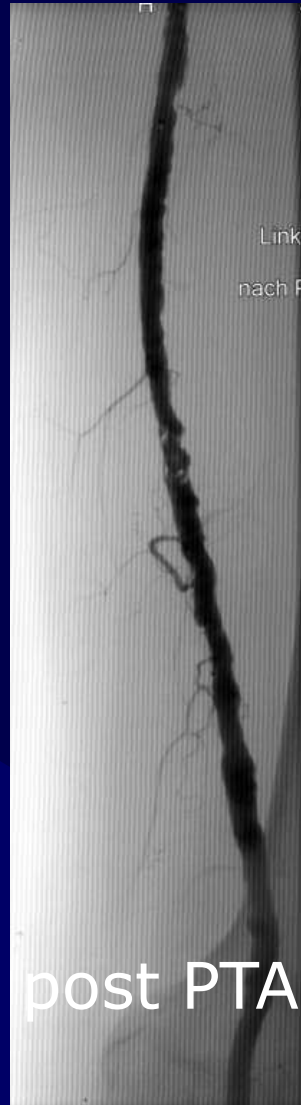




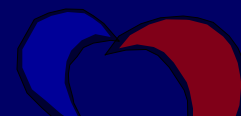
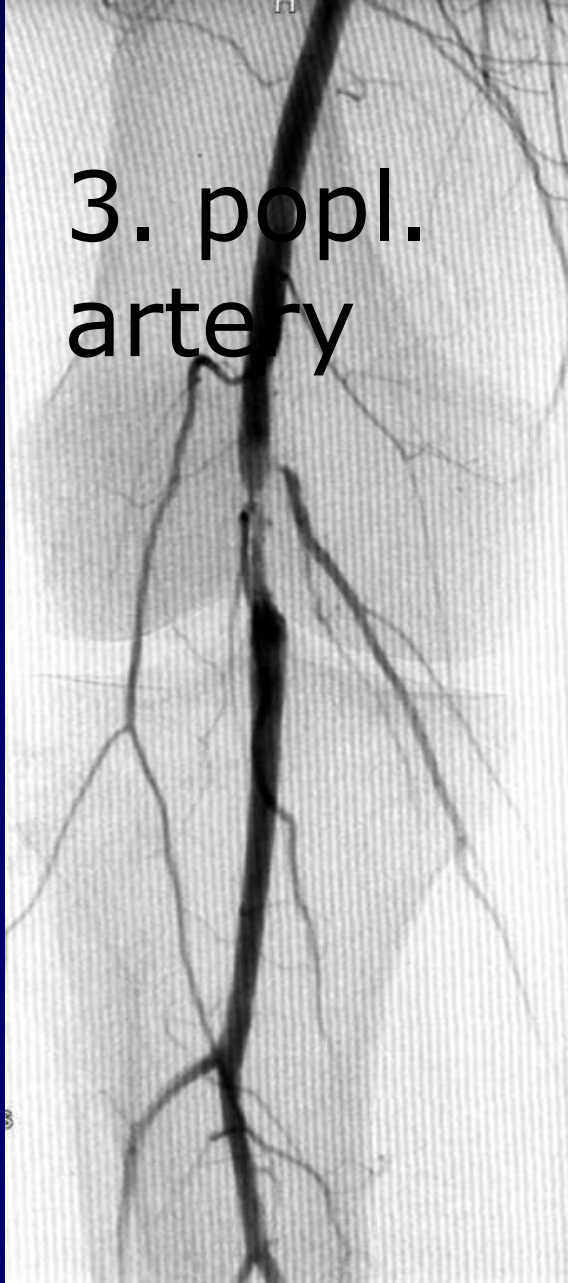


2. Left distal SFA

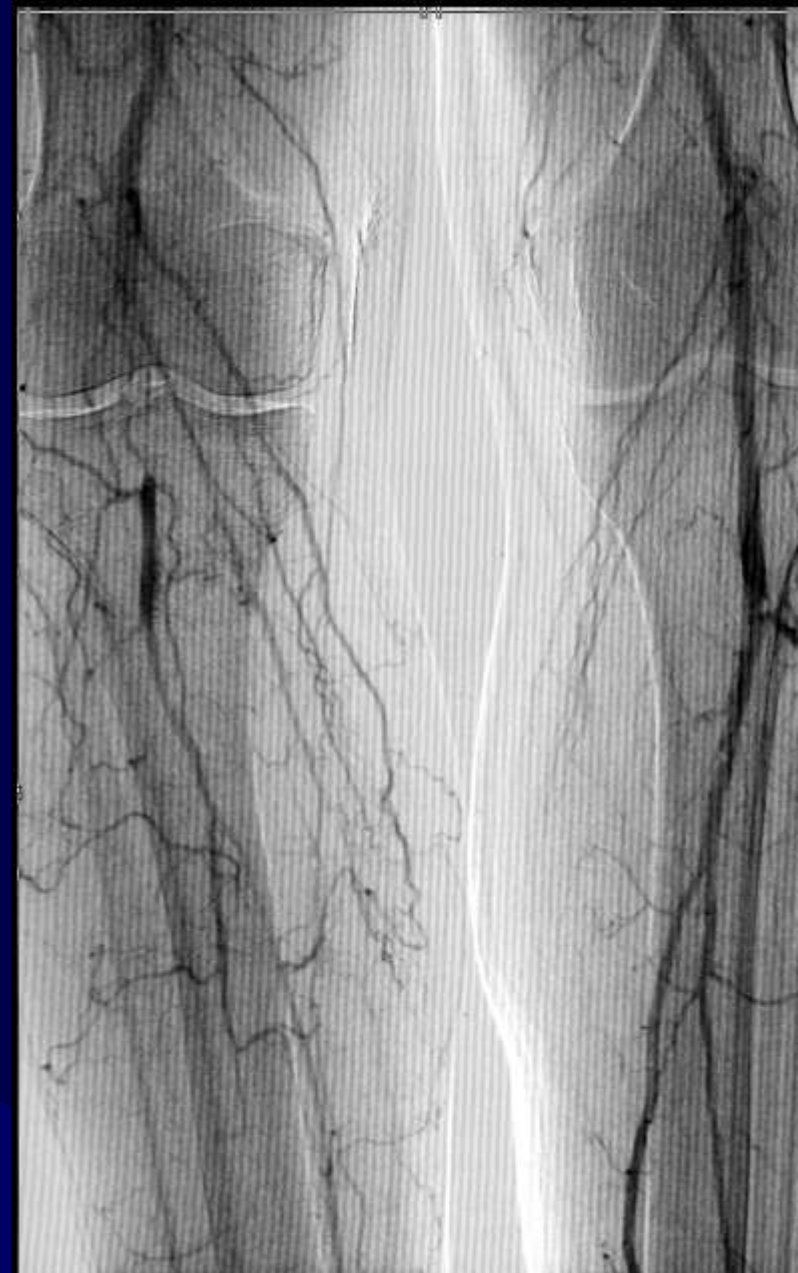


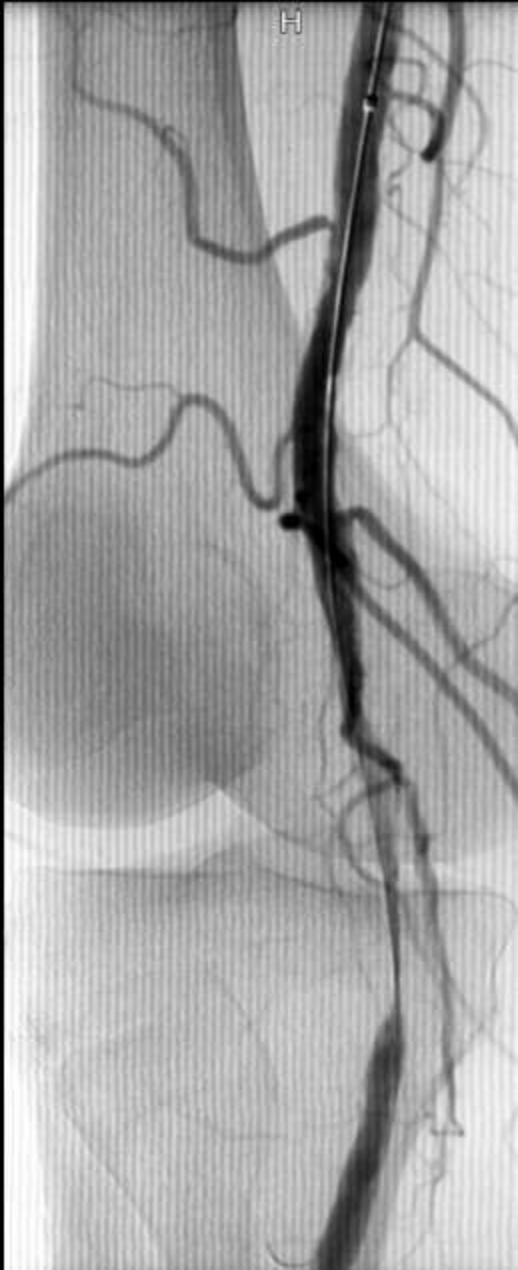


3. popl. artery

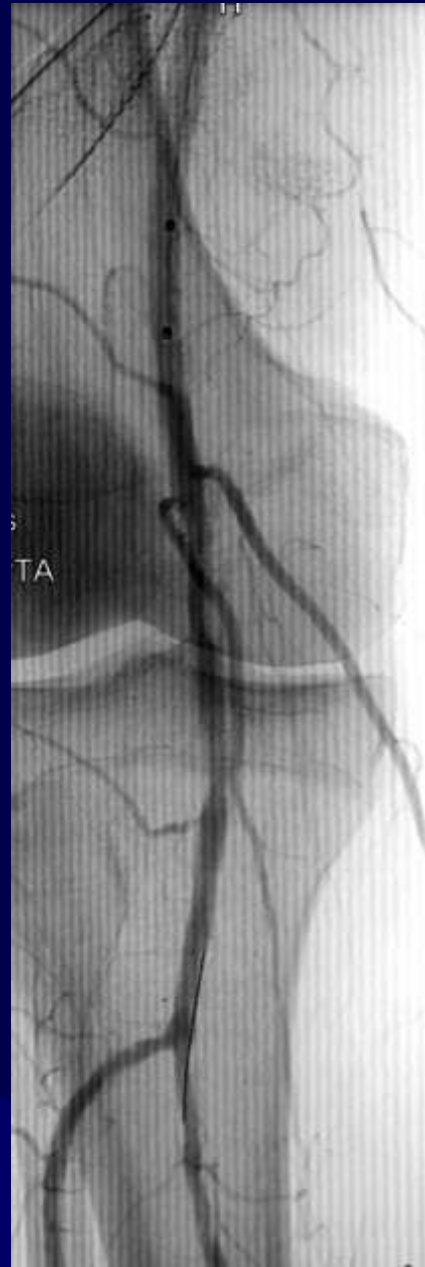


4.
K.K., male, 56 yrs.
Rest pain right leg (Rutherford 4)
Risk factors: Smoking, Hypertension,
LDL-C
Therapy: ASS, ACE-Inhibitor, Statin

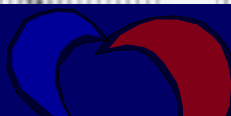
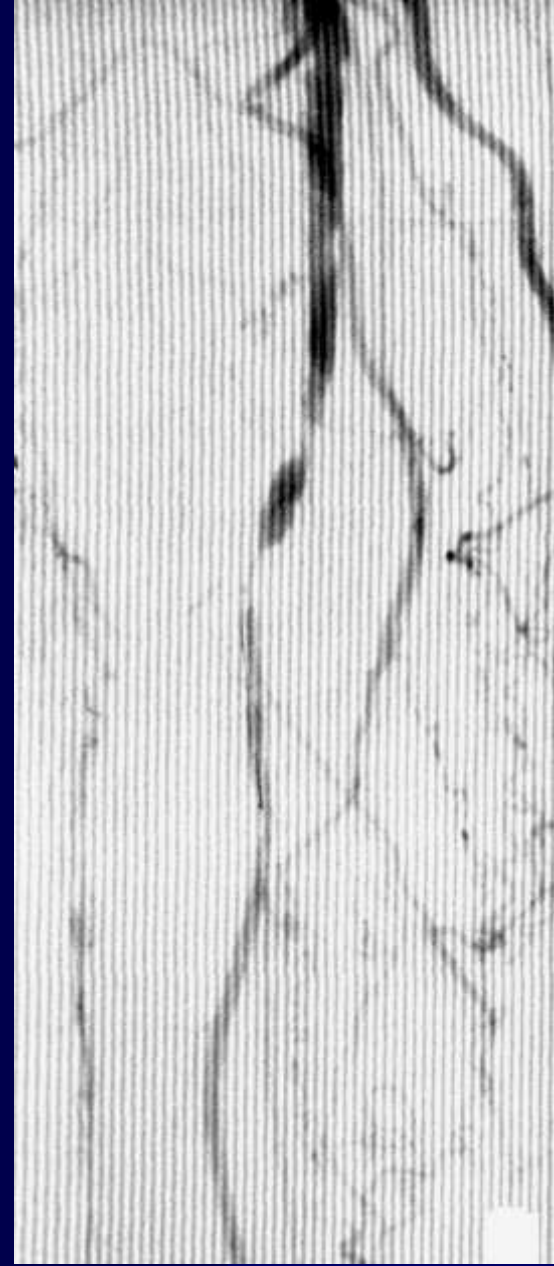
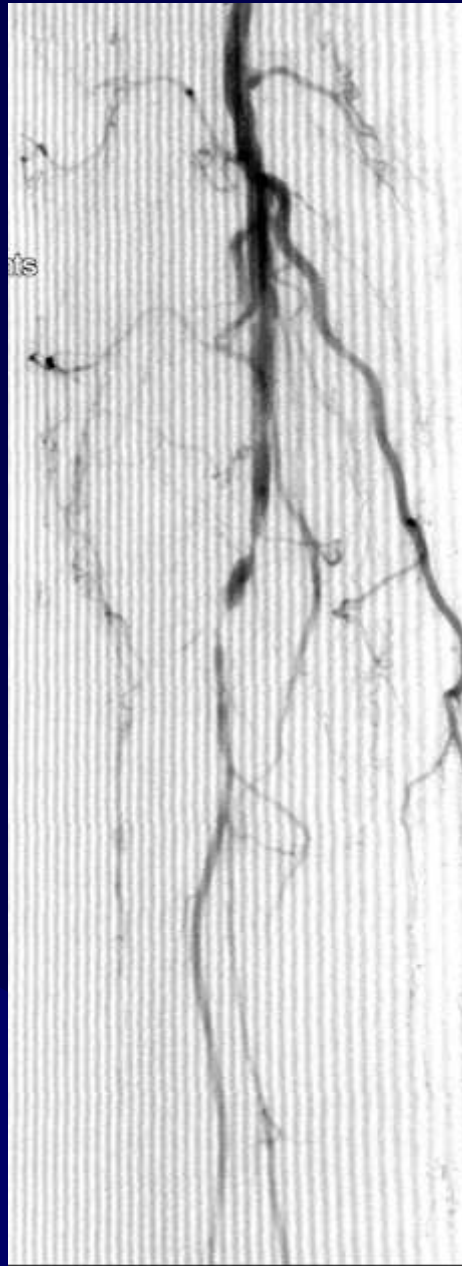


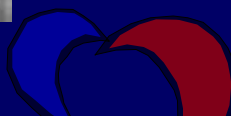
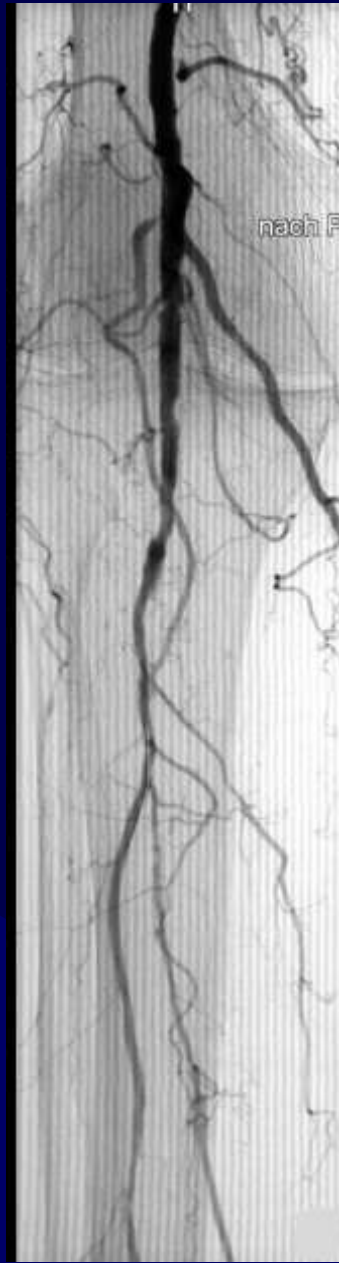


4x60 PTA,
4x30 Dior (2)



5.
H.W., male, 72 yrs.
CLI right leg (Rutherford 4)
Risk factors: Diab. (IDDM),
renal failure, dislipidemia
Therapy: Insulin, statin, ASA

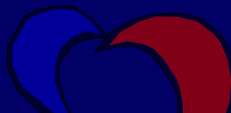




Summary of our EXPERIENCES

Femoro-popliteal and BTK-DEB-PTA
in 32 PAD-patients

6-month-restenosis-rate (Duplex)
24%



FREEWAY Stent study

Clinical Study Protocol

**Stent angioplasty with Paclitaxel-coated balloons
versus plain stent angioplasty for prevention of
restenosis due to intimal hyperplasia in peripheral
arterial occlusive disease**

Freeway Stent Study

Principal Investigator:

Prof. Dr. med. Josef Tacke

Institut für diagnostische und interventionelle Radiologie und Neuroradiologie

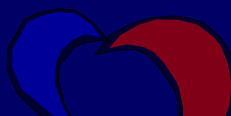
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94032 Passau

Germany

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FREEWAY Stent study

Study phase

Phase III study

Study design

Randomized, prospective, multicenter, open study

Number of subjects planned

200 included patients

Randomization

Internet based

Number of treatment arms

2 treatment arms:

- a) Stent with uncoated balloon catheters
- b) Stent with paclitaxel coated balloon catheters

Investigational product, manufacturer, dosage, route of administration, and duration of treatment

Paclitaxel: dosage $3\mu\text{g}/\text{mm}^2$

Coated balloons: Eurocor

Type of balloon catheters: Freeway PTA balloon

Dose: $3\mu\text{g}$ paclitaxel/ mm/ balloon surface

Route of administration: intra-arterial

Duration of treatment: single treatment inflation 45 - 60 sec.

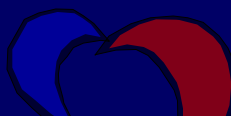
Endpoints

Primary endpoint:

Rate of clinically driven target lesion revascularization at 6 and 12 months

Secondary Endpoints:

- Late lumen loss, i.e. the difference between the minimum lumen diameter after intervention and during the follow-up at 6 and 12 months determined by colour-coded duplex sonography and/or angiography



FREEDOM study

FREEDOM-STUDY

FREEway ranDOMized Angioplasty STUDY

Prospective, Randomized, Controlled, Multicentre, Open Study

**Release of Paclitaxel during PTA versus PTA alone for the treatment of
de-novo occluded, stenotic or, reoccluded, restenotic
superficial femoral (SFA) or popliteal arteries**

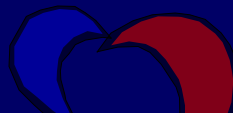
Lead Principal Investigator: Prof. Dr. med. Karl-Ludwig Schulte
Vascular Center Berlin /Dept. Internal Medicine
Ev. Hospital Königin Elisabeth Herzberge
Academic. Teaching Hospital of the Charité
Herzbergstraße 79, 10365 Berlin, Germany



FREEDOM-STUDY

Prospective, Randomized, Multicentre, Open Study
Release of Paclitaxel during *PTA versus PTA alone (incl. bail out stenting)* for the treatment of occluded or stenotic superficial femoral or popliteal arteries
(PI: K-L Schulte)

Investigational Devices	<ul style="list-style-type: none">- Freeway balloon catheter, Paclitaxel-elution- Balloon catheter \pm bail out stenting
Study Objective	To Investigate the inhibition of restenosis by the Paclitaxel-eluting PTA balloon Freeway versus PTA or stenting-PTA (bail-out) in the treatment of occluded or stenotic superficial femoral or popliteal arteries
Study Design	Randomized, prospective, multicentre, open study
Primary Endpoints	Absence of clinically driven target lesion revascularization at 6, 12 (and 24) months
Number of Patients	280 patients
Number of sites	\leq 15 sites world-wide
Patient Population	Patients with symptomatic one or two legs ischemia, requiring treatment of SFA or popliteal artery (2 or more by Rutherford classification) Patients with documented symptomatic occlusion and/or $>70\%$ stenosis of SFA or popliteal artery in one or both legs



Role of DEB in infrainguinal interventions

Summary

- First promising study-results for treatment of femoro-popliteal lesions have been published
- Which drug and which coating technology?
- We need more RCT's

Technical Problems

- Loss of drug concentration on the long way down to the lesion?!
- Is there need of long protecting introduction catheters?
- Predilatation is a must!

