

Endovascular Brachytherapy with Rhenium-188

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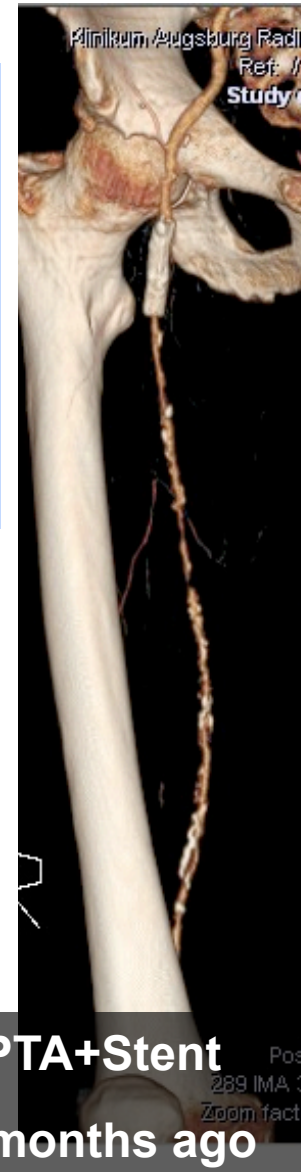
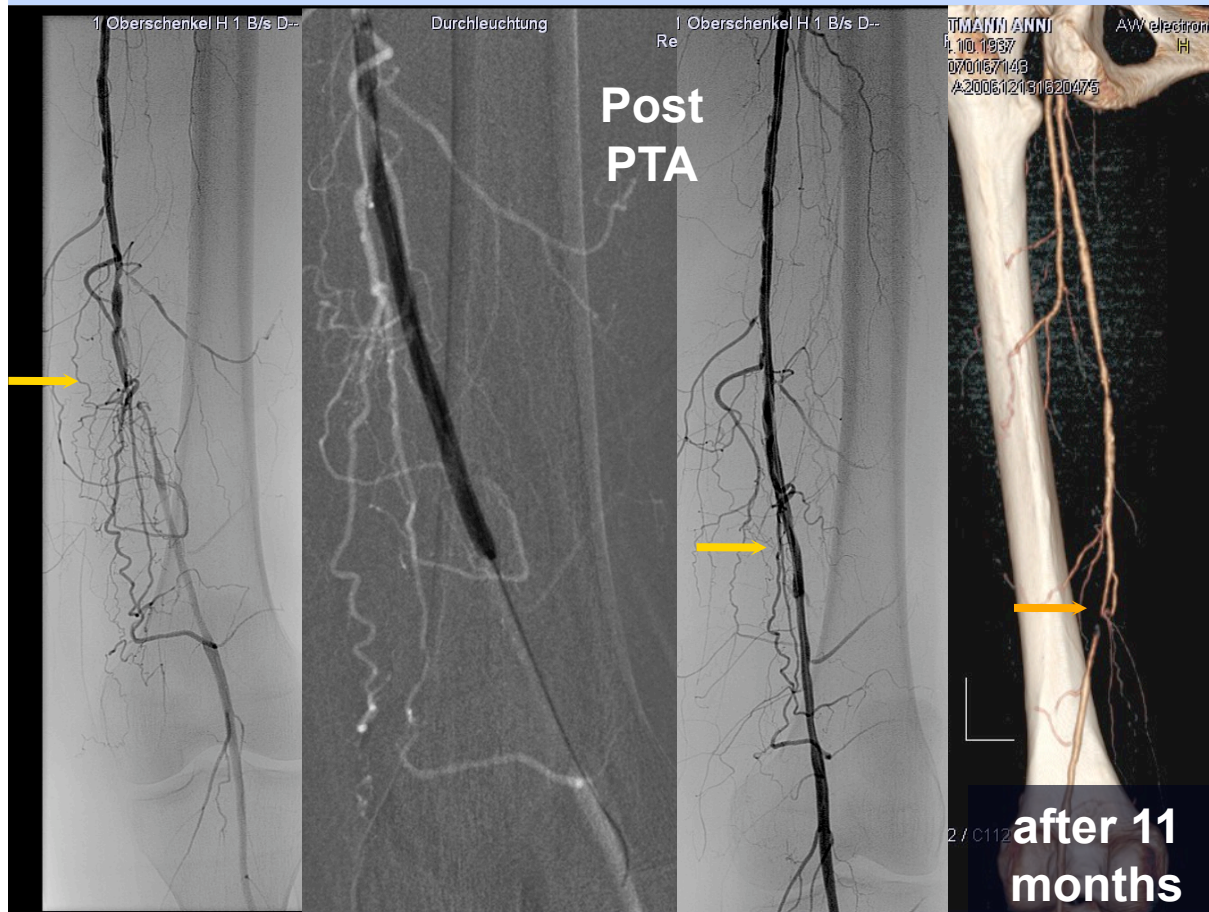
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Rate of Restenosis after PTA +/- Stent 30 - 80 %

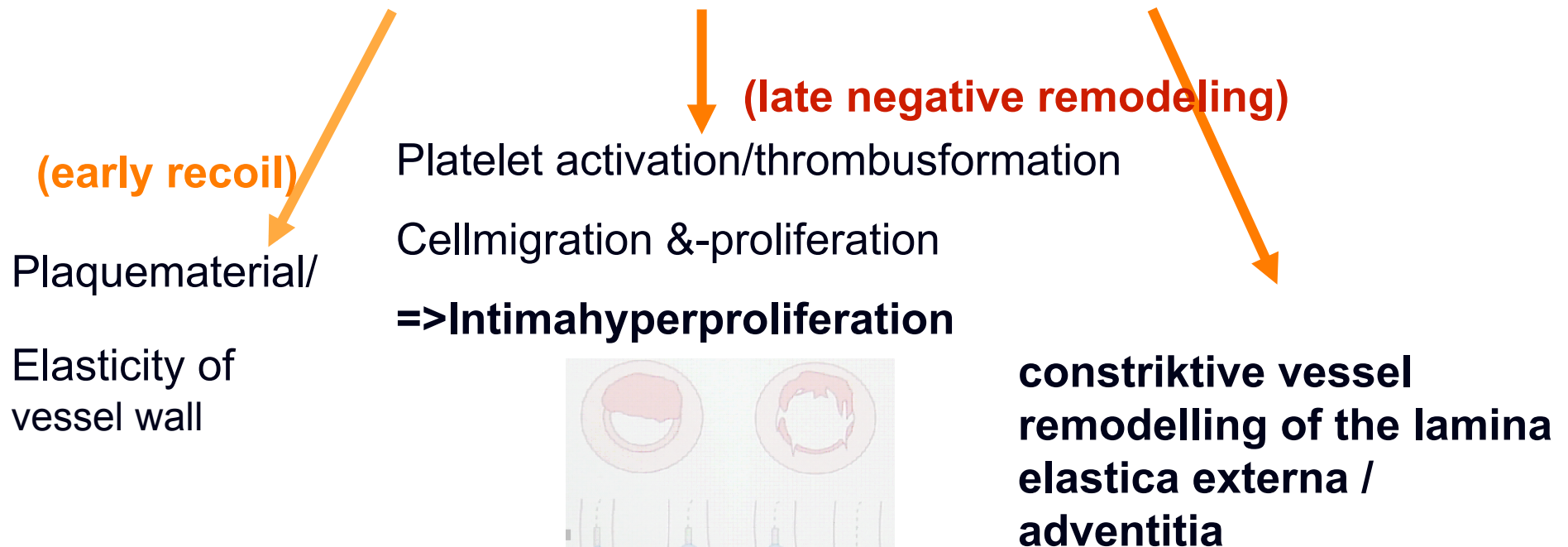
Criteria: DeNovo/Recurrence, Morphology, Localisation, Length...

(Capek P et al; Circulation 1991;83(suppl2):I70-I807 Murray RR Jr, et al. Radiology 1987;162:473-47699)

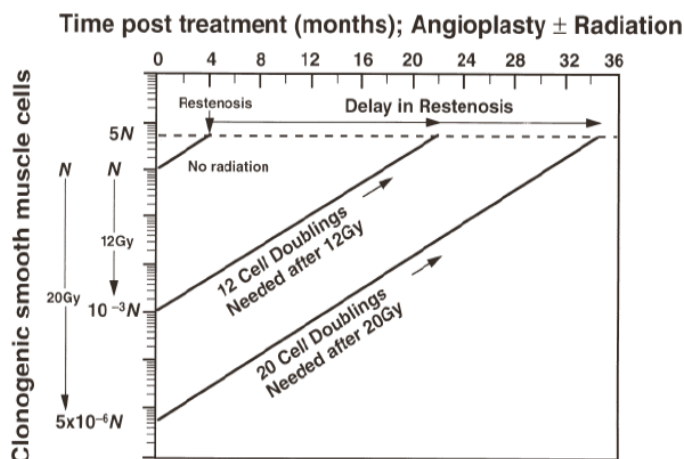
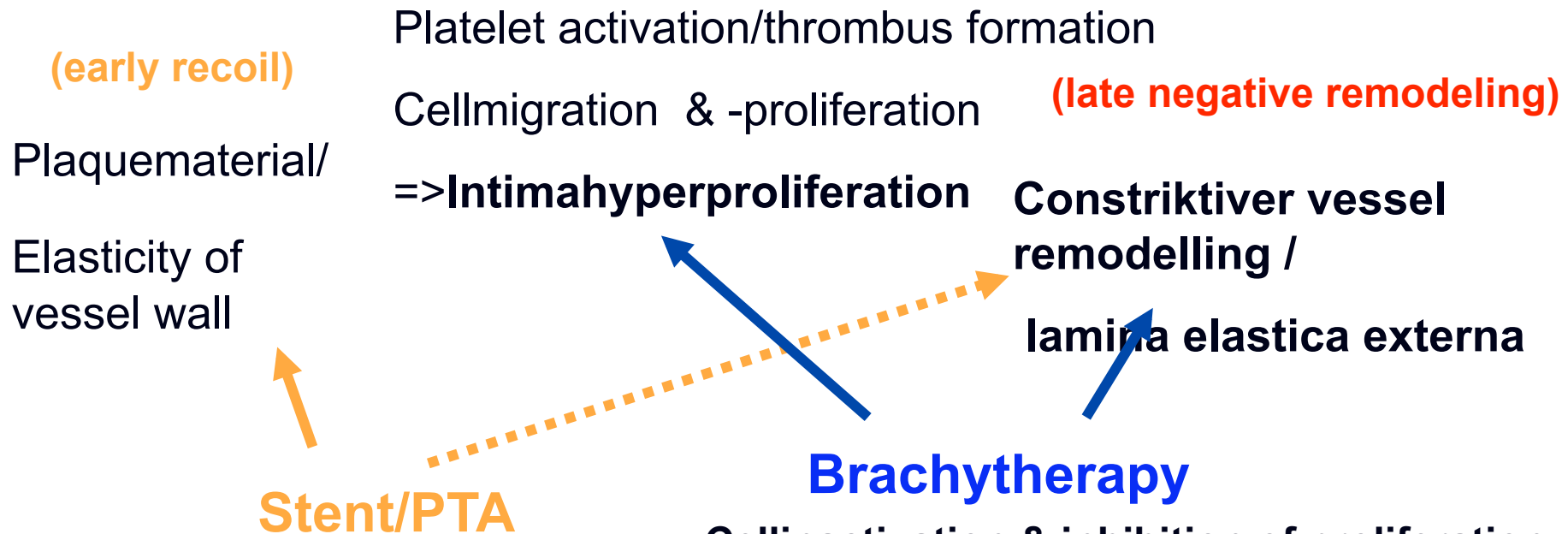


Cause of Restenosis after Angioplasty:

1. Progress of arteriosclerosis
2. Response of vessel wall to PTA-trauma



Femoropopliteal Restenosis Prevention



Cell inactivation & inhibition of proliferation of smooth muscle cells & myofibroblasts in the media/adventitia transition

M. Schillinger, E. Minar; J Endovasc Ther (2004); 11 (Suppl II) 180-191

W. A. Wohlgenuth, G. Leissner et al; Cardiovasc & Intervent Radiol (2008) 31, 698-708



Vascular wall-resident **stem cells**

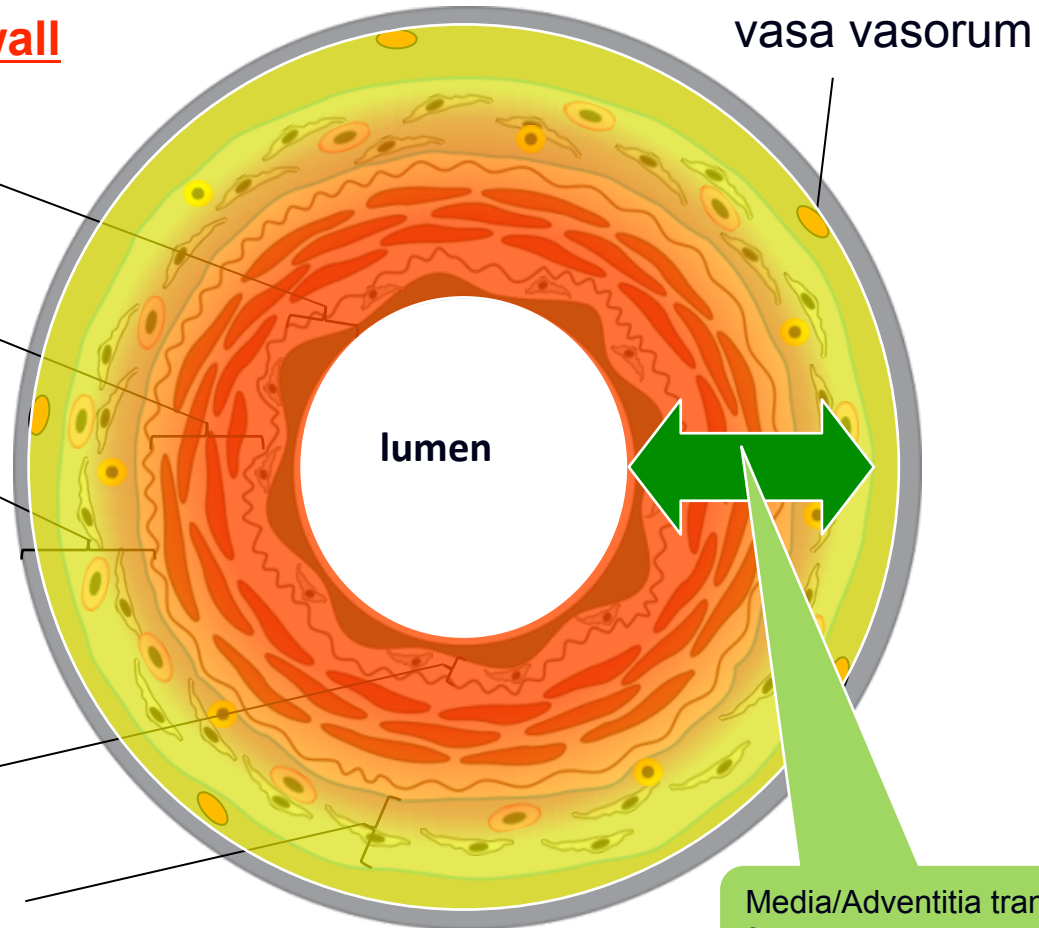
Endothelial Progenitor Cells (EPCs)
Mesenchymal Stem Cells (MSCs)

Layers of the vessel wall

Tunica intima
Tunica media
Tunica adventitia

Niches of the VW-SCs

Sub-endothelial zone
„Vasculogenic zone“



Media/Adventitia transition
fem.-pop. = 1,9 mm
(own IVUS measurements)

Tilki et al., Trends in Molecular Medicine, 2009

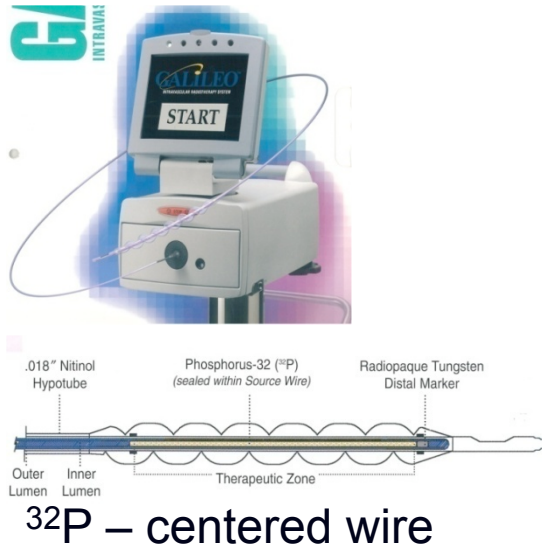
Klinikum Augsburg

Akademisches Lehrkrankenhaus der Ludwig-Maximilians-Universität München

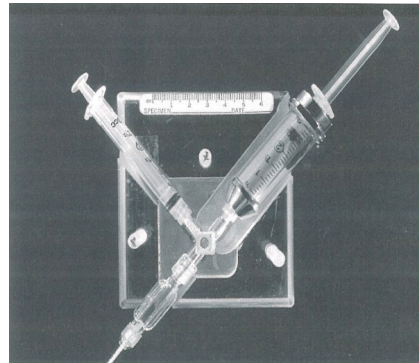


Earlier Methods for endovascular Brachytherapy

Guidant



„Homemade“



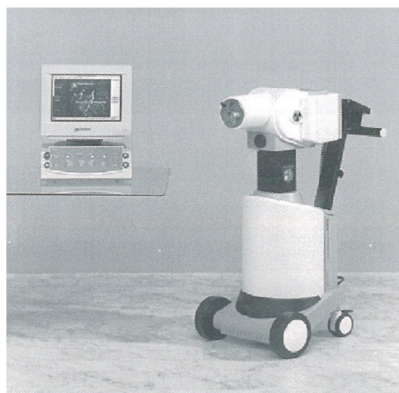
^{188}Re – filled balloon catheter

Novoste



^{90}Sr / ^{90}Y sources „trains“ uncentered

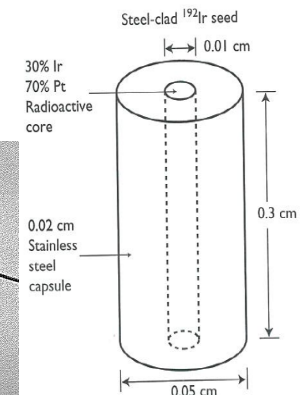
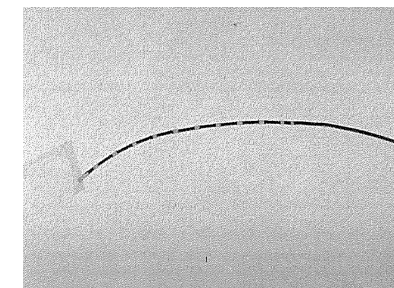
Nucletron



^{188}W / ^{188}Re -wire
oder
 ^{32}P - wire

Best Medical

^{192}Ir - wire

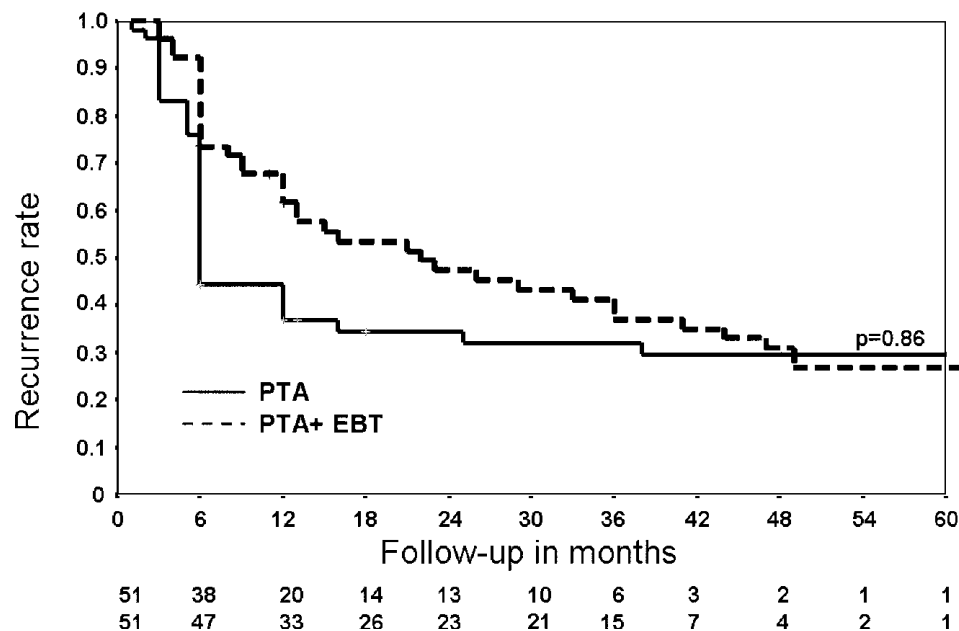


Endovascular Brachytherapy for Prophylaxis of Restenosis after Femoropopliteal Angioplasty:

Five-year Follow-up—Prospective Randomized Study¹

Wolfram RM; E Minar ;Wien
Radiology 2006; 240:878-884

51 Pat. PTA + Brachytherapy with Iridium 192
51 Pat. PTA alone
Restenosis = >50%
only ASS !
12 Gray 3 mm off Center; uncentered



At 5-year follow-up, PTA followed by gamma radiation EBT with a dose of 12 Gy resulted in a delay but not an inhibition of restenosis when compared with that of PTA alone.

During follow up „late catch-up henomenon“

=> after 5 years alignment of restenosis rate EVBT&PTA

Problem : Centering of the radiation source ?!

**Wolfram R et al;
Endovascular Brachytherapy: Restenosis in deNovo versus
Recurrent Lesions of Femoropopliteal Artery;
Radiology 2005; 236:338-342**

100 Pat. PTA + Brachytherapy

99 Pat. PTA

Restenosis = >50%

18 Gray centered; in 2-4 mm distance

Restenosis Rate after 12 months

	DeNovo- stenosis	Recurrent- stenosis
PTA	44% _(30/68)	71%
PTA/ Brachytherapy	36% _(24/66)	26%

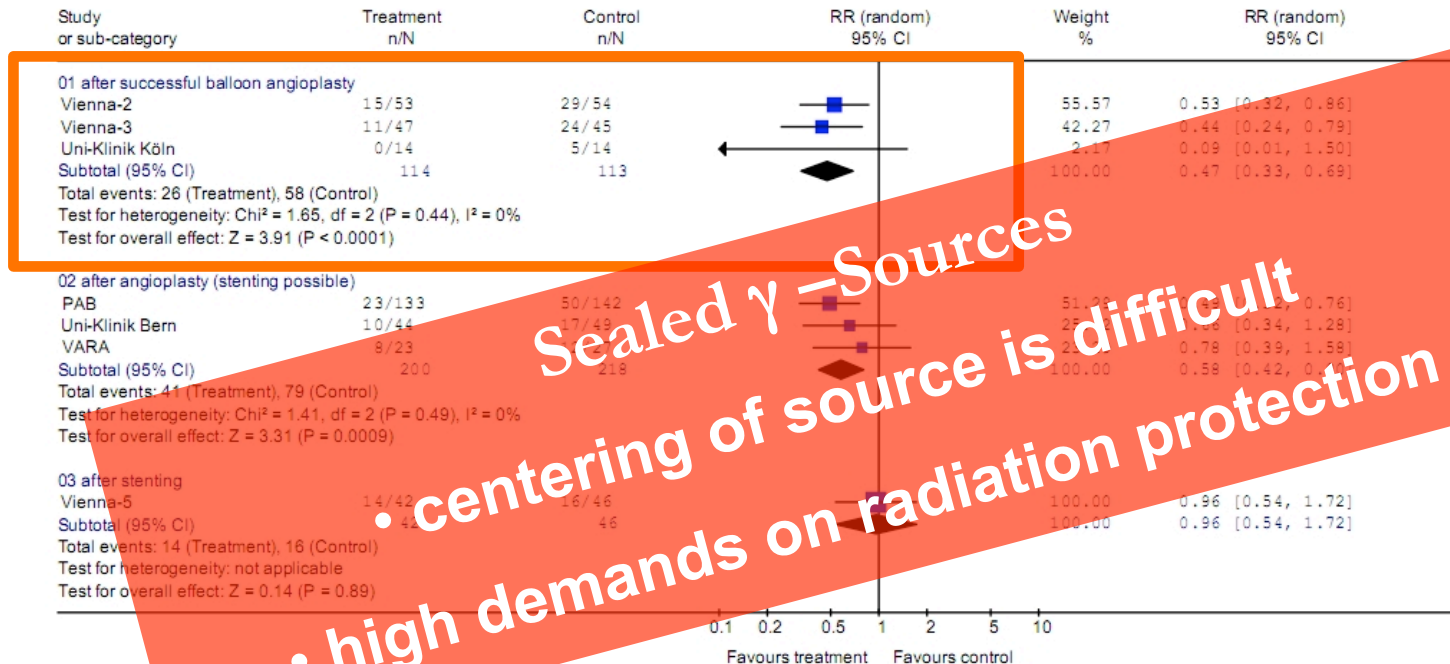
=> Improvement in prevention of recurrent stenosis



Large amount of studies (approx. 35 studies, 20 in Cardiology, 15 in Radiology)

... medizinischen Bewertung zieht der Bericht ⁽¹⁾ zwölf Publikationen zu sieben randomisierten kontrollierten Studien heran...

Review: Intravascular Brachytherapy for peripheral vascular disease
Comparison: 01 Brachytherapy vs. no brachytherapy
Outcome: 01 Rate of Restenosis (per protocol / as treated)



Englisch, eigene Berechnungen. 95 % CI = 95 % Konfidenzintervall. RR = Relatives Risiko.

Abbildung 1: Metaanalyse für Restenoserate nach sechs bzw. zwölf Monaten aus per-Protokoll-Daten

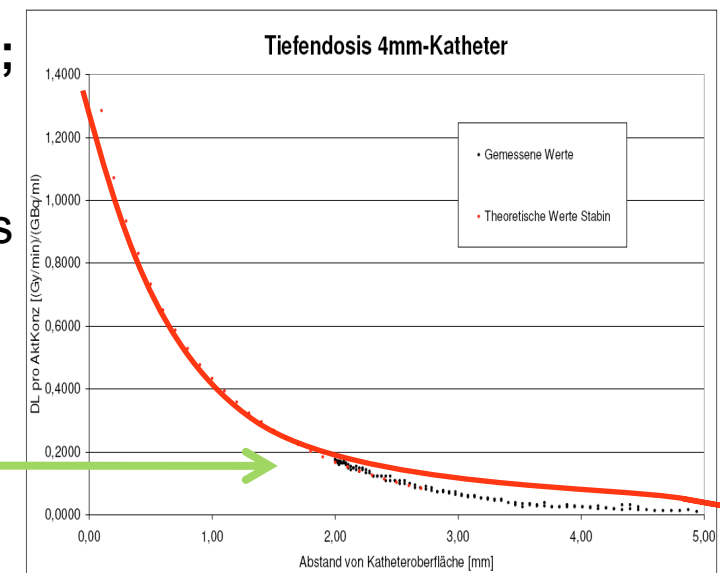
...prove that brachytherapy following a successful balloondilatation of a blood vessel reduces the **rate of restenosis**. Also the time period to develop a new stenosis is decreased.

(1) hta Bericht: Intravaskuläre Brachytherapie bei pAVK; Schriftenreihe Health Technology Assessment, Bd.75: 1864-9645 1. Auflage 2008

β - Source /Rhenium-188

- Strictly local irradiation of the vessel wall according to the steep decrease of dose (**13,3 Gy in 2mm depth of vessel wall tissue**) (own measurements)
- **Therapy can be done in the angiography cabinet**
- The filling of the balloon with liquid Re-188 using low pressure **centers the source**
- **Phys.half-life of Rhenium-188 is approx. 17 h;**
biol. Half-life approx. 7-9 h
(biphasic excretion: 3,6 hours for 60%
of the incorporated activity and 12,3 hours
for the residual 40%)

In 2 mm distance from the catheter surface the dose is about 1/8 of the dose at the surface of the balloon

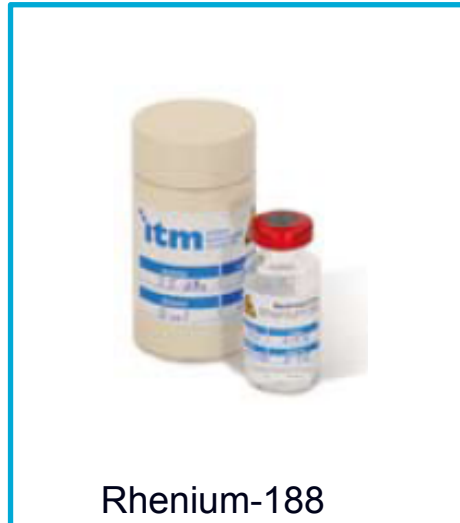


„Hardware“ for Rhenium-PTA (β -source)

The system components are certified medical products class CE IIb (CE 1275) since 09/2008 .



Application device



Rhenium-188



PTA-Catheter
(Clearstream)



PTA-single use-set



Total equipment with all accessories
(1,waste disposal box, 2,shielding rings, 3,transport
trolley)

Requirements for Application

Organisation

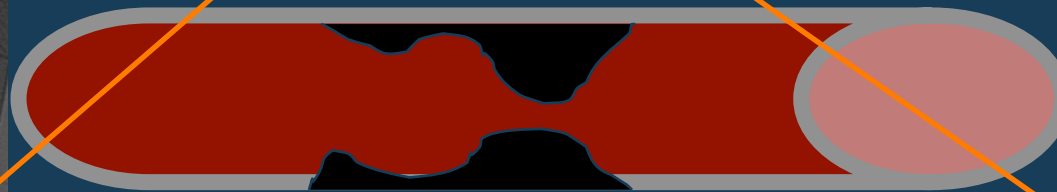
- Radiologist/interventionalist
- Medical physicist
- Nuclear Medicine physician

Others

- Specified licence for use of open sources including disposal of waste



Stenosis



Durchleuchtung

SUBTRACTION

/40 mm

0 MM

PTA of stenosis

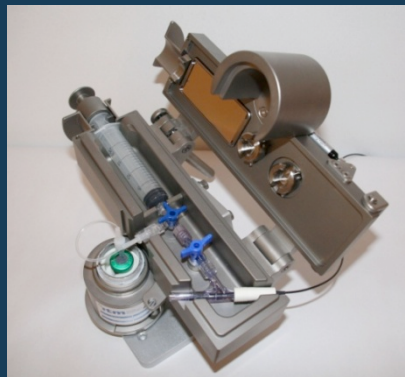


Intravascular irradiation with Rhenium-188

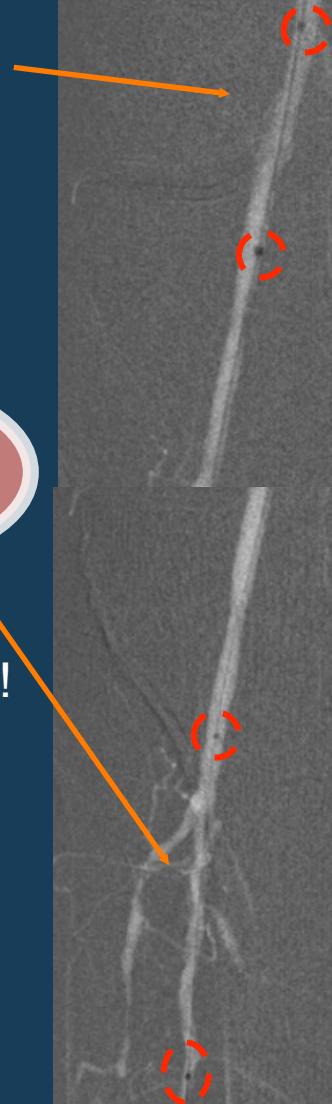
5/100 mm

13,3 Gy in 2mm tissue depth

EVBT-Ballonlength proximal & distal 1 cm longer!



Rhenium Applikator
made of tungsten



1 Oberschenkel H 1 B/s D---

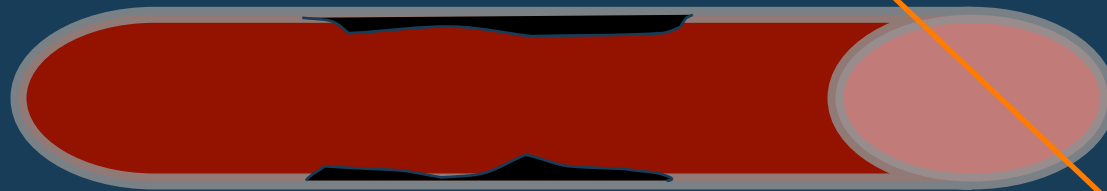
SUBTRACTION

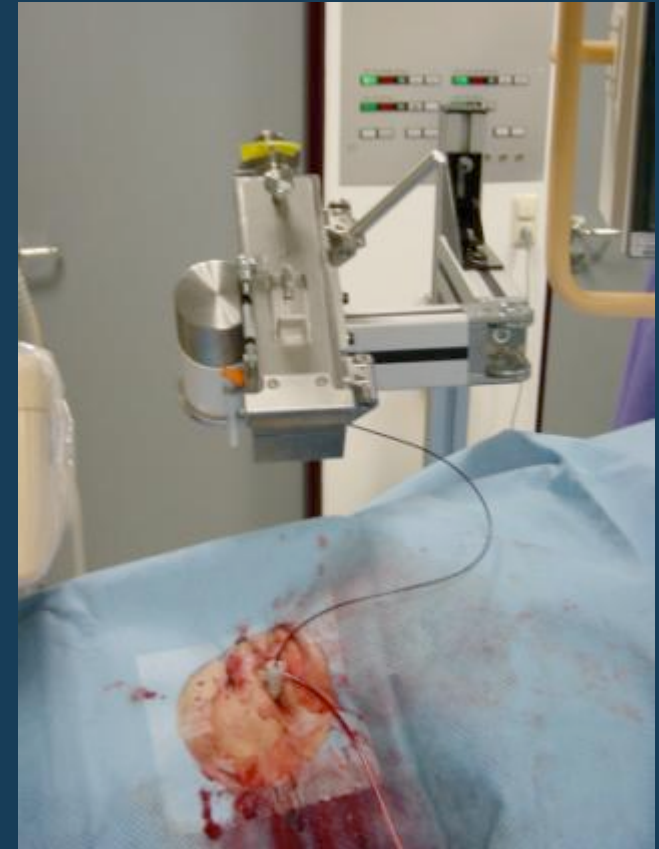
EVBT =>

**Final
situation**

henium

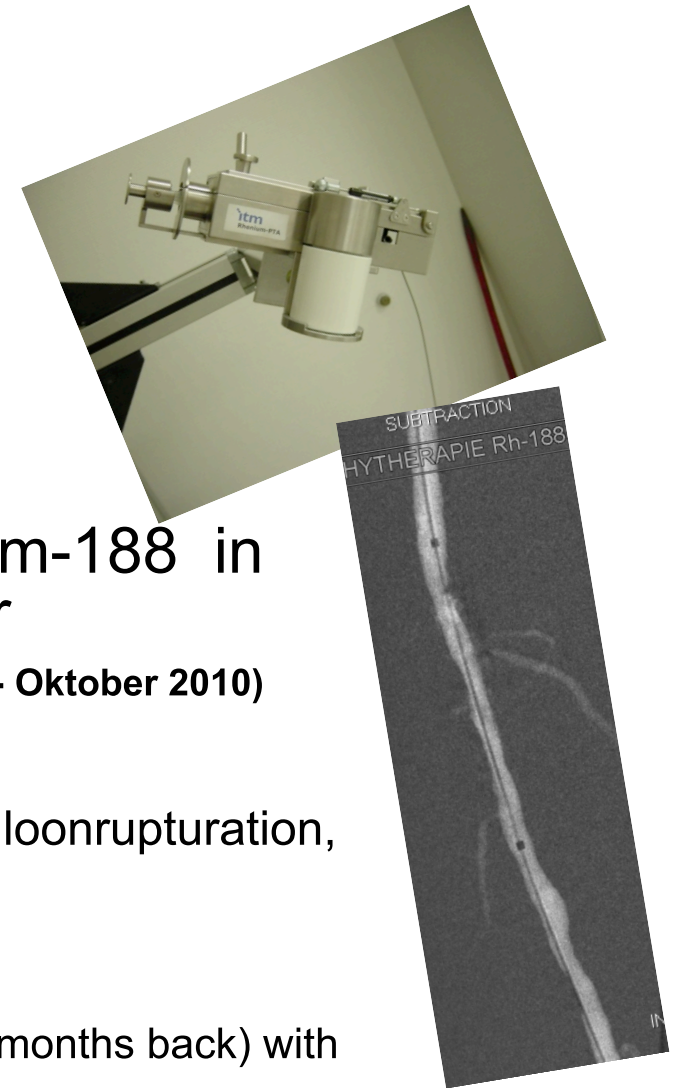
BT =>





Results

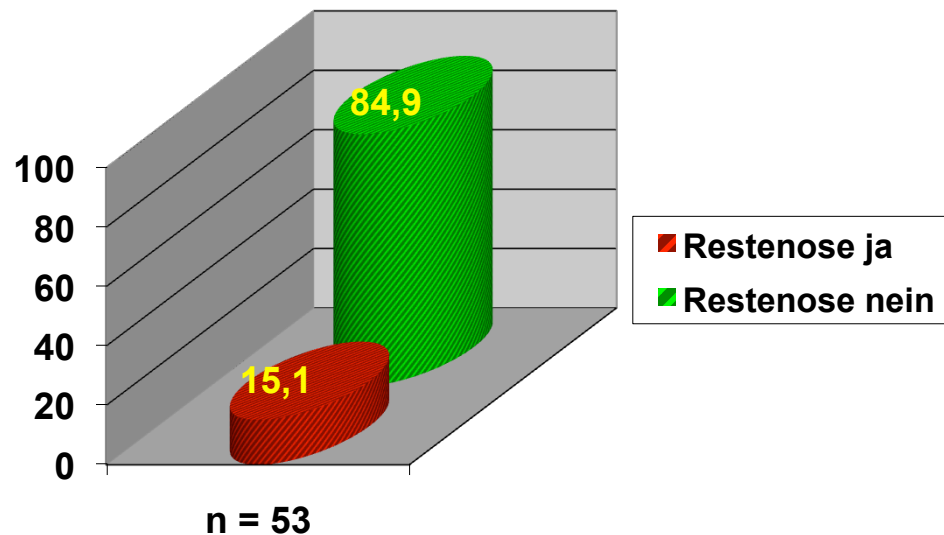
- Endovascular brachytherapy mit Rhenium-188 in **135 femorocrural lesions (105 pat.)** for reststenosisprevention post PTA. (März 2006- Oktober 2010)
- **No periprocedural complications** (e.g balloonrupturation, vessel occlusion, pat.-contamination...).
- Follow-up of **40 pat. /53 lesions** (EVBT >6 months back) with clinical exam, KD, stresstest und FKDS)



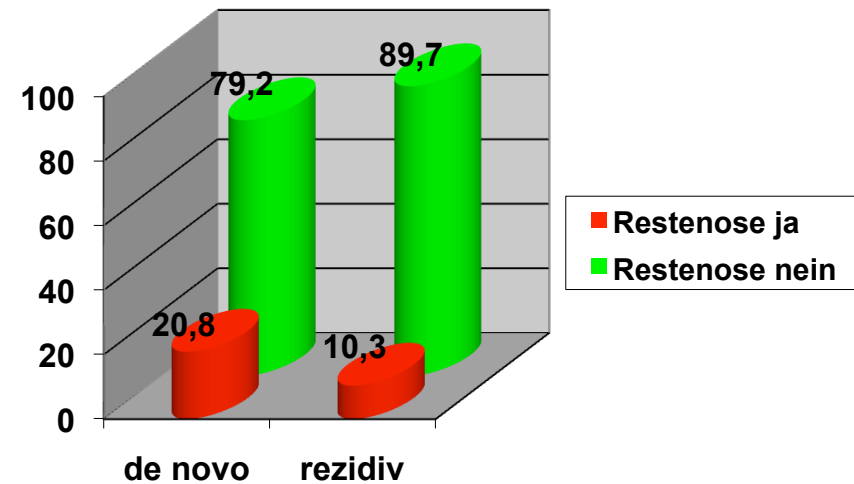
	N	Minimum	Maximum	Mean value	Standarddev.
Ballondim. primary PTA (mm)	53	3	5	4,66	0,706
Ballonlänge primary PTA (mm)	53	20	220	58,30	45,520
Ballonlength Rh-PTA (mm)	53	40	240	80,00	47,394
Activityconcentration (MBq/ml)	53	1937	8204	4817,75	1261,684
Irradiation time (min)	53	5,1	25,0	10,608	3,9904



Total-Restenosisrate (%)

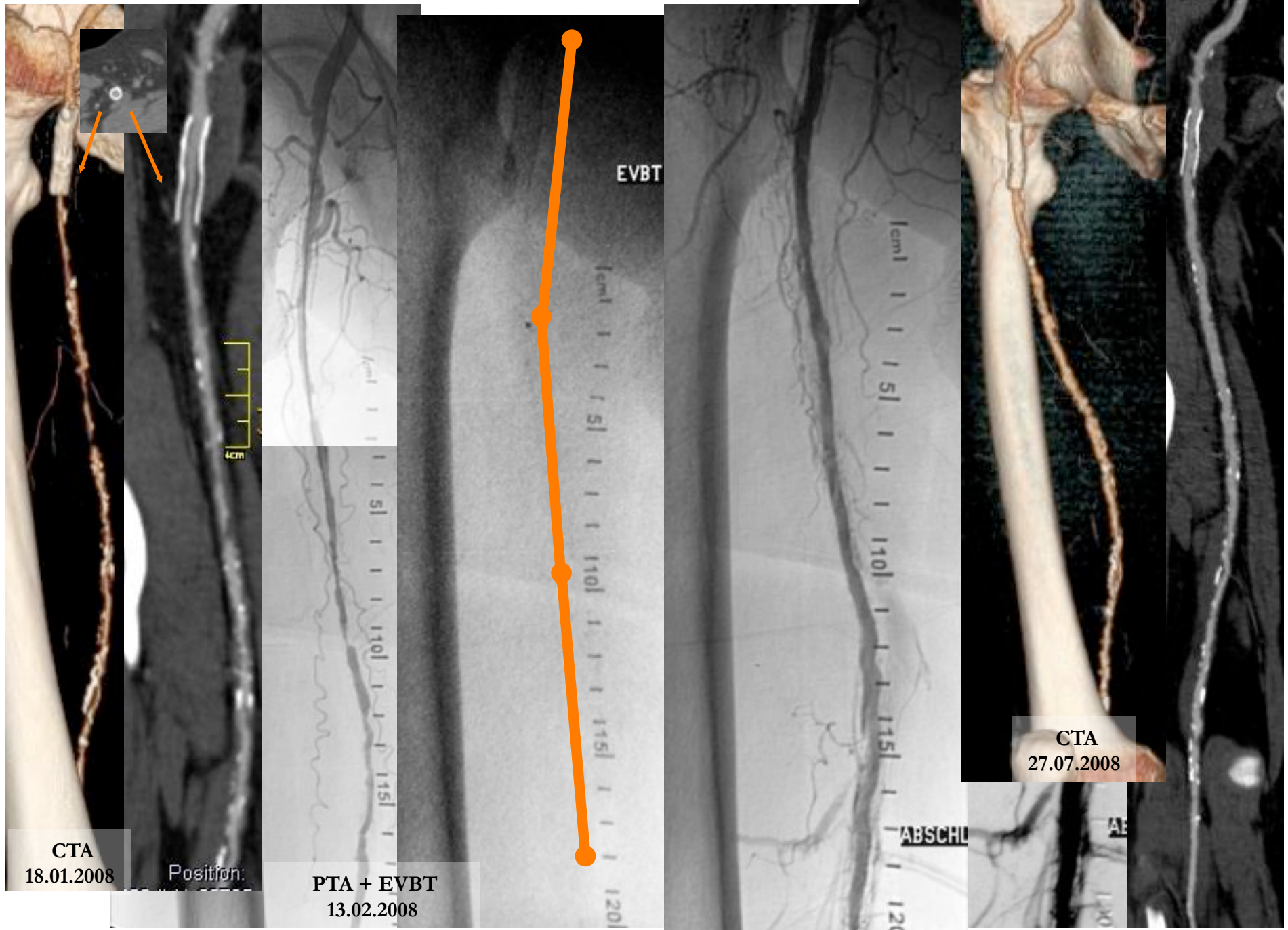


Restenosisrate (%) in dependence of de novo- or recurrant-lesions

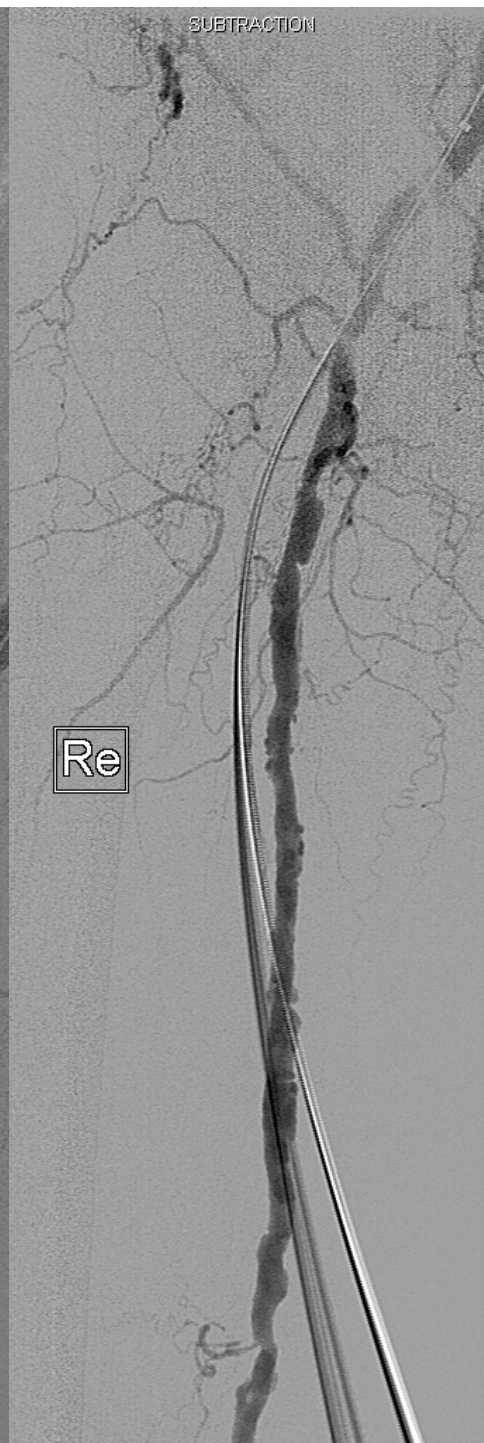
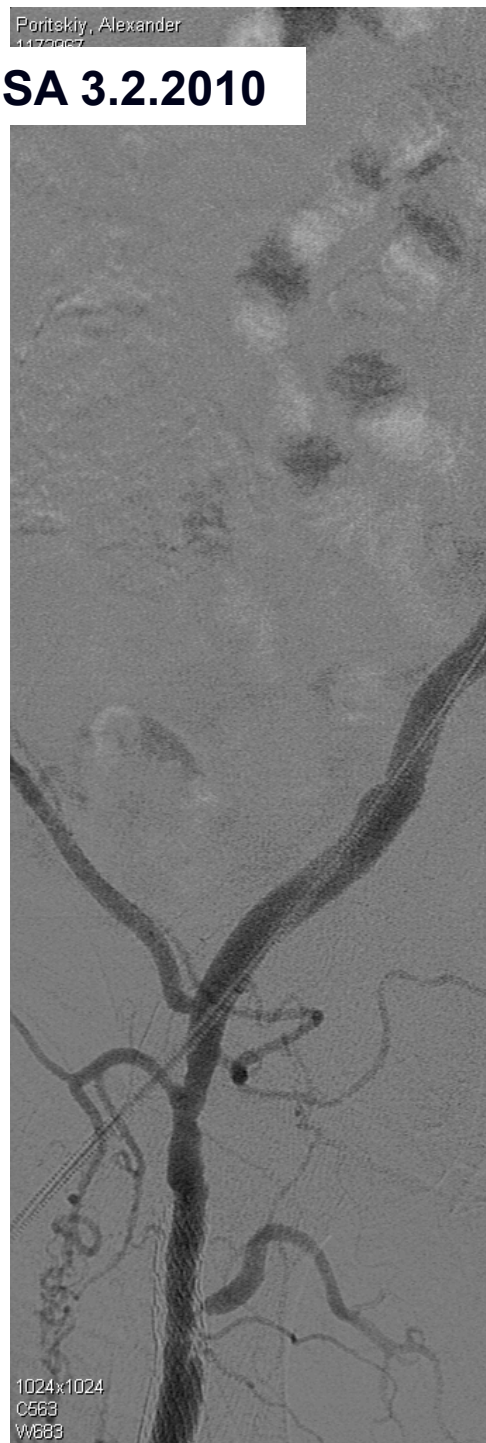


		Restenosis		Total
		yes	no	
De Novo oder Recurrence	de novo	5 (20,8%)	19 (79,2%)	24 (100%)
	recurrence	3 (10,3%)	26 (89,7%)	29 (100%)
Total		8 (15,1%)	45 (84,9%)	53 (100%)

71 years, pAVK III, PTA+Stent 7 months ago; dual TAH



DSA 3.2.2010



Where, what dose?

Optimal dosage is still unclear, because of

- problems in comparability of dose informations given in studies
- uncentered sources used in various studies

„Usual Dose“

Coronaries: 6 – 18 Gy (2mm from center)

periph. vessels: 7 - 20 Gy (2mm tissue depth)

Dose limitation:

After percutaneous irradiation of 47-70 Gy fractionated total dose
arterial obstructions can occur (latency 11-18 years)



„Augsburg“ Dose-Protocol:

Dose documentation in defined target structure:

Dose at transition media/adventitia:
(max. distance of media to balloon)

more than 10 Gy

e.g. fem.-pop. arteries (d=5mm)

13,3 Gy in 2 mm

e.g. crural arteries

13,3 Gy in 1,5 mm





Thank you for your attention!

Organ	Spezifische Organdosis (nach Stabin 2000) ohne Perchlorat [Gy/GBq]	Spezifische Organdosis (nach Kotzerke 1998) mit Perchlorat [Gy/GBq]	Organdosis bei 15 GBq inkorporierter Aktivität ohne Perchlorat nach Stabin [Gy]	Organdosis bei 15 GBq inkorporierter Aktivität mit Perchlorat nach Kotzerke [Gy]	Toleranzdosis TD5/5 (Seegenschmiedt 2000) [Gy]
Gefäße (außer Bestr.-Abschnitt)	0,0445	0,068	0,7	1,0	50
Gehirn	0,0435	0,067	0,7	1,0	45
Brust	0,0434	0,067	0,7	1,0	50
Gallenblasenwand	0,0466	0,068	0,7	1,0	50
Dickdarm	1,9750	0,069	30	1,0	45
Dünndarm	0,0497	0,068	0,8	1,0	40
Magen	0,4330	0,067	0,7	1,0	50
Herz	0,0442	0,068	0,7	1,0	40
Nieren	0,0448	0,067	0,7	1,0	30
Leber	0,0446	0,067	0,7	1,0	30
Lunge	0,0438	0,067	0,7	1,0	17,5
Muskeln	0,0445	0,067	0,7	1,0	100
Ovarien	0,0499	0,069	0,7	1,0	2
Rotes Knochenmark	0,0448	0,068	0,7	1,0	2,5
Knochenoberfläche	0,0452	0,067	0,7	1,0	60
Haut	0,0435	0,066	0,7	1,0	50
Hoden	0,0447	0,067	0,7	1,0	5
Schilddrüse	1,1000	0,067	17	1,0	45
Harnblasenwand	1,5100	1,500	23	23	65
Gebärmutter	0,0487	0,070	0,7	1,0	100
Ganzkörper	0,0574	0,069	0,89	1,0	