Prevention of Restenosis
in CLI Patients

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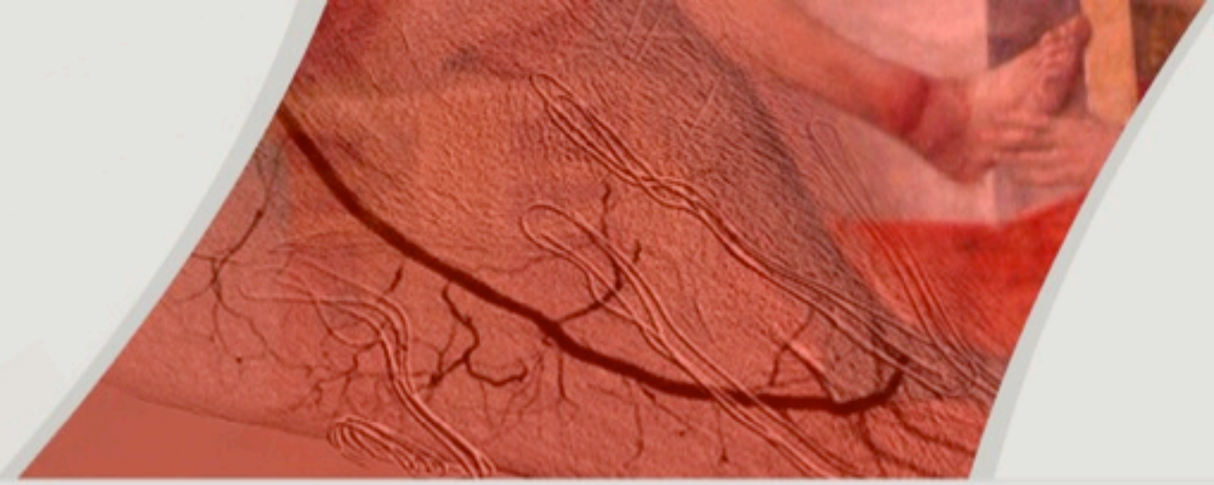
Italy

Prevention of Restenosis

in CLI Patients



Clinical Experience Milan 2010-2013

CLI disease patterns

Revascularization targets and lesion mean length

BTK-CLI treatment (devices)

Studies and Clinical Cases Evidence

Healing time in RTF 5-6 Patients

Restenosis Rate and Significance in CLI patients

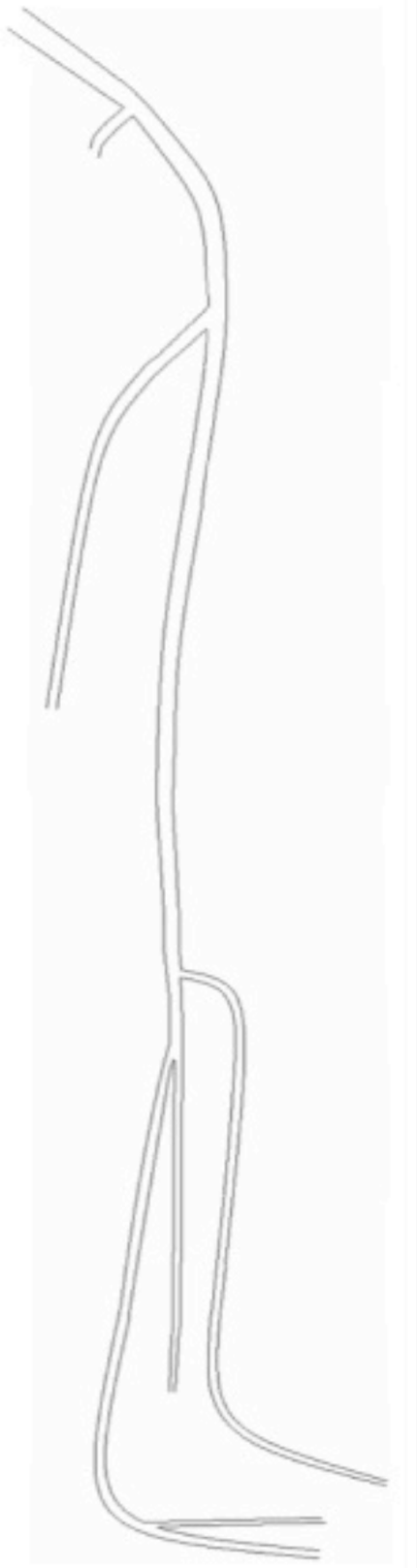
- Case 1

Restenosis in BTK vessels

Conclusions

1) Pattern of disease in CLI patients

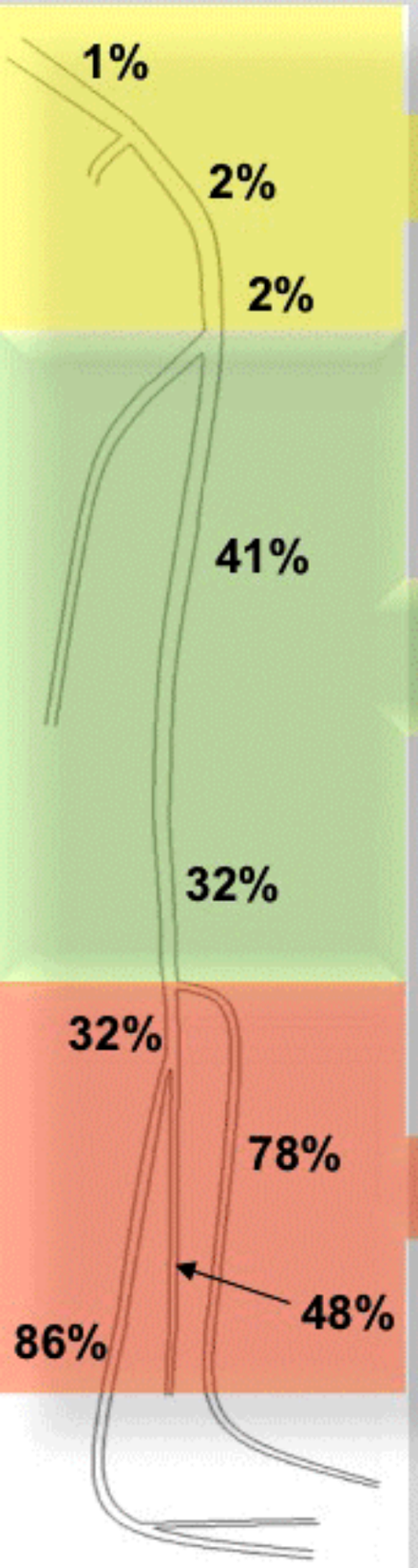
Pattern of disease in CLI patients



CLI “real world” patients 2010-2013, our diabetic foot clinic

- 1,343 patients →1,589 legs (first angiographic study)
- All CLI patients (Rutherford 4-5-6)
- Mean age 72 yrs
- 82% DM
- 46% smokers/ex-smokers
- 20% end-stage-renal-disease in hemodialysis
- 75% high blood pressure

Pattern of disease in CLI patients



5% above-the-groin (ATG)

53% FEM-POP

95% BTK

TPT	32%	
0 BTK vessel	5%	
1 BTK vessel	15%	
2 BTK vessels	43%	80%
3 BTK vessels	37%	

Pattern of disease in CLI patients

5% above-the-groin (ATG)

53% FEM-POP

95% BTK

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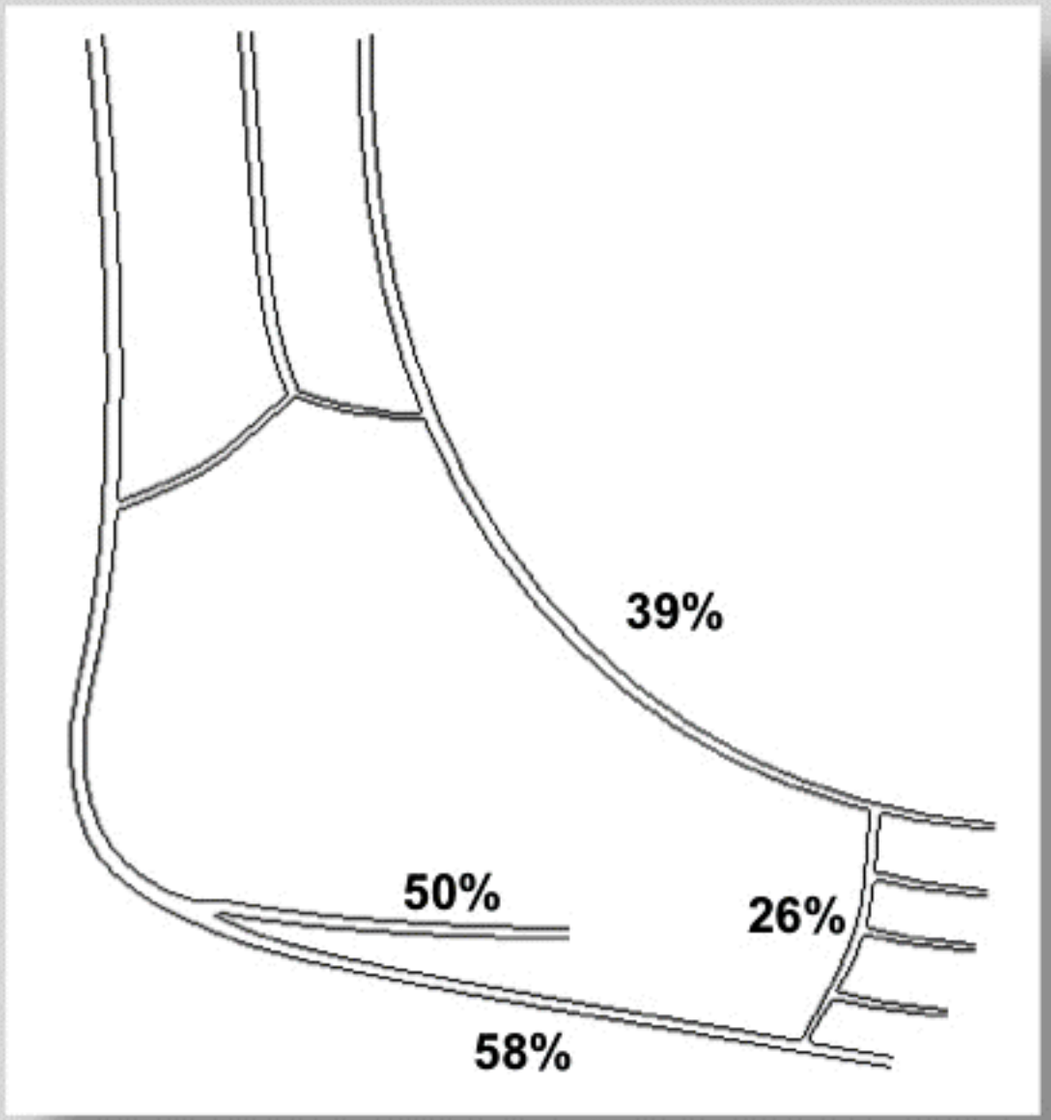
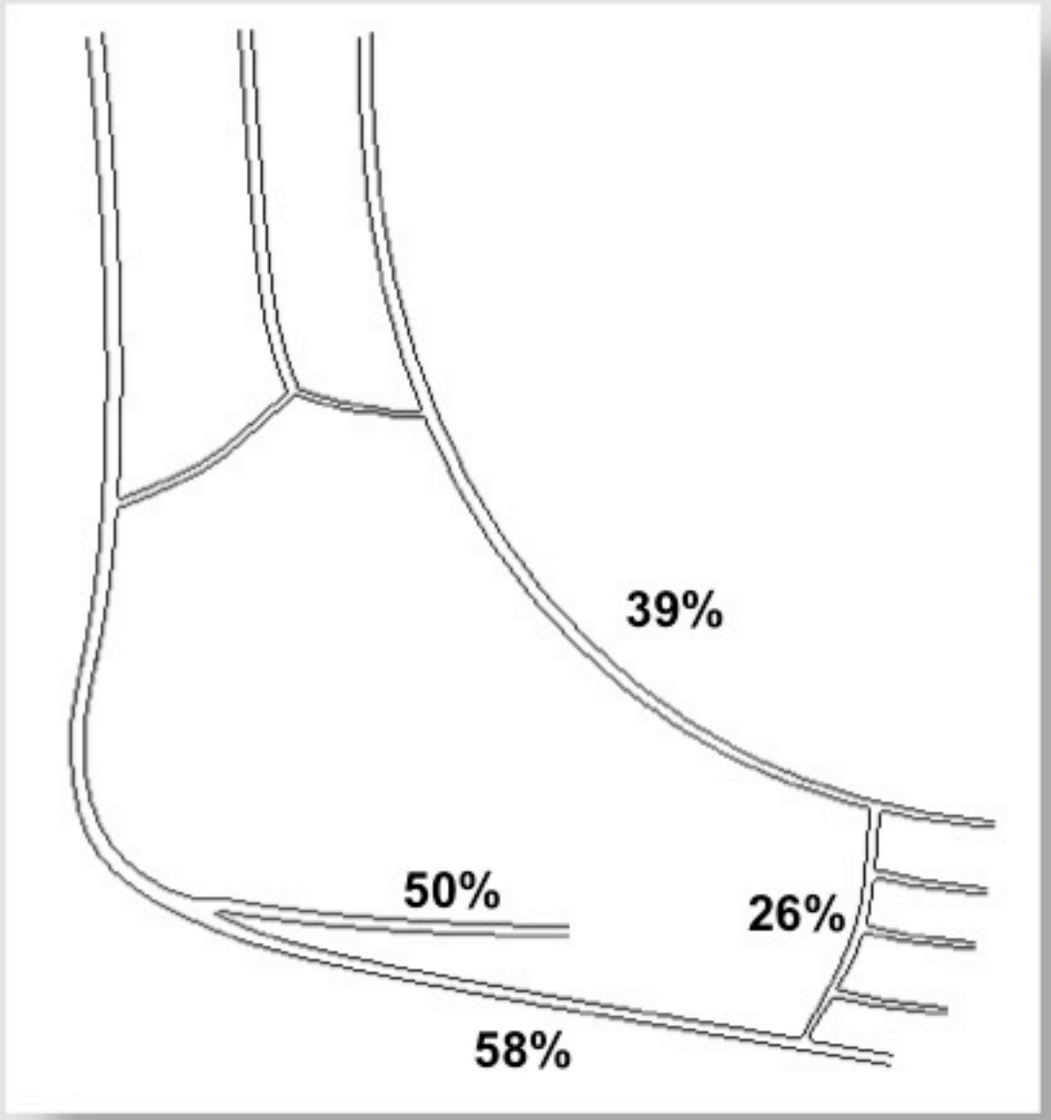
Pattern of disease in CLI patients



0 FOOT vessel	**26%**	
1 FOOT vessel	**22%**	
2 FOOT vessels	**31%**	**52%**
3 FOOT vessels	**21%**	
ARCH	**26%**	

Pattern of disease in CLI patients



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3 FOOT vessels	**21%**	
ARCH	**26%**	

Pattern of disease in CLI patients

5% ATG

53% FEM-POP

95% BTK

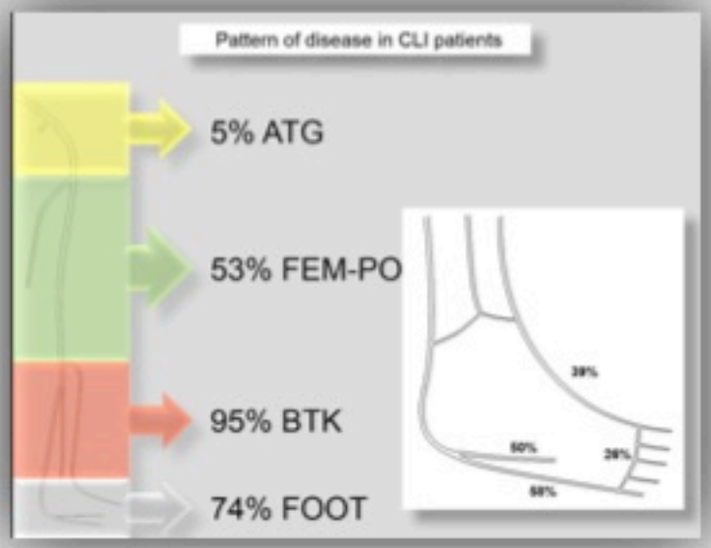
74% FOOT

Conclusions

1. Above-the-groin disease is not common in a diabetic-foot clinic, because this localization is not related to diabetes

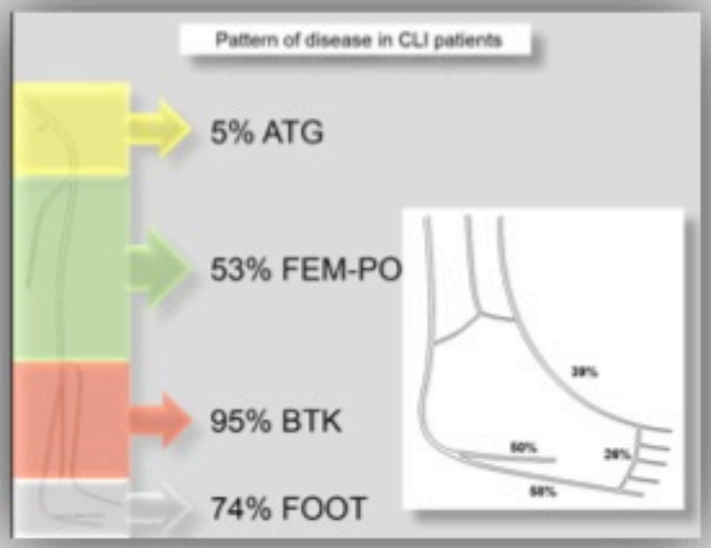
2. Fem-pop disease is present in more than half of the patients

3. BTK & FOOT vessel disease is an emergent cause of CLI: 80% of the patients have 2 or 3 BTK vessels disease, 52% of the patients have 2 or 3 FOOT vessels disease



1)

…epidemic of OLD-DM-ESRD-CLI pts: multilevel disease & extensive involvement of BTK&FOOT vessels



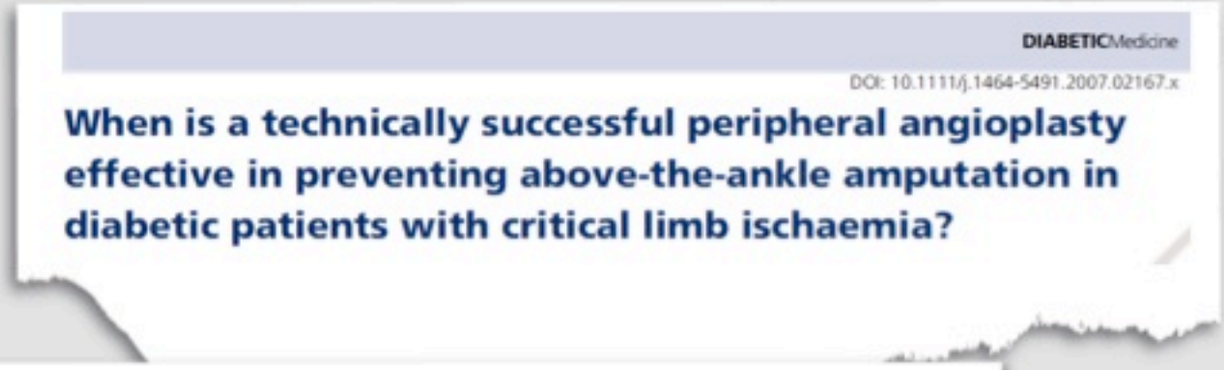
1) …epidemic of OLD-DM-ESRD-CLI pts: multilevel disease & extensive involvement of BTK&FOOT vessels

2) **Targets in CLI revascularization**

Targets in CLI revascularization

1. Complete revascularization

- 1 vessel better than 0
- 2-3 vessels better than 1
- Tibials better than peroneal



DIABETICMedicine

DOI: 10.1111/j.1464-5491.2007.02167.x

When is a technically successful peripheral angioplasty effective in preventing above-the-ankle amputation in diabetic patients with critical limb ischaemia?

Cardiovasc Intervent Radiol (2010) 33:720–725
DOI 10.1007/s00270-010-9881-3

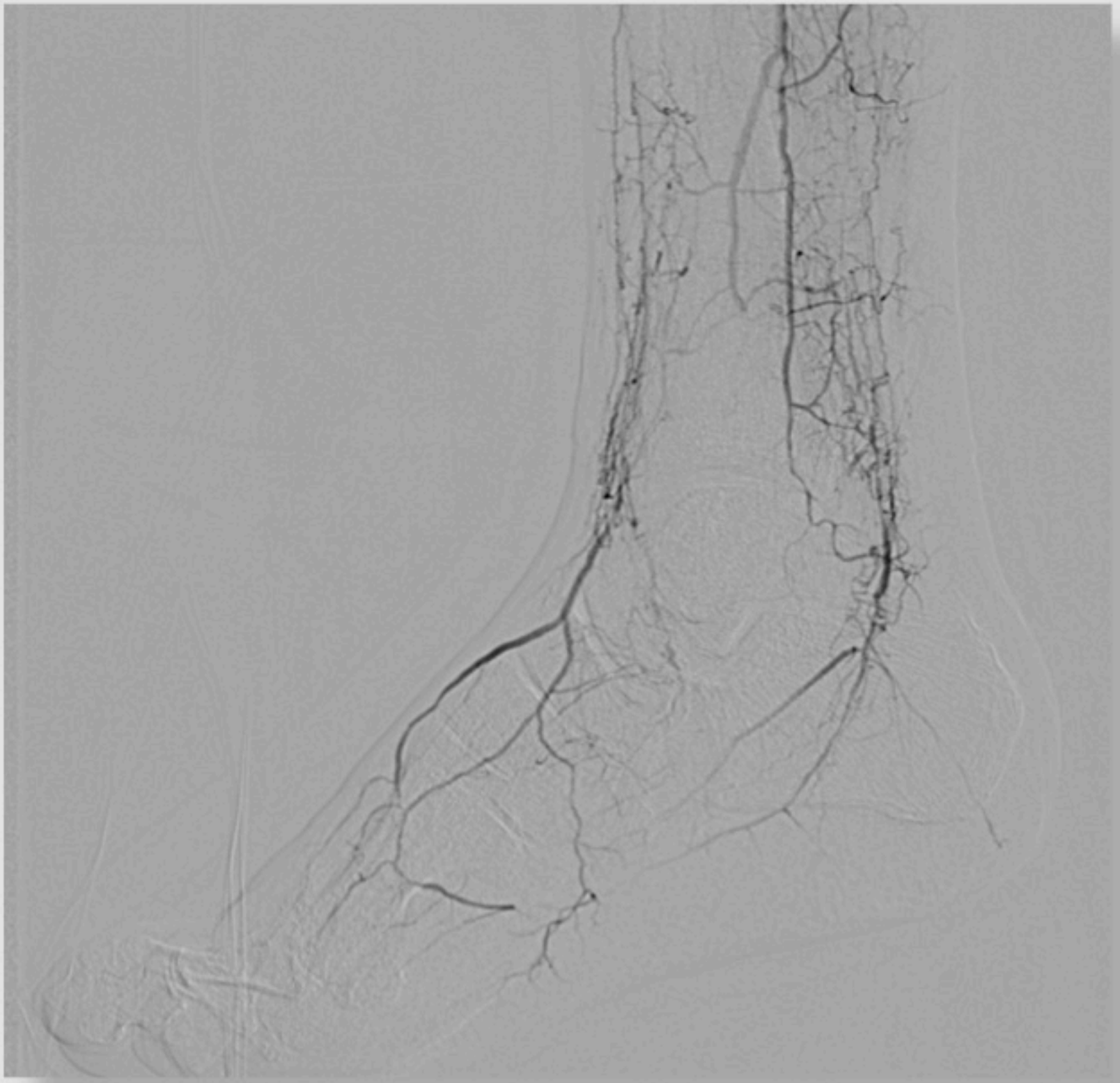
CLINICAL INVESTIGATION

PTA of Infrapopliteal Arteries: Long-term Clinical Follow-up and Analysis of Factors Influencing Clinical Outcome

Jan H. Peregrin · Boris Kožnar · Josef Kováč · Jarmila Laštovičková · Jiří Novotný · Daniel Vedlich · Jelena Skibová

Healing is a blood-flow dependent phenomenon and the first principle guiding our revascularization strategy must be giving to the foot the best possible blood supply.

Complete revascularization



Complete revascularization

Targets in CLI revascularization

1. Complete revascularization

2. WRA Revascularization

Complete revascularization could not be possible to achieve in many cases due to different reasons:

- Technical failure
- Time failure (patient stress, contrast dye amount, etc.)

Revascularization of a Specific Angiosome for Limb Salvage: Does the Target Artery Matter?

Richard F. Neville,[1] Christopl
Michael Thomassen,[2] and An

Importance of the Angiosome C
Endovascular Therapy in Pati
Critical Limb Ischemi

Osamu Iida,[1] MD, Shinsuke Nanto,[2*] MD, PhD, Masaaki Uematsu,
Kuniyasu Ikeoka,[1] MD, Shin Okamoto,[1] MD, Tomoharu Dohi,[1] MD,
Masashi Fujita,[1] MD, PhD, Hiroto Terashi,[3] MD, PhD,
and Seiki Nagata,[1] MD, PhD

A reliable approach to diabetic neuroischemic foot wounds: below-the-knee angiosome-oriented angioplasty.

Alexandrescu V, Vincent G, Azdad K, Hubermont G, Ledent G, Ngongang G, Filimon AM

WRA rev. in a “desert foot”

PATIENT DATA

- 69-year-old male
- Type 2 DM
- ESRD in hemodialysis
- Forefoot plantar ulcer

Targets in CLI revascularization

1. Complete revascularization

- 1 vessel better than 0
- 2-3 vessels better than 1
- Tibials better than peroneal

2. WRA Revascularization

- Direct revascularization (bypass or PTA) better than indirect revascularization

How much vessel have we to treat to achieve these goals?

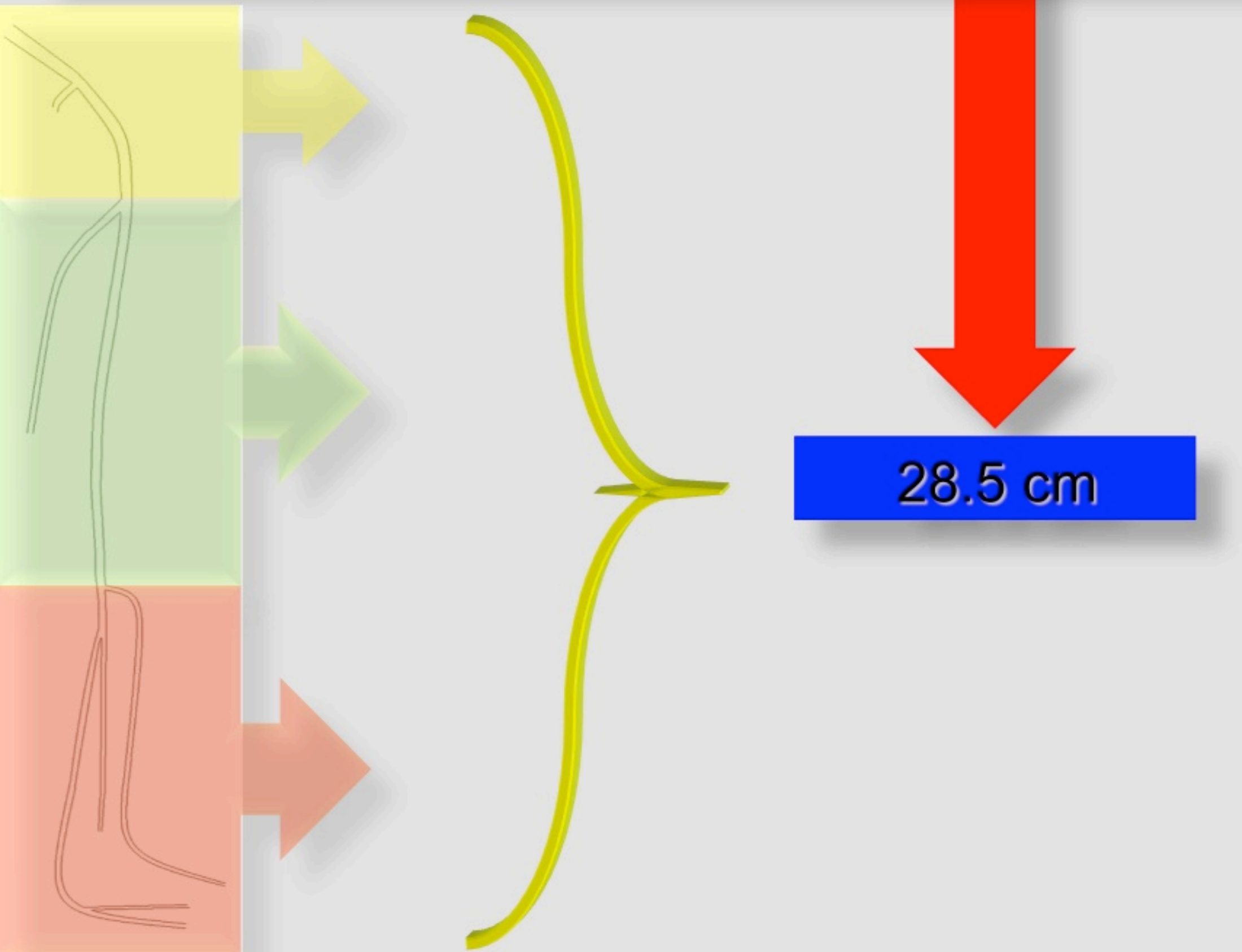
Mean length of the single treated lesion

5% ATG → 60±53 mm

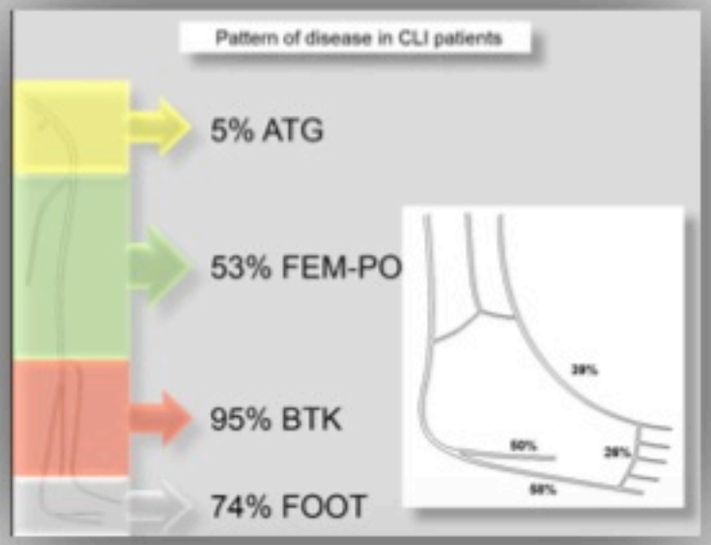
53% FEM-POP → 121±113 mm

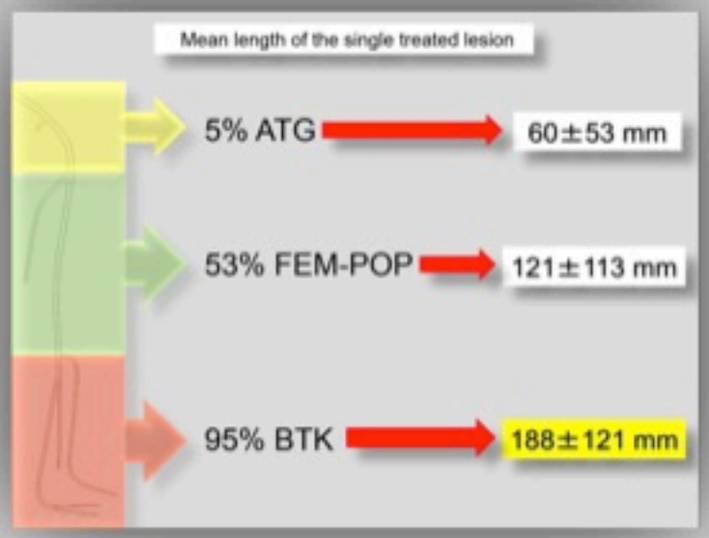
95% BTK → 188±121 mm

Mean length of the treated vessel in a single limb/procedure



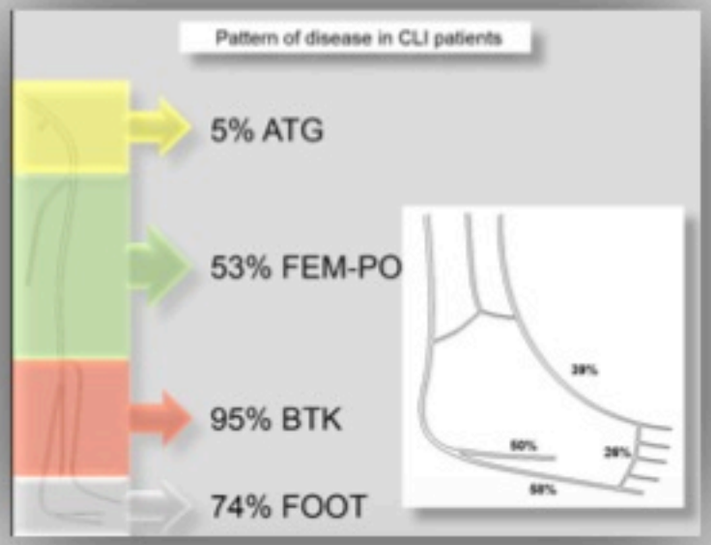
28.5 cm

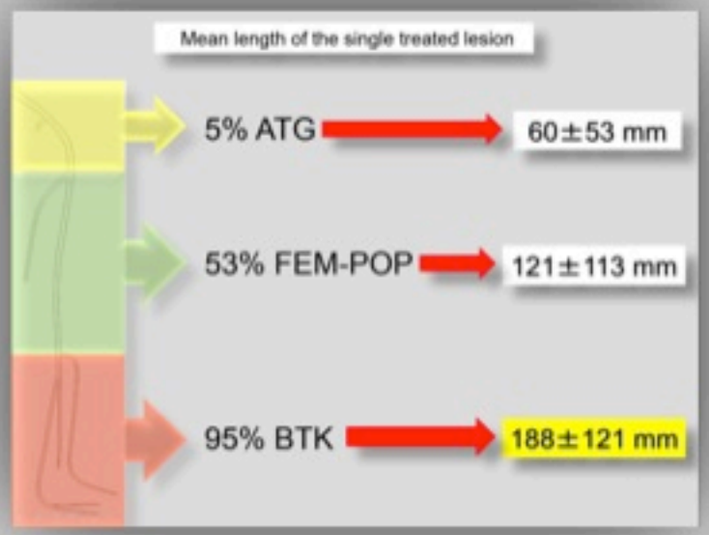




1) …epidemic of OLD-DM-ESRD-CLI pts: multilevel disease & extensive involvement of BTK&FOOT vessels

2) **Complete/WRA PTA → we have to treat a lot of vessel to gain healing!**





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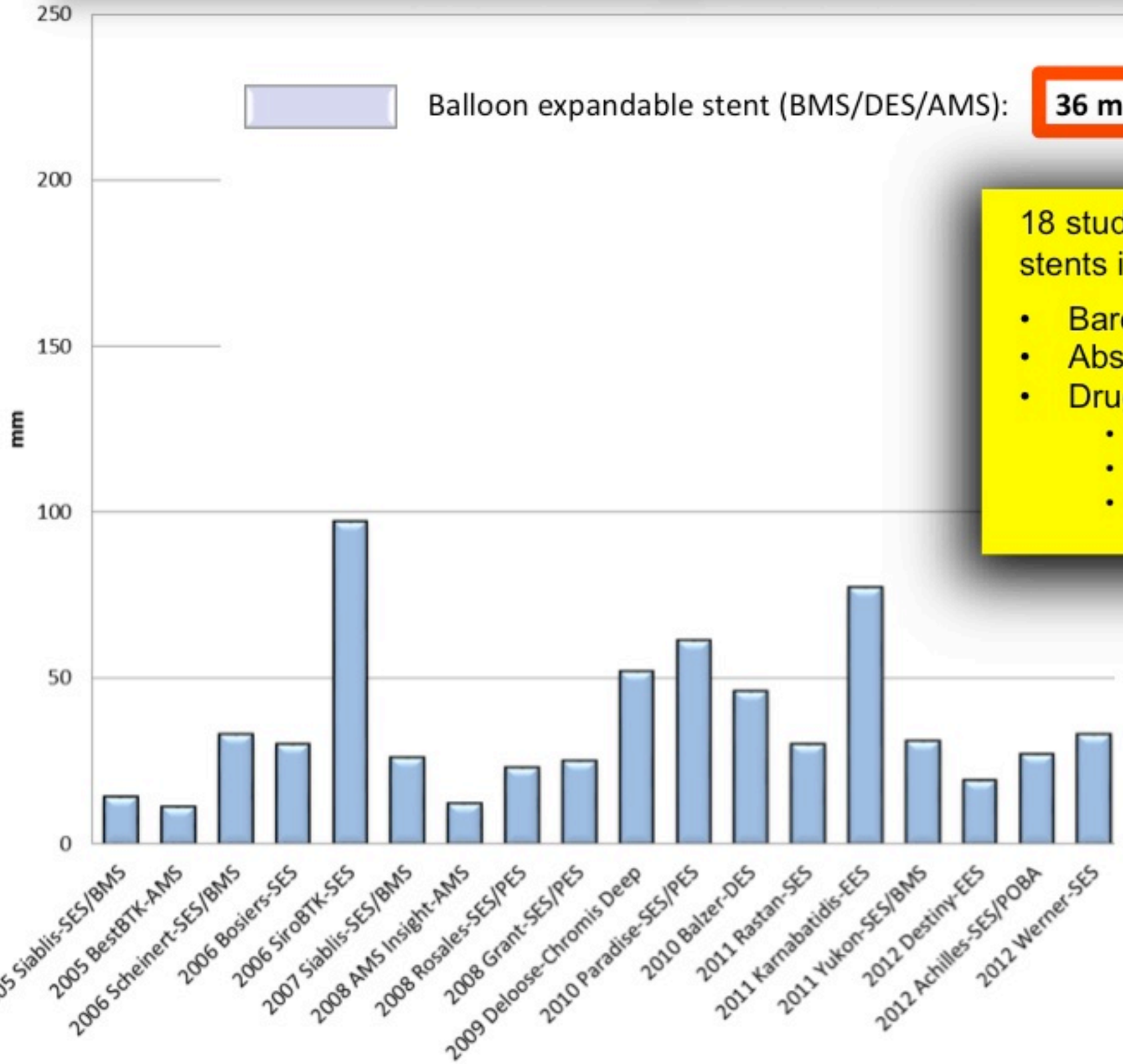
3) **BTK-CLI angioplasty**

Mean length of the treated lesion

Balloon expandable stent (BMS/DES/AMS): **36 mm (11-97)**

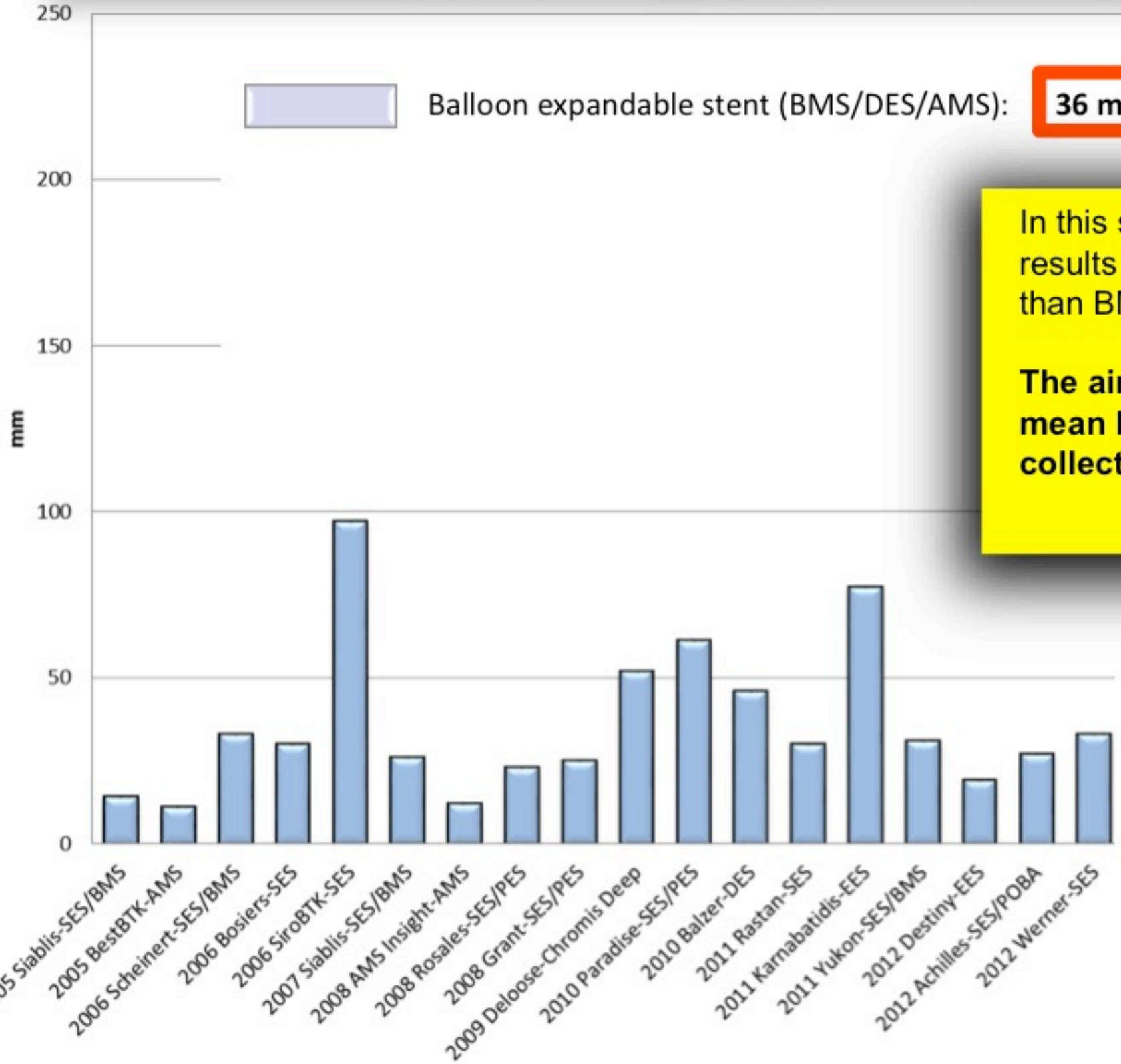
18 studies with Balloon expandable stents in BTK arteries:

- Bare Metal Stents (BMS)
- Absorbable Metal Stent (AMS)
- Drug-Eluting Stents (DES)
  - Sirolimus-Eluting Stent (SES)
  - Everolimus-Eluting Stent (EES)
  - Paclitaxel-Eluting Stent (PES)



Published studies on BTK angioplasty

Mean length of the treated lesion



In this slide we don't want to show the results regarding patency (DES better than BMS better than POBA etc.).

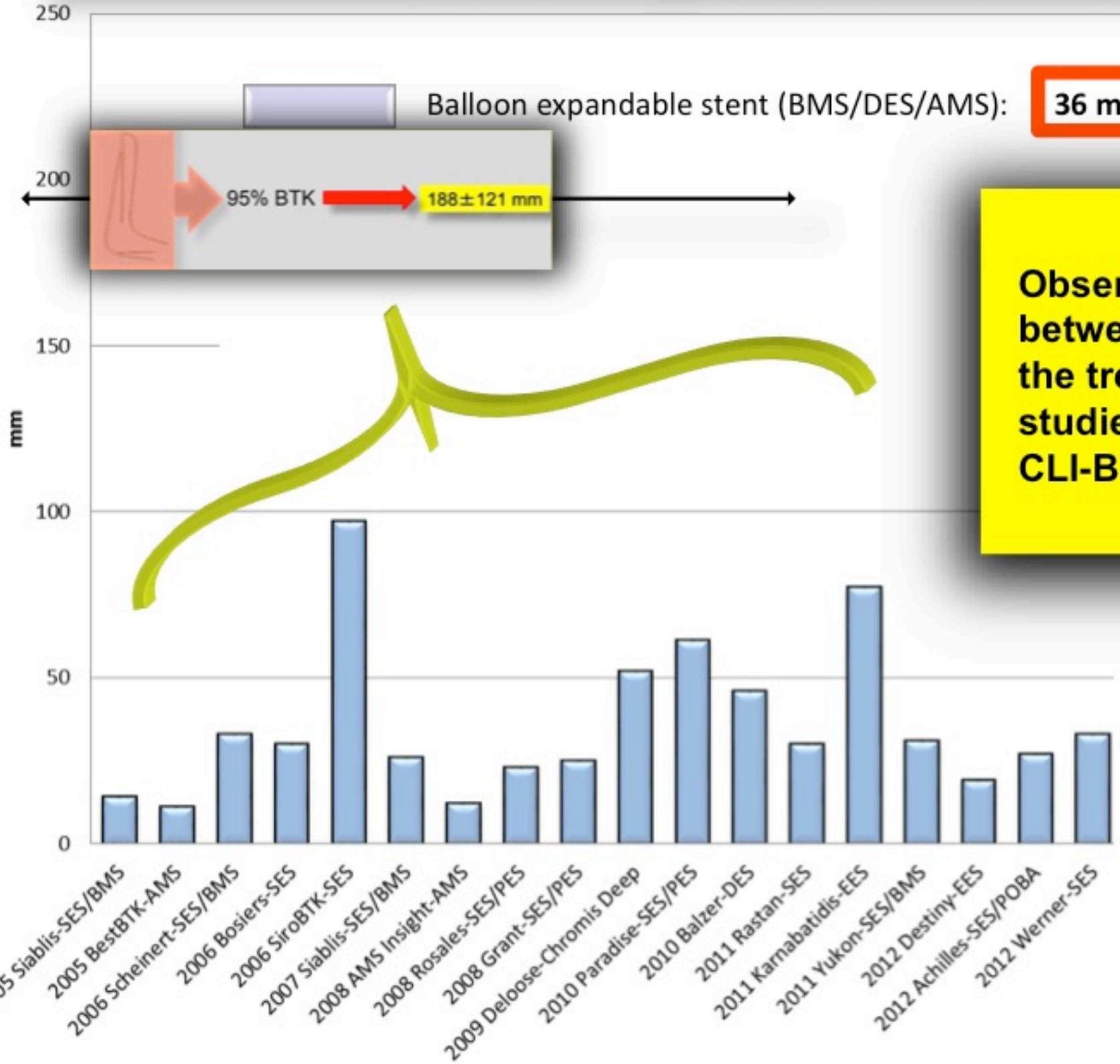
The aim of the slide is to show the mean length of the treated lesions collected in these studies!

Published studies on BTK angioplasty

Mean length of the treated lesion

Balloon expandable stent (BMS/DES/AMS): **36 mm (11-97)**

Observe the difference between the mean length of the treated lesion in these studies and our real world of CLI-BTK lesions!



Published studies on BTK angioplasty

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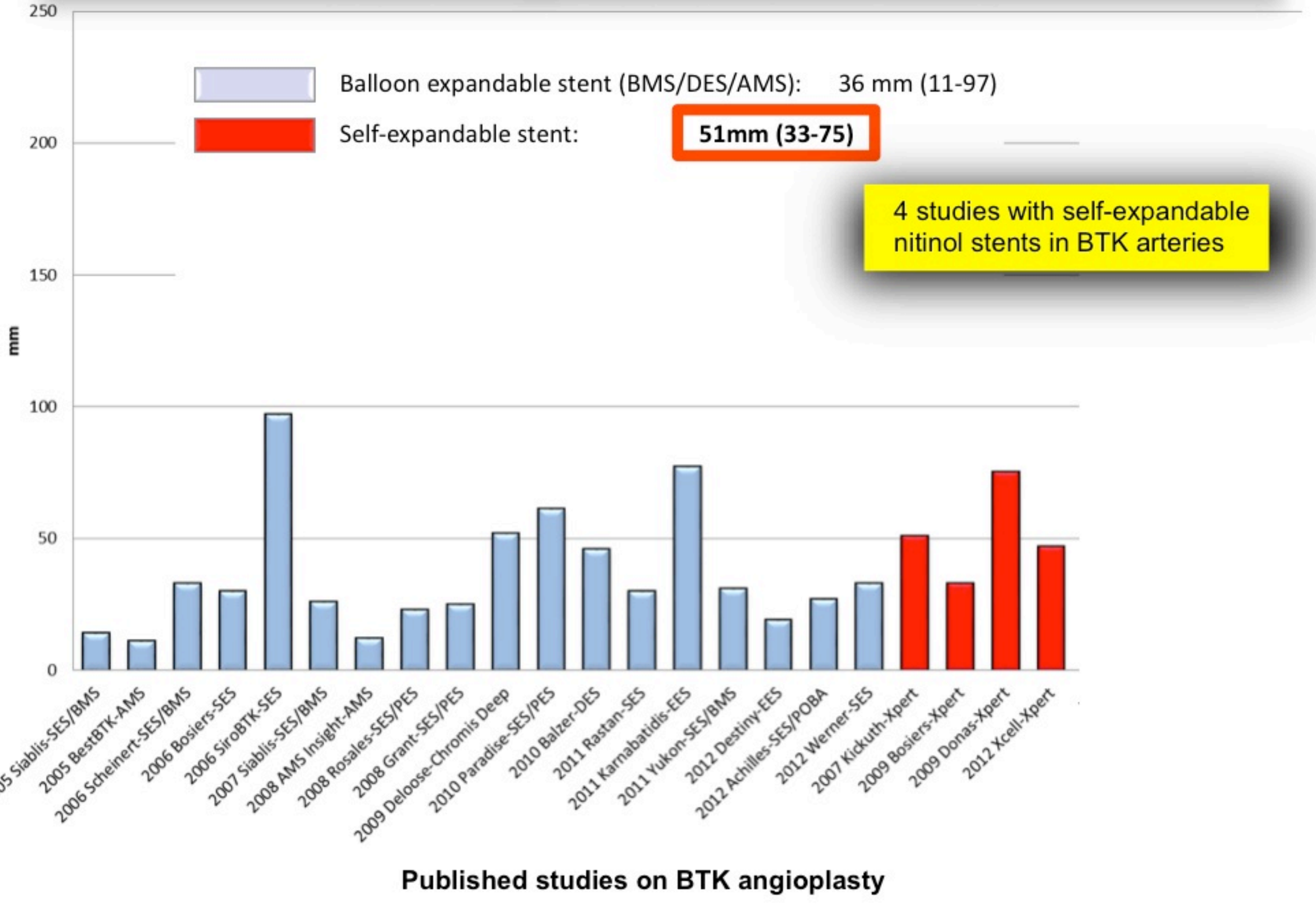

Published studies on BTK angioplasty

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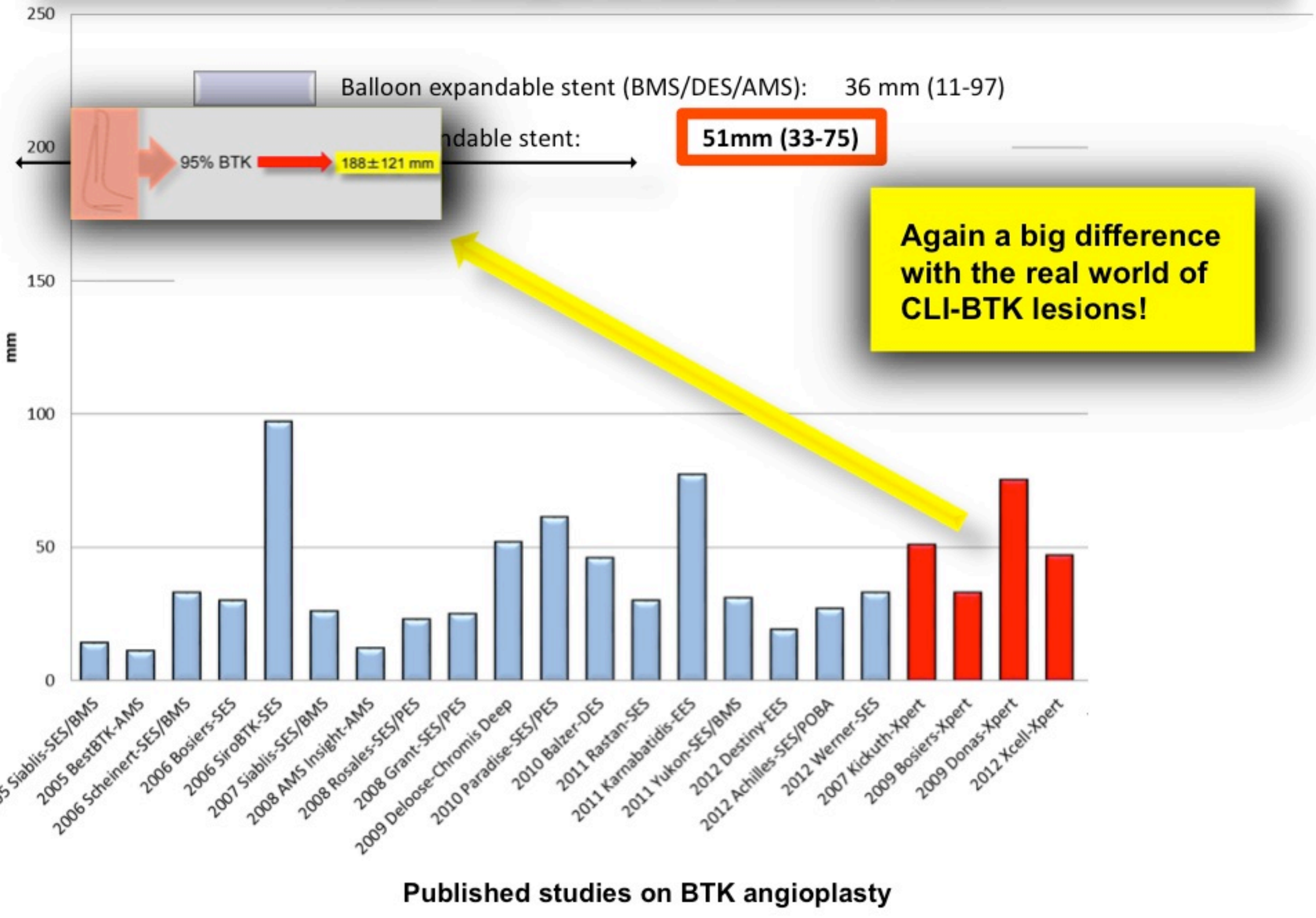

Published studies on BTK angioplasty

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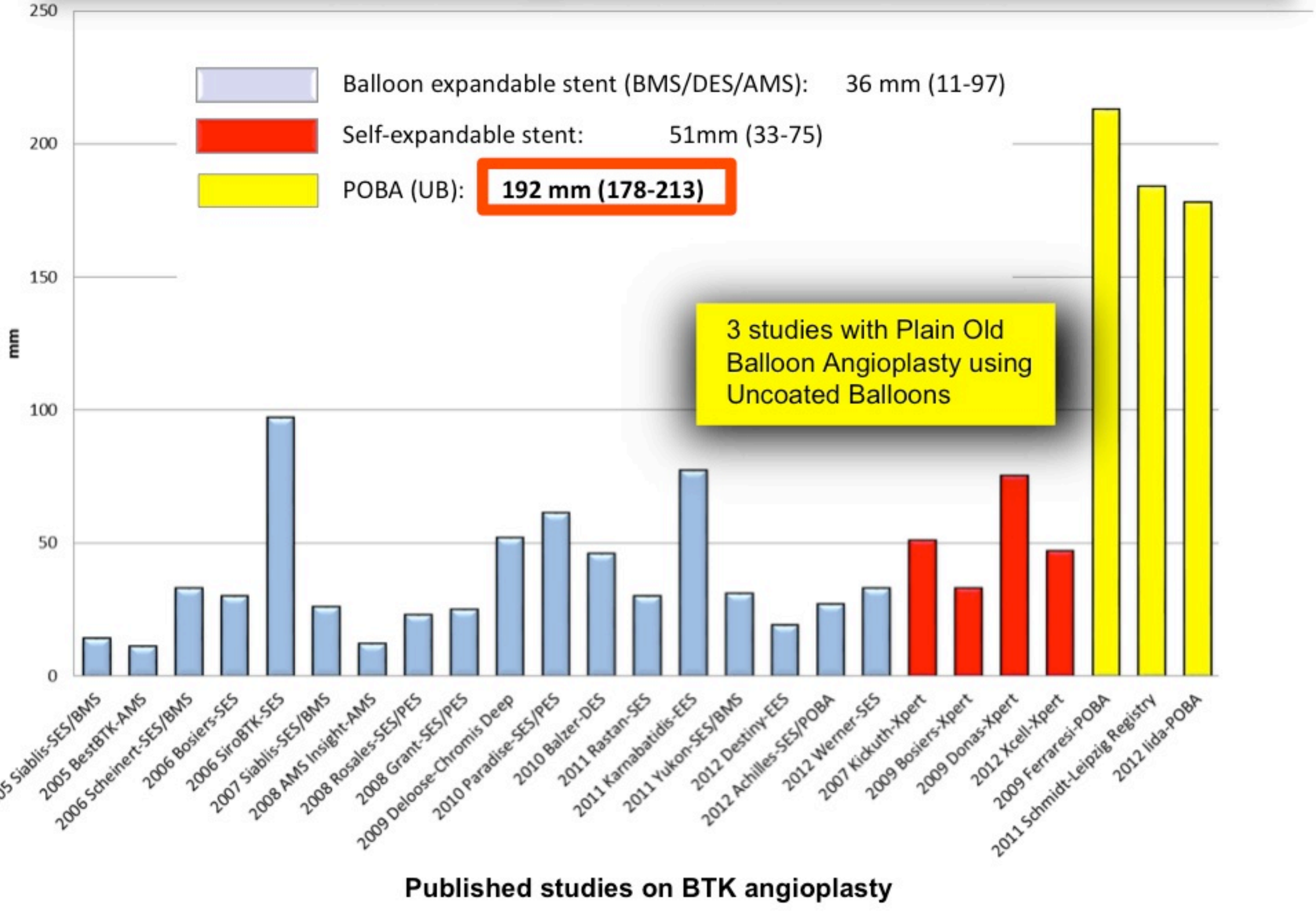

Published studies on BTK angioplasty

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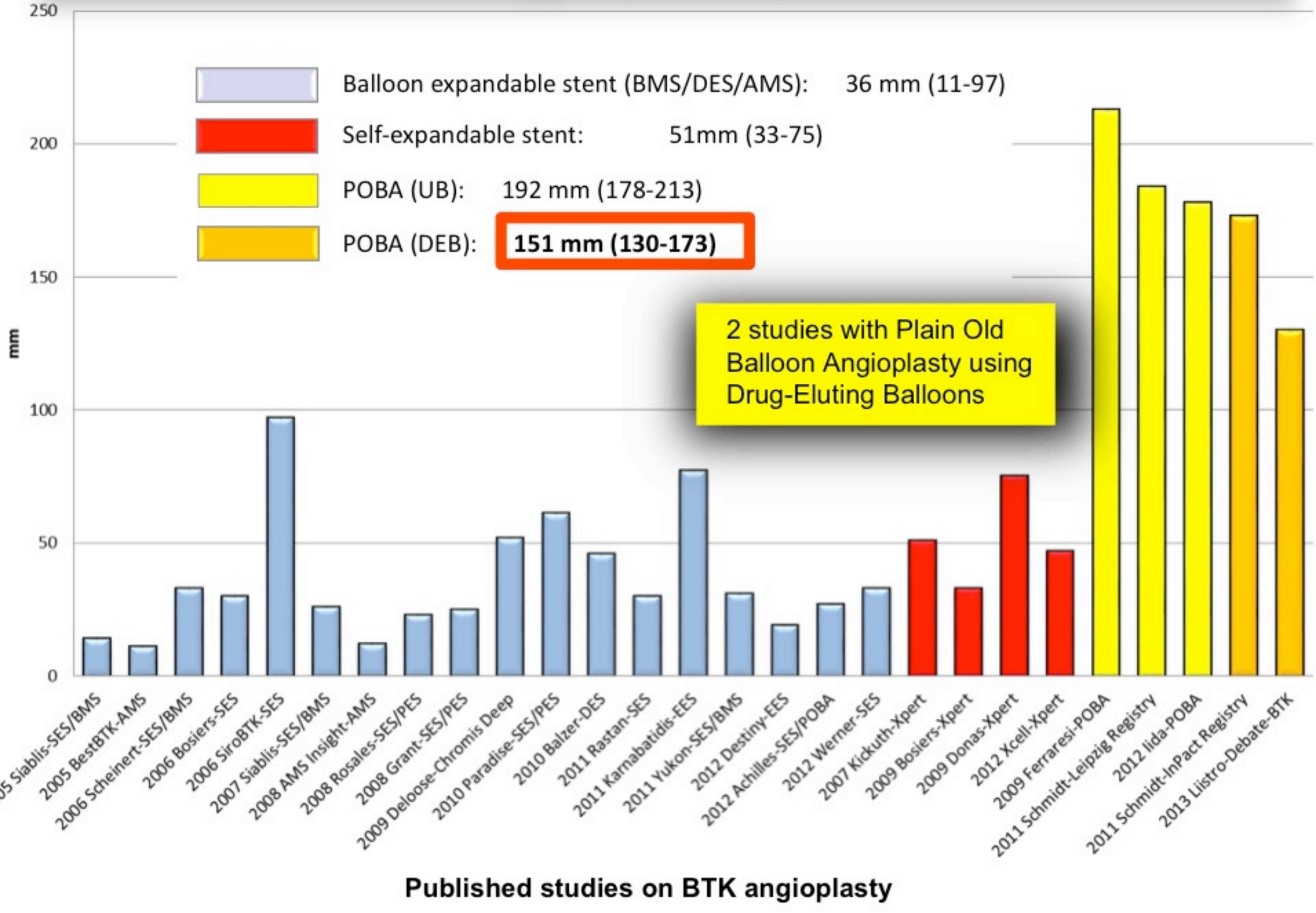
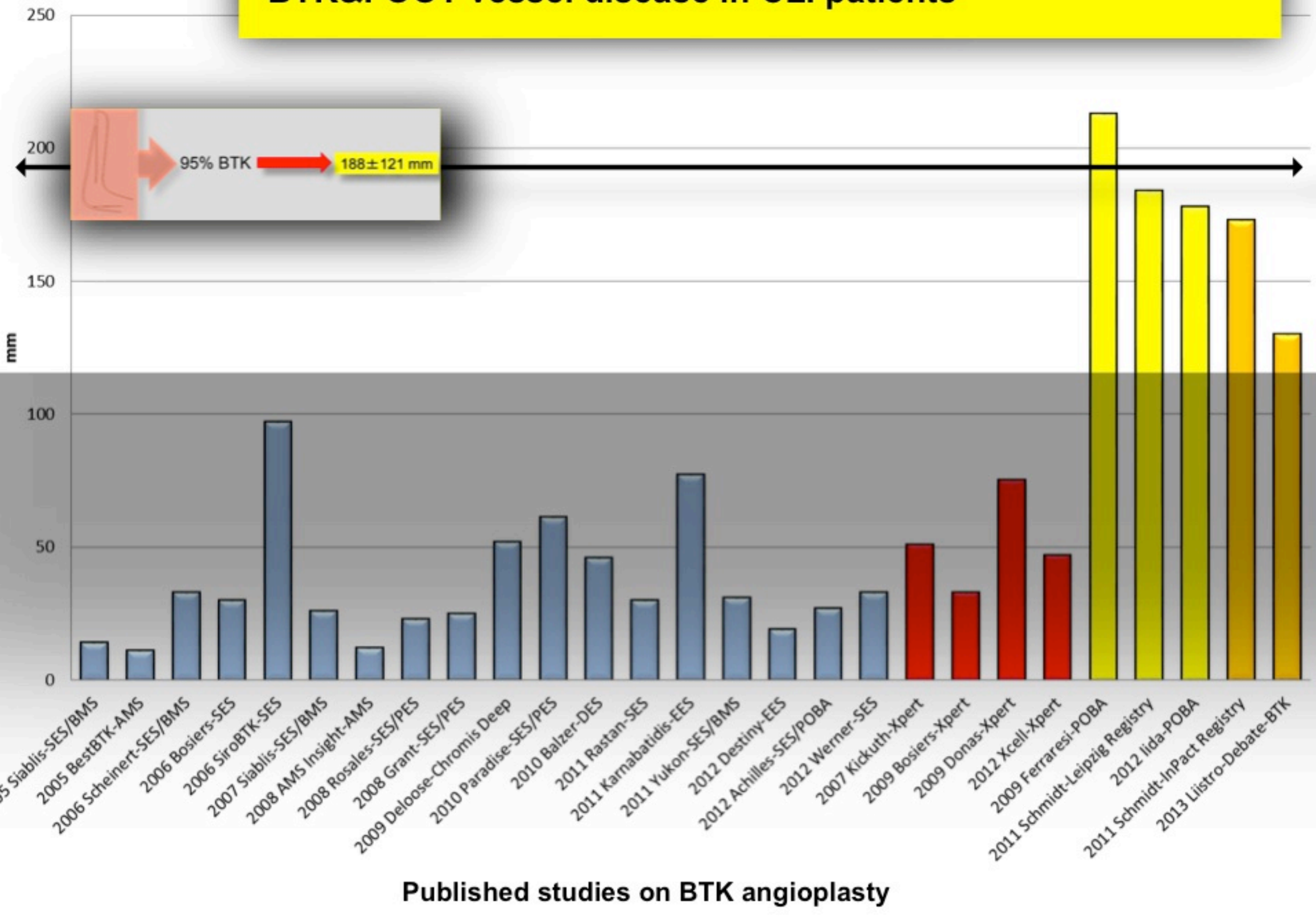
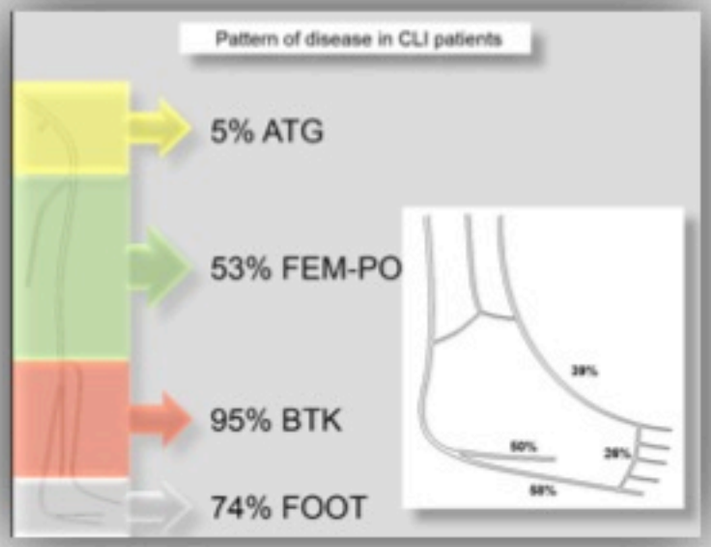


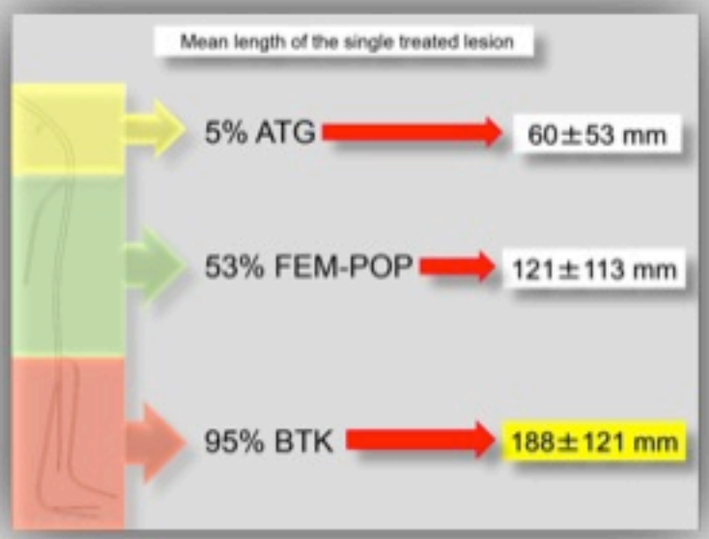
Published studies on BTK angioplasty

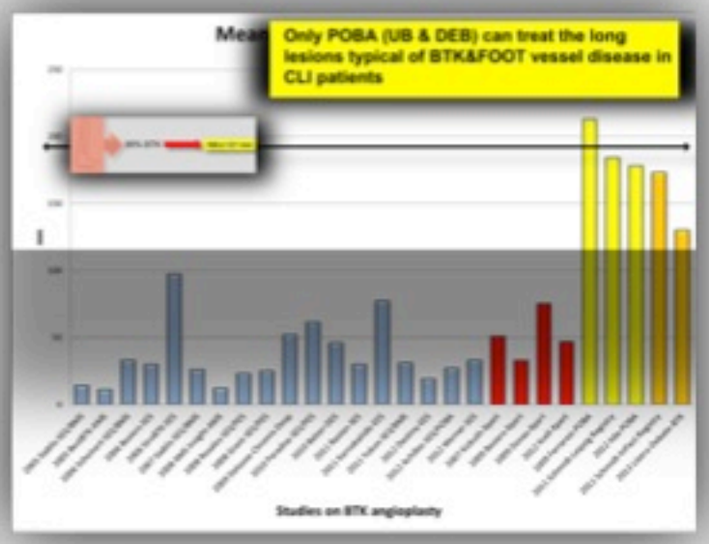
Only POBA (UB & DEB) can treat the long lesions typical of BTK&FOOT vessel disease in CLI patients



Published studies on BTK angioplasty







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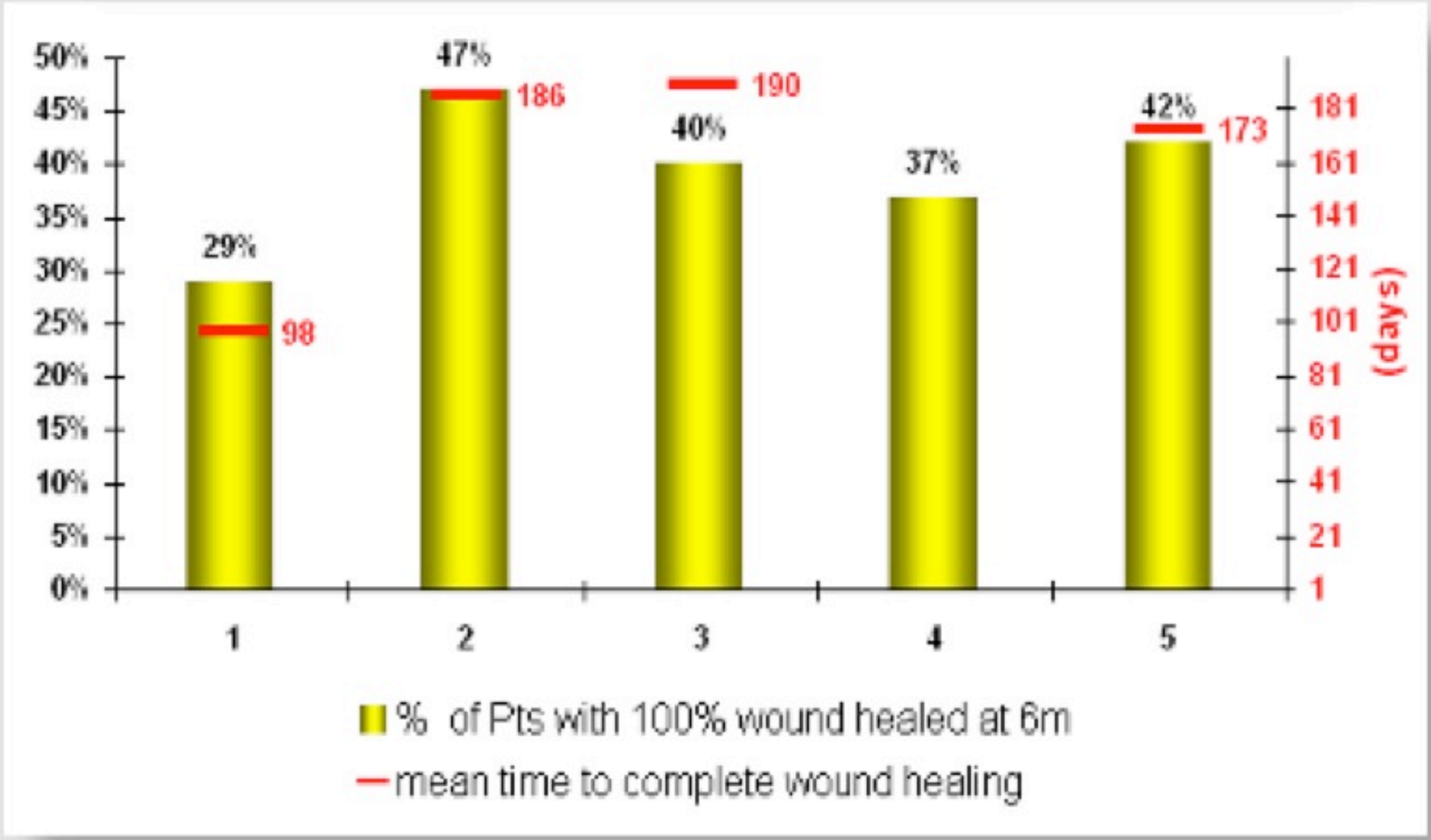
2) Complete/WRA PTA → we have to treat a lot of vessel to gain healing!

3) Only POBA (UB&DEB) can treat the long lesions typical of BTK&FOOT vessel disease

4) **Wound-healing time in Rtf 5-6 pts**

Healing time in Rutherford 5-6

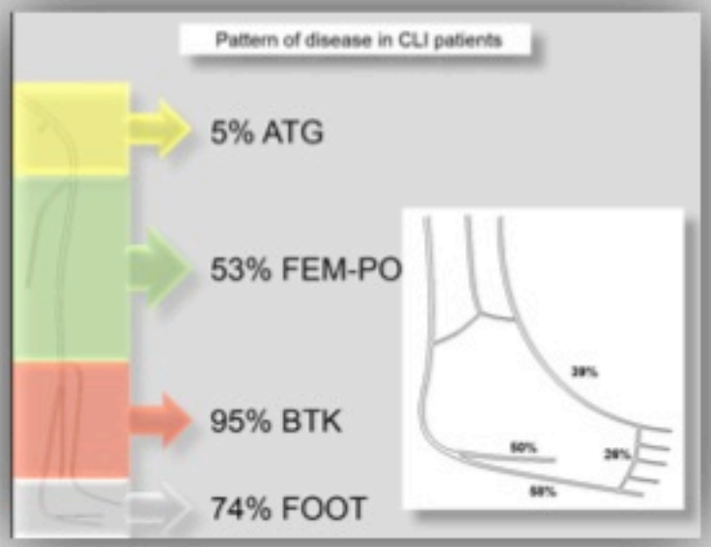


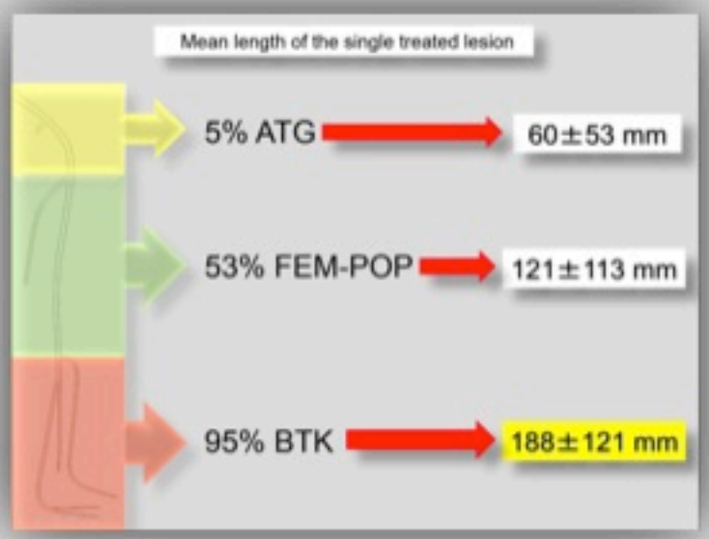
1. Xcell Trial – Rocha Sing 2011
2. Soderstrom, et al. Journal of Vascular Surgery 2009
3. Soderstrom, et al. Eur J Vasc Endovasc Surg 2008
4. Hoffman, et al. Eur J Vasc Endovasc Surg 2007
5. Chung, et al. Journal of Vascular Surgery 2006

Courtesy Rocha Sing 2011

≥ 6 months

The picture shows six Rutherford 6 feet when they arrived at our clinic and 6 months later





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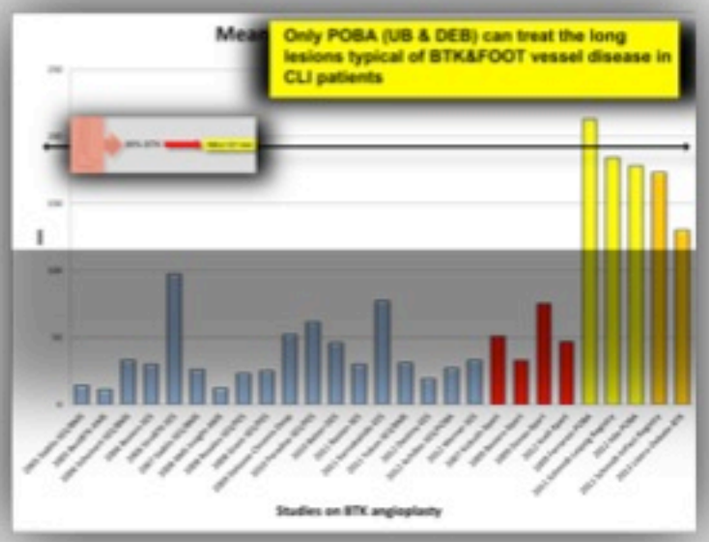
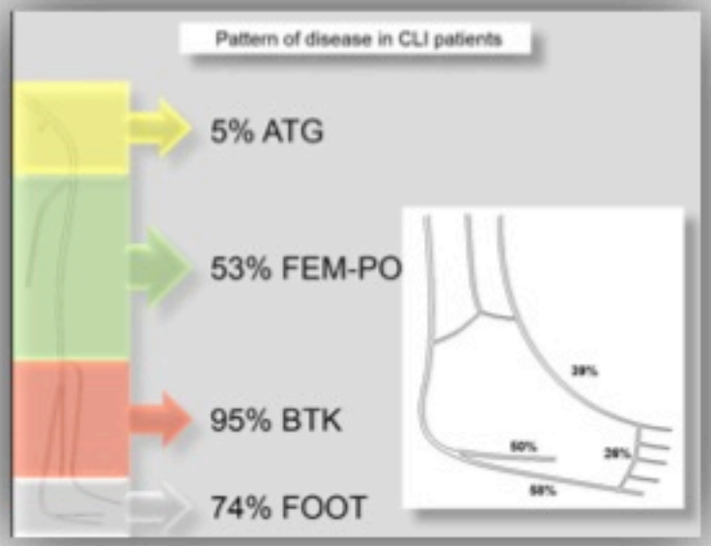
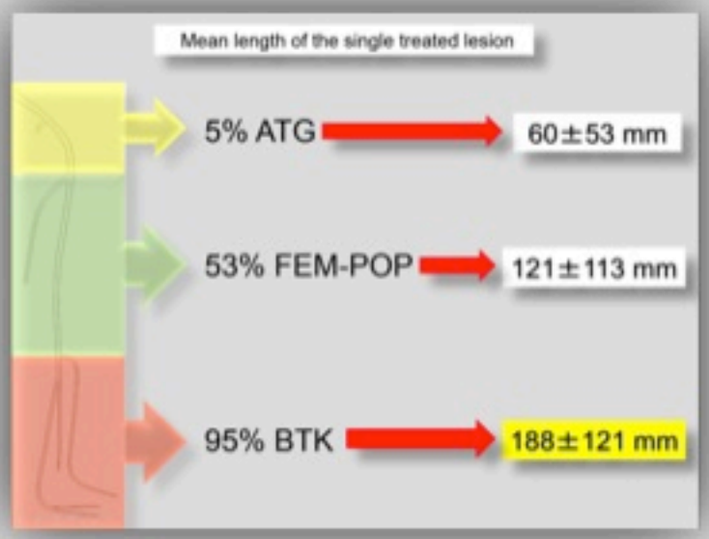
4) **Wound healing time in Rtf 5-6 pts is ≥6 m, and complete 6m healing rate <50%**







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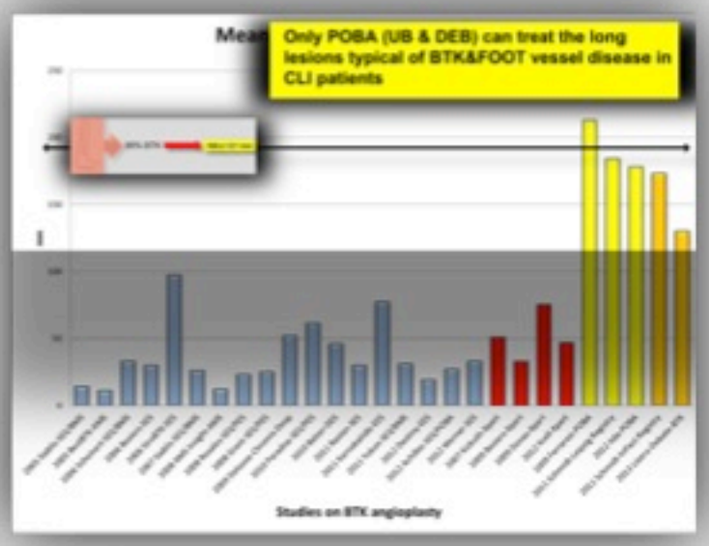
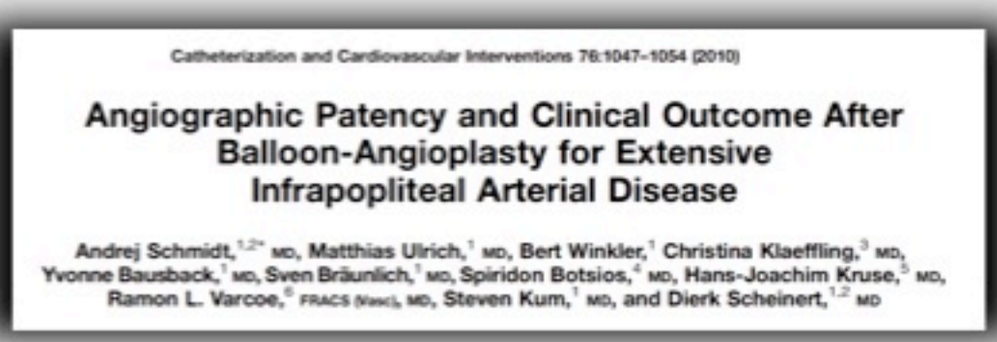
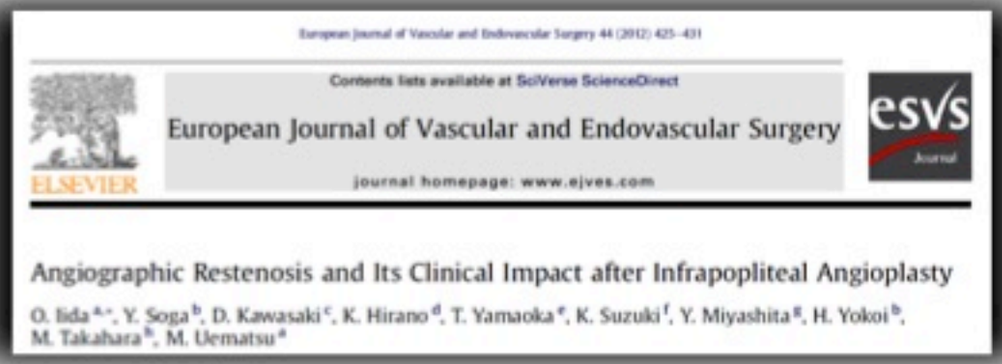


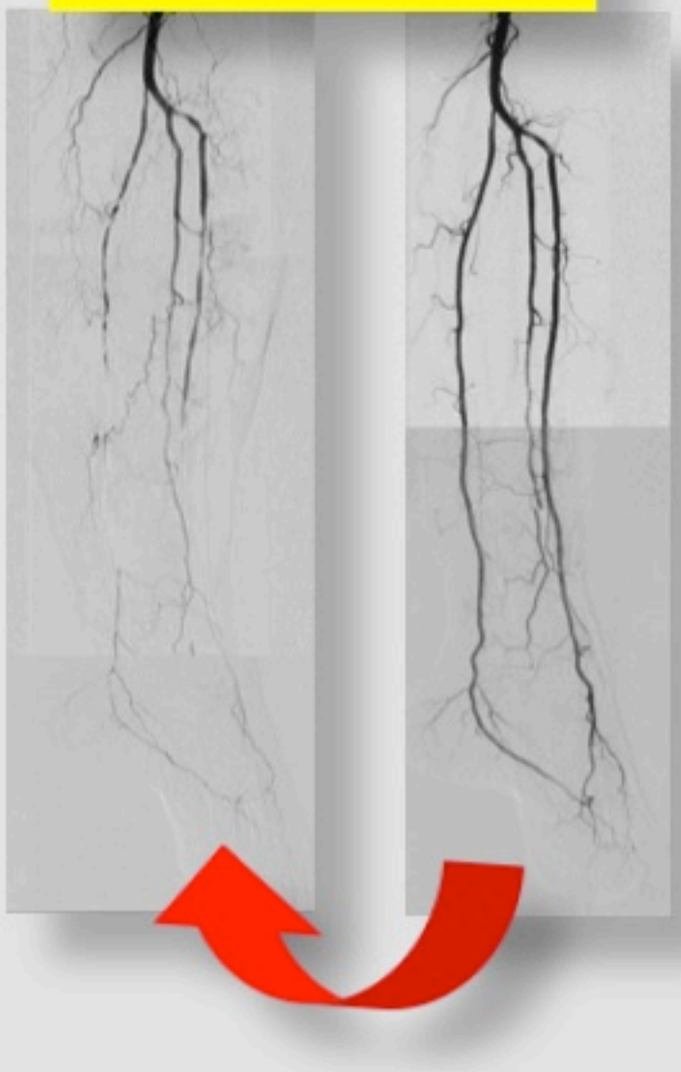
5) **Restenosis rate and significance in CLI patients**

Restenosis rate in real-world, long BTK vessels
Uncoated balloons

Study	limbs	Mean lesion length	Follow up	restenosis	TLR
 Catheterization and Cardiovascular Interventions 76:1047–1054 (2010) Angiographic Patency and Clinical Outcome After Balloon-Angioplasty for Extensive Infrapopliteal Arterial Disease Andrej Schmidt, Matthias Ulrich, Bert Winkler, Christina Klaeffling, Yvonne Bausback, Sven Bräunlich, Spiridon Botsios, Hans-Joachim Kruse, Ramon L. Varcoe, Steven Kum, and Dierk Scheinert	62	18.4 cm	3 m	69%	50%
 European Journal of Vascular and Endovascular Surgery 44 (2012) 425–431 Contents lists available at SciVerse ScienceDirect European Journal of Vascular and Endovascular Surgery journal homepage: www.ejves.com Angiographic Restenosis and Its Clinical Impact after Infrapopliteal Angioplasty O. Iida, Y. Soga, D. Kawasaki, K. Hirano, T. Yamaoka, K. Suzuki, Y. Miyashita, H. Yokoi, M. Takahara, M. Uematsu	68	14.0 cm	3 m	73%	40%
			12 m	82%	48%

Restenosis rate in real-world, long BTK vessels
Uncoated balloons

3 months!



Restenosis in extensive BTK-FOOT-PTA is precocious and aggressive: 70% at 3 months

Delay of healing in patients with restenosis

European Journal of Vascular and Endovascular Surgery 44 (2012) 425–431

Contents lists available at SciVerse ScienceDirect

European Journal of Vascular and Endovascular Surgery

journal homepage: www.ejves.com

Angiographic Restenosis and Its Clinical Impact after Infrapopliteal Angioplasty

O. Iida[a,*], Y. Soga[b], D. Kawasaki[c], K. Hirano[d], T. Yamaoka[e], K. Suzuki[f], Y. Miyashita[g], H. Yokoi[b], M. Takahara[h], M. Uematsu[a]

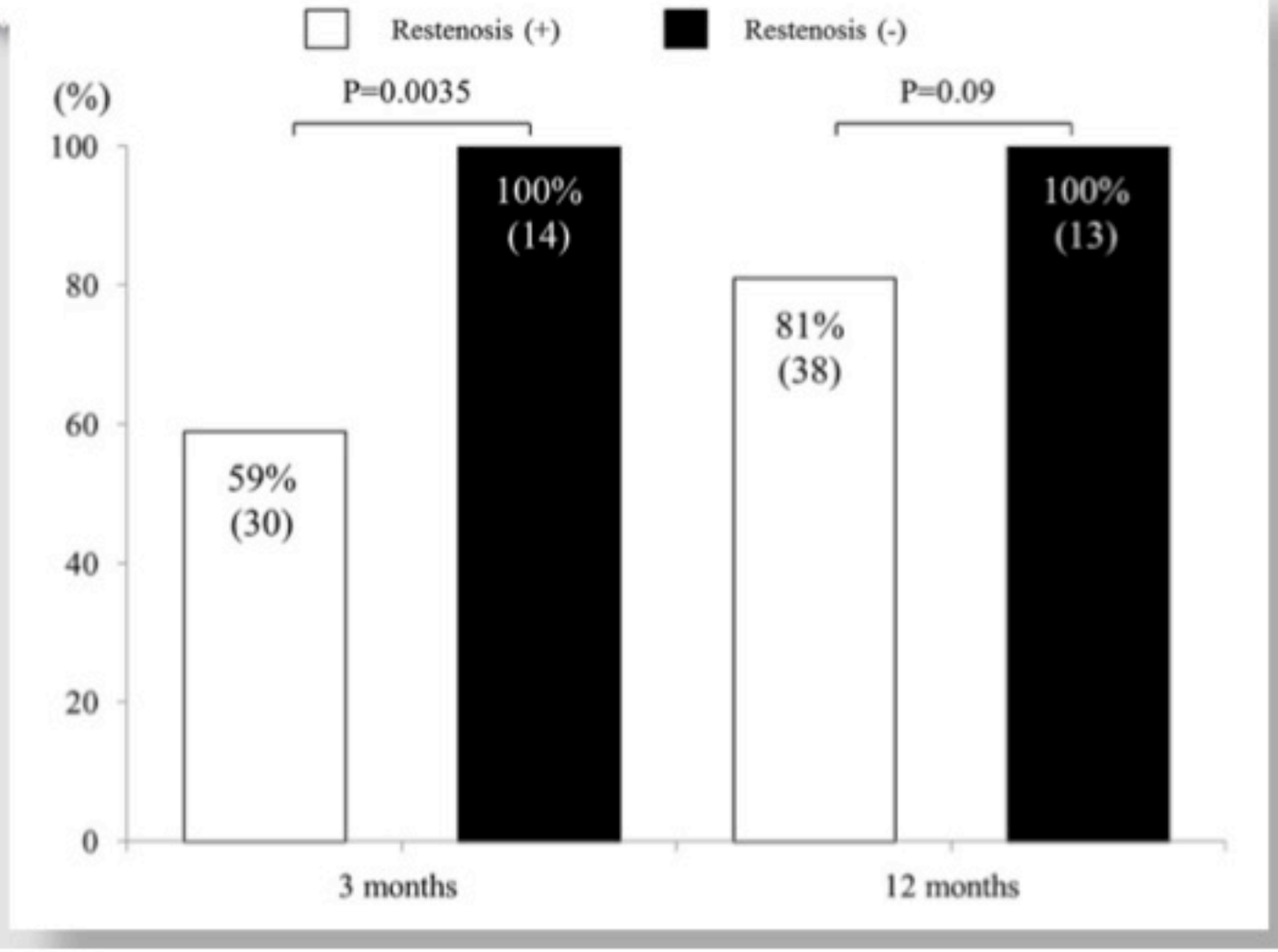


Figure 5. Comparison of frequency of complete ulcer healing or lack of rest pain with and without restenosis after 3 and 12 months.

Delay of healing in patients with restenosis

European Journal of Vascular and Endovascular Surgery 44 (2012) 425–431

Contents lists available at SciVerse ScienceDirect

European Journal of Vascular and Endovascular Surge

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Angiographic Restenosis and Its Clinical Impact after Infrapopliteal

O. Iida[a,*], Y. Soga[b], D. Kawasaki[c], K. Hirano[d], T. Yamaoka[e], K. Suzuki[f], Y. Miyashita[g], H. Yokoi[h], M. Takahara[h], M. Uematsu[a]

Restenosis delays healing of tissue lesions!

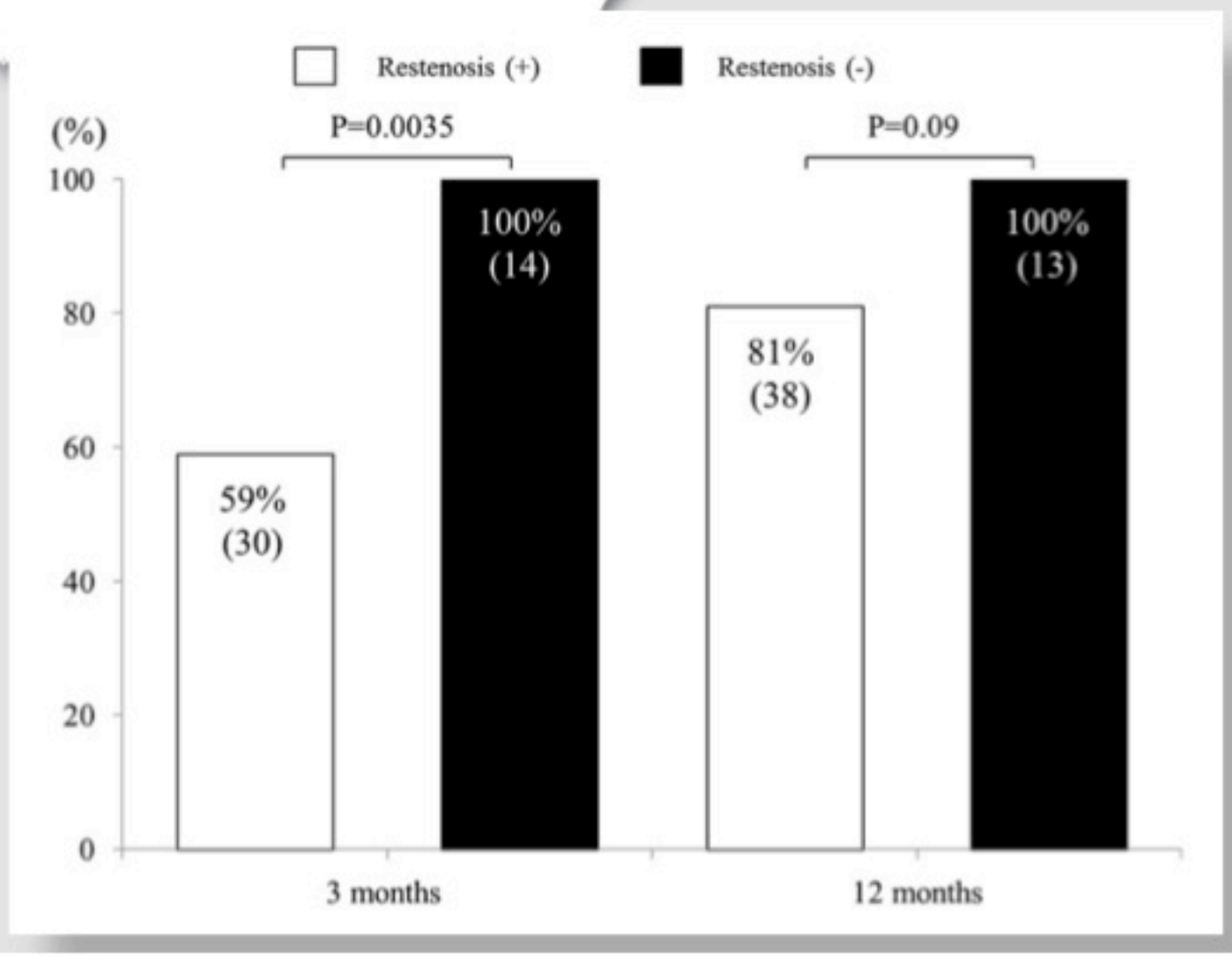


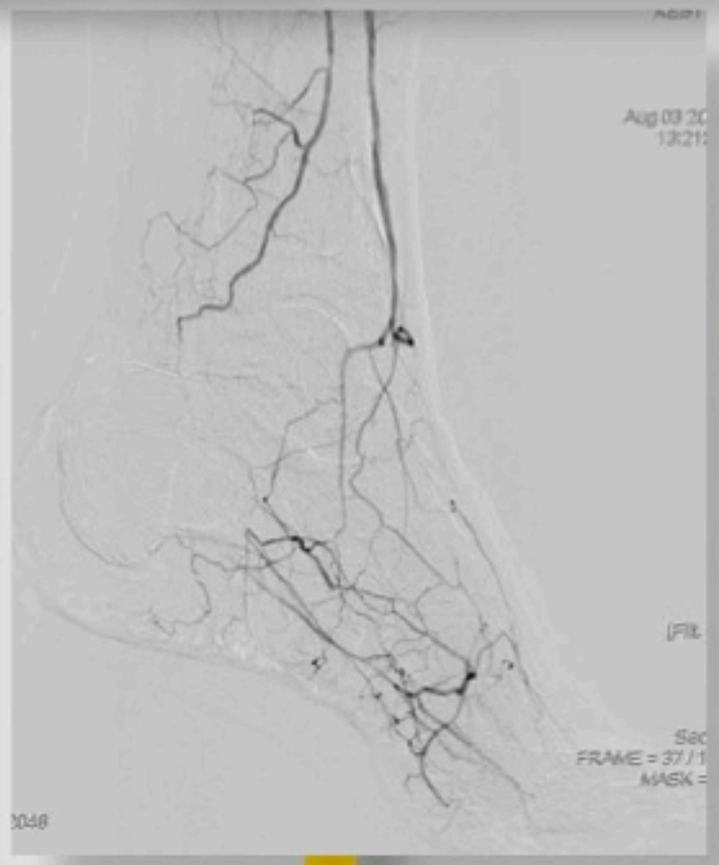
Figure 5. Comparison of frequency of complete ulcer healing or lack of rest pain with and without restenosis after 3 and 12 months.

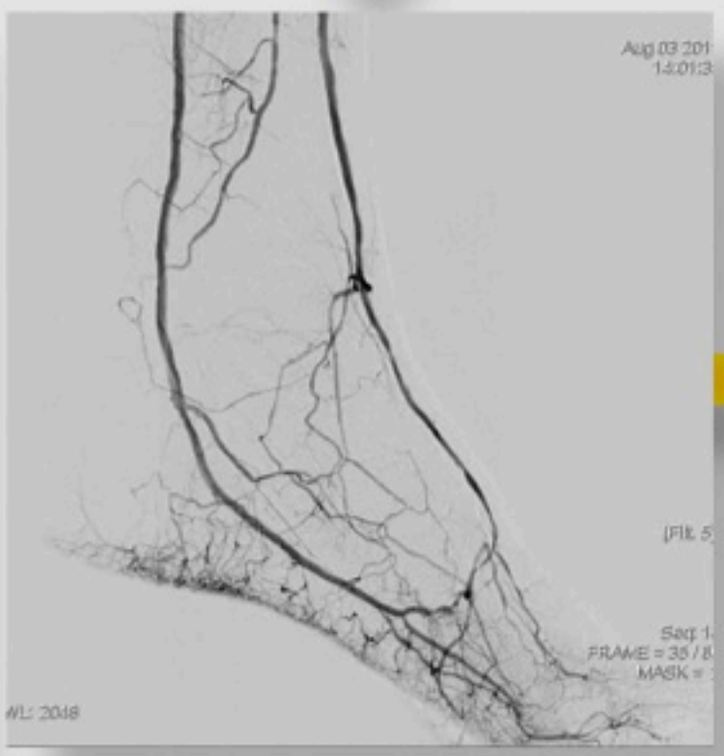
PATIENT DATA

- 84-year-old male
- Type 2 DM/HBP/ex-smoker
- Ischemic cerebrovascular disease
- Left foot: 1° toe gangrene → 1° toe amputation → dehiscence of the surgical wound

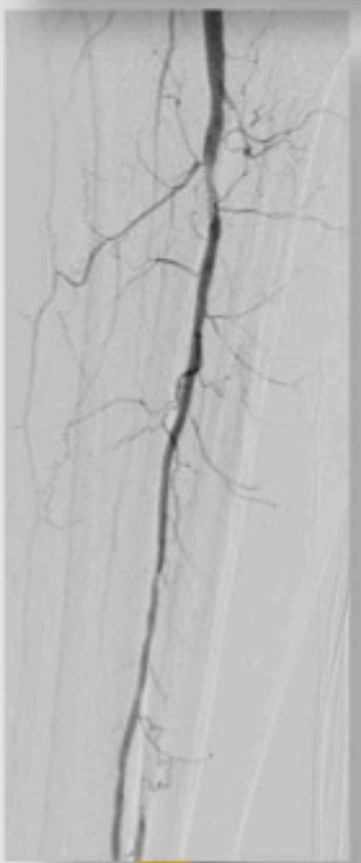
Sent to our diabetic foot clinic on August 2011

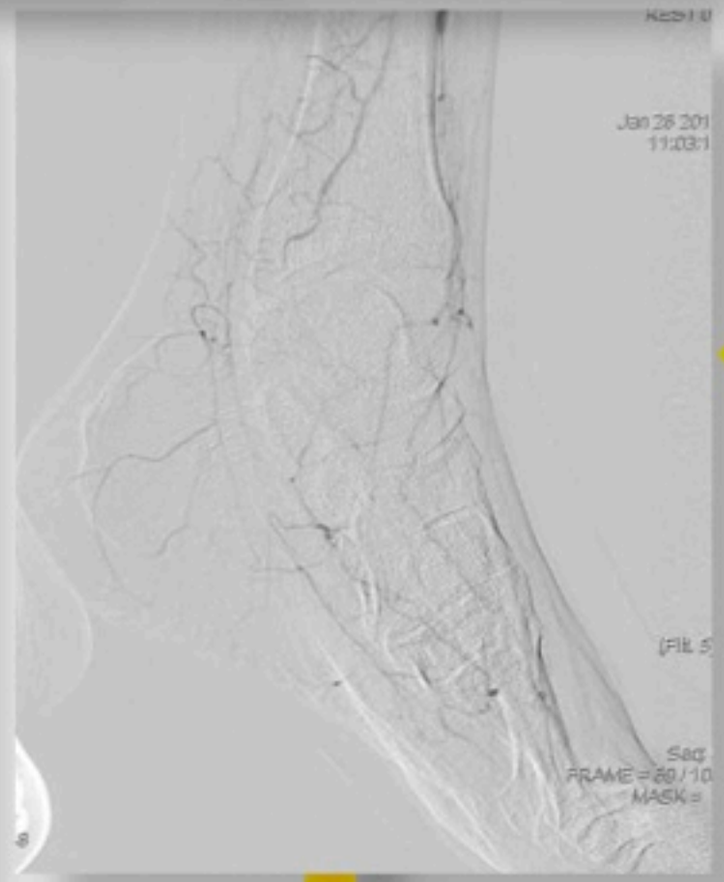
1° PTA: 3/08/2011 → basal

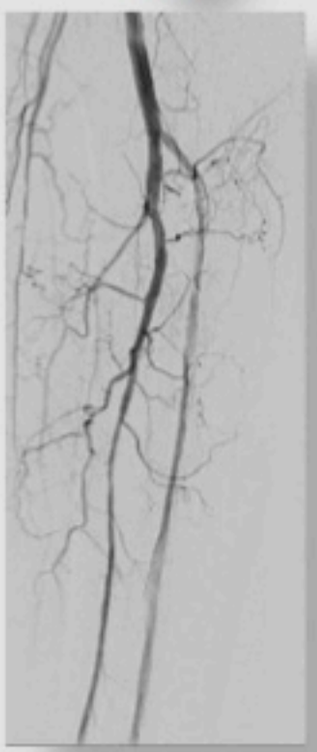


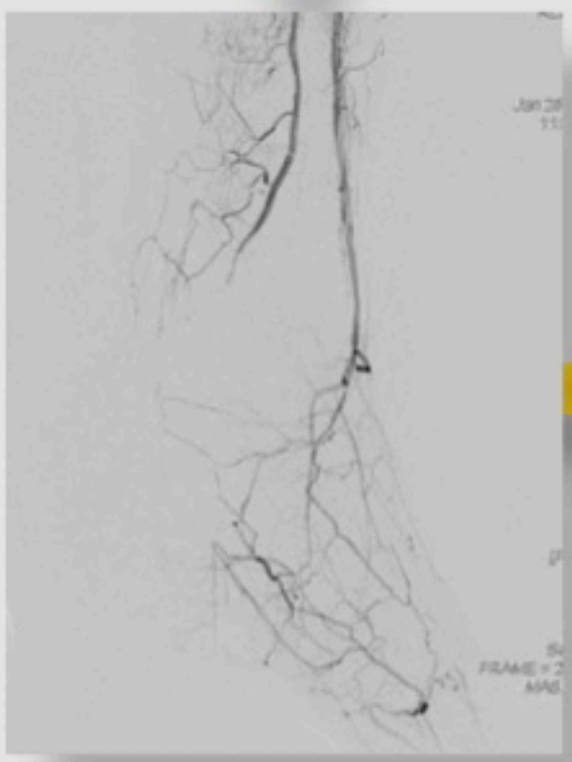


2° PTA: + 6 months → 6 m

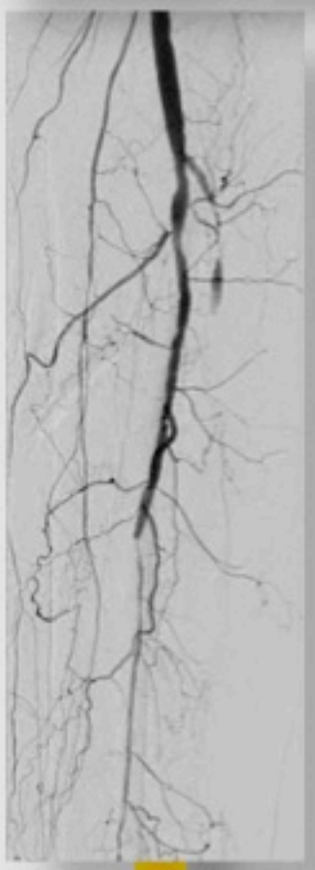


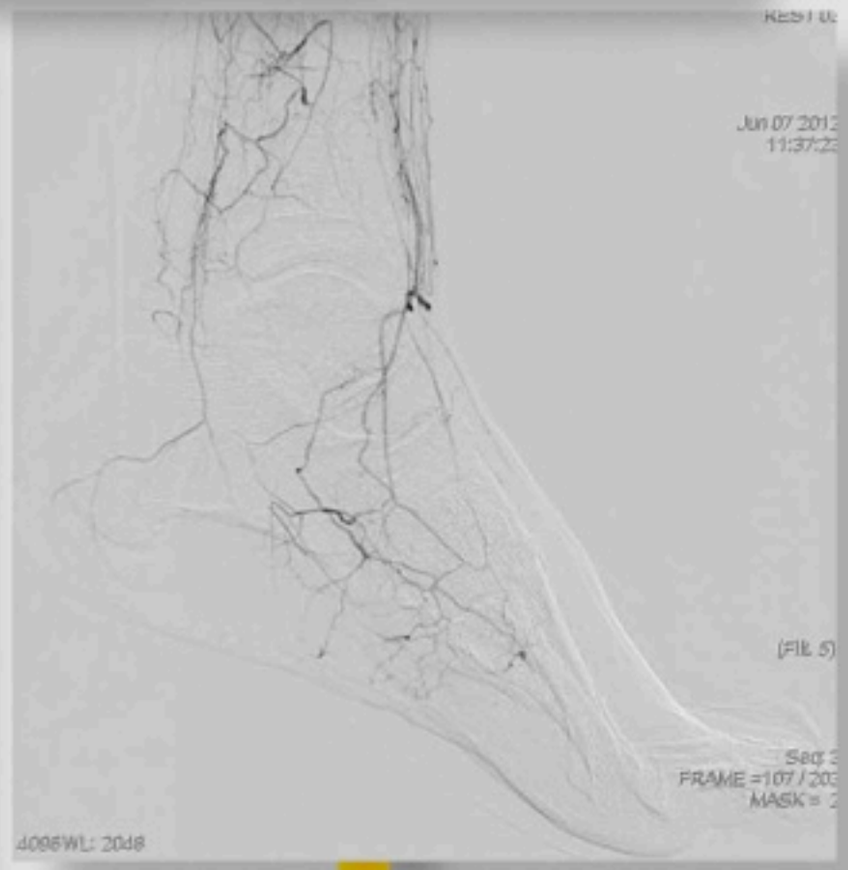


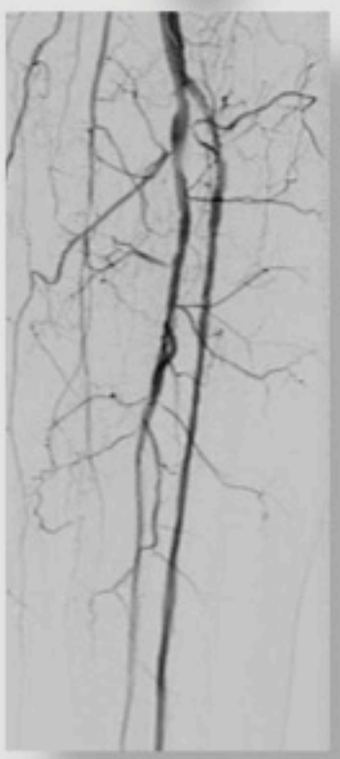


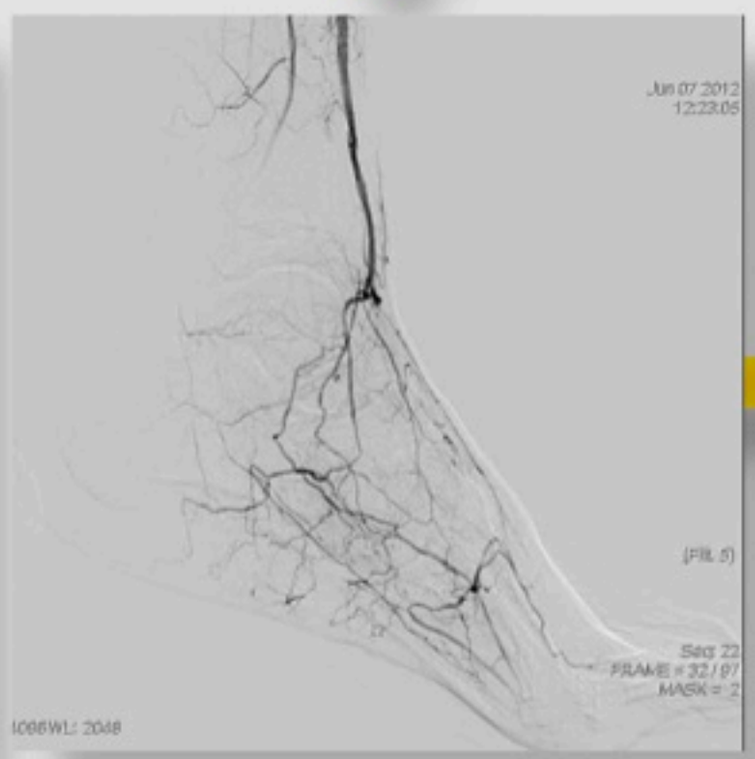


3° PTA: + 5 months → 11 m

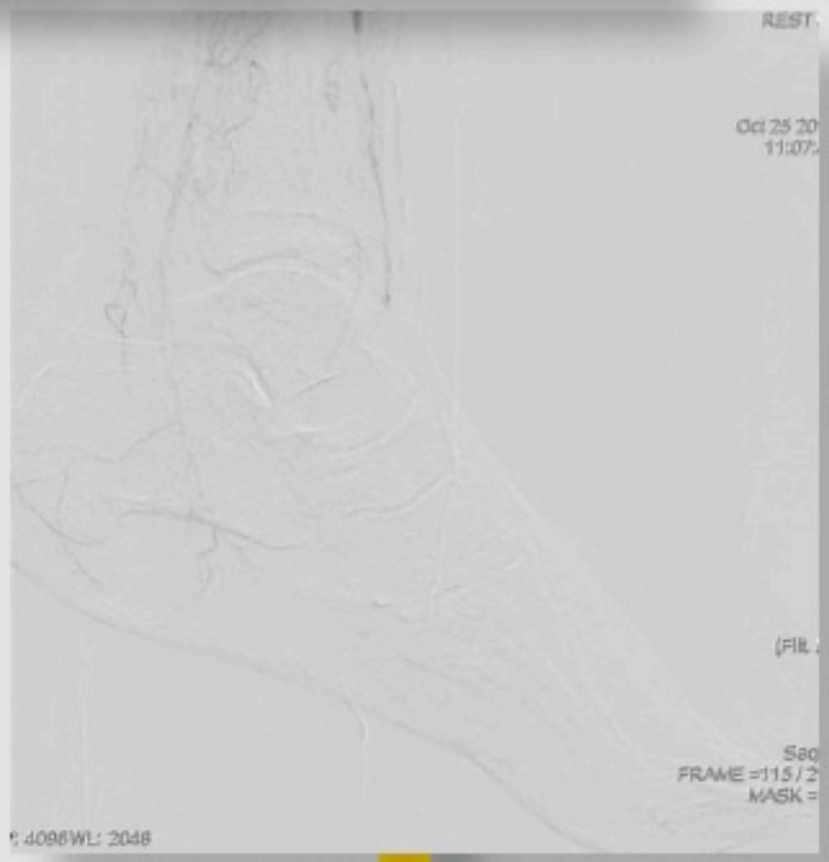


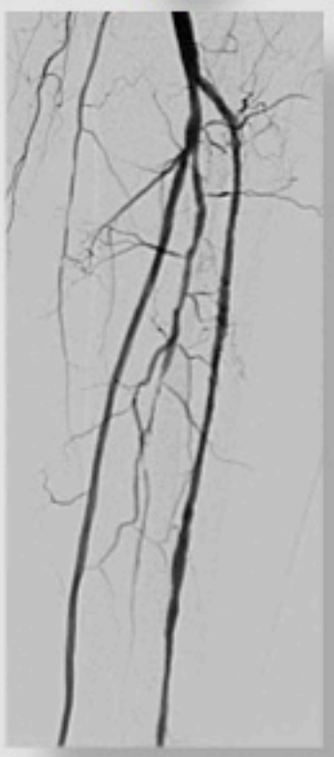


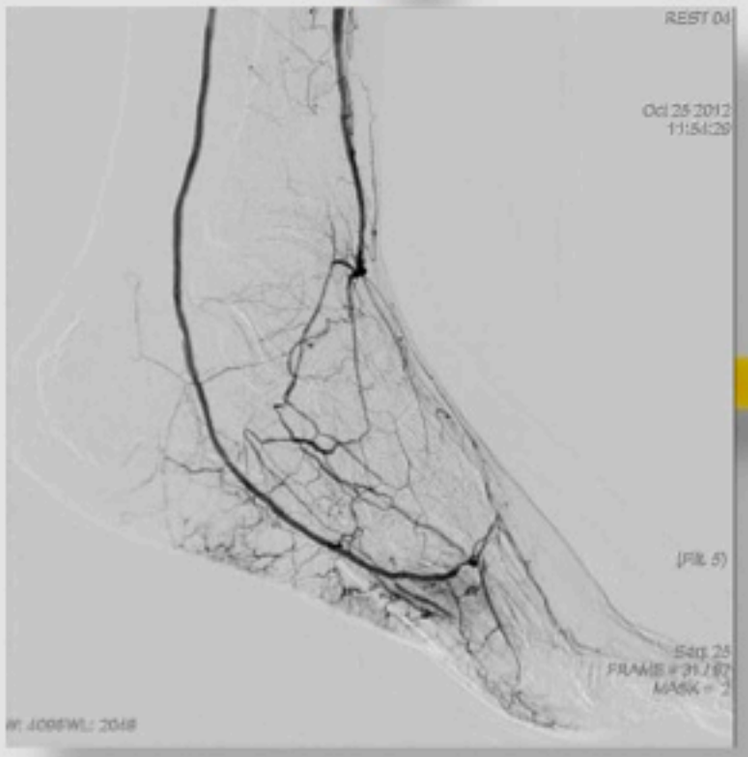




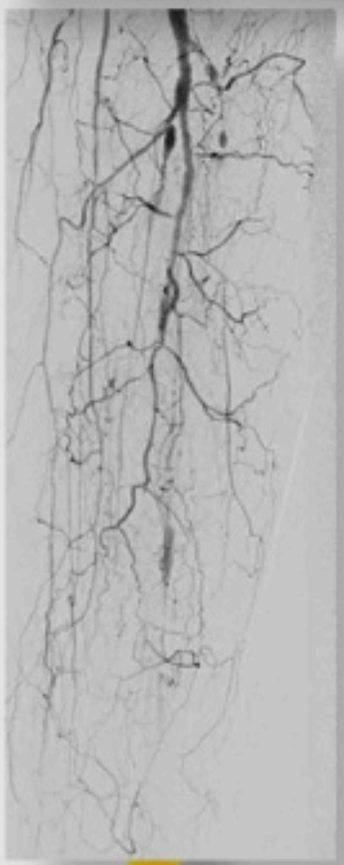
4° PTA: + 4 months → 15 m

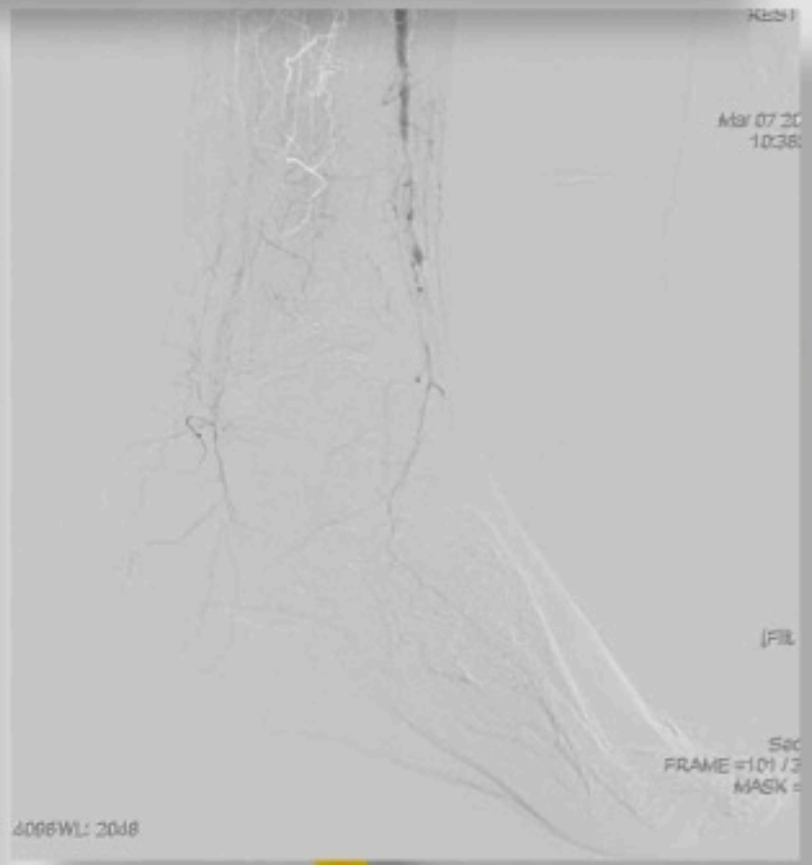


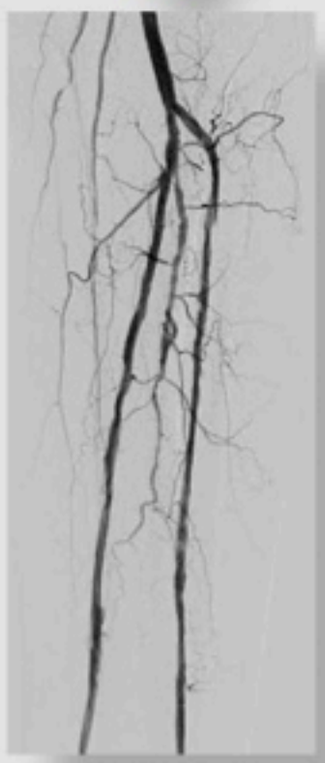


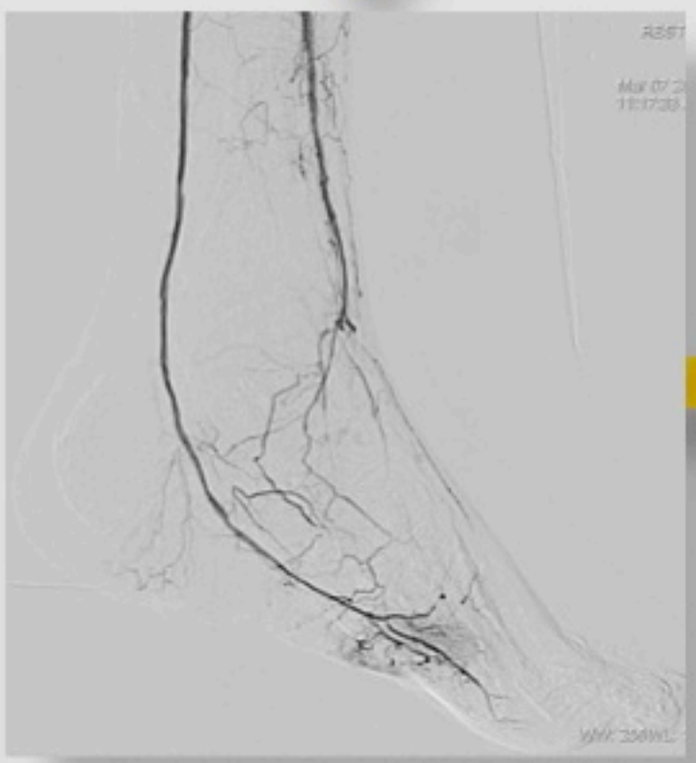


5° PTA: + 5 months → 20 m

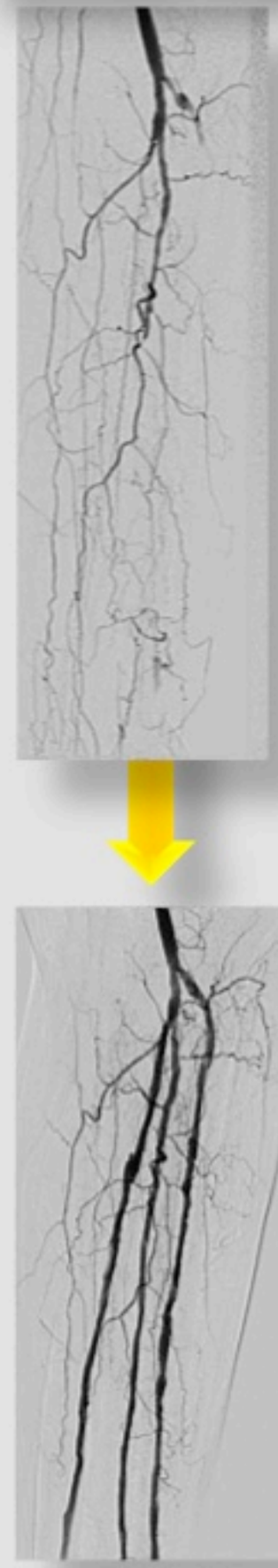


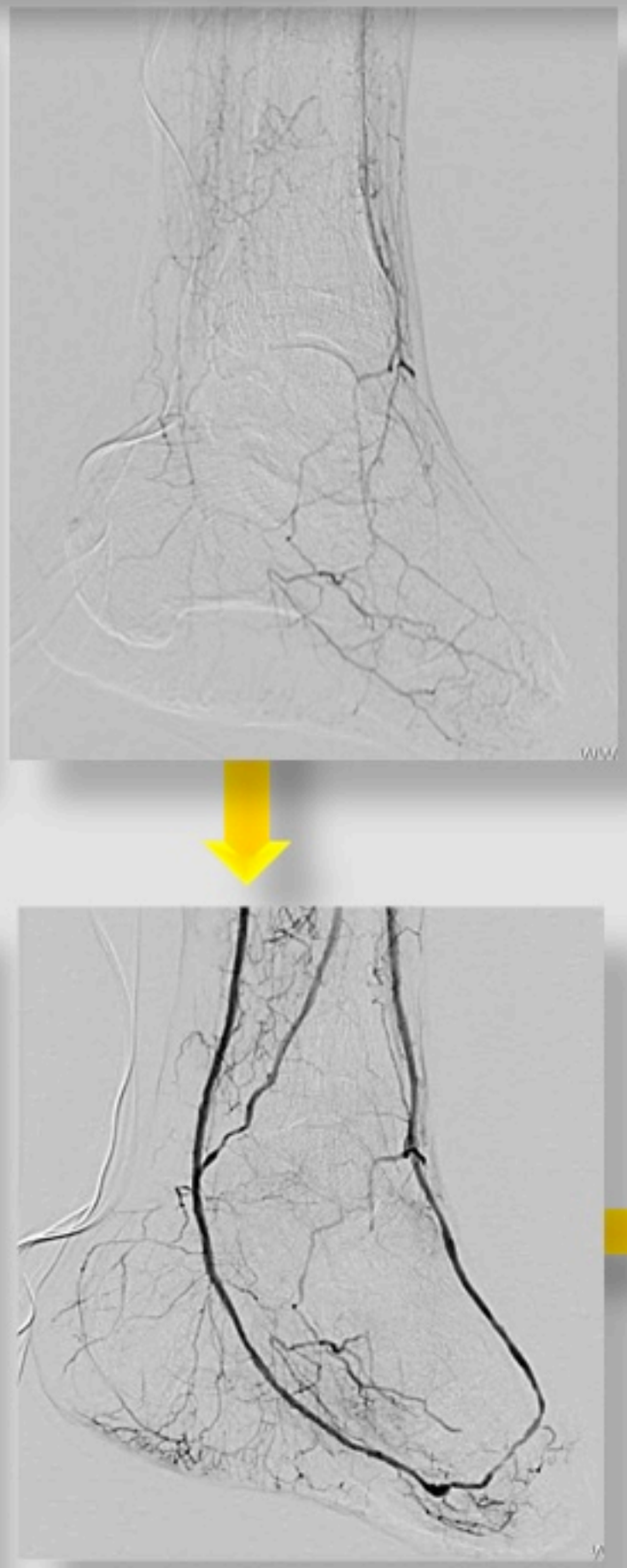






6° PTA: + 6 months → 26 m





?

1° PTA
3/08/2011

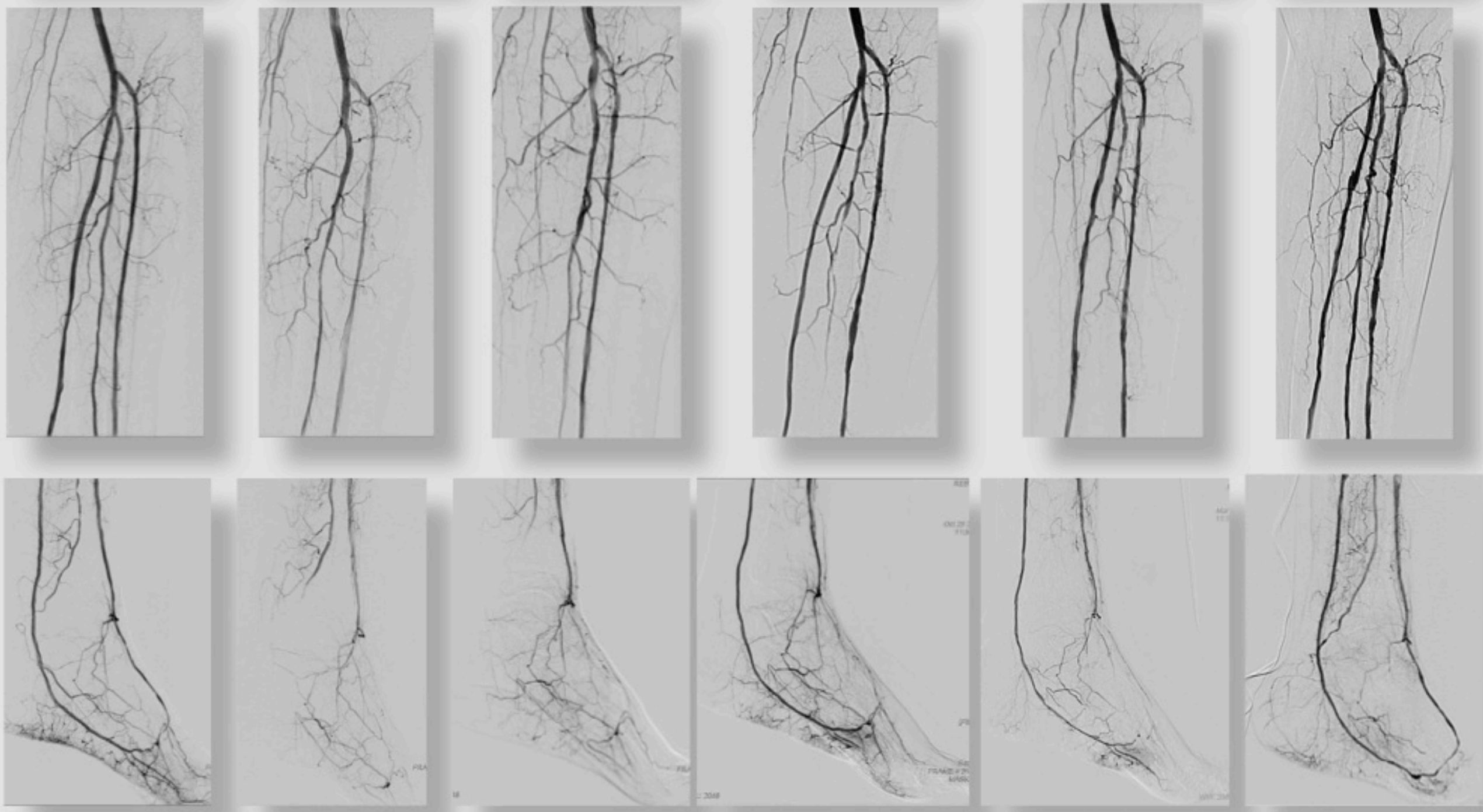
2° PTA
+ 5 months

3° PTA
+ 5 months

4° PTA
+ 4 months

5° PTA
+ 5 months

6° PTA
+ 6 months



Different operators → different results

1° PTA
3/08/2011

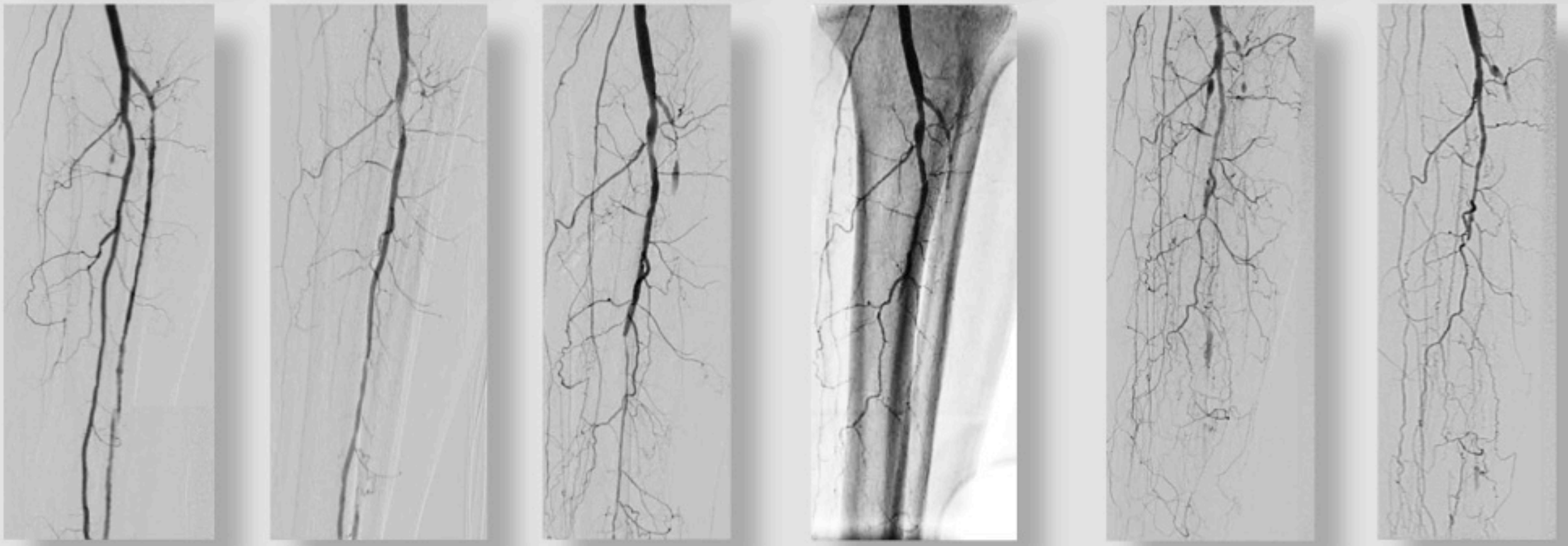
2° PTA
+ 5 months

3° PTA
+ 5 months

4° PTA
+ 4 months

5° PTA
+ 5 months

6° PTA
+ 6 months

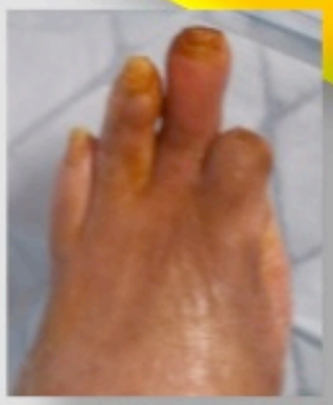


Restenosis after uncoated balloon angioplasty was always precocious and aggressive!

1° PTA
3/08/2011

2° PTA
+ 5 months

3° PTA
+ 5 months



4° PTA
+ 4 months

5° PTA
+ 5 months

6° PTA
+ 6 months

26 months of recurrent pain, inability to walk, infections, medications, hospitalizations, multiple "minor" amputations…
This is what we call "limb salvage"!

Restenosis rate in BTK vessels

Meta-analysis of infrapopliteal angioplasty for chronic critical limb ischemia

Marcello Romiti, MD,[a] Maximiano Albers, MD,[a] Francisco Cardoso Brochado-Neto, MD,[a] Anai Espinelli S. Durazzo, MD,[b] Carlos Alberto Bragança Pereira, PhD,[c] and Nelson De Luccia, MD,[b]
Santos and São Paulo, São Paulo, Brazil

30 articles between 1990-2006

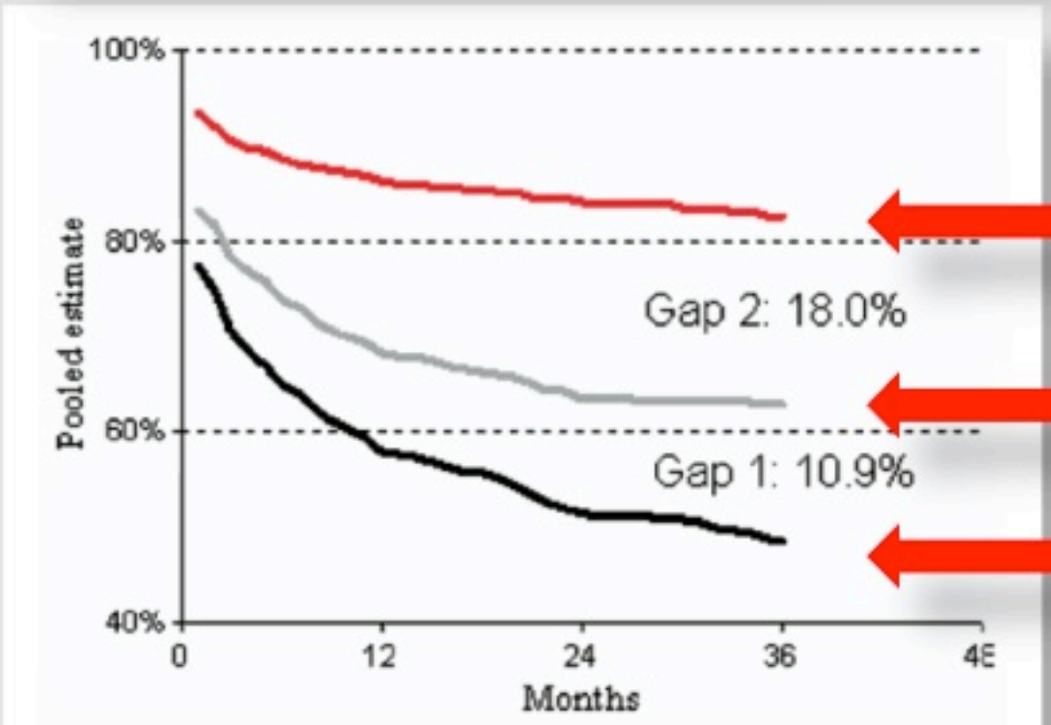


Fig 2. Meta-analysis estimates of primary patency *(black line)*, secondary patency *(gray line)*, limb salvage *(red line)*.

Limb salvage

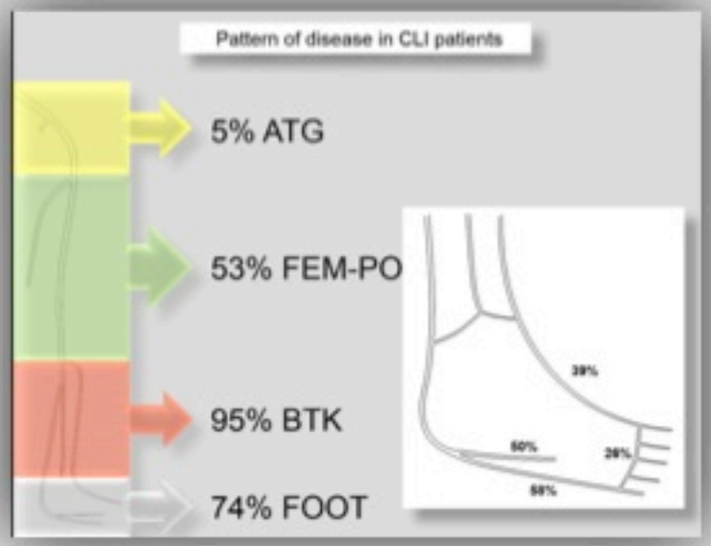
Secondary patency

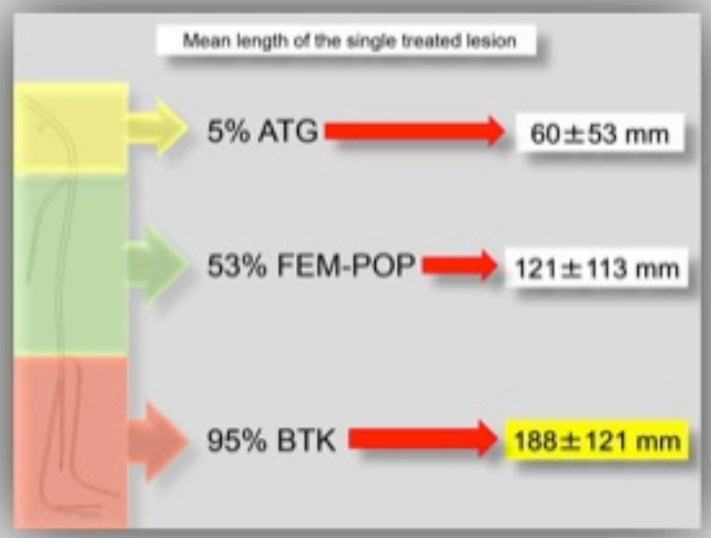
Primary patency

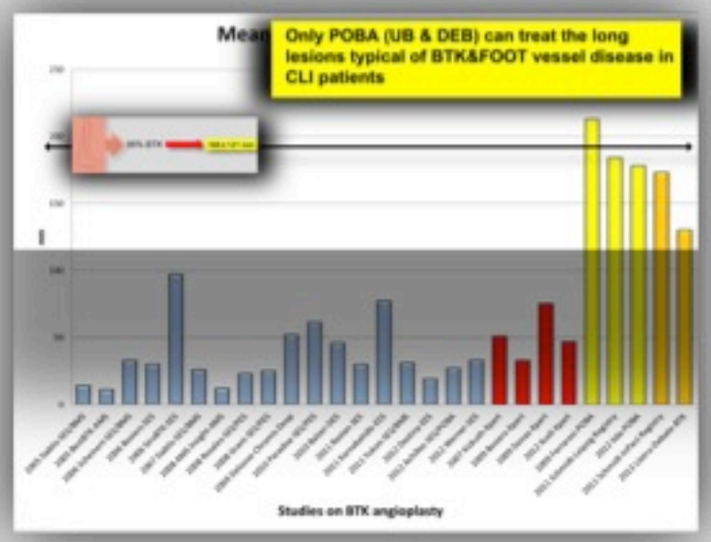
TLR

Primary angioplasty + TLR obtain a high limb salvage rate, but in the struggle against CLI we must pursue different and finer targets:

- Time to healing/Reulceration rate
- Time to walking/QoL evaluation







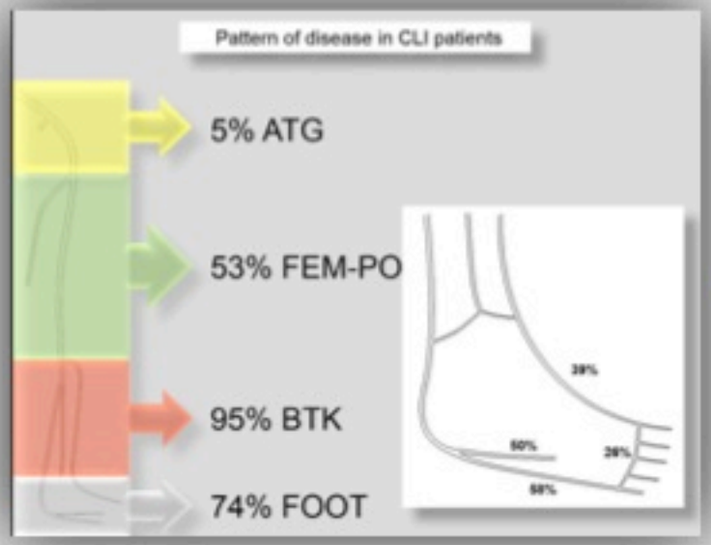
1) …epidemic of OLD-DM-ESRD-CLI pts: multilevel disease & extensive involvement of BTK&FOOT vessels

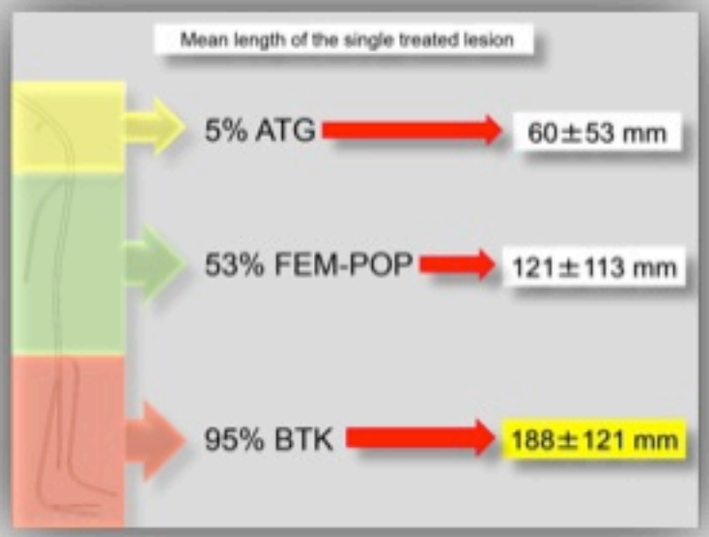
2) Complete/WRA PTA → we have to treat a lot of vessel to gain healing!

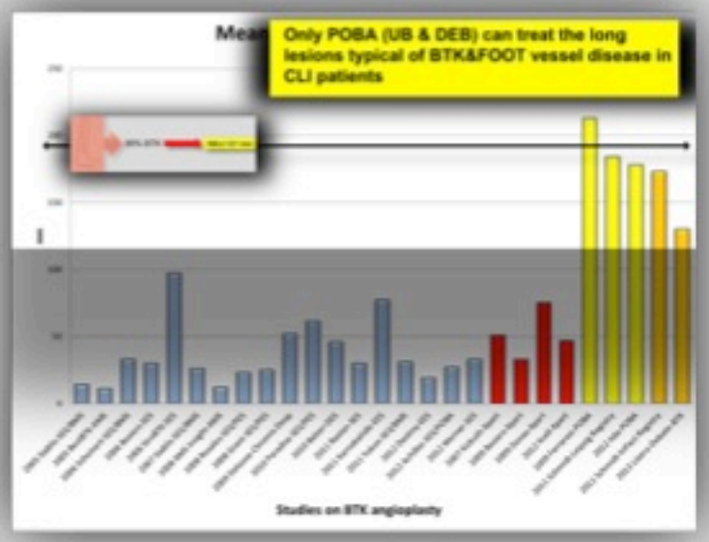
3) Only POBA (UB&DEB) can treat the long lesions typical of BTK&FOOT vessel disease

4) Wound healing time in Rtf 5-6 pts is ≥6 m, and complete 6m healing rate <50%

5) Restenosis rate and significance in CLI patients







We have got a problem! How can we fight restenosis in CLI patients?

1) …epidemic of OLD-DM-ESRD-CLI pts: multilevel disease & extensive involvement of BTK&FOOT vessels

2) Complete/WRA PTA → we have to treat a lot of vessel to gain healing!

3) Only POBA (UB&DEB) can treat the long lesions typical of BTK&FOOT vessel disease

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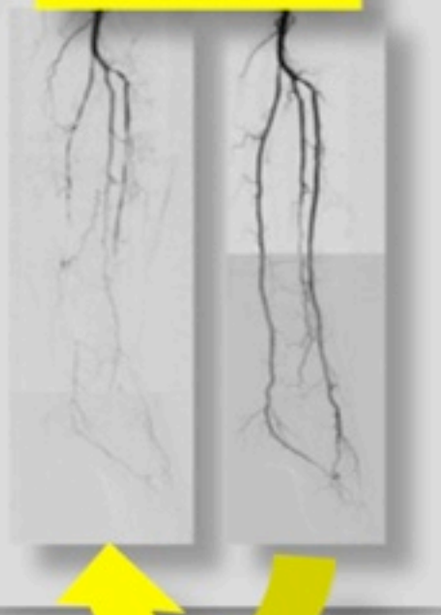
5) Restenosis rate and significance in CLI patients

≥ 6 months!

3 months!

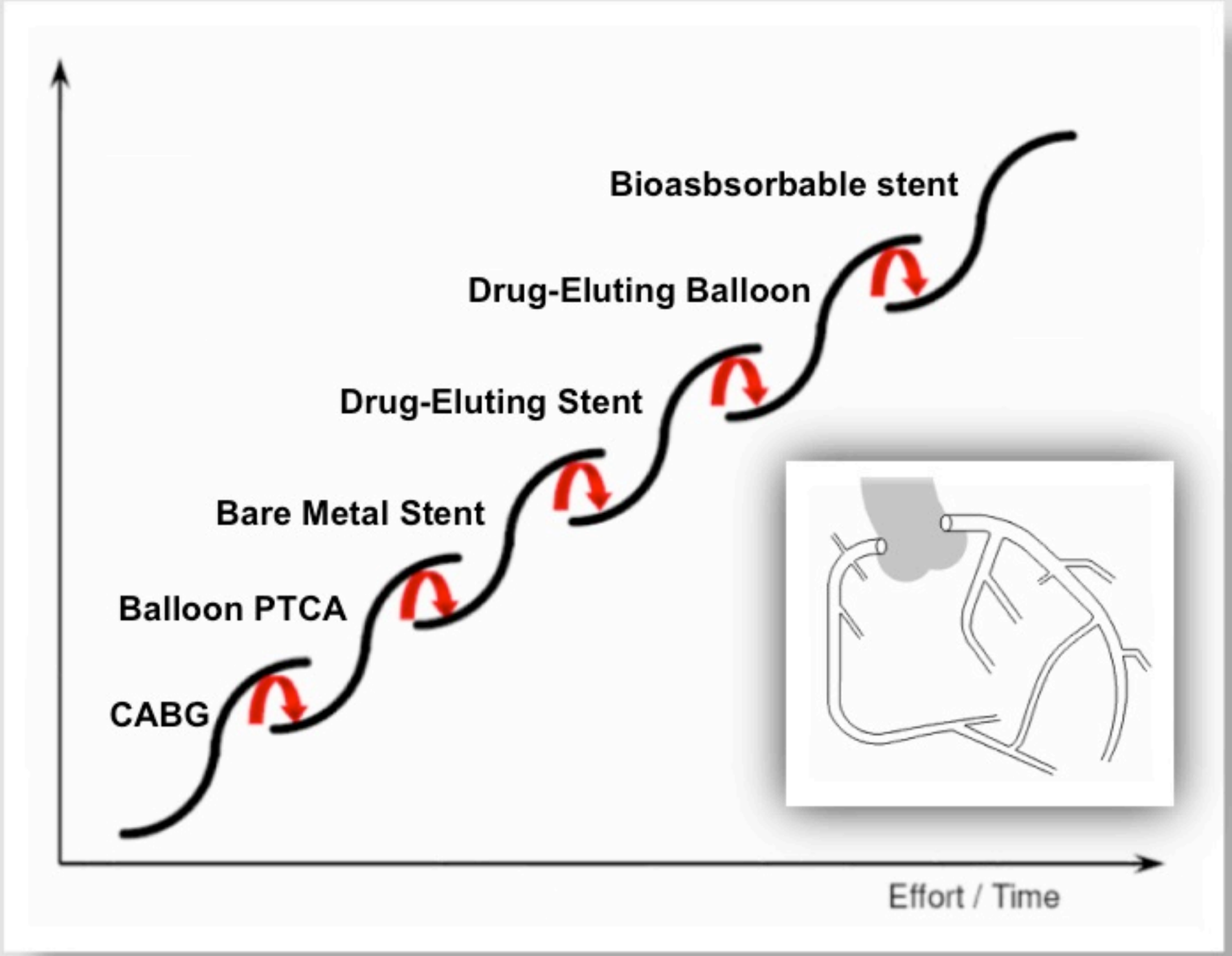


Percutaneous coronary intervention evolution

Decreasing incidence of restenosis

Decreasing invasiveness of surgical procedure

"Evolution fuel"



BTK-PTA: a coronary-like evolution?

Decreasing incidence of restenosis

Decreasing invasiveness of surgical procedure

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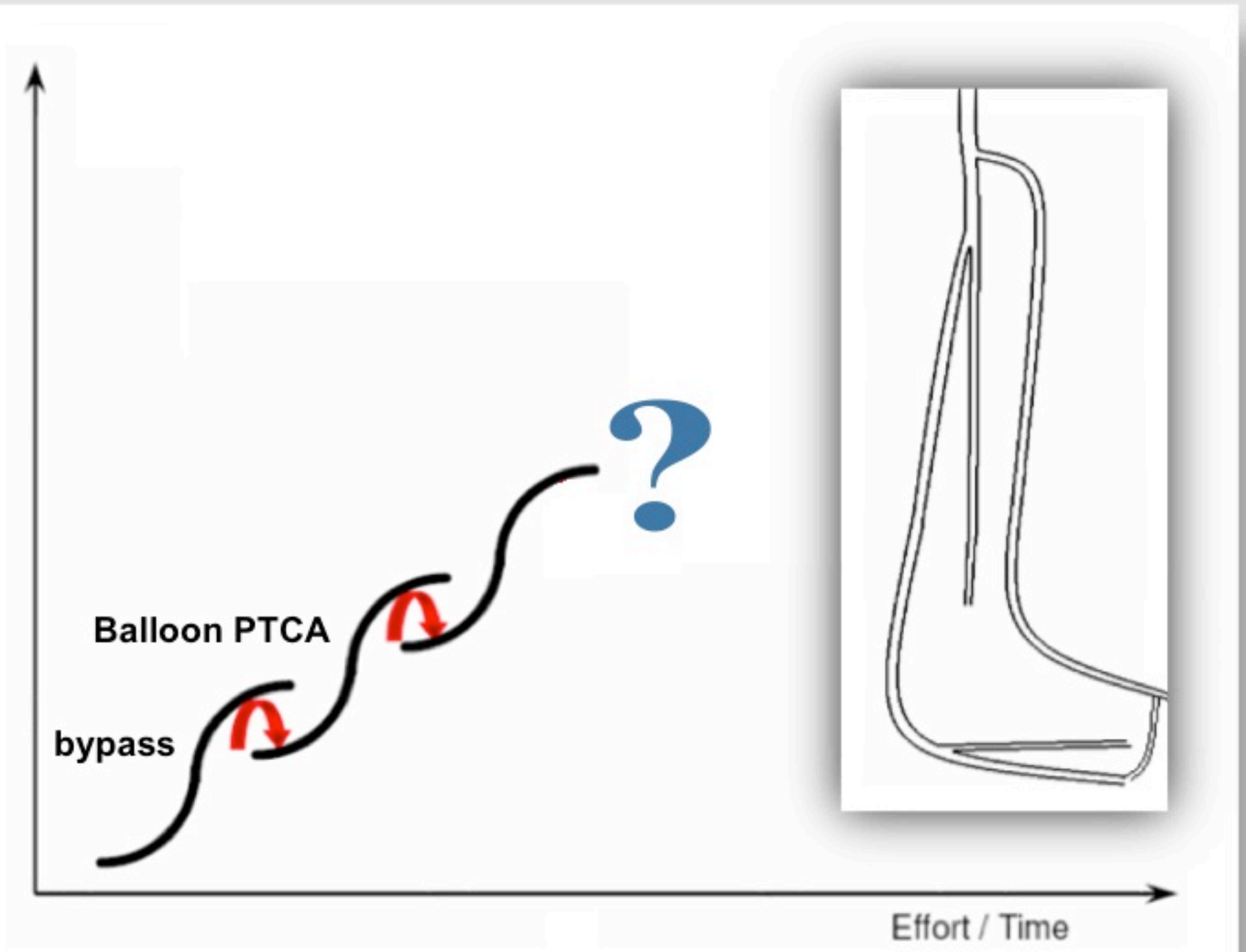

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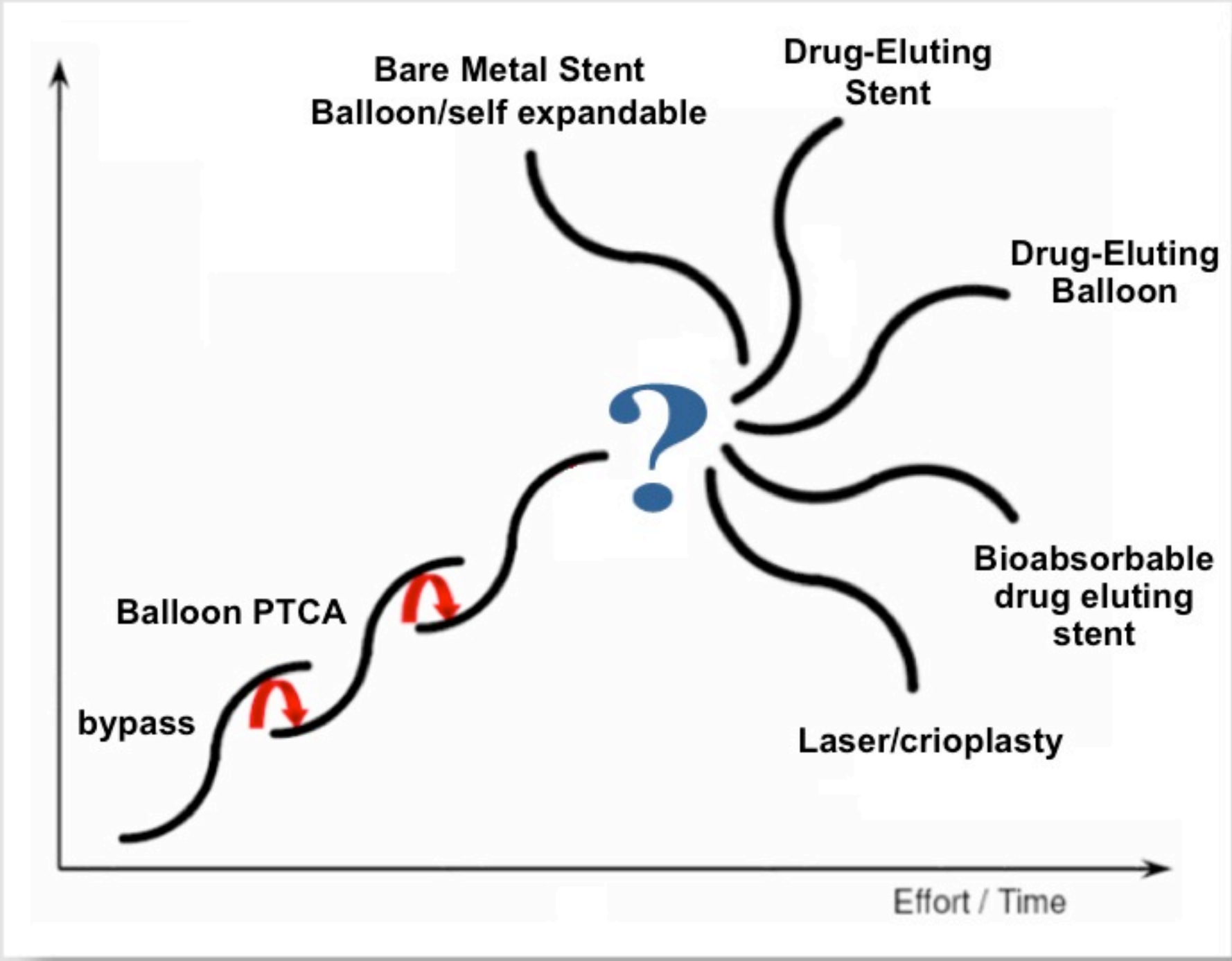

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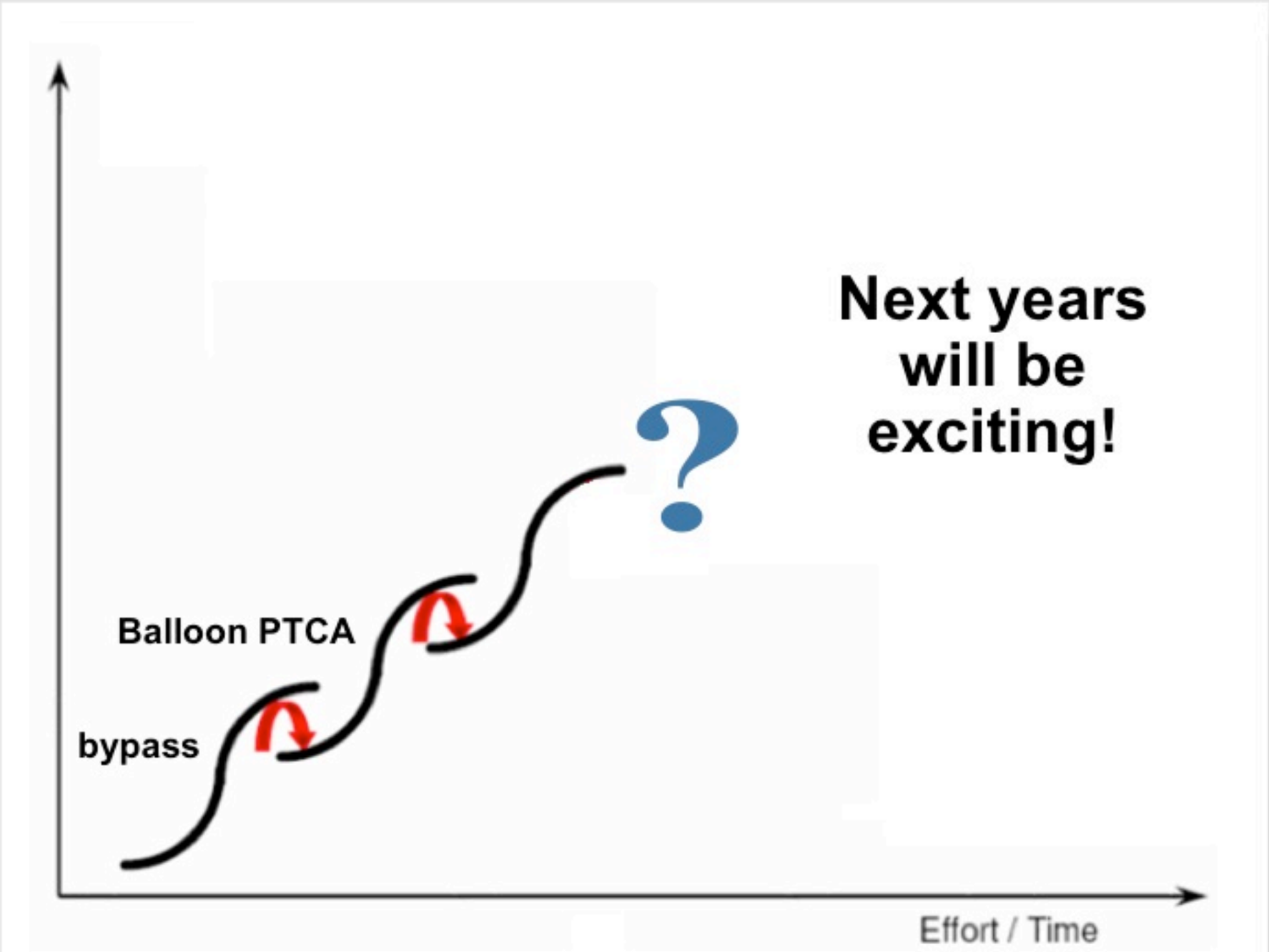

Conclusions

1) In short BTK lesions (<5cm) there is increasing evidence about good acute and mid-term results of primary stenting. BMSs, DESs and SESs seem to be promising devices in prevention of restenosis

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2) In long diffuse lesions (majority of CLI patients) the optimal endovascular treatment is POBA with dedicated BTK balloons + bailout stenting

Conclusions

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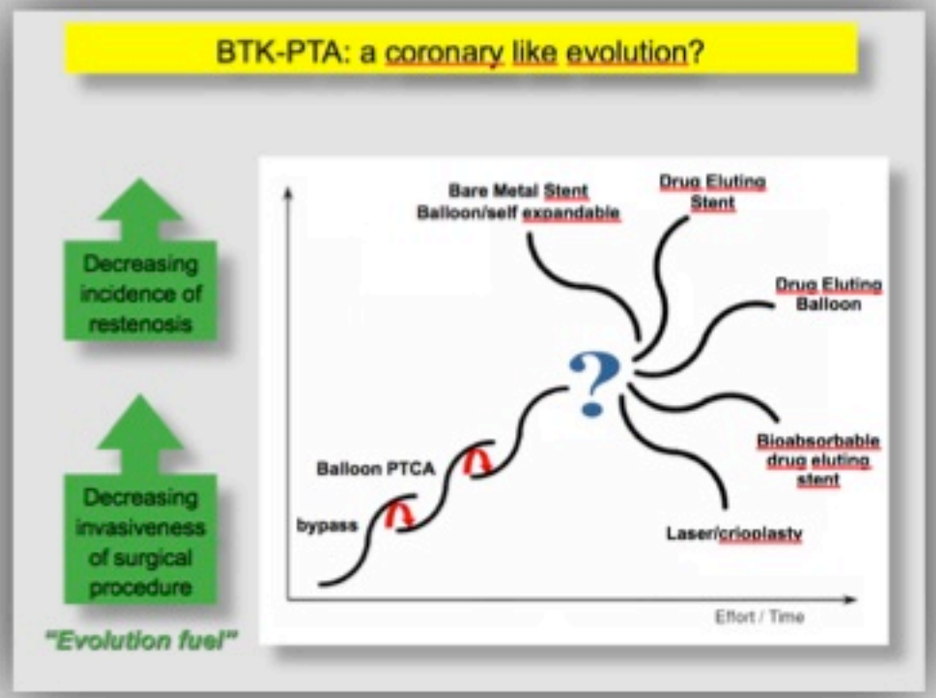
2) In long diffuse lesions (majority of CLI patients) the optimal endovascular treatment is POBA with dedicated BTK balloons + bailout stenting



3) **The future is open for every device able to demonstrate safety and efficacy in treating long BTK & FOOT vessel disease, improving patency, reducing TLR, healing time and reulceration rate**