CARDIOVASCULAR SUMMIT
TCTAP 2015

Below the Knee Intervention

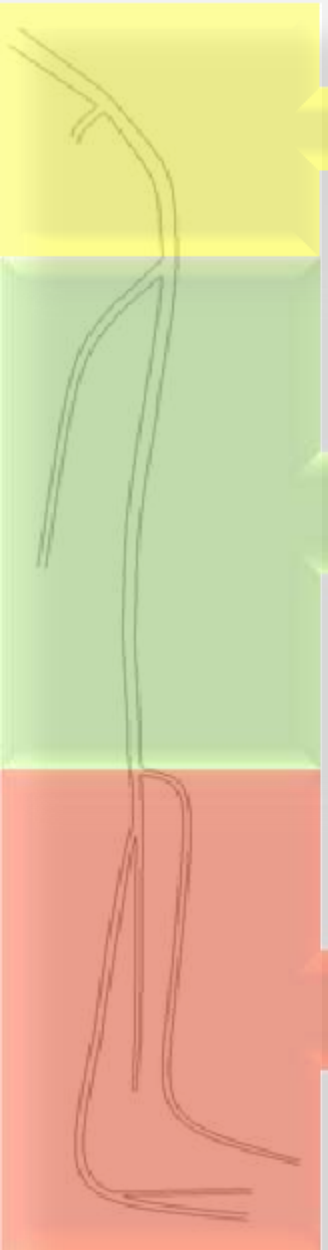
DEBATE-BTK and IN.PACT DEEP Trial: How to Apply DCB in BTK

GB Danzi, MD
Italy

Why to Apply DCB in BTK ?

- **Balloon angioplasty is the approach that best fits the type of lesions of diabetic patients with CLI**
- **The drawback of POBA is the high rate of restenosis**
- **DCB represents an intriguing option for high-risk lesions**

Mean length of the single treated lesion

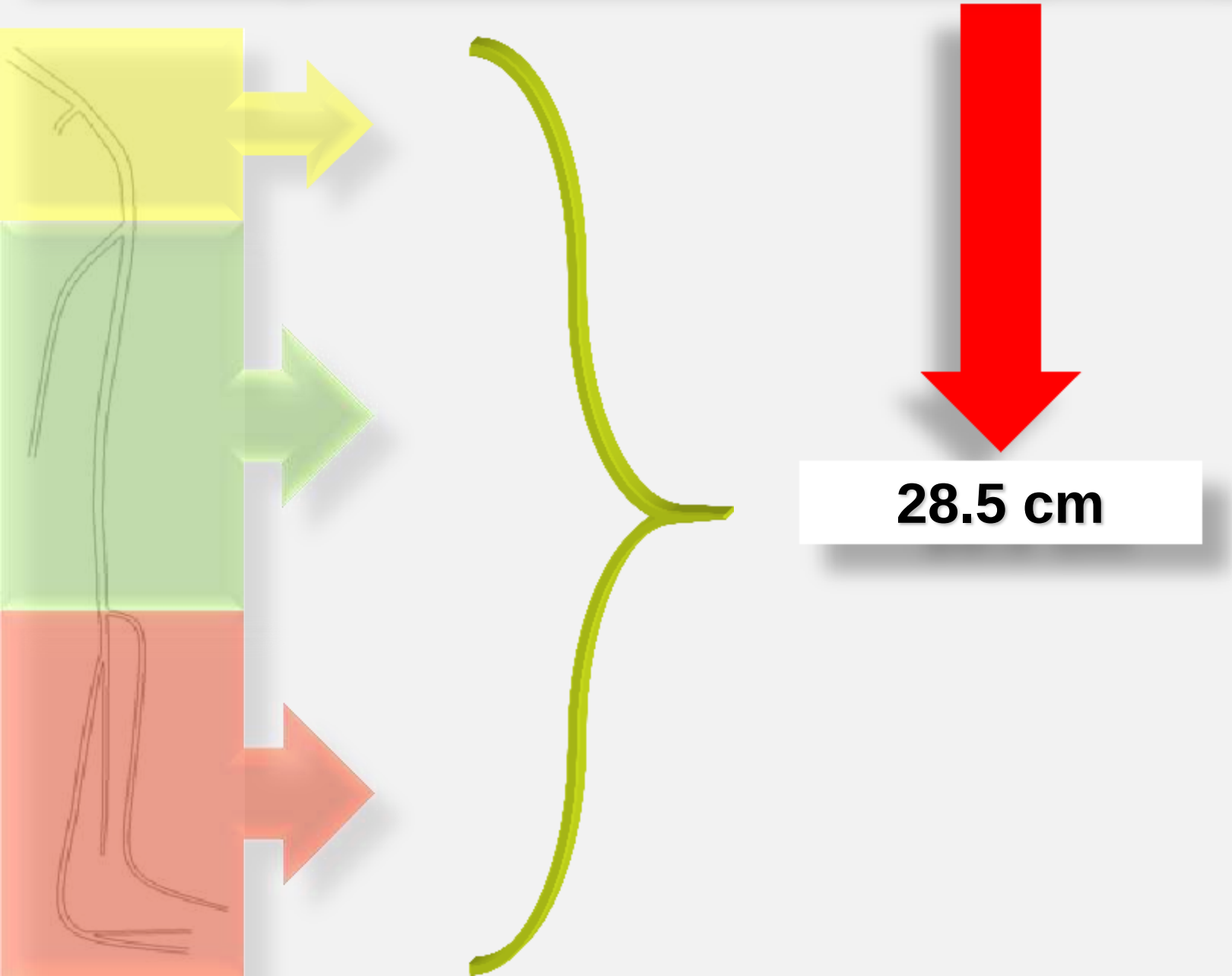


5% ATG → **60±53 mm**

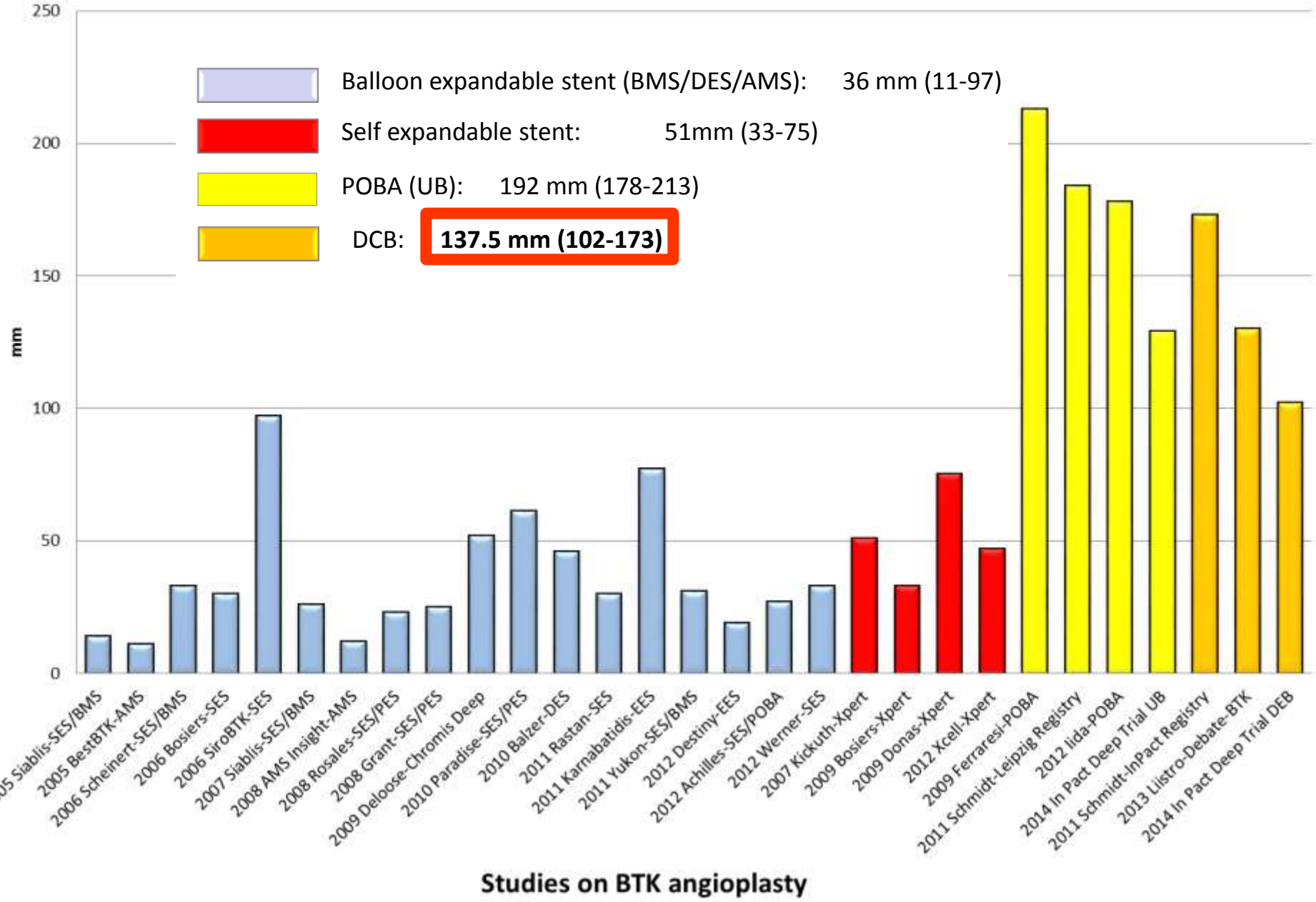
53% FEM-POP → **121±113 mm**

95% BTK → **188±121 mm**

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



Mean legth of the treated lesion



Why to Apply DCB in BTK ?

- Balloon angioplasty is the approach that best fits the type of lesions of diabetic patients with CLI
- The drawback of POBA is the high rate of restenosis
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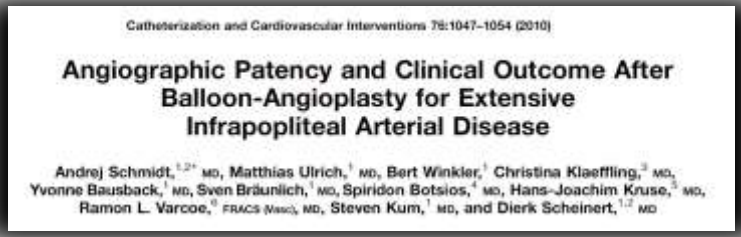
Restenosis rate of POBA in real world long BTK vessels

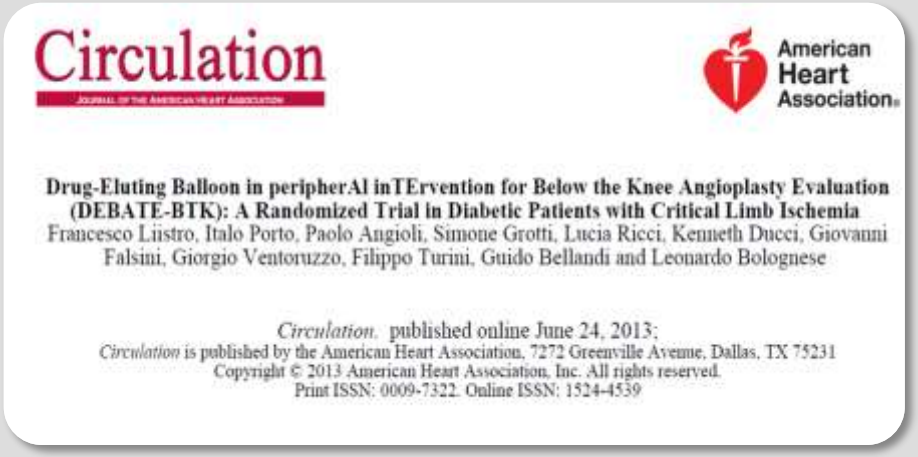
Study	limbs	Mean lesion length	Follow up	restenosis	TLR
 Catheterization and Cardiovascular Interventions 76:1047–1054 (2010) Angiographic Patency and Clinical Outcome After Balloon-Angioplasty for Extensive Infrapopliteal Arterial Disease Andrej Schmidt, Matthias Ulrich, Bert Winkler, Christina Klaeffling, 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 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%

Below the Knee Intervention

DEBATE-BTK and IN.PACT DEEP Trial: Disparate results between studies

DEBATE-BTK Study

IN.PACT Amphirion vs. PTA in pts with CLI and Diabetes



Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

Drug-Eluting Balloon in peripherAl inTErvention for Below the Knee Angioplasty Evaluation (DEBATE-BTK): A Randomized Trial in Diabetic Patients with Critical Limb Ischemia

Francesco Liistro, Italo Porto, Paolo Angioli, Simone Grotti, Lucia Ricci, Kenneth Ducci, Giovanni Falsini, Giorgio Ventoruzzo, Filippo Turini, Guido Bellandi and Leonardo Bolognese

Circulation. published online June 24, 2013;

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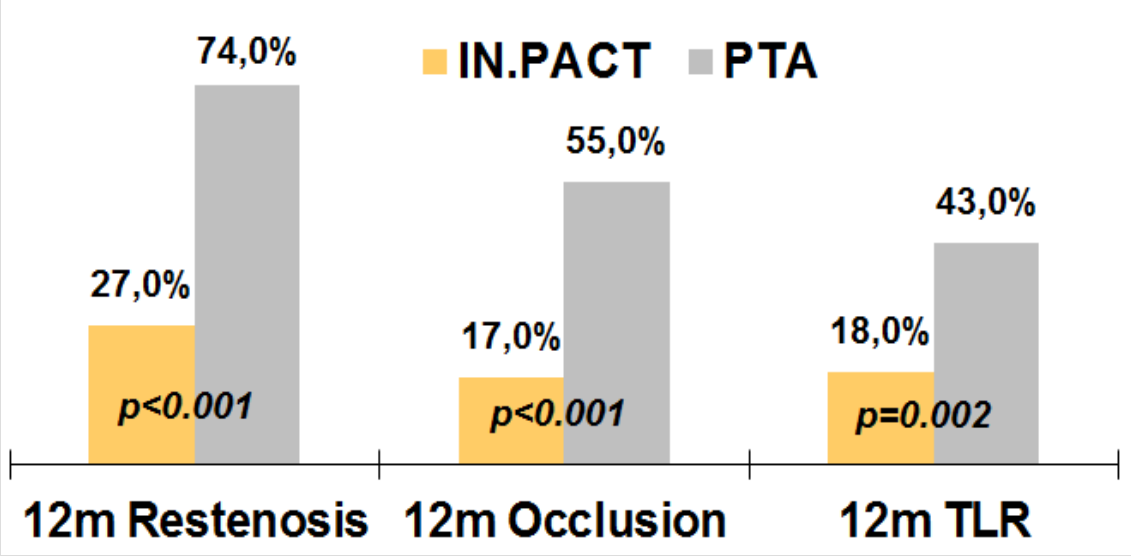
Single Center Randomized Trial

- 132 Patients
- CLI 100%
- Diabetes 100%
- Avg lesion length ~13 cm
- CTOs ~80%

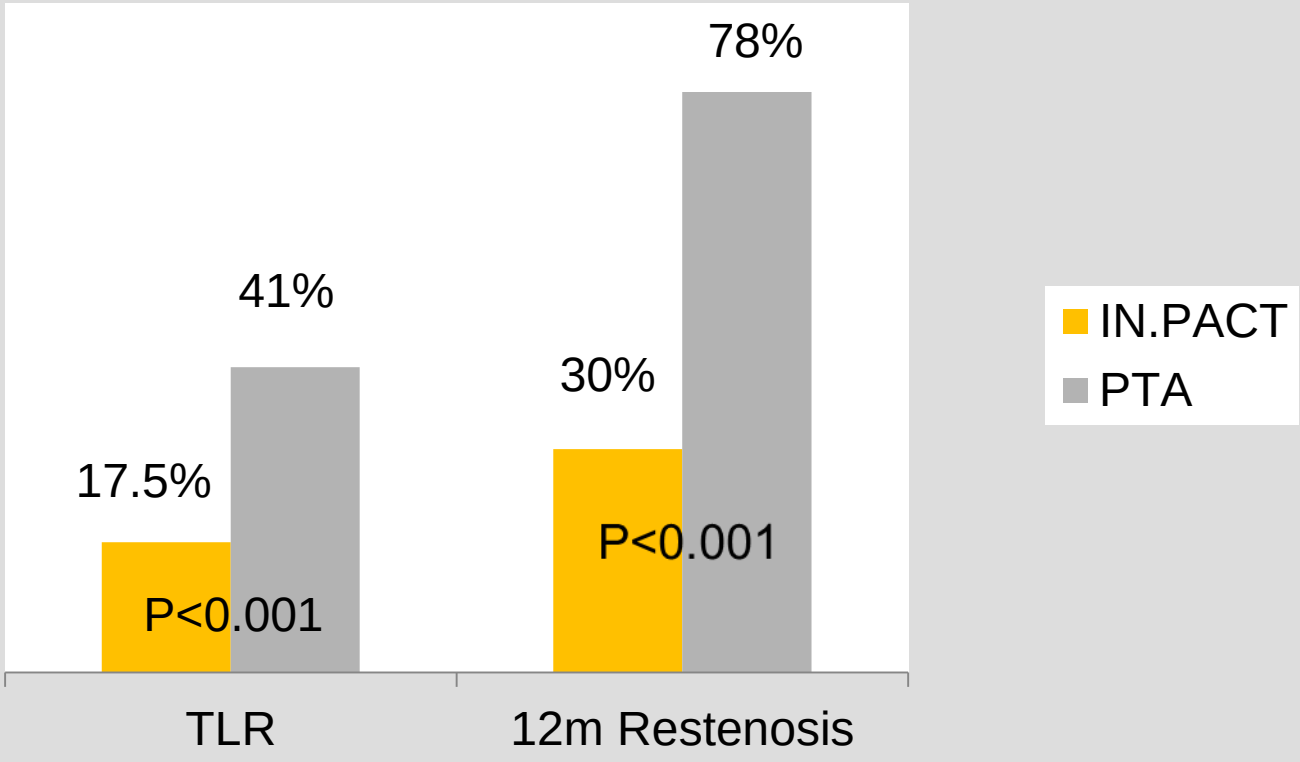
12-month Results



DEBATE-BTK Study

IN.PACT Amphirion vs. PTA in pts with CLI and Diabetes

24-month Results



Liistro F, *LINK* 2014

Multi center *vs*. single center trials

Larger treatment effect is usually reported by single- vs. multi-center Trials

Single Center Trials:

- **Typically borne "within highly expert endeavors, highly committed to the cause, dedicated and enthusiastic"**
- **May be affected by systematic (positive), unmeasured errors/confounders**
- **Mostly self-reported, self-adjudicated**
- **Mirror center's practice**
- **Limited generalizability**

INPACT.DEEP Trial

358-patient RCT (IN.PACT Amphirion *vs.* PTA)

- Prospective, Multicentre, Randomized
- Independent Data Safety Monitoring Board
- Independent CEC
- Independent Angiographic Corelab
- Independent Wound Corelab
- Wound Measurement (Electronic Reader)
- External Monitoring,
- 100% Source Verification

TABLE 4 12-Month Efficacy Endpoints

	IA-DEB	PTA	p Value
Late lumen loss,* mm	0.605 ± 0.775	0.616 ± 0.781	0.950
Binary restenosis*	41.0 (25/61)	35.5 (11/31)	0.609
Occlusion rate	11.5 (7/61)	16.1 (5/31)	0.531
Longitudinal restenosis†	62.7 ± 56.2	93.2 ± 60.8	0.167
Clinically driven TLR (AFS subjects)	9.2 (18/196)	13.1 (14/107)	0.291
Clinically driven TLR (all ITT subjects)	11.9 (27/226)	13.5 (15/111)	0.682

Zeller T, *JACC* 2014;64:1568

INPACT.DEEP Trial

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- External Monitoring,
- 100% Source Verification

TABLE 5 Primary and Secondary Safety Endpoints

	IA-DEB	PTA	p Value
6-month primary safety endpoint	17.7 (41/232)	15.8 (18/114)	0.021*
12-month major amputation	8.8 (20/227)	3.6 (4/111)	0.080
12-month all-cause mortality	10.1 (23/227)	8.1 (9/111)	0.551
12-month death and amputations†	35.2 (80/227)	25.2 (28/111)	0.064
12-month death, major amputation or clinically driven TLR‡	26.9 (61/227)	23.4 (26/111)	0.496
Amputation-free survival	81.1 (184/227)	89.2 (99/111)	0.057

Zeller T, *JACC* 2014;64:1568

INPACT.DEEP Trial

358-patient RCT (IN.PACT Amphirion *vs.* PTA)

TABLE 3 Baseline Angiographic and Procedural Characteristics (ITT Population)

	IA-DEB	PTA	p Value
Lesion length, cm	10.15 ± 9.10	12.86 ± 9.46	0.002
Lesion length in angiography cohort, cm	5.91 ± 4.17	7.97 ± 7.46	0.060
Reference vessel diameter, mm	2.46 ± 0.69	2.41 ± 0.56	0.304
Pre-dilation	90.5 (325/359)	36.0 (68/189)	<0.001
Inflation time, s*	166.0 ± 138.4	137.7 ± 111.3	0.010
Maximum inflation pressure, atm	9.5 ± 2.4	10.3 ± 4.6	0.010

Zeller T, *JACC* 2014;64:1568

What about angiographic endpoints?

Angiographic Follow-up in DEB Studies

STUDY	N° of Pts	DEB Arm N° of Pts with Angio FU	POBA Arm N° of Pts with Angio FU	RVD
Schmidt A.	104	74 (176±88 mm)	-	-
DEBATE-BTK	132	65 (129±83 mm)	67 (131±79 mm)	2.9 mm
BIOLUX P-II	72	30 (113±88 mm)	35 (115±87 mm)	2.2 mm
IN.PACT DEEP	358	61 (102±91 mm)	31 (129±95 mm)	2.4 mm

INPACT.DEEP Trial

358-patient RCT (IN.PACT Amphirion *vs.* PTA)

TABLE 6 RC Subgroup Analysis (ITT Population)

Primary safety endpoint	IA-DEB	PTA
RC 4	12.12 (4/33)	20.0 (4/20)
RC 5	19.0 (37/195)	14.8 (13/88)
RC 6	0.0 (0/4)	20.0 (1/5)
12-month all-cause mortality	DEB	PTA
RC 4	6.3 (2/32)	10.0 (2/20)
RC 5	11.0 (21/191)	8.2 (7/85)
RC 6	0.0 (0/4)	0.0 (0/5)
12-month major amputation	DEB	PTA
RC 4	0.0 (0/32)	0.0 (0/20)
RC 5	10.5 (20/191)	3.5 (3/85)
RC 6	0.0 (0/4)	20.0 (1/5)

Zeller T, *JACC* 2014;64:1568

What about hard clinical endpoints?

LEIPZIG Registry

	DCB (12-month)	PTA (15 month)
Deaths	16.3%	10.5%
Limb Salvage	**95.6%**	**100%**
Wound healing	74.2%	78.6%

"…multiple factors contribute to wound healing and limb salvage, including local wound care and surveillance regimen, which may be equally as important as revascularization. It therefore may be difficult to prove the superiority of the DEBs over uncoated balloons for these clinical endpoints…"

- Schmidt A et al. J Am Coll Cardiol. 2011 Sep 6;58(11):1105-9
- Schmidt A et al. Catheter Cardiovasc Interv. 2010 Dec 1;76(7):1047-54

DEBATE-BTK

12-month Outcomes	DCB	PTA	*p*
Deaths	7.7%	4.5%	*0.4*
Major Amputation	**0%**	**1.5%**	***0.9***
Wound healing	**86%**	**67%**	***0.01***

"…once discharged, patients were followed in a multidisciplinary, dedicated foot clinic to facilitate healing process and recovery of the ambulatory function. Office visits were scheduled 2 days/week for the first 2 months, once a week for the third month and then every two weeks…"

- Liistro F et al. Circulation. 2013 Aug 6;128(6):615-21

Below the Knee Intervention
When to Apply DCB in BTK

- Disparate results among studies
- Costs related to DCBs
- Technical limitations of first-generation devices

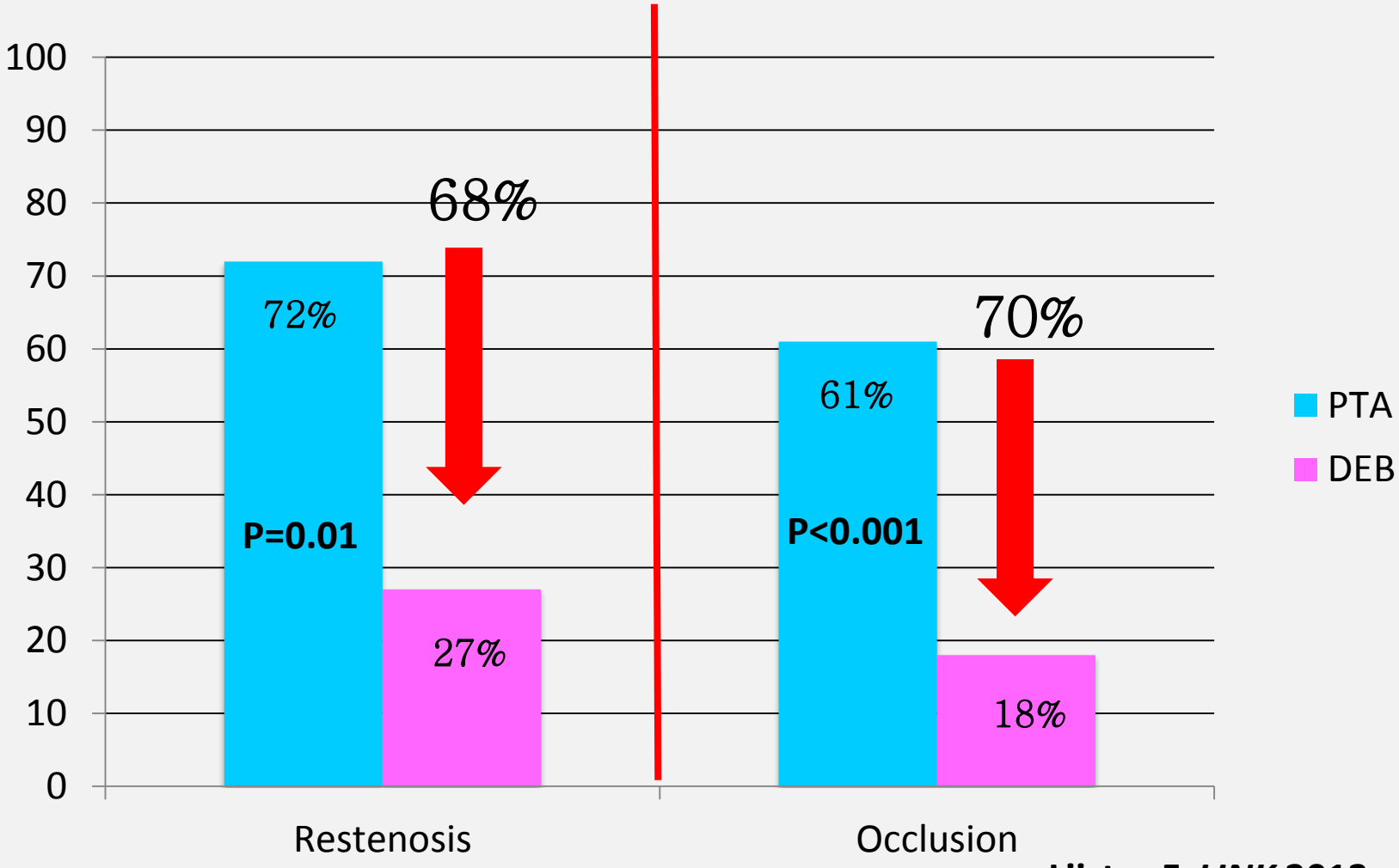
Need for a therapy that provides durable patency

Below the Knee Intervention

When to Apply DCB in BTK

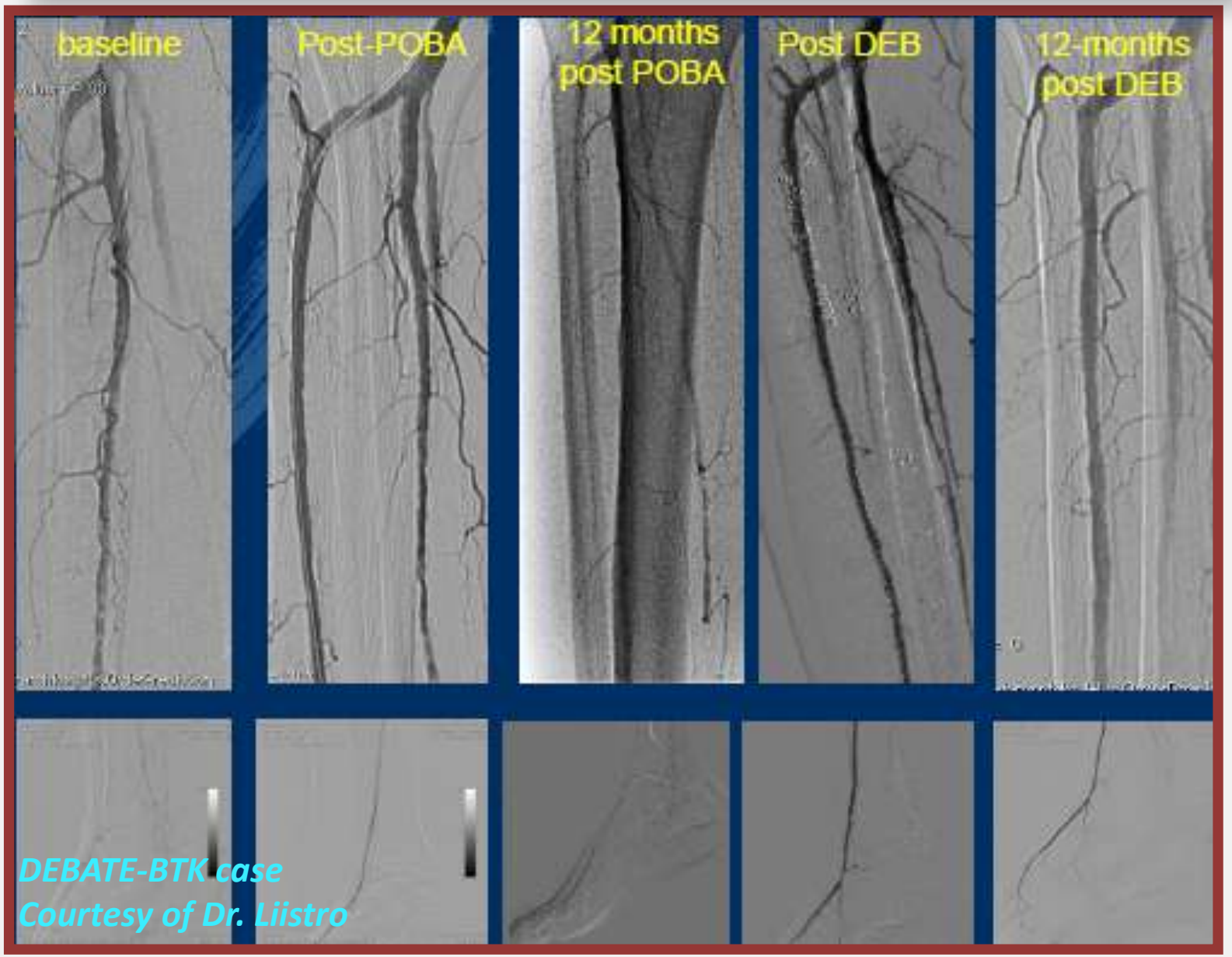
- Early aggressive restenosis after POBA
- Long occlusive restenosis
- Last remaining circulation

Restenosis / Occlusion in Totally Occluded Vessels

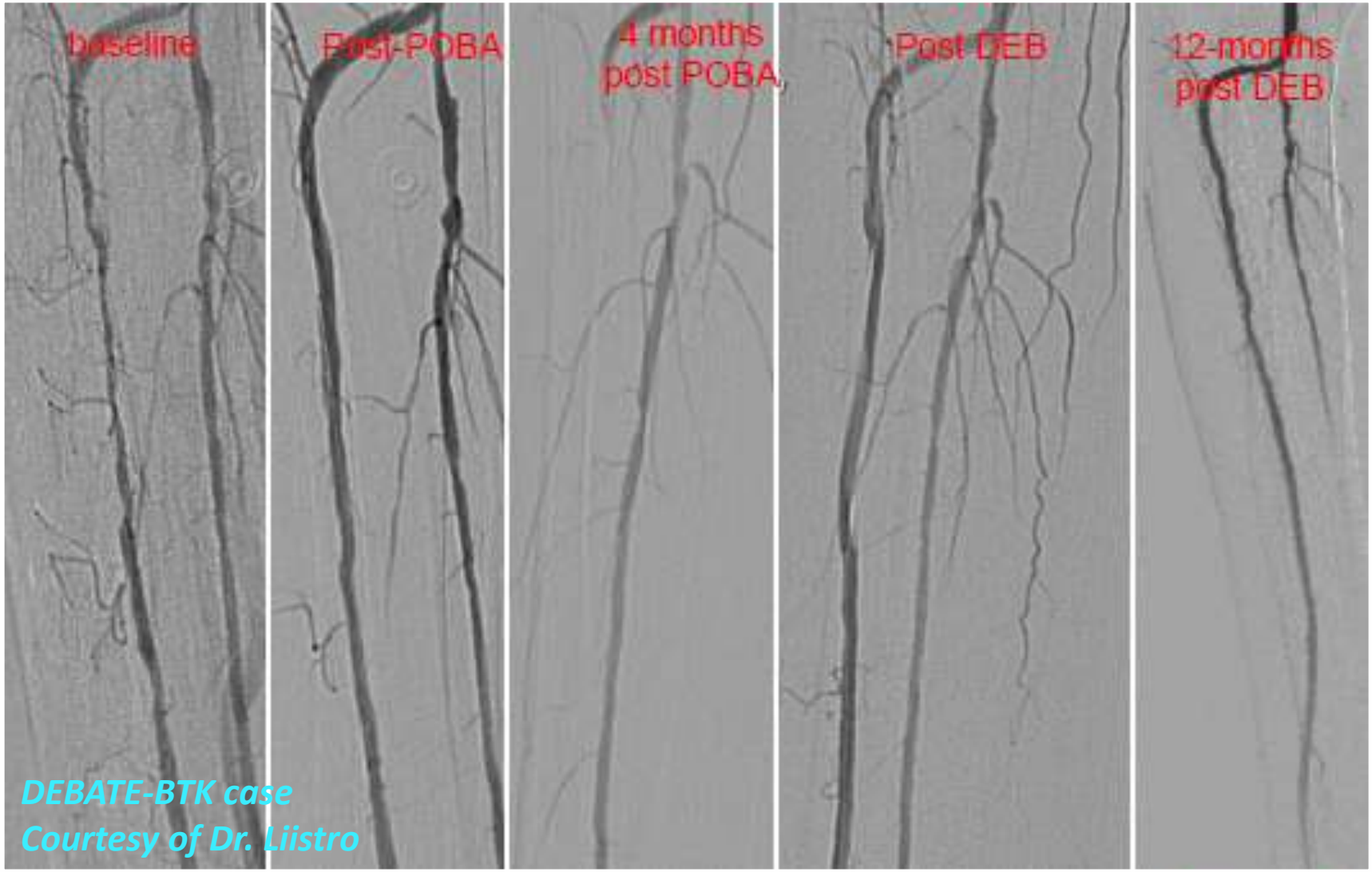


Liistro F, *LINK* 2013

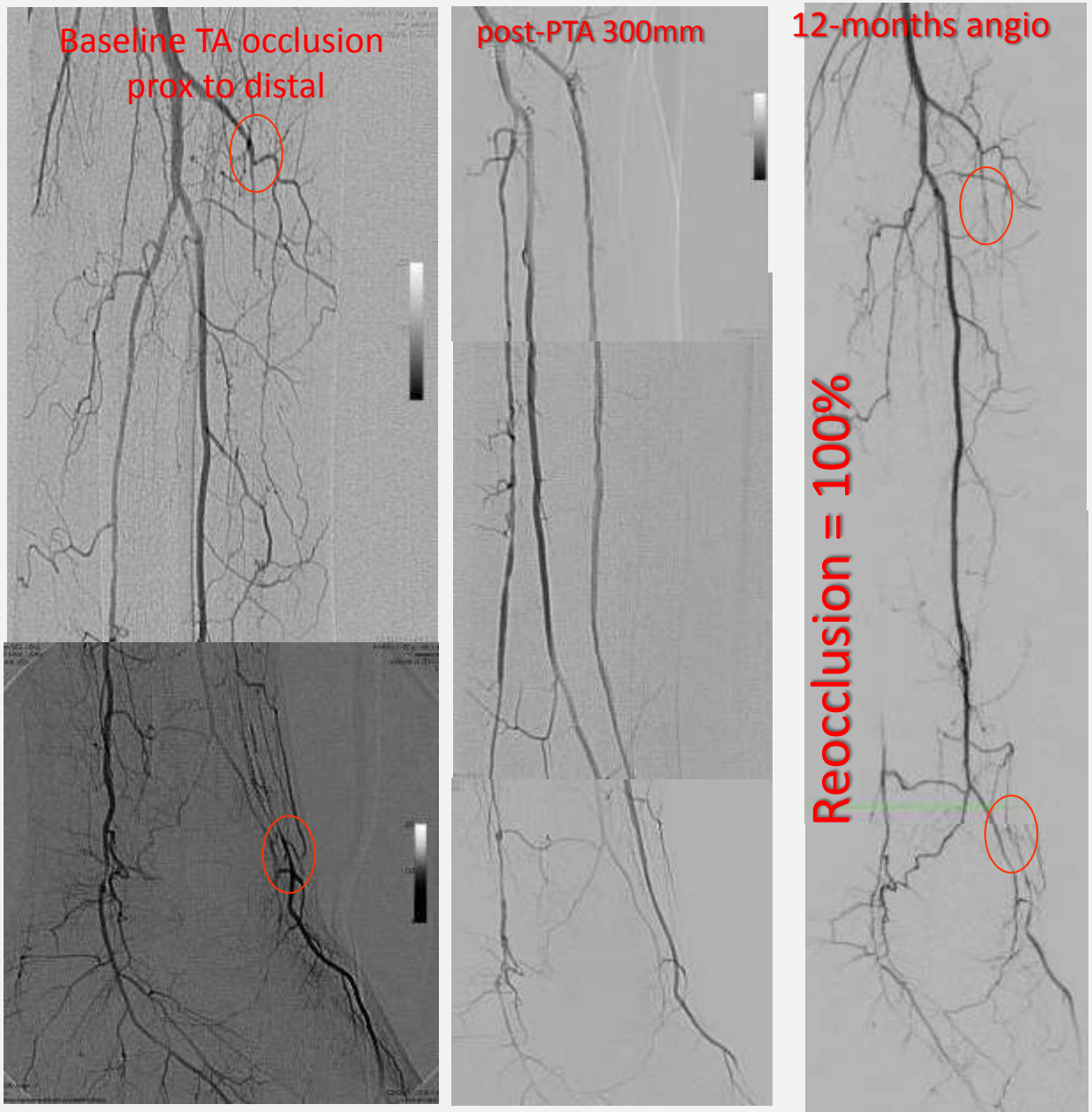
Occlusive Restenosis after POBA



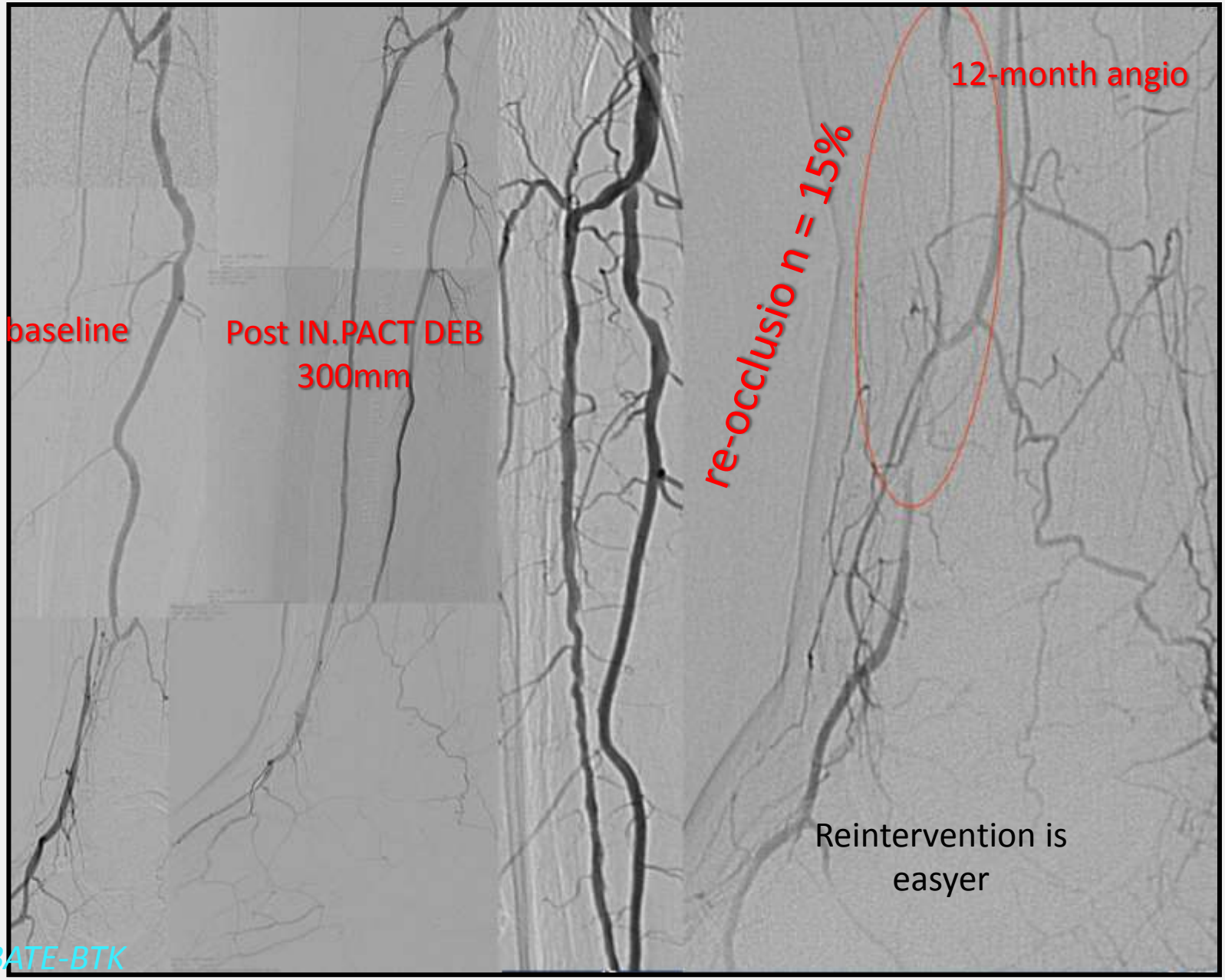
Occlusive Restenosis after POBA



POBA and Pattern of re-occlusion



DEB and Pattern of re-occlusion



DEBATE-BTK

When to Apply DCB in BTK

“Last Remaining Circulation“

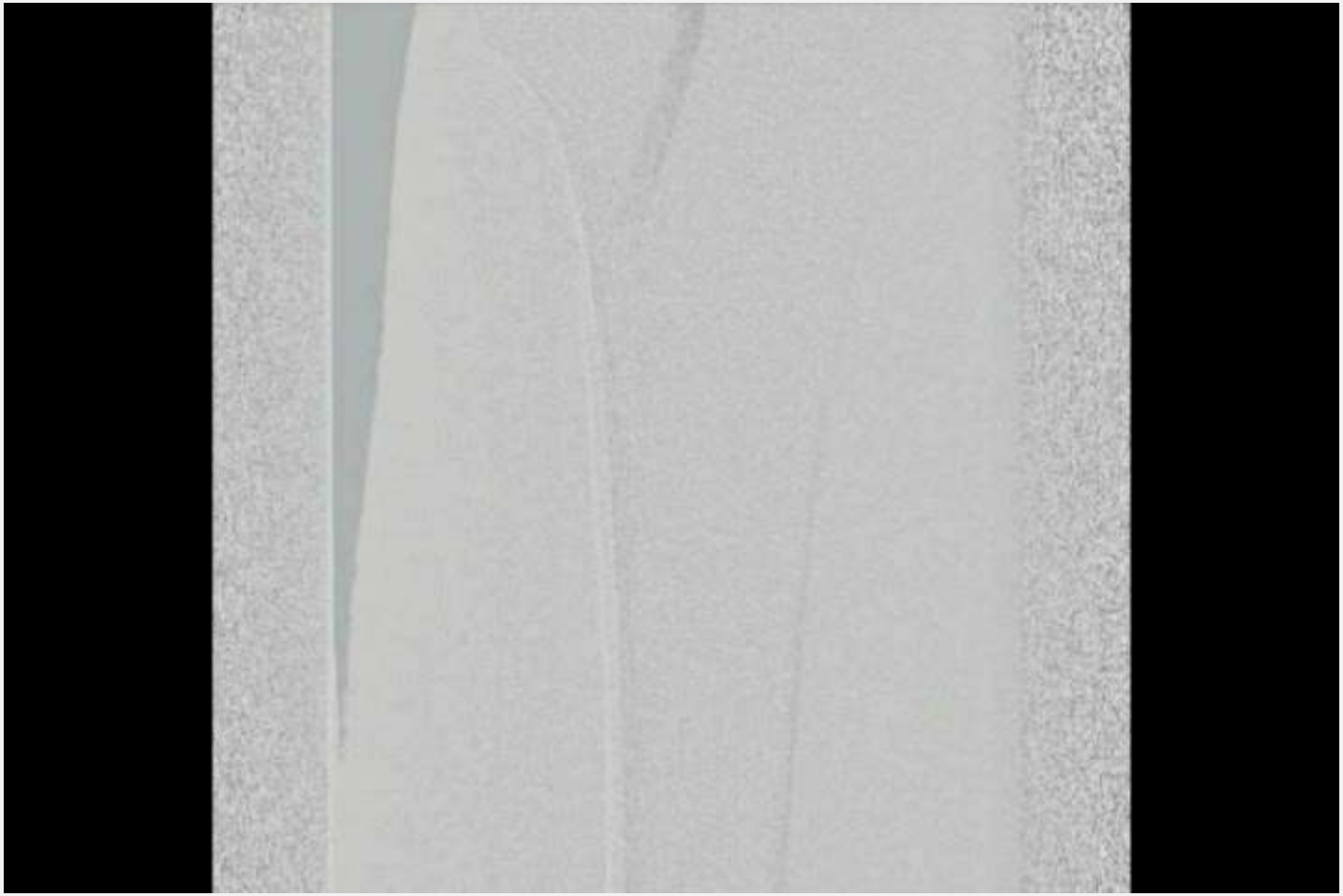
when the future of the foot resides on
a single flow line of blood

Trans-Collateral Approach

Peroneal Artery Branches PTA

- Male, 52 yy
- Type 1 DM
- ESRD-HD
- Previous Chopart amputation
- Ischemic suffering of plantar flap

Basaleline angio



Baseline angio

Ischemic suffering of the plantar flap of the amputation without healing

Treatment with DEB

Baseline angio

Final result

European Journal of Vascular and Endovascular Surgery 43 (2012) 73–80

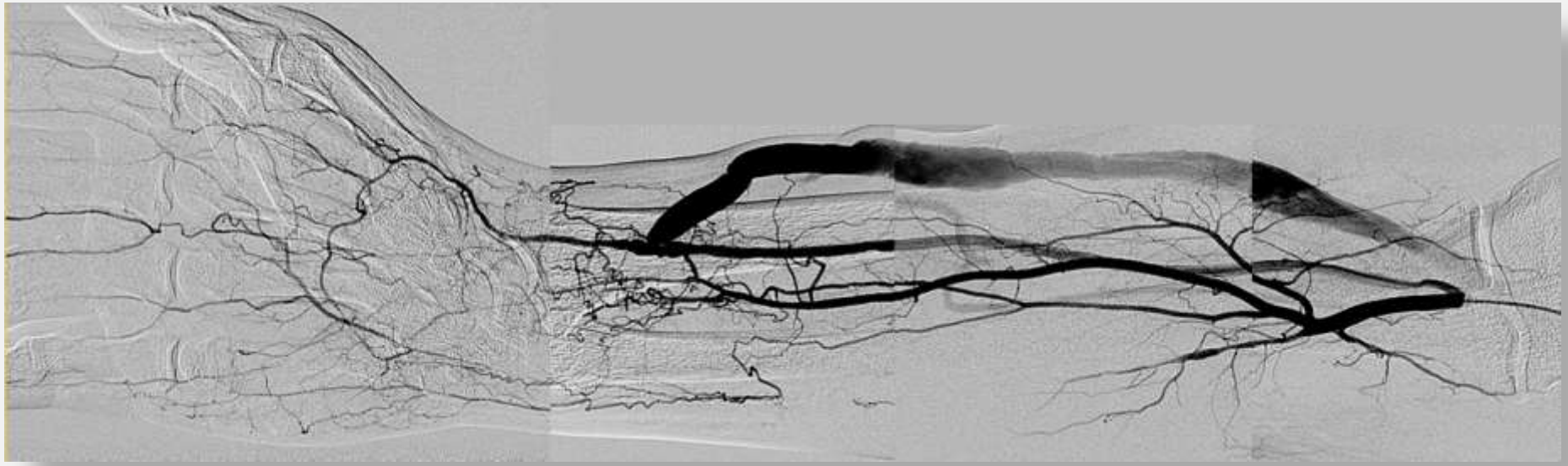
Contents lists available at SciVerse ScienceDirect

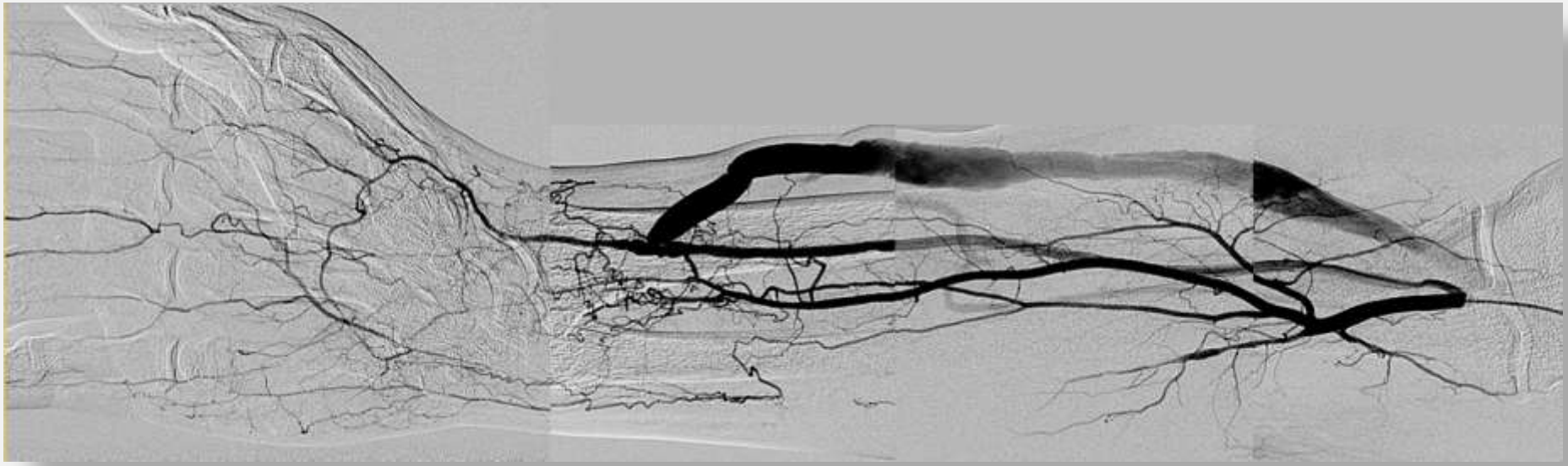
European Journal of Vascular and Endovascular Surgery

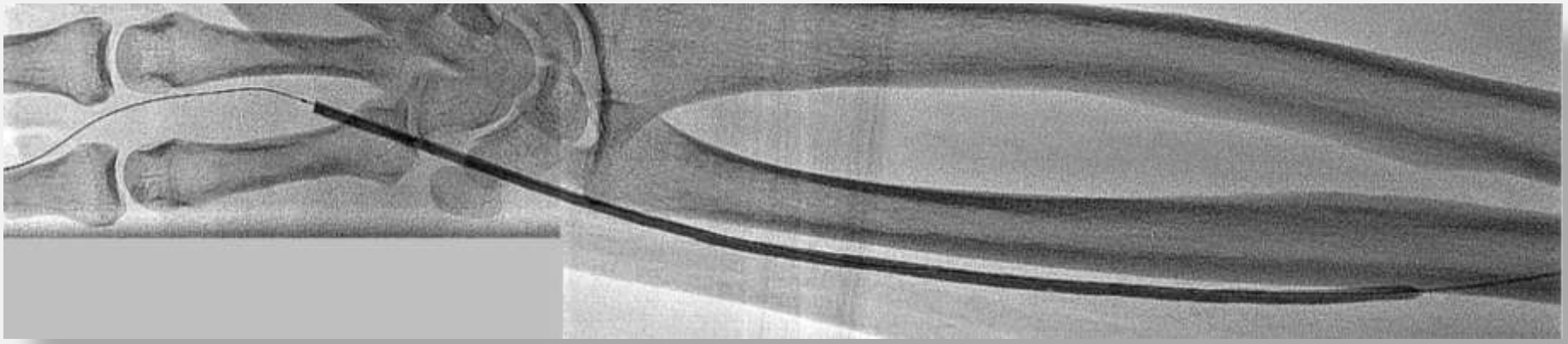
journal homepage: www.ejves.com

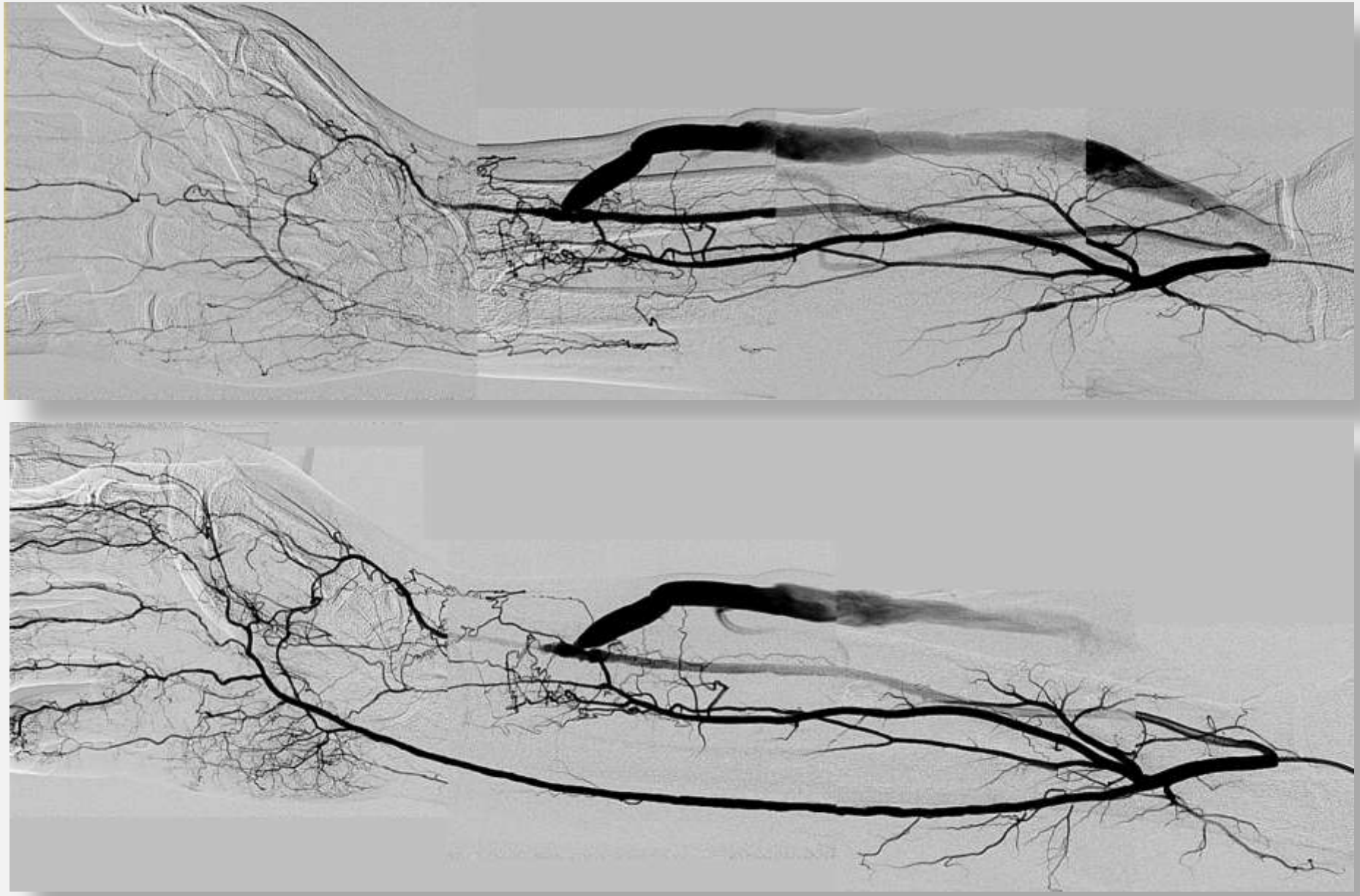
Angioplasty of Below-the-elbow Arteries in Critical Hand Ischaemia

R. Ferraresi [a,*], A. Palloshi [a], G. Aprigliano [a], C. Caravaggi [b], M. Centola [c], F. Sozzi [c], G.B. Danzi [c], M. Manzi [d]



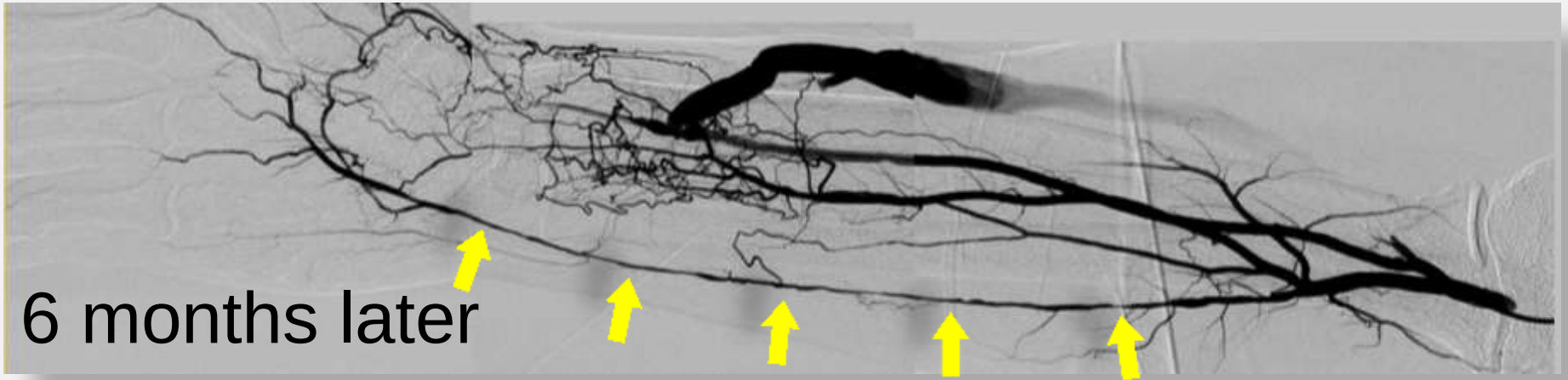







baseline


3 months later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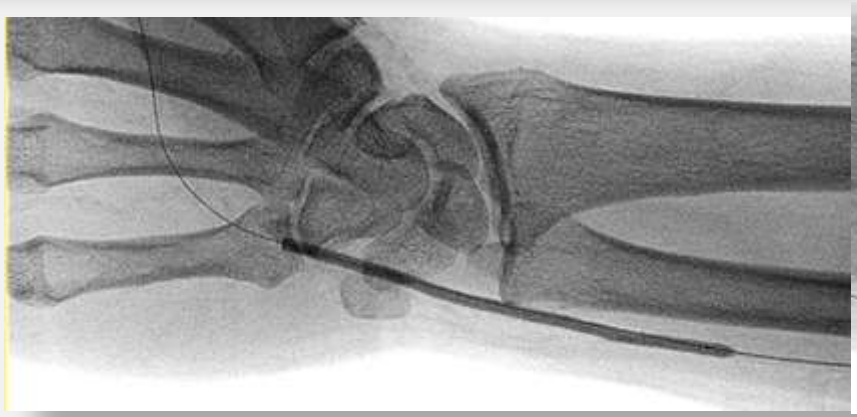
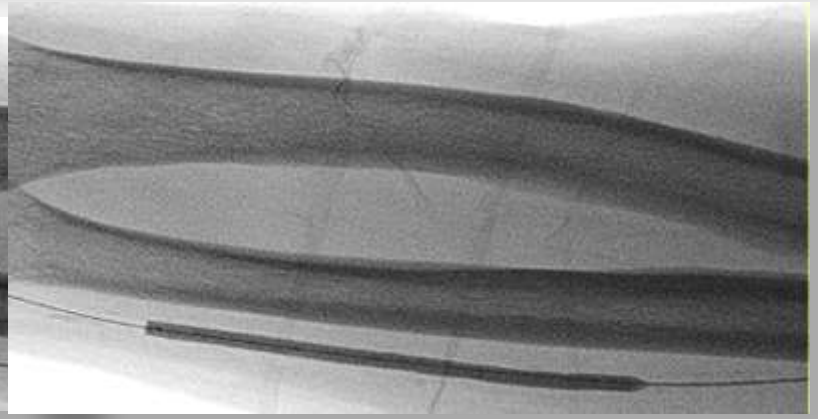
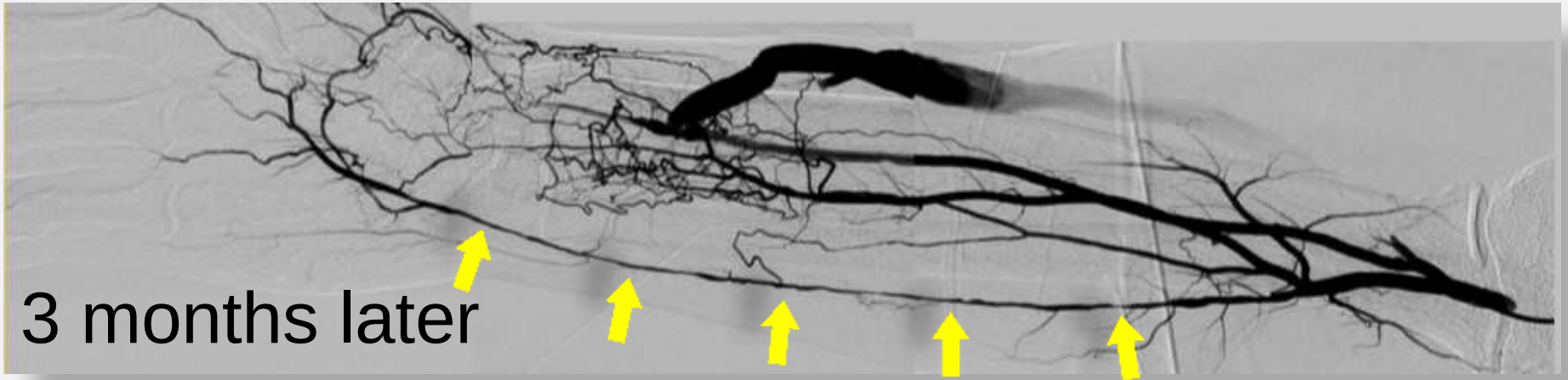
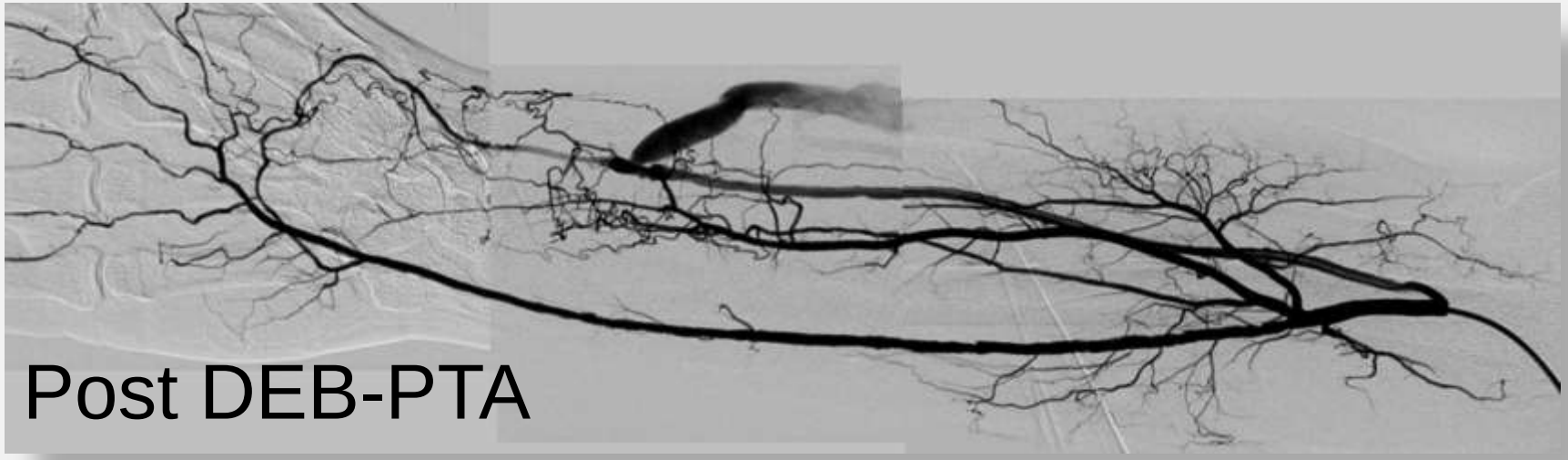
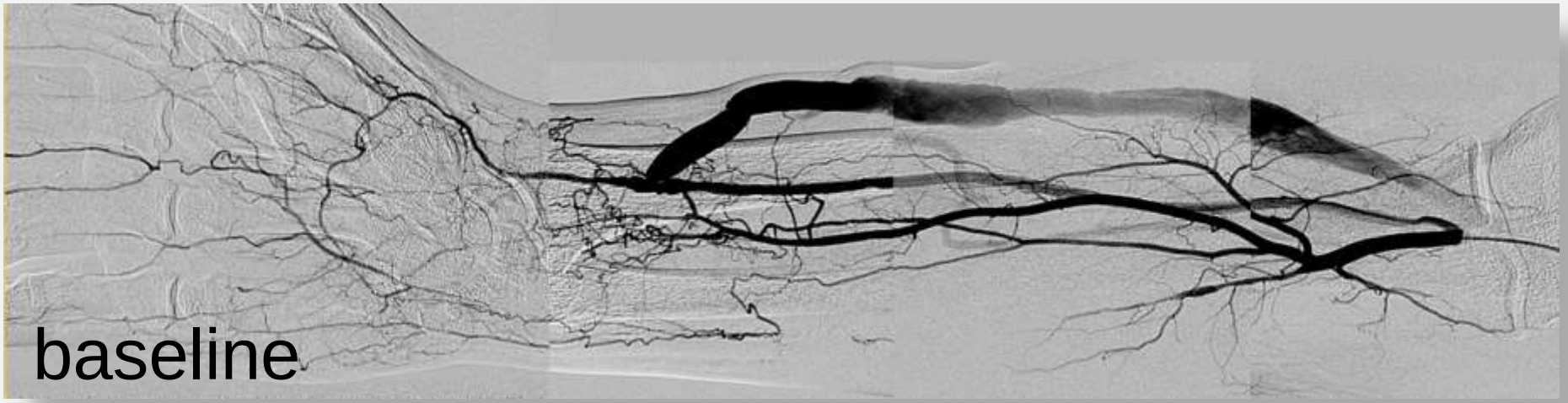





Novel Treatment Concept
IN.PACT
AMPHIRION
Paclitaxel-eluting PTA Balloon Catheter


3 months later


Post DEB-PTA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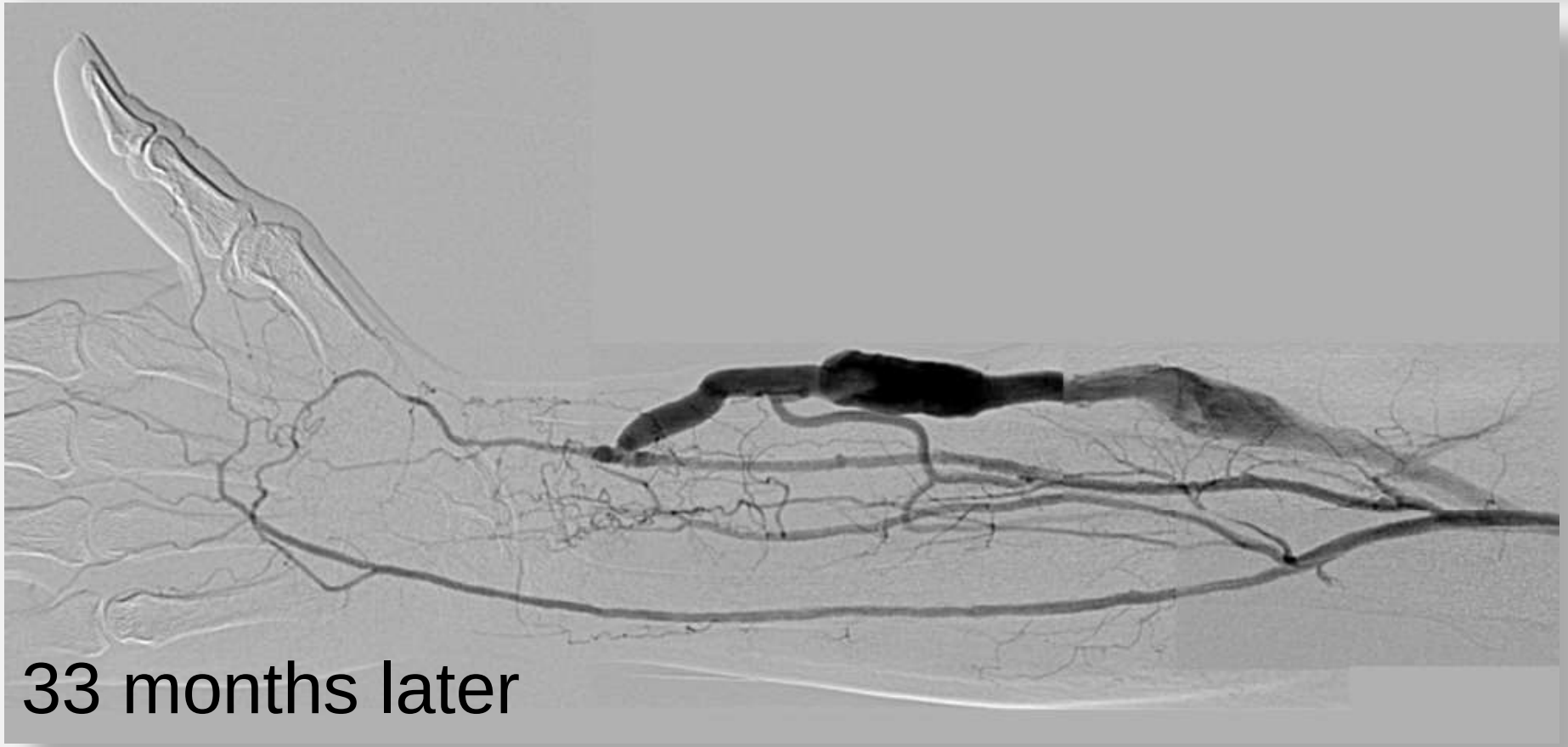
33 months later

BTK Angioplasty for CLI

Conclusions

- Strong need for a therapy that provides durable patency
- The results of studies with DCB are controversial
- However, DCBs represent the most intriguing approach to high-risk lesions in diabetic patients with CLI