DEB Lesson from the real Practice:Tips and Tricks for optimal Usage

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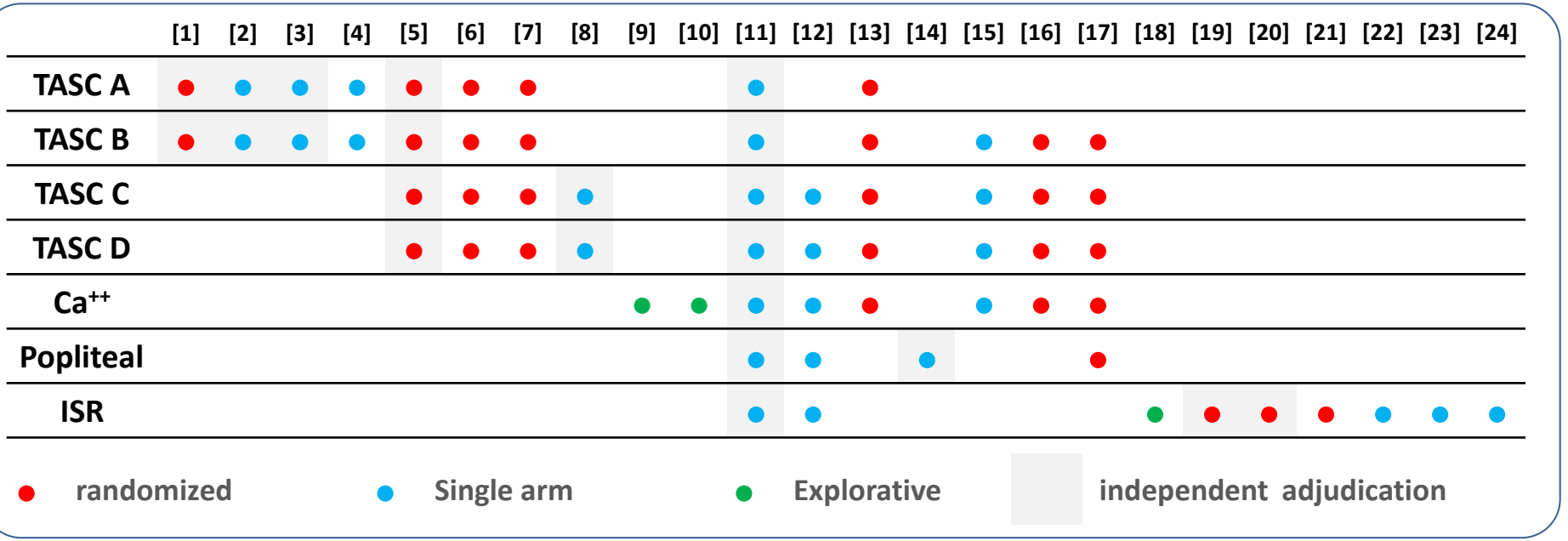
IN.PACT DCB fem-pop Clinical Program

24 IN.PACT Trials* (10 RCT), 4200+ Patients jointly covering the full spectrum of fem-pop PAD



[1] IN.PACT SFA; [2] IN.PACT SFA Japan; [3] IN.PACT SFA China; [4] IN.PACT SFA Italian Registry; [5] PACIFIER; [6] DEBELLUM; [7] ISAR STATH; [8] IN.PACT Long Lesions; [9] IN.PACT + Ather Ca++; [10] IN.PACT Ca++; [11] IN.PACT GLOBAL; [12] IN.PACT SFA Real World Leipzig; [13] DEBATE SFA; [14] IN.PACT Flexion; [15] DEB vs. DES retrosp; [16] DEB vs. DES Italy; [17] BE Diabetic IN.PACT Trial; [18] IN.PACT SFA ISR; [19] PHOTOPAC; [20] FAIR; [21] ISAR PEBIS; [22] PLAISIR; [23], DEBATE ISR; [24] IN.PACT ISR CDN

* **Medtronic and Investigator sponsored trials**

Background: Optimal PTA

Prolonged balloon inflations reduce dissection entity and rates and need for stents

	Inflation Time (sec)		
	30	180	*P* Value
Major dissection (grades 3 and 4)	16	5	.010
Minor or no dissection (grades 1 and 2)	21	32	.010
Further interventions	20	9	.017
Stent	4	1	
Further dilation (prolonged dilation, dilation with larger diameter)	16	8	
Residual stenosis (>30%)	12	5	.097
Complication (embolization, thrombosis)	1	1	
Mean ankle-brachial index (before, after intervention)	0.66, 0.87	0.65, 0.84	

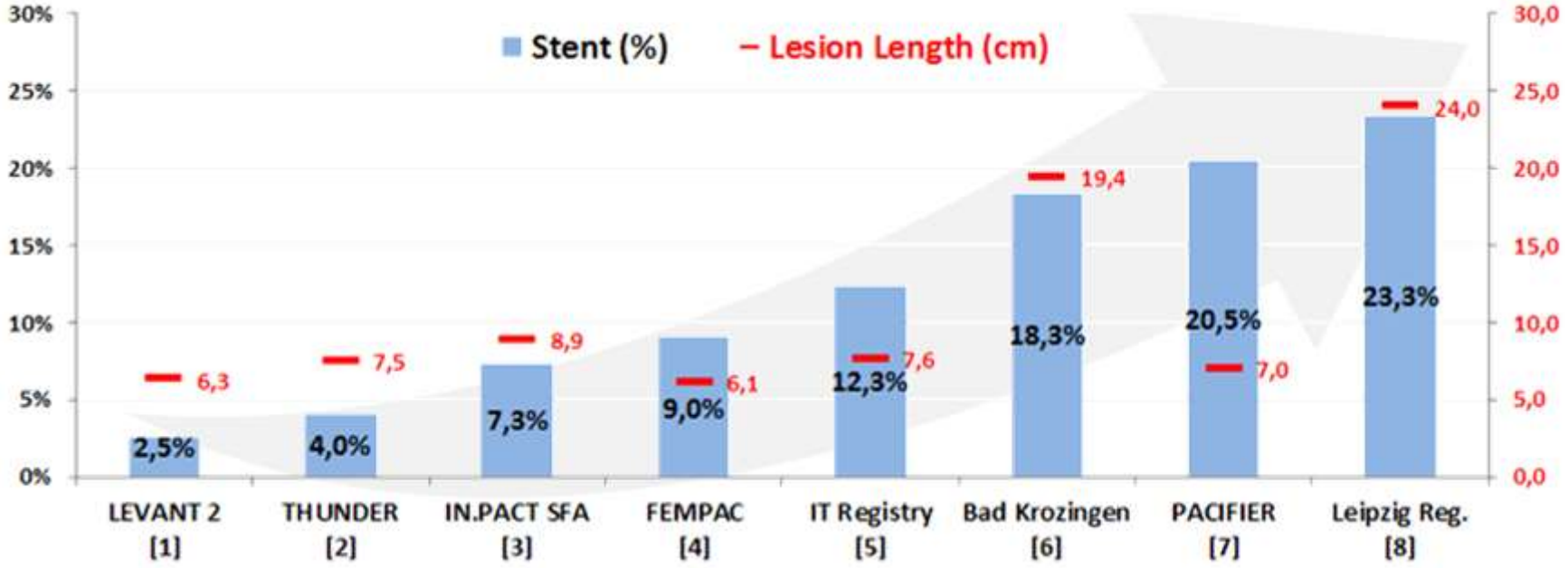
- Inflation times of 180 sec improve immediate infrainguinal PTA results vs. to a short dilation strategy
- Significantly fewer major dissections and a modest reduction of residual stenoses are observed

N. Zorger et al. Peripheral Arterial Balloon Angioplasty: Effect of Short versus Long Balloon Inflation Times on the Morphologic Results. J Vasc Interv Radiol 2002

Background: DCB and provisional Stenting

Scaffolds still needed, likely at rates proportional to lesion complexity

Provisional stent rates in DCB Trials are a function of lesion length



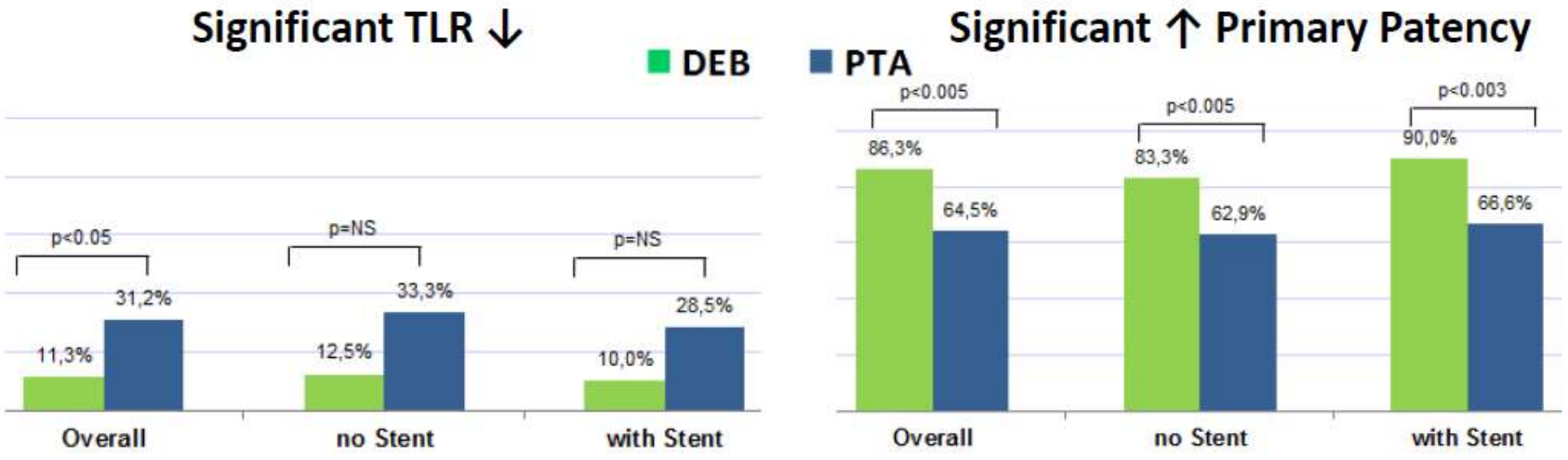
[1] Rosenfield K TCT 2013; [2] Tepe G et al. N Engl J Med 2008; [3] Tepe CX 2014; [4] Werk M et al. Circulation 2008; [5] Micari A et al. J Am Coll Cardiol Intv 2012; [6] Zeller T CX 2013 oral presentation; [7] Werk et al. Circ Cardiovasc Interv. 2012; [8] Schmidt A LINC 2013 oral presentation

IN.PACT ± Stent: DEBELLUM

Randomized, 50 Patients / 122 lesions (SFA and BTK):

- **Significantly ↓LLL and ↑Primary Patency vs. PTA at 6 and 12 months in SFA**
- **Stents do not compromise DEB outcomes**

IN.PACT vs. PTA in the SFA: 1-year results (with and without Stent):

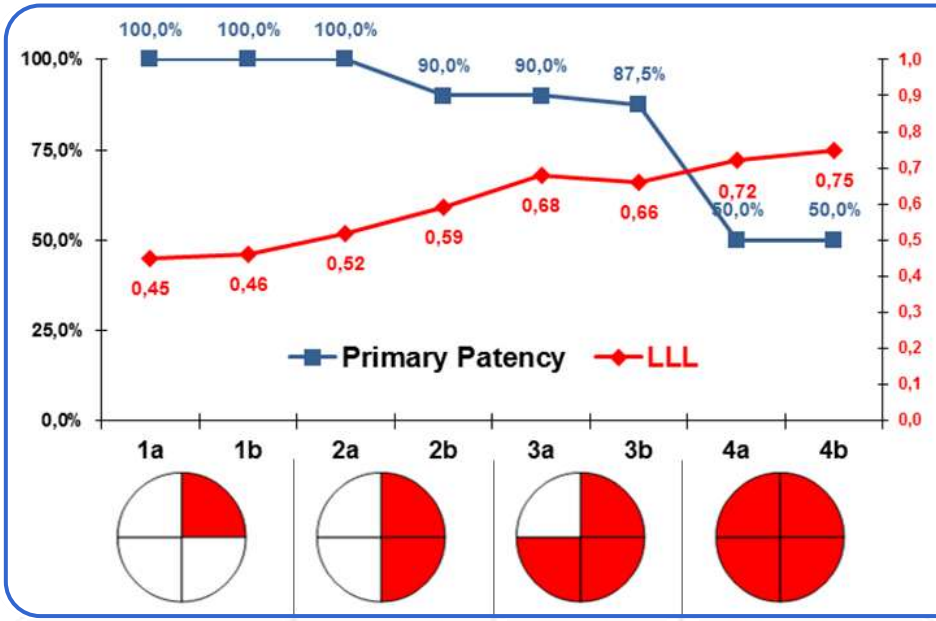


(Fanelli F et al. J Endovasc Ther. 2012)

Background: DCB and Calcium

GROUP	DIAMETER	LENGHT
1 a	0 – 90 °	< 3 cm
1 b		> 3 cm
2 a	90 – 180 °	< 3 cm
2 b		> 3 cm
3 a	180 – 270 °	< 3 cm
3 b		> 3 cm
4 a	270 – 360 °	< 3 cm
4 b		> 3 cm

- 60-patient registry
- SFA de-novo (~ 6 cm)
- CTO: 31.7%
- IN.PACT DCB with PTA pre-dil



- Calcium distribution and severity affect LLL and primary patency
- Ca++ represents a barrier to optimal drug absorption

Calcium distribution evaluation by CTA (circumf.) and DSA (longitud.)

(F.Fanelli LINC 2013)

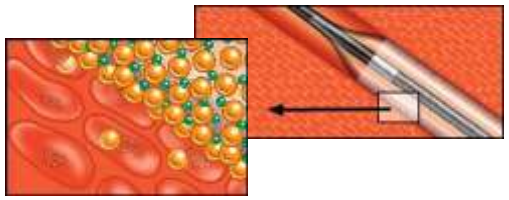
Method V

- DCA was performed with TurboHawk System.

TheSilverHawk™

- DEB used was Admiral In-Pact Paclitaxol-Eluting System. Sizing was 1:1 to Ref.Vessel Diam. and 10 mm longer than stenosis. Inflation time was at least 180 sec.

Admiral In-Pact Medtronic Invatec



- Drug: Paclitaxel (3µg /mm^2 ball. surface)
- Paclitaxel + Hydophilic Spacer: Urea

- IVUS was performed with Volcano technology (0,014" 20MHz) before and after DCA and DEB dilatation to evaluate DCA results and/or the presence of Flow limiting dissection.

DEB + Atherectomy in High Calcium

A.Cioppa LINC 2012

Singe center registry of IN.PACT Admiral + Atherectomy for SFA de-novo with severe calcifications

Angelo Cioppa MD

- **Primary Endpoint: 1y Prim. Patency**
- **30 patients**
  - **LLC / CLI = 6% / 94%**
  - **Diabetics = 60%**
  - **Mean lesion length = 115 ± 35 mm**
  - **Tot Occlusions = 13%**
  - **Calcium Score* 3 = 100%**
- **dist. Filter + TurboHawk + DEB**
  - **bail-out Stenting = 7%**

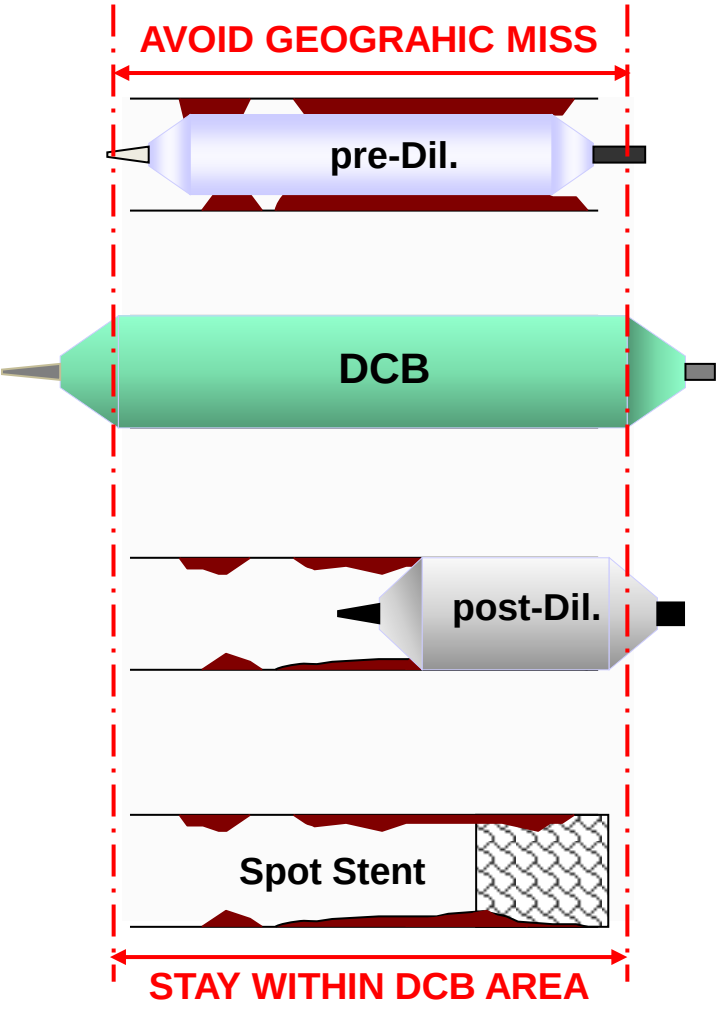
Initial, encouraging signals of performance in severely calcified SFA lesions with combined drug elution and debulking with nothing left behind

12-month FU

- **Primary Patency = 90%**
- **TLR = 10%**
- **Secondary Patency = 100%**

* 0= absence of calcium; 1= calcium on one side of lumen <1cm length; 2= calcium on both side <1cm length; 3=calcium on both side >1 cm length

DCB and Optimal PTA



1. **Pre-dilatation (CTOs, sub-occl. lesions, Ca++)**
   a. standard PTA Ø1 mm less than RVD
   b. Balloon length>lesion length or planned DCB length, whichever is longer
   c. inflation time ~ 2 minutes
   d. inflation pressure: < RBP as needed to reach full PTA balloon expansion

2. **DCB**
   a. DCB Ø: RVD = 1:1
   b. inflation time ≥ 3min
   c. inflation pressure: <RBP as required to reach full DCB expansion

3. **Post-Dilatation if residual stenosis >50% or flow limiting dissection**
   a. standard or high pressure PTA balloon Ø 1:1 to RVD
   b. short / focal length as necessary to treat the extent of residual stenosis or dissection
   c. inflation time ≥ 3 minutes

4. **Provisional Spot Stenting for persistent residual stenosis >50% or flow liniting dissections**
   1. Min. length as necessary to fully treat the residual stenosis or dissection

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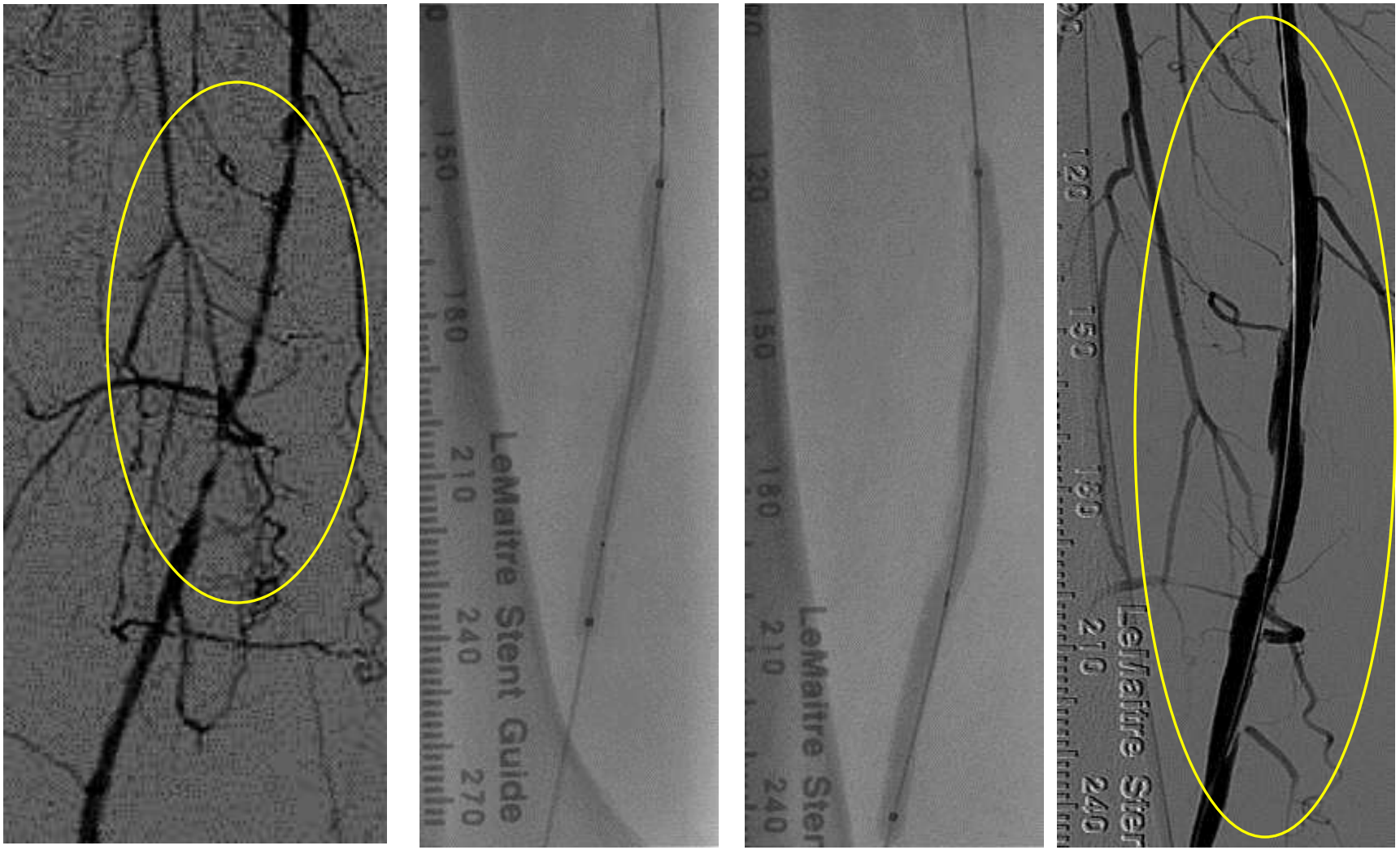
DCB and Optimal PTA:linear dissection



Pre-dilatation: Admiral 4.0-80 **DEB: In.Pact Admiral 5.0-120 mm**

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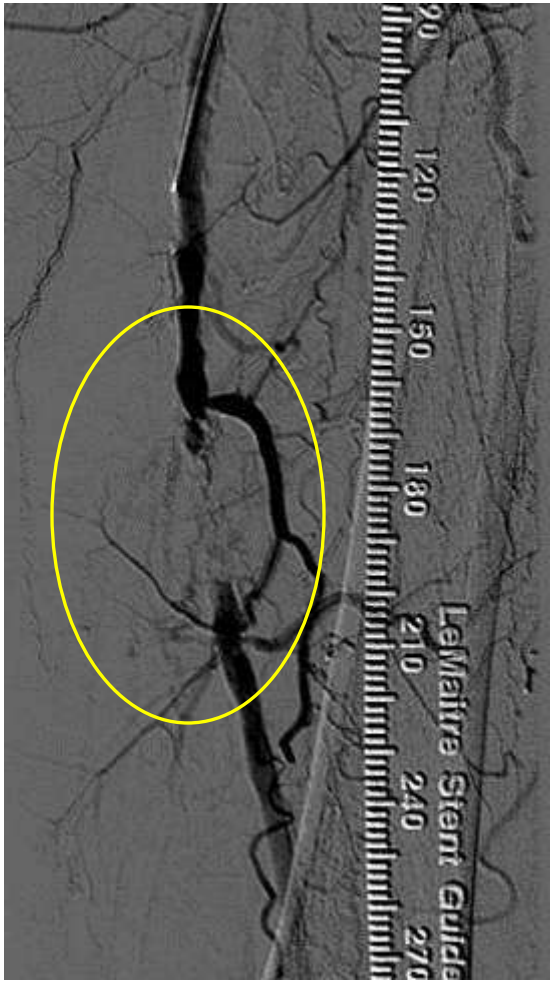
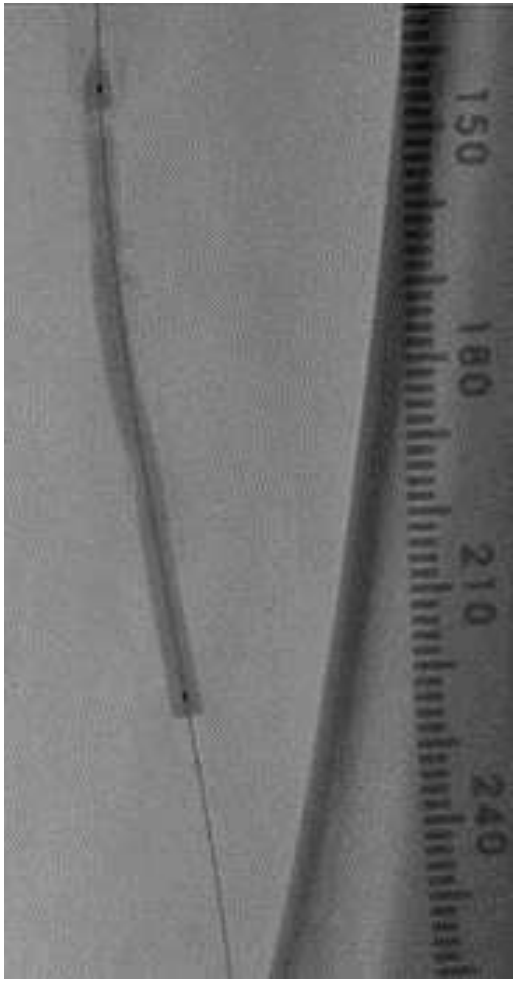
Predilation





Pre-Dilatation: Pacific 4.0-80 mm

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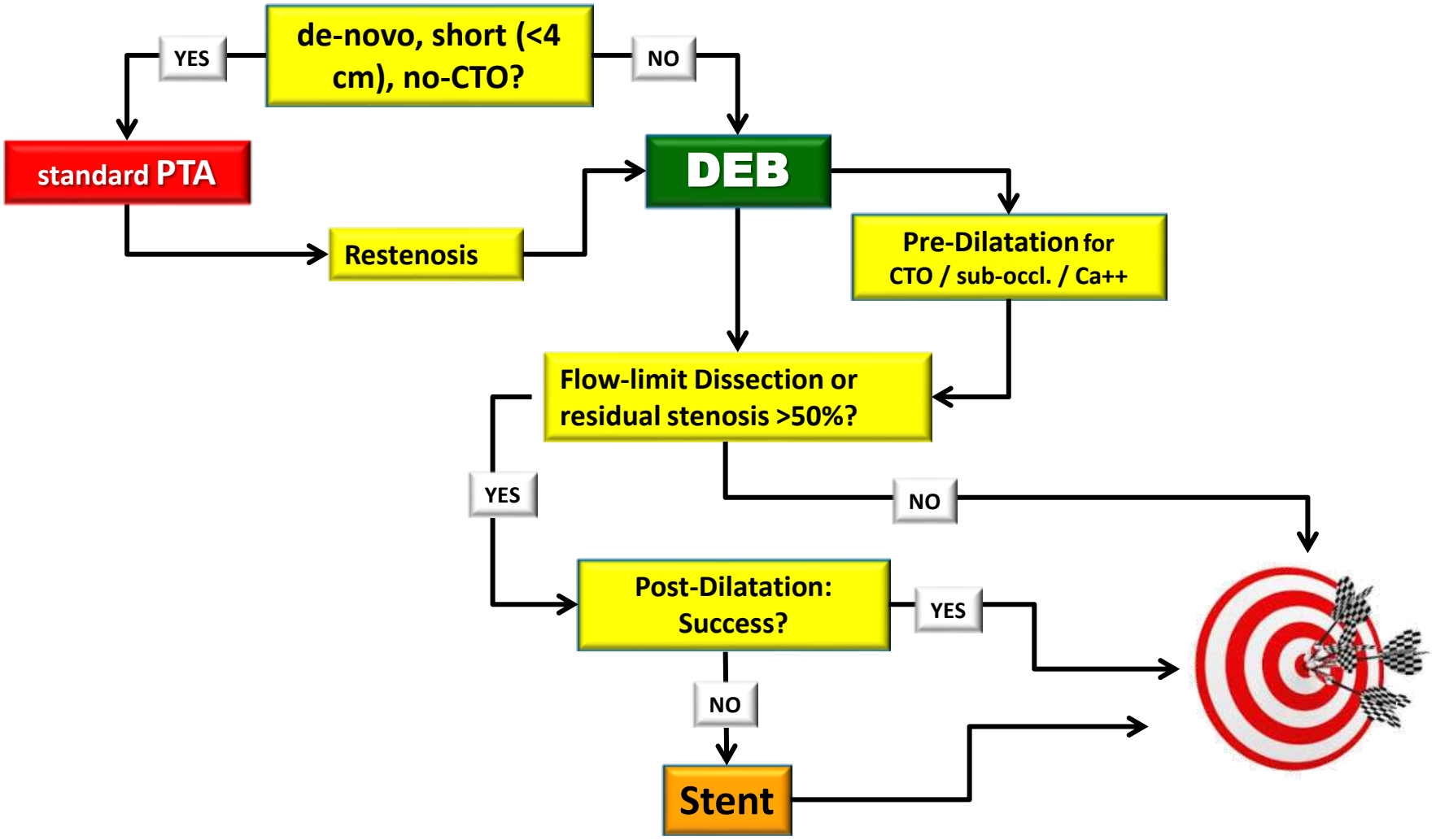
Predilation

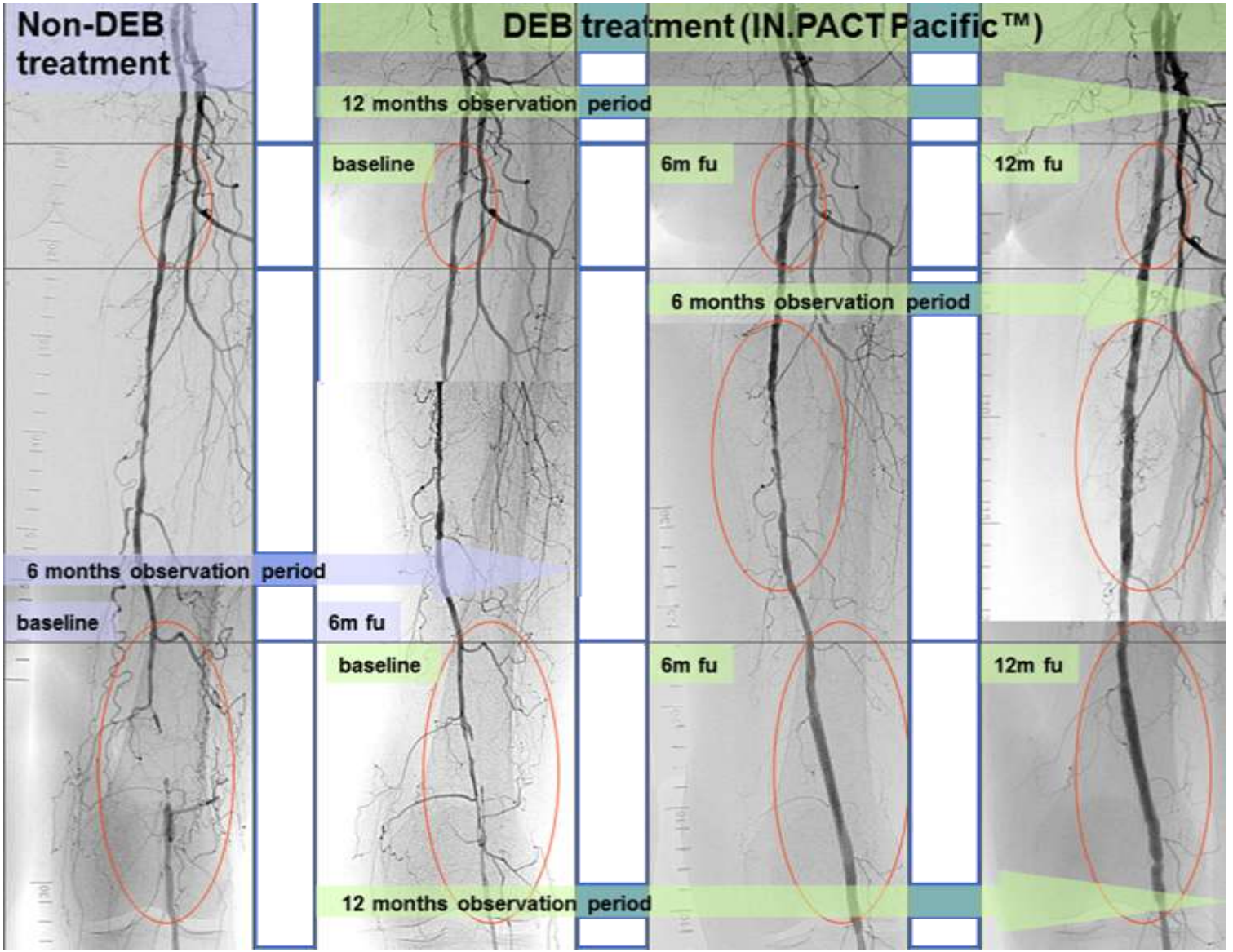
DEB: In.Pact Admiral 5.0-60 mm

Fem-pop treatment algorithm



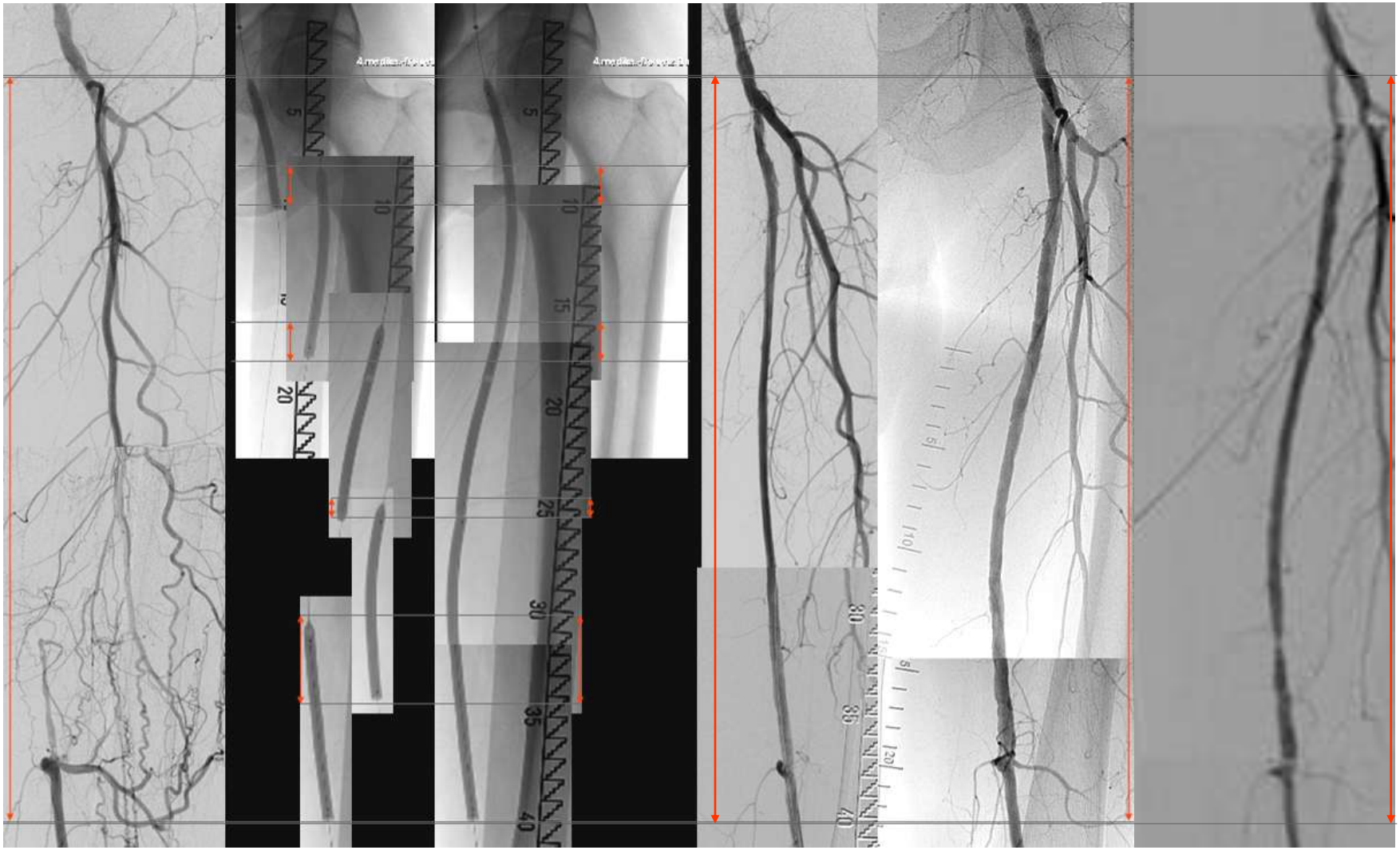
Case 1: PTA restenosis + de-novo treated by DEB

courtesy of M.Werk



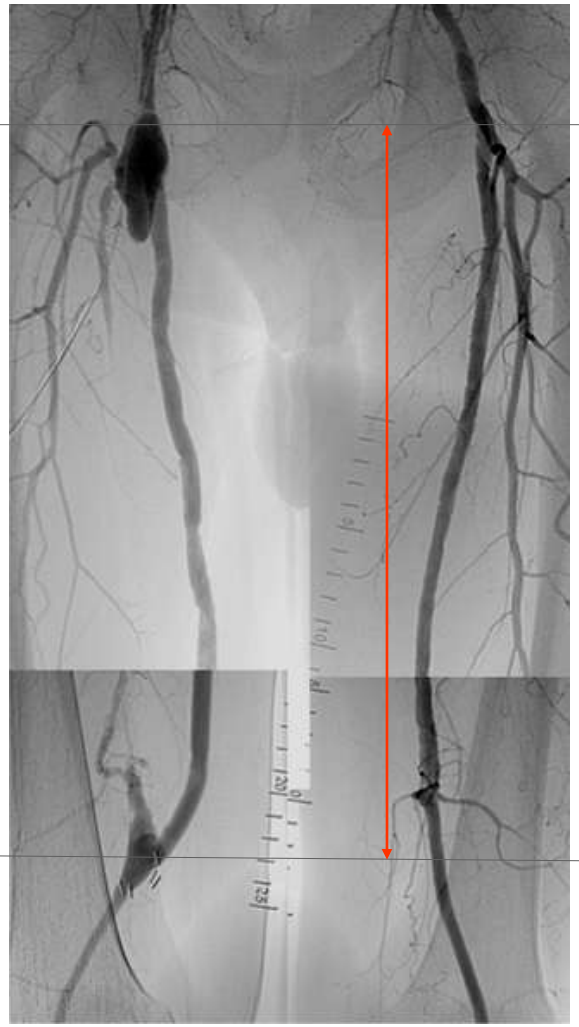
Case 2: Non-stented long occlusion

courtesy of M.Werk



Case 3: Non-stented long occlusion

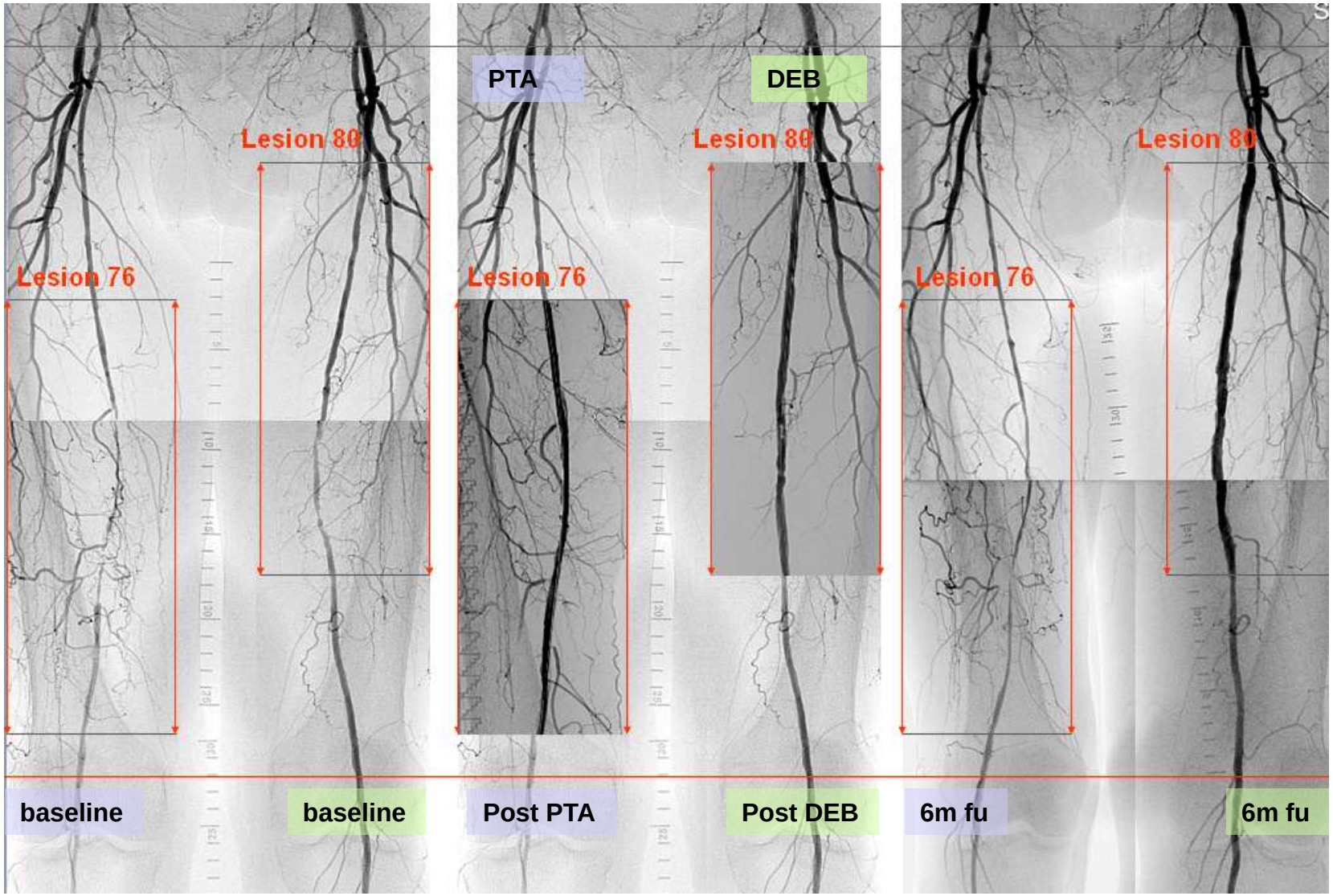
courtesy of M.Werk



baseline **6m fu** **24m fu**

Case 4: Bilateral SFA disease

courtesy of M.Werk



Summary

- Clinical Evidence Extent and Quality reassure on DEB Safety and Efficacy for femoro-popliteal indications
- DEBs are combination therapy devices
- Correct use will increase the efficacy
- The mentality of “Leaving nothing behind” is crucial to preserve future options
- IN.PACT DEB is a new quality standard in Clinical Evidence generation for PAD Therapies

IN.PACT SFA Pivotal RCT

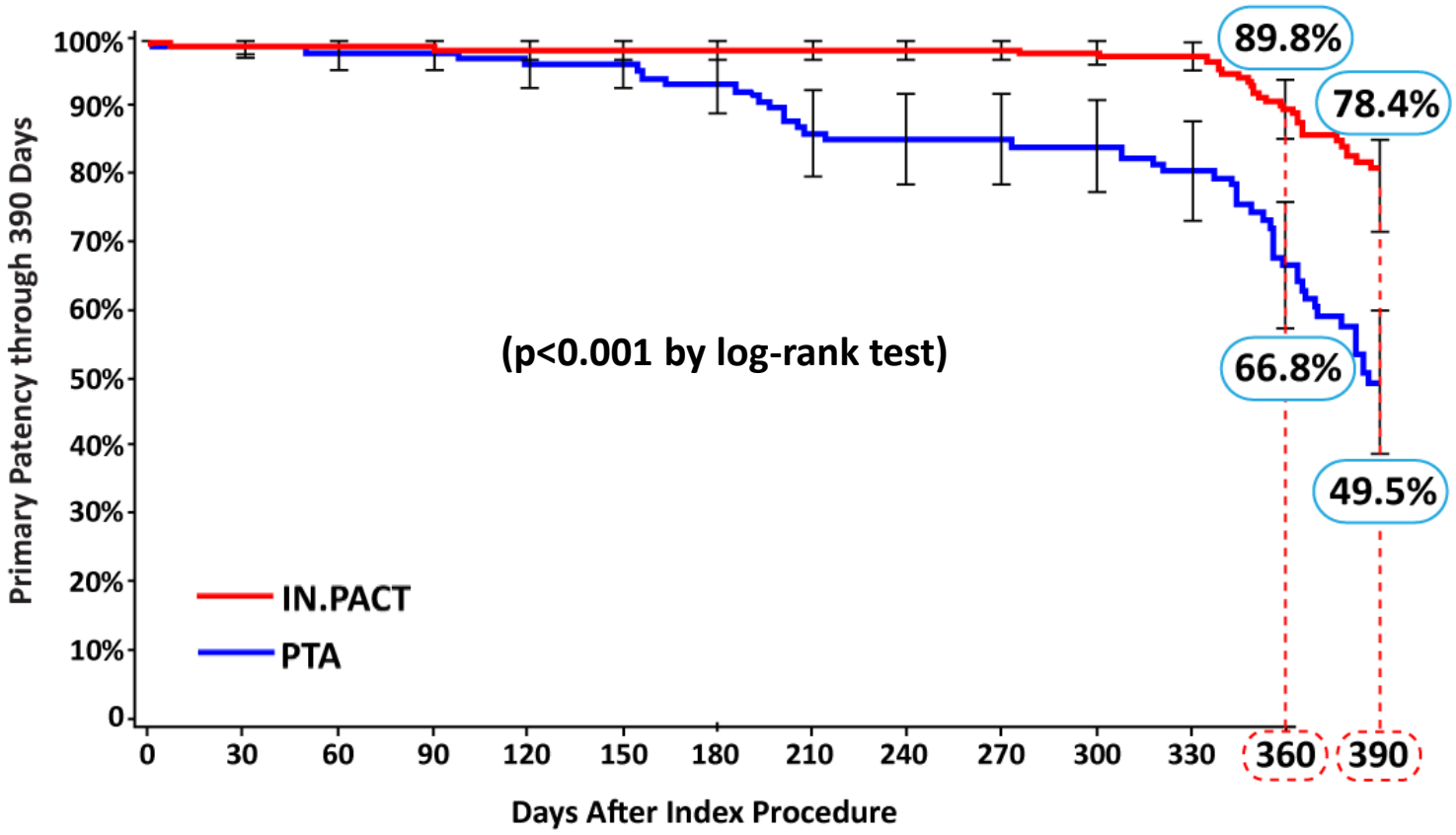
IN.PACT Admiral DCB vs. standard PTA
for the treatment of superficial femoral and proximal popliteal artery disease due to claudication and rest pain

- Prospective, multicenter EU and US, randomized (2:1), single blinded
- Independent and blinded Duplex Ultrasound Core Lab [1], Angiographic Core Lab [2], and Clinical Events Committee [3]
- Independent Data Safety Monitoring Board [3]
- External monitoring with 100% source data verification
- Subjects followed up to 5 years

Gunnar Tepe,
Charing Cross, London, UK, 4.5.2014,
on behalf of IN.PACT SFA Invesigators

IN.PACT SFA Pivotal RCT

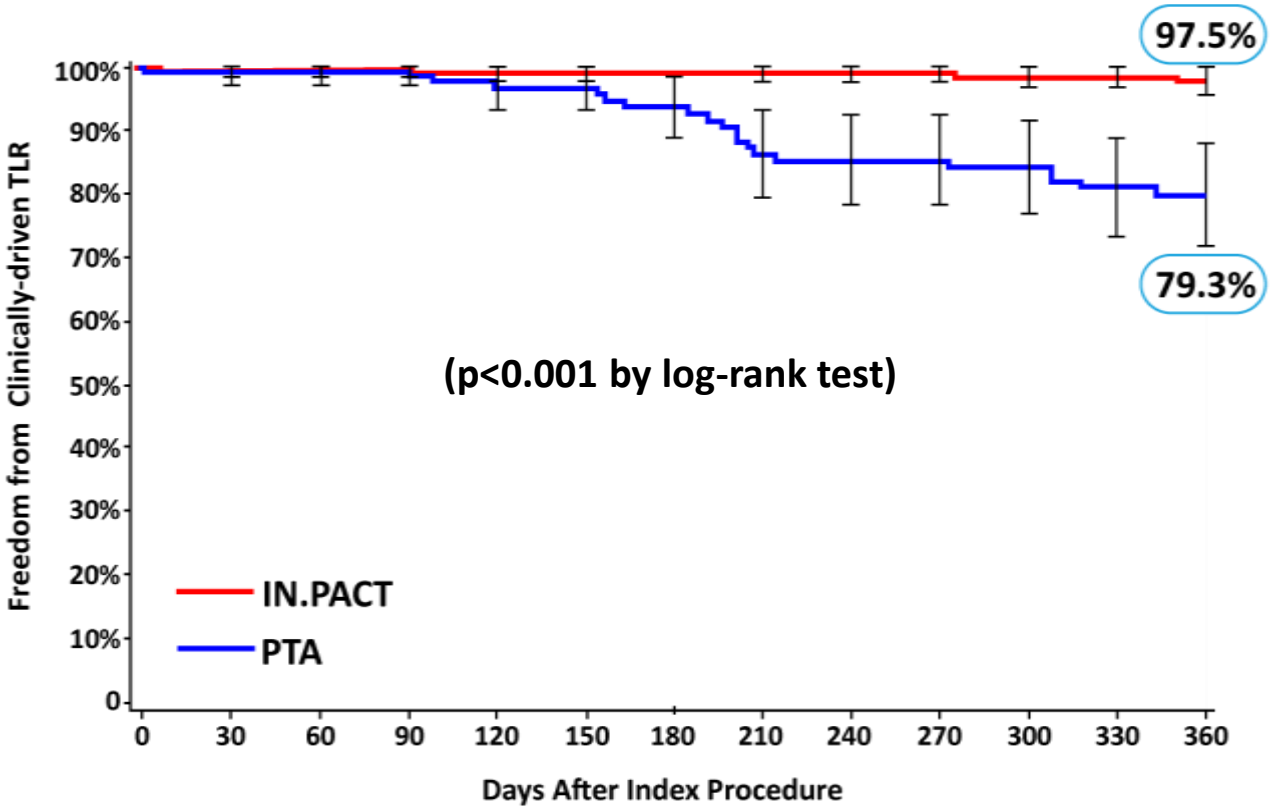
89.8% Primary Patency at 12-month



Gunnar Tepe,
Charing Cross, London, UK, 4.5.2014,
on behalf of IN.PACT SFA Invesigators

IN.PACT SFA Pivotal RCT

2.4% Clinically-driven TLR at 12-month



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IN.PACT in real world: IN.PACT GLOBAL

RC-2-3-4

- ☑ bilateral disease
- ☑ multiple lesions
- ☑ SFA and Popliteal
- ☑ TASC A
- ☑ TASC B
- ☑ TASC C
- ☑ TASC D
- ☑ Ca^{++}
- ☑ ISR

- 1500-patient, largest and rigorous all-comers single arm trial
- 67 centers WW
- Independent adjudication

1423 Patients enrolled as of March 28 (first 1-year results in Sep 2014)

Steering Committee: G.Tepe, M.Bosiers, P.Gaines, D. Dai-Do, A.Razuk, G. Ansel