Not Alone, Combination Might be Better, Which One Could Be Better: Atherectomy with DCB

Ravish Sachar MD, FACC

Physician-in-Chief

UNC – REX Heart and Vascular Service Line

University of North Carolina

Disclosures

Medtronic: SMAB

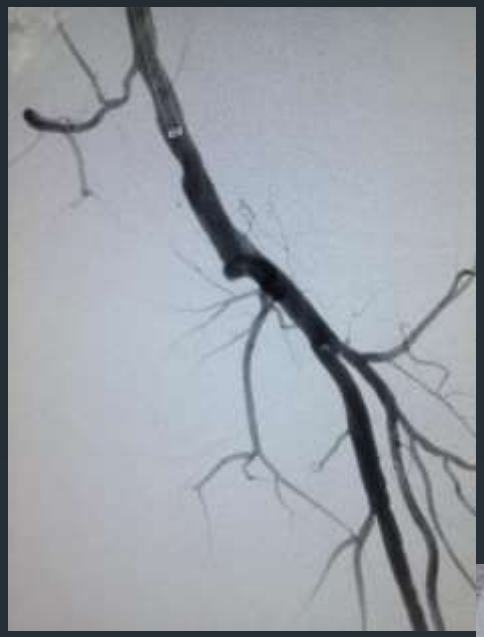
Spectranetics: Consultant

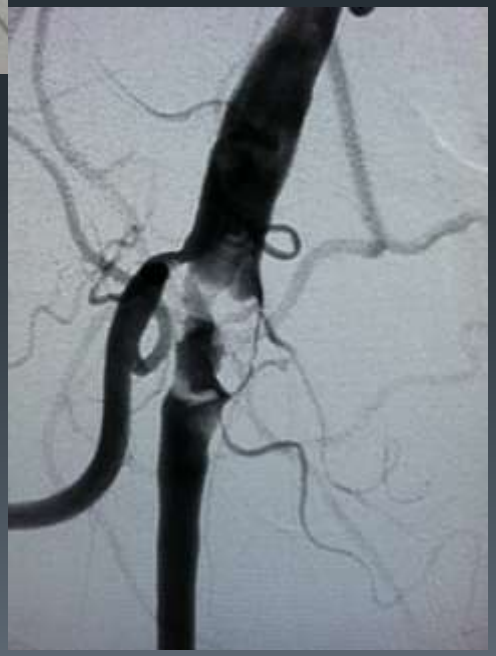
Boston Scientific: Consultant, DEB Steering Committee

Contego Medical: Share Holder

How should these lesions be treated in 2016?

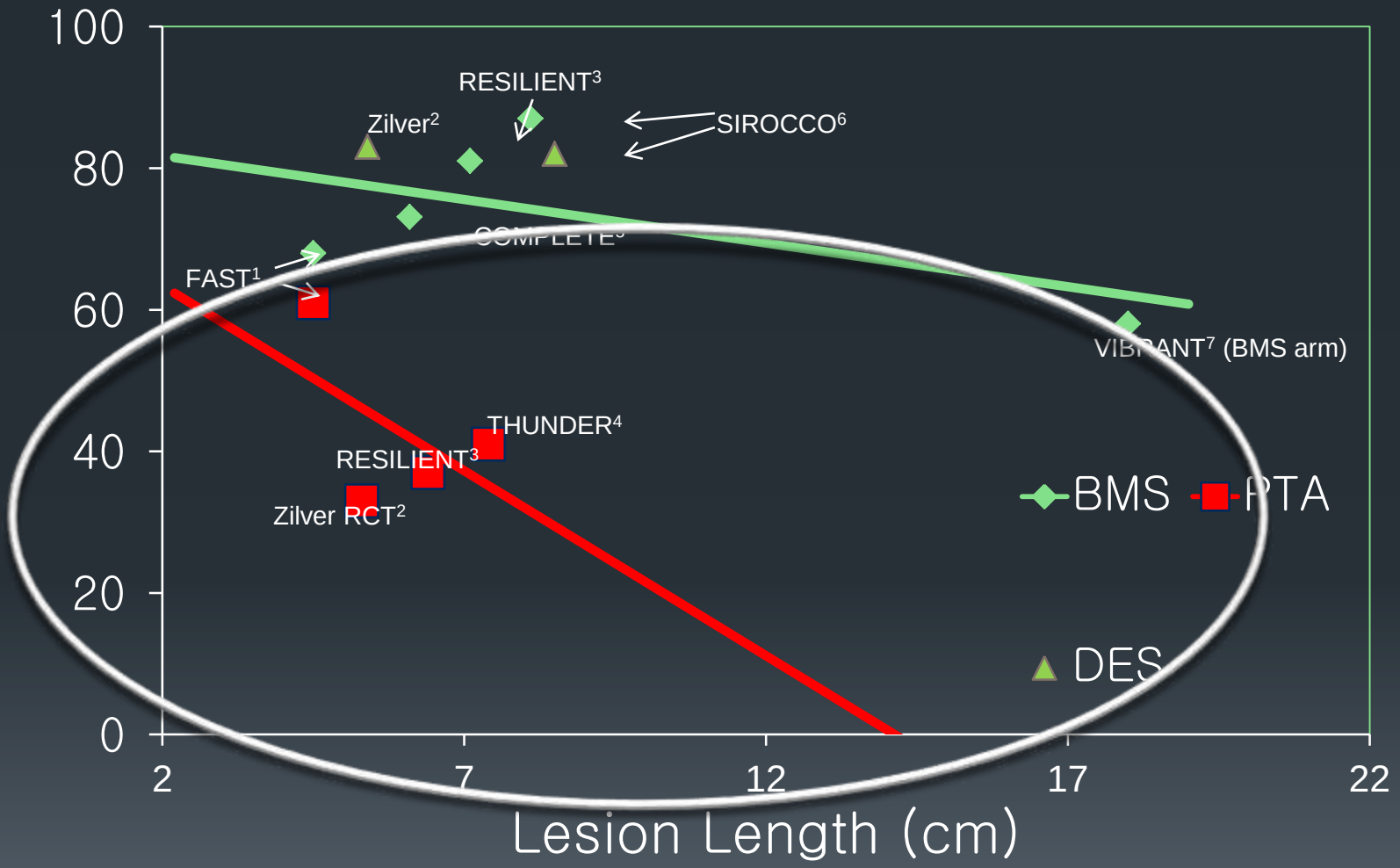
- PTA alone
- Bare Metal Stents
- Specialty Stents
- Atherectomy
- Drug Eluting Stents
- Drug Eluting Balloons
- Atherectomy + DEB
- Other Combination





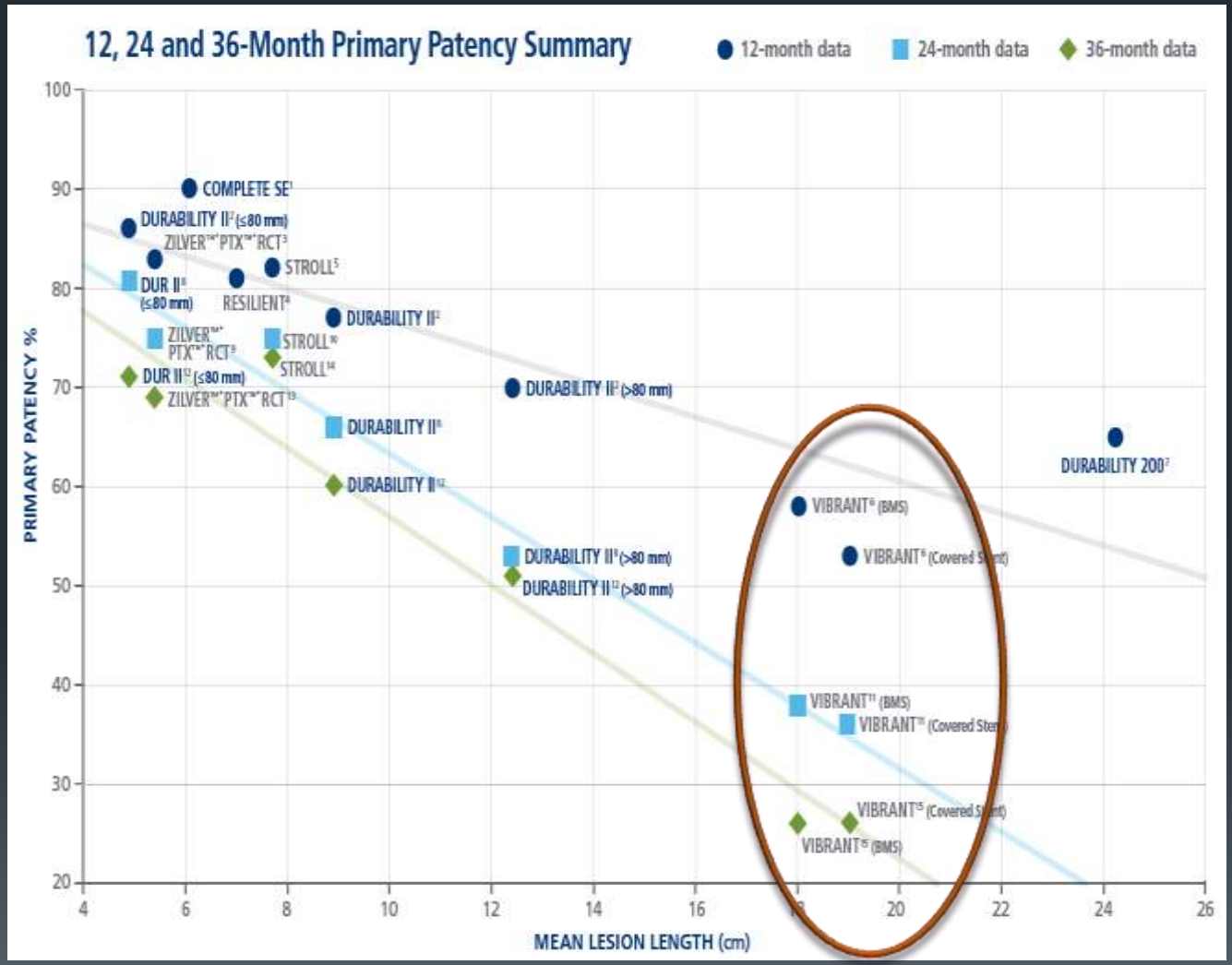
POA – SFA 12-Month Primary Patency

PTA, BMS, DES Sub-Analyses by Lesion Length



1. Krankenberg et al. Circulation. 2007; 116(3): 285-92
2. Dake et al. Circ Cardiovasc Interv. 2011:4:495-504)
3. Laird et al. Circ Cardiovasc Interv. 2010; 3: 267-276
4. Tepe et al. NEJM 2008:358:689-99
5. Laird, ISET 2012
6. Duda et al. J Endovasc Ther 2006; 13:701-710
7. Ansel, VIVA 2010

Nitinol Stents: Increased lesion length is an independent predictor of decreased patency.



[1]Freed MS, Manual of Interventional Cardiology, [2]Fanelli DEBELLUM, [3]Laird, CCI, June 2010, [4]SMART Control IFU, [5]Matusumura, DURABILITY IIJVS, July 2013, [6]Davaine, European Journal of Vascular and Endovascular Surgery 44 (2012)

Questions:

- Is Atherectomy the answer?
- Are DCBs the answer?
- Is Combination therapy better?
- Should Combination therapy always be used, or selectively used?

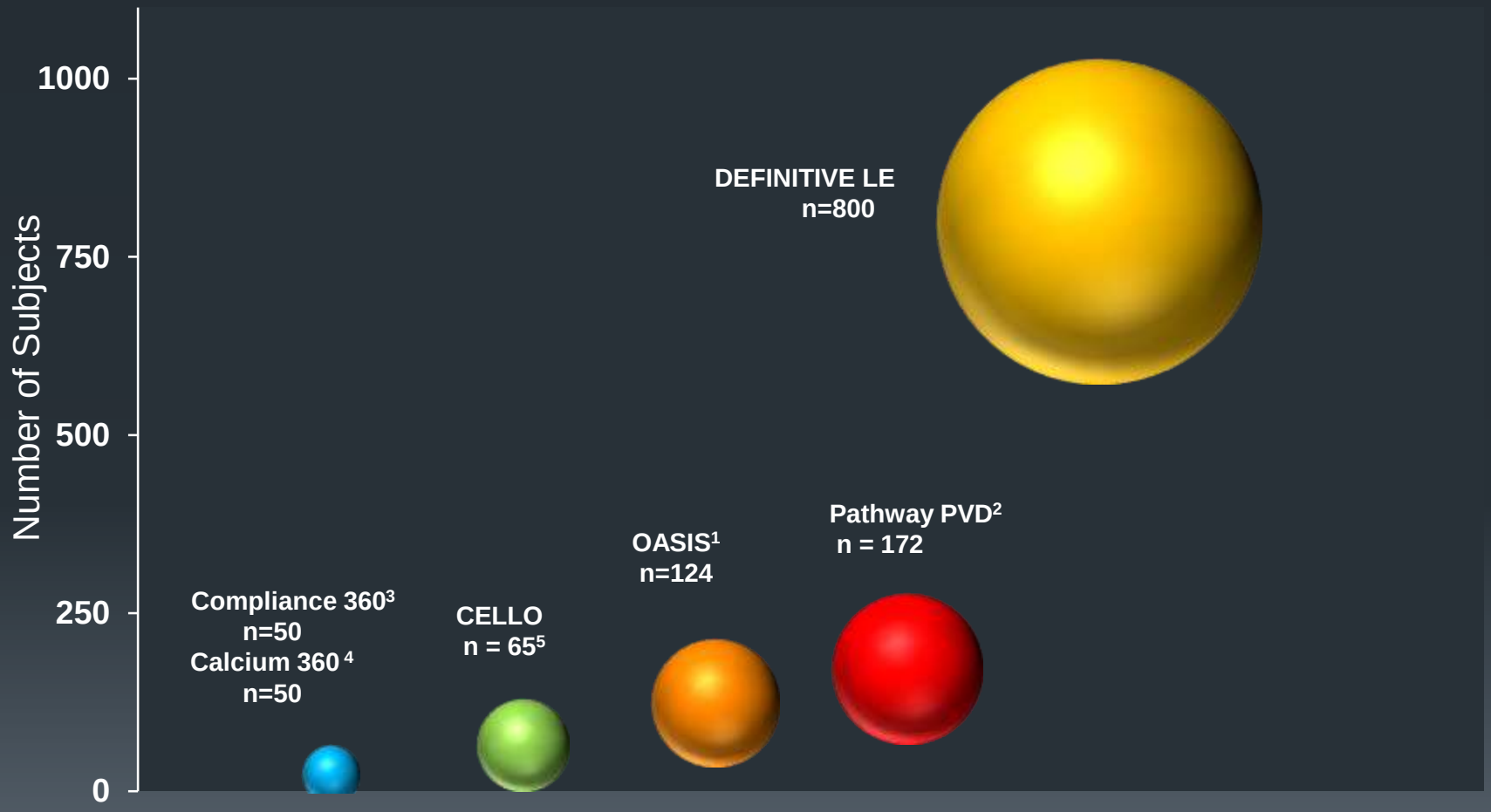
Answer:

We think we know, but we can’t prove it yet

Benefits of Atherectomy

- Treatment of no stent zones
- Treatment of severe calcification
- Prepares the vessel for combination therapy: DCB, or stent placement
- Protects side vessel branches by minimizing plaque shift
- Maintains treatment options
- Increase drug delivery in calcified lesions?

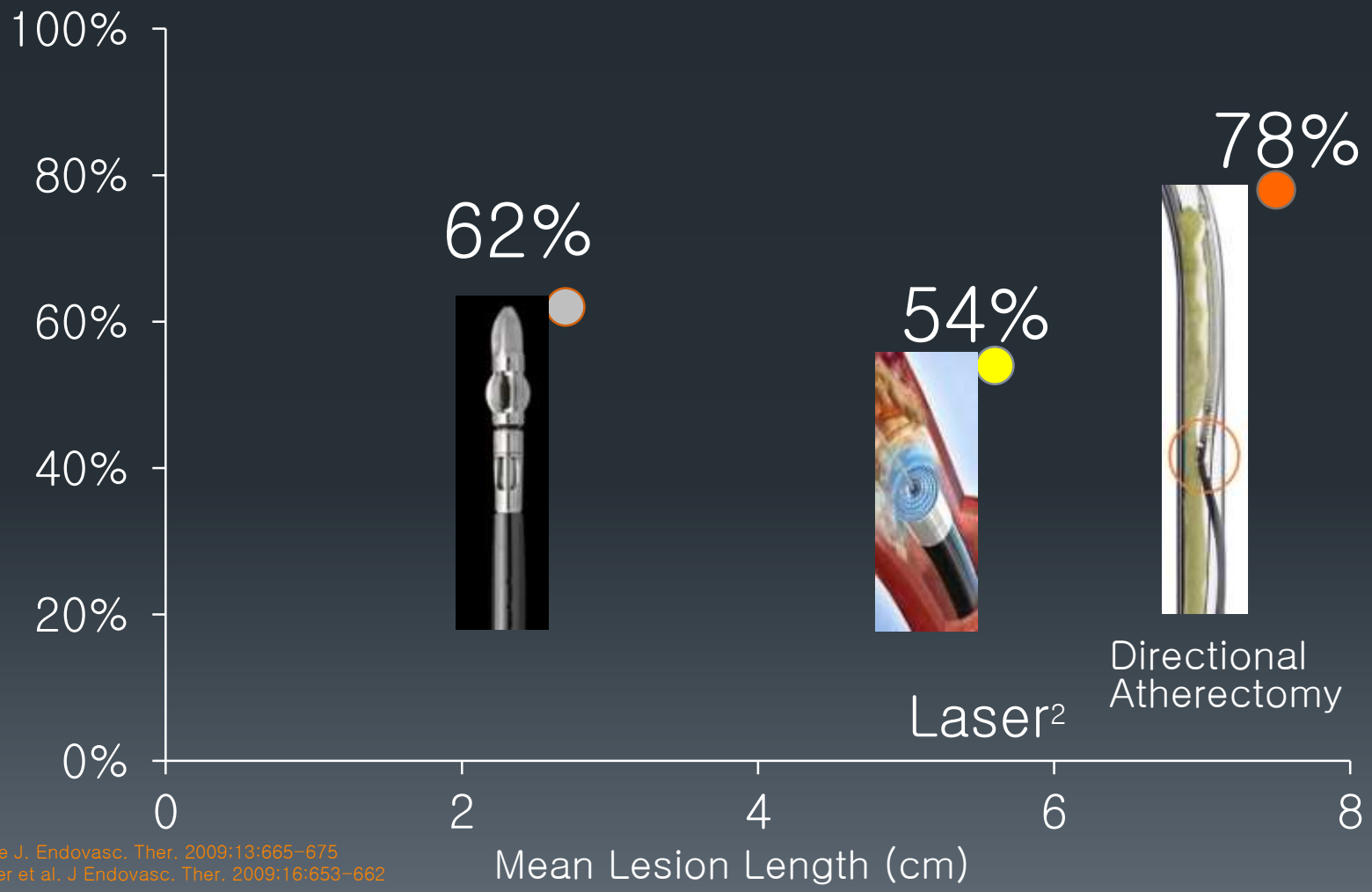
Atherectomy Trials in Fem-Pop Disease: Wide variation in sample size



1. Safian et al. Cath & Cardiovasc Interv 73:406:412
2. Zeller et al. J Endovasc Ther 2009;16:653-662
3. Dattilo, TCT 2011
4. Shammas et al. J Endovasc Ther 2012;19:480-488
5. Dave et al. J Endovasc Ther 2009;16:665-675

Atherectomy Trials

Core-Lab Adjudicated 12-mo. Patency



1. Dave J. Endovasc. Ther. 2009;13:665–675
2. Zeller et al. J Endovasc. Ther. 2009;16:653–662

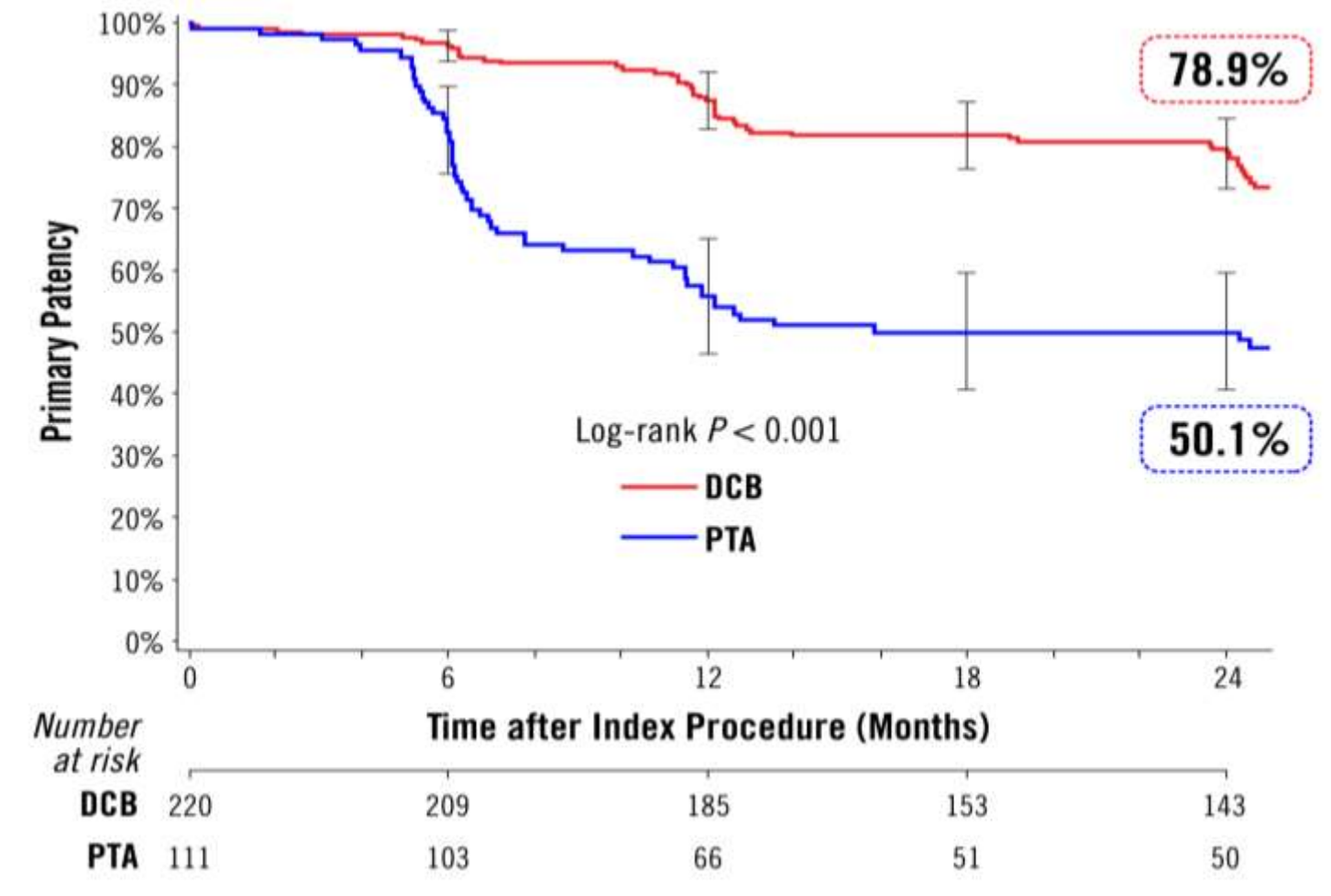
Directional Atherectomy: Challenging Subsets in Definitive LE

	Patency (PSVR ≤ 2.4)	Lesion Length (cm)
All Claudicants (n= 743)	**78%**	**7.5**
Lesion type		
Stenoses (n=611 lesions)	81%	6.7
Occlusions (n=128 lesions)	64%	11.1

Heavily Calcified Lesions Not Included

SUSTAINED PERFORMANCE BENEFIT OF IN.PACT™ ADMIRAL™ DCB OVER PTA THROUGH TWO YEARS

IN.PACT SFA TRIAL EFFICACY OUTCOMES THROUGH 2 YEARS



1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 24 months (adjudicated by a Clinical Events Committee blinded to the assigned treatment).
2. Number at risk represents the number of evaluable subjects at the beginning of the 30-day window prior to each follow-up interval.

In.Pact Long Lesion Subset

- 150 Patients
- Mean lesion length in this group was 26.4 cm.
- Primary patency at 360 days was 91.1%
- Provisional stenting was more common (>40%) in patients with lesion lengths greater than 25 cm.
- In those who did not require provisional stenting, the primary patency rate at 360 days was 92.5%.

CTO Subset n=127
Lesion/Procedural Characteristics

Lesion Characteristics	N = 128 Lesions
Lesion Type: **% (n)** De novo Restenotic (non-stented) In-stent Restenosis	 92.2% (118/128) 7.8% (10/128) 0.0% (0/128)
Lesion Length (cm ± SD)	22.90 ± 9.75
Occluded Lesion Length (cm ± SD)	11.97 ± 8.11
Calcification % (n)	71.2% (89/125)
RVD (mm ± SD)	5.056 ± 0.657
Diameter Stenosis (% ± SD)	100.0 ± 0.0
Dissections: 0 A-C D-F	 32.8% (42/128) 43.8% (56/128) 23.4% (30/128)

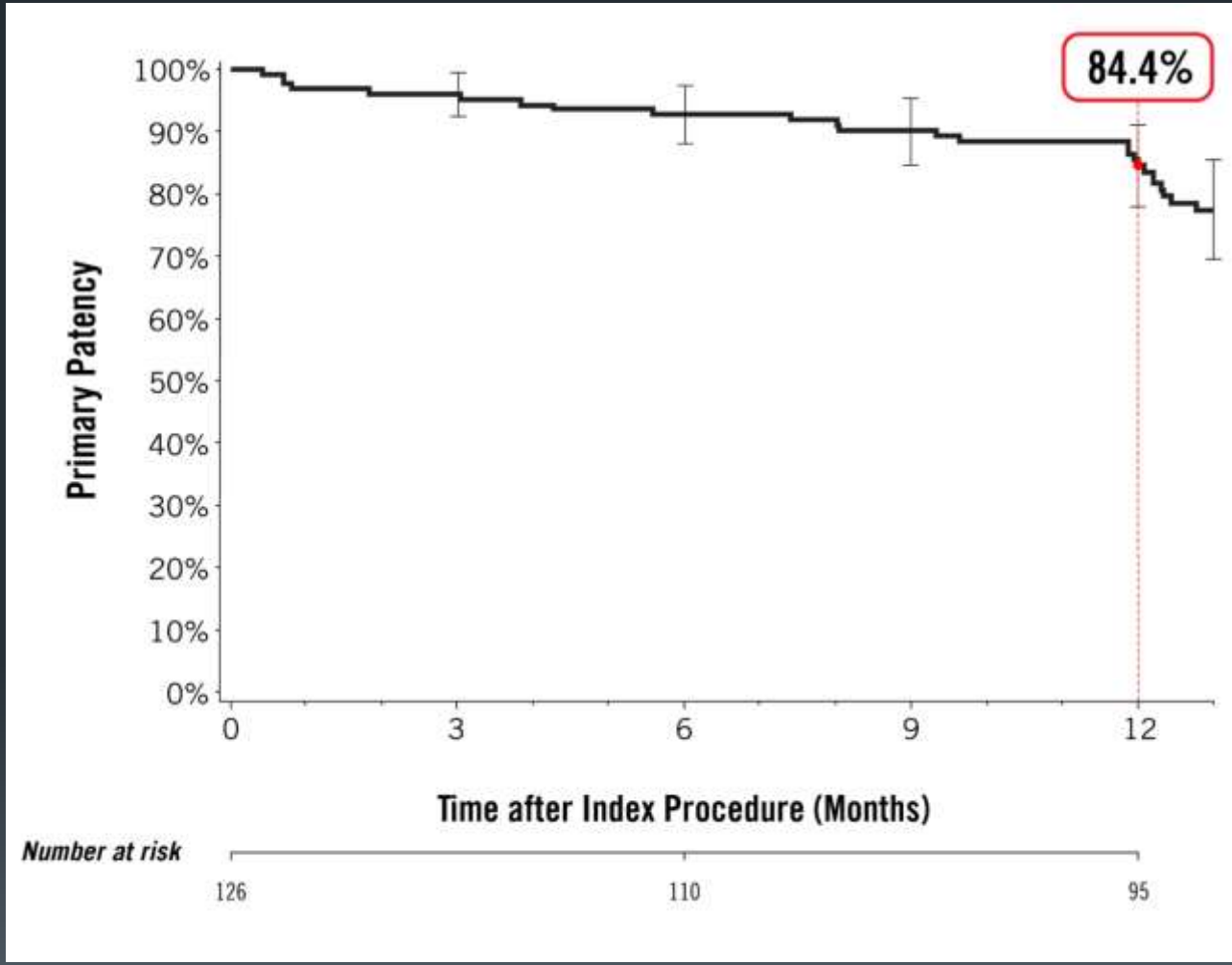
Procedural Characteristics	N = 126 Subjects N = 128 Lesions
Device Success[1] % (n)	99.3% (283/285)
Procedure Success[2] % (n)	100% (125/125)
Clinical Success[3] % (n)	99.2% (124/125)
Pre-dilatation % (n) Post-dilatation % (n)	94.4% (119/126) 50.0% (63/126)
Provisional Stent % (n)	46.8% (59/126)

1. Device success defined as successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP.

2. Procedure success defined as residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects) by core lab (if core lab was not available then the site-reported estimate was used).

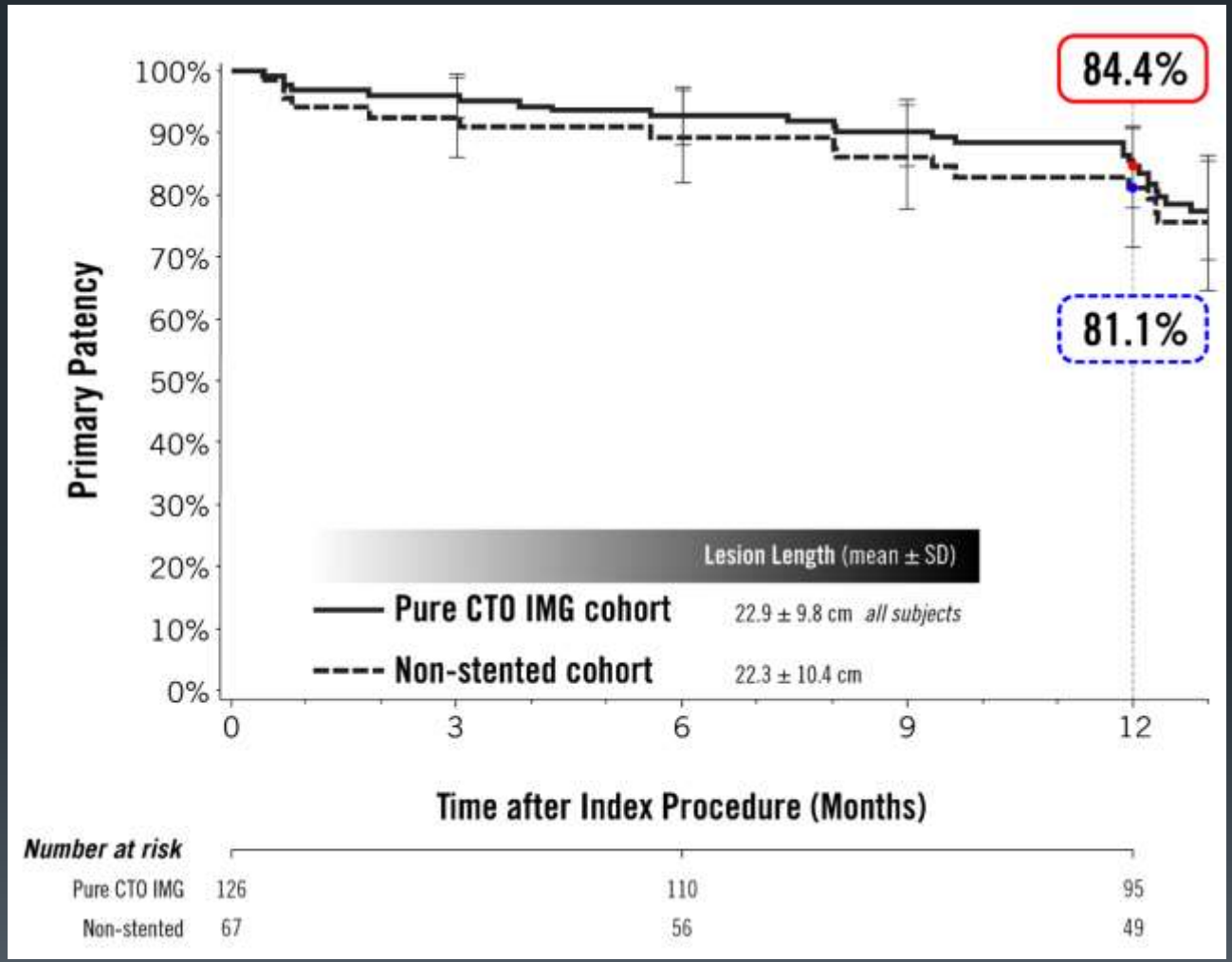
3. Clinical success defined as procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge.

CTO subset:
Primary Patency[1] Results through 1 Year



1. *Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 12 months (adjudicated by a Clinical Events Committee)*
2. *Number at risk represents the number of evaluable subjects at the beginning of the 30-day window and prior to each follow-up interval*

CTO Subset: Primary Patency[1] in Non-Stented Subgroup through 1 Year



1. *Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 12 months (adjudicated by a Clinical Events Committee blinded to the assigned treatment)*
2. *Number at risk represents the number of evaluable subjects at the beginning of the 30-day window and prior to each follow-up interval*

Illuminate 12 month Data

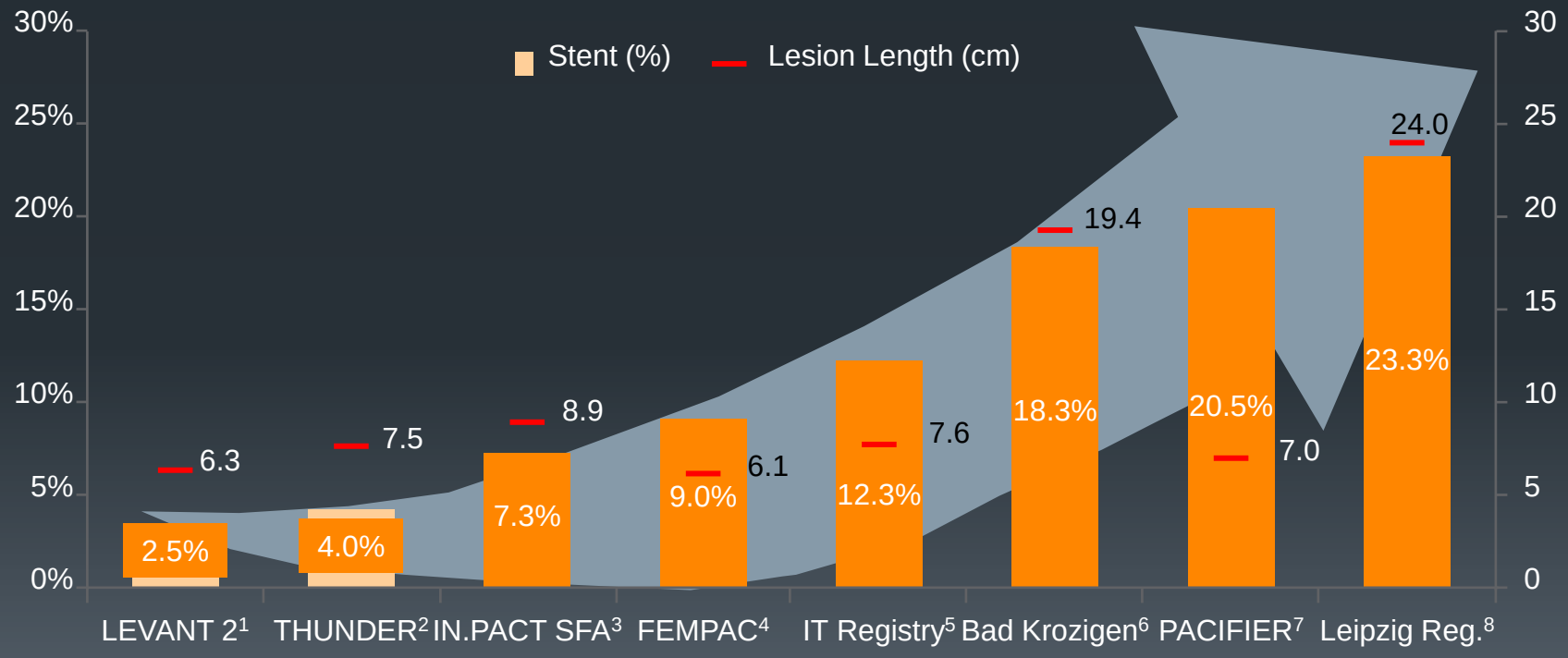
- Mean Lesion Length 7.3 cm
- 360 day patency 88.5%
- 365 day patency 84.7%
- Provisional Stent 12.6%

Are DCB's the Final Answer???

DCB and Provisional Stenting

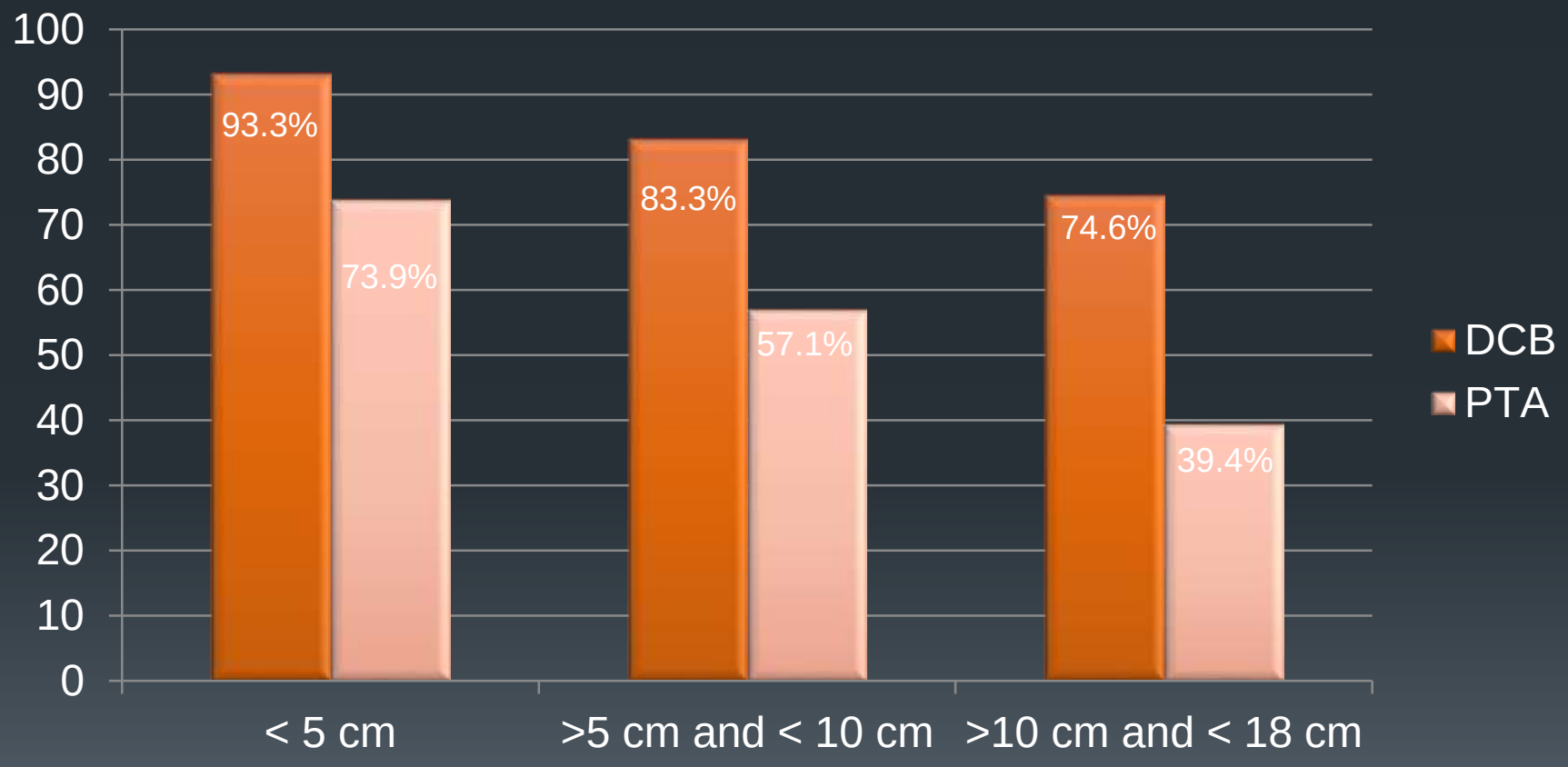
Scaffolds still needed, likely at rates proportional to lesion complexity

Provisional stent rates in DCB trials trend with lesion length



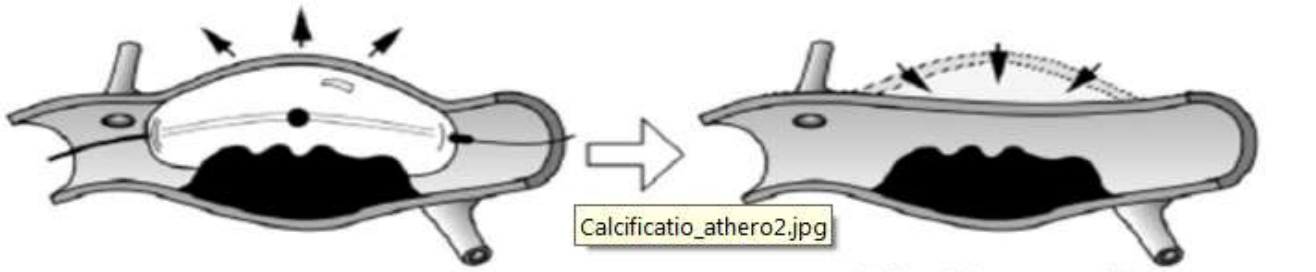
1. Rosenfield K TCT 2013; 2. Tepe G et al. *N Engl J Med*. 2008; 3. Tepe CX 2014; 4. Werk M et al. *Circulation*. 2008; 5. Micari A et al. *J Am Coll Cardiol Intv*. 2012; 6. Zeller T CX 2013 oral presentation; 7. Werk et al. *Circ Cardiovasc Interv*. 2012; 8. Schmidt A LINC 2013 oral presentation

IN.PACT SFA 12 Month Subgroup Analysis Lesion Length



Calcium Limits Vessel Expansion

Significant difference in vessel compliance leads to overstretch in non-diseased tissue causing dissections, recoil, excessive injury, and poor outcomes



Fully inflated balloon

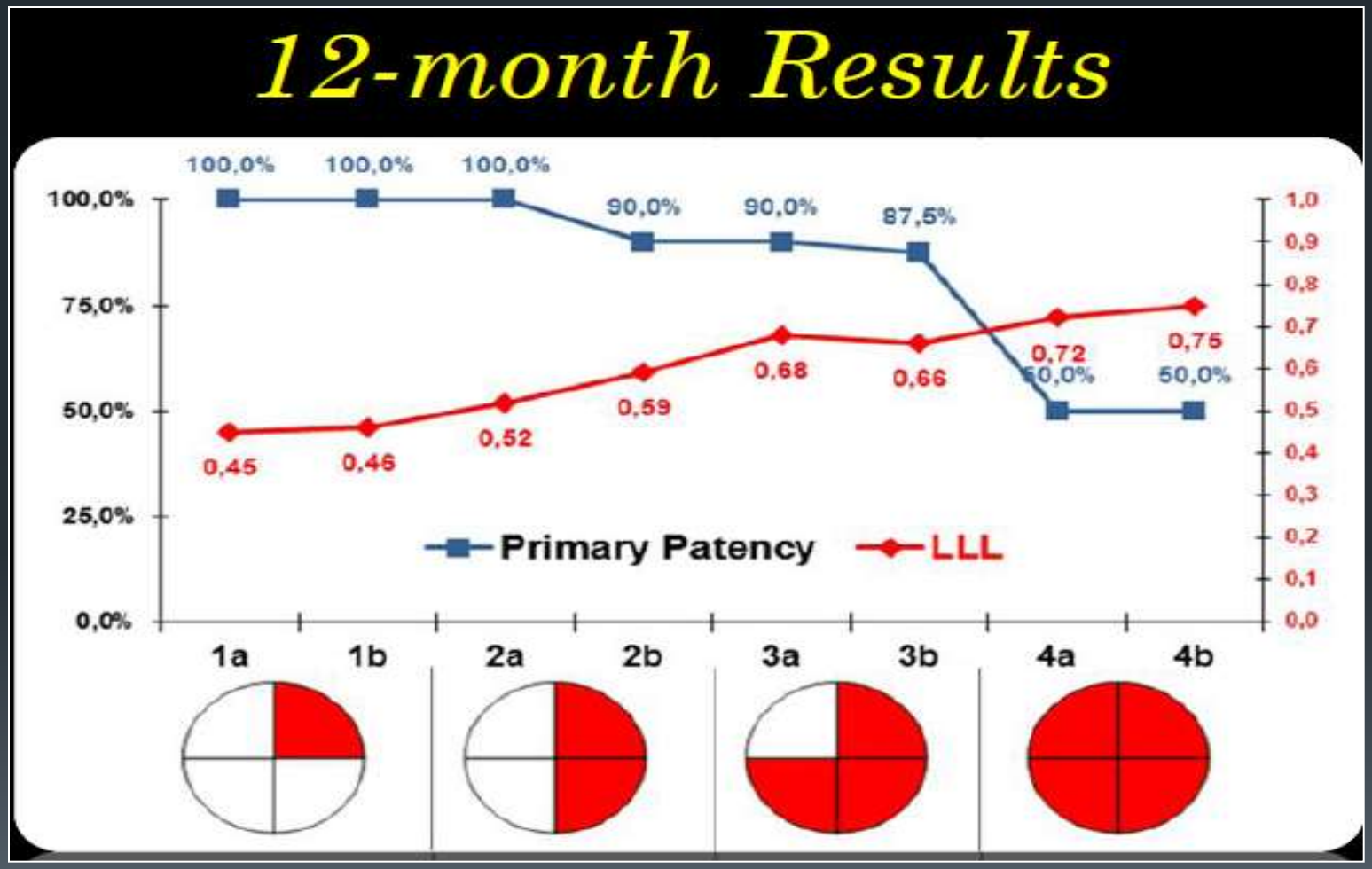
Elastic recoil
Residual, high-grade stenosis

Figure 12.1. Elastic Recoil After PTCA of Calcified Lesions

Rather than cracking the hard, calcified atheroma, PTCA causes stretching of the contralateral plaque-free wall segment and ineffective dilatation.

Freed MS, Safian RD; Manual of Interventional Cardiology, Ch. 12, 245-254

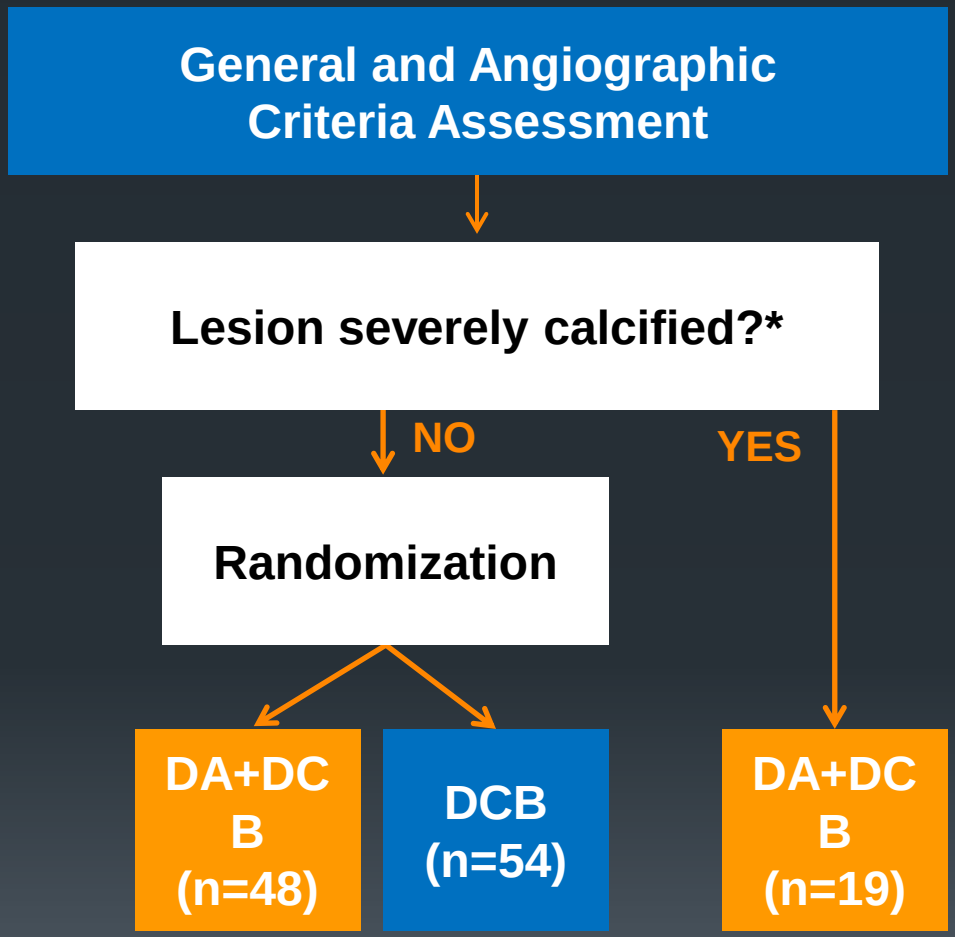
Calcium May Limit Drug Effect



1. Fanelli J Endovas Ther 2012;19:571-580. 2. Fanelli et al. Cardiovasc Intervent Radiol (2014) 37:898-907)

Is Combination Therapy the Right Answer?

Definitive AR: Study Design



Inclusion Criteria

- RCC Score of 2, 3 or 4
- ≥70% stenosis, restenosis or occlusion in the SFA and/or popliteal artery
- Target lesion(s) length is 7-15 cm
- Target vessel diameter is ≥ 4 mm and ≤ 7 mm

Exclusion Criteria

- In-stent restenosis
- Aneurysmal target vessel
- 2 or more lesions that require treatment in the target limb

*Defined as: dense circumferential calcification extending > 5 cm

Study Devices: *DCB was NOT IN.PACT Admiral*

Covidien's SilverHawk™ & TurboHawk™ peripheral plaque excision systems

Bayer HealthCare's Peripheral Paclitaxel-coated angioplasty catheter with Paccocath® Technology

Atherectomy + DEB: Higher Acute Technical Success

Defined as ≤ 30% residual stenosis following the protocol-defined treatment at the target lesion as determined by the Angiographic Core Laboratory.

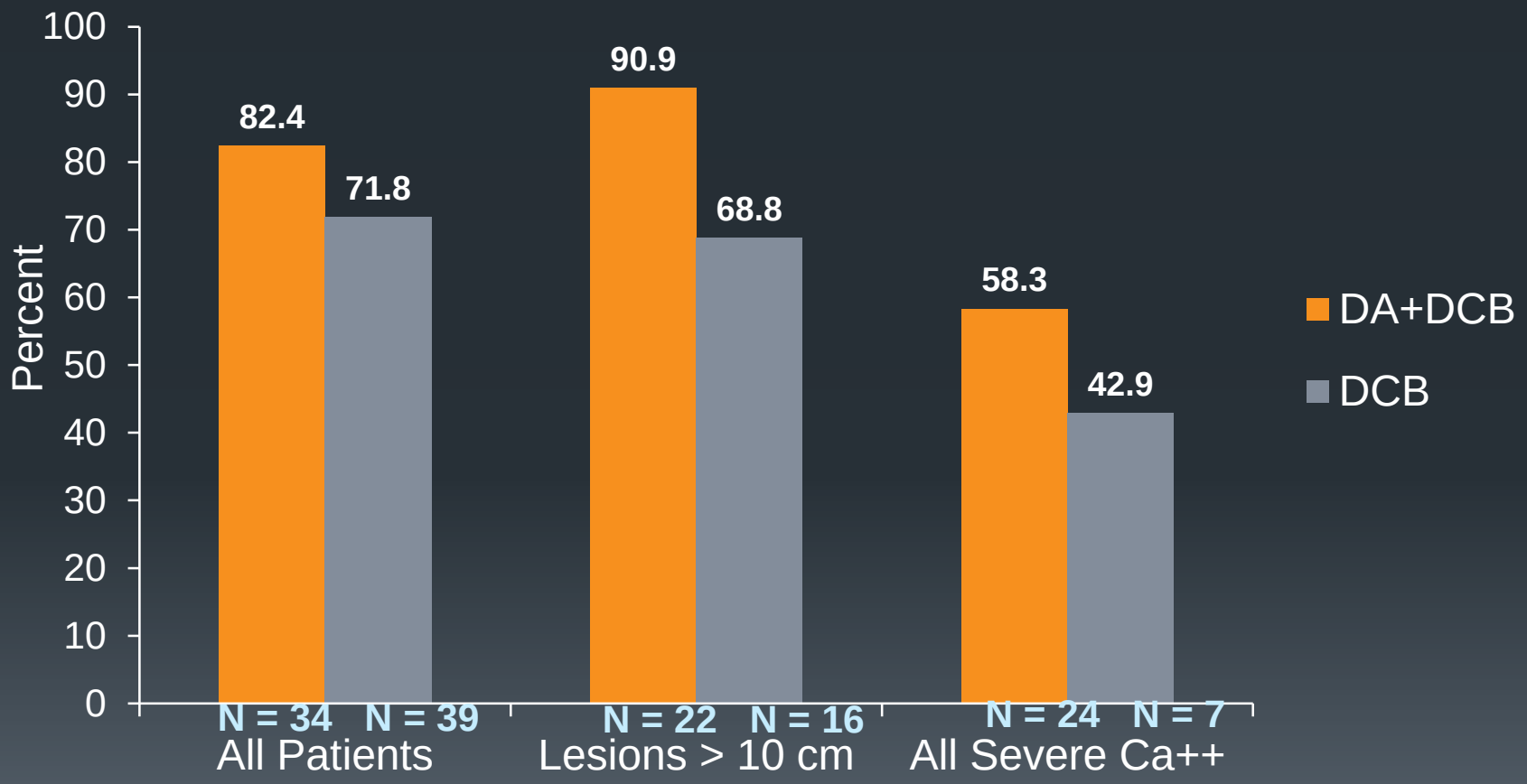
	DAART Severe Ca^{++}	DAART	DCB	P Value (DAART vs. DCB)
Technical Success	84.2%	89.6%	64.2%	0.004

Atherectomy + DEB: Lower need for post PTA and Bail Out Stenting

	DAART Severe Ca^{++}	DAART	DCB	P Value (DAART vs. DCB)
Adjunctive Therapy				
PTA (post-dil)	0	6.3% (3/48)	33.3% (18/54)	0.0011
Bail-out Stent	5.3% (1/19)	0	3.7% (2/54)	0.4968

Angiographic Patency at 12 Months

Angiographic Patency shows similar pattern

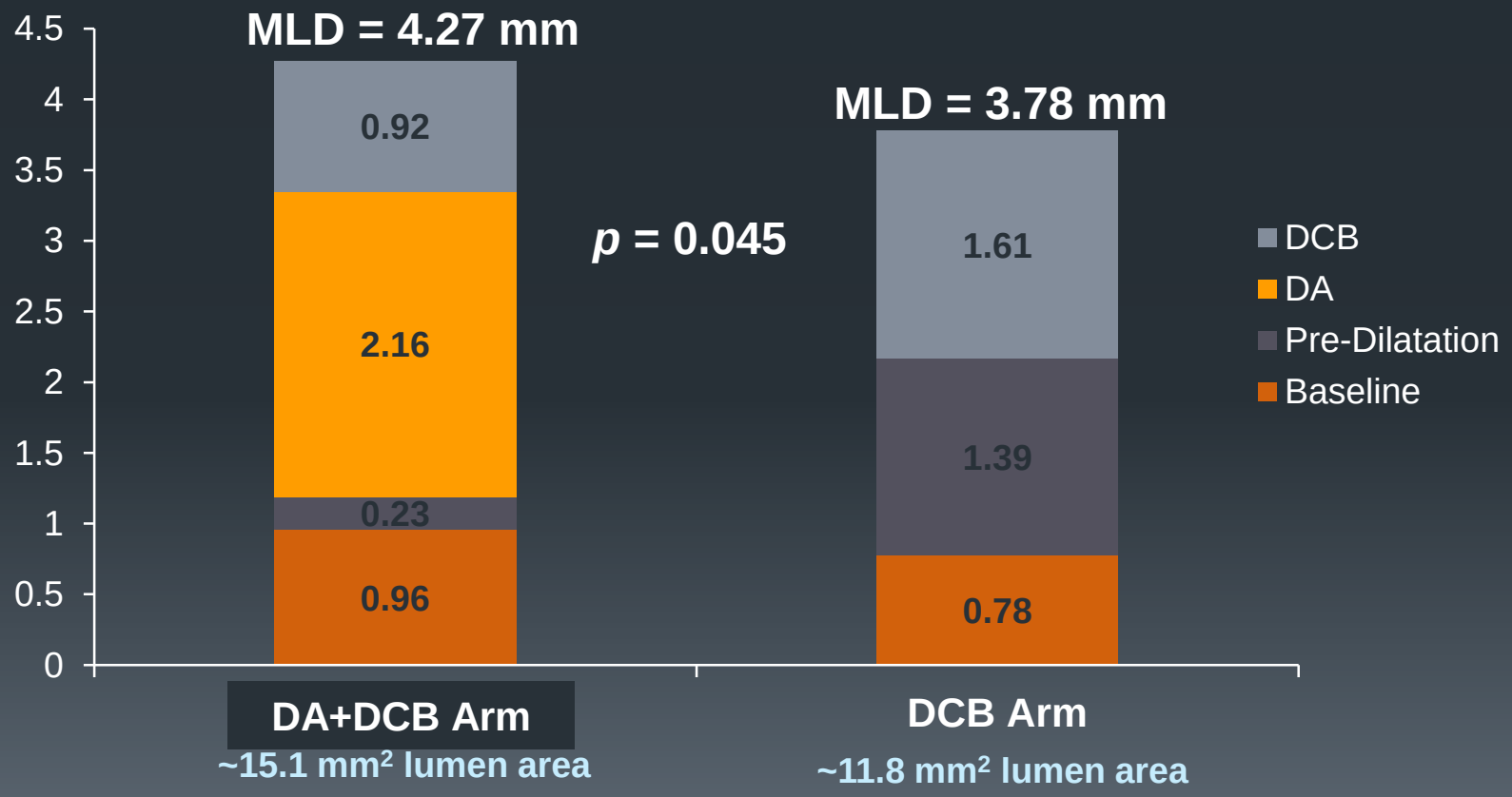


Per Core Lab Assessment. “All Severe Ca++ “ group includes all patients with severe calcium (including randomized and non-randomized. Results for all patients who returned for angiographic follow-up.

What is the Impact of Lumen Gain with DA+DCB?

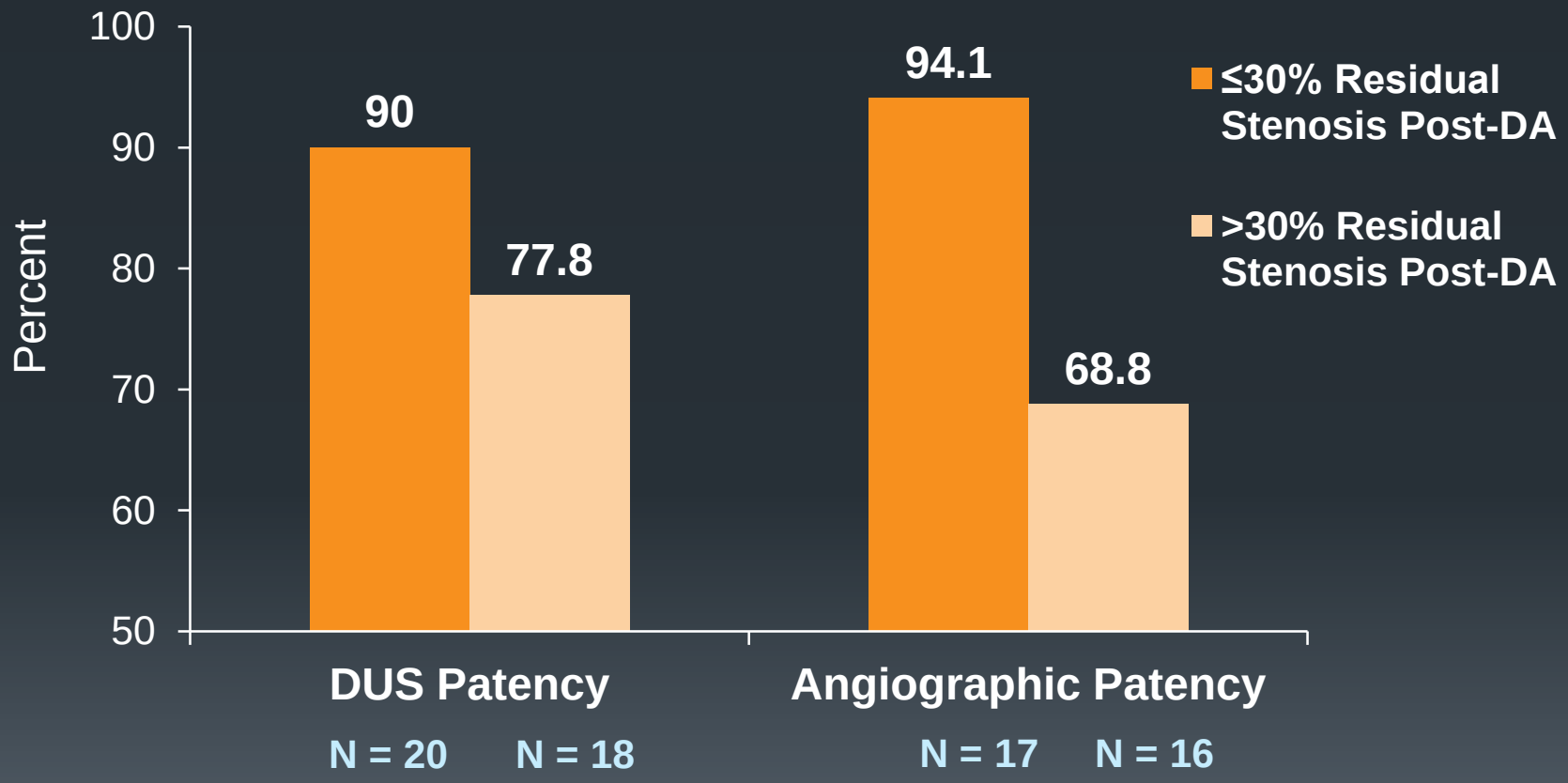
Post Procedure MLD (DA+DCB vs DCB alone)

DA+DCB resulted in a significantly larger minimum lumen diameter (MLD) following the protocol-defined treatment in DEFINITIVE AR



12-Month Patency: DA+DCB RCT Patients

Increased lumen gain with DA before DCB may result in improved 12-month patency

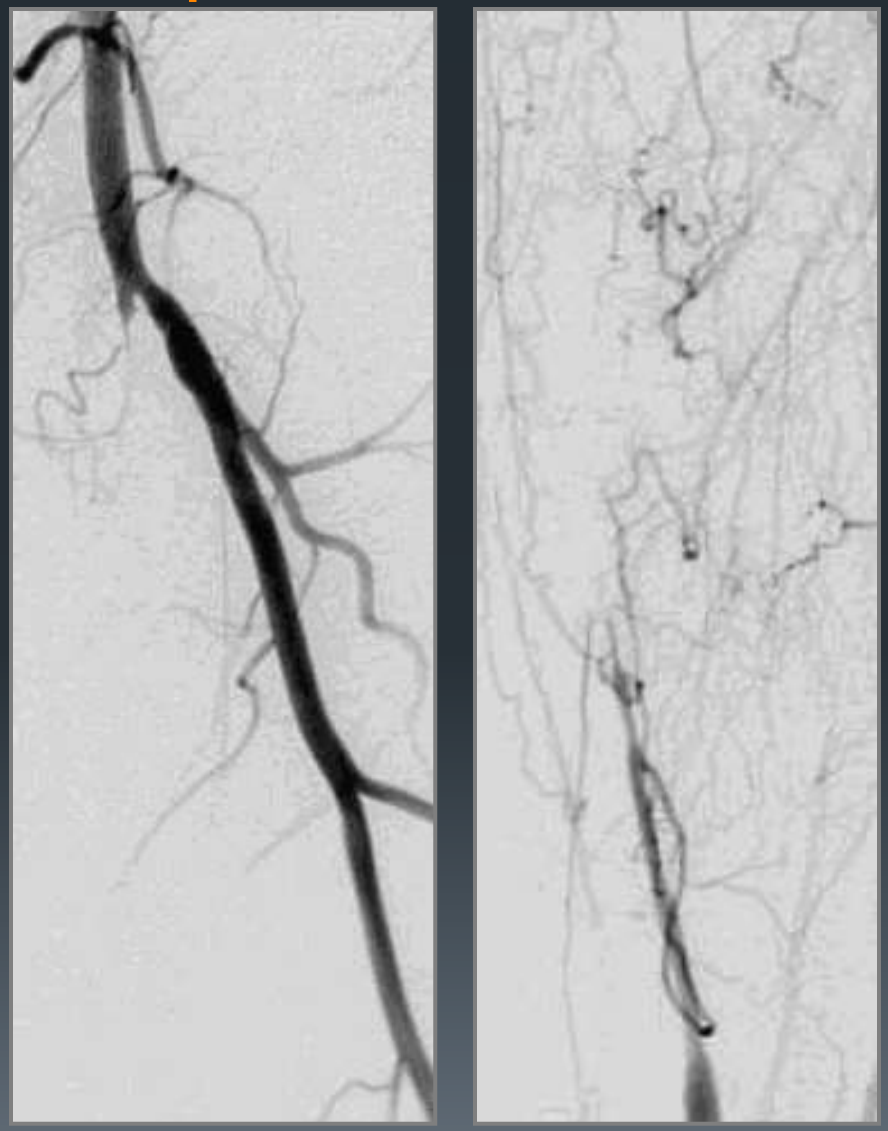


Hypotheses Generated

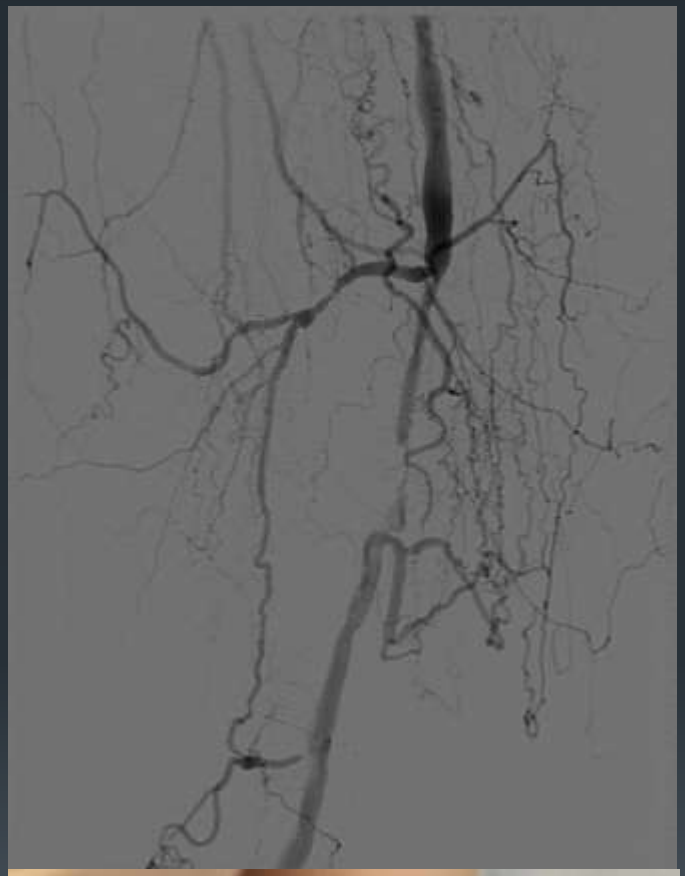
- Is there a benefit of using directional atherectomy before DEB in patients with
  - Long Lesions
  - Severe Calcification
  - Does A Larger MLD improve patency?

Best Strategy for Long Segment/Calcified Fem Pop Disease?

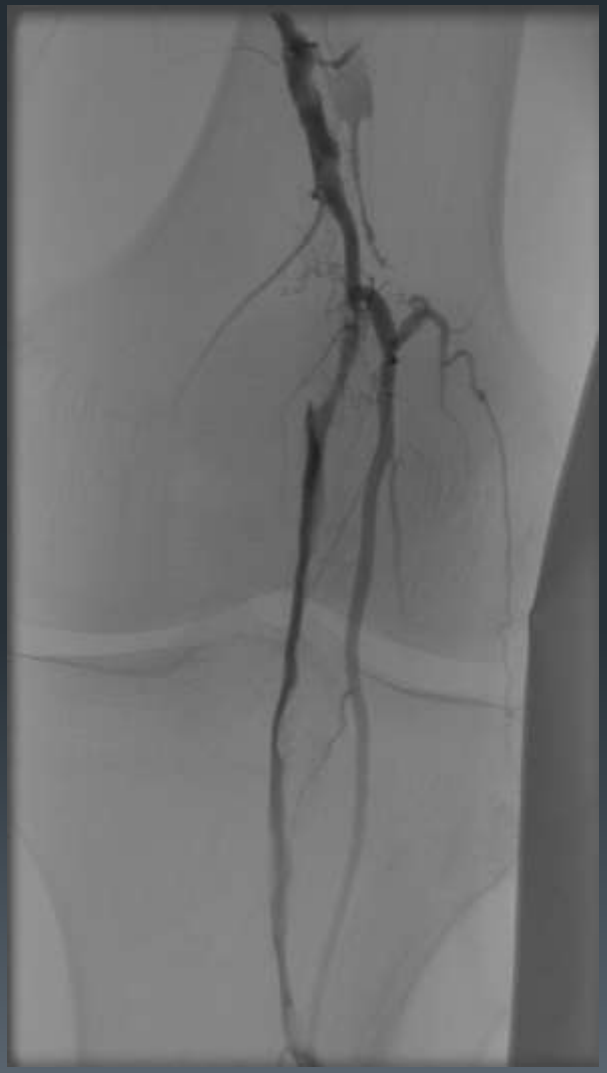
- Vessel Prep
  - Atherectomy – Directional
- Drug Eluting Balloon
  - Which Balloon?
  - Does **not** appear to be a class effect
  - Optimal PTA – long balloon inflations
- Spot stenting if needed for flow limiting dissection



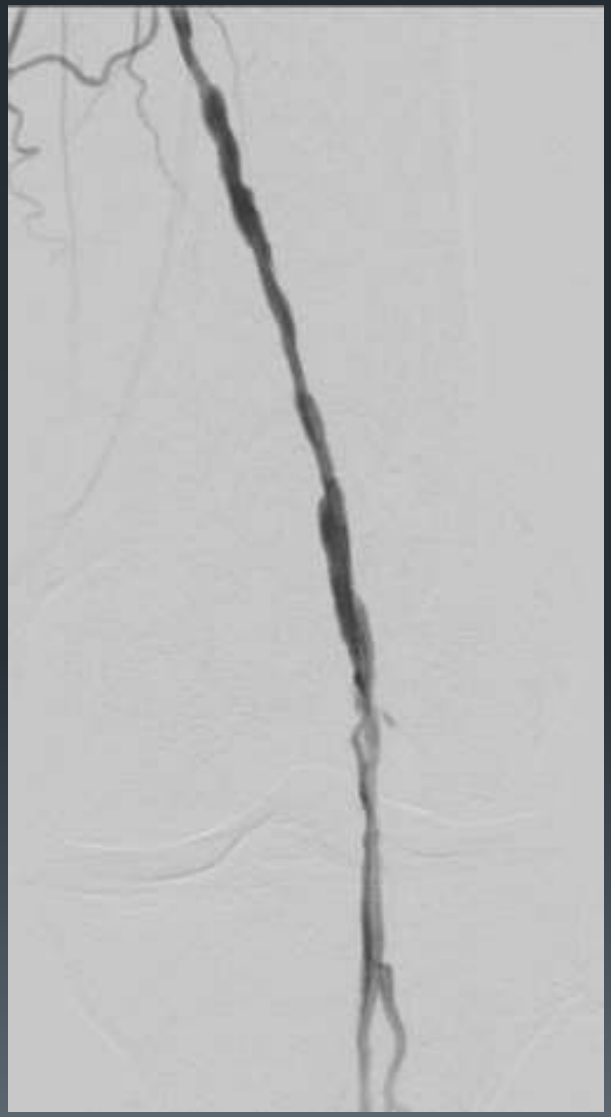
TurboHawk LXC with Admiral DEB

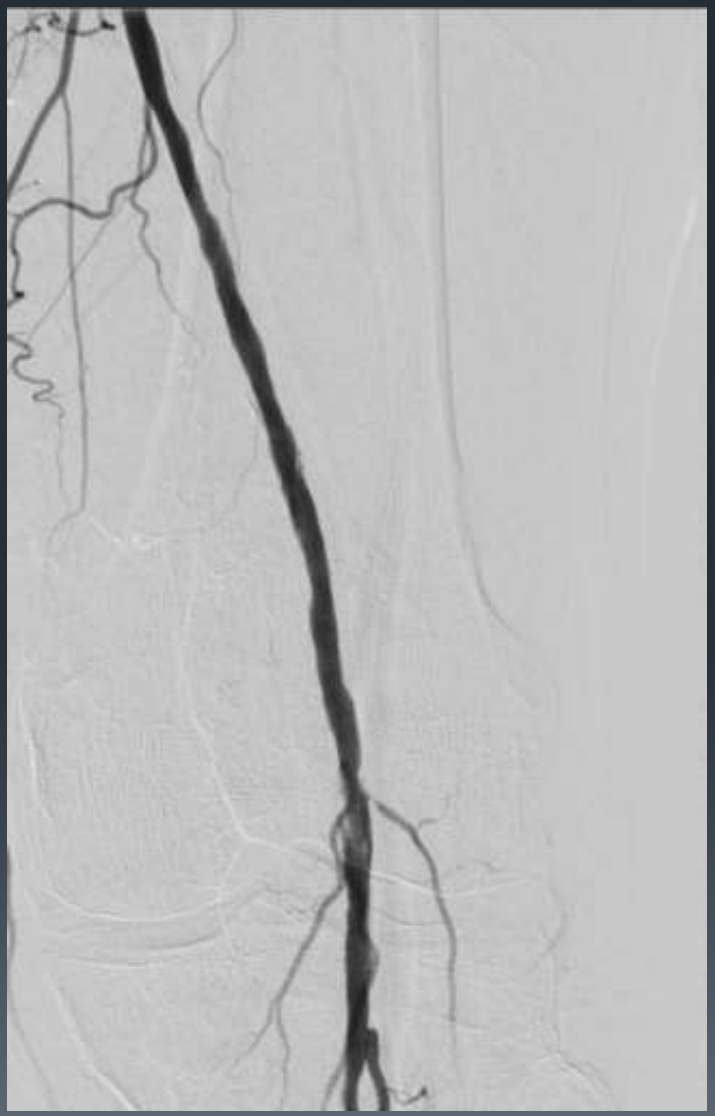


TurboHawk LXC with Admiral DEB

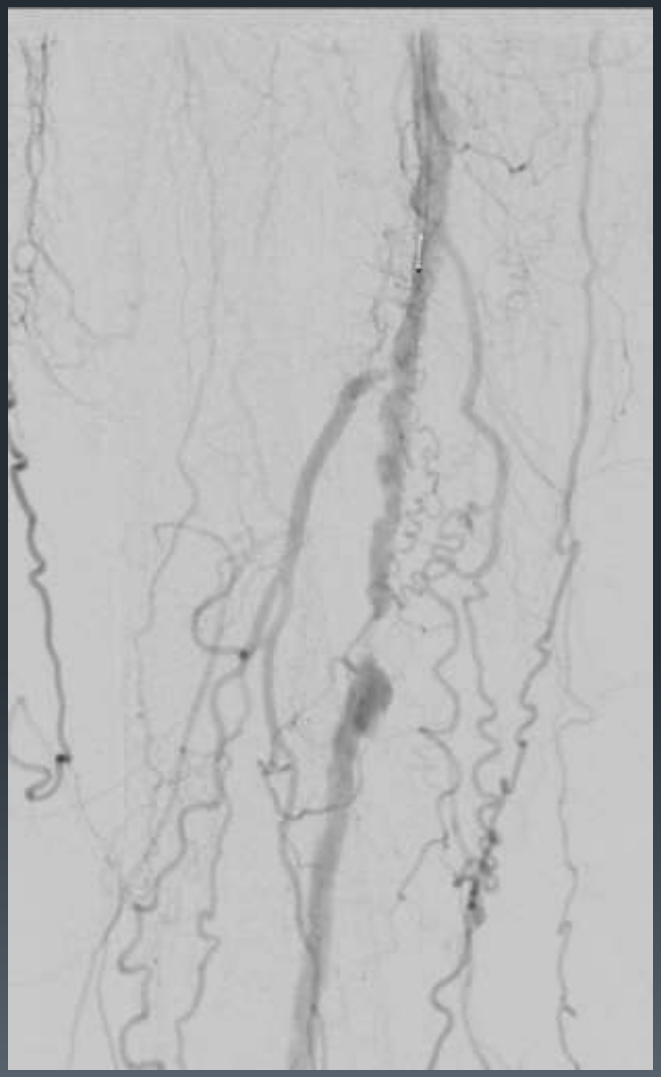


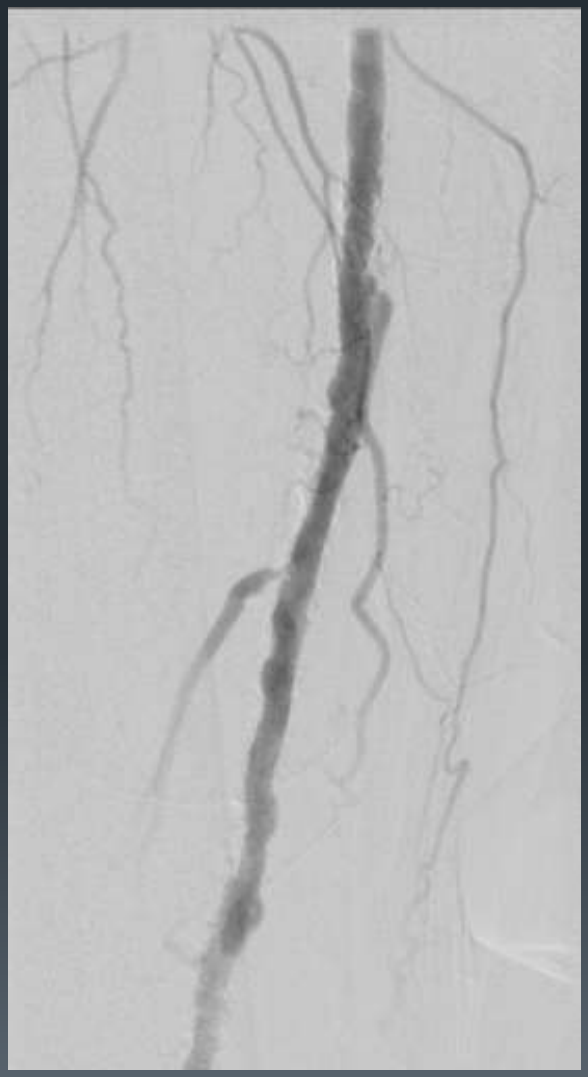
TurboHawk LXC with Admiral DEB





TurboHawk LXC with Admiral DEB





Summary

- Atherectomy and DEB both represent big advances in our ability to treat PVD, and have expanded our toolbox
- However, there is room for improvement
- My approach
  - Simple lesions < 8 cm – DCB alone
  - Complex Lesions - Combination therapy
    - Calcific Disease
    - Long Lesions
    - ISR – off label
    - This ends up being the majority of my patients
- But – We do no know the answer, and this is expensive
- Await start of the REALITY Study which will examine the the combination approach in a prospective manner in 250 patients
- Need long term Cost/Benefit Analysis

Thank You!