

Drug-Coated Balloons in the Femoro-popliteal Segment

Calcific Disease: All or Selective Use?

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Disclosure Statement of Financial Interest

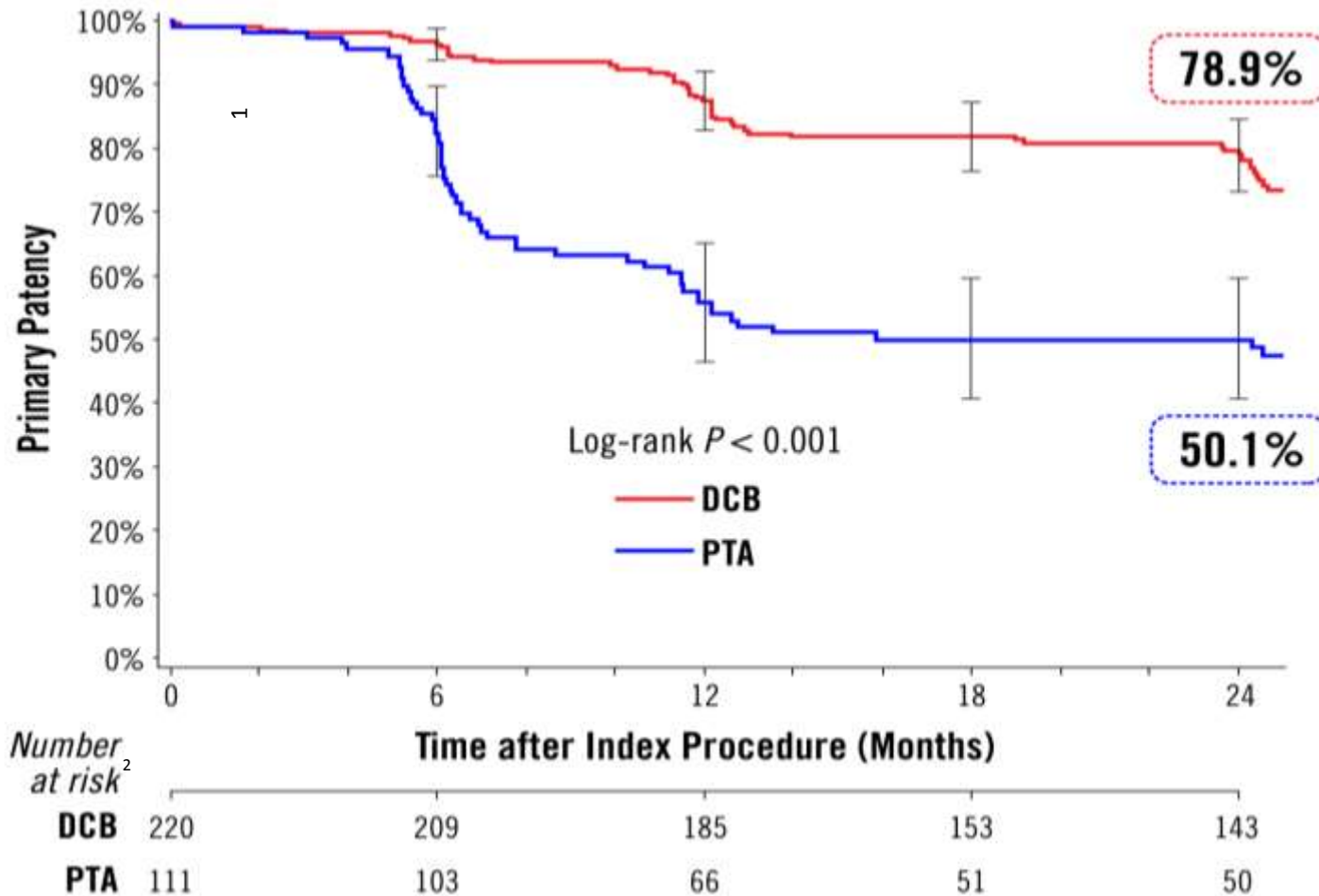
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Affiliation/Financial Relationship	Company
<ul style="list-style-type: none">• Grant/Research Support• Consulting Fees/Honoraria• Ownership/Founder• Other Financial Benefit	<ul style="list-style-type: none">• Medtronic, Boston Scientific, Gore• Medtronic, Boston Scientific, Spectranetics• Contego Medical• CardioMEMs

What do we know so far about DCB Efficacy and Vessel Calcification in the Fem Pop Segment?

- DCB are increasingly showing efficacy in RCTs, but long term data are lacking
- These trials excluded patients with severe calcification
- Hard to define severe calcification and definitions are not consistent across trials
- So when should we use DCBs as stand alone therapy???
- When should we use vessel prep technologies or resort to stenting???

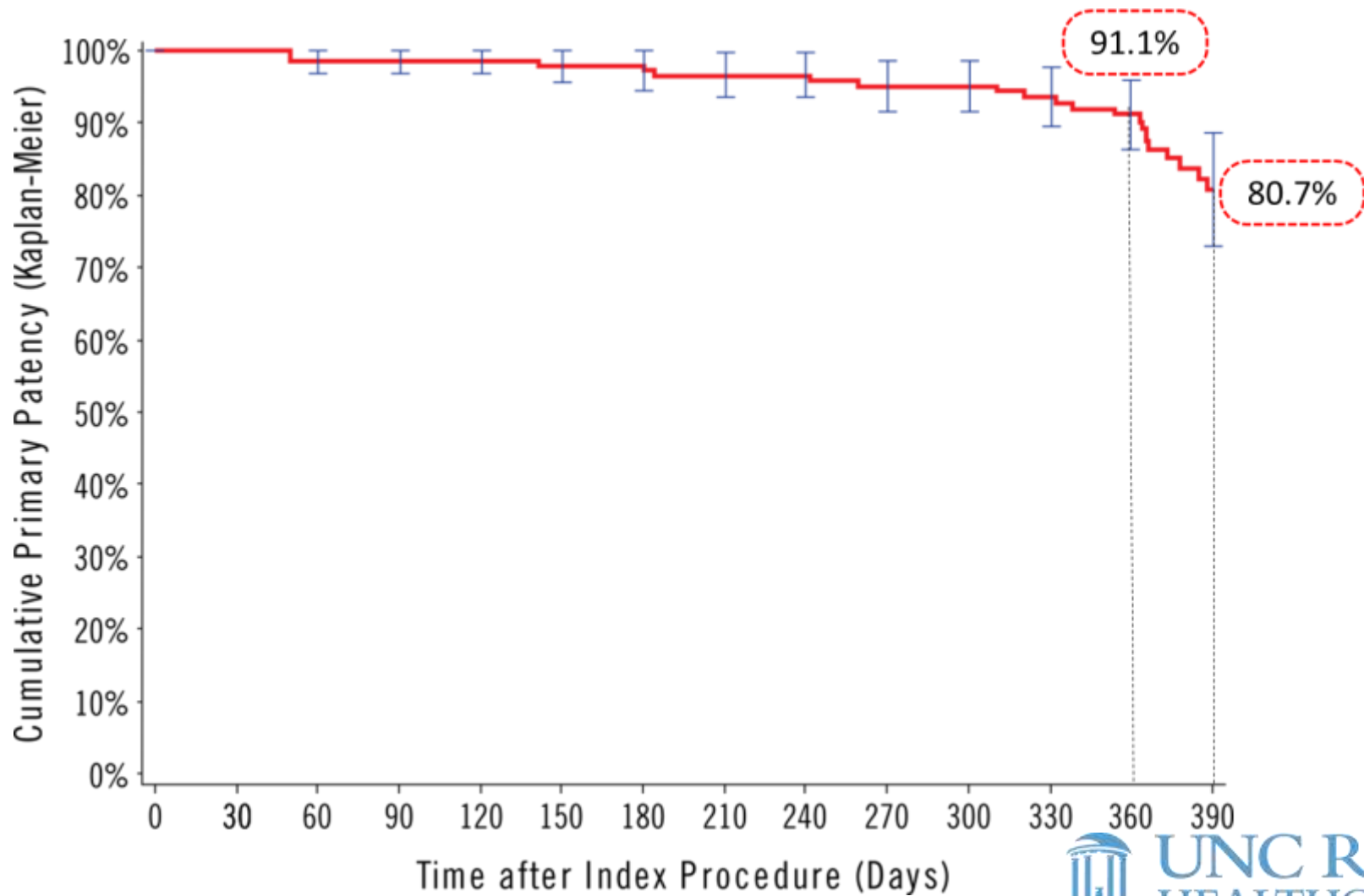
IN.PACT SFA TRIAL EFFICACY OUTCOMES THROUGH 2 YEARS



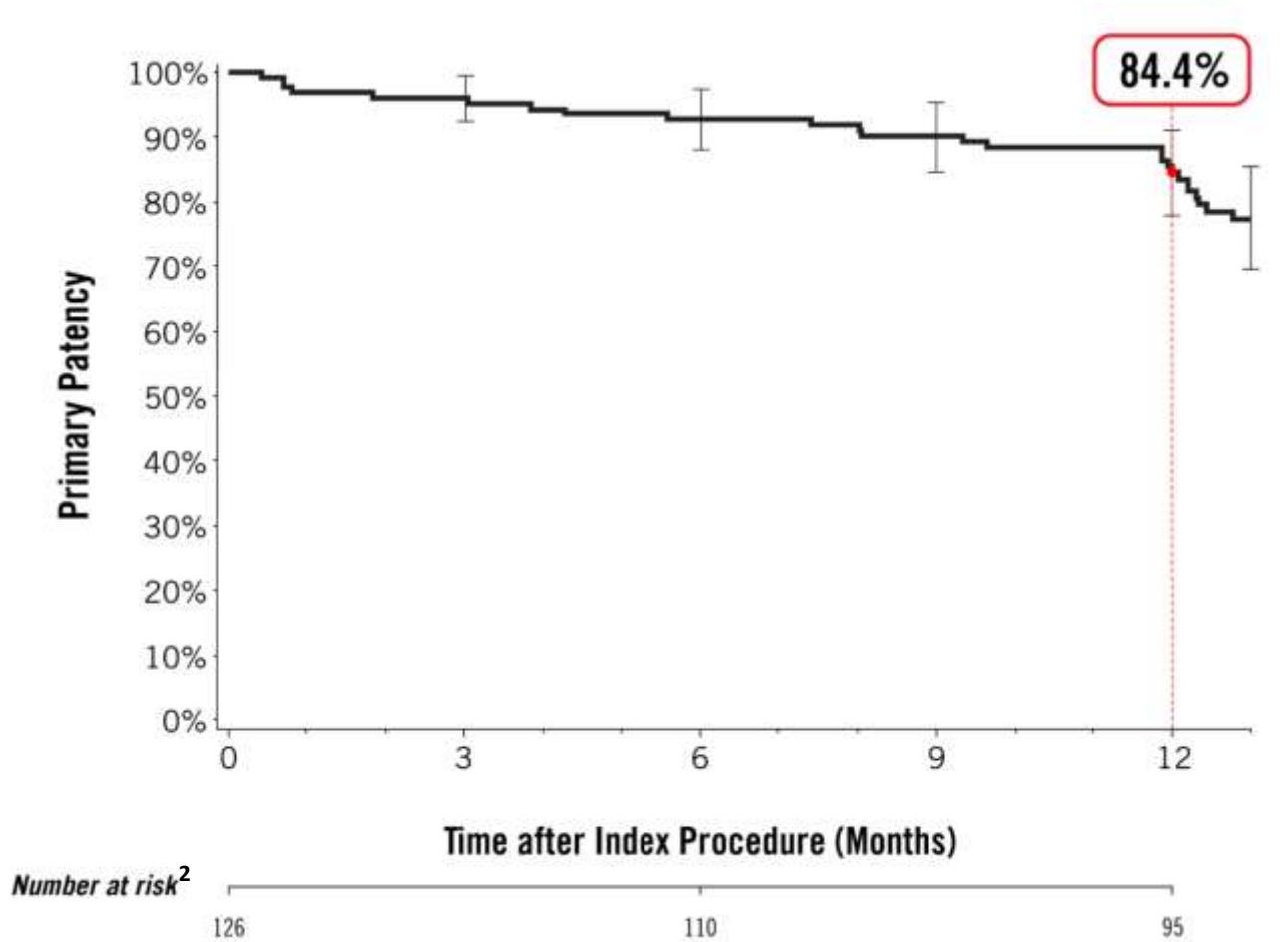
1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤ 2.4) or clinically-driven target lesion revascularization through 24 months (adjudicated by a Clinical Events Committee blinded to the assigned treatment).

2. Number at risk represents the number of evaluable subjects at the beginning of the 30-day window prior to each follow-up interval.

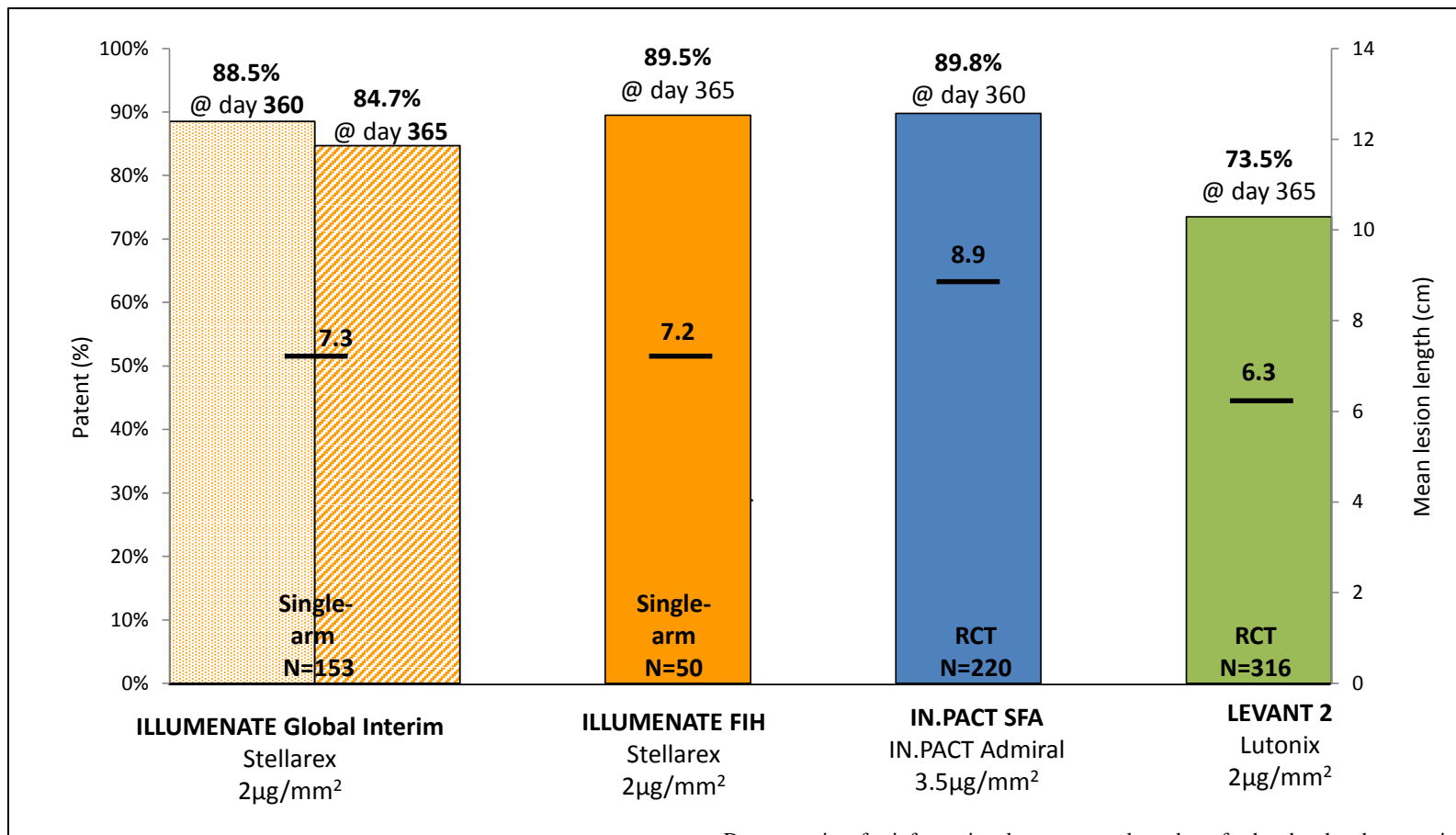
IN.PACT Global Long Lesion Imaging Cohort: Kaplan-Meier Estimate of Primary Patency



CTO subset: Primary Patency¹ Results through 1 Year



Illuminate Global Interim Data n=153



WHAT ABOUT PATIENTS WITH SEVERE CALCIFICATION?

IN.PACT SFA TRIAL: Severe Calcification

TABLE 1 Baseline Patient and Procedural Characteristics

	IN.PACT (n = 220)	PTA (n = 111)	p Value
Age, yrs	67.5 ± 9.5	68.0 ± 9.2	0.612
Male	65.0 (143/220)	67.6 (75/111)	0.713
Diabetes	40.5 (89/220)	48.6 (54/111)	0.161
Hypertension	91.4 (201/220)	88.3 (98/111)	0.431
Hyperlipidemia	84.5 (186/220)	82.0 (91/111)	0.637
Current smoker	38.6 (85/220)	36.0 (40/111)	0.719
ABI/TBI*	0.769 ± 0.228	0.744 ± 0.189	0.308
Rutherford clinical category			0.898
2	37.7 (83/220)	37.8 (42/111)	
3	57.3 (126/220)	55.9 (62/111)	
4	5.0 (11/220)	5.4 (6/111)	
5	0.0 (0/220)	0.9 (1/111)	
Lesion length, cm	8.94 ± 4.89	8.81 ± 5.12	0.815
Total occlusions	25.8 (57/221)	19.5 (22/113)	0.222
Severe calcification	8.1 (18/221)	6.2 (7/113)	0.662
Dissections			0.360
0	36.2 (80/221)	38.9 (44/113)	
A-C	63.8 (141/221)	60.2 (68/113)	
D-F	0.0 (0/221)	0.9 (1/113)	
Provisional stenting	7.3 (16/220)	12.6 (14/111)	0.110

In.Pact Global Baseline Lesion and Procedural Characteristics

Characteristic	IN.PACT (# Lesions=763)	Characteristic	IN.PACT (n=655)
Lesions per Patient	1.16	Pre-Dilatation	75.4% (494/655)
Popliteal Involvement	29.4% (224/763)	Post-Dilatation	31.0% (201/648)
De Novo Lesion	70.6% (539/763)	Provisional Stent	24.7% (160/648)
Restenotic Lesion (non-ISR)	8.0% (61/763)	Device Success	99.4% (1264/1271)
In-Stent Restenosis*	21.4% (163/763)	Procedure Success	99.8% (646/647)
Mean Lesion Length	12.23 cm ± 9.59	Clinical Success	99.5% (644/647)
Total Occlusions	35.8% (273/763)		
Severe Calcification	10.4% (79/763)		
RVD	5.2 mm ± 0.7		
Diameter Stenosis	88.7% ± 12.2		
Dissection: 0	60.2% (459/762)		
Dissection: A - C	33.9% (258/762)		
Dissection: D - F	5.9% (45/762)		

Calcium Limits Vessel Expansion

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

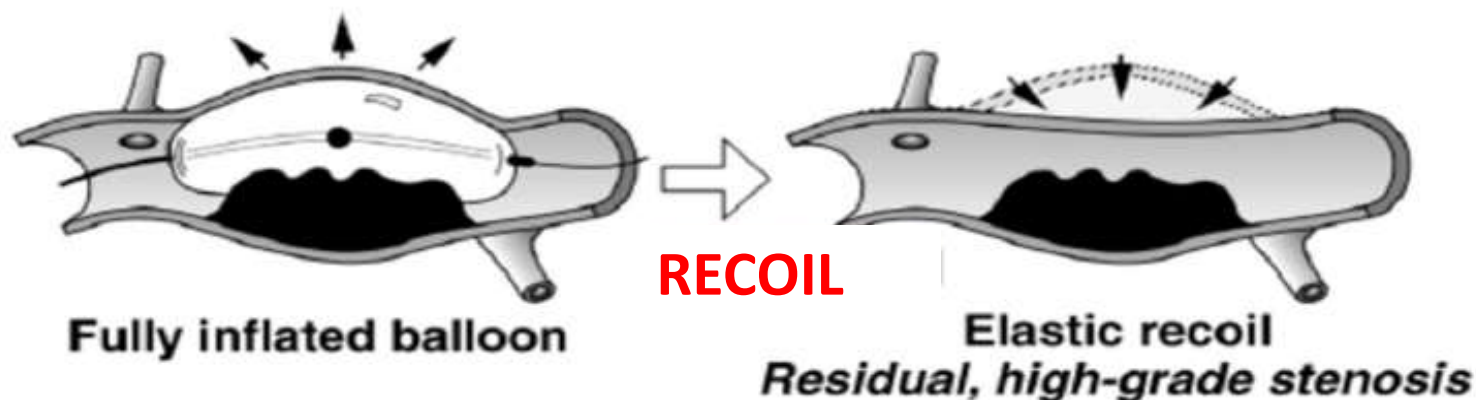


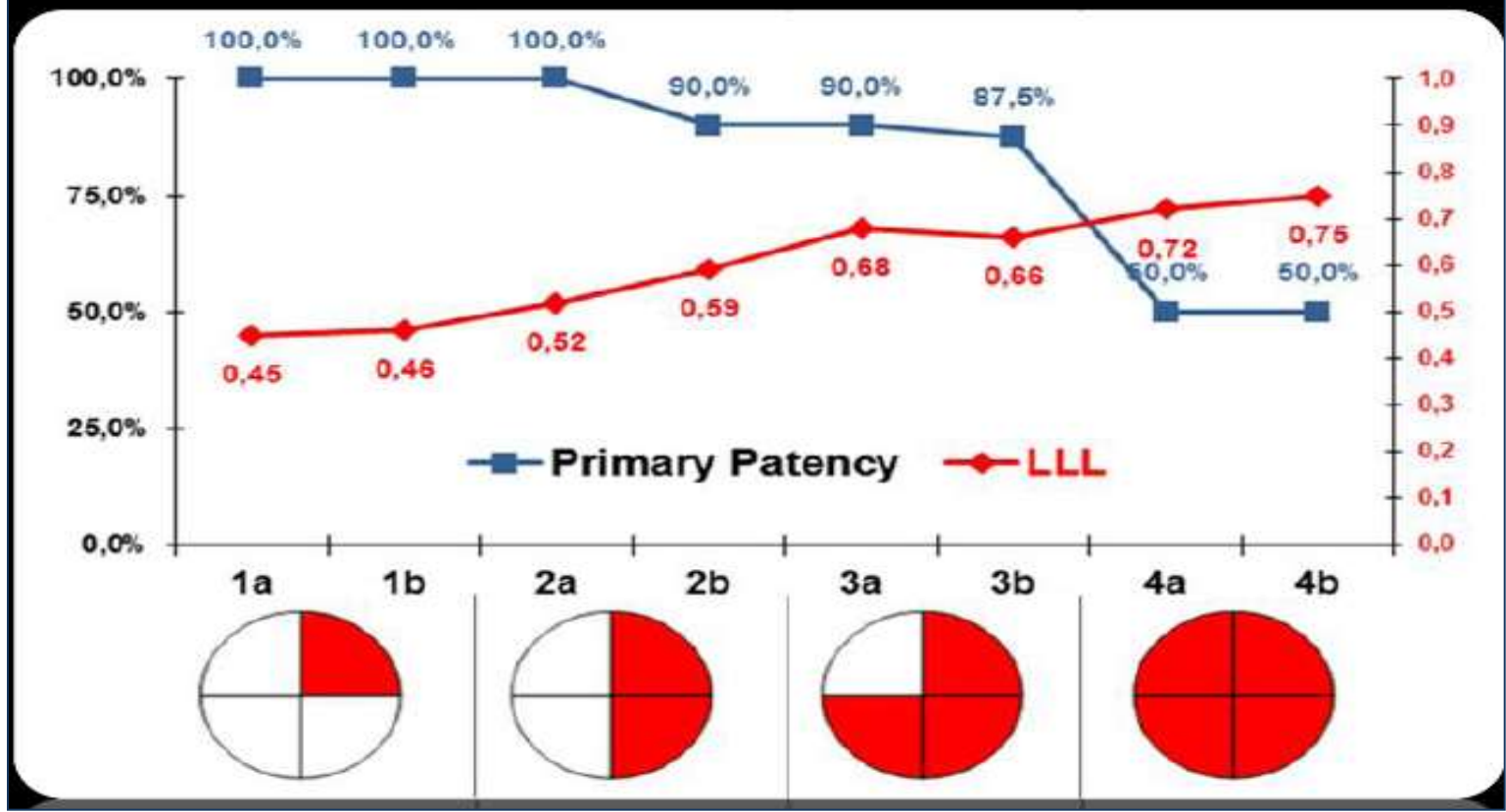
Figure 12.1. Elastic Recoil After PTCA of Calcified Lesions

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

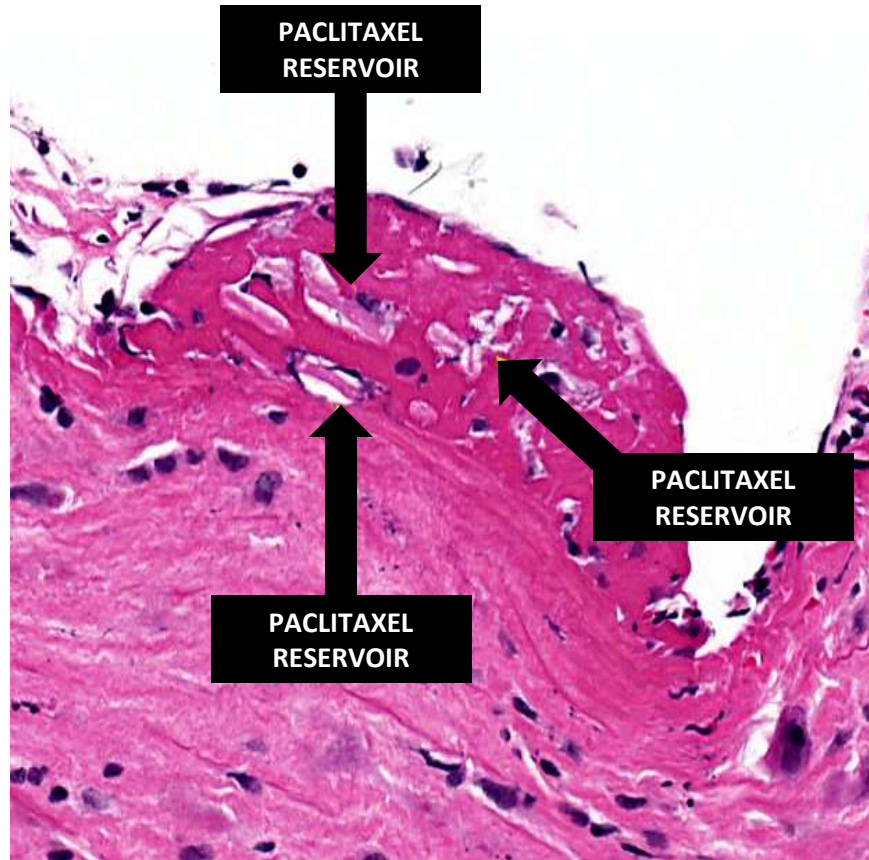
Freed MS, Safian RD; Manual of Interventional Cardiology, Ch. 12, 245-254

Calcium May Limit Drug Effect

12-month Results



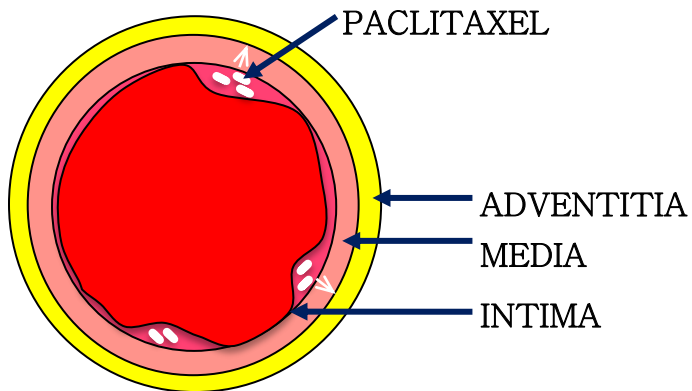
SUSTAINED DRUG, SUSTAINED BENEFIT. IMPORTANCE OF DRUG “RESERVOIRS”



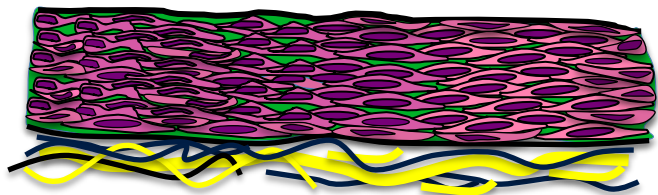
Solid-phase paclitaxel embeds in vessel wall, creating “reservoirs” of drug that are sustained over time.

Note: Study on file with Medtronic, represents 28-days post drug delivery.

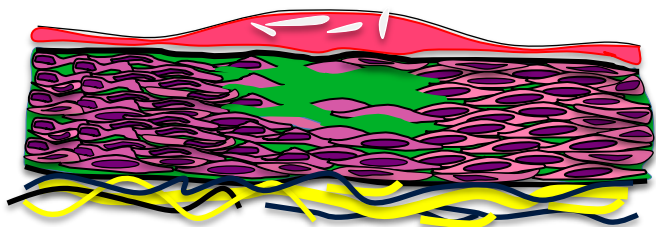
SUSTAINED DRUG, SUSTAINED BENEFIT. PACLITAXEL EFFECT ON SMOOTH MUSCLE CELL



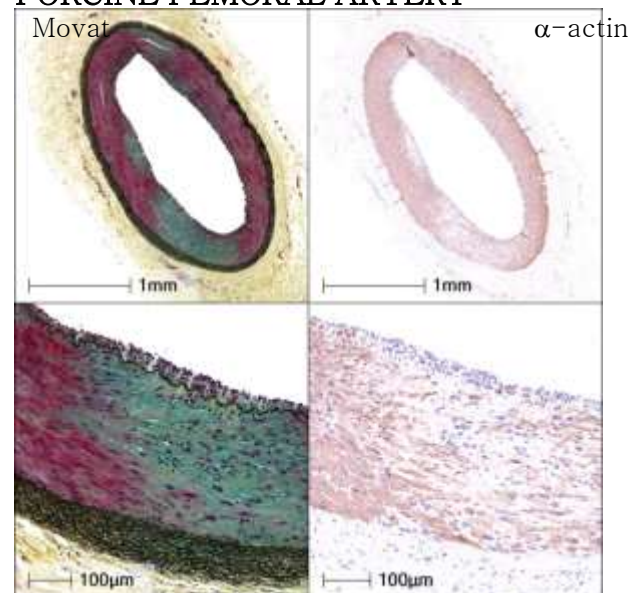
NORMAL ARTERIAL WALL



ARTERIAL MEDIAL WALL CHANGES FOLLOWING IN.PACT DCB

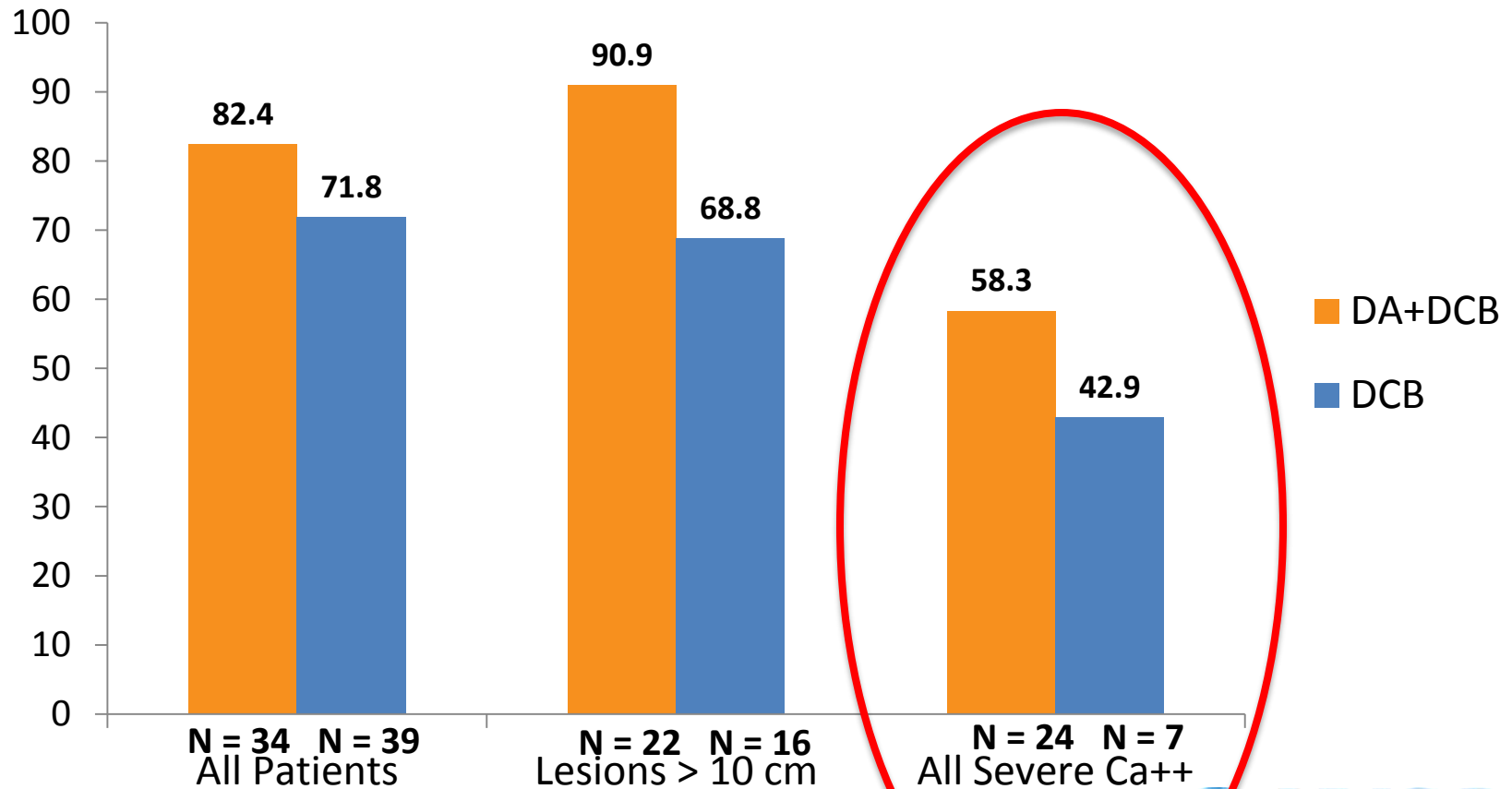


IN.PACT DCB TREATMENT
 PORCINE FEMORAL ARTERY



Are there any clinical data to support this?

Definitive AR: Angiographic Patency at 12 Months



Levant II Trial : Patients with Calcification

	DCB	Standard PTA	P-value
Two lesions treated	1.9%(6/316)	3.1%(5/160)	0.400
Total Lesion Length(mm)	62.9 ± 41.5(315)	63.6 ± 40.3(160)	0.866
Treated Length(mm)	107.7 ± 47.0 (316)	107.3 ± 49.3 (160)	0.933
Calcification	59.2%(187/316)	57.5%(92/160)	0.726
Total Occlusion	20.6%(65/316)	21.9%(35/160)	0.741
%DS post-treatment	23.4 ± 12.3(316)	23.8 ± 12.3(158)	0.703
Bail-outStenting	2.5%(8/316)	6.9%(11/160)	0.022
Dissection	63.7%(200/314)	72.3%(115/159)	0.060
Procedural Success (corelab)	88.9%(281/316)	86.8%(138/159)	0.497
DeviceSuccess(no of balloons)	99.5%(430/432)	100%(180/180)	0.367

Levant II Trial

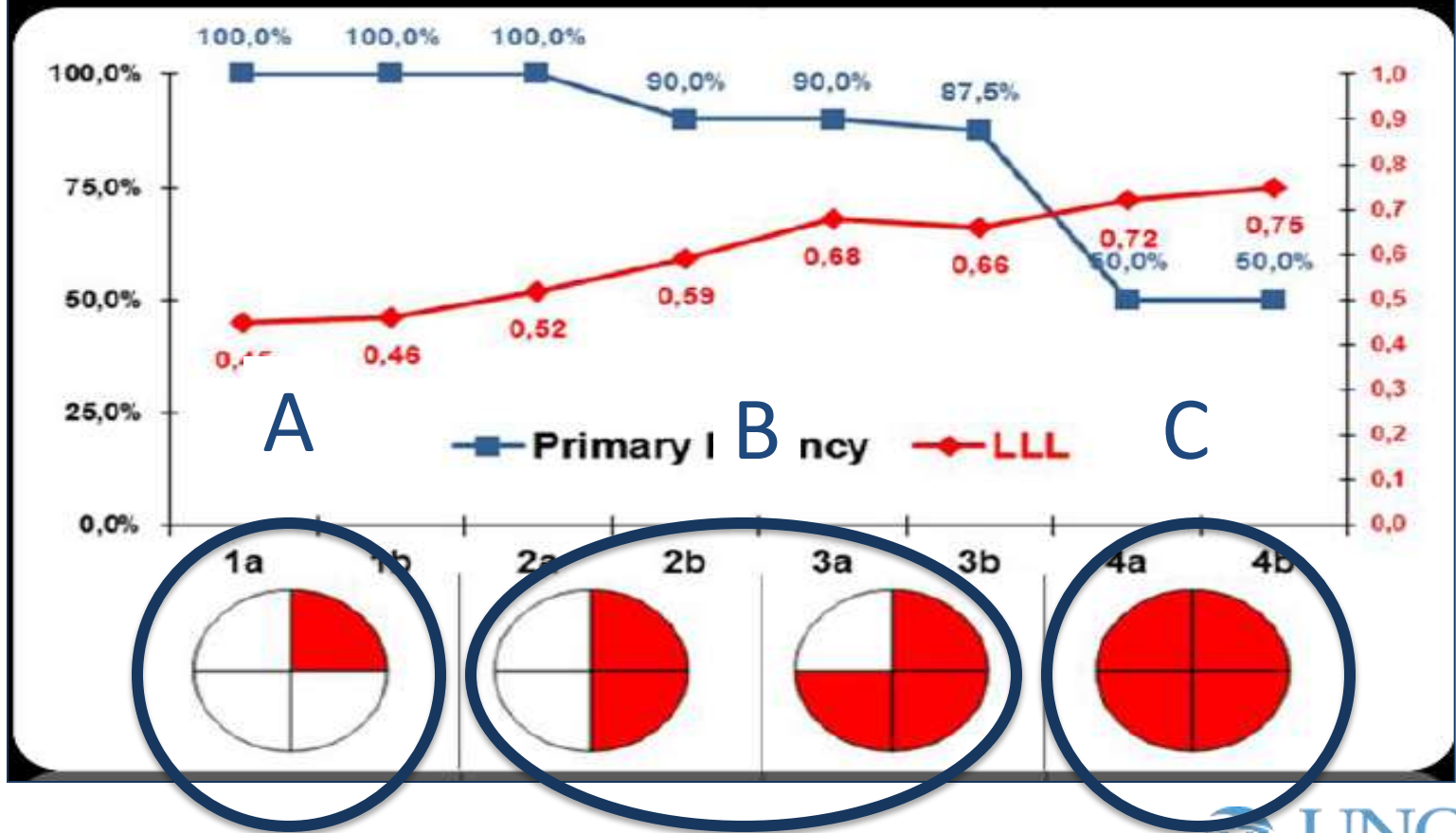
24 Month Primary Patency, Freedom from TLR, and Composite Safety

	Lutonix	PTA	
Patency @730 days	58.6%	53%	P=0.05
Composite Safety	78.7%	70.9%	P=0.08

***SO HOW SHOULD WE APPROACH OUR PATIENTS
WITH CALCIFIC DISEASE?***

Calcium May Limit Drug Effect

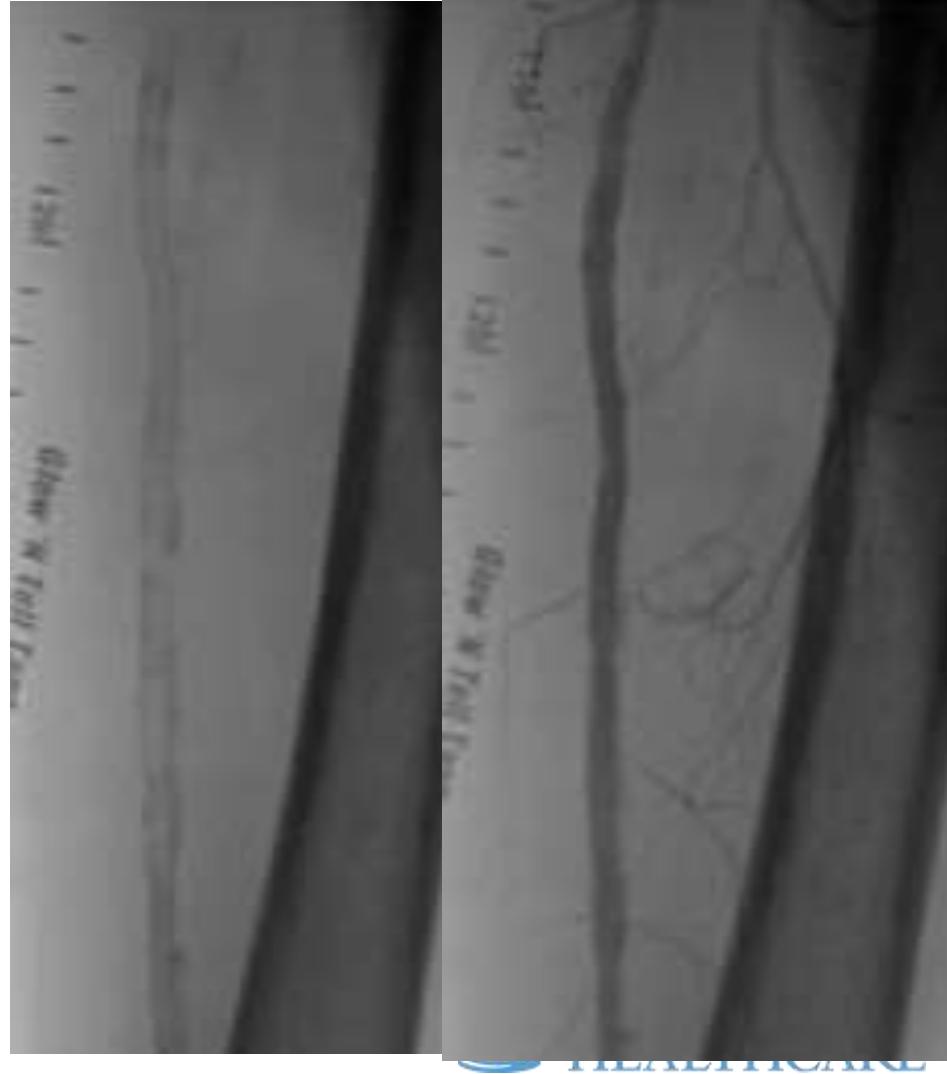
12-month Results



Treatment Algorithm Based on Calcification

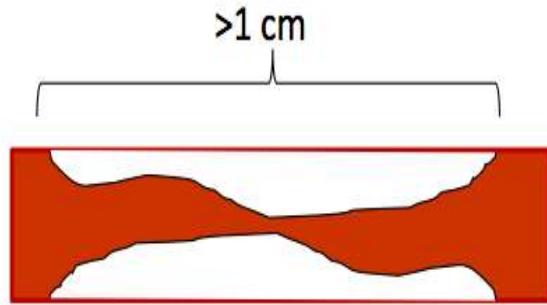
- A: Little to no calcification
 - DCB effective
 - Use Routinely
- C: Severe Circumferential Calcification
 - DCB alone likely ineffective
 - Consider prep with atherectomy or stent use
- B: Moderate Calcification – Majority of our Patients
 - Unclear Long-term Outcomes data
 - But, likely effective

Angiographic Assessment of Calcification is Not Always Accurate



DEFINITION OF SEVERE CALCIFICATION: DEFINITIVE CA⁺

Severe Calcification



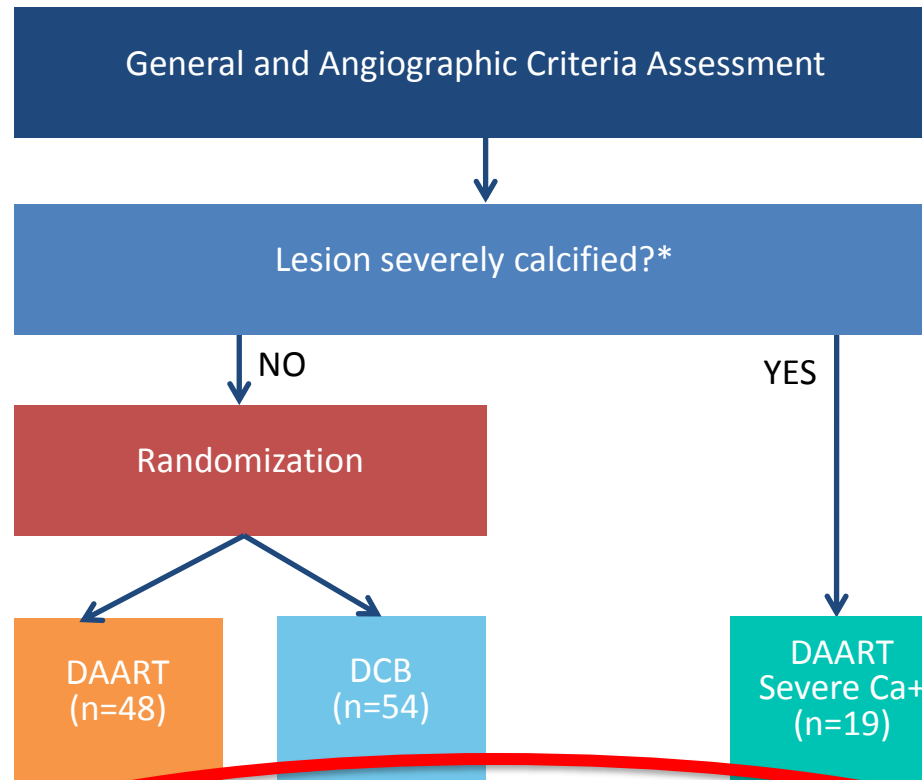
Radiopacities on both sides of arterial wall extending >1 cm

Moderate Calcification



Radiopacities on one side of arterial wall OR <1 cm

DEFINITION OF SEVERE CALCIFICATION: DEFINITIVE AR⁺

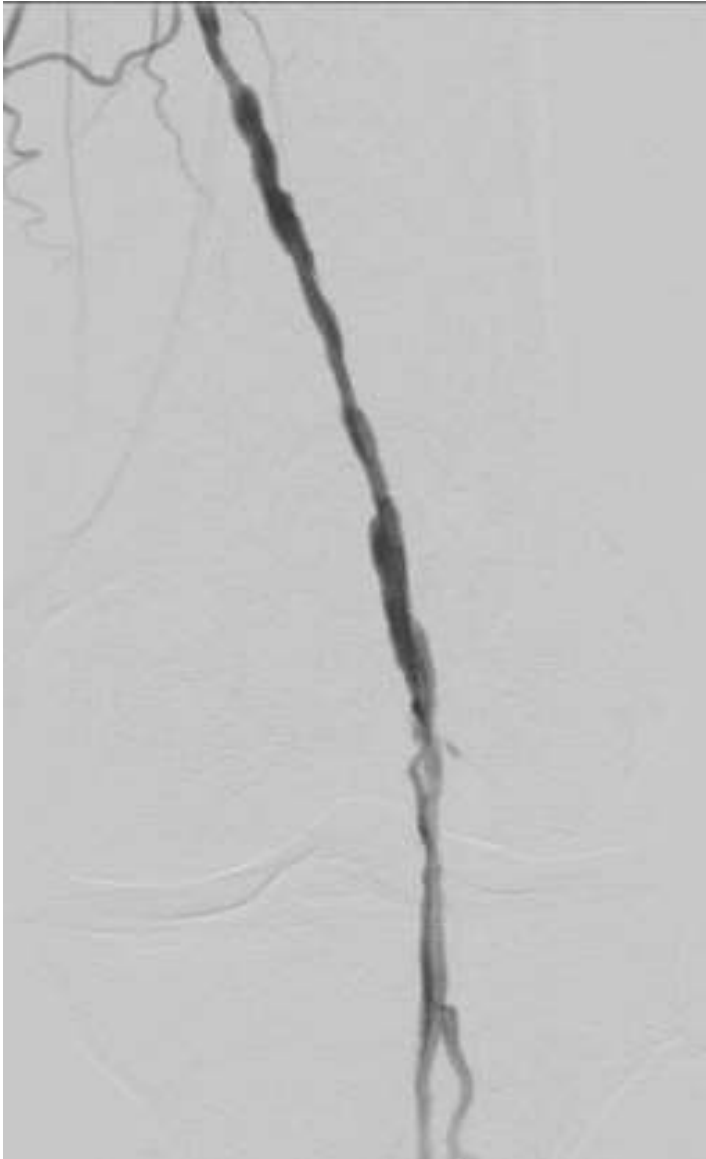


*Defined as: dense circumferential calcification extending > 5 cm

Group C: Severe/Circumferential Calcification

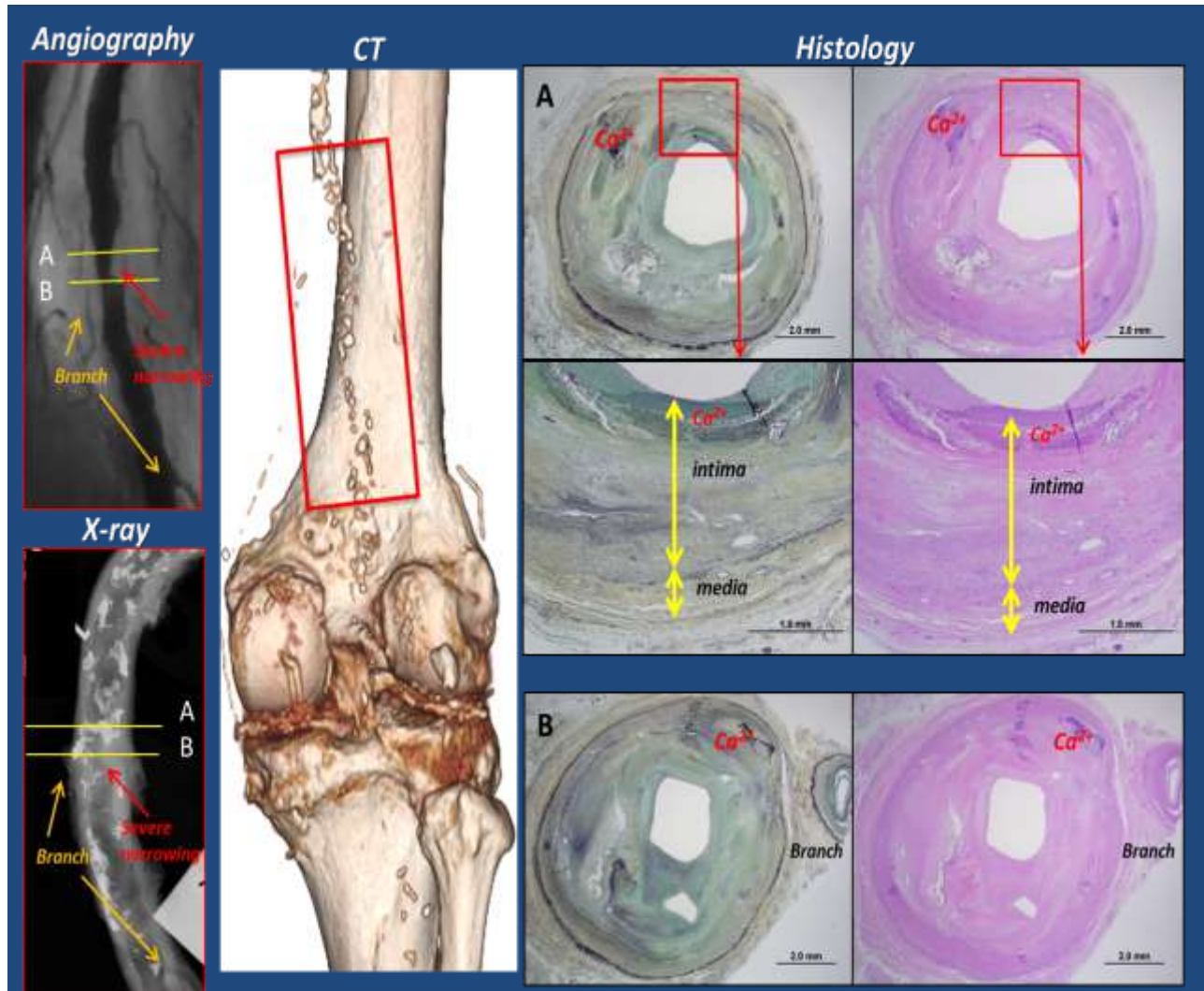


Do These Patients Have Moderate Or Severe Calcification??



UNDERSTANDING THE SCIENCE BEHIND THE OUTCOMES

INTIMAL MODERATE POPLITEAL CALCIFICATION



Courtesy of R. Virmani, MD

Conclusions

- **Severe circumferential calcium** – DCB alone probably will have reduced efficacy. Need some type of vessel prep.
- **Moderate calcium** – Routine use of DCBs will probably work.
 - What is moderate calcium?
 - Can we standardize the definition?
- In these majority of these cases DCBs should still be routinely used
 - Post dilate if needed
 - Follow up with spot stenting with BMS or DES as needed
- Await long term data from DCB trials, especially in patients with heavy calcification

Thank You!