

# **Durability, safety, and efficacy of a drug-coated balloon for the treatment of peripheral arterial disease in the SFA**

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# COI Disclosure

Speaker name :

*Osamu Iida, MD*

I have the following potential conflicts of interest to report:

- Consulting: NIPRO, Canon
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s) Honoraria : Medtronic, Boston Scientific, Gore, NIPRO, Canon, Kaneka, Cook
- I do not have any potential conflict of interest

# Background

- The use of drug-coated balloons (DCBs) for the treatment of femoropopliteal disease has demonstrated superiority over percutaneous transluminal angioplasty (PTA) in numerous trials.<sup>1-9</sup>
- While outcomes from numerous studies<sup>1-12</sup> have demonstrated effectiveness of DCBs through freedom from CD-TLR, **investigation into predictors of revascularization and restenosis have identified various predictors for failure.**<sup>10, 13-16</sup>
- This presentation from a large, multi-ethnic, pooled, independently-adjudicated drug-coated balloon (DCB) series will address **predictors of revascularization in complex lesions.**

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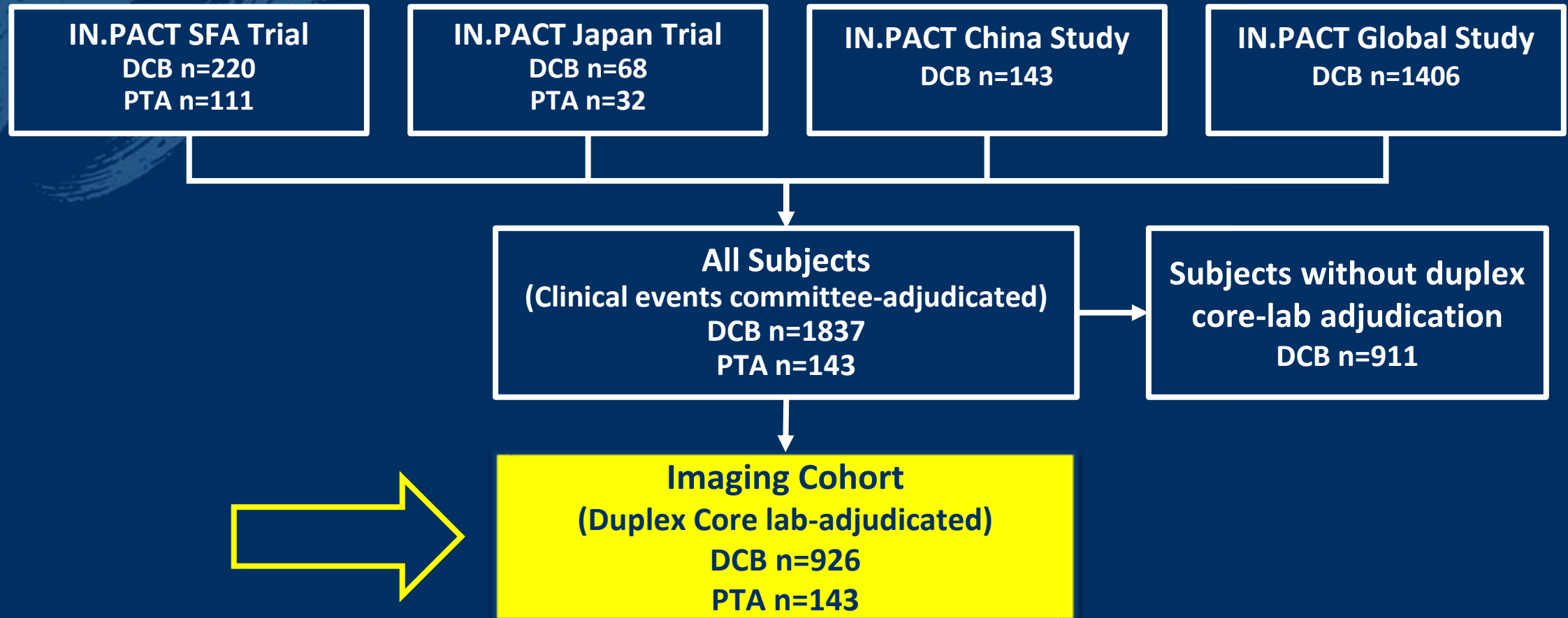
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# Total IN.PACT Architecture: **Imaging Analysis**

This analysis combines all subjects treated with the IN.PACT Admiral DCB and PTA across two RCT trials and two single arm studies across 147 sites and 28 countries



# Total IN.PACT **Imaging Cohort**

## Methodology for Statistical Analysis

Multivariable Analysis to identify predictors for **1) loss of primary patency** and **2) clinically-driven target lesion revascularization** included treatment with DCB vs PTA.

1. Univariate and stepwise multiple Cox regression model (with entry criterion of **p=0.20** and a stay criterion of **p=0.10**) was used.
2. Hazard ratios with two-sided 95% confidence intervals were calculated.
3. Level of statistical significance was set at  $p < 0.05$ .

# Total IN.PACT Imaging Cohort

## Baseline Clinical Characteristics

12-month Baseline		Total IN.PACT Imaging Cohort		
		DCB (N=926 Subjects)	PTA (N=143 Subjects)	P-value
Patient Status	Age	68.6 ± 9.7	69.4 ± 9.0	0.338
	Male	68.5%	70.6%	0.629
Risk Factors	Hypertension	83.9%	88.1%	0.216
	Dislipidemia	69.5%	81.1%	0.004
	Diabetes	40.4%	50.3%	0.029
	Active Smoker	37.2%	35.0%	0.642
Cardiovascular Disease	Coronary Heart Disease	44.6%	53.9%	0.045
	Coronary Artery Disease	25.1%	28.0%	0.454
Limb status	Rutherford Category			
	2	35.2%	42.7%	
	3	55.0%	51.7%	0.039
	4	8.0%	4.9%	
	5	1.8%	0.7%	
	ABI/TBI*(mmHg)	0.68 ± 0.22	0.74 ± 0.18	<0.001
	Previous Peripheral Revascularization	50.8%	52.4%	0.720
	Below-the-knee Disease of Target Leg	47.4%	49.0%	0.787

# Total IN.PACT Imaging Cohort

## Baseline Lesion Characteristics

12-month Baseline by Core Lab		Total IN.PACT Imaging Cohort		
		DCB (N=1054 Lesions)	PTA (N=143 Lesions)	P-value
Lesion Type	De Novo	75.5%	95.8%	<0.001
	Restenotic (non-stented)	6.2%	4.2%	0.451
	In-stent restenosis	18.3%	0%	-
TASC lesion type	A	32.4%	61.4%	<0.001
	B	26.6%	25.5%	0.841
	C	33.4%	13.1%	<0.001
	D	7.7%	0.0%	<0.001
Lesion Length (cm)		15.56 ± 10.35	8.83 ± 5.31	<0.001
Vessel diameter (mm ±SD)		4.68mm ± 0.82	4.68 ± 0.79	0.974
Minimum lumen diameter, mm		0.67 ± 0.75	0.93 ± 0.73	<0.001
Diameter stenosis %		86.84 ± 15.14	81.14 ± 13.36	<0.001
Outflow Impaired per limb		36.9%	12.0%	<0.001
100% Occluded Lesion		45.4%	18.6%	<0.001
Calcification		61.6%	56.6%	0.274

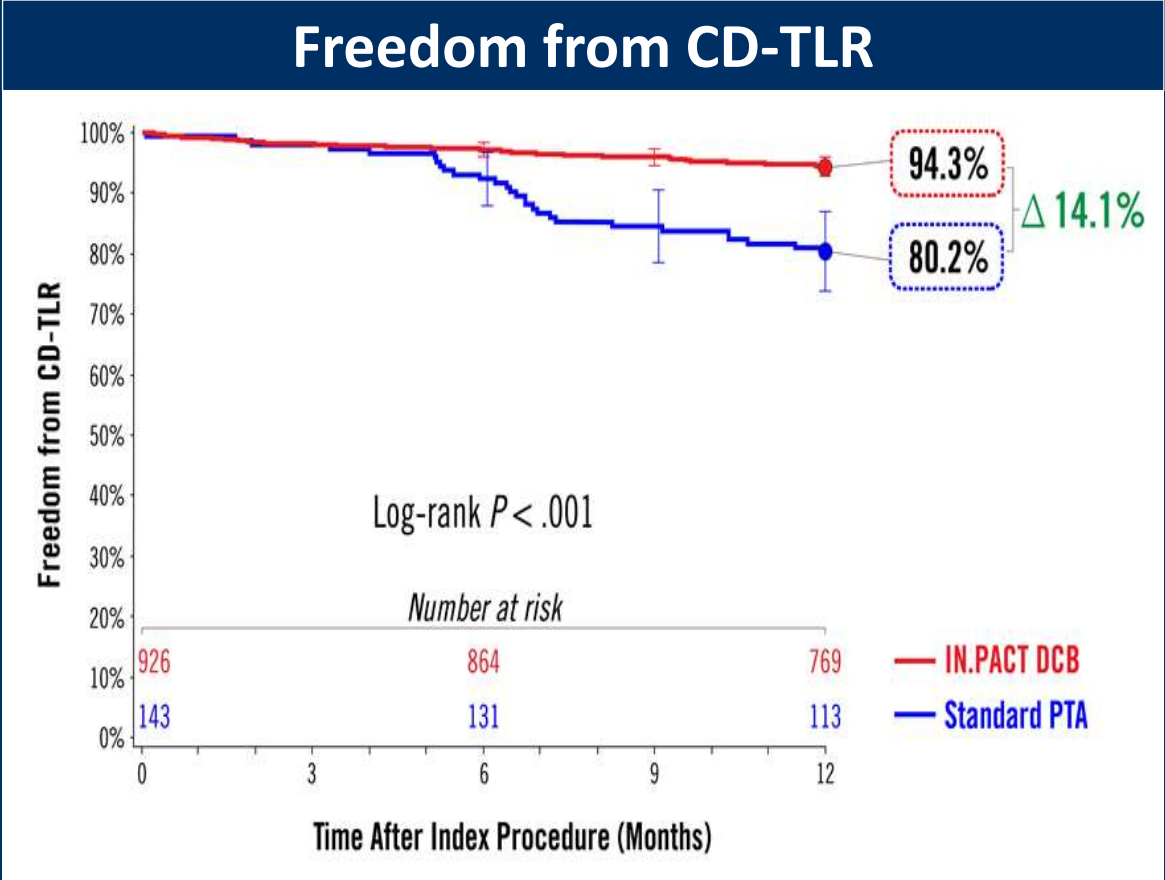
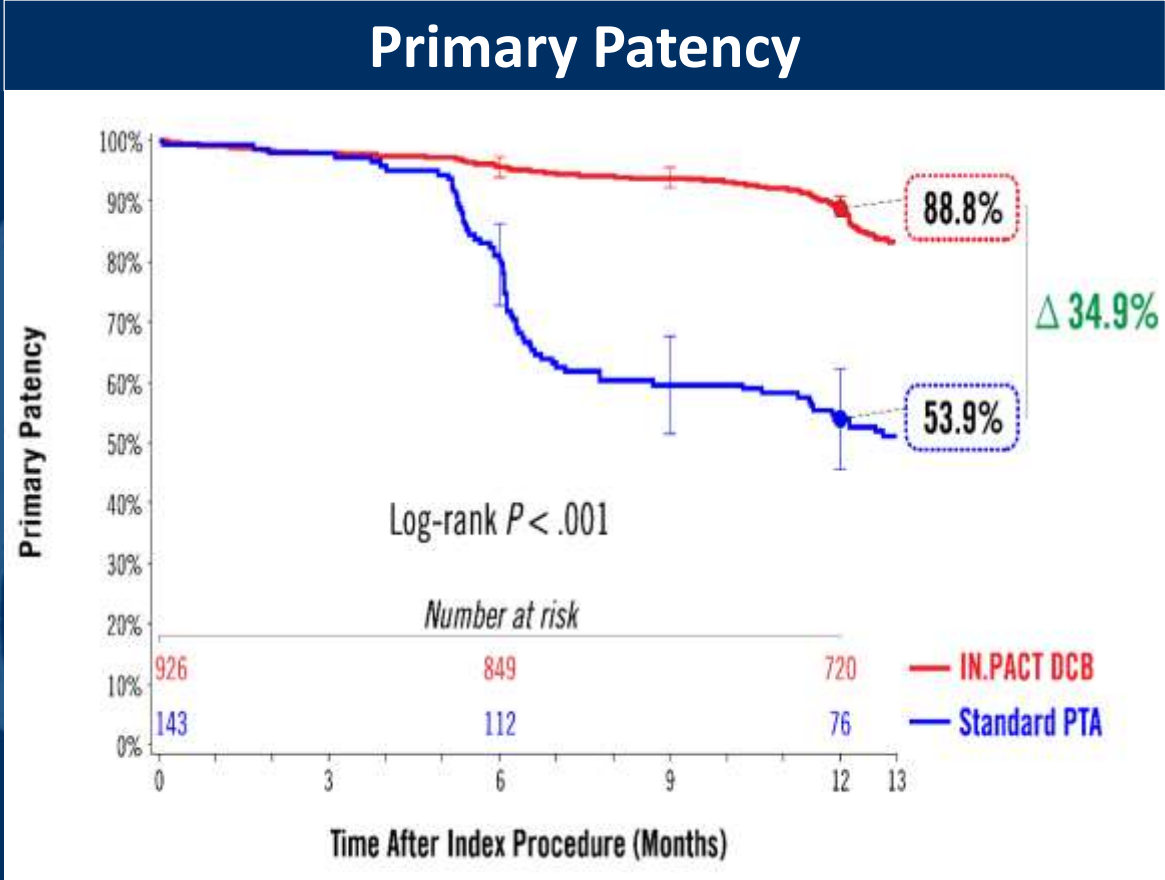
# Total IN.PACT **Imaging Cohort** Baseline Procedural\* Characteristics

12-month Baseline by Core Lab	Total IN.PACT Imaging Cohort		
	DCB (N=1054 Lesions)	PTA (N=143 Lesions)	P-value
Dissection Grade			
(No Dissection)	43.2%	36.6%	0.151
A	16.1%	40.7%	<0.001
B	19.5%	19.3%	1.000
C	11.3%	2.8%	<0.001
D	6.9%	0.0%	<0.001
E	2.5%	0.7%	0.239
F	0.5%	0.0%	1.000
Provisional Stent	19.4%	10.5%	0.008
Subjects with Pre-dilatation	89.7%	88.8%	0.768
Subjects with Post-dilatation	31.1%	18.9%	0.003

\* Core lab reported, except the target lesion type. The number of target limb and target lesions were determined from site-reported information; the number of target lesions was reported differently from the imaging core laboratory.



# Total IN.PACT Imaging Cohort Outcomes through 12 Months\*



\*Duplex Core lab and Independent clinical events committee-adjudicated

# Total IN.PACT **Imaging Cohort** Safety Outcomes through 12 Months

12-month Safety	Total IN.PACT Imaging Cohort		
	DCB (N=926 Subjects)	PTA (N=143 Subjects)	P-value
Primary Safety Endpoint <sup>1</sup>	94.1%	78.0%	<0.001
Major Adverse Events <sup>2</sup>	9.0%	22.7%	<0.001
All-cause death	2.6%	0.0%	0.061
Major Target Limb Amputation	0%	0%	-
Clinically-driven TVR <sup>3</sup>	6.4%	22.0%	<0.001
Thrombosis	2.4%	2.8%	0.767

1. Primary Safety Endpoint is a composite of freedom from device- and procedure-related mortality through 30 days, freedom from major target limb amputation and TLR within 12 months post-index procedure

2. Major adverse events is defined as all-cause mortality, clinically-driven TVR, major target limb amputation, thrombosis at the target lesion site

3. Clinically-driven TVR is defined as any re-intervention within the target vessel due to symptoms or drop of ABI of  $\geq 20\%$  or  $> 0.15$  when compared to post-index procedure baseline ABI

# Total IN.PACT Imaging Cohort

## Predictors of Loss of Patency Through 12 Months

Variables	Overall imaging cohort		Overall imaging cohort: DCB subjects only		Overall imaging cohort: PTA subjects only	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
<b>Clinical Characteristic Predictors</b>						
Age, years	–	–	0.98 (0.96-1.00)	.028	–	–
Diabetes mellitus (yes vs no)	1.53 (1.12-2.09)	.008	1.77 (1.18-2.64)	.006	–	–
Rutherford category ( >3 vs ≤3)	1.81 (1.14-2.86)	.012	2.23 (1.30-3.83)	.004	–	–
Previous peripheral revascularization on iliac (yes vs no)	1.63 (1.14-2.34)	.008	–	–	1.80 (1.05-3.09)	.032
Previous peripheral revascularization on popliteal (yes vs no)	1.58 (1.02-2.47)	.043	2.02 (1.24-3.30)	.005	–	–
<b>Lesion Characteristic Predictors</b>						
Lesion length, cm	–	–	–	–	1.10 (1.05-1.15)	<.001
Pre procedure Diameter Stenosis, %	–	–	1.02 (1.01-1.04)	.006	–	–
<b>Procedural Predictors</b>						
Treatment (DCB vs PTA)	0.15 (0.10-0.23)	<.001	–	–	–	–
No. of study balloons used (multiple vs single)	1.39 (0.94-2.04)	.096	–	–	–	–

# Total IN.PACT Imaging Cohort

## Predictors of Loss of Patency Through 12 Months

Predictors of loss of patency	DCB	PTA
	Age, years	✓
Diabetes mellitus (yes vs no)	✓	
Rutherford category ( >3 vs ≤3)	✓	
Previous peripheral revascularization on iliac (yes vs no)		✓
Previous peripheral revascularization on popliteal (yes vs no)	✓	
Lesion length, cm		✓
Pre procedure Diameter Stenosis, %	✓	

- DCB and PTA groups have different predictors for loss of patency in this multivariable analysis.
- The patients with these predictors need to be closely followed up.
- Lesion length, which is the strongest predictor for loss of patency in era of endovascular intervention, was not significantly associated with loss of patency in DCB group. On the other hands, % diameter stenosis was statistically significant.

# Total IN.PACT Imaging Cohort

## Predictors of Reintervention Through 12 Months

Variables	Overall imaging cohort		Overall imaging cohort: DCB subjects only		Overall imaging cohort: PTA subjects only	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
<b>Clinical Characteristic Predictors</b>						
Age, years	–	–	<b>0.96 (0.94-0.99)</b>	<b>.004</b>	–	–
Diabetes mellitus (yes vs no)	1.53 (0.97-2.41)	.065	–	–	–	–
Rutherford category (>3 vs ≤3)	2.85 (1.64-4.94)	<.001	<b>3.92 (2.02-7.61)</b>	<b>&lt;.001</b>	–	–
Coronary artery disease (yes vs no)	–	–	–	–	<b>2.78 (1.21-6.41)</b>	<b>.016</b>
BMI, kg/m <sup>2</sup>	–	–	–	–	<b>0.88 (0.80-0.97)</b>	<b>.009</b>
Previous peripheral revascularization on BTK arteries (yes vs no)	–	–	–	–	<b>4.12 (1.36-12.50)</b>	<b>.012</b>
Previous peripheral revascularization on femoral profunda (yes vs no)	–	–	–	–	<b>5.49 (1.25-24.21)</b>	<b>.024</b>

# Total IN.PACT Imaging Cohort

## Predictors of Reintervention Through 12 Months

Variables	Overall imaging cohort		Overall imaging cohort: DCB subjects only		Overall imaging cohort: PTA subjects only	
	HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
<b>Lesion Characteristic Predictors</b>						
Lesion length, cm	1.02 (1.00-1.05)	.065	–	–	–	–
Subject with totally occluded lesions (yes vs no)	2.39 (1.43-3.99)	<.001	2.43 (1.28-4.62)	.007	3.29 (1.41-7.66)	.006
No. of lesions per subjects	1.62 (1.17-2.26)	.004	1.73 (1.22-2.46)	.002	–	–
Outflow impaired (yes vs no)	–	–	1.95 (1.09-3.46)	.023	–	–
<b>Procedural Predictors</b>						
Treatment (DCB vs PTA)	0.15 (0.09-0.26)	<.001	–	–	–	–
Subject received no pre- or post dilation (yes vs no)	3.01 (1.61-5.62)	<.001	3.16 (1.42-7.02)	.005	–	–

# Total IN.PACT Imaging Cohort

## Predictors of Reintervention Through 12 Months

### Predictors of Reintervention

	DCB	PTA
Rutherford category >3	✓	
Subject received no pre- or post dilation	✓	
CTOs	✓	✓
No. of lesions per subjects	✓	
Age	✓	
Outflow impaired	✓	
BMI		✓
Coronary artery disease		✓
Previous peripheral revascularization on BTK arteries		✓
Previous peripheral revascularization on femoral profunda		✓

- DCB and PTA groups have different predictors for reintervention in this multivariable analysis.
- The patients with these predictors need to be closely followed up.
- Anatomical predictors such as lesion length, calcification and vessel diameter, which are usually considered as predictor of recurrence in the previous practice, did not show up as predictors in this analysis

# Total IN.PACT **Imaging Cohort** Predictors Through 12 Months in DCB arm

## Predictors of **loss of patency**

Age

Rutherford category >3

Diabetes mellitus

Pre procedure diameter Stenosis, %

Previous peripheral revascularization on popliteal

## Predictors of **reintervention**

Age

Rutherford category >3

No. of lesions per subjects

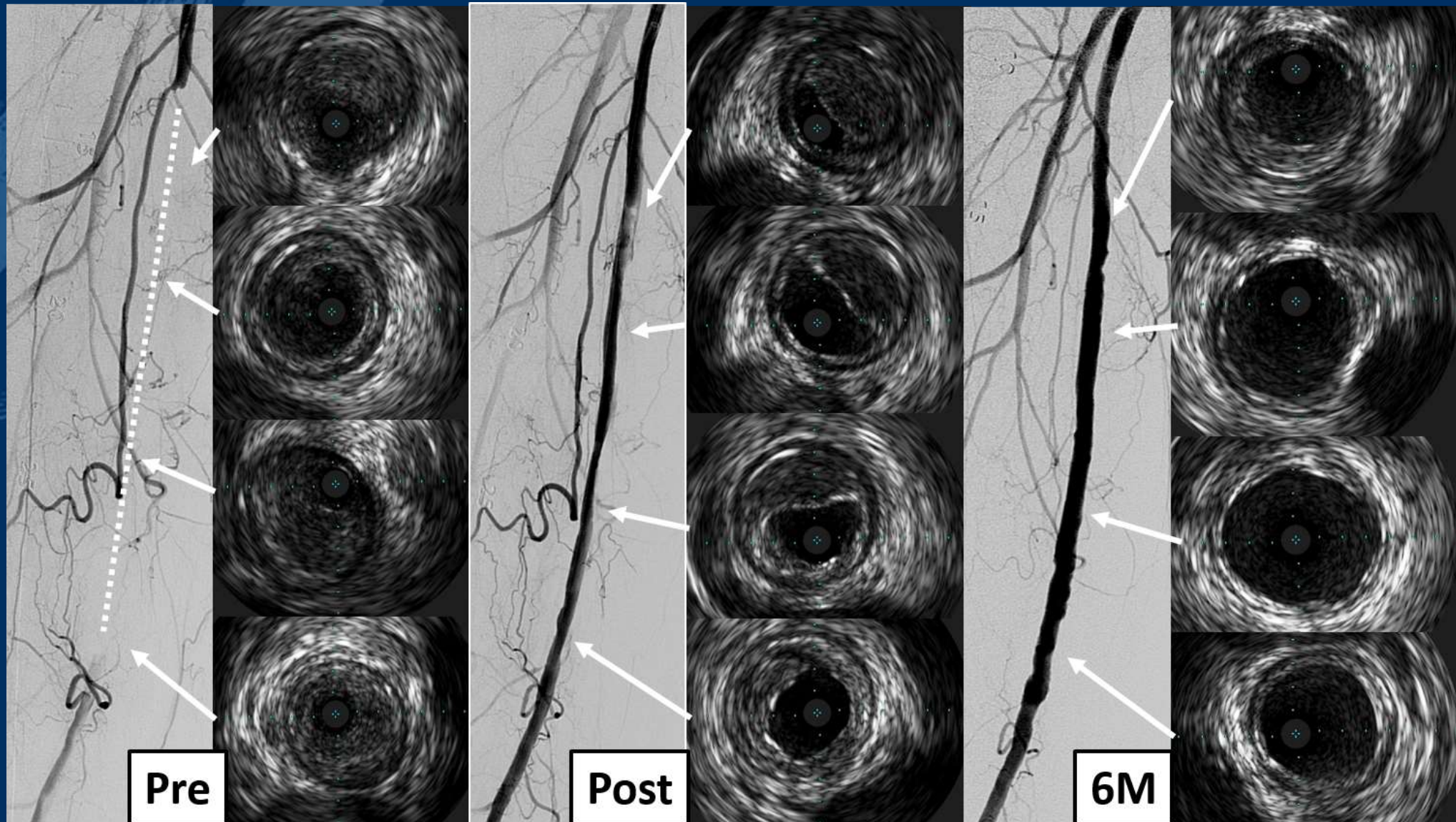
CTOs

Subject received no pre- or post dilation

Outflow impaired



# Small vessel and CTO but patent with positive remodeling@6-month



# Summary

- In this large, multi-ethnic, pooled, independently-adjudicated drug-coated balloon (DCB) series, the IN.PACT Admiral DCB demonstrated superior patency and freedom from reintervention over PTA through 12 months in the imaging analysis.
- The multivariable analysis from TOTAL IN. PACT showed that the dissection, calcification and lesion length were not the predictor of loss of primary patency or reintervention in DCB group. Those characteristics are usually considered as risk factors for occurrence of restenosis in previous SFA practice.
- Patients with CLI and greater degree of stenosis were common predictor for both loss of patency and reintervention after DCB treatment.
- There are more complex calcification and dissection in real practice. Further evaluation on vessel dissection and the level of calcification will be needed, where the efficacy of atherectomy is indicated.

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