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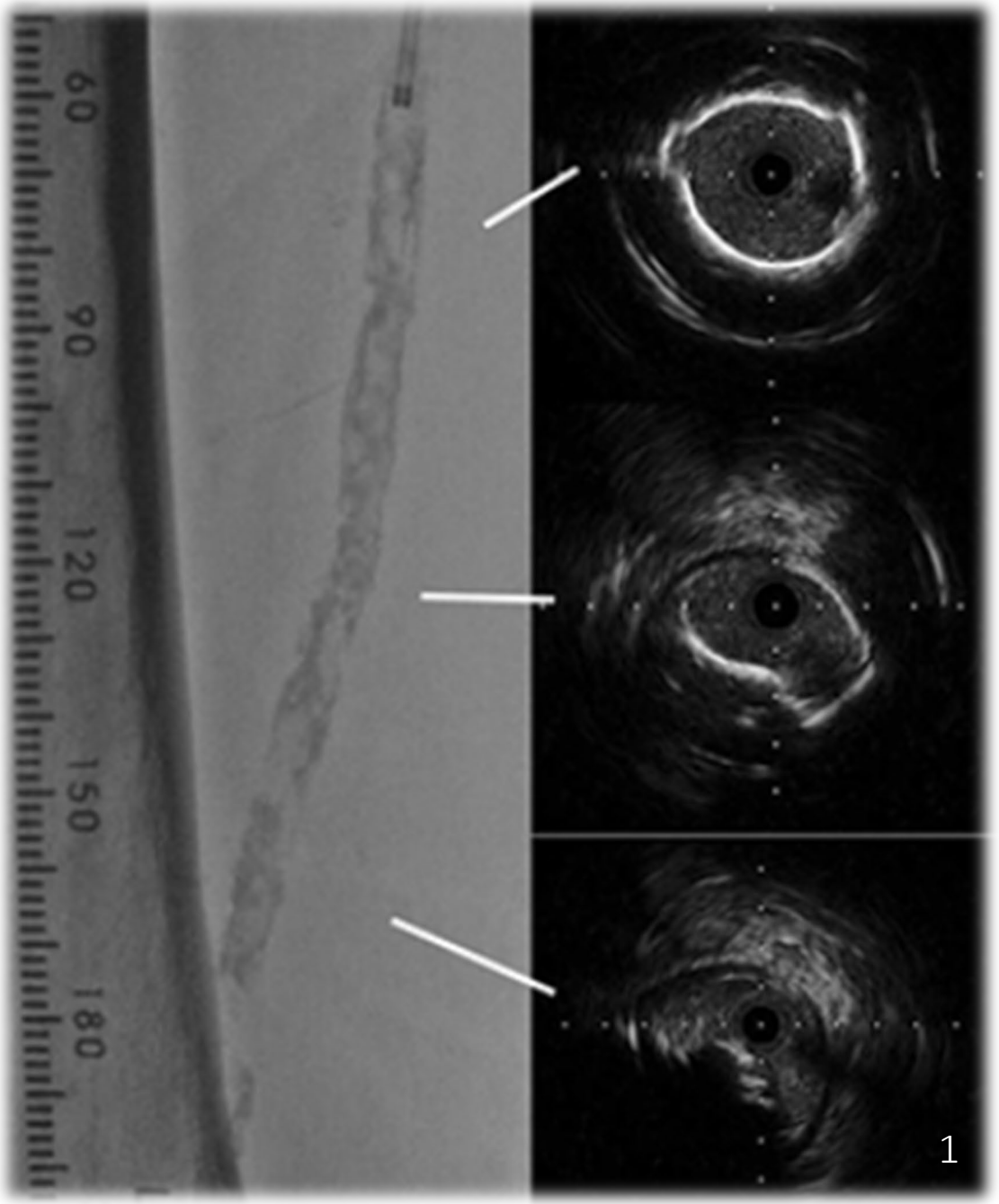
INTERVENTIONAL CHALLENGES IN CALCIFIED ARTERIES

Analysis of the BioMimics 3D® Vascular Stent System in Severe Calcium

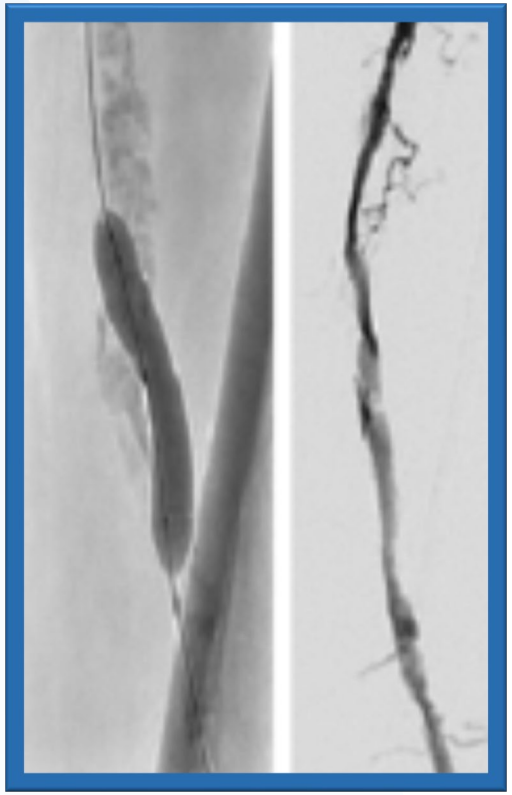


1. Fujihara, Masahiko, IntechOpen, 2017. 10.5772/67181.

TREATMENT CHALLENGES WITH CA+

DISSECTION

RECOIL



EMBOLIZATION

INADEQUATE EXPANSION

STUDIES SUGGEST 46-64% OF PATIENTS HAVE SEVERE FEMOROPOPLITEAL CALCIUM[1]

1. Kamenskiy A., et al, Arterioscler Thromb Vasc Biol. 2018;38(4):e48-e57

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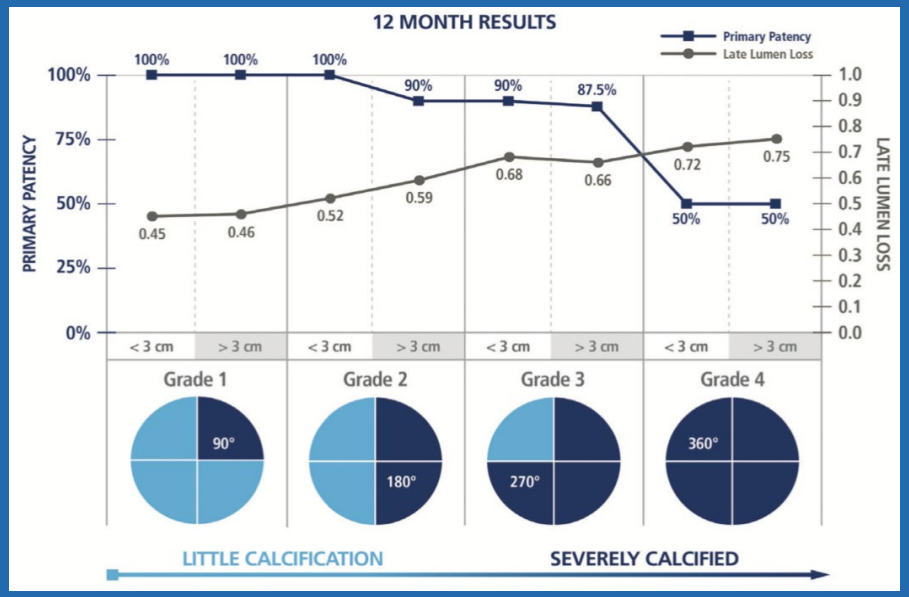
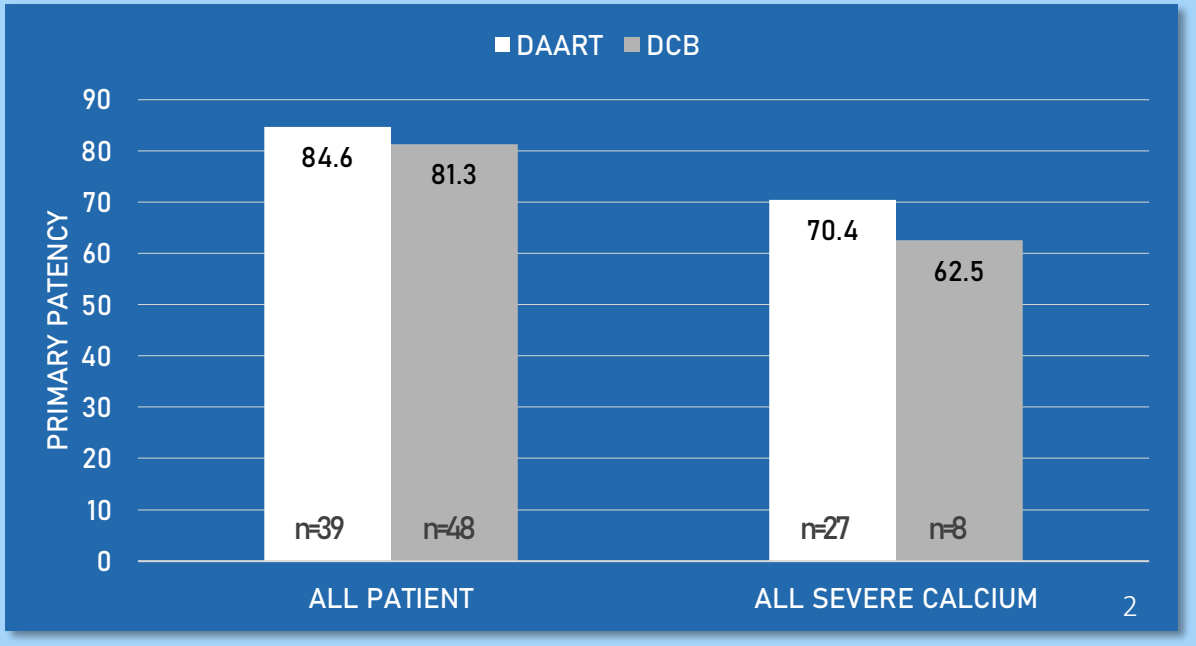
IMPACT OF CALCIUM ON DRUG ABSORPTION

CALCIUM IMPACT ON DCB



1

DEFINITIVE AR CALCIUM



2

BILATERAL WALL CALCIUM STRONGEST PREDICTOR OF POOR OUTCOME

1. Fanelli F, et al. Intervent Radiol. 2014 Aug;37(4):898-907
2. Zeller T, et al. Circ Cardiovasc Interv. 2017 Sep;10(9)

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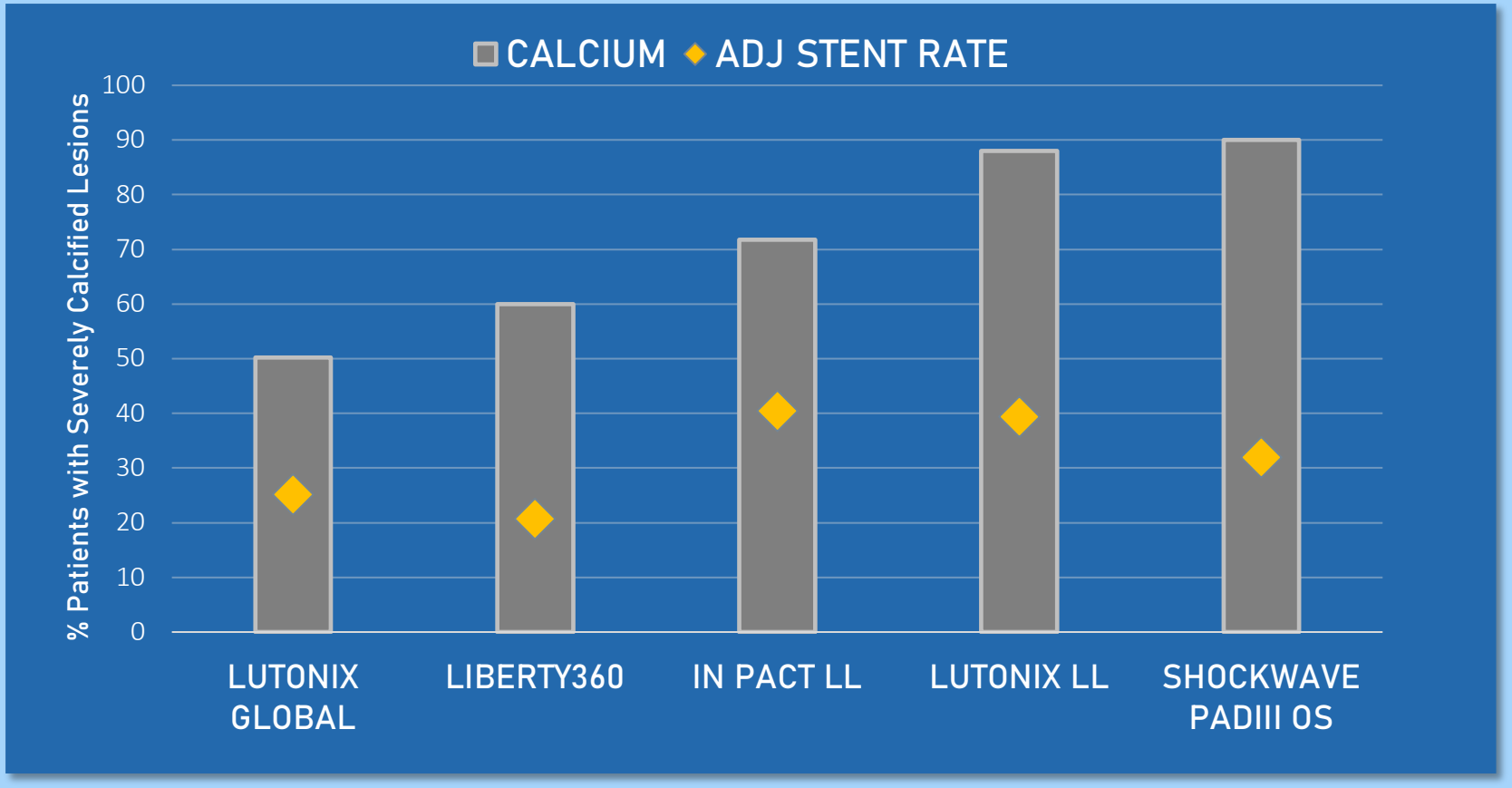
REQUIREMENTS OF ADJUNCTIVE STENTING IN REAL WORLD DATA SETS



STUDIES SUGGEST 20-40% OF PATIENTS REQUIRE SCAFFOLDING

1. Thieme M, et al. J Am Coll Cardiol Intv. 2017 Aug, 10 (16) 1682–1690
2. Mustapha J, et al. J Endovasc Ther. 2019 Apr;26(2):143-154
3. Ansel GM, et al. J Endovasc Ther. 2018 Dec;25(6):673-682
4. SHOCKWAVE: Intravascular Lithotripsy for Peripheral Artery Calcification: Interim Analysis of 752 Patients From the Disrupt PAD III Observational Study Ehrin Armstrong, MD VIVA 2021

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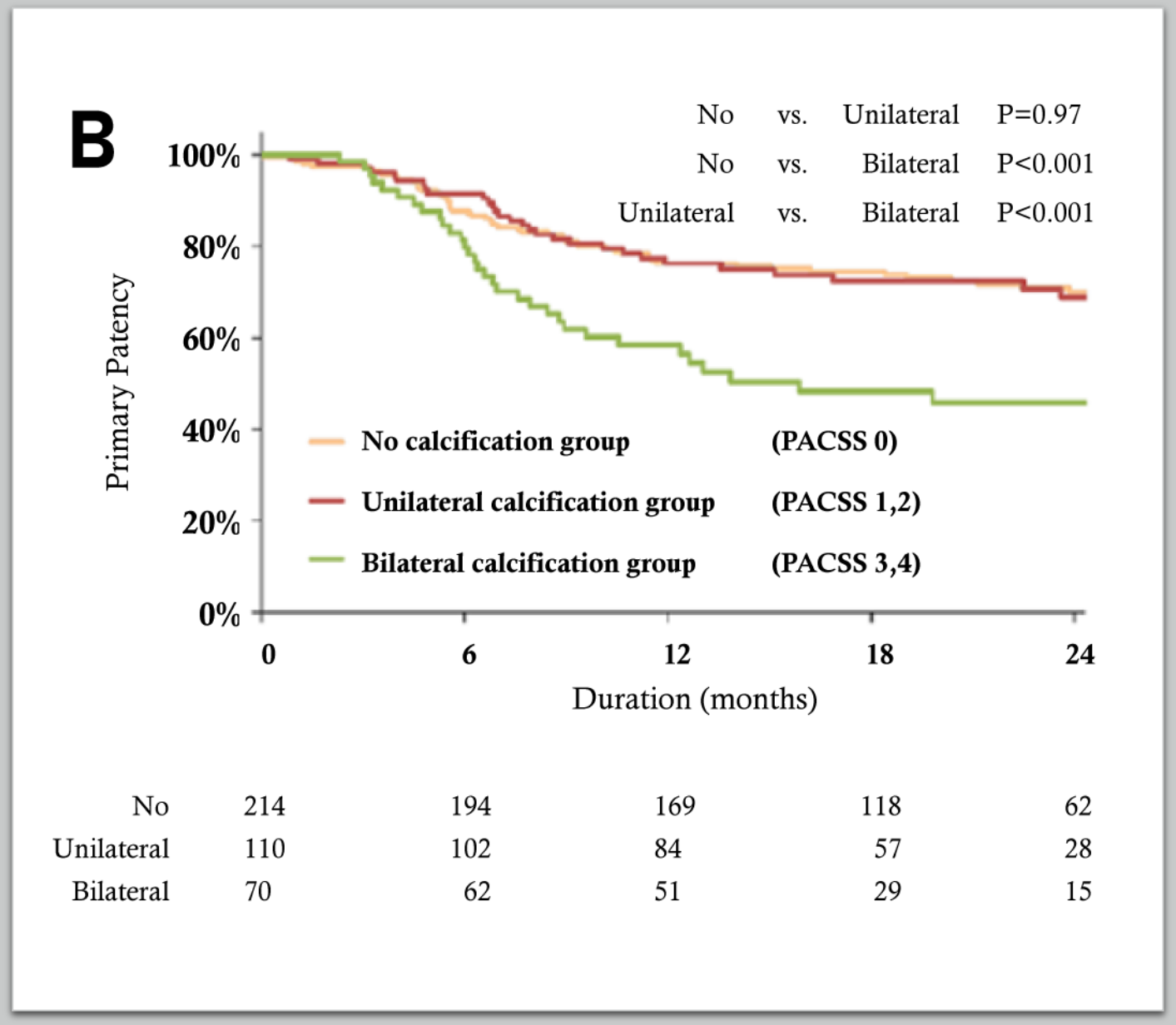
IMPACT OF SEVERE CALCIUM ON OUTCOMES

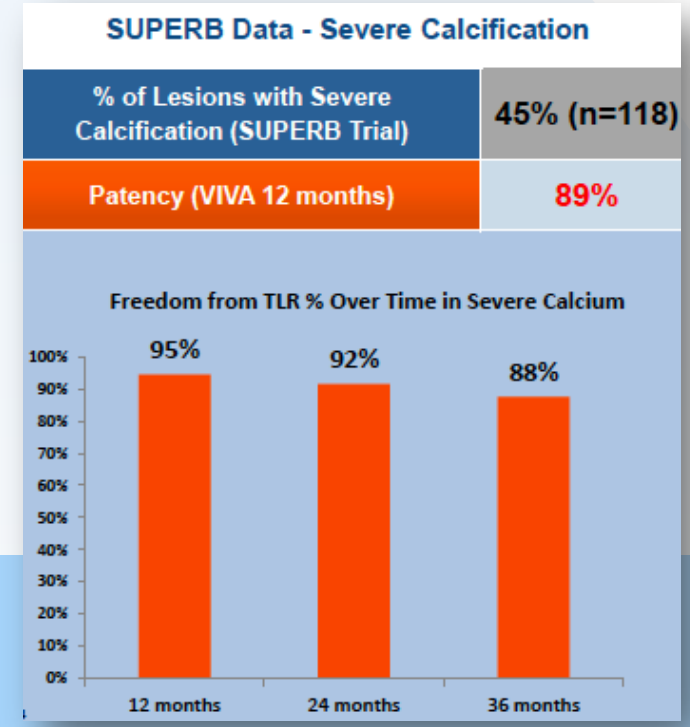
- 394 Consecutive patients analyzed to determine the impact of calcium on outcomes
- Most traditional stent platforms were included in the analysis (Zilver PTX)
- 18% of patients had bilateral wall Calcium
- Avg Lesion Length: 152mm

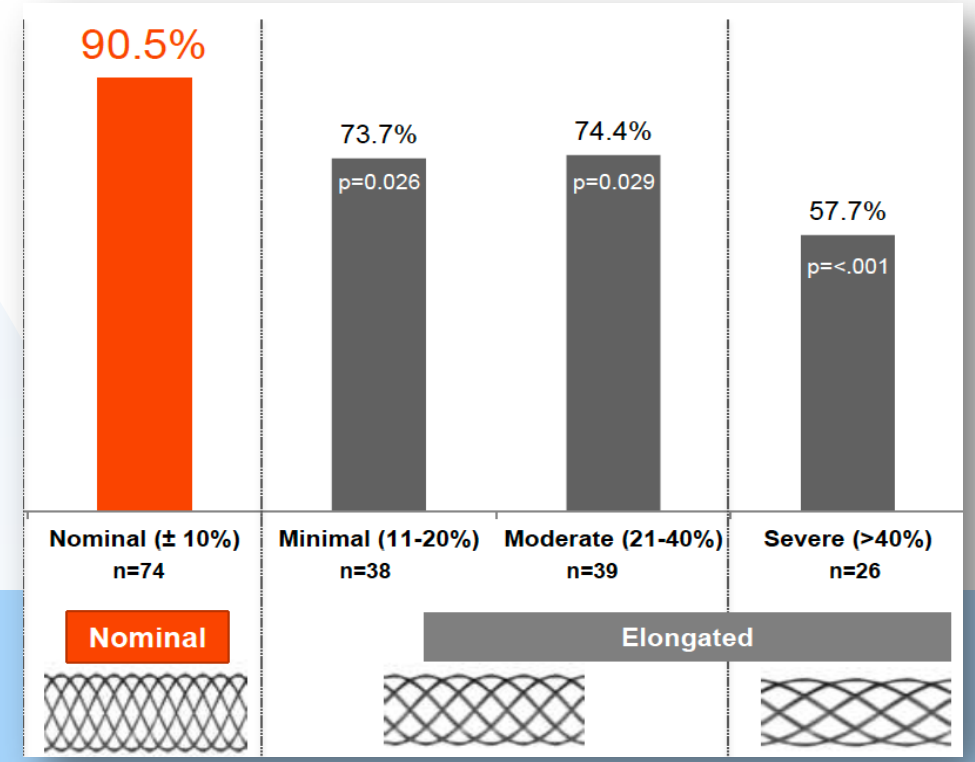
BILATERAL WALL CALCIUM ASSOCIATED WITH SIGNIFICANTLY WORSE OUTCOMES @ 2 YEARS

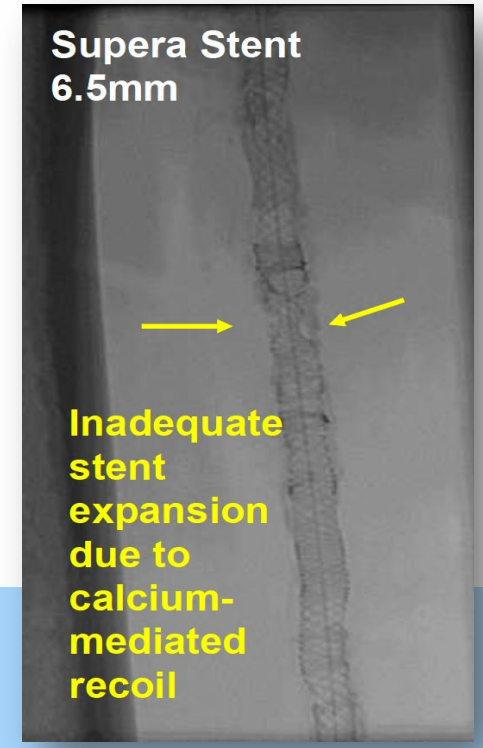


1. Okuno S, et al. J Endovasc Ther. 2016 Oct;23(5):731-7

OUTCOMES WITH SUPERA MIMETIC STENTS







EXCELLENT OUTCOMES, HOWEVER ELONGATION LEADS TO WORSE OUTCOMES

1. Garcia LA, et al. Catheter Cardiovasc Interv. 2017 Jun 1;89(7):1259-1267

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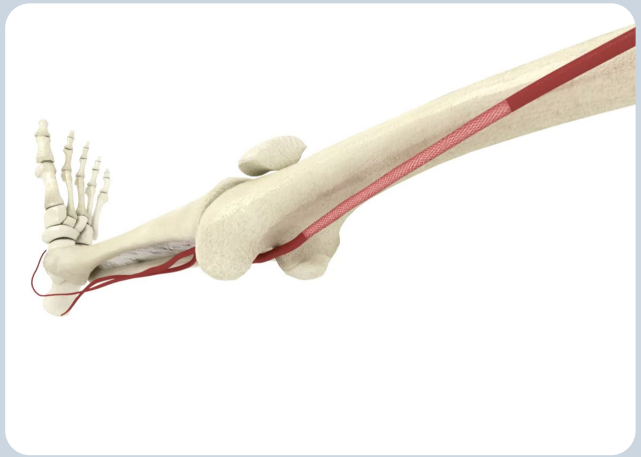
BioMimics 3D Purpose-built for the Femoropopliteal Segment

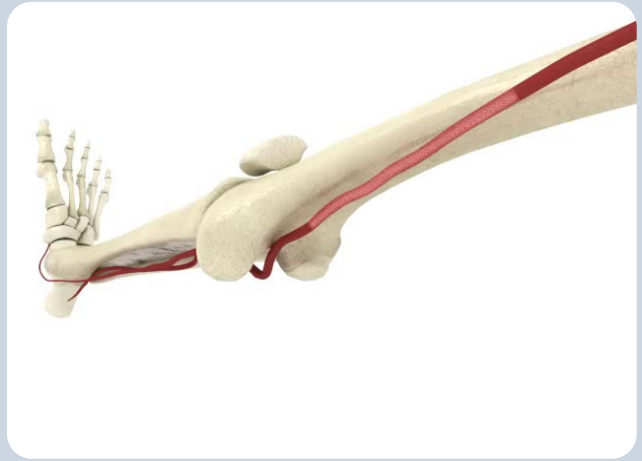
BIOMIMETIC DESIGN[1]

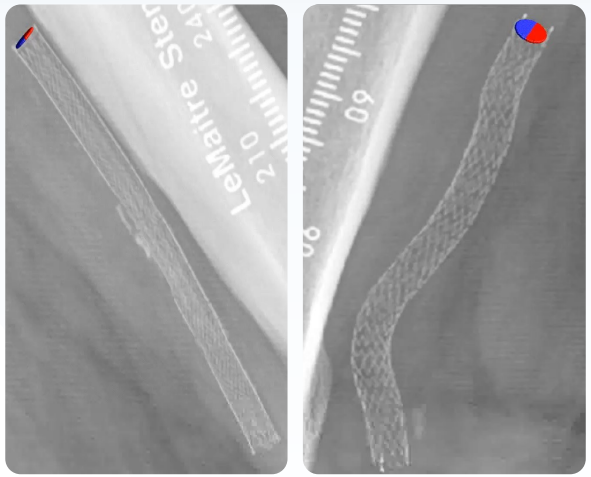
Mimics natural movement of the femoropopliteal segment

Aids in reducing localized trauma

Helps reduce risk of stent fracture in dynamic artery







ELEVATED WALL SHEAR STRESS[2]

Reduces restenosis by reducing thrombus formation and inflammation

Reduces Smooth Muscle Cell proliferation

Reduces neointimal hyperplasia

The BioMimics 3D Vascular Stent System has FDA, PMDA and CE Mark approval.
CAUTION: Federal law restricts this device to sale by or on the order of a physician.

1. Data on file at Veryan Medical
2. *Murphy EA,* Cardiovascular Engineering and Technology 2012

The MIMICS Clinical Program

MIMICS *FIH*	MIMICS *RCT*	MIMICS *2*	MIMICS 3D	MIMICS 3D *USA*	MIMICS *et seq*
N = 10 1 site Germany	N = 50 8 sites Germany	N = 271 43 sites USA/Japan/Germany	N = 507 23 sites Pan European	N = c. 500 c. 40 sites USA	N = c. 400 Multiple sites Europe
• First in Human • FU - 1 year • Completed	• Randomised controlled trial • FU - 2 years • Completed	• IDE Registry • FU - 3 years • Completed	• Prospective Registry • FU - 3 years • Completed	• Prospective Registry • FU - 3 years • Enrolment ongoing	• Physician initiated prospective and retrospective registries • Enrolment ongoing

1750+
patients

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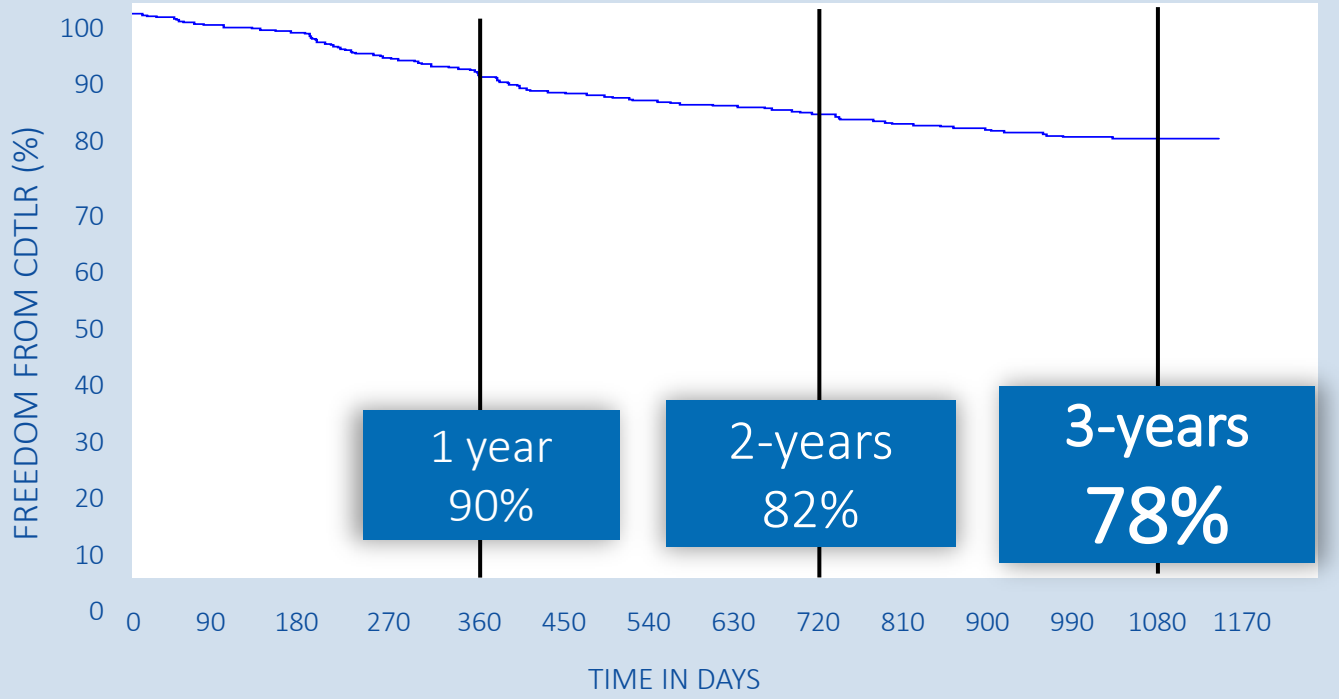
MIMICS 3D European Registry Results

Key baseline and procedural data

Mean lesion length	126mm +/-91mm
% CTO	57%
% Mod/Severe Ca++	53%
% CLI	24%
3-yr Primary Patency*	71%

Freedom from Clinically-Driven TLR at 3 Years



*ITT population. KM FF Loss of Patency at 36 mos. *PSVR >2.4*
Patency is defined as the composite of:
(1) freedom from more than 50% restenosis within the stented segment as observed by DUS or angiography and
(2) freedom from clinically-driven target lesion revascularization (TLR)
.

Data on file at Veryan Medical

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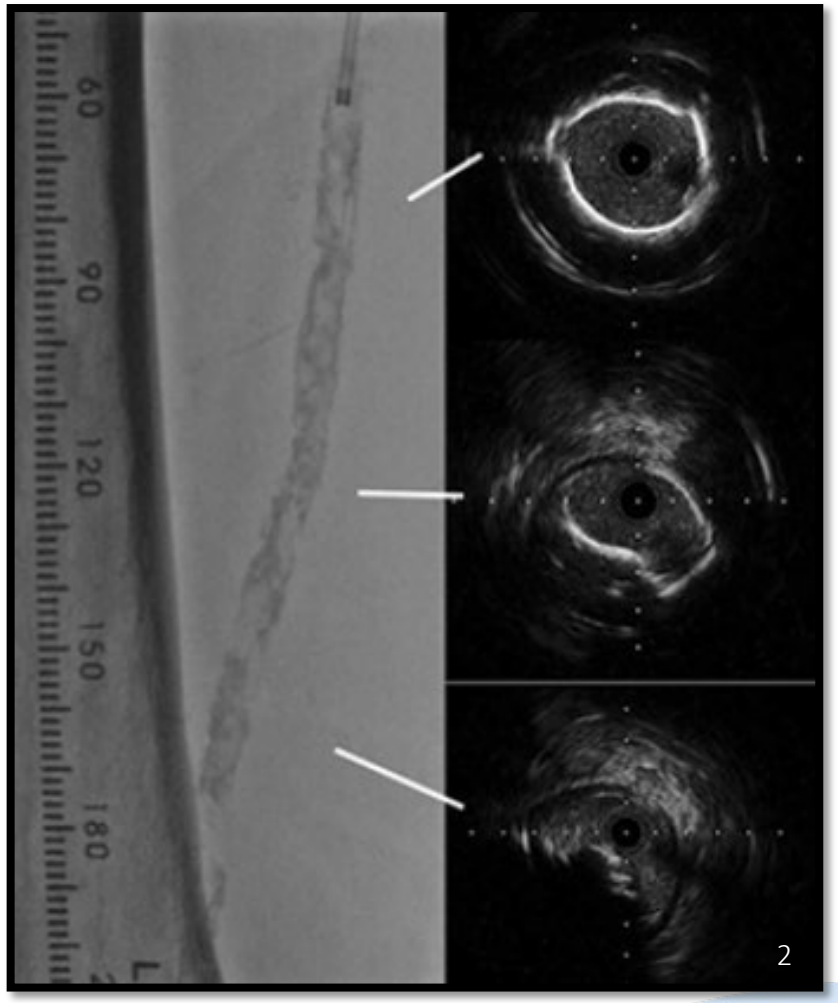
MIMICS 3D Calcium Subgroup Analysis[1]

As part of the 3-year follow up, a subgroup analysis was conducted to determine:

- Prevalence and severity of Calcium
- Impact on primary patency
- Impact on freedom from clinically-driven TLR
- Freedom from stent fracture



1. Data on File at Veryan Medical: MIMICS-3D database lock 07 Sept 2021
2. Fujihara, Masahiko, IntechOpen, 2017. 10.5772/67181.

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MIMICS 3D Patient Demographics

Table 1 Demographics and Medical History - ITT				
		PACSS Grade 2+	PACSS Grade 0/1	P-value
Age (years)	Mean±SD (n)	71.1 ± 10.2 (271)	68.8 ± 9.6 (234)	0.0140
	[min,max]	[45.0, 96.0]	[45.0, 88.0]	
Gender				
Male	n/N (%)	187 / 271 (69.0%)	144 / 234 (61.5%)	0.0910
Female	n/N (%)	84 / 271 (31.0%)	90 / 234 (38.5%)	0.0910
BMI	Mean±SD (n)	26.9 ± 4.5 (270)	26.7 ± 4.2 (233)	0.4635
	[min,max]	[15.9, 42.1]	[17.0, 44.2]	
Hypertension	n/N (%)	240 / 271 (88.6%)	193 / 234 (82.5%)	0.0561
Hypercholesterolemia / dyslipidemia	n/N (%)	183 / 271 (67.5%)	139 / 234 (59.4%)	0.0636
MI, CABG, PCI or coronary artery disease	n/N (%)	100 / 271 (36.9%)	65 / 234 (27.8%)	0.0362
Smoking	n/N (%)	174 / 271 (64.2%)	170 / 234 (72.6%)	0.0448
Current	n/N (%)	88 / 271 (32.5%)	102 / 234 (43.6%)	0.0128
Former	n/N (%)	86 / 271 (31.7%)	68 / 234 (29.1%)	0.5612
Diabetes mellitus	n/N (%)	111 / 271 (41.0%)	76 / 234 (32.5%)	0.0527
Renal insufficiency	n/N (%)	26 / 271 (9.6%)	15 / 234 (6.4%)	0.2526
Non-healing wound on the target limb	n/N (%)	44 / 271 (16.2%)	29 / 234 (12.4%)	0.2539
NOTE: P-value from Fisher's Exact test for categorical variables and from Student's t-test (means) or Wilcoxon Rank-Sum test (medians) for continuous variables.				

1. Data on file at Veryan Medical: MIMICS-3D database export 07 Sept 2021

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MIMICS 3D Lesion Characteristics

Table 3 Baseline Lesion Characteristics - ITT				
		PACSS Grade 2+	PACSS Grade 0/1	P-value
Number of Subjects	N	271	234	
Number of Lesions	N	277	239	
Max Reference Vessel Diameter (mm)	Mean±SD (n)	5.5 ± 0.8 (277)	5.4 ± 0.6 (239)	0.6345
Target Lesion Type				
De novo	n/N (%)	248 / 277 (89.5%)	218 / 239 (91.2%)	0.5533
Restenotic	n/N (%)	29 / 277 (10.5%)	21 / 239 (8.8%)	0.5533
Diameter Stenosis %	Mean±SD (n)	94.2 ± 8.5 (277)	95.1 ± 7.5 (239)	0.1834
	[min,max]	[50.0, 100.0]	[70.0, 100.0]	
Occlusions	n/N (%)	150 / 277 (54.2%)	143 / 239 (59.8%)	0.2125
Lesion Length (mm)	Mean±SD (n)	135.3 ± 93.6 (277)	115.3 ± 87.3 (239)	0.0017
	[min,max]	[10.0, 450.0]	[8.0, 400.0]	
Calcification				
None/Mild	n/N (%)	4 / 277 (1.4%)	239 / 239 (100.0%)	<.0001
Moderate	n/N (%)	126 / 277 (45.5%)	0 / 239 (0.0%)	<.0001
Severe	n/N (%)	147 / 277 (53.1%)	0 / 239 (0.0%)	<.0001
NOTE: P-value from Fisher's Exact test for categorical variables and from Student's t-test (means) or Wilcoxon Rank-Sum test (medians) for continuous variables. *Some patients presented with multiple lesions				

- 53% MOD/SEVERE CALCIFICATION
- 28% SEVERE/BILATERAL WALL CALCIFICATION

1. Data on file at Veryan Medical: MIMICS-3D database export 07 Sept 2021

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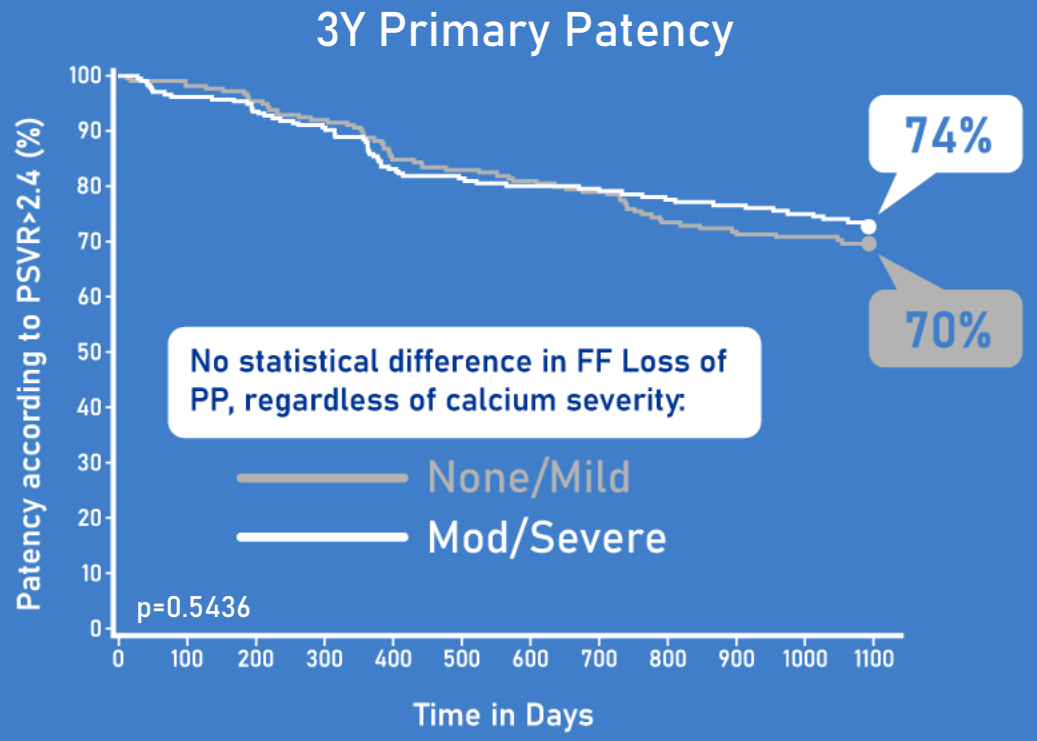
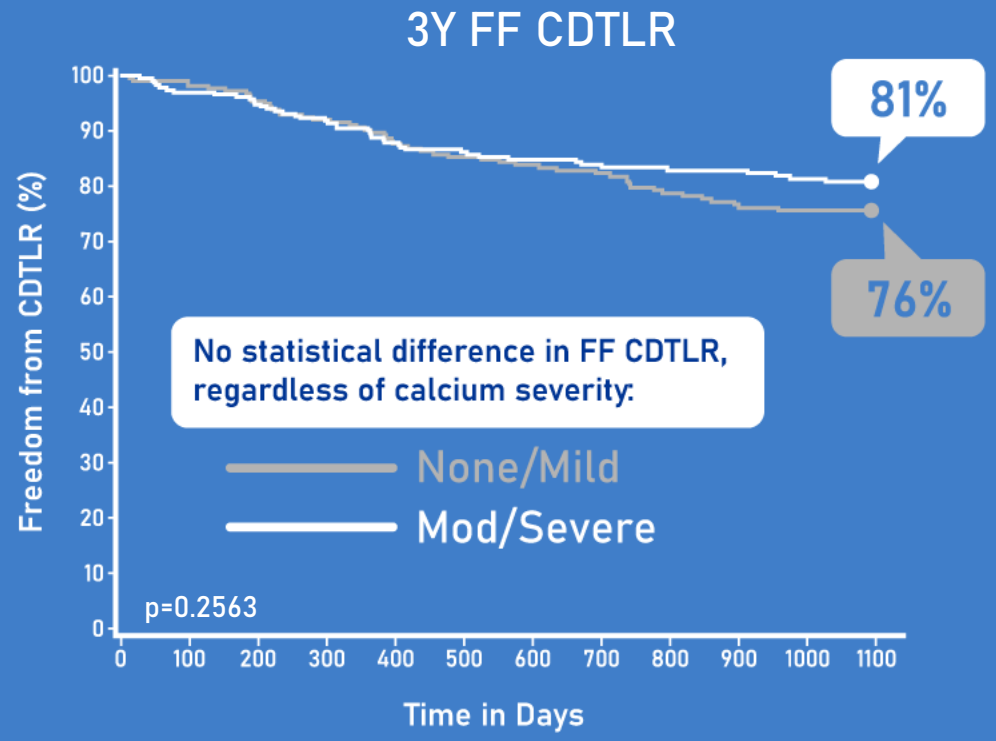
MIMICS 3D COMPARING OUTCOMES BASED ON CALCIUM SEVERITY





- 53% OF LESIONS PRESENTED WITH MOD/SEVERE CALCIUM
- NO STATISTICAL DIFFERENCE IN OUTCOMES BETWEEN COHORTS

1. Data on File at Veryan Medical: MIMICS-3D database lock 07 Sept 2021

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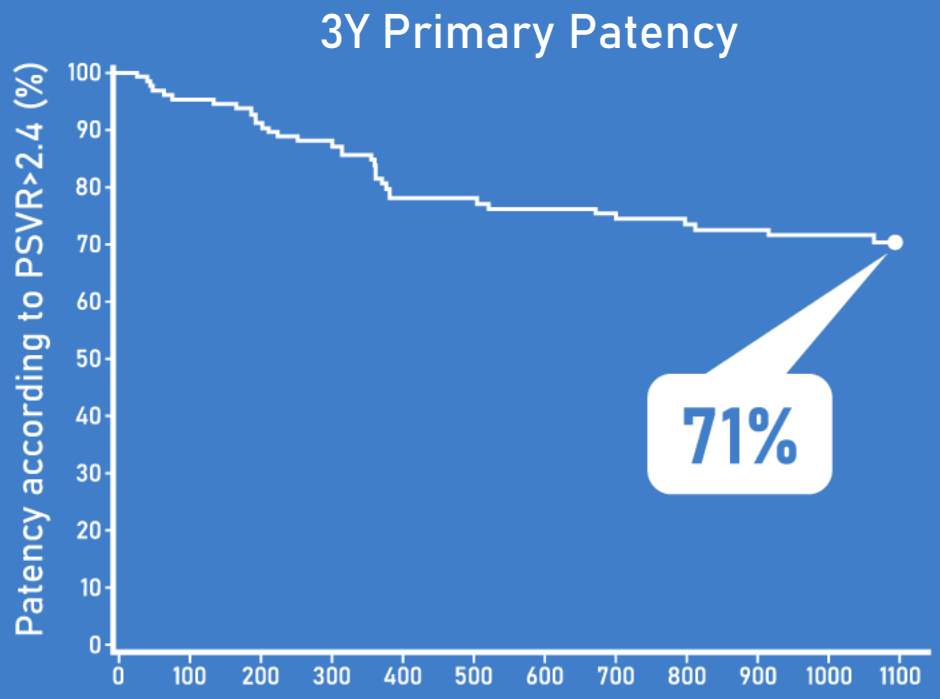
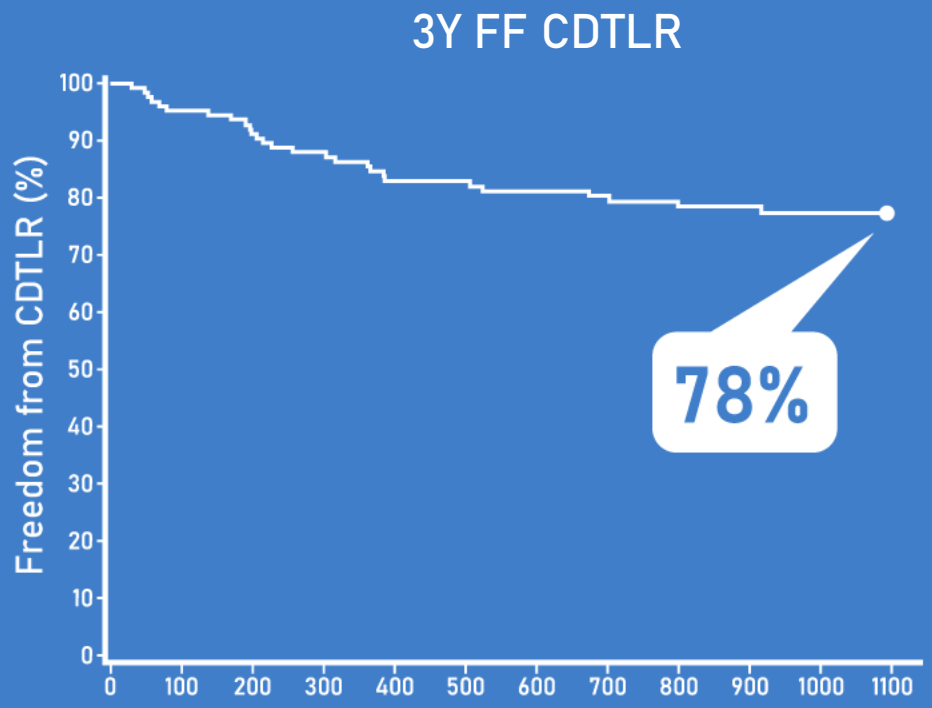
MIMICS 3D 3 YEAR OUTCOMES IN SEVERE CALCIUM COHORT





- 28% OF LESIONS HAD SEVERE/BILATERAL WALL CALCIFICATION
- 59% OF SEVERELY CALCIFIED LESIONS WERE CTO'S
- 144MM +/-94 AVG LESION LENGTH IN SEVERELY CALCIFIED COHORT

1. Data on File at Veryan Medical: MIMICS-3D database lock 07 Sept 2021

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CONCLUSIONS

Real world, prospective 500 patient registry with more complex patient and lesions demonstrate:

- 71% Freedom from loss of patency at 3 Years
- 78% Freedom from CDTLR at 3 Years

- Subgroup analysis performed to determine outcomes in patients with severe calcium
  - 53% of lesions exhibited moderate to severe calcification
  - 28% of lesions had severe, bilateral wall calcium
  - 3-year outcomes demonstrate:
    - 74% Primary patency at 3 years in mod/severe cohort
    - 71% Primary patency at 3 years in severely calcified cohort
    - No difference in between cohorts
    - 0.3% stent fracture rate through 3 year follow up in mod/severe subgroup

Data on file at Veryan Medical