

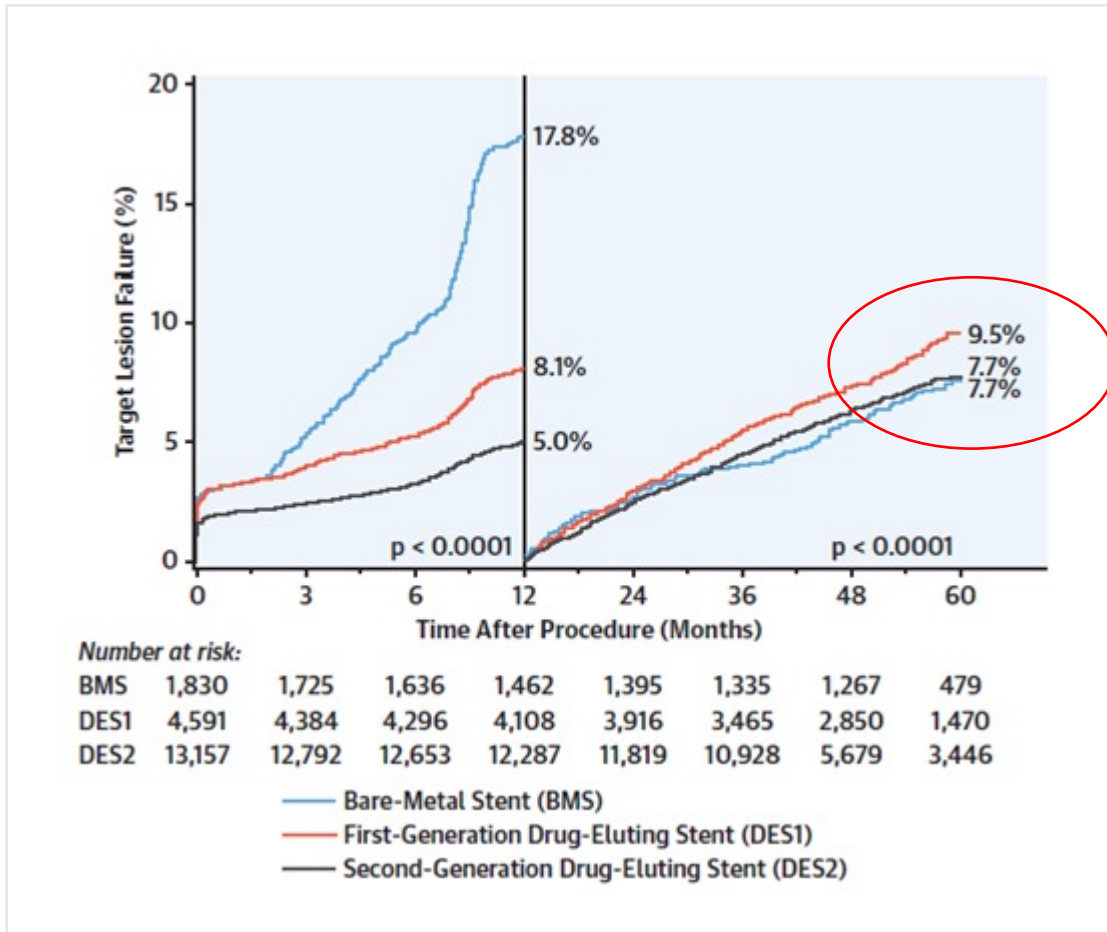
What is a bioadaptor

- Bioadaptor is a transforming adaptive implant designed to establish hemodynamic modulation, enabling vessel function and motion and restoration of homeostasis after PCI procedure.
- After the initial healing period post implantation, the bioadaptor:
 - Establishes pulsatility of the vessel
 - Modulates biphasic blood flow through the cardiac cycle
 - Enables rotational and axial movement of the vessel
 - Enables endothelial and smooth muscle cell biological exchange activating the plaque clearing mechanism of the artery



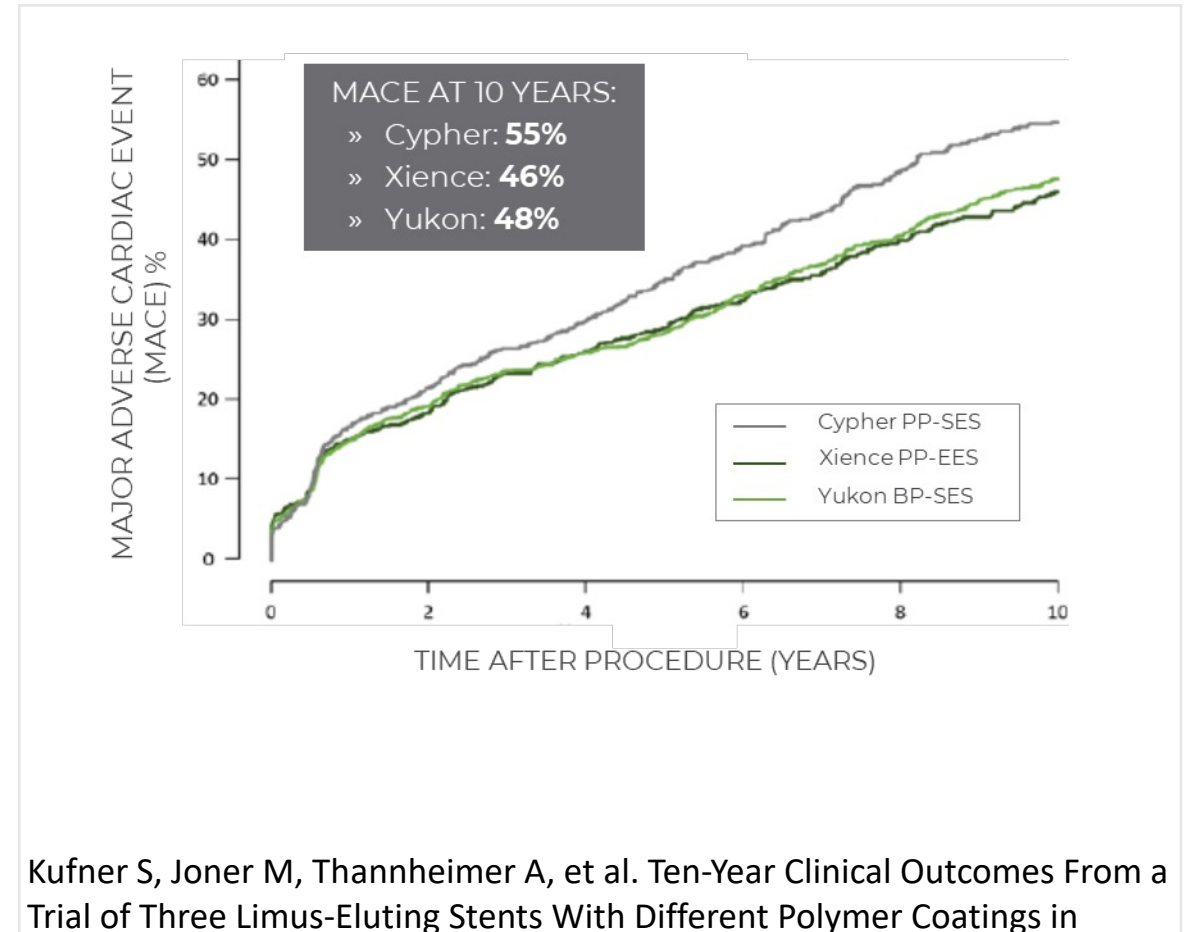
Persistent, Non-Plateauing 2-3% Annual Event Rate

TLF: BMS, 1st, 2nd Generation DES (meta-analysis)



Madhavan MV *et al.* J Am Coll Cardiol 2020;75:590-604

MACE: 10 Years – ISAR-TEST 4



Kufner S, Joner M, Thannheimer A, et al. Ten-Year Clinical Outcomes From a Trial of Three Limus-Eluting Stents With Different Polymer Coatings in Patients With Coronary Artery Disease – Results from the ISAR-TEST 4 Randomized Trial. *Circulation*. 2019;139:325-333

Adverse Events Remain High with Current DES

Research Original Investigation

JAMA Cardiology

Gregg W. Stone, MD; Takeshi Kimura, MD; Runlin Gao, MD; Dean J. Kerelakes, MD; Stephen G. Ellis, MD; Yoshinobu Onuma, MD, PhD; Bernard Chevalier, MD; Charles Simonton, MD; Ovidiu Dressler, MD; Aaron Crowley, MA; Ziad A. Ali, MD, DPhil; Patrick W. Serruys, MD, PhD

Although event-free survival for patients with coronary artery disease treated with metallic stents has improved with enhancements in technology and implantation technique, long-term studies have demonstrated an ongoing risk of restenosis or thrombosis arising from the implant site, which persists for at least 20 years, whether the stent was bare metal or drug eluting and regardless of the type of polymer or antiproliferative agent.¹⁻³ These adverse events, which occur after the first year at a rate of approximately 2% to 3% per year, may be attributed to strut fractures, loss of vessel compliance, vasomotion, and the capability for vascular adaptive remodeling, coverage of side branches, and the development of late neoatherosclerosis.⁴⁻⁷ A permanent implant may also impede noninvasive imaging (eg, computed tomographic angiography owing to blooming artifacts), may eliminate suitable bypass graft targets, and is suboptimal for treatment of stent failure owing to its obligate space-occupying effects. In addition, for cultural or religious reasons, many patients would prefer not to have a permanent implant. Drug-eluting bioresorbable scaffolds were designed to overcome many of these very late limitations of metallic drug-eluting stents (DES) by providing temporary mechanical support and antiproliferative effects similar to metallic DES but then completely resorbing within several years, normalizing vascular function and potentially improving late outcomes.⁸

The most widely studied bioresorbable scaffold is the poly-L-lactic acid (PLLA)-based everolimus-eluting Absorb bioresorbable vascular scaffold (BVS) (Abbott Vascular), which, in a porcine model, completely resorbs in approximately 3 years.^{9,10} Numerous randomized clinical trials

Key Points

Question Do the outcomes of bioresorbable scaffolds in patients with coronary artery disease vary during the course of their bioresorption?

Findings In this individual patient data pooled analysis and summary-level meta-analysis of 4 randomized clinical trials of a polymeric bioresorbable scaffold and a contemporary metallic drug-eluting stent in 3884 patients, scaffold-related adverse events increased within 3 years of implantation but not thereafter.

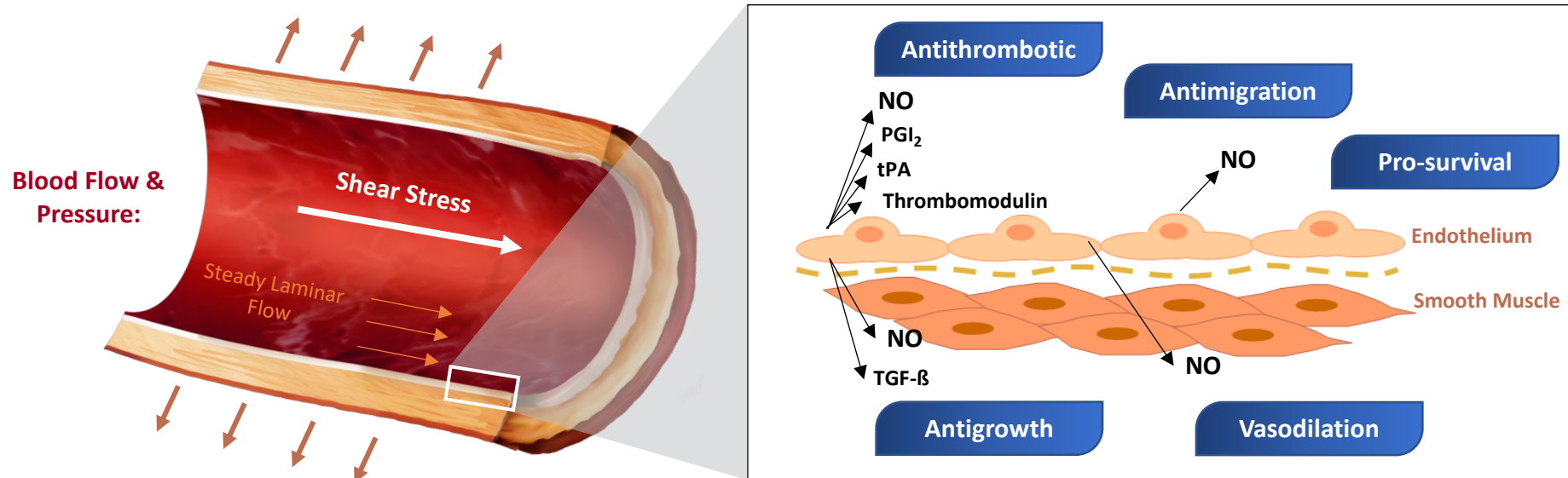
Meaning If new scaffolds are shown to have improved early results, bioresorbable scaffolds may be an acceptable alternative for many patients with coronary artery disease.

ing MEDLINE and the Cochrane database, <http://www.tctmd.com>, <http://www.clinicaltrials.gov>, <http://www.pcronline.com>, <http://www.clinicaltrialresults.org>, and <https://www.acc.org> using the keywords “randomized trial,” “drug-eluting stent,” “everolimus-eluting stent,” “Xience,” “bioabsorbable scaffold,” “bioresorbable scaffold,” “bioabsorbable stent,” and “bioresorbable stent” through July 21, 2019, in duplicate. The primary exclusion criteria were observational or nonrandomized study design, less than 5 years of follow-up data, lack of interval data between 0 to 3 years and 3 to 5 years, non-Absorb BVS, metallic DES with bioabsorbable polymers, editorials, letters, expert opinions, case reports/series, studies with duplicated data, and nonhuman studies. Two reviewers (Z.A.A. and G.W.S.) abstracted and reviewed the trials. Five-year data were available from 4 trials meeting these criteria in which pa-

“Adverse events, which occur after the first year at a rate of approximately 2% to 3% per year, may be attributed to **strut fractures, loss of vessel compliance, vasomotion, and the capability for vascular adaptive remodeling, coverage of side branches, and the development of late neoatherosclerosis.**”

Impact of Flow Dynamics on Vascular Health: *Optimal Flow & Shear Stress*

- In a **non-stented vessel**, under optimal biphasic flow dynamics, functional endothelial cells **protect** against **atherosclerosis and thrombosis** through the **production of nitric oxide (NO)** and other factors



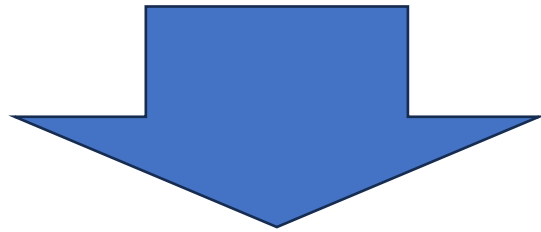
Adapted from Traub, O., et al., *Arterioscler Thromb Vasc Biol.* 1998; 18:677-685.

Stretching of the vessel wall (cyclic strain) during pulsatile flow leads to increased production of protective NO

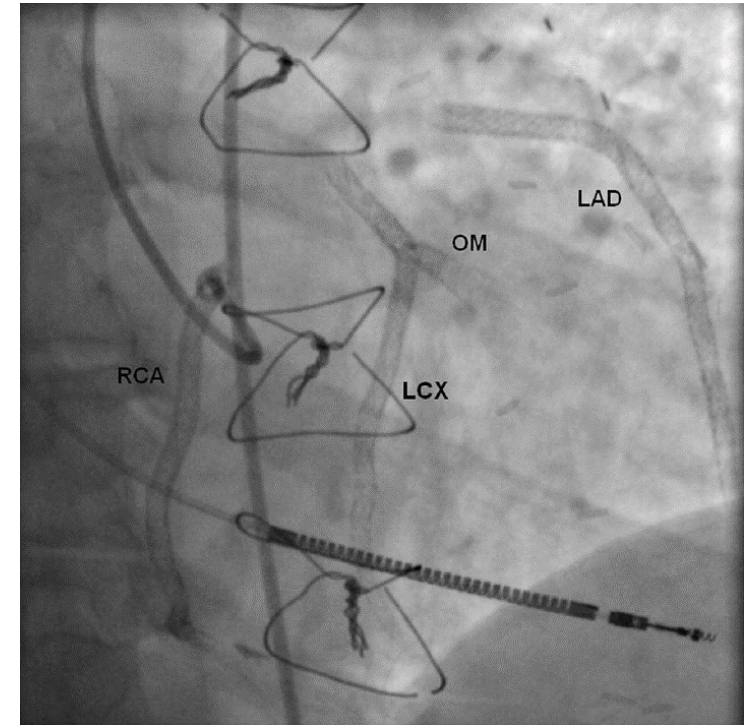
Pulsatile shear stress is also directly related to increased steady state levels of prostacyclin (PGI₂), the most potent natural inhibitor of platelet aggregation

Vascular homeostasis

The caging effect of stents drastically reduces natural vascular motion and physiology and can contribute to stent fractures, restenosis, myocardial infarctions, and cardiac death¹



Preserving the natural vascular motion and physiology by focusing on function, not only anatomy, is the modern standard of interventional coronary therapies^{2,3}




67 coronary stents: The patient had 28 catheterizations over 10 years, with stents placed in his native coronary arteries as well as in 3 bypass grafts. JACC Vol. 56, No. 19, 2010

1. Borovac JA, D'Amario D, Niccoli G. Neoatherosclerosis and Late Thrombosis After Percutaneous Coronary Intervention: Translational Cardiology and Comparative Medicine from Bench to Bedside. *Yale J Biol Med* 2017;90:463-70.
2. Julio Flavio Marchini, Vinicius Esteves, Pedro A. Lemos, Chapter 40 - Postpercutaneous Interventions: Endothelial Repair, Editor(s): Protásio L. Da Luz, Peter Libby, Antonio C.P. Chagas, Francisco R.M. Laurindo, *Endothelium and Cardiovascular Diseases*, Academic Press, 2018, Pages 591-596, ISBN 9780128123485,
3. EXPERT CONSENSUS Applied coronary physiology for planning and guidance of percutaneous coronary interventions. A clinical consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) of the European Society of Cardiology. *EuroIntervention* 2023;19:464-481. DOI: 10.4244/EIJ-D-23-00194

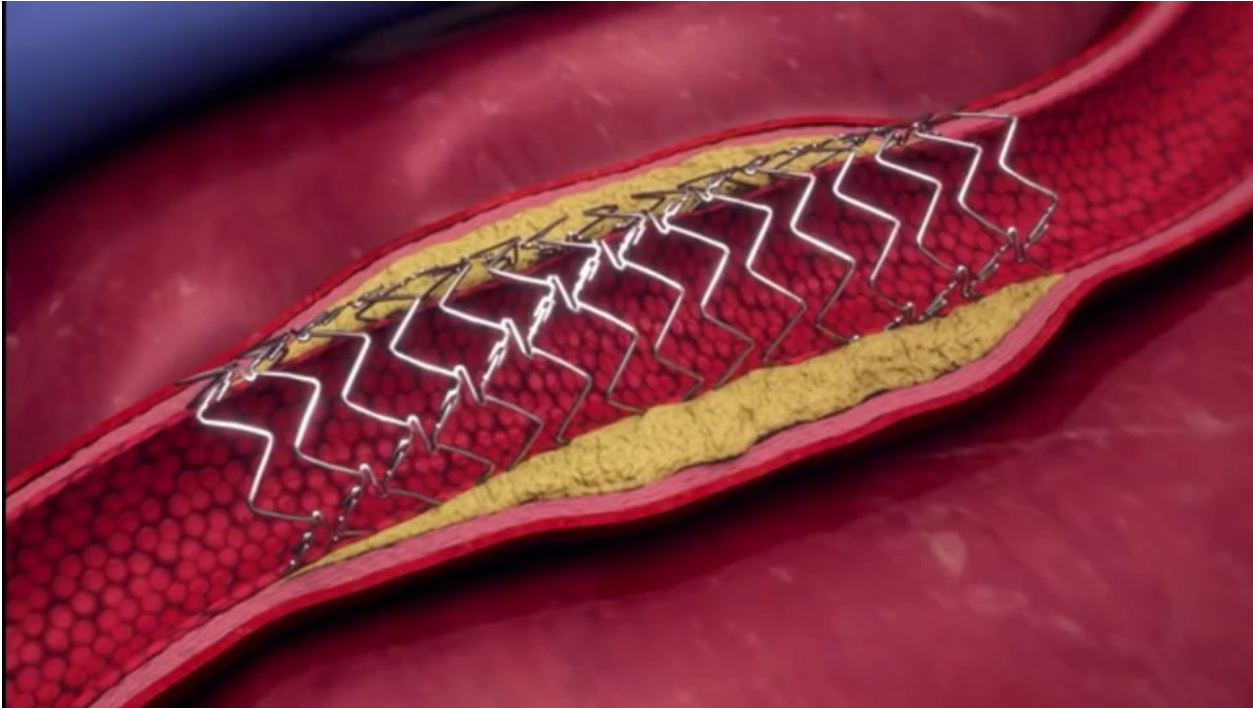
DynamX Coronary Bioadaptor System Design



- Three thin (71 μ m) Co-Cr helical sinusoid strands
- “Uncaging” expansion segments held by bioresorbable polymer , create temporary circumferential links connecting the helical strands
- Antiproliferative drug eluted over 3 months to control neointimal proliferation during vessel healing phase

Adaptive Hemodynamic Modulation

The thin polymer coating resorbs over six months allowing the three helical strands to separate and act as three independent prostheses embedded in the vessel wall, enabling hemodynamic modulation while providing dynamic support to the vessel.



- Establishes pulsatility of the vessel
- Modulates increased, biphasic blood flow through the cardiac cycle
- Enables rotational and axial movement of the vessel
- Enables endothelial and smooth muscle cell biological exchange activating the plaque clearing mechanism of the artery.



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Symposium Elixir

Du concept à la pratique clinique en passant par la physiologie

Julien Adjedj

Restaurer la physiologie



- Ouvrir l'artère (Ballon)
- Maintenir la lumière de l'artère (DES, BMS)
- Faire disparaître le scaffold (BVS)
- Redonner la mobilité à l'artère

Restaurer la physiologie

Strength and Deliverability

Sustained Dynamic Support of Diseased Vessel



RESTORE FLOW

*Acute
Performance
Similar to 2nd Gen*

- High device and procedure success
- High acute gain
- Low %DS



RELEASE

*The vessel to
enable motion
and function*

- Early uncaging at 6 months
- Restore pulsatility and compliance
- Increase blood flow volume
- Contractile SMC phenotype upregulation



RETURN

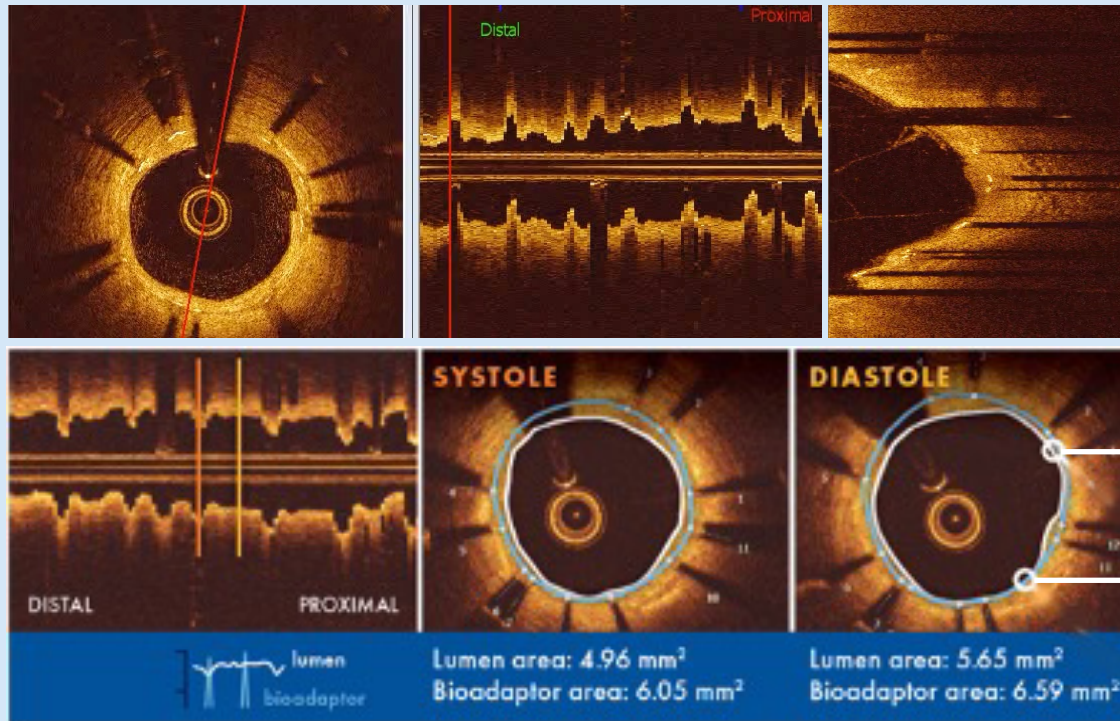
*Provide dynamic
scaffolding to
support natural
function*

- Reduce arterial stresses
- Improve hemodynamics
- Support positive remodeling
- Enable lesion/plaque stabilization

Restaurer la physiologie

RESTORATION OF PULSATILITY

Lumen area changes between systole and diastole cycles



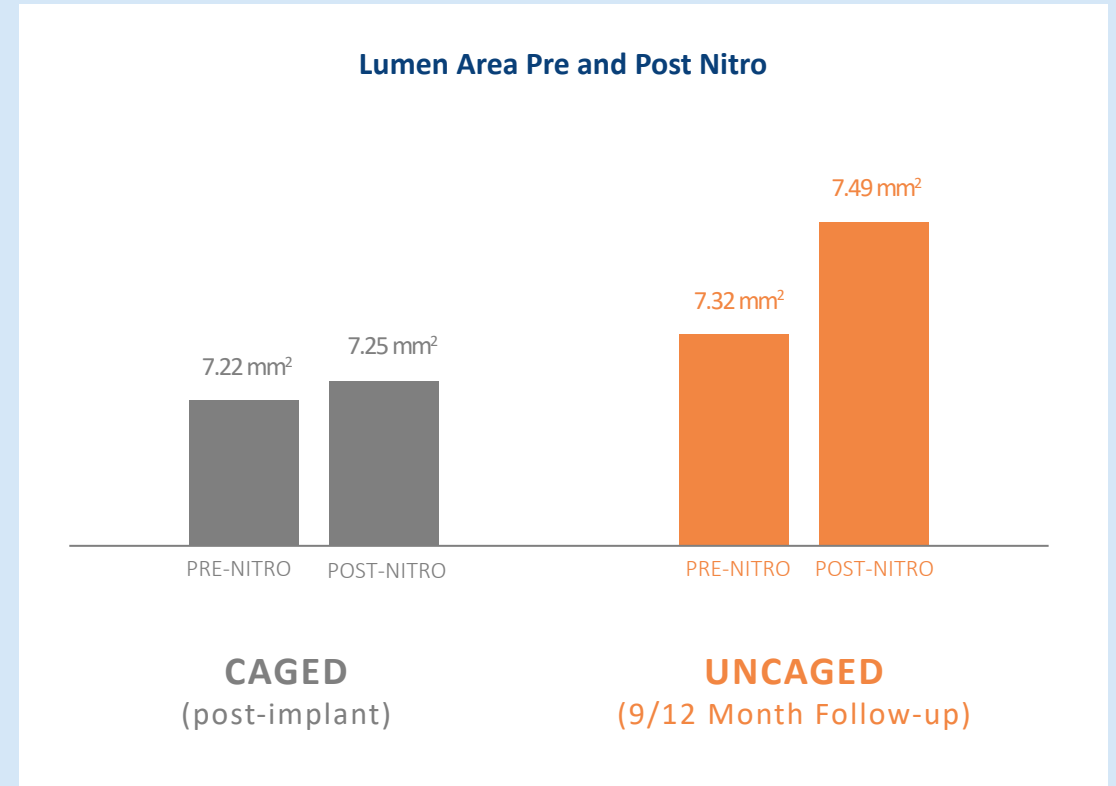
% increase between systole and diastole

Lumen area Δ 14%

Bioadapter area Δ 9%

RESPONSE TO CHEMICAL STIMULI

Uncaging allows the artery to respond to nitro



Paired IVUS-analysis (n=18)

Principe Physiologique

DynamX– Operating Principle To Restore Flow and Vessel Function



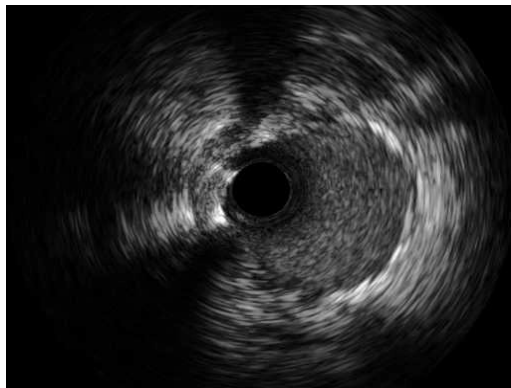
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Restoration of Flow

Restoration of Vessel Function

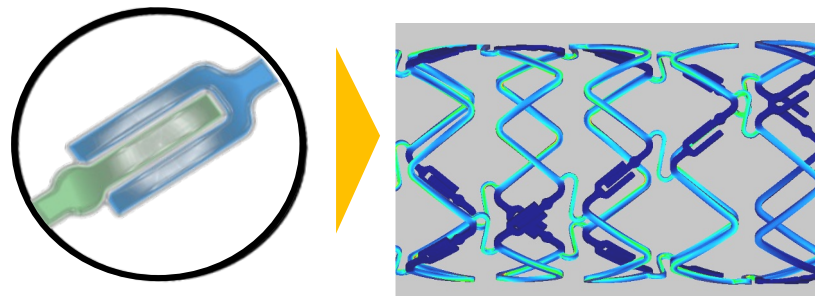


1. Connected, the device matches acute performance of standard of care DES

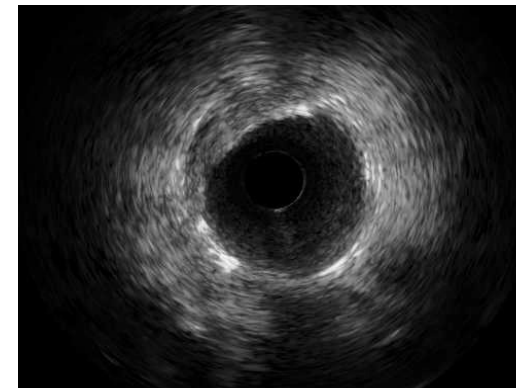


Patient image from Mechanistic study

2. By 6 months, the BASECOAT polymer resorbs separating the three helical strands



3. Return of normal vessel motion and function through the dynamic support of the vessel after unlocking the helical strands



Patient image from Mechanistic study

During neointima formation, helical strands become surrounded by smooth muscle cells* prior to unlocking of the device and uncaging the vessel while continuing to provide dynamic support of atherosclerotic vessel.

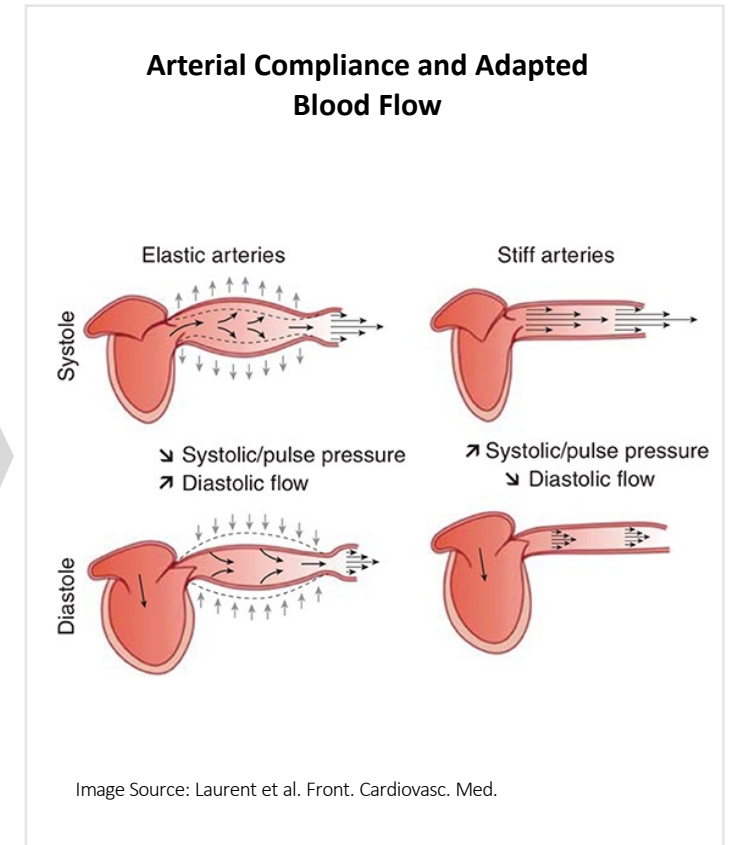
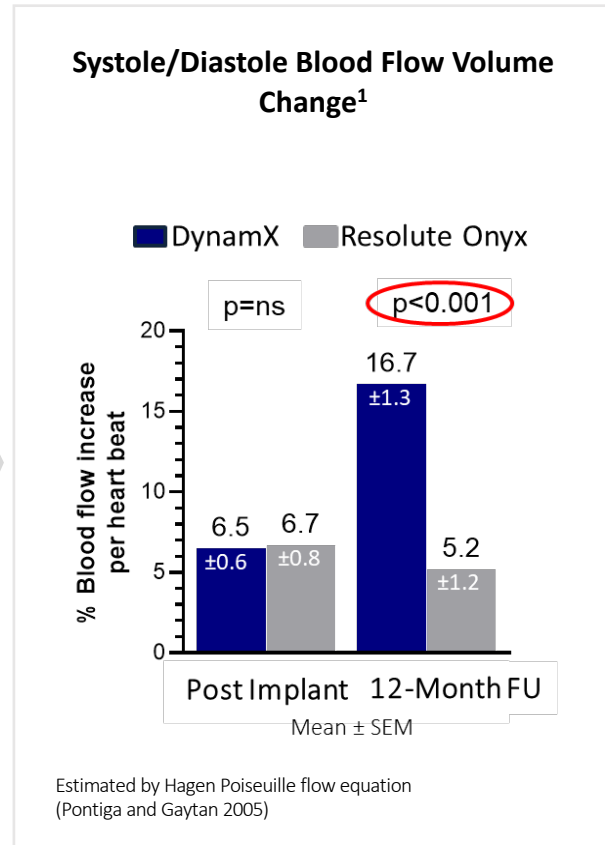
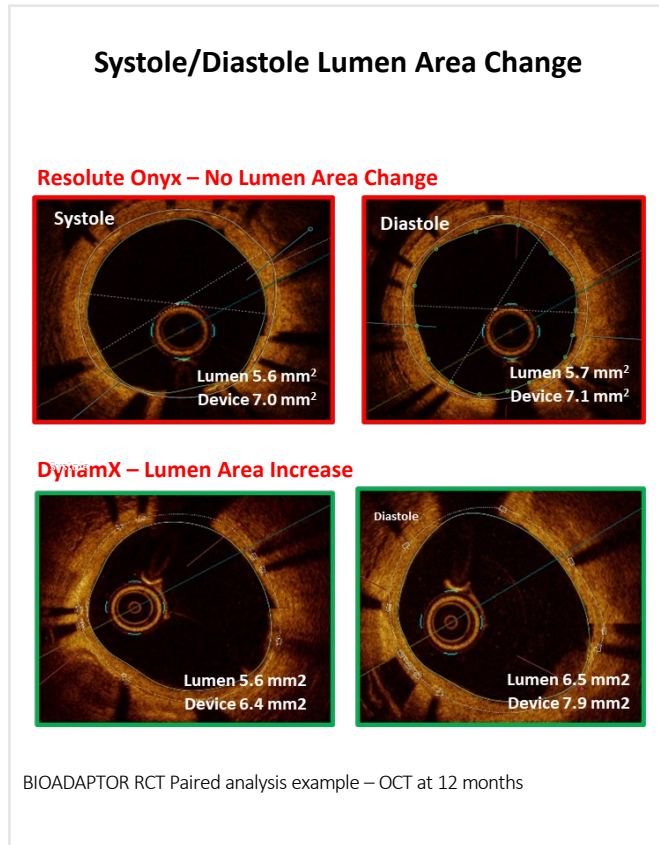
*Preclinical study. Data on file at Elixir Medical.

Principe Physiologique



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Return of Pulsatility Augmented Coronary Flow May Translate To Improved Microvascular Perfusion and Angina Symptoms

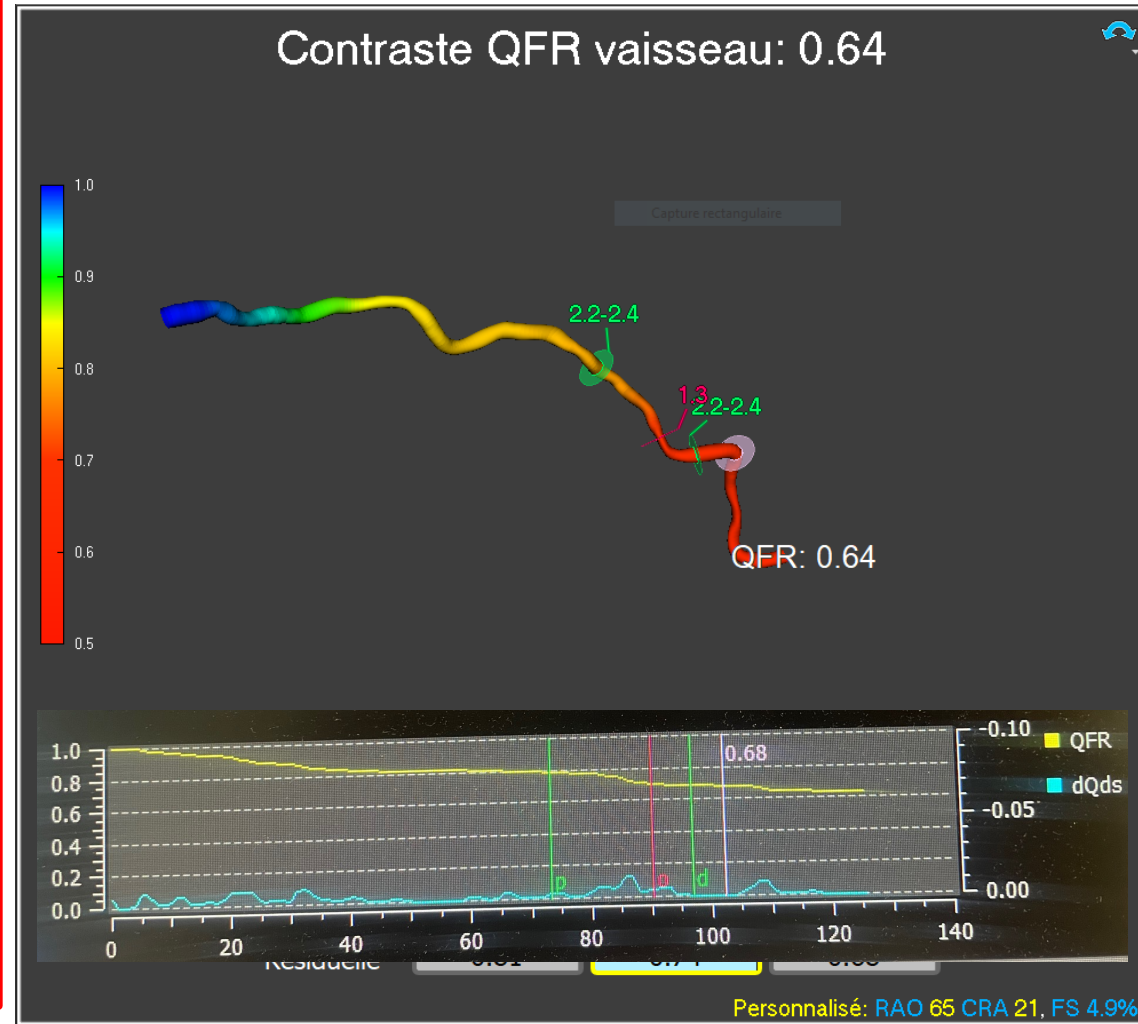


1. Saito S et al. 12-Months BIOADAPTOR-RCT. The Lancet eClinicalMedicine. 2023;65:102304.

Un cas pratique: patient de 81 ans



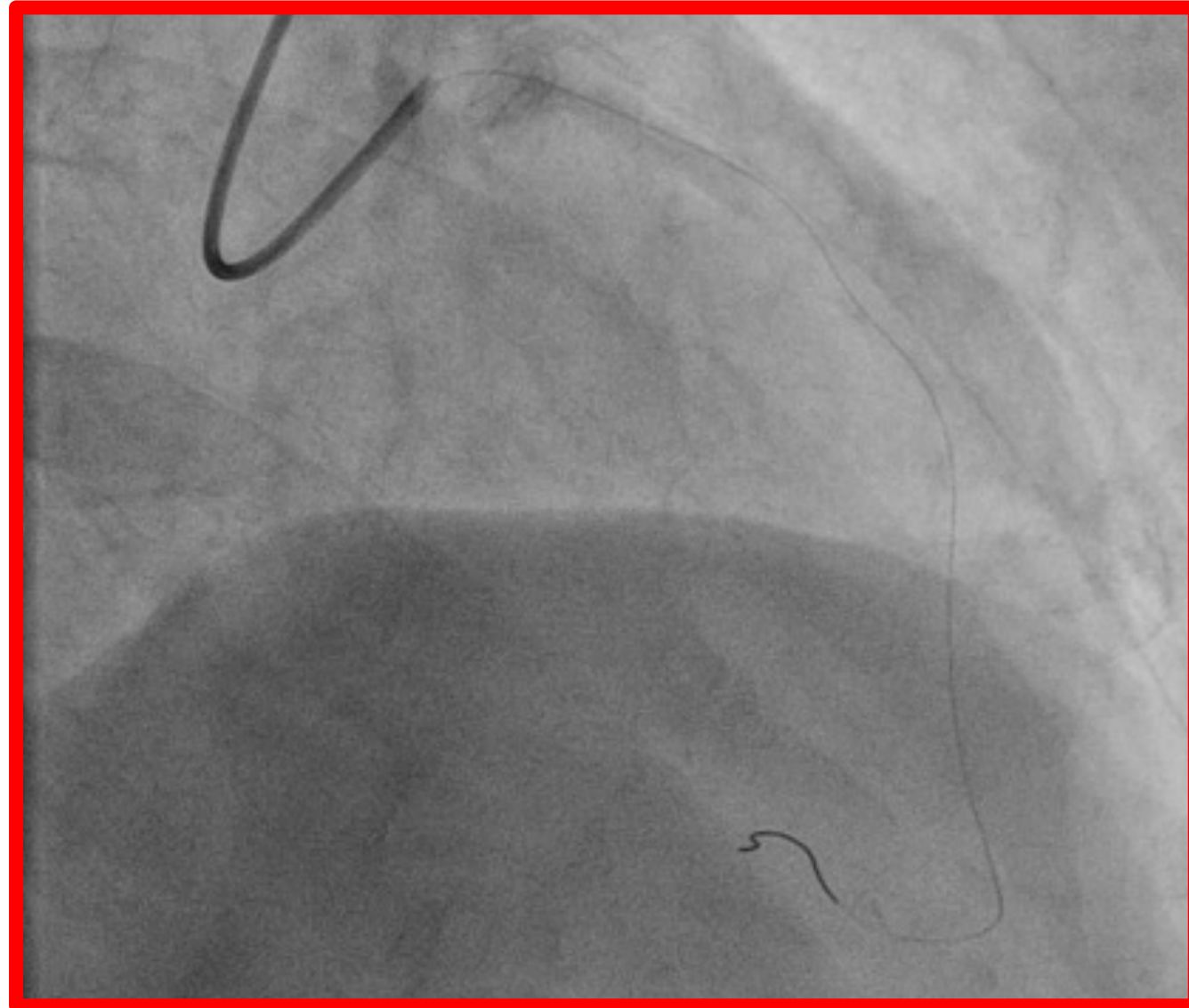
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Un cas pratique avec 3 Dinamix



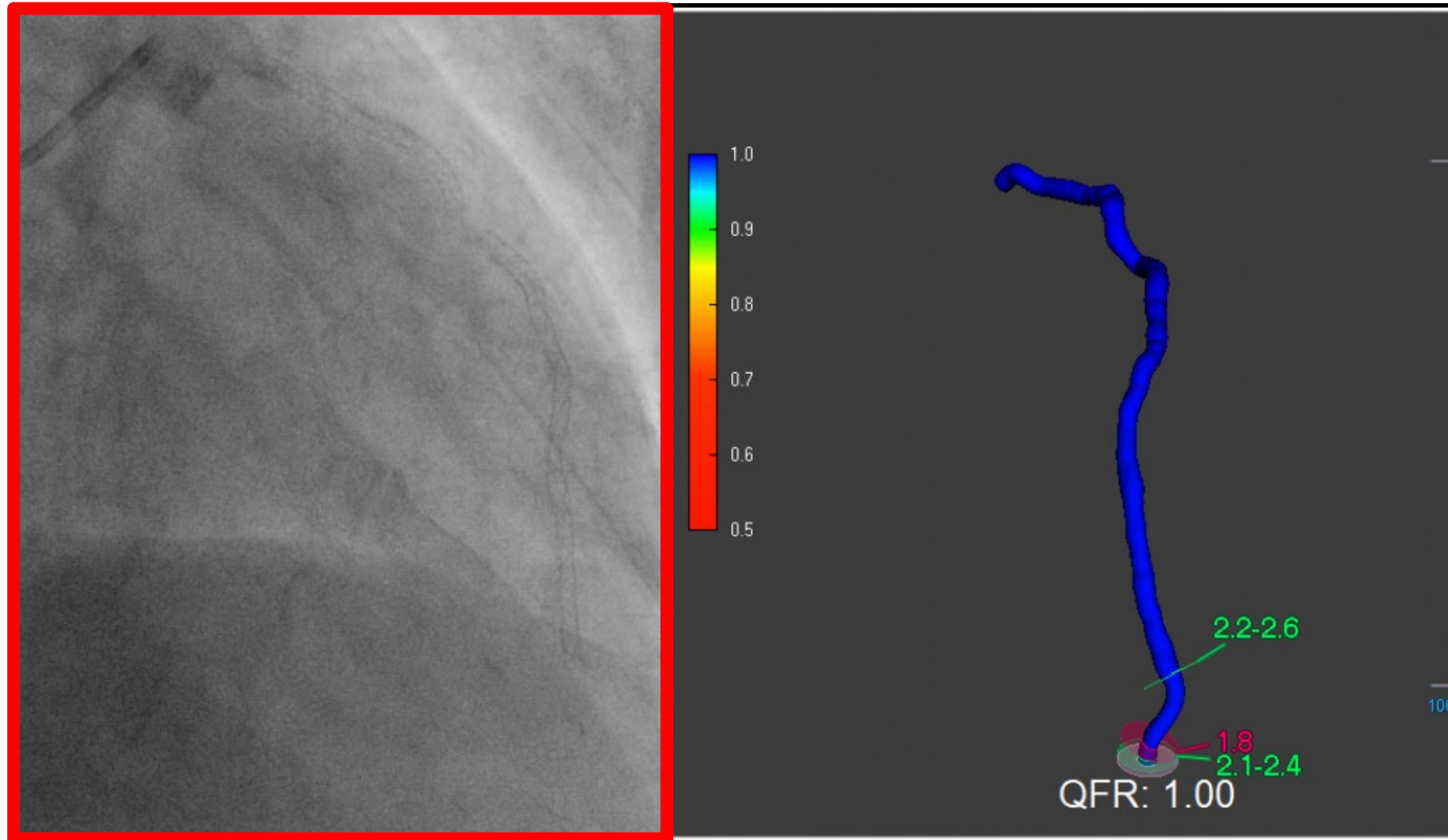
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Un cas pratique avec 3 Dinamix



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Merci @ vous



Cardio&vous



Centre hospitalier
universitaire vaudois

JOURNÉES DE PHYSIOLOGIE EN CARDIOLOGIE INTERVENTIONNELLE
5 & 6 AVRIL – 2024 – NICE



DynamX Coronary Bioadaptor System - Que dit la littérature?

Dr Vladimir Rubimbura

Interventional cardiologist

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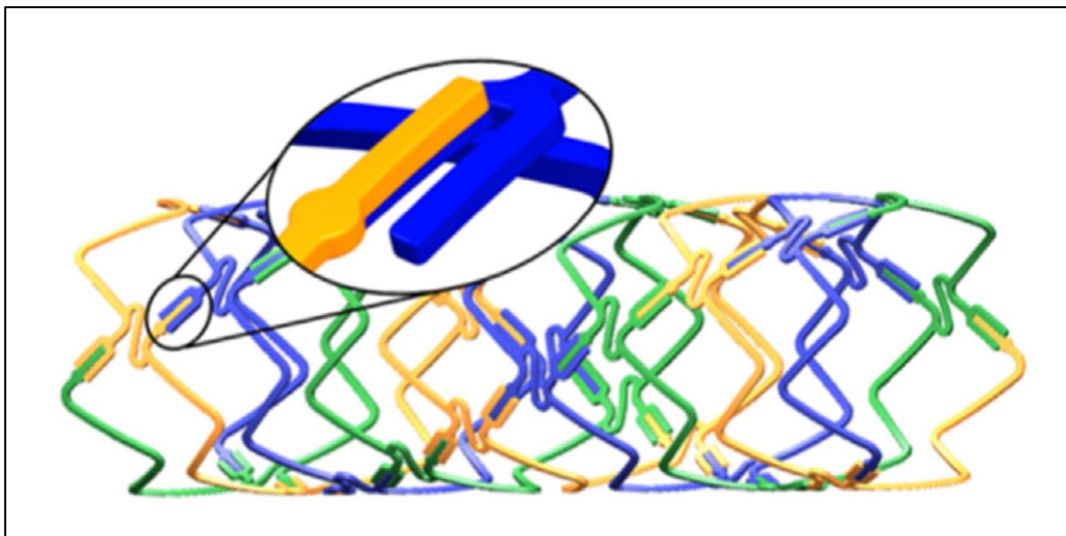
EHC (Morges) - CHUV (Lausanne)

Switzerland

COI

1. Support for this presentation: Elixir
 2. Grants: Terumo, Medtronic, Biotronik, Vascular Medical
-

DynamX Coronary Bioadaptor System Design



Ceci n'est pas un stent...mais un Bioadaptor!

DynamX evaluation

Study	Design	Control Arm	# of Pts Enrolled	Study Status
DynamX Mechanistic Study ¹	Single arm	N/A	50	Completed 3-year FU
DynamX NZ Imaging Study ²	Single arm	N/A	44	Completed 1-year FU
DynamX Hong Kong Registry ²	Single arm	N/A	50	Completed 1-year FU
BIOADAPTOR RCT ³ (Japan, Germany, Belgium, NZ)	RCT	Resolute Onyx	445	Completed 1-year FU
INFINITY SWEDEHEART (Sweden)	RCT	Resolute Onyx	2400	Completed enrollment; Results in 2025

1. Verheye, et al. Twelve-month clinical and imaging outcomes of the uncaging coronary DynamX Bioadaptor System. EuroIntervention 2020;16:e974-e981
2. Data on file at Elixir Medical
3. Saito S et al. BIOADAPTOR-RCT Collaborators. First randomised controlled trial comparing the sirolimus-eluting bioadaptor with the zotarolimus-eluting drug-eluting stent in patients with de novo coronary artery lesions: EClinicalMedicine. 2023 Oct 24;65:102304.

BIOADAPTOR RCT (N=445)

DynamX Coronary Bioadaptor vs. Resolute Onyx DES (1:1)

eClinicalMedicine

Part of THE LANCET *Discovery Science*

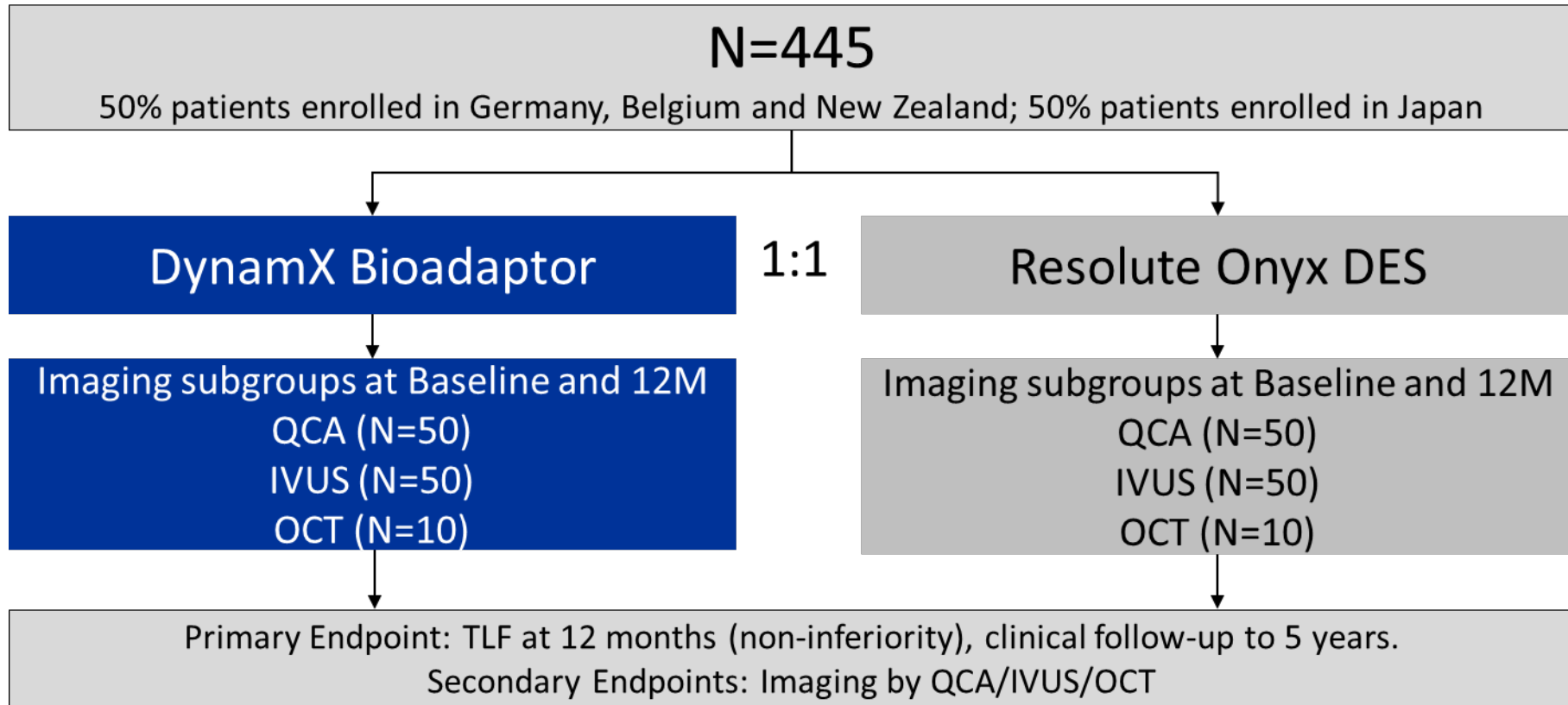
First randomised controlled trial comparing the sirolimus-eluting bioadaptor with the zotarolimus-eluting drug-eluting stent in patients with *de novo* coronary artery lesions: 12-month clinical and imaging data from the multi-centre, international, BIODAPTOR-RCT



Shigeru Saito,^{a,*} Johan Bennett,^b Halger M. Nef,^c Mark Webster,^d Atsuo Namiki,^e Akihiko Takahashi,^f Tsunekazu Kakuta,^g Seiji Yamazaki,^h Yoshisato Shibata,ⁱ Douglas Scott,^j Mathias Vrolix,^k Madhav Menon,^l Helge Möllmann,^m Nikos Werner,ⁿ Antoinette Neylon,^o Zlatko Mehmedbegovic,^o Pieter C. Smits,^o Marie-Claude Morice,^o and Stefan Verhey,^p BIODAPTOR-RCT Collaborators



BIOADAPTOR RCT Trial Design



Baseline characteristics

	DynamX (N = 223)	Resolute Onyx (N = 222)
Age (years)	67.1 (10.3)	66.2 (10.1)
Sex		
Male	144 (64.6%)	150 (67.6%)
Female	16 (7.2%)	9 (4.1%)
Race		
Japanese	18 (8.1%)	18 (8.1%)
Caucasian	6 (2.7%)	15 (6.8%)
Maori	15 (6.7%)	10 (4.5%)
Not permitted	24 (10.8%)	20 (9.0%)
Other		
Angina/ischemia status		
Stable angina	144 (64.6%)	150 (67.6%)
Unstable angina	16 (7.2%)	9 (4.1%)
Silent ischemia	18 (8.1%)	18 (8.1%)
Asymptomatic post myocardial infarction	6 (2.7%)	15 (6.8%)
Non-ST-elevation myocardial infarction	15 (6.7%)	10 (4.5%)
Other	24 (10.8%)	20 (9.0%)
Lesion characteristics	DynamX (N = 226 lesions)	Resolute Onyx (N = 230 lesions)
Target lesion classification		
B2/C	51 (22.6%)	49 (21.3%)
Target vessel		
LAD	114 (50.4%)	104 (45.2%)
LCX	35 (15.5%)	66 (28.7%)
RCA	77 (34.1%)	60 (26.1%)
Bifurcation	50 (22.1%)	55 (23.9%)
Calcified lesion (moderate/severe)	43 (19.0%)	47 (20.4%)
Tortuous lesion (moderate/severe)	53 (23.5%)	46 (20.0%)
Reference vessel diameter (mm)	3.1 (0.4)	3.0 (0.4)
Target lesion length (mm)	15.8 (6.0)	16.2 (6.0)

Saito S et al. BIOADAPTOR-RCT Collaborators. First randomised controlled trial comparing the sirolimus-eluting bioadaptor with the zotarolimus-eluting drug-eluting stent in patients with de novo coronary artery lesions: EClinicalMedicine. 2023 Oct 24;65:102304.

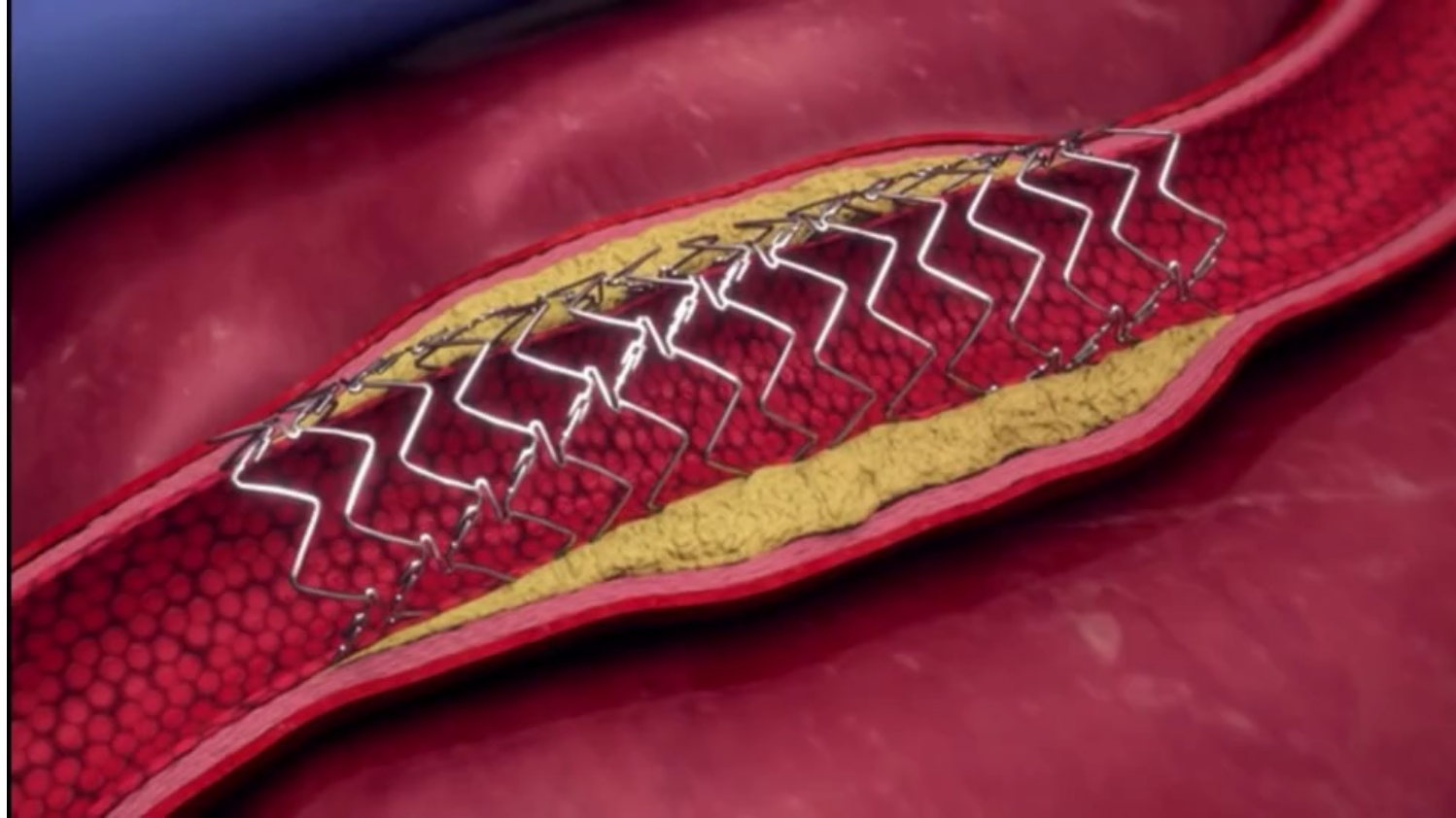
Results

	DynamX (N = 223)	Resolute Onyx (N = 222)	Difference (%)	CI of difference	p _{non-inferiority} ^a
Target lesion failure	4/221 (1.8%) [0.5; 4.6]	6/215 (2.8%) [1.0; 5.6]	-1.0%	[-3.3; 1.4]	<0.001
Cardiovascular death	0/221 (0.0%) [0.0; 1.7]	2/215 (0.9%) [0.1; 3.3]	-0.9%	[-3.4; 0.8]	-
Target vessel MI ^b	3/221 (1.4%) [0.3; 3.9]	4/213 (1.9%) [0.5; 4.7]	-0.5%	[-3.6; 2.3]	-
Clinically-driven TLR	2/221 (0.9%) [0.1; 3.2]	1/213 (0.5%) [0.0; 2.6]	0.4%	[-1.8; 2.9]	-
Definite or probable device thrombosis ^c	1/221 (0.5%) [0.0; 2.5]	1/214 (0.5%) [0.0; 2.6]	-0.0%	[-2.2; 2.2]	-

Data are displayed as n/N (%) [95% CI]. MI = myocardial infarction, TLR = target lesion revascularisation. ^aWald non-inferiority test statistic. ^bTwo periprocedural MI in the DynamX group and four in the Resolute Onyx group. ^cThe device thrombosis in the DynamX group occurred on day 3 in the patient with spontaneous target-vessel MI who was treated with a clinically-driven TLR; the device thrombosis in the Resolute Onyx group occurred in a patient with sudden death at day 1.

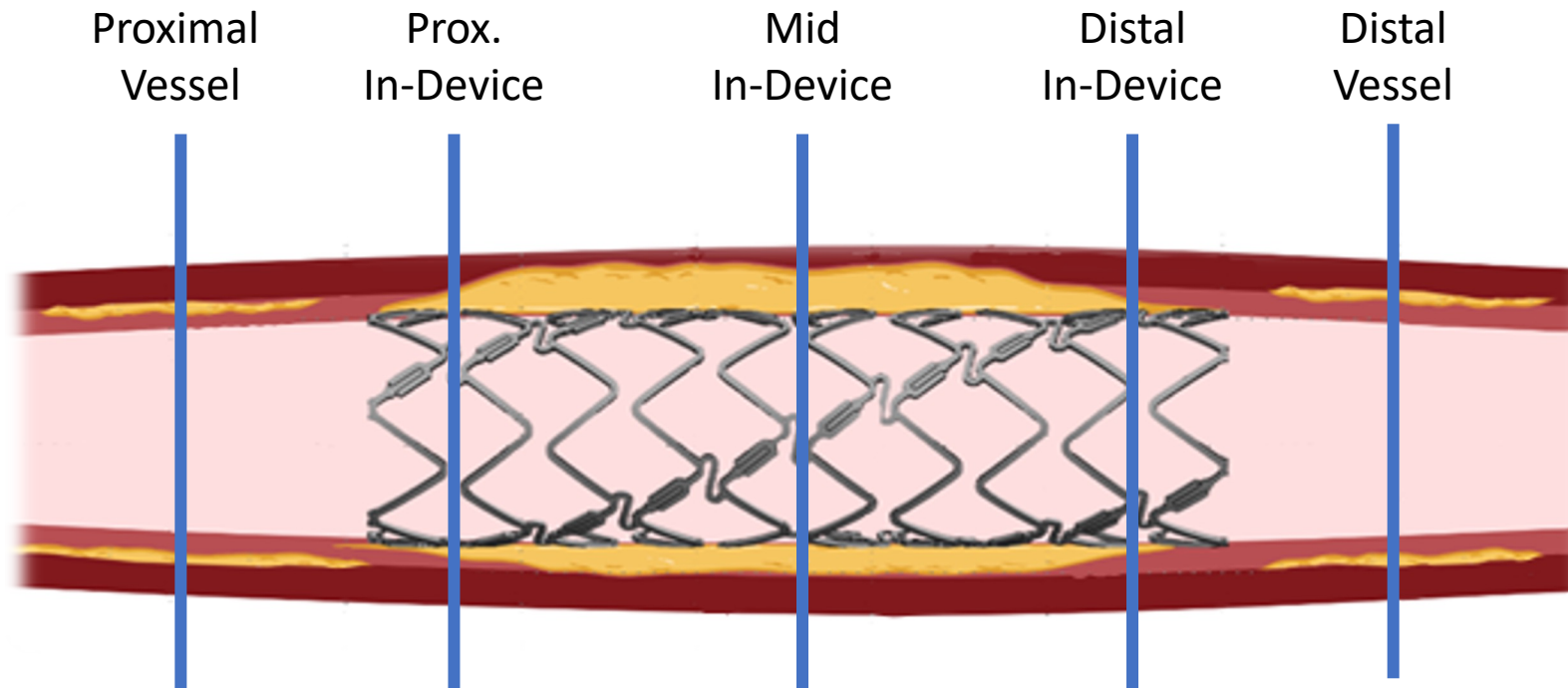
Table 2: Target lesion failure and device thrombosis at 12 months.

Imaging follow-up results (IVUS / OCT)

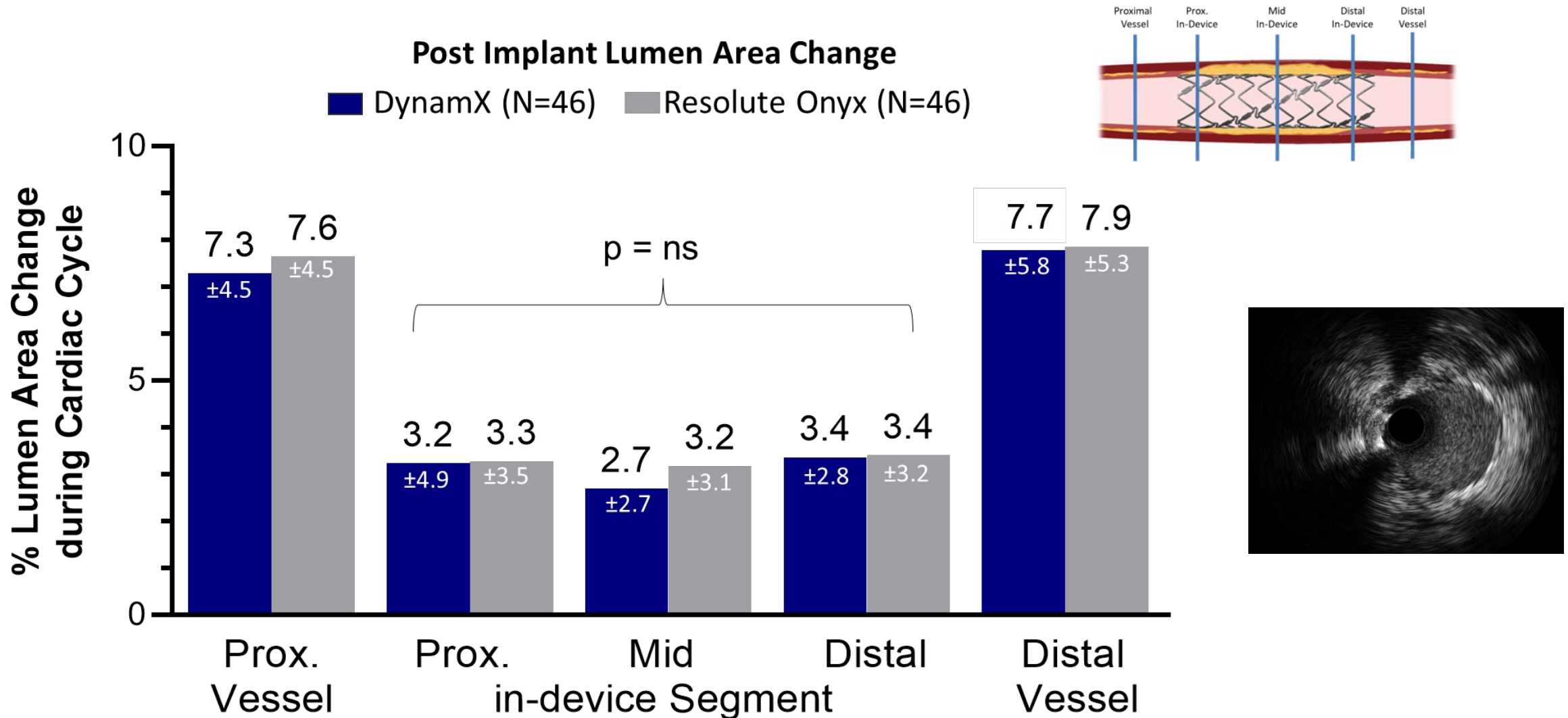


Stationary IVUS Pulsatility Paired Analysis

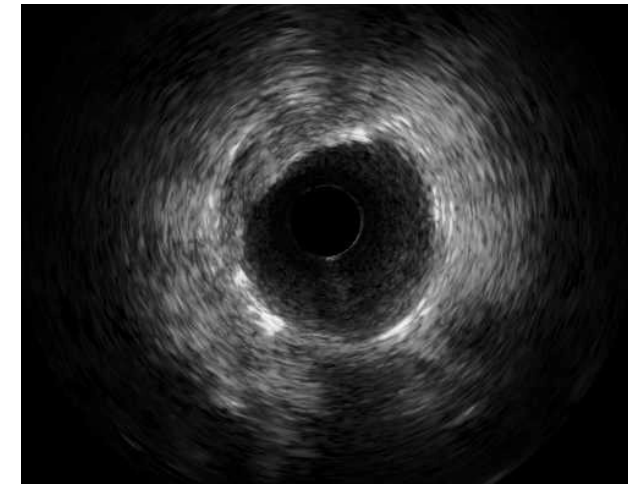
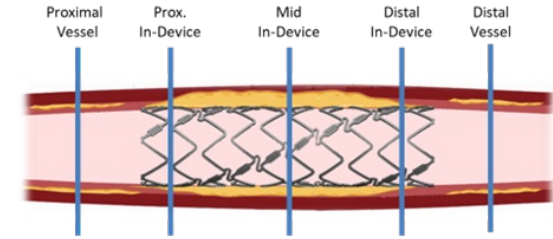
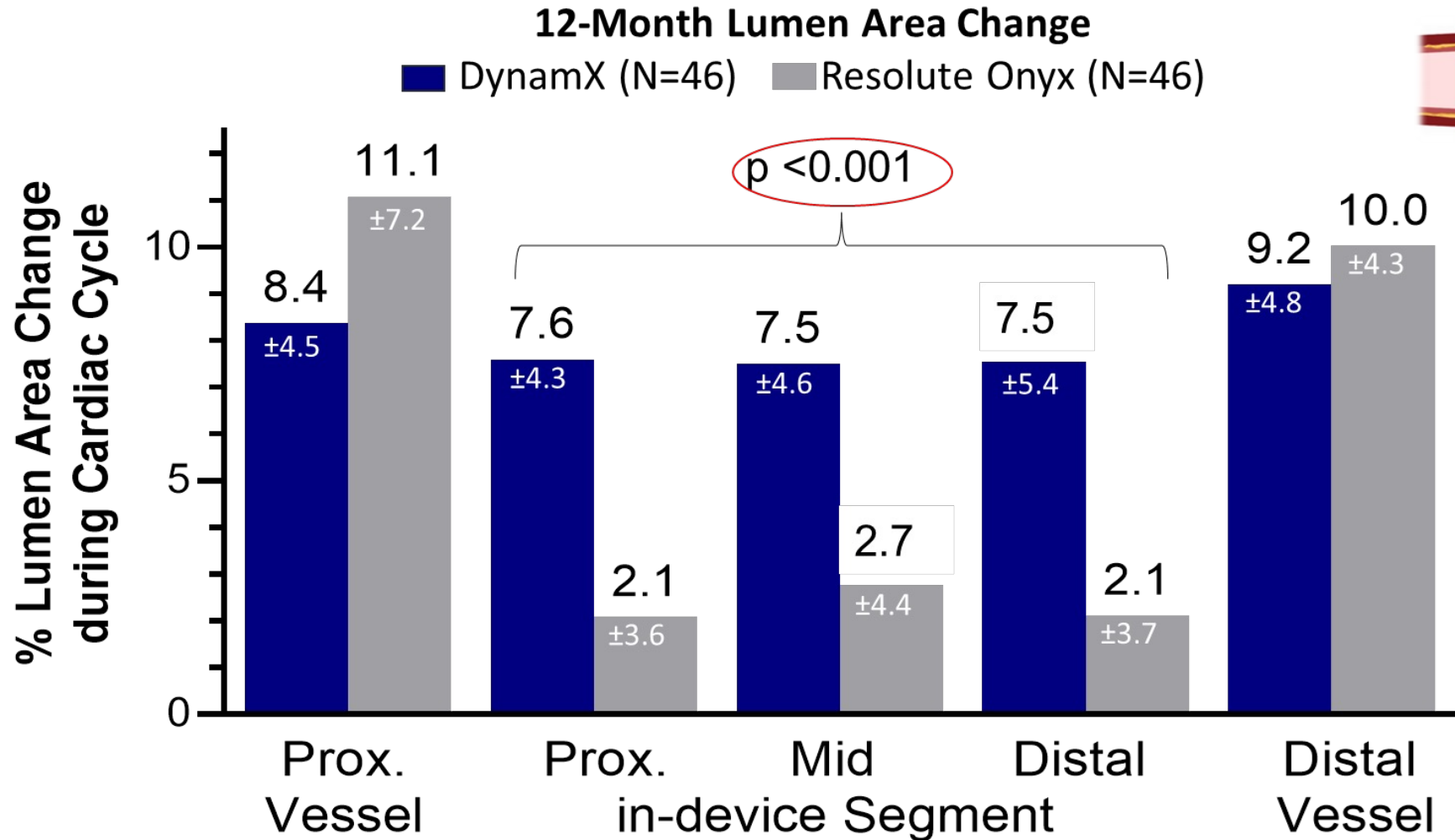
- Measured % change in Lumen Area between systole and diastole cycles
 - Measured across three cardiac cycles
- Recorded using the same frames at Post-Implant and 12-month follow-up



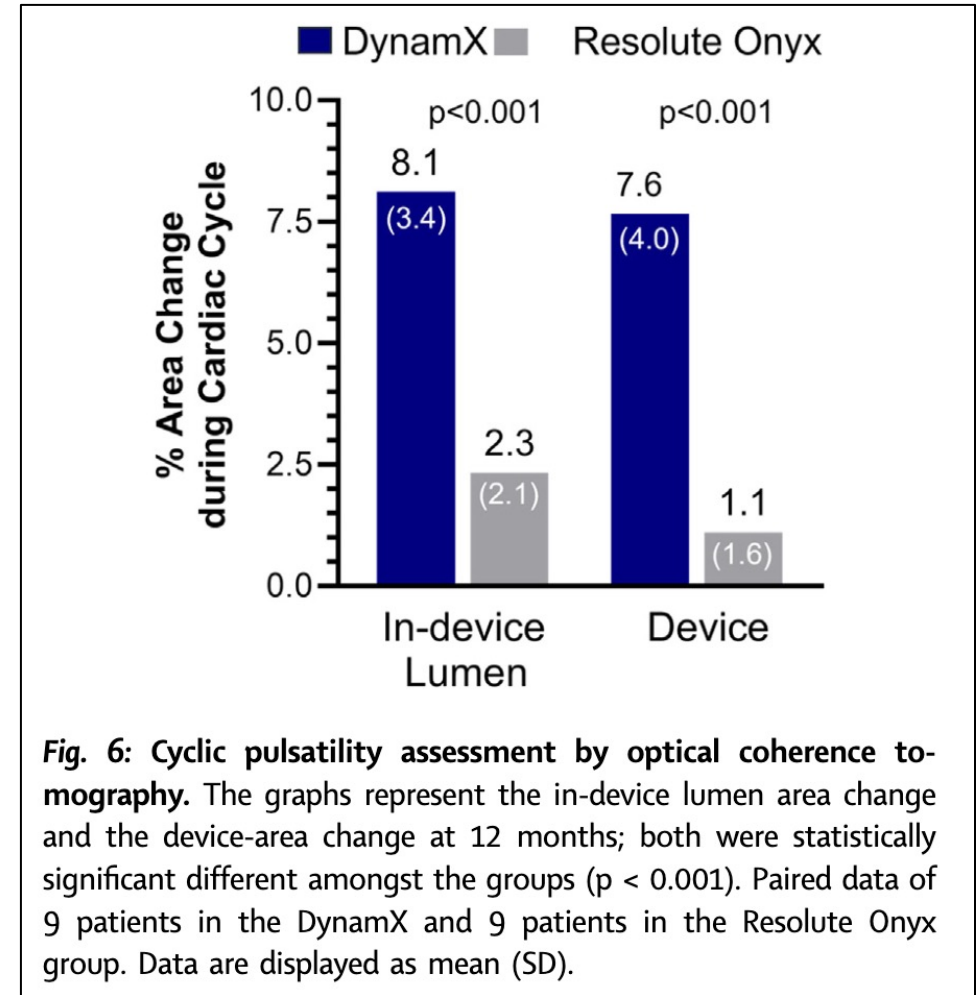
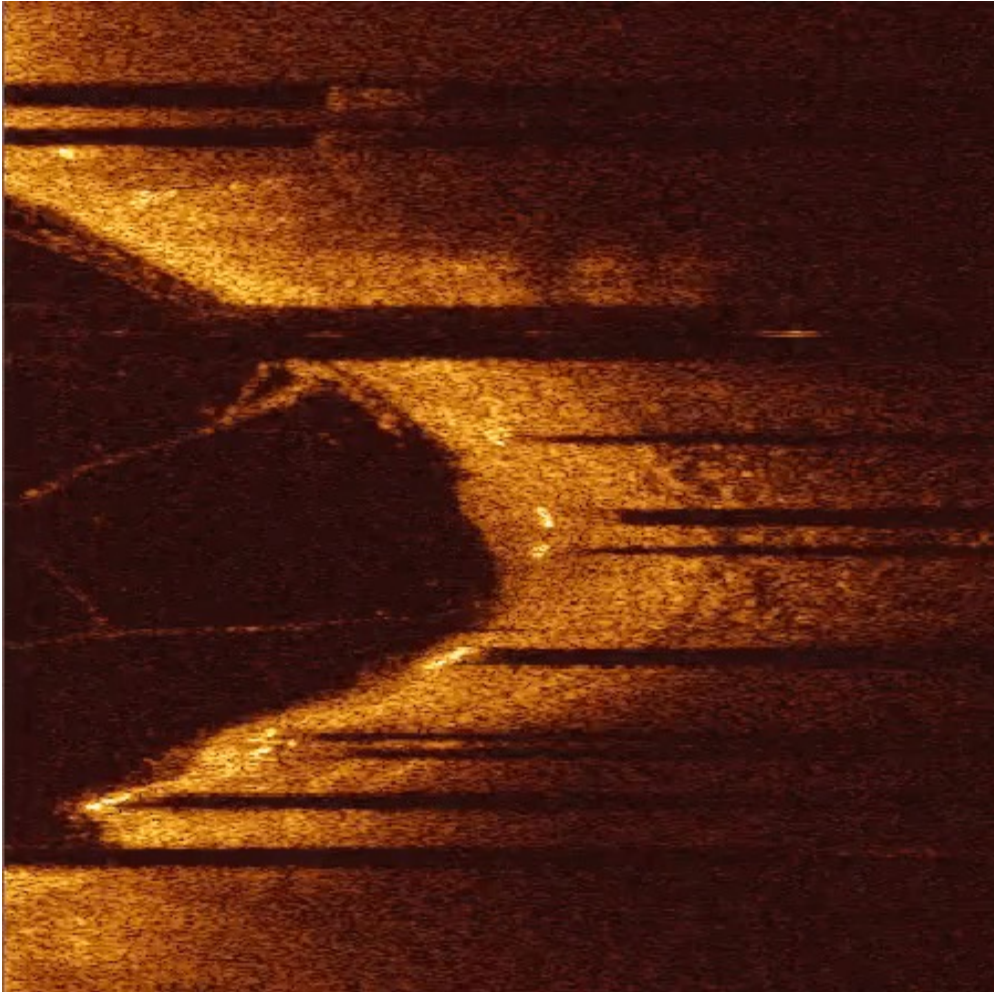
BIOADAPTOR RCT – No In-Device Pulsatility **Post Implant**



BIOADAPTOR RCT: Pulsatility evaluation (OCT) – 12 months



BIOADAPTOR RCT: Pulsatility evaluation (OCT)



DynamX Mechanistic study : Pulsatility evaluation

DynamX Mechanistic Study ¹	Single arm	N/A	50	Completed 3-year FU
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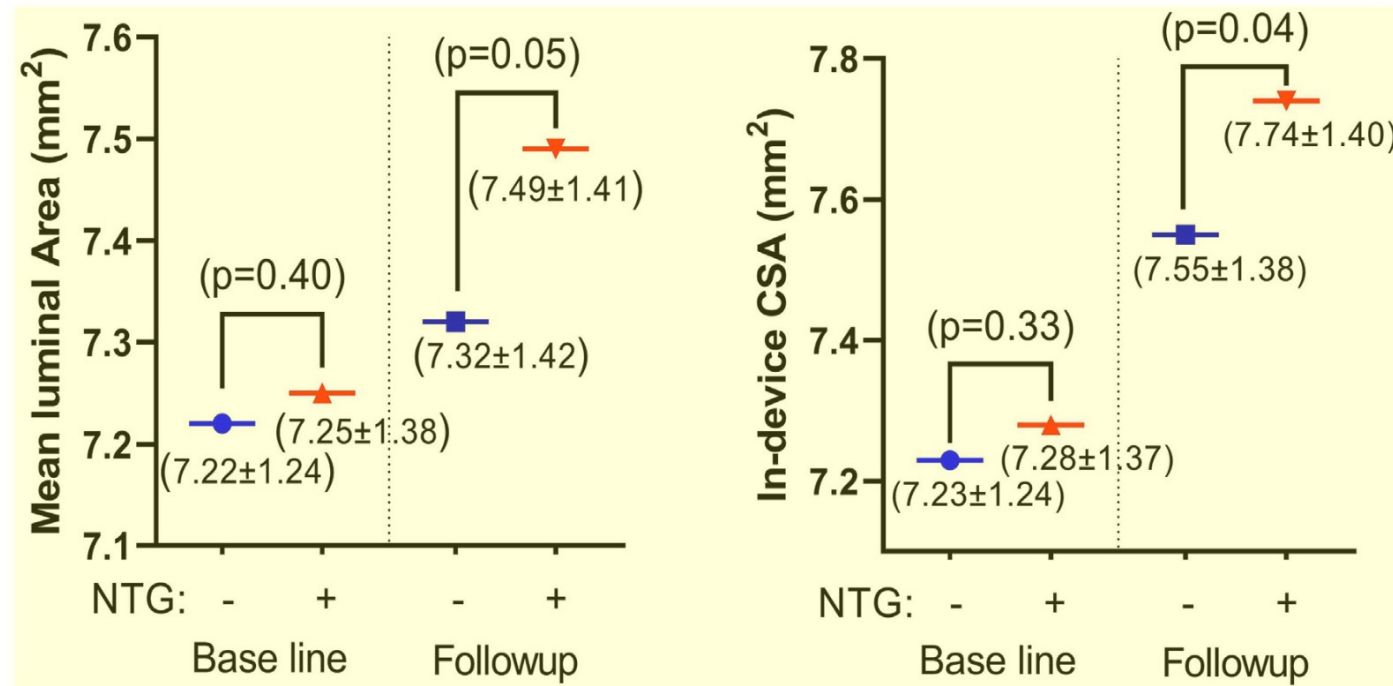
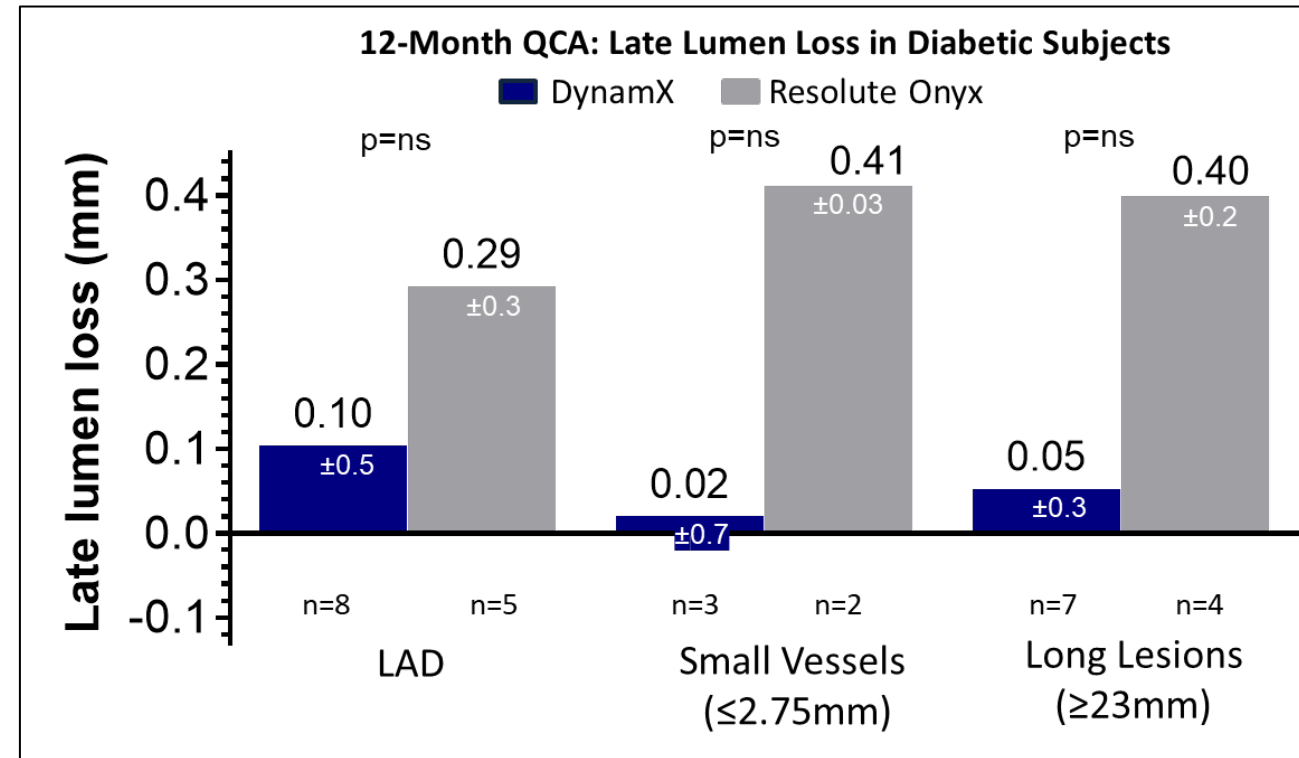
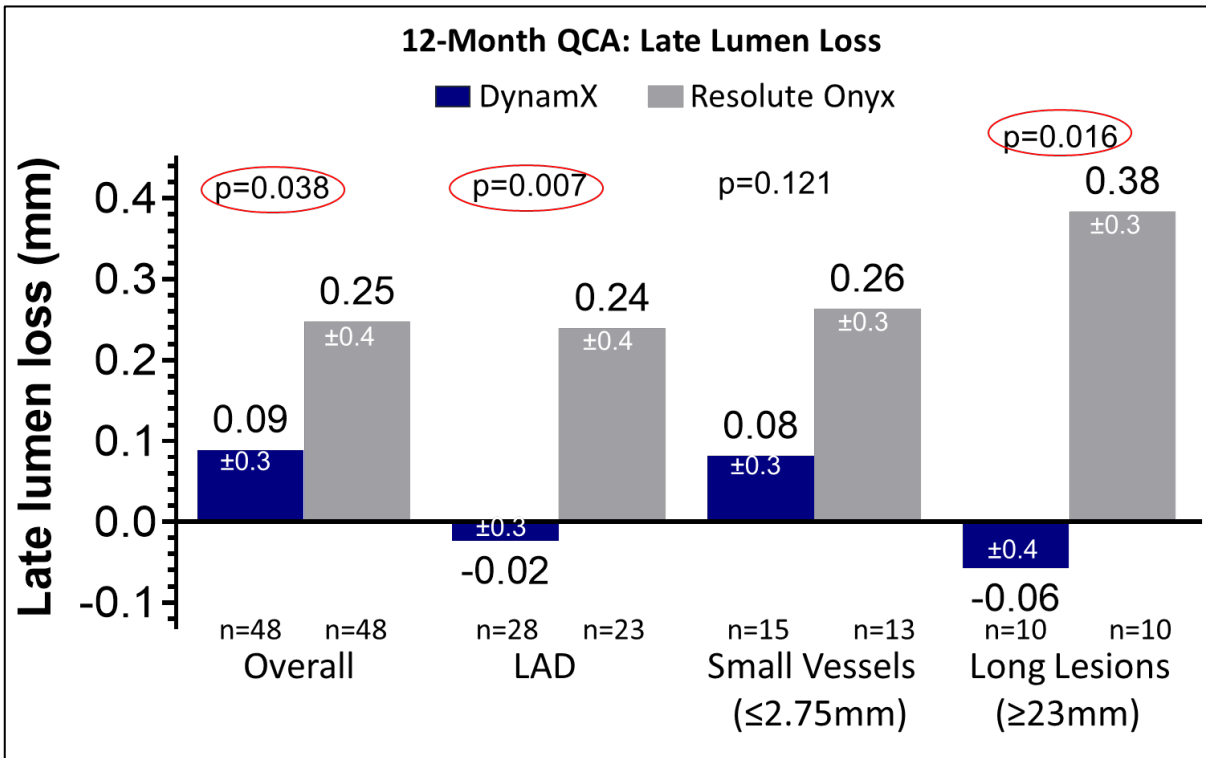
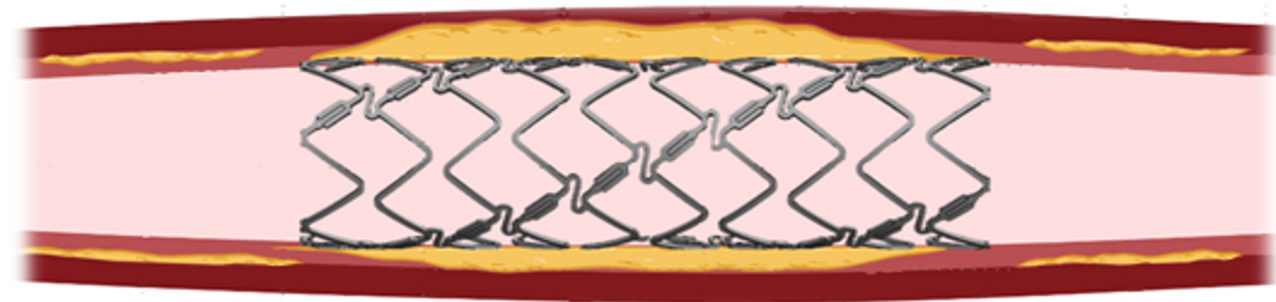
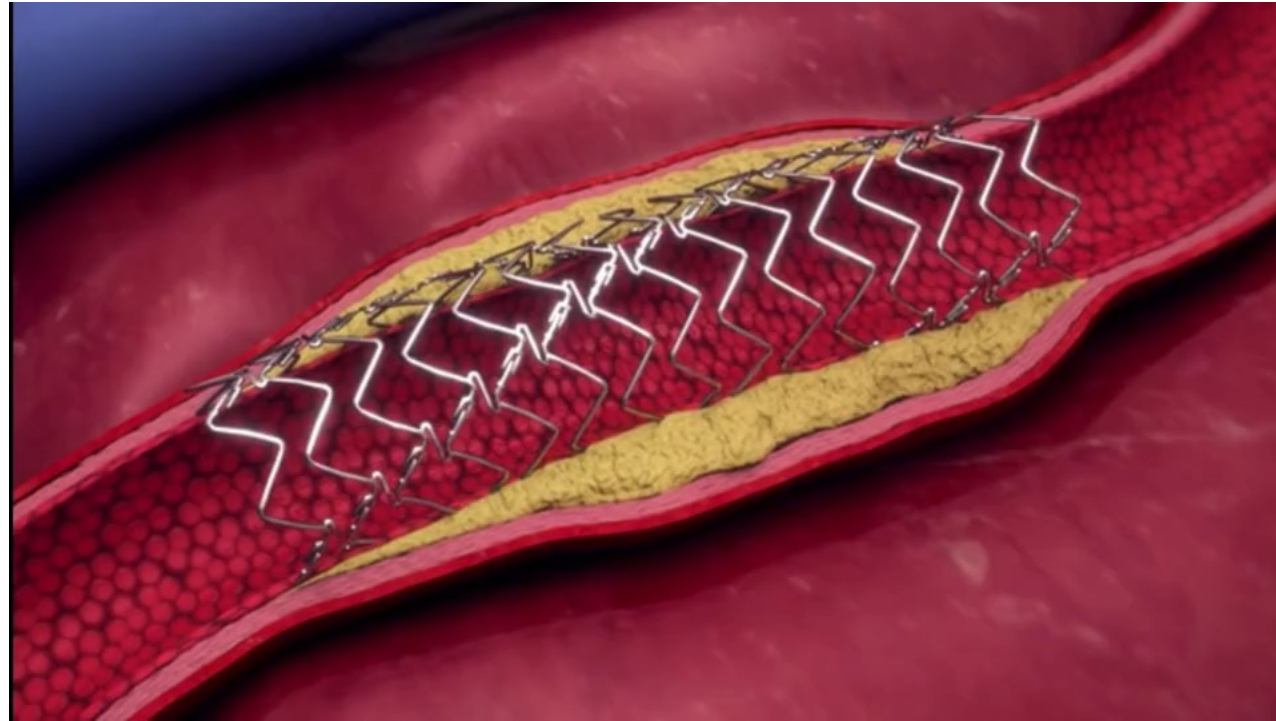


Fig. 2. Change in mean in-device lumen and cross-sectional area after nitroglycerin administration (assessed by intravascular ultrasound). In-device lumen (A) and cross-sectional (B) area significantly increased upon nitroglycerine administration in 18 patients at 9 to 12-month follow-up compared to baseline (paired data, mean \pm SD). The mean lumen area change was 0.17 mm² and the mean device area change was 0.19 mm² at follow-up. CSA-cross sectional area, NTG-nitroglycerine.

Late Lumen Loss with DynamX



Imaging follow-up results – impact on atherosclerosis



Plaque Changes **Outside** The Device – **12 months**

Lipid-lowering medication use	Screening/Baseline	Discharge	1 Month	6 Months	12 Months
DynamX	88%	90%	92%	92%	92%
Resolute Onyx	90%	94%	94%	94%	94%



Proximal

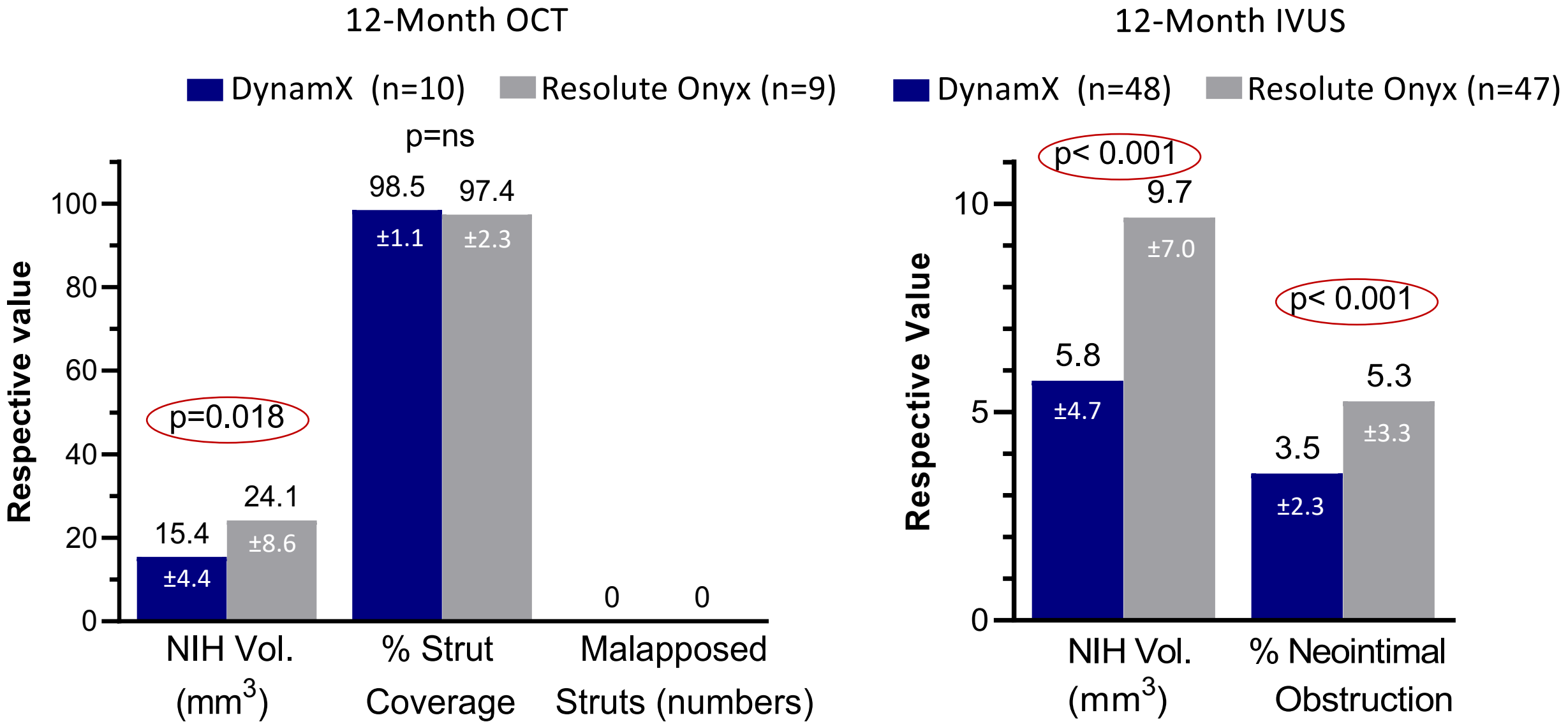
Absolute change in plaque volume normalized per length from baseline to 12M FU (mm ³)		
DynamX (N=42)	Resolute Onyx (N=42)	p-value
0.67 ± 1.45	0.42 ± 1.73	0.991

Distal

Absolute change in plaque volume normalized per length from baseline to 12M FU (mm ³)		
DynamX (N=41)	Resolute Onyx (N=42)	p-value
0.50 ± 1.34	0.41 ± 1.30	0.503

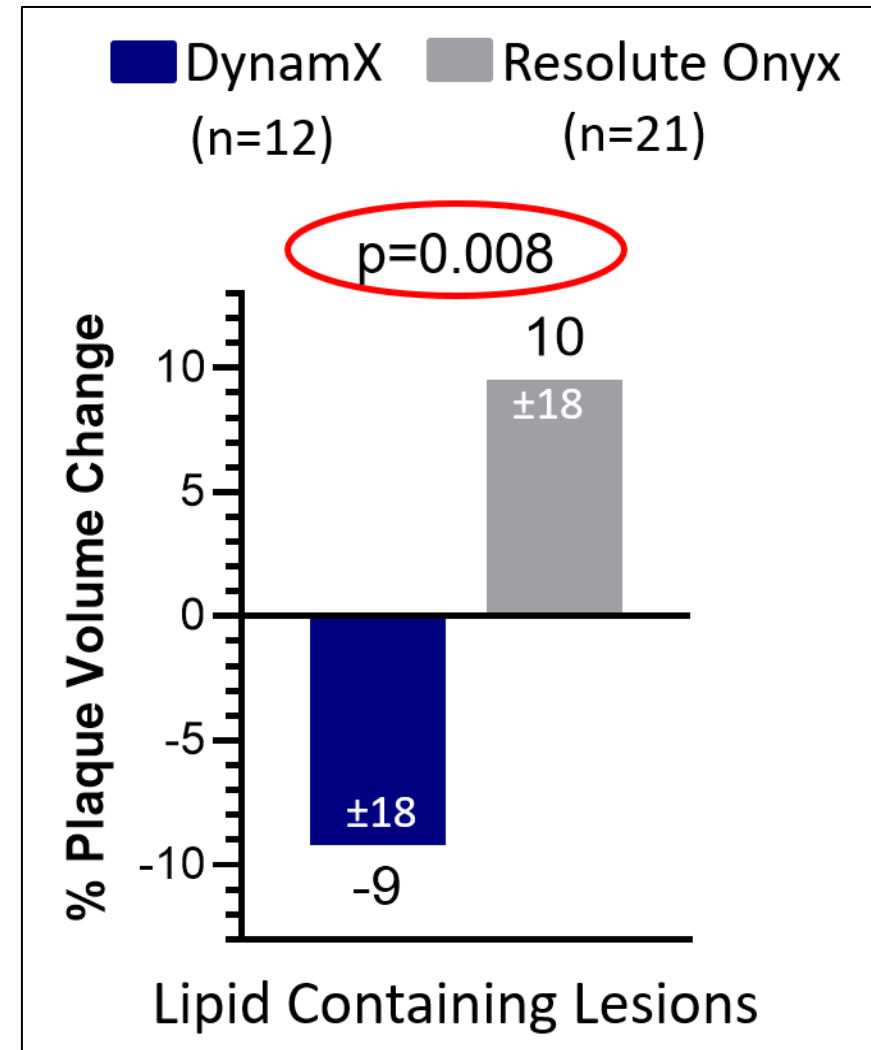
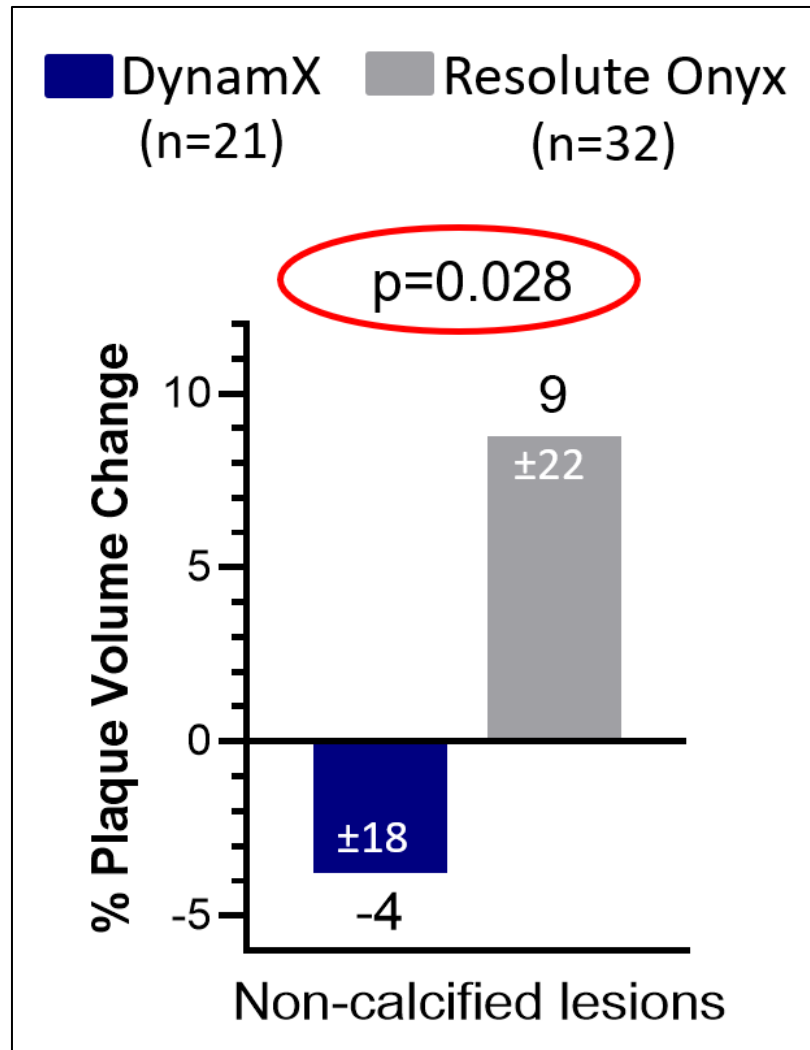
Saito S et al. BIOADAPTOR-RCT Collaborators. First randomised controlled trial comparing the sirolimus-eluting bioadaptor with the zotarolimus-eluting drug-eluting stent in patients with de novo coronary artery lesions: EClinicalMedicine. 2023 Oct 24;65:102304.

Bioadaptor: neointimal hyperplasia / struts coverage (OCT/IVUS)



Saito S et al. BIOADAPTOR-RCT Collaborators. First randomised controlled trial comparing the sirolimus-eluting bioadaptor with the zotarolimus-eluting drug-eluting stent in patients with de novo coronary artery lesions: EClinicalMedicine. 2023 Oct 24;65:102304.

Plaque changes **behind** the device



Take Home Messages

1. Le Bioadaptor DynamX “*n’est pas un stent*” mais offre la même sécurité d’un stent en termes de TLF à 12 mois
 2. Le respect de la physiologie artérielle, en termes de pulsatilité, est supérieur à 12 mois par rapport à un DES classique
 3. Il semble y avoir une meilleure évolution de la charge athéromateuse au niveau du site d’implantation du DynamX
 4. Les prochaines études randomisées nous donnerons plus de données sur l’impact clinique associé à l’implantation du Bioadaptor.
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A word cloud featuring various expressions of gratitude in multiple languages. The most prominent words are "THANK" and "YOU". Other visible phrases include "GRACIAS", "ARIGATO", "SHUKURIA", "JUSPAXAR", "DANKSCHEEN", "TASHAKKUR ATU", "YAQHANYELAY", "SUKSAM", "EKHMET", "MEHRBANI", "GRAZIE", "MAAKE", "KOMAPSUNNIDA", "GOZAIMASHITA", "EFCHARISTO", "BOLZIN", and "MERCII". The words are arranged in a roughly heart-like shape, with "THANK YOU" at the center and other phrases radiating outwards.