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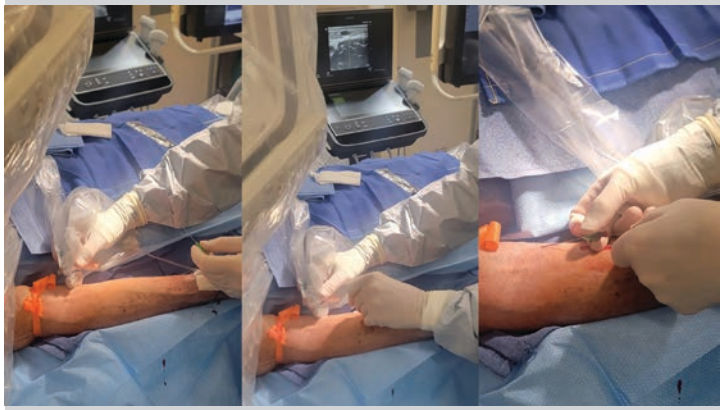

TECHNIQUE

Ultrasound-Guided Venous Access for Arm Cases

Marie E. Miranda, RN

In the cardiovascular lab, a right heart catheterization requires venous access, but sometimes it is not easy to gain access, which often needs a deft hand and finely tuned skills. I have been a vascular access nurse for 21 years, placing ultrasound-guided intravenous (IV) lines, midline, and peripherally inserted central catheters (PICC lines). Recently, I showed one of our staff interventionalists, Dr. Morton Kern, how to gain easy access to any vein. He said he learned something very helpful and it was worthy of sharing with a larger audience. Following are my thoughts on how best to perform ultrasound-guided venous access.

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RENAL DENERVATION

4 Cases: Treating Uncontrolled Hypertension With the Paradise™ Ultrasound Renal Denervation System (uRDN)

Surabhi Madhwal Atreja, MD, FACC, RPVI; Aravinda Nanjundappa, MBBS, MD; Wissam Gharib, MD, FACC, FSCAI, and Jordan King, MPAS, PA-C; Vamsee Yaganti, MD, MA, FACC, FSCAI

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NEW DEVICES

DynamX Bioadaptor: A Paradigm Shift in Percutaneous Coronary Intervention?

Dean J. Kereiakes, MD, FACC, MSCAI

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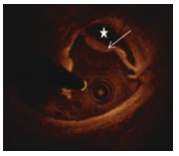
INTRAVASCULAR IMAGING

Intravascular Optical Coherence Tomography for the Diagnosis and Treatment of Peripheral Arterial Disease



Mehmet Cilingiroglu, MD; Thomas Milner, PhD; Ibrahim Halil Inanc, MD; Deniz Mutlu, MD; Kostas Marmagkiolis, MD; Cezar Iliescu, MD

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HMP Global

DynamX Bioadaptor: A Paradigm Shift in Percutaneous Coronary Intervention?

Dean J. Kereiakes, MD, FACC, MSCAI

The Problem of Late Adverse Coronary Prosthesis-Related Events

Percutaneous coronary intervention (PCI) has evolved from balloon angioplasty to bare metal stents (BMS), 1st and 2nd generation drug-eluting stents (DES), and subsequently, bioresorbable scaffolds (BRS). Iterations in metallic stent prostheses including drug elution, novel metal alloy composition, reduced strut thickness and improved polymer biocompatibility and/or resorption have contributed to improved stent-related clinical outcomes to 1 year following stent implantation (target lesion failure [TLF]; composite occurrence of cardiac-related death, target vessel-related myocardial infarction, and ischemia-driven target lesion revascularization). However, beyond 1 year there appears to be a 2%-3%/year annualized rate of TLF events extending at least 10-15 years post-implantation, regardless of device type (BMS, 1st or 2nd generation DES) (Figure 1).[1,2] Importantly, these device-related adverse events are not benign, and are associated with significant long-term morbidity and mortality.[3,4]

The pathophysiologic mechanism thought to be the driver for this annualized hazard is the common presence of a metallic prosthesis caging the vessel that mechanically distorts and constrains the vessel, limiting coronary vasomotion, autoregulation, and adaptive vessel remodeling via the Glagov phenomenon.[5] A metallic prosthesis also simultaneously serves as a persistent nidus for inflammation, neoatherosclerosis and/or strut fracture, with the consequent occurrence of myocardial infarction, thrombosis, and/or restenosis.[5] In this context, great enthusiasm surrounded the introduction of BRS, the concept of uncaging the vessel and "leave nothing behind" with the hope of restoring more normal vessel physiology. The largest cumulative clinical experience to date involves randomized comparative trials (RCT) of the Absorb bioresorbable vascular scaffold (BVS) (Abbott) compared with the metallic Xience everolimus-eluting stent (EES) (Abbott), and demonstrates a significant increase in adverse clinical events (TLF) through 5 years following implantation of Absorb BVS versus Xience EES (Figure 2A), driven by relative event rates occurring during the first 3 years (Figure 2B).[6]

The larger Absorb BVS device profile made procedural delivery more challenging and was associated with reduced device success rates and subsequent implantation of more unassigned devices in RCT comparisons with Xience EES. Importantly, beyond 3 years post implantation (time point for complete BVS resorption), the annualized rate of TLF remained 2%-3%/year through 5-year follow-up, and was similar following either Absorb BVS or Xience EES (Figure 2B).[6] The continued occurrence of TLF events despite complete scaffold resorption raises concerns that either prolonged (3-year) exposure to acidic polylactic acid resorption products may adversely impact the scaffolded segment and potentially accelerate neoatherosclerosis, or that there may be an additional mechanism that is missing from the "leave nothing behind" technologies that is essential and necessary to restore durable and more normal vessel functionality. Hence, the concept of a coronary prosthesis that circumferentially separates post-implantation, freeing the vessel, and which subsequently provides the essential and necessary mechanism of dynamic support to restore more normal functionality of the diseased vessel (restoration of coronary vasomotion, pulsatility, and adaptive remodeling), became extremely attractive.

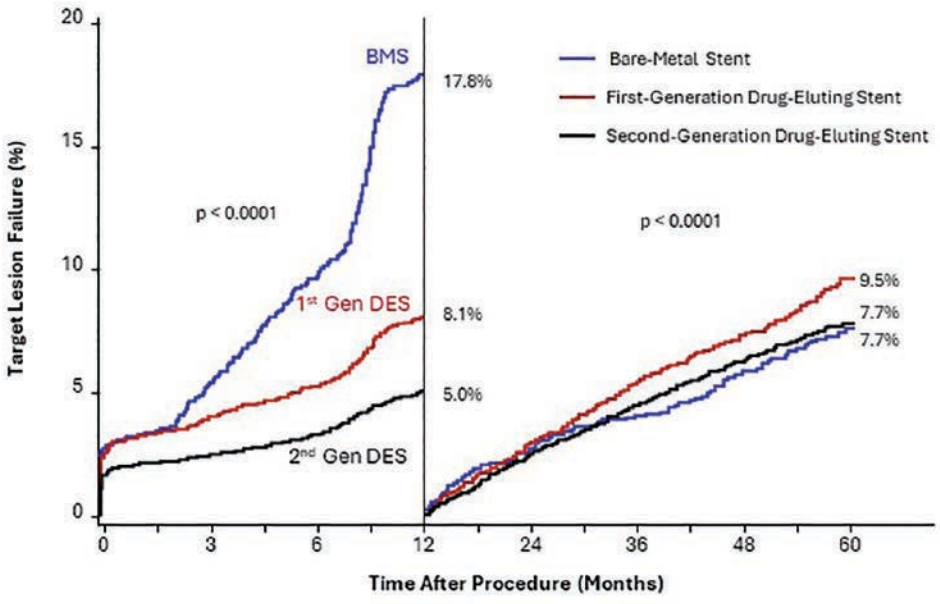

Figure 1. Meta-analysis of trials evaluating target lesion failure (TLF) following coronary stent implantation. Individual patient data level meta-analysis from 19 trials evaluating stent-related events (TLF: composite occurrence of cardiac-related death, target vessel myocardial infarction or clinically indicated target lesion revascularization) through 5-year follow-up after implantation. Despite a progressive reduction in events to 1 year from bare metal (BMS) to first-generation (1G) and second-generation (2G) drug-eluting stents (DES), beyond 1 year, there is a 2%-3% per year rate of events regardless of device.

Reproduced with permission from Madhavan MV, et al. Stent-related adverse events > 1 year after percutaneous coronary intervention. J Am Coll Cardiol. 2020;75:590-604.

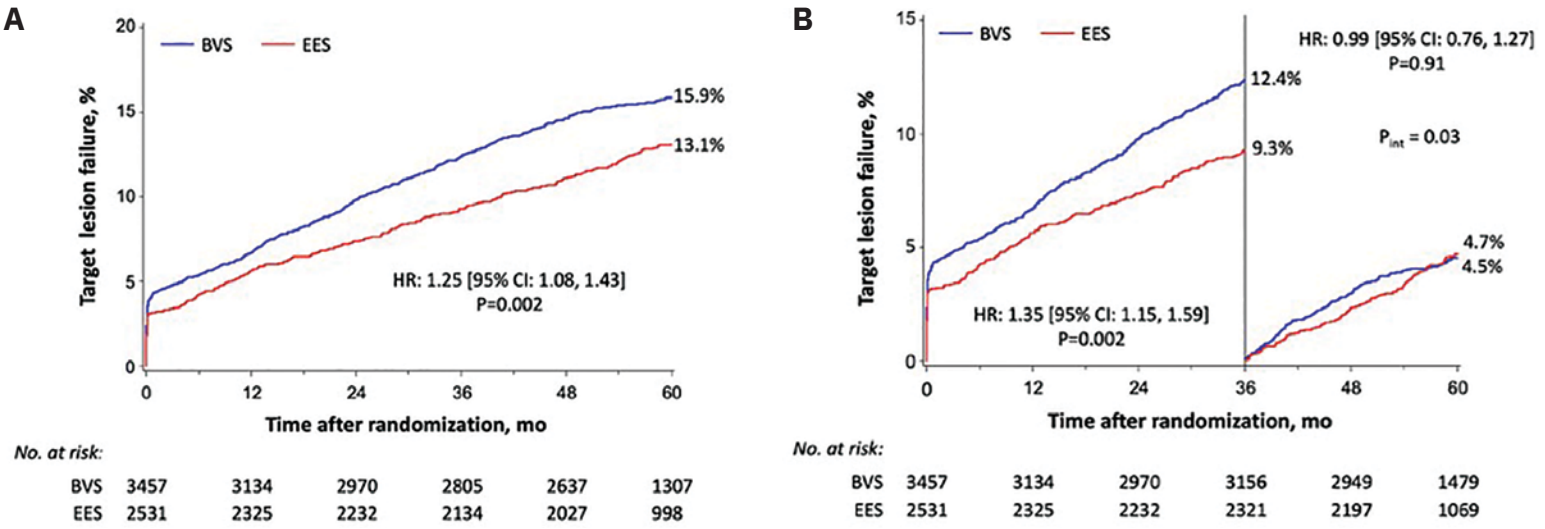

Figure 2. Pooled individual patient data analysis for target lesion failure (TLF) through 5-year follow-up from the ABSORB randomized trials comparing the Absorb bioresorbable vascular scaffold (BVS) and the Xience metallic everolimus-eluting stent (EES). (A) TLF rate was significantly increased to 5 years in the BVS treatment arm. (B) Beyond 3 years, the timepoint for complete scaffold resorption, TLF event rates were similar between the devices.

Reproduced with permission from Powers DA, Camaj A, Kereiakes DJ, et al. Early and late outcomes with the Absorb Bioresorbable Vascular Scaffold: Final report from the ABSORB clinical trial program. JACC Cardiovasc. Interv. 2025 Jan12;18(1):1-12.

The DynamX Bioadaptor

The DynamX bioadaptor (Elixir Medical) is comprised of three separate thin (71µ) CoCr sinusoidal helical strands that are temporarily locked to provide radial strength and strut integrity upon device expansion while maintaining longitudinal continuity of the helical prosthesis (Video).[7,8] The helical strands are coated and held together by a 9 µm dual layer conformal bioresorbable polymer, with the outer 3 µm composed of PLGA that resorbs over 3 months and elutes sirolimus, while the inner 6 µm basecoat is composed of a PLLA-based polymer that resorbs over 6 months with subsequent unlocking and separation of the helical strands.

This novel design of the DynamX bioadaptor creates a unique long-term mechanism of action to provide dynamic support of the diseased vessel, offsetting the burden of atherosclerotic disease while restoring the vessel function to a more natural state. The bioadaptor has three distinct phases:

(1) In the locked phase, designed for delivery and implantation, the bioadaptor establishes the blood flow lumen to achieve acute benefit of the angioplasty procedure.
(2) Unique to the bioadaptor, the second phase occurs when the device unlocks and separates after 6 months, permitting vessel motion and adaptive remodeling to maintain the established blood flow lumen.
(3) After the unlocking and separation phase, the final, functional phase provides dynamic support to restore vessel hemodynamic modulation by improving pulsatility, compliance, and adaptive blood flow volume.

Bioadaptor Pre-Clinical and Clinical Trials

Pre-Clinical Study. Circumferential unlocking of the bioadaptor is associated with enhanced flexibility/conformability and adaptive vessel remodeling which has been demonstrated in the adult porcine coronary model.[9,10] In this pre-clinical model, serial intracoronary imaging using optical coherence tomography (OCT) demonstrated a significant increase in both device and vessel lumen area at 12 months following bioadaptor implantation.

Insights From Intravascular Imaging. Subsequently, in a 50-patient, single-arm "proof of concept" trial involving clinically stable patients with non-complex coronary target lesions, intracoronary imaging with OCT and intravascular ultrasound (IVUS) performed at baseline (post procedure) and at 9- or 12-months post implantation demonstrated recovery in vessel pulsatility, as well as an increase in both device and vessel lumen area on late imaging follow-up (Figure 3A-B).[8,11]

The increase in device and lumen area appeared to offset neointimal hyperplasia ingrowth with resultant very low levels of angiographic late lumen loss by quantitative coronary angiography (QCA). Further, DynamX demonstrated restoration of coronary artery rotational motion after unlocking at 6 months and reduced geometric vessel distortion with more normal recovery in vessel angulation at late (9-12 month) QCA follow-up (Figure 3C-D).[12]

BIOADAPTOR Randomized Clinical Trial at 12 Months. More recently, the DynamX bioadaptor was compared (1:1 randomized RCT) to the Resolute Onyx zotarolimus-eluting DES involving 445 patients. The primary endpoint was TLF powered for non-inferiority at 12 months.[13] A key secondary endpoint included stationary IVUS pulsatility analysis of patient paired images obtained immediately post implant and at 12 months. Device, lesion, and procedural success rates were high and similar between devices, demonstrating excellent implantability and acute procedure success.

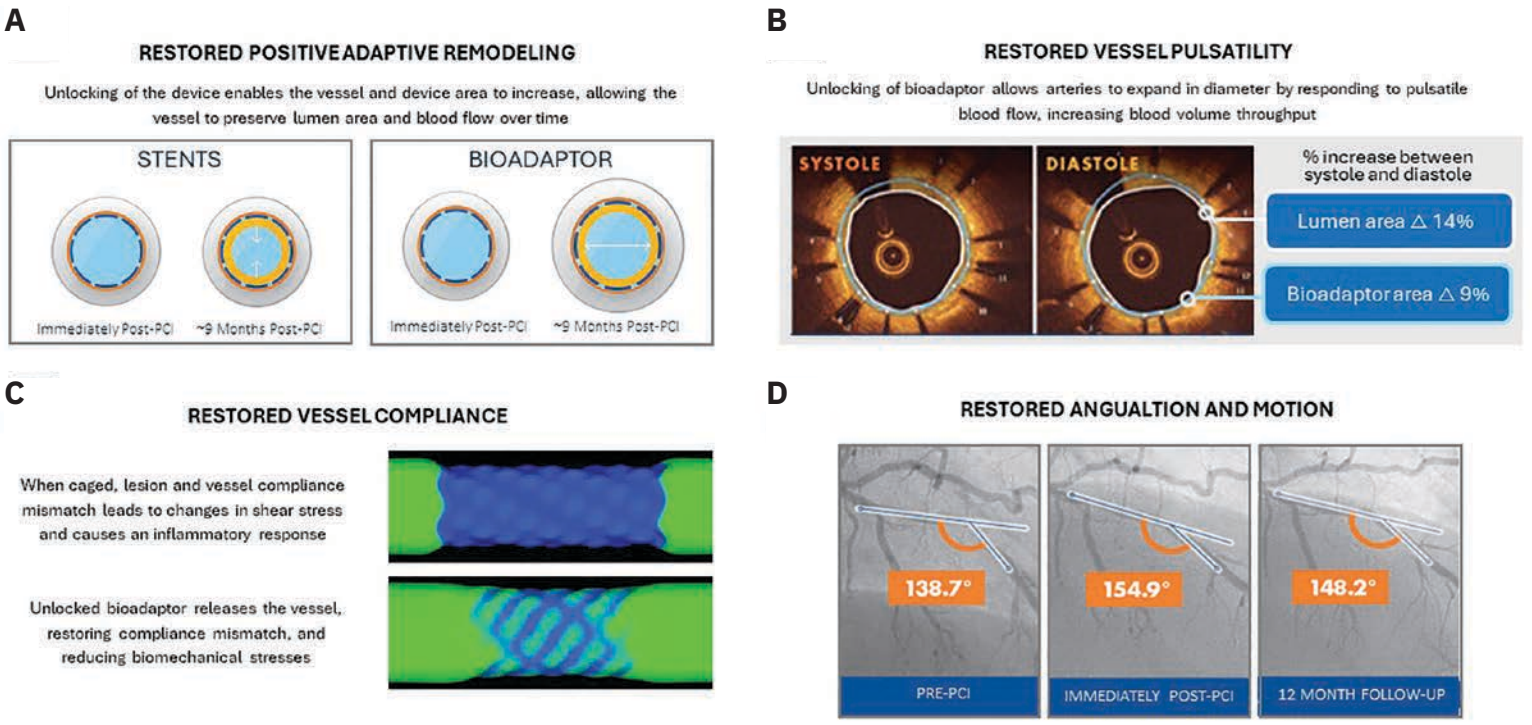

Figure 3. Bioadaptor mechanistic study documents recovery in vessel function. (A) Restoration of positive adaptive vessel remodeling as reflected by an increase in vessel and device lumen at late (9-12 months) follow-up. (B) Restoration of pulsatility with systematic variance in lumen area between systole and diastole in paired core-lab interpreted optical coherence tomographic images. (C) restoration of vessel compliance with reduction in shear stress abnormalities and geometric vessel distortion. (D) restoration of more normal vessel angulation by quantitative coronary angiography in late follow-up.

Adapted with permission from Verheye S, et al. Twelve-month clinical and imaging outcomes of the uncaging coronary DynamX bioadaptor system. EuroIntervention. 2020;16:e975-81.

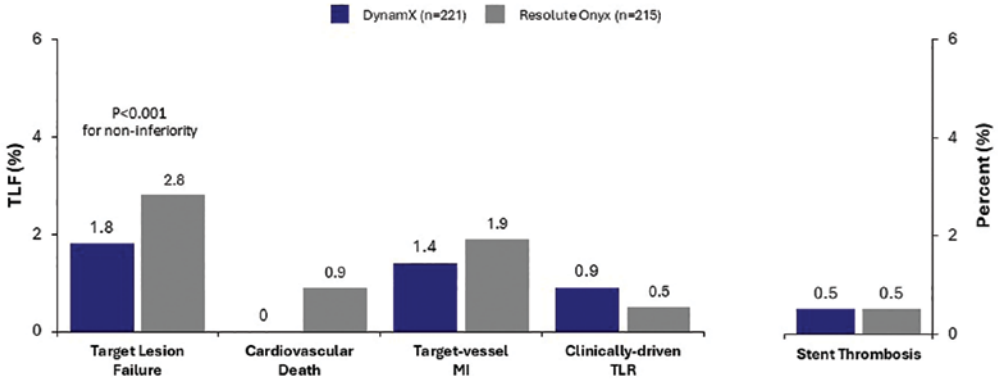

Figure 4. Primary endpoint and component events to 1-year in the BIOADAPTOR randomized trial. TLF was reduced in the bioadaptor arm, and the primary endpoint of non-inferiority was met. TLF components and stent thrombosis (ST) (definite/probable ST) were similar between devices.

Reproduced with permission from 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: 12-month clinical and imaging data from the mult-centre, international, BIODAPTOR-RCT. eClinicalMedicine. 2023;65:102304.

At 12 months, the primary endpoint was met (TLF 1.8% DynamX, 2.8% Onyx; *P*<.001 for noninferiority), and TLF component endpoints were similar between devices (Figure 4). In the IVUS sub-study, post implantation lumen area change during the cardiac cycle was similar between devices (Figure 5A).

However, at 12 months, significant differences were observed between devices involving the proximal, mid and distal in-device segments, consistent with a return in vessel pulsatility among DynamX-treated patients (Figure 5B). Although QCA performed at baseline demonstrated no difference in any angiographic measure between devices at 12 months, both the % diameter stenosis and the degree of late lumen loss favored DynamX (Figure 6A-B).

These QCA results were supported by paired IVUS images showing less neointimal hyperplasia volume and less % neointimal obstruction following DynamX.[13] An unexpected additional observation was made by IVUS comparing

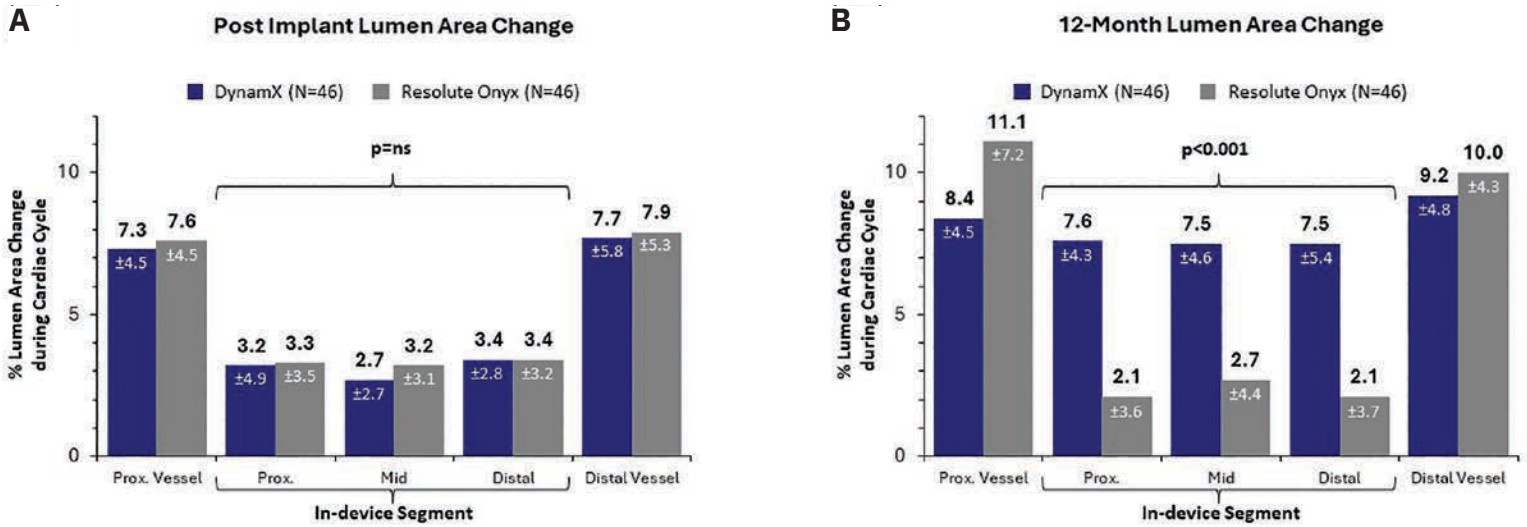

Figure 5. In-device pulsatility documented by lumen area change on late intravascular imaging. **(A) Percentage (%) lumen area change on intravascular ultrasound (IVUS) imaging through the cardiac cycle following device implantation in the 5 mm vessel segments proximal and distal to the device treated segment and within the proximal, mid- and distal device segment. No differences were observed immediately post-implant by device. (B) at 12-months follow-up, IVUS demonstrates no difference in lumen area change between devices at the proximal and distal margins, but significant differences within device for the bioadaptor. This observation is consistent with a return in vessel pulsatility.**

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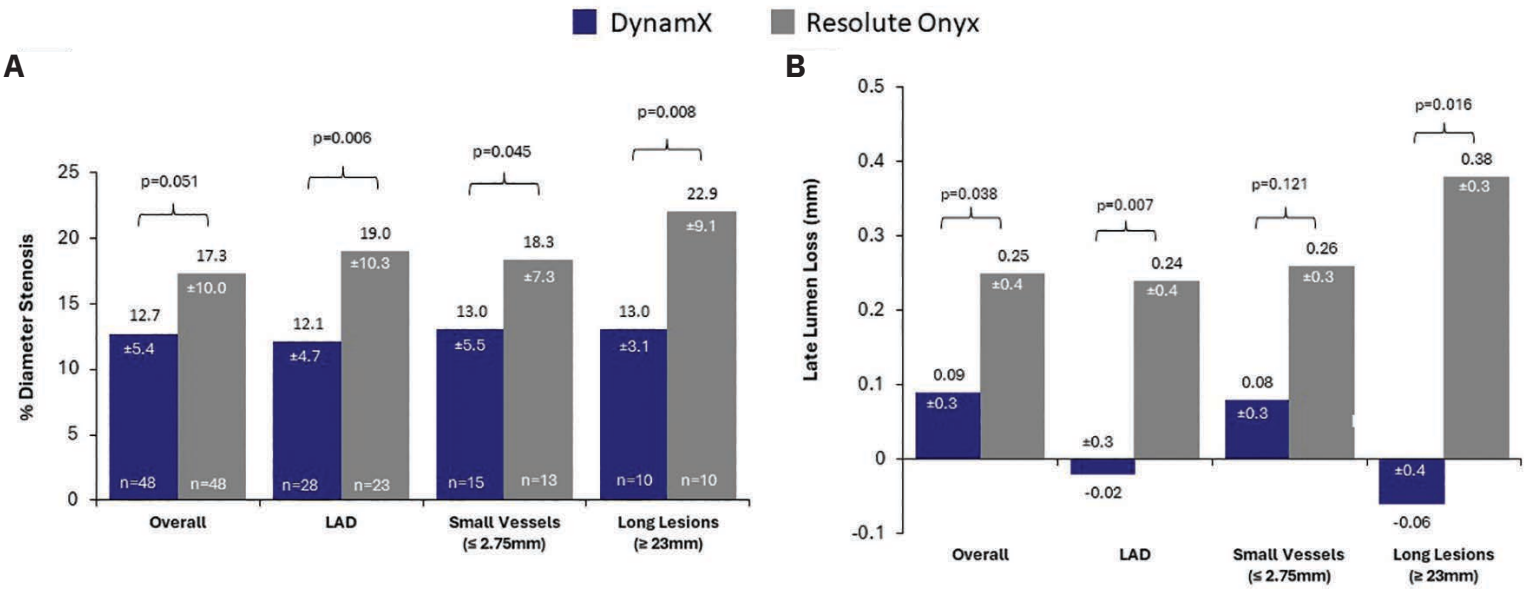
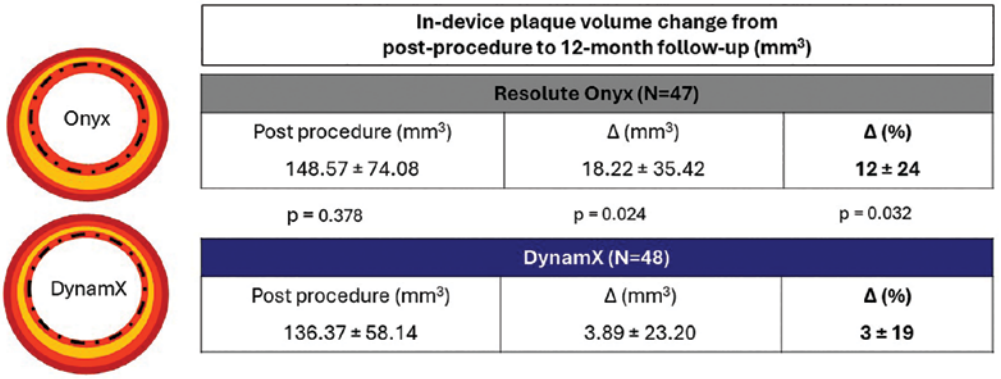


Figure 6. Angiographic diameter stenosis % and late-lumen loss at 12-month follow-up by device. **(A) Blinded, central angiographic core-lab analysis demonstrates a reduction in % stenosis overall and for specific high-restenosis subgroups. (B) Late-lumen loss at late follow-up was less among bioadaptor-treated subjects for the same subgroups analyzed in A.**

Reproduced with permission from 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: 12-month clinical and imaging data from the mult-centre, international, BIODAPTOR-RCT. eClinicalMedicine. 2023;65:102304.



In-device plaque volume change from post-procedure to 12-month follow-up (mm^3)		
Resolute Onyx (N=47)		
Post procedure (mm^3)	Δ (mm^3)	**Δ (%)**
148.57 ± 74.08	18.22 ± 35.42	**12 ± 24**
p = 0.378	p = 0.024	p = 0.032
DynamX (N=48)		
Post procedure (mm^3)	Δ (mm^3)	**Δ (%)**
136.37 ± 58.14	3.89 ± 23.20	**3 ± 19**

Figure 7. Plaque volume changes at 12 months. In-device plaque volume change (absolute and % change) by device in co-registered blinded core-lab analyses comparing baseline (post-procedure) to 12-month follow-up images. The bioadaptor was associated with significantly less plaque volume growth and regression among patients with lipid-rich, non-calcified plaque.

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plaque volume changes (mm^3) from baseline to 12 months post-device implantation. (Figure 7). This IVUS-derived evidence for plaque stabilization and regression following DynamX compared with plaque volume increase following Onyx treatment suggests the potential for lipid-lowering drug-device synergy with the restoration of more normal vessel physiology and function, and return of the plaque efflux mechanism. This observation should be considered hypothesis generating and requires further confirmatory evidence.

BIOADAPTOR Randomized Clinical Trial at 2 Years. Clinical events to 2 years from the BIOADAPTOR RCT were recently presented at the annual EuroPCR 2024 meeting.[14] These results demonstrated progressive divergence of the time-to-event curves for TLF for the ITT population and a statistically significant difference (for superiority) when the "per-protocol" or as treated populations were analyzed for TLF including a TLF assessment of left anterior descending (LAD) artery lesions. (Figures 8A-C).

This reflects the fact that one of the early adverse events in the bioadaptor arm occurred in a patient who was enrolled and treated for in-stent restenosis following BRS failure, which was a protocol exclusion. Indeed, in long-term follow-up, only a single event was observed in the bioadaptor arm between 6 months and 2 years compared to 6 events in Resolute Onyx arm. This extremely low annualized rate of TLF beyond 1 year, if sustained, will represent a new "gold standard" for long-term coronary device performance.

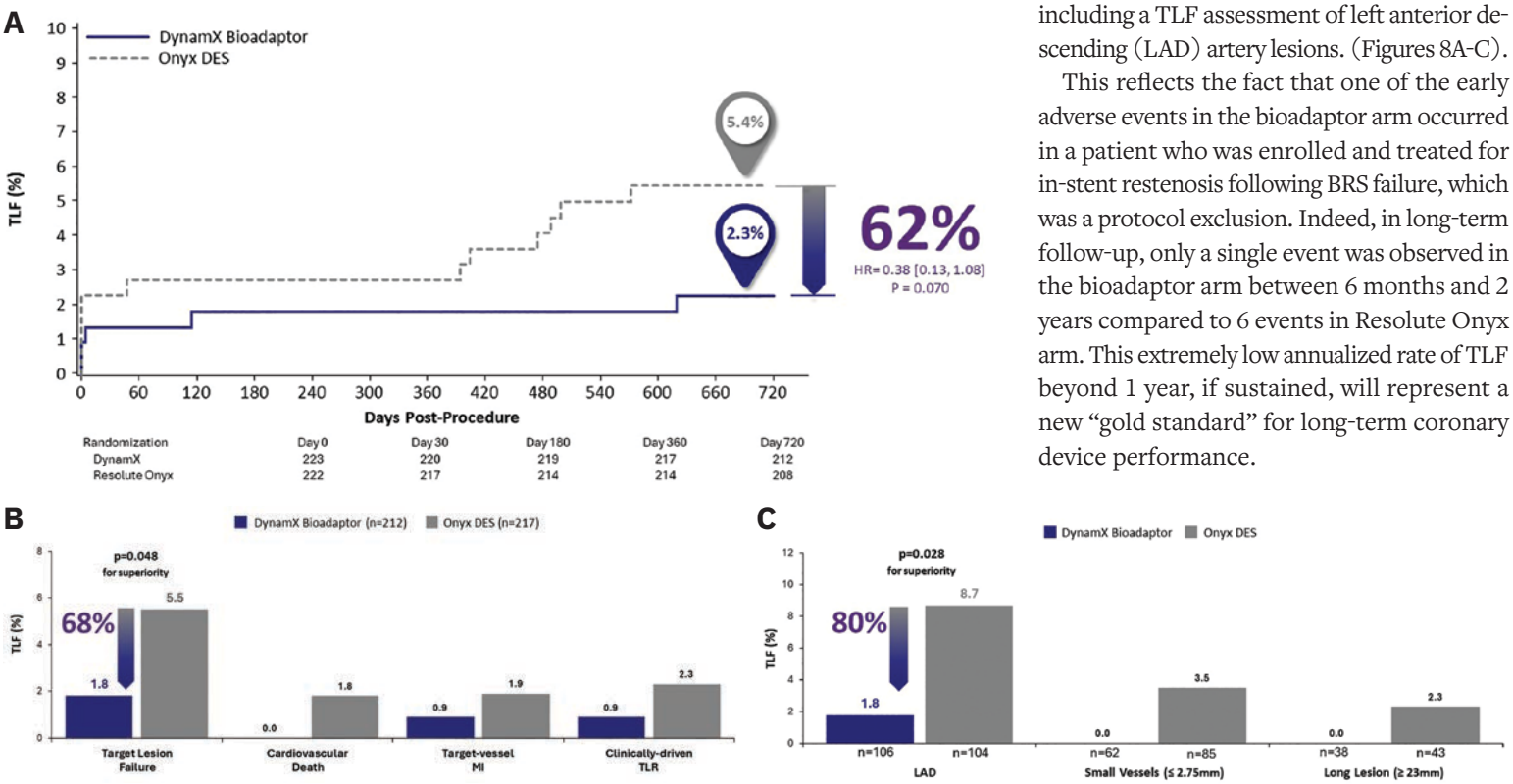

Figure 8. Target lesion failure events to 2 years by randomly assigned device. (A) Time to event curves for the intention-to-treat population shows a 62% relative reduction in events for bioadaptor-treated subjects. (B) Per-protocol analysis excluding protocol deviations (3 subjects in the bioadaptor arm were treated for in-stent restenosis with re-stenting) shows a statistically significant difference in TLF to 2-years favoring bioadaptor with the between-device difference in events widening over time. (C) Per-protocol analysis excluding protocol deviations shows a statistically significant reduction in TLF in LAD lesions to 2 years favoring bioadaptor.

Reproduced with permission from Saito S, et al; BIOADAPTOR-RCT Collaborators. Percutaneous coronary treatment with bioadaptor implant vs drug-eluting stent: 2-year outcomes from BIOADAPTOR RCT. JACC Cardiovasc Interv. 2025 Feb 26:S1936-8798(25)00497-2.

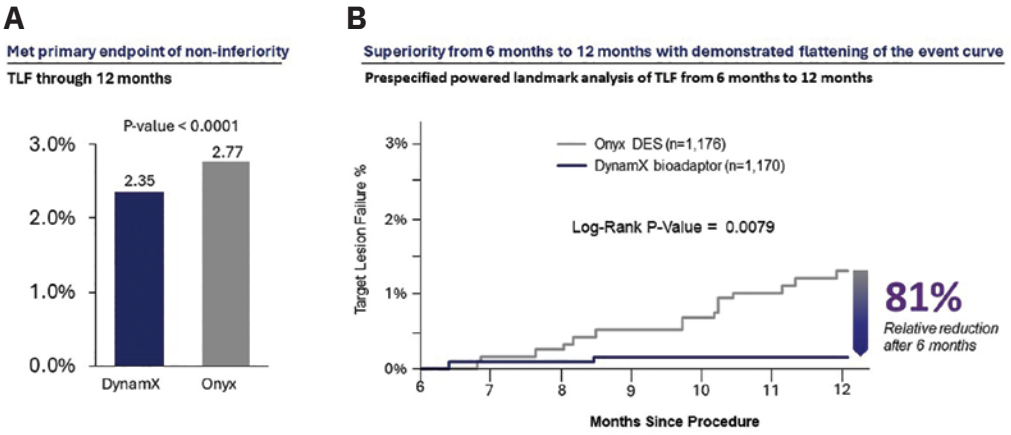

Figure 9. INFINITY SWEDEHEART Randomized (1:1) Controlled Trial of DynamX Bioadaptor versus Onyx (Medtronic). Primary endpoint analysis (A) proved non-inferiority of DynamX (versus Onyx) for TLF at 1-year. (B) Pre-specified landmark analysis of TLF from 6 months to 12 months demonstrates an 81% relative reduction in TLF (P=.0078 for superiority) compared with Onyx.

Reproduced with permission from Erlinge D, et al. Bioadaptor implant versus contemporary drug-eluting stent in percutaneous coronary interventions in Sweden (INFINITY-SWEDEHEART): a single-blind, non-inferiority, registry-based, randomised controlled trial. Lancet. 2024 Nov 2;404(10464):1750-1759.

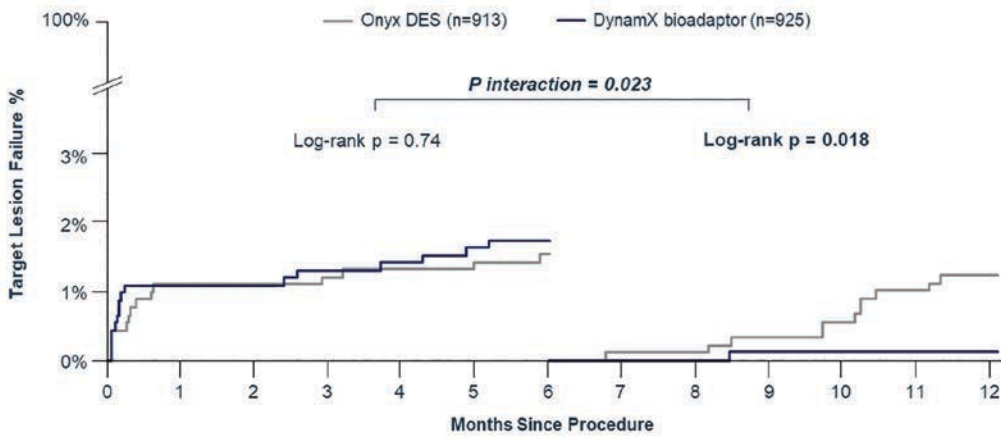

Figure 10. Cumulative event estimates for the powered secondary composite outcome of target lesion failure in patients with acute coronary syndrome at 12 months. Event estimates were calculated via the Kaplan–Meier method. Log-rank p values and p values for interactions are reported on time-to-event curves. No difference observed between 0 to 6 months while prespecified powered landmark analysis showed significant reduction in TLF rates and plateauing of curve after 6 months in the favor of bioadaptor.

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INFINITY-SWEDEHEART Randomized Clinical Trial. Finally, the large-scale INFINITY-SWEDEHEART RCT (NCT04562805) comparing DynamX with Onyx (1:1 randomized) in 2400 patients enrolled at 20 sites in Sweden, which includes a significant portion of acute coronary syndrome (ACS) patients, presented primary outcomes at the 2024 TransCatheter Therapeutics (TCT) meeting.[15] Both procedure and device success rates were similar for DynamX and Onyx. At 1 year, the rate of TLF observed for DynamX was non-inferior (2.35 versus 2.77%; *P*<.001) compared with Onyx. In a pre-specified, powered secondary endpoint, landmark analysis beyond 6 months post-device implantation, DynamX reduced the rate of subsequent TLF by 81% (*P*=.0079) (Figure 9).

The time-to-event curves for the powered landmark analysis of TLF in patients with ACS are shown in Figure 10. No differences in risk comparisons were observed between the study groups from 0 months to 6 months (log-rank *P*>.05). In the landmark analysis from 6 months to 12 months, Kaplan-Meier estimates of TLF in patients with ACS were 0.3% (events in two of 906) versus 1.8% (events in 12 of 895); hazard ratio: 0.17 [0.04–0.74]; *P*=.018, with *P* interaction = .023 demonstrating significant change in treatment effect after 6 months in the favor of the bioadaptor.

Conclusion: A Potential Paradigm Shift in PCI

Collectively, follow-up from multiple RCT patients forms a substantial body of evidence to establish objectively documented recovery in target lesion/vessel function that favorably impacts the 2%-3% annualized incidence of late adverse coronary prosthesis-related events documented with all prior PCI devices. If the DynamX bioadaptor provides "best-in-class" procedural performance followed by restoration of more normal vessel physiology and consequent improvement in clinical outcomes over time, a paradigm shift in PCI will occur. ■

References are available with the article online:

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Disclosures: Dr. Kereiakes reports he is a consultant for Elixir Medical, Inc, and will be the international co-principal investigator (along with Robert Yeh, MD) for the upcoming U.S. FDA IDE trial.

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