



# The Bioresorbable Vascular Scaffolds: Actual Knowledge and Future Prospects

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## Abstract

Coronary angioplasty was born in 1977, and since then it has not stopped evolving. Starting with plain old balloon angioplasty, the discipline knew the advent of the bare metal stent in 1986 and dual antiplatelet therapy since 1992. Due to the unacceptable rate of stent restenosis, the Drug Eluting Stents (DES) emerged in 2000, with a first generation that later knew an increase in late stent thrombosis. Therefore, the second-generation DES came with biocompatible or biodegradable polymers and thinner platforms; however very late stent thrombosis and late restenosis still remain at residual rate due to different DES components. Also, long-term vessel caging in particular impairs normal vasomotricity and long-term positive remodeling. To resolve these issues, the Bioresorbable Vascular Scaffolds (BVS) came into clinical practice in 2011, showing good initial results. Several randomized trials, meta-analyses and registries were performed, most of which with the Absorb Bioresorbable Vascular Scaffold System (Abbott Vascular, USA). This new technology is still hindered by some factors, such as the BVS radial strength, its strut thickness, and the inflammatory reaction related to scaffold degradation. Moreover, there is existing data showing a higher thrombosis rate observed with the Absorb BVS compared with the new generation of DES, despite not affecting cardiovascular death.

In this Review, we discuss the clinical procedural and technical evidence on BVS, with emphasis on their clinical impact. We finally tackle the future directions on device and procedural improvement while asking the question: is the bioresorbable technology still the way to the future?

**Keywords:** Percutaneous interventions; Bioresorbable vascular scaffolds; ST; ICI

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## Introduction

The extensive use of Drug-Eluting Stents (DES) as compared to Bare Metal Stents (BMS) led to a remarkable reduction in the rate of restenosis [1], but resulted in a progressive increase in late Stent Thrombosis (ST) [2]. The latter was reduced with the development of second-generation DES due to biocompatible or biodegradable polymers and thinner platforms. Although substantially reduced, ST-especially Very Late ST (VLST) -and late restenosis still remain major challenges [3]. ST is essentially linked to the presence of permanent metallic struts, chronic degeneration caused by an inflammatory response to the coating polymer, and/or adverse effects of antiproliferative drugs on endothelial regeneration. Furthermore, long-term vessel caging impairs arterial physiology hampering normal vasomotricity while promoting long-term positive remodeling.

In 2011, self-degrading coronary stents - the Bioresorbable Vascular Scaffolds (BVS or BRS) -were introduced into clinical practice, showing good short-term results [4]. The hypothesized benefits of BVS over current metallic stents are: (1) reduction in long-term adverse events from permanent materials; (2) restoration of the pulsatility and vasoreactivity of the treated vessel through bioresorption; (3) maintaining suitability for future treatment options in multivessel disease and long lesions; (4) implantation in STEMI patients (frequently young patients with less extensive disease); (5) pediatric applications and (6) feasibility of noninvasive imaging, such as computed tomographic angiography or magnetic resonance imaging [5].

Several studies were conducted, most of which were performed with the Absorb BVS System (Abbott Vascular, USA), with nearly 200000 devices implanted worldwide by June 2017 [6]. The Absorb BVS consists of a 150- $\mu$ m-thick bioresorbable poly (l-lactide) scaffold with a 7- $\mu$ m thick bioresorbable poly (D,L-lactide) coating, which elutes everolimus.

Intracoronary Imaging (ICI) studies support the distinctive attributes of BVS, with restoration of vasomotion by 12 months, and late lumen gain with plaque regression between 2 and 5 years [5].

Despite their potential benefits, BVS have several limitations including decreased radial strength, increased strut thickness, and an inflammatory reaction potentially related to scaffold degradation. Moreover, there is available data showing a higher thrombosis rate observed with Absorb BVS compared with the new generation of DES, despite not affecting cardiovascular death.

In this review, we will discuss the current data on technical and clinical evidence on BVS while discussing future directions.

## Characteristics and Procedural Aspects of the “Vascular Restoration”

### Biodegradation and vascular restoration

One of the most significant theorized benefits of BVS is the achievement of “vascular restoration” [7]. The actual reabsorption kinetics is largely variable, depending on several factors. These latter include the chemical composition, thickness, patient characteristics and design of scaffold struts [5]. In fact, overexpansion beyond proper design specifications is associated with faster degradation and erosion, with a loss of structural integrity and drug-release kinetics. An association was found between unfavorable BVS reabsorption and restenosis [8], however despite a lower Minimal Lumen Diameter (MLD) at 2 years after BVS implantation, the restenosis rate was similar to that in the Everolimus-Eluting Stent (EES) group. Noteworthy, data from randomized trials showed that at 12 and 24 months after BVS implantation, the restoration of vasoreactivity/vasomotion was directly proportional to the degree of reabsorption, was influenced by plaque composition and endothelial function and was maintained at 5 years [9].

### Procedural aspects of BVS deployment

It's established that BVS implantation is different from that of metallic DES, and the performance of a specific technique was associated with a reduced rate of ST [10]. Alternatively, implantation of an oversized Absorb scaffold in small vessels is associated with a higher rate of Major Adverse Cardiovascular Events (MACE) than implantation of a DES.

### The key steps in BVS implantation, known as PSP (Predilatation, Sizing, Postdilatation) are

#### Step 1: Lesion preparation with predilatation

Predilatation using an appropriate size balloon is mandatory to obtain a stent-like result before scaffolding, which should minimize the risk of thrombosis.

#### Step 2: Sizing, stepwise deployment, and balloon inflation

Severe under expansion was demonstrated in all reported cases of acute or subacute BVS thrombosis [10], which underlines the importance of careful BVS sizing. ICI might help to find the most favorable scaffold-artery ratio. As known, scaffold deployment should be performed in a stepwise fashion (2 atm every 5 seconds). Finally, balloon inflation should be maintained for  $\geq 30$  s to achieve optimal expansion. BVS are better deployed up to 12 atm to avoid proximal and distal injury [7].

#### Step 3: Post-dilatation with a noncompliant balloon

The lower the post-dilatation rate the higher the rate of Scaffold

Thrombosis (ScT). Current recommendations imply the use of a noncompliant balloon inflated at high pressure, with a nominal diameter up to 0.25 mm to 0.50 mm larger than the nominal scaffold diameter, depending on the scaffold-to-vessel ratio. ICI is very helpful in guiding post-dilatation, mainly to detect insufficient expansion or scaffold undersizing. Distinguishing underexpansion from undersizing is crucial to prevent rupture or strut fracture [7].

## Clinical Data on Bioresorbable Vascular Scaffolds

Several BVS with variable resorption from 1 to 3 years have been examined in clinical trials. All are impregnated with an antiproliferative limus family drug. The characteristics of the main available BVS are summarized in Table 1. The clinical/historical data are outlined as follows.

### First in man experience: the igaki-tamai stent

This was the first fully biodegradable scaffold tested in humans (Kyoto Medical Planning, Japan). A scaffold made from non-drug-eluting, high-molecular-weight Poly-L-Lactic Acid (PLLA) monofilaments [11] with a helical coil design and a strut thickness of 170  $\mu$ m. Long-term data from an observational, nonrandomized clinical trial of 50 patients reported in 2012 showed that survival rates free of cardiac death and MACE were 98% and 50% respectively. Most importantly, long-term imaging showed positive vessel remodeling and lumen enlargement. This paved the way for future development of BVS.

### The Absorb BVS

#### Absorb BVS in randomized clinical trials (RCTs) (Table 2)

- o In the ABSORB II trial, BVS was compared with the Xience metallic EES (Abbott Vascular, USA). At 1 year, the rate of first time or worsening angina was lower with BVS than with EES (20% vs. 30%;  $P=0.04$ ), whereas non-significant differences were reported for the Device-Oriented Composite End point (DOCE). At 3-year follow-up, the vasomotor reactivity and non-inferior Late Luminal Loss (LLL) for the Absorb BVS was found to be significantly lower in the Xience group. A higher rate of DOCE due to target vessel MI, including peri-procedural MI, was observed in the Absorb group. The patient-oriented composite endpoint, angina status, and exercise testing were not statistically different between both devices at 3 years [12].

- o ABSORB Japan was a single-blind, multicenter, randomized trial. The rate of TLF was numerically higher in the BVS arm than in the EES arm, although this difference was not statistically significant ( $p=0.18$ ). VLST was observed only in the BVS arm at a rate of 1.6% between one and two years [13].

- o The EVERBIO II trial showed no significant differences in clinical outcomes at 2 years between BVS and EES. Event rates were numerically higher in BVS-treated patients. However, when BVS were compared to Biolimus Eluting Stent alone, the occurrence of device related adverse events was significantly increased [14].

- o The randomized ABSORB-STEMI TROFI II trial studied patients with ST-Segment Elevation MI (STEMI) treated with Absorb or Xience stent. The Optical Coherence Tomography (OCT)-based healing score at 6 months was lower in Absorb than in EES (1.74 vs. 2.80;  $p<0.001$  for non-inferiority). The DOCE was similarly low in the two groups [15].

- o In the randomized ABSORB III trial at 1-year follow-up,

**Table 1:** BVS are summarized.

Scaffold	Manufacturer	Polymer	Eluted drug	Strut thickness (µm)	Resorption time (months)	Development status
Igaki-Tamai	Kyoto Medical	PLLA	None	170	24–36	CE mark
Absorb 1.1	Abbott Vascular	PLLA	Everolimus	156	24–48	CE mark - FDA
DESolve	Elixir Medical	PLLA	Novolimus	150	12–24	CE mark
Magmaris	Biotronik	BIOLute coating	Sirolimus	150	12	CE mark
ART 18Z	Terumo	PDLLA	drug free	160	18–24	CE Mark
DESolve Cx	Elixir Medical	PLLA	Novolimus	120	12–24	Clinical testing
Fantom	Reva Medical	PTD-PC	Sirolimus	125	Unknown	Clinical testing

CE: Conformité Européenne; NA: Not Available; PDLLA, Poly-DL-Lactic Acid; PLGA: Poly Lactic-co-Glycolic Acid; PLLA: Poly-L-Lactic Acid; PTD-PC: Poly-Tyrosine-Derived Polycarbonate

the primary end point of TLF was non inferior in the BVS group compared with the EES group. No significant difference was also seen for cardiac death (0.6% vs. 0.1%;  $P=0.29$ ), target-vessel MI (TVMI; 6.0% vs. 4.6%;  $P=0.18$ ), or ischemia-driven TLR (3.0% vs. 2.5%;  $P=0.50$ ). Device Thrombosis (DT) occurred in 1.5% of patients with BVS and in 0.7% of patients with EES ( $P=0.13$ ) [16]. Notably, the enrollment in ABSORB III was restricted to patients with relatively stable symptoms and noncomplex coronary lesions, not generalizable to *real-life* clinical practice.

Despite this restriction, at 25 months' follow-up, MACE was more prevalent with Absorb compared to Xience (TLF 10.9% vs. 7.8%;  $p=0.03$ ). The increased event rate was mainly in the smallest-caliber treated vessels with a reference vessel diameter (RVD) of <2.25 mm by quantitative coronary angiography (QCA) [16].

Based on the above data, the Food and Drug Administration released a safety alert on March 18, 2017 recommending the adherence to Dual Antiplatelet Therapy (DAPT) during BVS use while avoiding its use in small vessels to help decrease MACE [17]. Three-year data for the ABSORB III trial then came out with the BVS group having higher event rates than EES, particularly TVMI and DT.

o The AIDA trial (Amsterdam Investigator-Initiated Absorb Strategy All-Comers Trial) randomly allocated 1845 patients undergoing Percutaneous Coronary Intervention (PCI) to receive either a BVS or a DES. The primary end point was target-vessel failure (TVF, a composite of cardiac death, target-vessel MI, or target-vessel revascularization). The data and safety monitoring board recommended early disclosure of the study results because of safety concerns. In the 2-year follow-up, definite or probable DT occurred in 3.5% vs. 0.9% (hazard ratio, 3.87;  $P<0.001$ ) with cardiac death occurring in 2.0% and 2.7%, respectively [18]. Pre-dilation and post-dilation were performed in the majority of patients (98.6% and 74%, respectively) in the BVS group, yet the 2-year rate of definite or probable ScT remained unacceptably high.

#### Absorb BVS in registries and retrospective analyses

The large number of patients included in real-life registries with heterogeneous clinical and angiographic characteristics allowed the assessment of less common clinical end points, such as thrombosis, which was higher than expected. That led to the design of randomized studies targeting that issue [10].

The ABSORB Extend study (*first* 512 patients enrolled; 12-month MACE 4.3) [19] showed that minor systematic oversizing of the BVS followed by high pressure post-dilatation is safe and effective with a low rate of MACE and no reported ScT events. In the Polish National registry (591 patients) [20], early in-hospital results found no

significant differences between BVS and EES in the primary composite MACE end point in patients with Acute Coronary Syndrome (ACS) and those with complex lesions. However, the early registries were single centered with a follow-up within 12-month.

In the large multicenter Ghost-EU registry of 1189 patients, researchers assessed the performance of the Absorb BVS in a real-world setting [21]. The incidence of TLF was 4.4% at 6 months, and diabetes mellitus was the only independent predictor of TLF (HR 2.41,  $P=0.006$ ). However, the cumulative incidence of definite or probable ScT was 1.5% at 30 days and 2.1% at 6 months. Ostial lesions ( $P=0.049$ ) and impaired left ventricular ejection fraction ( $P=0.019$ ) were independent predictors of ScT. Most importantly, in this registry and in BVS registry Gottingen the rates of device-related complications with BVS were found not negligible and they did not decline over time [22].

Finally, the ISAR-ABSORB registry included 419 patients undergoing PCI with BVS, including 39% of patients with ACS [15]. At 12 months, the incidence of TLR among these patients was 13.1%, whereas definite ST occurred in 2.6% of patients [23]. The 2-year data found a disturbing 21.6% MACE rate with ABSORB BVS. The rate of definite or probable ST at 2 years was 4.2% [23].

#### Absorb BVS in meta-analyses

o Lipinski et al. [24] analyzed 10510 patients and showed that patients treated with BVS were at higher risk of MI (OR 2.06,  $p=0.002$ ) and definite or probable ScT (OR 2.06,  $p=0.03$ ) than those treated with DES. However, no significant difference was found for all-cause and cardiovascular mortality. Conversely, BVS post-dilatation was performed in only 52% of treated lesions [24].

o Collet C et al. [25] studied 16830 patients treated with ABSORB. The overall rate of definite or probable ScT was 1.8%, and the residual percent diameter stenosis was the only factor associated with ScT [5]. A similar meta-analysis of 1730 patients was conducted by the same authors with 24 months follow-up [25]. Patients treated with Absorb BVS were found to have a higher risk of DT compared with those treated with EES. 92% of the Very late ScT in the BVS group occurred in the absence of DAPT. Patients treated with Absorb had a trend towards higher risk of TLF (OR 1.48;  $P=0.09$ ), driven by a higher risk of TVMI and ischemia-driven TLR. No difference was found in cardiac death.

o Polimeni et al. [26] showed in 5219 patients, higher rates of TLF (9.4% vs. 7.2%; OR=1.33;  $p=0.008$ ) and DT (2.3% vs. 0.7%; OR=3.22;  $p<0.0001$ ) in BVS compared with EES. The incidence of both early (within 30 days after implantation) and very-late DT (>1 year) was also higher with BVS. They concluded that BVS was

**Table 2:** Randomized clinical trials comparing BVS and DES.

Clinical trial (year)	Number of patients (BVS:DES)	Primary end point	Primary outcome	DOCE rate (%; BVS versus DES)	Scaffold thrombosis rate (%; BVS versus DES)
ABSORB II (2015)	501 (2:1)	Vasomotion/minimal lumen diameter (3 years)	Ongoing (3-year follow-up)	5 vs. 3 ( $P=0.35$ )	0.9 vs. 0 ( $P=0.55$ )
ABSORB China (2015)	480 (1:1)	In-segment lumen loss (1 year)	0.19 ± 0.38 mm vs. 0.13 ± 0.38 mm ( $P=0.01$ )	3.4 vs. 4.2 ( $P=0.62$ )	0.4 vs. 0 ( $P=1.00$ )
ABSORB Japan (2015)	400 (2:1)	Target-lesion failure (1 year)	4.2% vs. 3.8% ( $P_{ni}<0.0001$ )	NA*	1.5 vs. 1.5 ( $P=1.00$ )
EVERBIO II (2015)	240 (1:2)‡	Late lumen loss (9 months)	0.28 ± 0.39 vs. 0.25 ± 0.36 ( $P=0.30$ )	12 vs. 9 ( $P=0.6$ )	1.3 vs. 0
STEMI-TROFI II (2015)	191 (1:1)	Healing score§ (6 months)	1.74 vs. 2.80 ( $P_{ni}<0.001$ )	1.1 vs. 0	1.1 vs. 0
ABSORB III (2015)	2,008 (2:1)	Target-lesion failure (1 year)	7.8% vs. 6.1% ( $P=0.16$ , $P_{ni}=0.007$ )	10.9 vs. 7.8% ( $P=0.03$ )	1.5 vs. 0.7 ( $P=0.13$ )
AIDA (2015)	1,845	24-month TVF	11.7% vs. 10.7% ( $P=0.43$ )	NA*	3.5% vs. 0.9% (hazard ratio, 3.87; $P<0.001$ )

BVS: Bioresorbable Vascular Scaffold; DES: Drug-Eluting Stent; DOCE: Device-Oriented Composite End Point; NA: Not Available;  $P_{ni}$ :  $P$  value for noninferiority \*DOCE corresponds to the primary end point. ‡Patients with DES were treated 1:1 with either everolimus-eluting stents or biolimus-eluting stents. §Score based on optical coherence tomography imaging.

associated with worse two-years clinical outcomes compared with EES in patients with coronary artery disease [26].

o Elias et al. [27] analyzed 3258 patients treated with BVS and 2319 with EES. The primary outcome of TLF occurred more frequently in BVS (OR 1.34;  $p=0.003$ ). Overall definite/probable DT occurred more frequently with the BVS (OR 2.86;  $p<0.001$ ) and this extended beyond 1 year of follow-up (OR 4.13;  $p<0.001$ ). Clinically indicated or ischemia driven TLR and all MI were more frequently seen in BVS, however, cardiac death was not significantly different [27].

o Sorrentino S et al. [28] compared the effectiveness of Absorb vs. metallic EES in 5583 patients undergoing PCI with a median follow-up of 2 years. Compared with EES, the risk of TLF with BVS was 9.6% vs. 7.2% (number needed to harm: 41;  $p<0.003$ ) and of ST was 2.4% vs. 0.7% (number needed to harm: 60;  $p<0.0001$ ). The increased risk for ScT was concordant across the early (<30 days), late (30 days to 1 year), and very late (>1 year) periods [28].

o Cassese S et al. [29] compared the mid-term clinical outcomes of 5583 patients treated with BVS vs. EES. Those former displayed higher risk of TLF (odds ratio =1.35;  $p=0.0028$ ) and ScT (OR 3.24;  $p<0.0001$ ) compared to EES particularly after 1year from implantation [29].

## Actual CE-Mark Approved BVS

### DESolve

The DESolve (Elixir Medical) BVS, like Absorb, has a PLLA backbone but elutes the antiproliferative drug novolimus. The coating polymer is a biodegradable polylactide-based polymer. The important features of the DESolve distinguishing it from other BVSs are (1) intrinsic self-correcting deployment properties that become operative in the event of minor strut malapposition, and (2) relative elasticity/ductility that provides a wide range of expansion without risk of strut fracture [30].

The first series of the DESolve showed a LLL at 6 months of 0.19 ± 0.19 mm, which was comparable to that seen with contemporary DES. The second series of the DESolve was assessed in the DESolve Nx trial. LLL at 6 months was 0.20 ± 0.32 mm; MACE rate at 24 months was 7.4%. No definite ScT were observed [30].

### ART Pure

This BVS has a PDLLA or poly (l-lactide-co-d, l-lactide) backbone with 170 µm strut thickness, but elutes no antiproliferative drug. There

are few clinical data concerning this scaffold. The ARTDIVA trial (Arterial Remodeling Transient Dismantling Vascular Angioplasty), the first-in-man trial enrolling 30 patients, demonstrated 1 case of ischemic-driven TLR at 6 months. No other clinical result is available to date [31].

### Absorbable Magnesium Scaffold (AMS)

They were developed in parallel to the PLLA polymeric scaffolds [32]. Potential advantages of AMS are the good radial strength with negligible early elastic recoil and a better compliance to vascular anatomy. Single step inflation makes their implantation similar to that of DES, and their electropolishing, improves their trackability. A recent pooled outcomes study of BIOSOLVE-II and BIOSOLVE-III with 184 patients aimed to assess respectively the safety and performance of the DREAMS 2G scaffold (i.e. 2<sup>nd</sup> generation; Magmaris, Biotronik AG). At 24 months, the TLF rate was 5.9%, TVMI was 0.9%, and TLR was 3.4%, with no definite or probable ScT. Finally, that study offered additional evidence on the safety of DREAMS 2G in a population with predominantly non-complex lesions. More robust data are still needed [32].

## Current Limitations of BVS

### Mechanical integrity

The mechanical properties of bioresorbable materials are primarily different from those of metal alloys and have three core limitations [33].

- Insufficient ductility, which impacts scaffold retention on balloon catheter and limits the range of scaffold expansion during deployment.
- Low tensile strength and stiffness, which require that struts be thick to prevent recoil during vessel remodeling.
- Limited elongation-to-break, which defines the opening range of the BVS.

Because of these intrinsic limitations, there is a need for a larger profile device with larger strut thickness leading to a difficulty in delivery through tortuous and noncompliant arteries.

## Clinical and Imaging Concerns

At present, ScT is the main ongoing limitation of BVS, followed by restenosis and TVR.

- o **Scaffold thrombosis: modifiable and non-modifiable**



## features

A systematic review of all reported ScT cases analyzed by ICI was conducted [34]. Malapposition (24%), incomplete lesion coverage (18%), and under-deployment (12%) were most frequently found, whereas in late/very late cases, malapposition (35%), late discontinuity (31%), and peri-strut low-intensity areas (indicating the presence of neointima [19%]) were the predominant features.

Hence, to decrease the potential risk of ScT, it might be very helpful that operators try to avoid suboptimal results [34]. However, late discontinuity and peri-strut low-intensity areas are less likely to be modified by an optimized implantation strategy.

Late discontinuity is a benign change during the bioresorption process and does not cause any problems if the scaffold struts are well covered by neointima. However, during bioresorption, struts might not be fully covered by neointima which brings thrombogenic proteoglycan into contact with blood; then, late discontinuity could be a malignant potential cause of VLScT [34].

That late discontinuity relative to Intraluminal Scaffold Dismantling (ILSD) was often observed by OCT imaging at the time of BVS VLST and was said to be causally related to the thrombotic event [13].

- o Moreover, thick stent struts, such as the 150- $\mu$ m struts in the Absorb scaffold, could make the loss of laminar flow more frequent. This results in areas of oscillatory shear stress that could promote platelet activation *or* thrombogenicity especially when they are left malapposed [35].

- o The first generation of BVS was limited by a high rate of scaffold restenosis and TVR, which was similar to that reported for BMS [8]. Such event could be related to either a suboptimal elution of antiproliferative drug or the complex implantation technique required and the resultant injury. ICI including 3D OCT in symptomatic BVS restenosis showed extensive neointimal thickening [36].

## Future Directions of BVS

### Device development

Newer BVS with better characteristics were reported, with promising results:

- The DESolve Cx novolimus-eluting BVS, Elixir
- The Fantom sirolimus-eluting BVS, Reva Medical
- The MeRes 100 sirolimus-eluting BVS, Meril Life Sciences
- The Fortitude, Magnitude, and Aptitude sirolimus eluting BVSs, Amaranth Medical
- The MIRAGE sirolimus-eluting bioresorbable microfiber scaffold (Manli Cardiology, Singapore)
- The Firesorb sirolimus-eluting BVS, Shanghai MicroPort Medical

Therefore, thinner struts, lower crossing profile and fast absorption characteristics could be the way to go. Also, maintaining strong radial force because of new post-processing of the polymer looks encouraging and could reduce the risk of BVS-specific issues.

## Procedural Optimization

The first issue is whether the clinical outcomes could be modified

by improving the implantation technique. Researchers have been investigating the influences of device sizing and implantation techniques on acute device performance indices, including acute gain, expansion index, asymmetry index, eccentricity index, and strut embedment [37].

Optimal predilatation and postdilatation are expected to improve the expansion index of the device. BVS-specific implantation technique has proved to reduce the rate of ScT from 3.3% to 1.0%, which remained significant after multivariate adjustment (hazard ratio, 0.19;  $P=0.012$ ) [10]. However, this has not been proven by randomized studies [10].

## Duration of DAPT after BVS Implantation

The latest American guidelines advocate DAPT following DES for at least 6 months in patients with stable ischemic heart and for at least 12 months in patients with ACS. However, the interruption of DAPT accounted for around 1/3 of BVS thromboses, and also VLScT. Stone G suggested that if ILSD is visualized on OCT, prolonged DAPT has to be considered, especially in patients with low bleeding risk. Restenting with a metallic DES may also be appropriate in severe cases of ILSD.

Therefore, the increased risk of ScT up to 2 years provides a good rationale for continuation of DAPT for that period.

## Summary and Conclusion

The added value of this “vascular restoration therapy” is still waiting for a proof of evidence, while safety concerns have emerged, together with the challenging device implantation, the worse trackability, the longer procedural times, and the larger amounts of contrast used [5]. Serious research is being conducted in that regard. Furthermore, the PLLA based BVS have lower tensile strength ranging from 45 to 70 MPa compared with 1449 MPa for cobalt-chromium based stents. The elongation at break for polymers is 2% to 6% compared with 40% for metallic stents [8,33]. These gaps in mechanical properties are a challenge to surmount, and despite the progress in improving the polymer composition, structure, and production process, the performance of the currently available polymer-based BVS technology appears to remain inferior to the second-generation metallic DES. Late dismantling of the polymer can also occur at the final stages of resorption, with the risk of ScT [12,16]. To surmount the tensile strength and stiffness deficiency, the first-generation BVS structure consisted of thick struts (150  $\mu$ m), however not suitable for small vessels, and at higher risk for ScT. In addition, the polymeric BVS require meticulous implantation technique (PSP) [6].

To address that issue, ABSORB IV was a prospective, randomized study, a continuation of ABSORB III. Two important design changes were made compared with ABSORB III: all treated vessels had to have a RVD of  $>2.25$  mm, and a PSP technique of pre- and post-dilation and appropriate sizing was followed routinely. Although the results are better for BVS compared with ABSORB III, results in the EES arm improved as well. Therefore, the primary outcome, TLF for BVS vs. Xience at 30 days, was 5.0% vs. 3.7%,  $p$  for noninferiority = 0.02,  $p$  for superiority = 0.11 [38].

Magnesium BVS appears to have better mechanical properties compared with PLLA-based polymers, with tensile strength ranging from 220 to 330 MPa and elongation at break of 40%. Although there is limited experience, no ScT has been reported so far in any of the

current clinical trials. The Magnesium BVS may become the way to go especially that it combines the physical properties of the metallic stents while being the fastest-dissolving device currently available, over just a 12 months' period [6,32].

At the end, this review article aimed to be broad, comprehensive and updated concerning the actual knowledge on BVS. Thinner struts, newer design characteristics, appropriate patient selection, and standardized techniques of implantation may lead to better outcomes and improve the care of our patients. In Euro PCR 2018 [39], Gregg Stone said that "we've learned a tremendous amount", and with the ongoing developments "we can get very close, if not equivalent, to metallic DES. And then the promise comes after 3 years."

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