Coronary angioplasty was first introduced in 1977. From plain old balloon angioplasty to the introduction of bare metal stents in 1986 and dual antiplatelet therapy in 1992 to much more later on. Due to the unacceptable rate of stent restenosis, drug eluting stents (DES) were introduced in 2000. The first generation showed an increase in late stent thrombosis which led to the introduction of the second generation DES with biocompatible or biodegradable polymers and thinner platforms. However very late stent thrombosis and late restenosis might still pose problems in the latter. Furthermore, there has been major debate regarding the impact of long-term vessel caging on normal vasomotricity and long-term positive remodeling. To resolve these issues, the bioresorbable vascular scaffolds (BVS) were launched into the real world in 2011, showing promising initial results. Multiple randomized trials, meta-analyses, and registries were performed, mainly with the Absorb Bioresorbable Vascular Scaffold System (Abbott Vascular, Chicago, IL, USA). This new technology is hindered by certain features, such as the BVS radial strength, its strut thickness, and the inflammatory process related to scaffold degradation. Moreover, there is known data indicating higher thrombosis rate with the Absorb BVS compared with the new generation of DES, despite similar 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: is the bioresorbable technology still the way to the future?

Keywords
Percutaneous interventions; Bioresorbable vascular scaffolds; Outcomes

1. Introduction
Drug-eluting stents (DES) caused a remarkable reduction in the restenosis rate [1], but led to a progressive increase in late stent thrombosis (ST) [2]. The latter was reduced with the development of second-generation DES which provided thinner struts with a biocompatible or biodegradable polymer. Despite that, there still remains cases where ST - especially very late ST (VLST) - and late restenosis occur [3]. ST remains an issue due to the permanent metallic struts, possible inflammation caused by polymer degeneration, and/or negative effects of antiproliferative drugs on endothelial regeneration. Furthermore, long-term vessel caging impairs arterial physiology impeding normal vasomotricity while promoting long-term positive remodeling. With all that, DES still conferred excellent outcomes with very low restenosis rates and even much lower VLST (occurring more than 1 year).

In 2000, the first in man use of the self-degrading Igaki-Tamai coronary stent [4] -the first bioresorbable vascular scaffold (BVS or BRS)- showed favorable outcomes. BVS necessarily had to be compared to DES which already conferred very low rates of adverse events. In 2011, BVS were finally introduced into clinical practice, showing good initial short term outcomes [5]. It was thought they conferred multiple advantages over metallic stents including: reduction in long-term adverse effects of permanent materials, restoration of vasoreactivity in the long term, maintaining the applicability of future treatment options for multivessel disease and long lesions, use in STEMI patients who might have less extensive disease, pediatric applications and the relevance to perform noninvasive imaging, such as computed tomographic angiography or magnetic resonance imaging [5, 6].

Several studies were conducted, mainly with the Absorb BVS System (Abbott Vascular, USA), with nearly 200,000 devices implanted worldwide by June 2017 [7]. The Absorb BVS consists of a 150-μm-thick bioresorbablepoly(l-lactide) scaffold with a 7-μm thick everolimus eluting bioresorbable poly(d,l-lactide) coating.

Intracoronary imaging (ICI) studies highlighted the potential advantage of BVS showing recovery of pulsatility at 12 months, and late lumen gain with plaque regression between 2 and 5 years [5, 6]. However, multiple studies showed that those scaffolds still had multiple limitations like low radial strength while having thick struts. This made BVS less ideal for complicated and calcified lesions where deliverability and stent expansion would be problematic. Furthermore, there was concern regarding higher episodes of stent thrombosis that was seen in the Absorb BVS as compared to DES. This was postulated to be due to scaffold degeneration causing local inflammation and consequently thrombosis.
In this review, current data regarding technical and clinical evidence on BVS will be discussed while considering future directions.

2. 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 promoted BVS are summarized in Table 1. The clinical/historical data are outlined as follows:

2.1 First in man experience: the Igaki-Tamai stent

It’s made from non-drug-eluting, high-molecular-weight poly-l-lactic acid (PLLA) monofilaments [4] with a helical coil pattern and a strut thickness of 170 μm. It is the first fully BVS tested in humans (Kyoto Medical Planning, Japan). In 2012, an observational, nonrandomized clinical trial of 50 patients showed that survival rates free of cardiac death and major adverse cardiovascular events (MACE) were 98% and 50% respectively. Imaging also showed positive vessel remodeling and lumen enlargement. This experience paved the way for future development of BVS.

2.2 The absorb BVS

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

- In the ABSORB II trial, BVS was compared to the Xience metallic EES (Abbott Vascular, USA). At 1 year, use of BVS conferred lower rates of unstable angina as compared to EES use (20% vs. 30%; P = 0.04), while non-significant difference was seen for the device-oriented composite end point (DOCE). At 3-year follow-up, the Xience group had a significantly lower vasomotor reactivity with a non-inferior late luminal loss (LLL); while the Absorb group showed a higher rate of DOCE due to target vessel MI, including peri-procedural MI. The patient-oriented composite endpoint, angina status, and exercise testing were not statistically different among both devices [8].

- In ABSORB Japan, a single-blind, multicenter and randomized trial, the rate of TLF was non-significantly higher in the BVS than in the EES arm. Only the BVS arm had VLST and this was seen at a rate of 1.6% between one and two years [9]. Authors concluded that under-expansion of BVS was associated with greater negative remodeling and LLL which might explain the worse outcomes of BVS compared to EES [10].

- The EVERBIO II trial showed that the use of BVS was associated with a non-significant increase in device related adverse events at 2 years as compared to EES and a significant increase in device related events as compared to Biolimus Eluting Stent [11].

- The ABSORB-STEMI TROFI II randomized trial studied the use of Absorb vs. Xience stents in patients presenting with STsegment elevation MI (STEMI). The Absorb group showed a lower optical coherence tomography (OCT)-based healing score at 6 months than the EES group (1.74 vs. 2.80; P < 0.001 for noninferiority). The DOCE was similarly low in the two groups [12]. BVS resulted in more evident endothelium-dependent and -independent vasomotion of the infarct related artery, compared with EES at 3 years. Also, BVS and EES had mostly adequate and similar functional microcirculatory parameters. Remaining strut footprints and larger number of intraluminal scaffold dimpling (26.3% vs. 0%; P = 0.049) were seen on OCT in the BVS group. Clinical significance and implications of these findings are discussed further [13].

- In the ABSORB III randomized trial, the primary end point of TLF at 1-year follow-up was non inferior in the BVS group relative to the EES group. Cardiac death (0.6% vs. 0.1%; P = 0.29), target-vessel MI (TVMI; 6.0% vs. 4.6%; P = 0.18), and ischemia-driven TLR (3.0% vs. 2.5%; P = 0.50) were not significantly different. However, device thrombosis (DT) occurred in 1.5% of patients with BVS compared to 0.7% with EES (P = 0.13) [14]. However, patients with stable symptoms and noncomplex lesions were excluded, limiting the generalizability of this data. At 25 months, Absorb had higher MACE compared to Xience (TLF 10.9% vs. 7.8%; P = 0.03) which were mainly seen in the smallest-caliber treated vessels with a reference vessel diameter (RVD) of < 2.25 mm by quantitative coronary angiography (QCA) [14].

Based on the above data, the Food and Drug Administration released a safety alert in March 2017 recommending the adherence to dual antiplatelet therapy (DAPT) during BVS use while avoiding their use in small vessels to help decrease MACE [15]. 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. Finally, a recent 5-year Follow-Up of the ABSORB III Trial, showed a higher rate
of cumulative adverse event after BVS compared with EES which mainly ended at 3 years, coincident with complete scaffold resorption [16].

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 [17]. Target-vessel failure (TVF, a composite of cardiac death, target-vessel MI, or target-vessel revascularization) was the primary end point. Because of safety concerns, the data and safety monitoring board advocated early disclosure of the study results. 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 [8]. In the majority of patients (98.6% and 74%, respectively), pre and post-dilation were performed in the BVS group, however the 2-year rate of definite or probable ScT remained unacceptably high.

### 2.2.2 Absorb BVS in registries and retrospective analyses

Registries included a large number of patients with different plaque morphologies and clinical presentations allowing us to detect both common and uncommon features of using BVS. Stent thrombosis remained to raise a lot of concern which led to the design of randomized studies targeting that issue.

Initial registries were single centered and/or had 12 months’ short term follow up. For example, the ABSORB Extend study (first 512 patients enrolled; 12-month MACE 4.3) [18] showed that minor routine oversizing of the BVS followed by high pressure post-dilation was safe with a low rate of MACE and no reported ScT. In the Polish National registry (591 patients) [19], in patients with acute coronary syndrome (ACS) and those with complex lesions, early in-hospital results showed no significant differences between BVS and EES in the primary composite MACE endpoint. More recently, in the RAI Registry, a total of 1,505 patients were enrolled with predilatation and post-dilatation performed in practically all the cases. At one-year follow-up, TLR and ScT rates were 3.3% and 1.3%, respectively. TLR was significantly higher in the off-label group (4.0% vs. 2.2%; P = 0.05) while a trend towards a higher ScT rate was observed in the off-label group (1.7% vs. 0.6%; P = 0.06). At multivariate analysis, treatment of in-stent restenosis, chronic total occlusion and BVS diameter were independent predictors of TLR [20].

In the large multicenter Ghost-EU registry, authors looked at 1189 patients who underwent angioplasty with the Absorb BVS [21]. The only independent predictor of TLF was diabetes (HR 2.41, P = 0.006) and TLF occurred at a rate of 4.4% at 6 months. The cumulative incidence for definite or probable ScT was concerning with 1.5% at 30 days and 2.1% at 6 months. Independent predictors in this registry included ostial lesions (P = 0.049) and impaired left ventricular ejection fraction (P = 0.019). In both this registry and the BVS registry Gottingen, the rates of device-related complications with BVS were not negligible and did not decline over time [22].

Finally, the ISAR-Absorb registry included 419 patients (39% with ACS) undergoing PCI with BVS [23]. The incidence of TLR and definite ST at 12 months were 13.1% and 2.6% respectively. At 2 years, there was a 21.6% MACE rate and a 4.2% rate of proven or probable ST [23].

### 2.2.3 Absorb BVS in meta-analyses

Lipinski et al. looked at 10510 patients treated with BVS where post-dilatation was performed in 52% of lesions. Compared to DES, there were higher rates of MI (OR 2.06, P = 0.002) and definite or probable ScT (OR 2.06, P = 0.03) in the BVS group [24]. No significant difference was found for all-cause and cardiovascular mortality.

### Table 2. Randomized clinical trials comparing BVS and DES

<table>
<thead>
<tr>
<th>Clinical trial (year)</th>
<th>Number of patients (BVS : DES)</th>
<th>Primary end point</th>
<th>Primary outcome</th>
<th>DOCE rate (%; BVS Scaffold thrombosis rate vs. DES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSORB II (2015)</td>
<td>501 (2 : 1)</td>
<td>Vasomotion/minimal lumen diameter (3 years)</td>
<td>Ongoing (3-year follow-up)</td>
<td>5 vs. 3 (P = 0.35) 9 vs. 0 (P = 0.55)</td>
</tr>
<tr>
<td>ABSORB China (2015)</td>
<td>480 (1 : 1)</td>
<td>In-segment lumen loss (1 year)</td>
<td>0.19 ± 0.38 mm vs. 0.15 ± 3.4 vs. 4.2 (P = 0.62) 0.4 vs. 0 (P = 1.00)</td>
<td></td>
</tr>
<tr>
<td>ABSORB Japan (2015)</td>
<td>400 (2 : 1)</td>
<td>Target-lesion failure (1 year)</td>
<td>4.2% vs. 3.8% (Pni &lt; 0.0001) NA*</td>
<td>1.5 vs. 1.5 (P = 1.00)</td>
</tr>
<tr>
<td>EVERBIO II (2015)</td>
<td>240 (1 : 2)†</td>
<td>Late lumen loss (9 months)</td>
<td>0.28 ± 0.39 vs. 0.25 ± 0.36 (P = 12 vs. 9 (P = 0.6) 1.3 vs. 0</td>
<td></td>
</tr>
<tr>
<td>STEMI-TROFII (2015)</td>
<td>191 (1 : 1)</td>
<td>Healing score# (6 months)</td>
<td>1.74 vs. 2.80 (Pni &lt; 0.001) 1 vs. 0 1.1 vs. 0</td>
<td></td>
</tr>
<tr>
<td>ABSORB III (2015)</td>
<td>2,008 (2 : 1)</td>
<td>Target-lesion failure (1 year)</td>
<td>7.8% vs. 6.1% (P = 0.16, Pni 10.9 vs. 7.8% (P = 1.5 vs. 0.7 (P = 0.13)</td>
<td></td>
</tr>
<tr>
<td>AIDA-2015</td>
<td>1,845</td>
<td>24-month TVF</td>
<td>11.7% vs. 10.7% (P = 0.43) NA*</td>
<td>3.5% vs. 0.9% (hazard ratio, 3.87; P &lt; 0.001)</td>
</tr>
</tbody>
</table>

BVS, bioresorbable vascular scaffold; DES, drug-eluting stent; DOCE, device-oriented composite endpoint; NA, not available; Pni, P value for non-inferiority. *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.
Collet C. et al. looked at 16,830 patients treated with ABSORB. There was 1.8% overall rate of definite or probable ScT, and the residual diameter stenosis percentage was the only factor associated with ScT [25]. A similar meta-analysis of 1730 patients was conducted by the same authors with 24 month follow-up [26]. There was a higher incidence of DT in patients treated with Absorb BVS compared to those treated with EES, with 92% of the very late ScT occurring in the absence of DAPT. They also had a higher tendency for TLF (OR 1.48; \( P = 0.09 \)) driven by a greater risk of TVMI and ischemia-driven TLR. No difference was found for cardiovascular mortality.

Polimeni et al. looked at 5219 patients and had similar findings for BVS with 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; \( P < 0.0001 \)) compared with EES. BVS were associated with worse clinical outcomes at two-years and higher incidence of both early (within 30 days after implantation) and very-late (> 1 year) DT [27].

Elias et al. looked at 3258 patients treated with BVS and 2319 with EES. The BVS group had higher rates of TLF (OR 1.34; \( P = 0.003 \)) and DT (2.4% vs. 0.7% with number needed to harm: 60; \( P < 0.0001 \)) extending beyond 1 year of follow-up (OR 4.13; \( P < 0.001 \), clinically indicated or ischemia driven TLR, and all-cause MI. There was no significant difference with respect to cardiac death [28].

Sorrentino S et al. looked at 5,583 patients undergoing Absorb vs. metallic EES with a mean follow-up of 2 years. There was a higher incidence of TLF (9.6% vs. 7.2% with number needed to harm: 41; \( P < 0.003 \)) and ST (2.4% vs. 0.7% with number needed to harm: 60; \( P < 0.0001 \)) in the BVS group. The increased risk for ScT was consistent across early (< 30 days), late (30 days to 1 year), and very late (> 1 year) periods [29].

A meta-analysis by Cassese S et al. compared BVS vs. EES in 5583 patients for mid-term clinical outcomes. BVS displayed a higher risk of TLF (odds ratio = 1.35; \( P = 0.0028 \)) and ScT (OR 3.24; \( P < 0.0001 \)) compared to EES particularly after 1 year from implantation [30].

De Rosa et al. recent meta-analysis on 2,318 patients aimed to assess the safety and efficacy of everolimus eluting-BVS vs. EES in ACS patients undergoing PCI. There was a higher risk of definite ST/ScT in patients treated with BVS compared to EES (2.3% vs. 1.08%, \( P = 0.03 \)) and an increased risk of TLR at mid-term (9.5 months) follow-up [31]. Finally, two recent meta-analyses done on 10 and 6 randomized controlled trials respectively with 3 years follow-up found that BVS was inferior to second-generation DES in both safety and efficacy [32, 33].

2.3 Special situations where BVS has been studied

2.3.1 Acute coronary syndromes (ACS)

Mid-term outcome data for BVS and 2nd generation DES were compared in a recent systematic review and meta-analysis on a total of 1758 patients in the setting of ACS. BVS had higher risk of TLR and ScT at follow-up than the 2nd generation DES. ScT was the key factor determining the decreased safety and effectiveness of BVS relative to DES [34]. Other studies cited in this article (like AIDA and TROFI II trials) have also included patients with ACS and shown comparable results.

2.3.2 In-stent restenosis (ISR)

The prospective multicenter study RIBS VI included 141 patients treated with BVS for either BMS-ISR or DES-ISR. The study suggested that the use of BVS in patients with ISR was effective and safe. In this challenging anatomic scenario, BVS obtained late angiographic and clinical results similar to DEB but inferior to EES [35].

2.4 Actual CE-mark approved BVS

2.4.1 DEStent

Like Absorb, the DEStent (Elixir Medical) BVS, has a PLLA backbone with a biodegradable polylactide-based polymer coating that elutes the antiproliferative drug novilimus. The unique features of the DEStent scaffold include (1) intrinsic self-correcting deployment that becomes operative in the event of minor strut malapposition, and (2) relative elasticity/ductility which provides a wide range of expansion without risk of stent fracture [36].

The first series of the DEStent showed a LLL at 6 months of 0.19 ± 0.19 mm, which was similar to that seen with contemporary DES. The second series of the DEStent was assessed in the DEStent 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 [36].

2.4.2 ART pure

This BVS has a 170 \( \mu \)m PDLLA or poly (l-lactide-co-d, l-lactide) backbone with no antiproliferative drug. The ART-DIVA trial (Arterial Remodeling Transient Dismantling Vascular Angioplasty), the first-in-man trial enrolled 30 patients, demonstrated 1 case of ischemic-driven TLR at 6 months. No other clinical result is available to date [37].

2.4.3 Resorbable magnesium scaffold (RMS)

It was developed in parallel to the PLLA polymeric scaffold [38]. However, RMS has a good radial strength with minor early elastic recoil and a superior compliance to vascular anatomy. They are electropolished which helps with trackability. Their implantation is more practical because of single step inflation. The safety and performance of the DREAMS 2G scaffold (i.e. 2nd generation; Magmaris®, Biotronik AG) was assessed in a pooled outcomes study of BIOSOLVE-II and BIOSOLVE-III with 184 patients assessed respectively. At 24 months, the TLF, TVMI, and TLR rates were 5.9%, 0.9%, and 3.4% respectively with no definite or probable ScT. The BIOSOLVE-IV was a single-arm, multicenter registry that included data of 400 patients with a 12-month follow up. RMS showed similar performance to second-generation DES [39].
However, available evidence is currently limited to small observational studies. Positive outcomes have been reported for up to 3 years after second-generation drug-eluting RMS implantation in clinical trials. However, evidence is still lacking for this novel device, and more long-term clinical outcomes from the BIOSOLVE trials and further randomized trials involving other clinical and lesion subsets are needed in the future [39].

3. Characteristics and procedural aspects of the “vascular restoration”

3.1 Biodegradation and vascular restoration

The main theoretical advantage for BVS was thought to be restoration of vasomotoricity [6, 40]. Data from randomized trials showed that the restoration of vasoactivity/vasomotion was directly proportional to the degree of BVS reabsorption -12 and 24 months after implantation and was influenced by plaque composition and endothelial function [6, 40]. Furthermore, it was noted that the resorption process of the scaffold was variable depending on scaffold design and thickness along with certain patient characteristics [40]. For example, if the scaffold was overexpanded, it was associated with faster degradation and consequently high rates of restenosis [41]. With a similar restenosis rate as compared to everolimus-eluting stent (EES), the minimal lumen diameter (MLD) at 2 years was similar.

3.2 Procedural aspects of BVS deployment

It was established that to obtain better outcomes with BVS and decrease the rates of ST and decrease the rates of ST and decrease the rates of MACE [43]. Data from randomized trials showed that the restoration of vasoactivity/vasomotion was directly proportional to the degree of BVS reabsorption -12 and 24 months after implantation and was influenced by plaque composition and endothelial function [6, 40]. Furthermore, it was noted that the resorption process of the scaffold was variable depending on scaffold design and thickness along with certain patient characteristics [40]. For example, if the scaffold was overexpanded, it was associated with faster degradation and consequently high rates of restenosis [41]. With a similar restenosis rate as compared to everolimus-eluting stent (EES), the minimal lumen diameter (MLD) at 2 years was similar.

3.3 Procedural optimization

The first issue is whether the clinical outcomes could be modified by improving the implantation technique. Studies have looked at the impact of device sizing and implantation techniques on acute device performance indices, including acoustic gain, expansion index, asymmetry index, eccentricity index, and strut embedment [45].

Optimal predilatation and postdilatation were expected to improve performance and reduce the rate of ScT from 3.3% to 1.0%, which still remained significant even after multivariate adjustment (hazard ratio, 0.19; P = 0.012) [43, 46]. However, this has not been proven by randomized studies.

3.4 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 [47]. However, the interruption of DAPT accounted for around 1/3 of BVS thromboses, and also VLScT. Stone G suggested that if intraluminal scaffold dismantling (ILSD) is visualized on OCT, prolonged DAPT has to be considered, especially in patients with low bleeding risk. Re-stenting with a metallic DES may also be appropriate in severe cases of ILSD [48]. Therefore, the increased risk of ScT up to 2 years provides a good rationale for continuation of DAPT for that period [47].

4. Current limitations of BVS

4.1 Mechanical Integrity

BVS differ from their metallic counterparts when it comes to their intrinsic mechanical properties [49]. They have sub-optimal ductility, which affects scaffold retention on balloon catheter and limits the range of scaffold expansion during deployment. Second, they have thick struts to offset their low radial strength and help prevent recoil during vessel remodeling. Finally, they have limited elongation-to-break, which defines the opening range of the BVS. This makes BVS less practical options for difficult lesions whether in tortuous vessels or calcified lesions, among others.

4.2 Clinical and imaging concerns

Imaging is crucial in assessing ScT, restenosis, and TVR in patients undergoing BVS implantation.

4.2.1 Scaffold thrombosis: modifiable and non-modifiable features

A systematic analysis of all reported ScT cases evaluated by ICI was conducted [49]. Malapposition (24%), incomplete lesion coverage (18%) and under-deployment (12%) were most frequently observed. 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.
Table 3. Next Generation BRS with Thinner Struts (≤ 150 μm)

<table>
<thead>
<tr>
<th>Scaffold</th>
<th>Manufacturer</th>
<th>Backbone</th>
<th>Coating</th>
<th>Eluted drug</th>
<th>Strut thickness (μm)</th>
<th>Resorption (months)</th>
<th>time to Development</th>
<th>status</th>
</tr>
</thead>
<tbody>
<tr>
<td>DESolve Cx</td>
<td>Elixir</td>
<td>PLLA</td>
<td>Biodegradable polymer</td>
<td>Novolimus</td>
<td>120</td>
<td>2 years</td>
<td></td>
<td>CE mark</td>
</tr>
<tr>
<td>Absorb BVS gen 2</td>
<td>Abbott Vascular</td>
<td>PLLA</td>
<td>poly-lactic-co-glycolic acid</td>
<td>Everolimus</td>
<td>≤ 99</td>
<td>36 months</td>
<td></td>
<td>CE mark</td>
</tr>
<tr>
<td>MeRes 100</td>
<td>Meril Life Sciences</td>
<td>PLLA</td>
<td>PDLLA</td>
<td>Sirolimus</td>
<td>100</td>
<td>50% at 4-6 mo; complete resorption</td>
<td>2 years</td>
<td>CE mark</td>
</tr>
<tr>
<td>FORTITUDE</td>
<td>Amaranth Medical</td>
<td>Ultra-high weight PLLA</td>
<td>molecular- PDLLA</td>
<td>Sirolimus</td>
<td>150</td>
<td>10 mo</td>
<td></td>
<td>CE mark</td>
</tr>
<tr>
<td>Mirage</td>
<td>Manli Cardiology, PLLA</td>
<td>PLLA</td>
<td>PDLA</td>
<td>Sirolimus</td>
<td>125</td>
<td>≈ 14 mo</td>
<td></td>
<td>CE mark</td>
</tr>
<tr>
<td>Firesorb</td>
<td>Shanghai MicroP-Port Medical</td>
<td>PLLA</td>
<td>PDLA</td>
<td>Sirolimus</td>
<td>100-125</td>
<td>3 years</td>
<td></td>
<td>CE mark</td>
</tr>
</tbody>
</table>

DOCE indicates device-oriented composite end point; MACE, major adverse cardiac event; NA, data not available; PLLA, poly-l-lactide; PDLLA, poly(l-lactide-co-d,lactide); POCE, patient-oriented composite end point; RCT, randomized controlled trial; ScT, scaffold thrombosis; and TVF, target vessel failure.

This provides evidence that optimizing stent sizing and deployment might help to decrease the potential risk of ScT [42, 49]. This, however, does not address late discontinuity and peri-strut low-intensity areas.

Late discontinuity is a benign change during the biore sorption process and doesn’t cause any complications if the scaffold struts are well covered by neointima. However, during bioreosption, 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 [49].

That late discontinuity relative to ILSD was often observed by OCT imaging at the time of BVS VLST and was considered to be causally related to the thrombotic event [50].

Moreover, thick stent struts may lead to turbulence in flow and areas of oscillatory shear stress that could promote platelet activation or thrombogenicity especially when struts are left malapposed [51].

The first generation of BVS was limited by a high rate of scaffold restenosis and TVR, which was similar to that reported for BMS [52]. Such event could be related to either a suboptimal elution of antiproliferative drug or the complex implantation technique required and the subsequent injury. ICI including 3D OCT in symptomatic BVS restenosis showed extensive neointimal thickening [53].

5. Future directions of BVS

5.1 Device development

Newer BVS with better characteristics were reported, with promising results (Table 3):
- The DESolve Cx novolimus-eluting BVS, Elixir
- The Absorb BVS 2nd generation, Abbott Vascular
- The MeRes100 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 MicroP-Port Medical

Therefore, thinner struts, lower crossing profile, and fast resorption characteristics could be the way to go. Also, obtaining strong radial force because of new post-processing of the polymer looks encouraging and might help improve outcomes.

6. Summary and conclusions

The added value of this “vascular restoration therapy” is still waiting for a proof of evidence, while safety concerns are already known, together with the challenging device implantation, the worse trackability, the longer procedural times, and the larger amounts of contrast used [52]. 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 [52, 54]. These gaps in mechanical properties are a challenge to overcome, 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 [50]. To overcome the tensile strength and stiffness deficiency, the first-generation BVS structure consisted of thick struts (150 μm) which made them unsuitable for small vessels and at higher risk for ScT. In addition, the polymeric BVS requires a meticulous implantation technique (PSP) [6].
To address that issue, ABSORB IV was a prospective, randomized study, a continuation of ABSORB III. However, two new criteria were implemented: all treated vessels had to have a RVD of > 2.25 mm, and a PSP technique of pre- and post-dilation and appropriate sizing were followed routinely. Results in both the BVS and EES arm improved as compared to prior studies, but BVS remained to have worse outcomes compared to EES (30 day TLF was 5.0% vs. 3.7%, P for non-inferiority = 0.02, P for superiority = 0.11) [55].

The Resorbable Magnesium scaffold 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%. The RMS 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-month period [38, 54]. Up to 3 years post implantation, RMS had good outcomes with only 2 ScT reported so far having strut malapposition as their underlying cause [39]. More data are still needed to prove their non-inferiority as compared to DES.

In summary, and to date, BVS have failed to demonstrate a clinical benefit over the conventional metallic stent. Further development of the bioreabsorbable technology is needed to overcome the limitations of first-generation BVS [56].

To conclude, 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 EuroPCR 2018 [57], 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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