The introduction of bioresorbable vascular scaffolds (BRS) is changing the landscape of percutaneous coronary revascularization and is considered by many the 4th revolution in interventional cardiology. To date, BRS have shown promising short- and long-term results in the treatment of simple de novo lesions. Even though the feasibility, efficacy and safety of BRS implantation for more complex lesion subsets remain unknown, reports are emerging aiming to identify the role of BRS in everyday practice. In the current review we are aiming to summarize the results from ‘all-comer’ BRS studies and identify strengths and limitations of BRS when tackling specific complex lesion subsets.

Keywords: acute coronary syndrome • bifurcation • bioresorbable scaffold • BRS • BVS • calcific • complex • left main • ostial • outcomes

The introduction of bioresorbable vascular scaffolds (BRS) is changing the landscape of percutaneous coronary revascularization and is considered by many the 4th revolution in interventional cardiology. The emergence of drug-eluting stents (DES) and more potent antiplatelet drugs has improved patient outcomes by reducing the incidence of restenosis and stent thrombosis [1,2]. Despite improvements in the safety profile of DES [3], late lumen loss, late stent thrombosis and permanent vessel caging are bitter reminders of the inherited limitations of inserting a foreign material in the walls of the coronary arteries. BRS are the product of the attempts to overcome these limitations by temporarily providing support to the vessel wall with a scaffold that will subsequently disappear in 2–4 years’ time. Even though increases in the plaque size in the first couple of years post implantation compared with their metallic counterparts have been observed, bioresorbable scaffolds compensate by facilitating plaque regression [4] and by promoting expansive remodeling [5] at long-term follow-up. Despite the positive early experience with BRS in de novo simple lesions, the efficacy and long-term behavior of BRS implanted in complex lesions remains unknown. In recent days several real-world registries have published their early experiences with BRS and will be discussed in the current review.

**Bioresorbable vascular scaffolds clinical studies**

The initial experience with BRS implantation in de novo simple lesions has proven remarkable. Excellent long-term outcomes (major adverse cardiovascular events 3.4%) have been demonstrated in the 5-year follow-up of the ABSORB (Bioresorbable Everolimus Eluting Vascular Scaffold) Cohort A [6] where 30 patients with single simple de novo lesions were treated with the Absorb version v1.0. From 6-months to 2-year, the luminal dimensions in vessels treated with BRS Absorb v1.0 were increased [7] due a decrease in plaque size without change in vessel size suggestive of positive remodeling. The Absorb v1.1 [8] multi-imaging modality study revealed unchanged late luminal loss after the first year, whereas on intravascular ultrasound (IVUS), mean lumen, scaffold, plaque and vessel area showed enlargement...
up to 2 years. Subsequently between 2nd and 3rd year mean lumen and scaffold area remained stable whereas significant reduction in plaque behind the struts occurred. In the 3-year period the major adverse cardiovascular event (MACE) event rate was 10% [9]. In the ABSORB II randomized controlled trial [10], 335 patients treated with the BRS Absorb v1.1 where compared with 166 patients treated with an everolimus eluting metallic stent (Xience, Abbott Vascular, CA, USA). The ABSORB II included patients with 1 or maximum 2 de novo relatively simple lesions (ostial, left main, bifurcation, chronic total occlusion, heavily calcified or in stent restenosis lesions were all excluded). Despite the lower post implantation acute lumen gain observed in lesions treated with BRS, 1-year target lesion failure (composite of cardiac death, target vessel myocardial infarction or clinically indicated target lesion revascularization) was similar between the two groups (BRS vs EES; 5% vs 3%, p = 0.035). Early experience with other BRS platforms has also been favorable for simple de novo lesions. In the BIO-TRONIKS-Safety and Clinical Performance Of The First Drug-Eluting Generation Absorbable Metal Stent In Patients With de Novo Lesions in NatiVE Coronary Arteries (BIOSOLVE-I) study [11], the Drug Eluting Absorbable Metal Scaffold (DREAMS-I) platform (paclitaxel-eluting bioabsorbable magnesium scaffold) tested on 45 patients demonstrated a target lesion revascularization (TLR) and MACE rate of 6.5% at 12 months. In its first clinical evaluation [12], the DESolve Biodegradable coronary scaffold was implanted in 16 patients with de novo simple coronary artery lesions. At 12 months no MACE directly attributable to the scaffold occurred whereas late lumen loss at 6 months was 0.19±0.19 mm. In the DESolve NX study [13] (Novolimus Eluting Biodegradable Coronary Scaffold System) of 120 patients, the DESolve, Elixir Medical (Sunnyvale, CA) Novolimus eluting BRS demonstrated a TLR of 1.6% and MACE of 3.25% at 6 months.

Real world registries

Simple de novo lesions however only reflect a very small portion of real world practice. The aging population and the increasing prevalence of diabetes, renal disease and other risk factors have led to complex lesions becoming the bread and butter of interventional cardiologists. The safety and performance of BRS in the treatment of complex lesion is therefore of great interest. All relevant studies to date (baseline, procedural characteristics and outcomes) are presented in Tables 1–3. A small propensity matched study from Costopoulos et al. [14], demonstrated similar 1-year outcomes in all-comer patients treated with Absorb BRS versus newer generation everolimus eluting stents. The European GHOST EU (Gauging coronary Healing with biOabsorbableScaffolding plaTforms) registry [15] consisting of 1189 patients with coronary artery disease is the largest ‘all comers’ BRS (Absorb) registry to date. Target lesion failure (TLF), defined as cardiac death, myocardial infarction (MI) related to target vessel and clinically driven TLR, was observed in 67 out of 1189 patients (3.5%) at the median follow-up time of 109 days. The Kaplan Meier estimated TLF at 6 months of 4.4% and 10.1% at 1 year. Diabetes, chronic kidney disease, current smoking and acute coronary syndromes (ACS) on presentation showed preponderance to TLF. However, the only independent predictor of TLR was diabetes mellitus with a hazard ratio (HR) of 2.51 (1.55 to 4.06). Definite stent thrombosis (ST) was recorded in 20 and probable ST in 3 of 1189 patients at a median of 6.5 days (IQR 1.5–34) and resulted in cardiac death in three of 23 patients (13%) and nonfatal reinfarction in 15 of 23 (65%) cases. Even though overall 1-year TLF rates are acceptable, considering the complexity of patients and lesions treated, the GHOST-EU registry revealed some worrying signals of ST (1.5% at 30 days, 2.1% at 6 months) which exceed the incidences reported in newer generation all-comer registries (the incidences of definite or probable scaffold thrombosis at 30 days with zotarolimus- and everolimus-eluting stents were 0.8% and 0.4% in the large E-FIVE and XIENCE V USA registries, respectively [16,17]). However, these differences could be attributed to baseline confounding which can only be eliminated by randomized controlled studies. In the GHOST EU registry [15], 70% of ST cases occurred in the first month after percutaneous coronary intervention (PCI), at a median of 5 days, and most cases resulted in death or recurrent myocardial infarction. Mechanisms of ST differ depending on the time frame after PCI, with early events mostly attributable to procedural issues (such as dissection, incomplete stent apposition, incomplete stent expansion) and late events more likely linked to stent factors, antiplatelet cessation therapy and vascular response [18]. This highlights the importance of post implantation intravascular imaging to ameliorate the risk of an early ST. The association between strut thickness and the risk of thrombosis has been previously suggested in ex vivo experimental models [19], with thick-strutted platforms (i.e., Absorb BVS, first-generation DES, thick-strutted bare metal stents) described as being 1.5-fold more thrombogenic than their thin-strutted counterparts (such as second-generation DES or even thin-strut bare metal stents).

In the German multicenter ASSURE (ABSORB: Postmarketing Surveillance Registry to Monitor the
## Table 1. Demographic characteristics of ‘real world’ studies of patients treated with bioresorbable scaffolds.

<table>
<thead>
<tr>
<th>Study</th>
<th>Group</th>
<th>n</th>
<th>Age (years)</th>
<th>Male gender (%)</th>
<th>DM (%)</th>
<th>Previous CABG (%)</th>
<th>Previous MI (%)</th>
<th>LVEF (%)</th>
<th>ACS (%)</th>
<th>SYNTAX score</th>
<th>Multivessel disease (%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costopoulos et al.</td>
<td>BRS</td>
<td>92</td>
<td>64.2</td>
<td>89.1</td>
<td>29.3</td>
<td>9.8</td>
<td>28.3</td>
<td>55.3 ± 7.7</td>
<td>10.9</td>
<td>17.2 ± 9.8</td>
<td>51.1</td>
<td>[14]</td>
</tr>
<tr>
<td>Propensity matched cohorts</td>
<td>EES</td>
<td>92</td>
<td>62.5</td>
<td>84.8</td>
<td>26.1</td>
<td>9.8</td>
<td>34.8</td>
<td>55.2 ± 8.1</td>
<td>12.0</td>
<td>15.4 ± 8.8</td>
<td>50.0</td>
<td>[20]</td>
</tr>
<tr>
<td>ABSORB EXTEND Registry</td>
<td>BRS</td>
<td>512</td>
<td>62</td>
<td>74.0</td>
<td>26.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muramatsu et al.</td>
<td>BRS</td>
<td>102</td>
<td>62.2</td>
<td>71.6</td>
<td>100.0</td>
<td>21.6</td>
<td>25.5</td>
<td></td>
<td></td>
<td></td>
<td>31.4</td>
<td>[23]</td>
</tr>
<tr>
<td>Propensity matched cohorts</td>
<td>EES</td>
<td>172</td>
<td>62.2</td>
<td>66.9</td>
<td>100.0</td>
<td>31.4</td>
<td>26.2</td>
<td></td>
<td></td>
<td></td>
<td>31.4</td>
<td></td>
</tr>
<tr>
<td>Liang et al. Registry</td>
<td>BRS</td>
<td>35</td>
<td>54.7</td>
<td>85.7</td>
<td>17.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>51.4</td>
<td>[22]</td>
</tr>
<tr>
<td>GHOST EU Multicenter registry</td>
<td>BRS</td>
<td>1189</td>
<td>62.2</td>
<td>79.4</td>
<td>24.8</td>
<td>4.6</td>
<td></td>
<td>53.4 ± 9.1</td>
<td>47.4</td>
<td>11.3</td>
<td></td>
<td>[15]</td>
</tr>
<tr>
<td>AMC registry et al. Registry</td>
<td>BRS</td>
<td>135</td>
<td>59.0</td>
<td>73.0</td>
<td>20.0</td>
<td>25.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>50.0</td>
<td>47.0</td>
</tr>
<tr>
<td>Elabbassi et al. Registry</td>
<td>BRS</td>
<td>140</td>
<td>53.8</td>
<td>81.0</td>
<td>45.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>88% (STEMI 33%)</td>
<td>17 ± 9</td>
</tr>
<tr>
<td>L’Allier P et al. Registry</td>
<td>BRS</td>
<td>339</td>
<td>65</td>
<td>23.0</td>
<td>5.0</td>
<td>55</td>
<td></td>
<td>75.0</td>
<td></td>
<td></td>
<td>75.0 (STEMI 22%)</td>
<td></td>
</tr>
<tr>
<td>ASSURE Registry</td>
<td>BRS</td>
<td>183</td>
<td>64</td>
<td>25.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>48.3%</td>
<td></td>
</tr>
<tr>
<td>ABSORB FIRST Registry</td>
<td>BRS</td>
<td>1200</td>
<td>58.9</td>
<td>80.2</td>
<td>25.1</td>
<td>24.0 (CABG or PCI)</td>
<td>19.3</td>
<td></td>
<td></td>
<td></td>
<td>53.0</td>
<td>17.2</td>
</tr>
</tbody>
</table>

ACS: Acute coronary syndrome; BRS: Bioresorbable scaffold; CABG: Coronary artery bypass surgery; DM: Diabetes mellitus; EES: Everolimus eluting stents; LVEF: Left ventricular ejection fraction; MI: Myocardial infarction, STEMI: ST segment elevation myocardial infarction.
Table 2. Lesion characteristics of patients included in ‘real world’ bioresorbable scaffold studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Group</th>
<th>Lesions (n)</th>
<th>B2/C (%)</th>
<th>Bifurcations (%)</th>
<th>Moderate/Severe calcification (%)</th>
<th>CTO (%)</th>
<th>In stent restenosis (%)</th>
<th>Rotablation (%)</th>
<th>Ostial (%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costopoulos et al.</td>
<td>BRS</td>
<td>137</td>
<td>83.9</td>
<td>45.2</td>
<td>20.4</td>
<td>7.3</td>
<td>5.8</td>
<td>5.8</td>
<td></td>
<td>[14]</td>
</tr>
<tr>
<td>Propensity matched cohorts</td>
<td>EES</td>
<td>124</td>
<td>77.4</td>
<td>40.3</td>
<td>16.4</td>
<td>5.6</td>
<td>11.3</td>
<td>4.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABSORB EXTEND Registry</td>
<td>BRS</td>
<td>548</td>
<td>41.0</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td>[20]</td>
</tr>
<tr>
<td>Muramatsu et al.</td>
<td>BRS</td>
<td>108</td>
<td>39.8</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td>[21]</td>
</tr>
<tr>
<td>Propensity matched cohorts</td>
<td>EES</td>
<td>183</td>
<td>44.8</td>
<td>NA</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liang et al. Registry</td>
<td>BRS</td>
<td>41</td>
<td>75.0</td>
<td>14.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>[22]</td>
</tr>
<tr>
<td>GHOST EU Multicenter registry</td>
<td>BRS</td>
<td>1343</td>
<td>51.2</td>
<td>23.1</td>
<td>6.7</td>
<td>3.4</td>
<td></td>
<td></td>
<td></td>
<td>[15]</td>
</tr>
<tr>
<td>AMC registry Registry</td>
<td>BRS</td>
<td>159</td>
<td>67.0</td>
<td>15.0 1-stent 54%, 2-stent 46%</td>
<td>11.0</td>
<td>8.0</td>
<td>3.0</td>
<td></td>
<td>[23]</td>
<td></td>
</tr>
<tr>
<td>Elabbassi et al. Registry</td>
<td>BRS</td>
<td>221</td>
<td>62.0</td>
<td>9.0 1-stent 73%, 2-stent 27%</td>
<td>3.0</td>
<td></td>
<td></td>
<td></td>
<td>[24]</td>
<td></td>
</tr>
<tr>
<td>L’Allier P et al. Registry</td>
<td>BRS</td>
<td>504</td>
<td>41.0</td>
<td>5.0</td>
<td>14.0</td>
<td>5.0</td>
<td>1.2</td>
<td>16.0</td>
<td></td>
<td>[25]</td>
</tr>
<tr>
<td>ASSURE Registry</td>
<td>BRS</td>
<td>198</td>
<td>64.6</td>
<td>14.1</td>
<td>15.7</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td>[26]</td>
</tr>
<tr>
<td>ABSORB FIRST Registry</td>
<td>BRS</td>
<td>1454</td>
<td>46.7</td>
<td>12.2</td>
<td>17.0</td>
<td>10.9</td>
<td></td>
<td>6.0</td>
<td></td>
<td>[27]</td>
</tr>
</tbody>
</table>

BRS: Bioresorbable scaffold; CTO: Chronic total occlusion; EES: Everolimus eluting stents.
Table 3. Outcomes of ‘real world’ patients treated with bioresorbable scaffolds.

<table>
<thead>
<tr>
<th>Study</th>
<th>Group</th>
<th>n</th>
<th>Follow-up time (months)</th>
<th>MACE (%)</th>
<th>All-cause mortality (%)</th>
<th>Cardiovascular mortality (%)</th>
<th>MI (follow-up; %)</th>
<th>TLR (%)</th>
<th>TVR (%)</th>
<th>ST (%)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costopoulos et al.</td>
<td>BRS</td>
<td>92</td>
<td>6</td>
<td>3.3</td>
<td>0</td>
<td>0</td>
<td>3.3</td>
<td>3.3</td>
<td>0 (d)</td>
<td></td>
<td>[14]</td>
</tr>
<tr>
<td>Propensity matched cohorts</td>
<td>EES</td>
<td>92</td>
<td>6</td>
<td>7.6</td>
<td>2.2</td>
<td>1.1</td>
<td>0</td>
<td>5.4</td>
<td>6.5</td>
<td>0 (d)</td>
<td></td>
</tr>
<tr>
<td>ABSORB EXTEND Registry</td>
<td>BRS</td>
<td>512</td>
<td>12</td>
<td>4.3</td>
<td>NA</td>
<td>0.4</td>
<td>2.9</td>
<td>1.8 (ID)</td>
<td>3.0</td>
<td>0.8 (d/p)</td>
<td>[20]</td>
</tr>
<tr>
<td>Muramatsu et al.</td>
<td>BRS</td>
<td>102</td>
<td>12</td>
<td>7.8</td>
<td>0</td>
<td>0</td>
<td>2.9</td>
<td>2.0</td>
<td>1 (d)</td>
<td></td>
<td>[21]</td>
</tr>
<tr>
<td>Propensity matched cohorts</td>
<td>EES</td>
<td>172</td>
<td>12</td>
<td>11.0</td>
<td>1.2</td>
<td>1.2</td>
<td>2.9</td>
<td>4.1</td>
<td>1.7 (d)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liang et al. Registry</td>
<td>BRS</td>
<td>35</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>[22]</td>
</tr>
<tr>
<td>GHOST EU Multicenter registry</td>
<td>BRS</td>
<td>1189</td>
<td>6</td>
<td>10.1 (TLF)</td>
<td>1.3</td>
<td>1.0</td>
<td>2.7</td>
<td>2.5</td>
<td>4.0</td>
<td>2.1 (d/p)</td>
<td>[15]</td>
</tr>
<tr>
<td>AMC registry Registry</td>
<td>BRS</td>
<td>135</td>
<td>6</td>
<td>8.5</td>
<td>0.8</td>
<td>2.2</td>
<td>6.3</td>
<td>8.5</td>
<td>3 (d)</td>
<td></td>
<td>[23]</td>
</tr>
<tr>
<td>Elabbassi et al. Registry</td>
<td>BRS</td>
<td>140</td>
<td>12</td>
<td>7.2</td>
<td>4.3</td>
<td>0.7</td>
<td>2.9 (ID)</td>
<td></td>
<td></td>
<td></td>
<td>[24]</td>
</tr>
<tr>
<td>L’Allier P et al.</td>
<td>BRS</td>
<td>339</td>
<td>In hospital</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>1.2 (d)</td>
<td></td>
<td>[25]</td>
</tr>
<tr>
<td>ASSURE Registry</td>
<td>BRS</td>
<td>183</td>
<td>12</td>
<td>5</td>
<td>0.5</td>
<td>1.6</td>
<td>2.8</td>
<td>0</td>
<td></td>
<td></td>
<td>[26]</td>
</tr>
<tr>
<td>ABSORB FIRST Registry</td>
<td>BRS</td>
<td>1200</td>
<td>1</td>
<td>0.8</td>
<td>0</td>
<td>0</td>
<td>0.8</td>
<td></td>
<td>0.42 (d/p)</td>
<td></td>
<td>[27]</td>
</tr>
</tbody>
</table>

BRS: Bioresorbable scaffold; d: Definite stent thrombosis; d/p: Definite/probable stent thrombosis; EES: Everolimus eluting stents; ID: Ischemia driven; MACE: Major adverse cardiovascular events; MI: Myocardial infarction; ST: Stent thrombosis; TLF: Target lesion failure; TLR: Target lesion revascularization; TVR: Target vessel revascularization.
Everolimus-eluting Biodegradable Vascular Scaffold in Patients With Coronary Artery Disease) registry [26], 183 patients treated with BRS Absorb were followed up for 1 year. Of note, this study excluded long lesions (>28 mm) and lesions with a vessel diameter of >3.3 mm. One year MACE rate was 5%, TLR 2.8%, MI 1.6% whereas no stent thrombosis was observed. In the BVS Expand [28] single center registry, which excluded patients with ST elevation MI and previous coronary artery bypass surgery (CABG), 200 patients were recruited. The MACE rate at 6-months was 3.3%, TLR 2.2%, MI 1.7% whereas 4 (2.2%) definite scaffold thrombosis were observed. The ABSORB EXTEND registry [20] recruited patients with less severe disease compared with the BVS Expand one. The 1-year MACE rates amongst its 512 participants was only 4.3% with ischemia driven target lesion revascularization (TLR) rates of 1.8%. Despite its name, the ABSORB EXTEND study excluded a large number of patients encountered in everyday PCI practice; namely patients presenting with acute MI, those with EF less than 30%, patients with unstable arrhythmias, renal insufficiency and use of chronic anticoagulation. Furthermore patients with left main lesions, in stent restenosis, chronic total occlusions, bifurcations with a side branch of ≥ 2 mm in diameter, excessive tortuosity, heavy calcification or visible thrombus were also excluded. Hence results from the ABSORB extend study apply only to certain population subgroups and should not be considered as a true ‘all-comers’ study. In the dutch AMC (Academic Medical Center) registry [23] 135 real world patients (159 lesions) treated with the Absorb v1.1 scaffold where followed up for 6 months. Two third of the lesions treated were type B2/C, while 40% of patients presented with ACS. Cumulative target vessel revascularization (TVR) rate was 8.5% including a 6.3% TLR rate, a 3% rate of MI and a 3% rate of definite scaffold thrombosis (three subacute and one late). The latter, alongside the higher ST rates in the GHOST registry suggest that these early generation BRS with significantly thicker struts compared with new generation DES may indeed be more thrombogenic, particularly when underexpanded or malapposed. The ABSORB first registry [27] is a multicenter, prospective global registry of ‘real world’ patients treated with the Absorb v 1.1 scaffold. A total of 1800 patients had been recruited by August 2014. Of 1200 patients analyzed, 55.8% presented with ACS. Of 1454 lesions, 46.7% were type B2/C classification, 17% were moderately/severely calcified, 10.9% were chronic total occlusions (CTOs), 12.2% bifurcations, 6% ostial and 10.7% tortuous, reflecting a ‘real world’ setting. In the first 30-days, total rate of MI was 0.8%, whereas no cardiac deaths were reported. Definite or probable stent thrombosis rates were 0.42%. Excellent 1-year outcomes were also reported in a registry from the United Arabic Emirates (UAE). Elabbassi et al. [24] recruited 140 all-comer patients, majority of whom presented with ACS (88%). Total MACE at one year was 7.2%, with only 2.9% ischemia driven TLR and no definite or probable stent thrombosis.

Complex lesion subsets

Even though several small sized studies of BRS use in complex lesions have emerged, it should be emphasized that many lessons remain to be learned on the long-term behavior of BRS in this lesion subsets. The currently commercially available BRS are bulky devices (strut thickness -150 μm) with suboptimal deliverability. Hence, optimal guide catheter selection to maximize support, often with the use of mother in child and extension catheters, such as the Guideliner™ (Vascular Solutions, MN, USA), and optimal lesion preparation (with noncompliant, scoring balloons and even rotablation in calcific undilatable lesions) are of paramount significance to avoid stent injury or dislodgement and achieve successful BRS implantation. Of note, the BRS compliance charts are suboptimal in predicting the final scaffold expansion; hence the risk of malapposition is high, particularly in complex lesions. This highlights the importance of IVUS use after implantation in order to assess the need for postdilatation or other optimization manoeuvres. Another area of uncertainty in BRS for complex lesions is the duration of dual antiplatelet therapy (DAPT). Even though currently most studies apply the 1-year DAPT strategy adopted from metal stent studies, reports of very late stent thrombosis after discontinuation of DAPT [29] and presence of uncovered struts 18 months after the index procedure [30] raise concerns regarding the optimal duration of DAPT. Large studies with long-term follow-up are needed to establish the optimal duration of DAPT in complex lesions treated with BRS, particularly in long lesions with overlapping BRS segments or bifurcating/ostial lesions with overlapping BRS struts or plastic neocarinas. In the meantime at least 1 year of DAPT is recommended. Furthermore, additional optical coherence tomography (OCT) studies are required to provide insight in the reabsorption times, and potential presence of residual tissue bridging [31,32], of struts covering jailed sidebranches or struts overhang at ostia (either into aorta, or left main stem [LMS]). Reabsorption times in these locations may differ compared with the 2–3 years needed for struts apposed to the vessel wall. Hereby we discuss the available evidence on the use of BRS in various complex lesion subsets.
**Calcified lesions**

Coronary calcification (Agaston >0 on computed tomography) is as high as 60% in males and 40% in females [33] in the asymptomatic population (aged 45–84 with no clinical history of cardiovascular disease). Moderate/severe calcification is prevalent angiographically in 38% of lesions whereas IVUS detects calcium in 73% of lesions [34]. Lesions with extensive calcifications remain a challenge for the interventional cardiologist despite the advent of low-profile, non-compliant, high pressure, bladed or scoring balloons. In tertiary centers, rotablation is used in up to 5% of cases [35]. MACE rates after treatment of calcific lesions are worse compared with the general PCI population regardless of the use of rotational atherectomy [36–39]. On some occasions, despite meticulous lesion preparation, optimal strut apposition is not possible [40]. The increased strut thickness and reduced radial force have raised concerns regarding the feasibility, performance and the clinical outcomes of BRS in the treatment of calcific lesions.

A recent study [41] investigated the 9-month clinical outcome data after implantation of BRS in 62 patients (63.8±10.5 years and 54 (87.1%) male) with at least one calcific lesion (defined as calcium arc = 90° on IVUS or at least moderate lesion calcification on angiography). In this cohort a high prevalence of diabetes mellitus 35.5% and a high average SYNTAX score were observed. Results were encouraging with a MACE rate of 6.5%, MI of 1.6% TLR of 4.5% and TVR of 6.5% at median follow-up with one case of definite late stent thrombosis. Meticulous lesion preparation was carried out for all lesions using scoring balloons and rotablation when necessary (Figure 1). Future larger studies with angiographic/intracoronary imaging follow-up and longer clinical follow-up are required to assess

**Figure 1. Importance of optimal lesion preparation prior to bioresorbable scaffold implantation in calcific lesions.**

A tight lesion in mid circumflex (LCx) with circumferential calcification on intravascular ultrasound and an area of 2.55 mm² was treated initially with a noncompliant 2.5 mm balloon to 12 atm (suboptimal balloon expansion). In view of the circumferential calcification a 2.5 mm Angiosculpt (Angioscore, CA, USA) balloon at 18 atm was used. This enlarged the lumen area and led to successful, optimally expanded bioresorbable vascular scaffold implantation (Absorb 3.0 x 18 mm, CA, USA).
Bifurcations

In everyday interventional practice, approximately 20% of patients will require PCI of a bifurcation lesion. In an in vitro model with a 75° angle, a variety of bifurcation techniques commonly used in everyday practice were performed using BRS in order to improve our understanding of the morphological appearance of the scaffolds at the end of the procedure. The conclusions were that even though feasible, certain contemporary two-stent bifurcation techniques such as culotte or crush produced suboptimal results using BRS and a provisional strategy should be preferred where possible. In case a 2-stent strategy is required, T-and protrusion (TAP) (>75°) or mini-crush (<75°) using DES in the sidebranch (Figure 2) should be the first choice. Culotte stenting with 2 BVS may be technically feasible if good backup support is present, however the long-term results are uncertain given the presence of a double layer of thick struts some of which (those belonging to the sidebranch) may have been disrupted from the proximal optimization technique (POT) or the final kissing balloon (FKB). A 2 BRS T-stenting can be an option for high-angle bifurcations. FKB should be avoided to avert possible overexpansion or even fracture of the scaffold. When necessary, FKB inflation should be performed at low pressures, well below the maximal diameter limit for the BVS implanted. The combined balloon diameter should be maintained below the upper diameter limit of the BRS (Finet’s adaptation: proximal main vessel diameter [MVd] = 0.678 [distal MVd + sidebranch (SB) diameter]). Some of

Figure 2. Hybrid 2-stent double kissing mini crush without final kissing balloon inflation for the treatment of a bifurcation lesion. After deployment of a 2.5 × 16 mm Promus Element (Boston Scientific, MA, USA) in the diagonal branch with mini-crush technique with kissing balloon inflation, a 3.0 × 18 mm ABSORB (Abbott Vascular, CA, USA) was implanted in the proximal LAD without final kissing balloon inflation. Cross-sections of different levels of the bifurcation are shown in images (A–C).

EES: Everolimus eluting stents; Diag: Diagonal; LAD: Left anterior descending; OCT: Optical coherence tomography; Pre: Previous.
Yellow arrow: EES strut; Red arrow: BVS strut.
For color images please see online: www.futuremedicine.com/doi/full/10.2217/ICA.14.71
these recommendations are supported by the recent bench study by Ormiston et al. [44]; in their study, they demonstrated that a low pressure (5 atm) mini-kissing (the sidebranch balloon proximal marker is just proximally to the carina) balloon postdilatation (also called snuggling balloons) in a 3.0 mm scaffold with 3.0 mm balloons did not cause any scaffold fractures. This bench study [44] also highlighted the fact, that single sidebranch balloon dilatation cause distortion of main branch scaffolds and either postdilatation of the MB or of both branches with low pressure mini-kissing balloon are required to resolve it without risking fracturing the scaffold.

Some investigators presented their preliminary results on the treatment of bifurcation lesions: Chan et al. [45] reported results on the treatment of 23 bifurcation lesions, mainly (96%) located in the left anterior descending (LAD)-diagonal (D) bifurcation, using BRS. True bifurcation lesions were 13/23. The preferred bifurcation technique was provisional stenting (21/23) with proximal optimization performed in almost half of cases (12/21). T-stenting was reserved for two cases. FKB was performed in a third of the cases (8/23). At median follow-up of 115 days, there was one death, one TLR, two TVR and one probable subacute stent thrombosis. Naganuma et al. [46] also presented data on BRS treatment of bifurcation lesions (side branch [SB] = 2.25 mm), in a cohort of 63 patients, 48 (68.5%) of which with true bifurcation lesions, predominantly located in LAD-Diagonal 53 (75.7%). Out of 70 bifurcations treated, provisional single stenting technique was selected for the majority 50/70 (71.4%) whereas systematic double stenting was reserved for 14 (20%) cases. In the 6 (8.6%) remaining cases only the SB ostium was treated. Out of those who underwent provisional stenting, two were crossed over to two-stenting TAP using DES in the SB. FKB with minimal protrusion of SB was performed in six cases whereas single dilatation at the SB ostium in four. Out of the 14 cases where double stenting was the preferred strategy, BRS in both branches were used in 9 cases whereas a hybrid strategy with BRS in MB and DES in SB was used in 5. The predominant bifurcation technique used was T-stenting (10/14) whereas mini crush was used in the remaining 4/14 cases. Angiographic success (defined as residual stenosis of ≤ 30% in MB and ≤ 30% in SB after stenting or ≤ 50% without stenting) was 98.6% (69/70). At a median follow-up of 182 days three MACE (4.8%), no deaths, three TVR (4.8%), two (2.9%) TLR and no scaffold thrombosis were observed. Of note, BRS have been associated with a higher incidence of post-procedural SB occlusion compared with EES [47]. This effect was more pronounced with small side branches with a reference vessel diameter =0.5 mm. In the same study, multivariable analysis revealed that BRS was an independent predictor of postprocedural SB occlusion (odds ratio: 2.09; 95% confidence interval [CI]: 1.18–3.68).

Treatment of bifurcations with BRS differs compared with metallic stent and appears more challenging particularly when it comes to a two stent strategy. One should take the following under consideration: provisional stenting with POT, as with all stents, should be the preferred strategy where feasible; FKB should only be performed when deemed necessary rather than as routine practice—FKB at low pressure with minimal protrusion of the SB balloon (‘snuggling balloon’) does not appear to be associated with in vitro scaffold disruption [44]; when a crossover to a two-stent technique is deemed necessary, T or TAP stenting in high angle bifurcations ≥75 is a feasible option. In narrower angle bifurcations a mini crush with a DES in the sidebranch could be the preferred strategy (hybrid approach); IVUS or preferably OCT imaging is essential to assess for disrupted BRS struts, particularly when FKB or dilation of sidebranch struts has been performed. These recommendations should by no means be considered panacea. Once again we need to highlight the urgent need for future, large bifurcation studies with long-term follow-up in order to understand the long-term behavior of BRS and optimal strategies in the treatment of bifurcation lesions.

In-stent restenosis

Even though newer generation stents have markedly reduced the incidence of in-stent restenosis (ISR), the latter is still haunting interventional practice. Paclitaxel eluting balloons and first generation paclitaxel stents have shown superior results to plain balloon angioplasty in the treatment of restenosis [48]. In the recent RIBS V trial (Restenosis Intrastent of Bare Metal Stents: Paclitaxel-eluting Balloon vs Everolimus-eluting Stent) [49] new generation EES and DEB demonstrated similar efficacy (1-year outcomes) for the treatment of BMS restenosis. Even though one would favor a DEB strategy to avoid double or more metallic stent layers, it should be noted that in RIBS V, EES provided superior late angiographic findings compared with DEB which have been attributed to the longer lasting antiproliferative effect. One would therefore hypothesize, that a temporary scaffold that could elute for longer the more powerful antiproliferative compound everolimus but subsequently disappear would be an ideal treatment for ISR. This hypothesis was tested in the study by Ielasi et al. [50], who treated 25 cases (14 de novo and 11 recurrent) of ISR with Absorb BRS. Mean age of participants was
68.3±12.3 years whereas the majority were males (76%). Diabetes prevalence was 24%, chronic kidney disease (CKD) 16% and previous CABC 8%. The majority of restenotic lesions where of the focal pattern (53.3%) whereas diffuse pattern was mainly observed in patients with recurrent restenosis. The restenosis was in previously implanted DES in 46.7% of cases and in a quarter of cases it involved a bifurcation lesion (26.74%). The average BRS length used for the treatment of restenotic lesions was 34.8±18.4 and the average diameter was 3.2±0.4 mm. Angiographic success was achieved in all cases. On discharge 16% of patients were on dual antiplatelet therapy with ticagrelor whereas the remaining were on aspirin and clopidogrel. At a mean angiographic follow-up of 9 months TLR was observed in two patients (8%) and was successfully treated with re-PCI, whereas non target vessel MI was seen in one patient (4%). In another small cohort,[51] 27 patients (31 lesions) with a mean age of 63±9 and predominantly males (92%) were treated with BRS for ISR. Prevalence of diabetes was high at 40%, 78% had suffered a previous MI and 7% had undergone previous CABC. Focal restenosis was observed in 27% of cases whereas diffuse in 71%. The majority of ISR occurred in previously implanted DES (63%). Recurrent restenosis was prevalent in 20% of cases. The average length of BRS length was 39±15.2 mm whereas the average diameter 3.02±0.3 mm. Procedural success was observed in 100% of cases. At 9-month follow-up two patients died (8%), one underwent ischemia driven TLR (4%) and two (8%) target vessel revascularization. The results from the afore-mentioned studies demonstrated the feasibility, safety and short-term efficacy of BRS for ISR treatment. However, given their small sample sizes they should only be viewed as hypothesis generating. The increased BRS strut thickness remains a cause of concern when treating ISR as it can potentially result in lumen compromise, particularly in the absence of adequate lumen gain after balloon dilation of the restenosed stent or in ISR in small vessels where BRS should be avoided. Further studies with longer follow-up (extending beyond BRS absorption time) are urgently warranted to clarify the role of BRS in the treatment of ISR and compare its performance against the current gold standards, second-generation metallic stents and drug eluting balloons.

**Ostial lesions**

Treatment of ostial lesions can be challenging as suboptimal positioning can either lead to geographic miss or floating struts.[52] Furthermore, ostial locations are more often fibrotic, calcified and more prone to recoil. These could promote restenosis or thrombosis and increase the difficulty of reaccessing the coronary artery. Gori et al.[53] were the first to put BRS to the test by reporting the first clinical data on angiographic and short-term clinical outcomes of BRS implanted for the treatment of ostial lesions. A total of 37 patients (39 lesions) were included. In the majority of cases patients were male (88%) with no history of previous MI and a preserved LV ejection fraction. A third of cases were treated for stable angina, 40% for non ST segment elevation MI (NSTE MI) or unstable angina (UA) and 28% for STEMI. In the majority of cases the ostium of the LAD was treated (58%) whereas the LCx ostium in 30% and RCA ostium in 13%. In this cohort, after 6 months there was one death (of unknown cause), and one STEMI secondary to definite in-stent thrombosis. Promising though these result may seem, a couple of recent case reports have demonstrated scaffold disruption and recoil with significant neointimal hyperplasia in BRS implanted in the ostium of the circumflex artery.[54] It should be noted, however, that in the anatomical location of the LCx ostium, even conventional metallic stents have failed to produce consistent favorable outcomes.[55] This fact may be attributed to the acute angulation and hinge motion at the LMS-LCX junction, where a stent/scaffold is subjected to torsion, flexion and rotational forces[56,57] that may lead to stent/scaffold fatigue, fracture and subsequent restenosis or thrombosis at follow-up. This is more likely to occur in a scaffold that is dilated beyond its recommended limits or that has started to be reabsorbed, hence losing its radial strength. Even though of interest, the sample size in all the aforementioned studies is too small to draw any solid conclusions on the use of BRS for ostial lesions. Future large studies with long-term follow-up are required to assess the feasibility and efficacy of BRS in this type of lesions.

**Long, diffuse disease**

Diffuse lesions have been always problematic to treat, as it is well established that longer stent lengths increase the risk of stent thrombosis and restenosis[58]. Treatment of diffuse disease with biodegradable scaffolds, offering a ‘cage free’[59] approach to intervention, appears most appealing for the treatment of this lesion subset (Figure 3).[60] The first study to show feasibility and efficacy of BRS for long diffuse disease is the one by Wiebe et al.[61], on 73 patients treated with at least 28 mm of Absorb scaffold. Median age was 63 years and 76.7% were males with a remarkable 52.1% of diabetics and 68% having multivessel disease with a quarter of lesions being CTOs. In hospital MACE was 2.7% (2/73) with one STEMI due to scaffold thrombosis after cessation of dual antiplatelet therapy for a planned aortic aneurysm surgery. During a median follow-up of 180 (63.5 to 309.5) days, MACE rate was 5.5 (4/73), scaffold thrombosis seen
Figure 3. Use of bioresorbable vascular scaffolds for the treatment of diffuse disease. Hybrid percutaneous coronary revascularization with use of EES in the proximal left anterior descending (LAD)-first diagonal bifurcation and 3 BVS (3.0 x 18) from the proximal-mid to distal LAD. Intravascular imaging at the end of index procedure (cross-sections A–F) revealed excellent result with well apposed struts and optimally expanded scaffolds. Two-year follow-up OCT (cross-sections A’–F’) revealed acceptable lumen dimensions and partially reabsorbed BVS struts.

BVS: Bioresorbable vascular scaffold; EES: Everolimus eluting stents; OCT: Optical coherence tomography; Pre: Previous.

in 2.9% (2/70), TVR in 4.3% (3/70) and TLR in 2.9% (2/70). Future large studies are required to establish the role of BRS in the treatment of diffuse disease (Figures 3 & 4).

Chronic total occlusions

Chronic total occlusions (CTOs) are present in up to 30% in patients undergoing diagnostic angiography [62]. The figures are much higher in patients who have already undergone coronary artery bypass surgery (CABG), reaching up to 80% of cases [62]. Even though randomized trials are still lacking, CTO recanalization has been associated with significant reductions in residual or recurrent angina and reduced need for future CABG [63]. In certain cases of patients with occluded grafts on optimal medical therapy, CTO recanalization is the sole remaining option for symptomatic relief. Several features of the BRS render them an attractive alternative for the treatment of CTO. BRS offer the required transient radial strength to protect from acute vessel recoil, while at a later stage, unlike metallic stents, they are fully resorbed, leading to restoration of the vessel’s biological properties. This ‘cage free’ strategy is of particular importance in the treatment of long lesions, a frequent encounter in CTO cases. The risks inherited to ‘full metal jackets’ [64], including late restenosis and thrombosis, make the concept of a ‘full plastic BVS jacket’ which will subsequently disappear, a very attractive alternative. A BRS CTO strategy appears even more appealing in younger patients since reabsorption of scaffolds will likely reduce risks for late events and allow future surgical revascularization should the need arise (Figure 5). A case series of ten patients with CTOs treated with BVS by two expert CTO operators [65] was reported by Garbo et al. Mean age was 66.7±8.3 years and nine out of ten were males, two diabetics, three had
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Figure 4. Treatment of diffuse left anterior descending disease with bioresorbable scaffolds in a 29-year-old patient with Type 1 diabetes and recent renal transplantation. Implantation of three BRS from proximal to mid-distal LAD and distal LAD plain old balloon angioplasty. Acceptable final angiographic and intravascular ultrasound (IVUS cross-sections A–D) result, albeit with the loss of a small septal branch, highlighting one of the limitations of thick-strutted BRS in treating long lesions. Patient has been asymptomatic for a year postindex procedure and will return for follow-up angiography at 2 years.

BVS: Bioresorbable vascular scaffold; KBI: Kissed balloon inflation; LAD: Left anterior descending; POBA: Pre: Previous.

Perspective
Panoulas, Sato, Miyazaki, Kawamoto, Colombo & Chieffo

To date there is limited experience in BRS implantation in bypass graft lesions [67–70]. The available literature cases reports suggest that implantation of BRS in arterial and venous grafts is feasible; however, larger series with longer follow-up are required to establish the safety and efficacy of BRS in this lesion subset. One of the current limitations of BRS is that their largest commercially available size is 3.5 mm which can be postdilated to 4.2 mm. This prohibits the use of BRS in venous grafts whose diameter exceeds 4.0 mm. Another concern in venous graft PCI relates to the risk of distal embolization. It remains unknown whether BRS with their thick struts would provoke this complication compared to previous MIs and one previous CABG. In eight cases CTO involved the RCA, total stent length was 85 mm and an average of 3.6 stents were used. At a mean follow-up time of 197.9 days no events were noted. A recent case report [66] demonstrated an excellent result at 1-year OCT follow-up after recanalization of an LAD CTO tackled with retrograde approach at index procedure. There was some partial scaffold malapposition, which could have been attributed to subintimal space hematoma absorption, scaffold recoil or low sensitivity of IVUS to detect its presence at the time of BRS implantation. Either way, this case highlights the importance of reabsorption in scaffolds that are implanted in the subintimal space, where hematomas may have formed during the index procedure, or in vessels chronically underperfused which are likely to be subject to positive remodeling in the future post successful revascularization. A shorter reabsorption period may be desirable to limit the risk of transient malapposition. Long-term results from large CTO BRS registries are eagerly awaited and expected to revolutionize the field.

Coronary artery bypass grafts

To date there is limited experience in BRS implantation in bypass graft lesions [67–70]. The available literature cases reports suggest that implantation of BRS in arterial and venous grafts is feasible; however, larger series with longer follow-up are required to establish the safety and efficacy of BRS in this lesion subset. One of the current limitations of BRS is that their largest commercially available size is 3.5 mm which can be postdilated to 4.2 mm. This prohibits the use of BRS in venous grafts whose diameter exceeds 4.0 mm. Another concern in venous graft PCI relates to the risk of distal embolization. It remains unknown whether BRS with their thick struts would provoke this complication compared
Figure 5. Treatment with bioresorbable scaffolds of diffuse left anterior descending disease with a chronic total occlusion in the mid segment. The first diagonal branch was treated with drug eluting balloon IN.PACT Falcon (Medronic, MN, USA) 2.5 × 40 mm at 8 atm for 60 s. The LAD was treated with three Absorb BRS (Abbott Vascular, CA, USA) 3.5 × 28, 3.0 × 28 and 2.5 × 28 mm and an everolimus eluting stent at the distal cap of the CTO where reference vessel diameter was 2.25 mm. Optical coherence tomography (OCT) at 18 months reveals excellent result (cross-sections A–D) with fully covered BRS struts. In frames B & C double struts can be seen at the overlap sites whereas in D the metallic struts of the EES can be seen. Of note the diagonal ostium at 18 months is free from struts (cross-sections i, ii) despite no final kissing balloon inflation at index procedure.

BVS: Bioresorbable vascular scaffold; CTO: Chronic total occlusion; DEB: Everolimus eluting stents; EES: Everolimus eluting stents; LAD: Left anterior descending; OCT: Optical coherence tomography; Prox: Proximal.
with their metallic counterparts and future studies are required to demonstrate non inferiority.

**Left main disease**

Left main PCI for patients with low or intermediate SYNTAX risk scores has been demonstrated to be a viable therapeutic option\(^{[71,72]}\). Even though direct comparisons of newer generation DES with CABG are eagerly awaited, previous studies have demonstrated a trend toward superior outcomes in LMS PCI when newer versus first generation DES were used\(^{[73]}\). Although a stent that disappears with time is most appealing, BRS implantation for left main lesions is associated with particular challenges. These include the larger size of LMS which often exceeds the dilatation limit of 4.2 mm of the Absorb BRS scaffold 3.5 mm and even the 4.5 mm limit of other platforms such as the DESolve. Furthermore, LMS bifurcation stenting can be challenging particularly when operators wish to perform kissing balloon inflation in a sidebranch with a reference vessel diameter of >2.5–3.0 mm. As described above this could cause BRS scaffold disruption and potentially worse future clinical outcomes. All limitations regarding BVS bifurcation stenting discussed above apply also for LMS lesions. In a case series of three LMS lesions treated with BRS, Miyazaki et al.\(^{[74]}\) describe LMS lesions ‘suitable’ for BRS stenting; these include ostial LAD lesions (Medina 0.1.0) requiring cross-over stenting and distal bifurcation lesions not involving the LCx ostium. BRS strategy is not recommended for cases where the LCx ostium is larger than 2.5 mm and requires intervention due to large plaque burden. Furthermore, crossover stenting from LMS into LCx should be avoided due to branch angulation and increasing risk for restenosis. BRS implantation could be feasible even for vessel sizes of more than 4.2 mm as long as the lesion characteristics do not allow expansion of lumen diameter to more than 4.0 mm. A minimal scaffold area of 12.6 mm\(^2\) (the area occupied by an expanded 4.0 balloon) is considered a satisfactory result for LMS from the coronary physiology point of view\(^{[75]}\). Even though hybrid two-stent strategies\(^{[76]}\) (using BRS for the ostium of Cx) and DES for LMS-LAD) have been proposed for certain anatomies (angle >60°) their efficacy can only be assessed when follow-up clinical and angiographic data are available. These recommendations however should be viewed with caution and large studies with long-term follow-up are eagerly awaited to establish the role of BRS stenting in LMS disease.

**Bioresorbable scaffolds in acute coronary syndromes**

The majority of studies focus on BRS implantation in stable coronary artery disease. However, in recent days there has been growing interest in the treatment of unstable disease with BRS. In a study from Germany, Gori et al.\(^{[77]}\) reported similar 30-day outcomes in 150 patients with ACS treated with BRS compared with 103 patients treated with DES (Xience Prime, Abbott vascular, Santa Clara, CA, USA) at the same period (MACE BRS vs EES: 10.7% vs 15.5%, p > 0.8). Of note in that study, BRS was not implanted in LMS lesions, lesions involving a sidebranch of >2 mm, calcified lesions preventing effective predilatation as well as in stent restenosis/thrombosis. Three definite in-scaffold thrombosis were noted in the BRS group versus 2 in the Xience group.

The first to report outcomes in 11 patients with STEMI treated with BRS were Kajiyaa et al.\(^{[78]}\) who demonstrated the feasibility of BRS implantation in this particular group. In the ‘Prague 19’ study\(^{[79]}\) 142 consecutive patients presenting with ST elevation were treated with BRS or DES as per study inclusion criteria. Patients with Killip III-IV class (n = 24) or those where no stent was implanted, where excluded. A BRS was not implanted in long lesions (where more than one scaffold was needed), calcific or tortuous lesions, in cases with reference vessel diameters (RVD) lower than 2.3 or higher than 3.7 mm, in the presence of stent thrombosis, poor DAPT compliance, anticoagulation or comorbidity with limited survival expectancy. As such, patients treated with BRS (about 30% of the total STEMI population) were lower risk patients with very low diabetes (2.5% vs 24.6%, p = 0.003) and prior MI prevalence (2.5% vs 12.3%, p = 0.137) compared with the controlled group treated with metallic stents. Authors report a case of subacute thrombosis after cessation of the dual antiplatelet therapy in the BRS arm. During the short-term follow-up (less than half patients followed-up at 6 months), a total of two patients suffered a MACE in the BRS compared with four in the metallic stent group. No statistical significance was observed in outcomes between the two groups, however caution is recommended due to the small sample sizes and the unadjusted baseline confounders (e.g., diabetes). In another relatively small registry, Diletti et al.\(^{[80]}\) described their experience in BRS implantation in 49 STEMI patients. Of the total 267 consecutive STEMI patients in the study period, 49 (18%) were included in the study (exclusion criteria included previous metallic stent, left main disease, previous CABG, age >75). Device success was 97.9% whereas at OCT analysis, 7/31 (22.6%) patients had >5% malapposed struts. This could be attributed to the low rate of postdilatation (20.4%) in the STEMI setting. Regarding outcomes only one NSTEMI case occurred in a non-target vessel whereas no cases of
recent case report from our group suggesting no clear preponderance for stent thrombosis amongst patients presenting with ACS. In a real world study included 27% diabetics, 23% patients with previous PCI and 8% with previous CABG. In this registry delivery and device success were 100%. In two cases there was slow flow, in one distal embolization and in six another bail-out BRS was required. At 1-year follow-up TVR was 1.1%, TLR 0% and MI 3.2% (including two periprocedural MIs). One subacute definite stent thrombosis was documented in a patient who did not take any medication after discharge. However, despite these excellent outcomes, we suggest caution when interpreting the results from the POLAR ACS study, as despite the presence of a definite scaffold thrombosis, authors report no follow-up TLR. In the largest BRS registry reported to date, the GHOST EU (n = 1189) there were 192 patients with STEMI, 214 with non-STEMI and 157 with unstable angina. There was a trend for a higher prevalence of ACS patients in those who suffered TLF at follow-up (58.2% vs 46.7%), p = 0.067. However, this trend was lost (HR for TLF 1.45, 95% CI: 0.74–2.84) when adjusting for other confounders including diabetes. In the same study 12/23 (52.2%) patients who suffered stent thrombosis presented with an ACS. This percentage is similar to the prevalence of ACS patients included in the study (47.4%), suggesting no clear preponderance for stent thrombosis amongst patients presenting with ACS. In a recent case report from our group [82], however, we described a case of acute stent thrombosis in a patient presenting with anterior STEMI and proximal LAD occlusion with high thrombus burden. Despite loading with bivalirudin, prasugrel and aspirin and an optimal angiographic result (though with evidence of some material protrusion through the struts on IVUS), patient suffered an acute stent thrombosis within 2 hours from index procedure. Even though BRS use in patients with unstable angina or NSTEMI appears safe, it is important to highlight that BRS for STEMI has certain limitations; in STEMI patients and particularly in thrombotic lesions, lesion preparation is kept to the bare minimum or more often not performed to avoid distal embolization and slow flow. In this setting the inferior trackability of the current generation BRS may limit their use to less complex lesions (larger minimum luminal diameters (MLDs), not calcific or tortuous, similar to the inclusion criteria of Prague 19 study [79]). Furthermore, often in an acute MI setting (particularly STEMI with presence of thrombus), baseline IVUS measurement of vessel size and postdilatation are omitted, hence scaffold malapposition may occur. The ~20% presence of >5% malapposed struts in the OCT arm study by Diletti et al. [80] however, does not differ to the percentages observed in contemporary studies of balloon expandable metallic stents [83,84]. Even though early outcomes with BRS in STEMI patients are acceptable, the impact of malapposed thick struts on long-term outcomes requires further investigation.

**Future perspective**

Bioresorbable scaffolds are here to stay and evolve. Questions remain on the efficacy and performance of BRS in the long term, the optimal duration of DAPT, the short- and long-term outcomes in the treatment of complex lesions and their head to head comparison with new generation DES. In May 2014, Elixir Medical Corporation (Sunnyvale, CA, USA), received CE (Conformité Européenne) Mark approval for its DESolve® 100 μm Novolimus Eluting Bioresorbable Coronary Scaffold System, whereas other manufacturers are also working on reducing strut thickness, increasing radial strength, increasing size range, reducing absorption time to ~1 year and improving BRS deliverability. An improved BRS with those features will be able to tackle most complex lesions described above as: its improved radial and scaffold strength and conformability would suffice to support vessel lumen in ostial, calcific and fibrotic lesions and allow sidebranch dilatation, without worrying for scaffold fracture with kissing balloons; its wider range of sizes and reduced strut thickness will allow the treatment of most left main and graft lesions as well as small vessel disease; its reduced strut thickness and improved deliverability will allow treatment of most STEMI patients whereas; its reduced absorption time would necessitate DAPT for 1 year without worrying for very late events (restenosis or thrombosis) after DAPT cessation. For the time being, there remain a lot of lessons to be learned particularly when treating complex lesions. When the new generation BRS become commercially available, a new cycle of feasibility, safety, performance and ‘head to head comparison with DES’ studies will need to be carried out. However, BRS are the exciting new development in coronary interventions and with appropriate collaborations between device industry, academia and physicians, they are likely to become the mainstream devices for coronary intervention in the near future.
### Executive Summary

#### Bioresorbable scaffold clinical studies
- The initial experience with bioresorbable scaffolds implanted for simple de novo lesions has lived up to the expectations, producing similar major adverse cardiovascular event (MACE) rates to new generation drug-eluting stents (DES).

#### Real world registries
- The emerging results from real world registries suggest acceptable intermediate outcomes (up to 1 year). In the largest registry to date (GHOST EU) there are some worrying signals regarding higher rates of stent thrombosis (particularly acute/subacute); however, randomized controlled trials with DES are required to confirm/dispute this finding.

#### Complex lesions
- Even though several small studies have emerged regarding the use of bioresorbable vascular scaffolds (BRS) in complex lesions, several lessons remain to be learned on the efficacy and long-term outcomes after BRS implantation for complex lesions. In the meantime, optimal lesion preparation, good guide catheter support and intracoronary imaging are key for a successful BRS implantation. Future studies are needed to inform clinicians regarding optimal duration of dual antiplatelet therapy after BRS implantation, particularly for complex lesions.

#### Calcified lesions
- Even though evidence on BRS implantation for calcific lesions is sparse, meticulous lesion preparation with noncompliant or scoring balloons and even rotablation where required is key.

#### Bifurcations
- Even though future large studies are required to establish the role of BRS in the treatment of bifurcation lesions, early experience and in vitro studies have shown that bifurcation treatment with BRS, particularly when it comes to two stent strategies, can be challenging. The following recommendations should be considered when treating bifurcation lesions: provisional stenting with proximal optimization technique (POT) should be the initial strategy with mini-kissing at low atmospheres when required. In high angle bifurcations, when a double stent strategy cannot be avoided, T-and protrusion (TAP) or T-stenting techniques are feasible options. In shallow angle bifurcations a double kissing mini-crush technique (final kissing not necessary if sidebranch ostium not compromised) using a DES for the sidebranch is recommended.

#### In stent restenosis
- Despite small studies demonstrating the feasibility of BRS implantation for restenotic lesions, caution is recommended particularly when considering to use this strategy in vessels with small reference diameter. The thick-strutted BRS could potentially compromise the lumen area and lead to adverse events.

#### Ostial lesions
- Even though BRS use is particularly appealing given that any overhanging struts in aorta or left main would disappear in future years to come, the propensity of ostial lesions, often fibrotic and calcified, for recoil alongside the inferior radial strength of BRS, makes use of BRS for this lesion subset a matter of concern.

#### Long diffuse disease
- Treatment of diffuse disease with bioresorbable scaffolds, offering a ‘cage free’ approach, appears most appealing. Some small studies and case reports have shown the feasibility of this strategy however larger trials are required to establish the efficacy and safety of BRS in long diffuse disease.

#### Chronic total occlusions
- Often after chronic total occlusion (CTO) recanalization a long segment of a chronically hypoperfused artery is stented. BRS may reduce the rates of stent malapposition at follow-up and offer a ‘full plastic jacket’ option that will subsequently allow restoration of vessel vasomotion and permit future surgical revascularization if needed. Even though appealing as a strategy, it is still early days for any conclusions on the BRS performance in the treatment of CTOs.

#### Left main disease
- Use of BRS for left main disease is limited by its currently commercially available size and its propensity to fracture when final kissing balloon is performed in a large size sidebranch (>3 mm with >5 atm pressure). However, in certain LMS lesions which do not involve the ostium of the LCx and when LCx size is 3.0 mm or below, provisional stenting from LMS into LAD with BRS is a feasible option when LMS size allows.

#### Acute coronary syndromes
- Early experience of BRS use in unstable angina and NSTEMI patients suggests feasibility with acceptable outcomes, albeit with a large registry (GHOST EU) cautioning a slightly higher rate of stent thrombosis in the BRS group when compared with new generation DES registries. A few small registries suggest that BRS for the treatment of STEMI is feasible in a particular subset of less complex lesions. However, in STEMI patients, particularly those with high thrombus burden where pre- and postdilatation are better avoided and a direct stenting strategy preferred, the limitations of BRS (inferior trackability, scaffold thickness) become more evident and scaffold implantation more challenging. Future studies are needed to demonstrated efficacy and safety of current and newer generation BRS implantation in ‘all-comers’ STEMI patients.
Bioresorbable scaffolds for the treatment of complex lesions

Conclusion
Bioresorbable vascular scaffolds (BRS) have shown promising short- and long-term results in the treatment of simple de novo lesions. Several clinical studies have emerged describing the use of BRS for complex, ‘real world’ coronary lesions. Initial results appear promising; however, larger cohorts and longer follow-up times are required to establish the role and the limitations of BRS in the treatment of complex lesions.

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