ABSORB BVS Implantation in Bifurcation Lesions – Current Evidence and Practical Recommendations

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Abstract

The introduction of the ABSORB bioresorbable vascular scaffold (BVS) provides a new tool for stenting in interventional cardiology. Initially, relatively simple coronary artery lesions were treated with this novel device; nowadays, we are gaining clinical experience when treating a wide variety of lesions with the ABSORB BVS, including bifurcation lesions. Unfortunately, data are limited in terms of the use of the ABSORB BVS in coronary bifurcation lesions, so little is known about the safety and feasibility of these procedures. Bench testing and case reports showed that single provisional scaffold placement is feasible with fenestration of the scaffold towards the side branch and sequential non-compliant balloon inflation in the side and main branches. However, no prospective randomised clinical data with optical coherence tomography (OCT) imaging for different bifurcation stenting techniques are available. Based on the available data and our own experience we would recommend the use of the provisional single scaffold technique and only to fenestrate the scaffold if a severely pinched ostium combined with impaired flow seen on angiogram.

Keywords

Percutaneous coronary interventions, bioresorbable vascular scaffold, bifurcation lesions, optical coherence tomography

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In the past three decades, significant progress has been made in the treatment of coronary artery disease. From the introduction of balloon angioplasty by Andreas Grüntzig in 1977¹ to metallic drug-eluting stents with thin stent struts coated with cytotoxic or cytostatic drugs,^{2,3} with biocompatible/biodegradable polymers,⁴ with or without endothelial progenitor cell-capturing technology.⁵ However, current standard treatment with metallic stents has its shortcomings, such as late in-stent restenosis, late and very late stent thrombosis, impaired vasomotion in the stented segment^{6–8} and hindrance of repeat revascularisations. To potentially overcome the shortcomings of metallic stents, fully bioabsorbable stents (i.e. scaffolds) were developed.⁹ After preclinical testing and clinical evaluation in relatively simple coronary artery lesions,^{10–12} the ABSORB everolimus-eluting bioresorbable vascular scaffold (BVS) received CE-mark approval on 14 December 2010 and is since then increasingly being used in clinical practice across Europe and the rest of the world. This adoption in clinical practice led to a broad extension of, officially off-label, indications in which the ABSORB BVS is being used, such as ST-segment elevation myocardial infarction (STEMI),¹³ chronic totally occluded (CTO) arteries and bifurcation lesions.

The use of bioresorbable technology in coronary bifurcation lesions may have potential benefits compared with metallic stents. For example, bioresorbable scaffolds could prevent permanent obstruction of a side branch (SB) after full absorption of the struts in front of this SB, leading to increased blood flow in the SB. Another

potential benefit of the ABSORB BVS in bifurcation lesions might be a lower risk of late stent thrombosis, due to the absorption of non-apposed SB (NASB) struts at long term. These NASB struts are known to be often uncovered and thus a potential nidus for stent thrombosis.¹⁴ However, in all preclinical and clinical trials on the BVS, patients with SB ≥ 2 mm were excluded from enrolment, so limited data are available about the use of the BVS in bifurcation lesions. Therefore, the 'Instructions for use' of the ABSORB BVS does not indicate the use of the device in lesions involving a SB >2.5 mm. This led to some practical concerns about the use of the ABSORB BVS in coronary bifurcation lesions. For example, does the ABSORB BVS, with a strut thickness of 150 μm , allow for the same bifurcation techniques being used in metallic stent? Is the BVS, due to the lactic acid material, easier to fracture? This article will focus on data provided from *in vitro* and *in vivo* assessment of the ABSORB BVS in coronary bifurcation lesions and will provide practical recommendations based on these data and our own experience.

In vitro evaluation

Džavik and Colombo recently reported several bifurcation bench tests in which the ABSORB BVS is evaluated in a synthetic arterial model.¹⁵ Bifurcation stenting techniques tested included provisional stenting with final kissing balloon inflation (FKBI), modified T-stenting with a FKBI, double or two-step crush technique, mini-crush technique and culotte technique. The investigators used non-compliant (NC) balloons only, to prevent overexpansion of the scaffold due to increased

Figure 1: *In vitro* Bench Test of the Double-crush Procedure

In vitro model of a double-crush procedure (A), with a 3.0x18 mm ABSORB bioresorbable vascular scaffold (BVS) in the main vessel and a 2.5x28 mm scaffold in the side branch, showed a small area of carinal malapposition (arrow). Micro-computed tomography reconstruction showed a good paving of the main branch lumen with one strut protruding into the lumen (B); however, no protruding struts in the side branch BVS (C). View through the main branch BVS into the side branch revealed good opening and coverage of the side branch ostium (D). Source: Džavik and Colombo, 2014.¹⁵ Copyright Elsevier. LAD = left anterior descending; RCx = right circumflex artery.

balloon diameters. All procedures were assessed visually and by scanning electron microscopy (single scaffold techniques) and by micro-computed tomography (two scaffold techniques).

The investigators did not see any malapposition or strut fractures after FKBI in provisional stenting of a 3.0x18 mm BVS. FKBI in the provisional stenting technique was performed with a 2.5x20 mm balloon in the SB and 3.0x20 mm balloon in the main branch, both inflated at 8 atmospheres. Strut fractures were observed when FKBI was performed after T-stenting technique using a 3.0x18 mm BVS in the main branch (MB) and a 2.5x18 mm BVS in the SB and 3.0x20 mm (MB) and 2.5x20 mm (SB) balloons inflated at 10 atmospheres. The double- and mini-crush techniques both resulted in mild protrusions of BVS struts in the main branch. Even so, the double-crush technique showed a small area of malapposition between the carina and the two overlying scaffolds (see *Figure 1*). Likewise, a small area of malapposition was seen if the culotte technique was used, this technique also led to a thick circumferential two-layer scaffold wall in the proximal segment of the MB as well as a bulky BVS neocarina.

Based on their observations, the authors recommended to use provisional stenting in the majority of cases, with sequential non-compliant balloon inflation in the SB and the MB and reserving FKBI only if absolutely necessary. Restricted use of planned two-stent techniques, like crush or culotte, was recommended as more bench testing is needed to evaluate the feasibility of these techniques. These recommendations are supported by other bench test studies, performed by White et al. presented at Transcatheter Cardiovascular Therapeutics (TCT) 2013.¹⁶

In vivo Evaluation

Systematic evaluation of side branches ≤ 2 mm jailed by the ABSORB BVS was performed by Okamura et al.¹⁷ Furthermore, few case reports described the treatment of true bifurcation lesions with involvement of SB ≥ 2 mm.¹⁸⁻²¹ To allow full assessment of the ABSORB BVS SB struts, optical coherence tomography (OCT) was used in all these reports. OCT allows visualisation of the vessel wall and the ABSORB BVS struts at high resolution²² and with a high degree of reproducibility.²³

Okamura et al. assessed jailed side branch struts at baseline with three-dimensional (3D) OCT reconstruction, allowing the SB orifices to be evaluated visually. In total, 40 SB ostia of 25 patients enrolled in the ABSORB Cohort B study were analysed. In total, 24 orifices were jailed and showed different degrees and patterns of compartmentalisation (Type V, T and H) (see *Figure 2*).

Further insight in the use of the ABSORB BVS in coronary artery bifurcation lesions emerges from case reports combined with OCT images. Okamura et al. described a patient with an obstructed SB of ≤ 2 mm. Serial OCT imaging was performed at 2-year follow up showing an open SB ostium with intimal bridges creating a neo-carina, persisting after absorption of the scaffold.²⁴ Van Geuns et al. demonstrated the feasibility of crossing the ABSORB BVS struts into the SB with a coronary guidewire after deployment of a 3.0x18 mm ABSORB BVS in a left anterior descending (LAD) artery bifurcation lesion (Medina classification 1,1,0).²¹ Gogas et al. were first to describe side branch balloon dilatation of a LAD/second diagonal bifurcation lesion (Medina 1,1,1) treated with a single ABSORB BVS in the main branch. After deployment of a 3.0x18 mm ABSORB BVS

Figure 2: Three-dimensional Assessment of Non-jailed and Jailed Side Branch

Extra-luminal views (A) and intraluminal views (B) from three-dimensional offline reconstructions shows non-jailed and Types V, T, and H jailed ≤ 2 mm side branch (SB). Source: Okamura et al., 2010.¹⁷ Copyright Elsevier.

in the midLAD, there was impaired flow and pinching of the ostium of the second diagonal, after which the scaffold was fenestrated towards the SB and dilated with a 1.5x12 mm Trek-compliant balloon. 2D OCT images and offline 3D-OCT reconstructions showed an open ostium of the SB and well-apposed struts in the SB segment.²⁰ Finally, Grundeken et al. showed a successful deployment of a 3.5x18 mm ABSORB BVS in the left main coronary artery (LMCA) in the direction of the LAD, crossing the left circumflexus artery (LCx). However, after placement of the scaffold plaque shift towards the ostium of the LCx was observed on angiography. Therefore, the BVS was fenestrated towards the LCx and the LCx ostium was dilated with 2.0x20mm and 2.5x15mm Sapphire II compliant balloons at 8 atmospheres. Offline 3D-OCT reconstructions of the scaffold before fenestration showed multiple struts jailing the ostium of the LCx. After dilatation of the LCx ostium there is an opening of the stent cell seen towards the LCx without scaffold disruption (see Figure 3). These case reports illustrated that implantation of the ABSORB BVS and scaffold fenestration towards the SB with subsequent SB post-dilatation is feasible. Furthermore, these cases described the role of OCT to guide optimal scaffold placement.

Practical Recommendations

Although more clinical studies are needed to verify the optimal strategy in bifurcation lesions using ABSORB BVS, we would like to make the

Figure 3: Three-dimensional Optical Coherence Tomography Evaluation of a Left Main Bifurcation Lesion Treated with ABSORB Bioresorbable Vascular Scaffold

Initial angiography showed a left main coronary artery (LMCA) lesion (A), after placement of a 3.5 x 18 mm ABSORB bioresorbable vascular scaffold (BVS). (B) Plaque shift (white arrow) was observed towards the left circumflexus artery (LCx) (C). Therefore, the BVS was fenestrated towards the LCx with a traverse wire and the LCx ostium was dilated with 2.0x20 mm and 2.5x15 mm Sapphire II compliant balloons at 8 atmospheres (D). Final angiogram showed a good result (E). Longitudinal two-dimensional optical coherence tomography (OCT) pullback (I) indicating the viewing points at the LCx ostium of figures (F), (G), (H), (J), (M) and (N). Offline three-dimensional reconstructions before fenestration showed multiple BVS struts jailing side branch (H), (K), (M) and dividing the LCx ostium in five compartments (F). After fenestrating the ABSORB BVS, with guidewire positioned through the distal cell (G) (I), the ABSORB could be opened without BVS deformity at the level of the carina (L) (N). Source: Grundeken MJ et al., 2013.¹⁸ Copyright Elsevier.

following recommendations based on previously described data and our own experience. In accordance with the recommendation of the European Bifurcation Club, based on randomised data on one- versus two-stent techniques using metallic stents, we would recommend the provisional single stenting technique in the majority of the lesions (see Figure 4), as previously suggested by Džavík and Colombo.¹⁵

Adequate lesion preparation and optimal sizing of the ABSORB BVS is essential prior to scaffold placement. Stent sizing with metallic stents is recommended to be based on the distal diameter with subsequent postdilatation of the proximal main branch with a larger balloon to ensure stent apposition in the proximal main branch (proximal optimisation technique [POT]).²⁵ This technique is considered to prevent carinal shift and subsequent ostial pinching of the SB. However, post-dilatation of the BVS with balloons >0.5 mm larger than the BVS size is discouraged due to the increased risk of strut fractures. Therefore, we recommend to choose the BVS size based on the proximal diameter. Intravascular imaging, such as intravascular ultrasound (IVUS) or OCT, or online quantitative coronary angiography (QCA) can be used for optimal sizing of the ABSORB BVS.

Figure 4: Provisional Single-scaffold Placement in a Coronary Bifurcation Lesion

Initial angiography of a 64-year-old male patient without a medical history showed a Medina 0,1,1 left anterior descending (LAD)/first diagonal branch (D1) lesion (A). After pre-dilatation with a 2.0x20 mm balloon of both the LAD (12 atm) and ostium of D1 (10 atm), a 3.0x18 mm ABSORB bioresorbable vascular scaffold (BVS) was delivered in the LAD (B) and (C). Subsequently, the scaffold was post-dilated with a 3.0x12 mm non-compliant balloon at 16 atmospheres. Final angiography showed a good result in the LAD and a slightly pinched ostium of the D1 (D). Two-dimensional optical coherence tomography (OCT) images showed some non-apposed side branch struts, and an open ostium of D1 (E) and (F). Offline three-dimensional reconstructions showed a pinched ostium of the D1, probably because of carina shifting (G), multiple BVS struts jailing the side branch (H) and (I) and dividing the D1 ostium in three compartments. Due to TIMI III flow in the D1 at final angiogram, the scaffold was not fenestrated. At 9-months follow-up the patients is still without complaints.

After deployment of the scaffold, we recommend to guide further need for fenestration and post-dilatation of the scaffold on the angiographic result and OCT images. If a lesion after deployment of the scaffold has a severely pinched ostium on angiography combined with impaired flow, Thrombolysis In Myocardial Infarction (TIMI) flow 1 or 2, we recommend the fenestration of the scaffold towards the SB. Online 3D-OCT reconstructions, which are available at the newest OCT consoles, could guide the optimal guidewire position during recrossing towards the SB. Recrossing through the most distal compartment is recommended, as distal recrossing leads to a reduction of incomplete stent apposition (ISA) at baseline in metallic stents.²⁶ In our experience, fenestration of the scaffold towards the SB is feasible with a 2.0 mm or a 2.5 mm balloon in the SB ostium to a maximum of 6 to 8 atmospheres.

Final OCT pullback after fenestration could be performed to detect whether the scaffold is well apposed in the whole stented area and to control for any struts out of the expected range. The latter is a sign of strut fracture, which could be treated with additional stenting. Due to lack of clinical data, we recommend repeat angiography to be performed combined with OCT at 9 months after scaffold placement, even if the patient is without any complaints. This allows assessment of the TIMI flow in the SB and MB, intimal tissue bridging in front of the SB and intimal formation in the distal MB. Treatment of ABSORB BVS re-stenosis has not been investigated in clinical trials; however, Nakatani et al. showed a case series of six patients with in-stent restenosis who have been treated with additional stenting using Xience drug-eluting stents.²⁷

Discussion

The ABSORB BVS is currently being used in daily clinical practice around the world. Unfortunately, very limited data are available about the use of the BVS in coronary bifurcation lesions. Several case reports have shown that treatment of bifurcation lesions and fenestration of the scaffold towards the side branch is feasible, which is supported by *in vitro* testing. However, all recommendations made in the treatment of coronary bifurcation lesions are not supported by any long-term clinical or *in vivo* data and are solely based on either expert opinion or limited *in vitro* data.

Džavik and Colombo are the first to publish *in vitro* benchmark testing. The tests performed are extensive; however, only one or two experiments were performed in each bifurcation stenting procedure. For example, a double-crush procedure could be successful once or twice but what if the experiment is repeated multiple times, will these results still hold? Although silicone models provide us with valuable insights into BVS geometry, *in vitro* models almost always have their limitations, which makes it difficult to deduce these results in terms of *in vivo* use. Silicone models are in general more rigid compared with coronary arteries, which makes it harder to overstretch and fracture the ABSORB BVS. Furthermore, the radial force of these models differ from coronary arteries, which makes assessment of non-apposed struts less reliable.

Okamura et al. provided a detailed description of how the ABSORB BVS obstructs SB orifices at baseline and the patterns of compartmentalisation and the number of compartments obstructing the SB. These observations are intellectually interesting; however, it is uncertain what implications it has for everyday clinical practice. Furthermore, the clinical outcome in relation with the pattern of

compartmentalisation and number of compartments is still unknown and needs further investigation.

Moreover, the effect of different bifurcation stenting procedures at follow up is unknown. Different stenting procedures could alter the endothelial shear stress patterns and coronary blood flow in different ways, hypothetically leading to different neointimal formation patterns at 1-year follow up.²⁸ The effect of all these factors could alter the neo-intimal bridge formation in front of the side branch in two ways. At follow-up this could potentially lead to increased neo-intimal formation with obstruction of the SB, although also non-covered NASB struts can persist.

Due to the lack of data, we believe that there is an urgent need for prospective randomised clinical data with OCT imaging for different bifurcation stenting techniques using the ABSORB BVS. In the absence of these data we recommend the use of the single scaffold provisional stenting strategy in coronary artery bifurcation lesions as is recommended by the European bifurcation club for metallic stents.

Conclusion

Based on case reports and *in vitro* testing ABSORB BVS placement in coronary bifurcation lesions seems to be feasible. The potential theoretical advantage of BVS of better access to side branches due to the disappearance over time of obstructing struts needs to be confirmed. Complex multiple BVS-bifurcation constructions, such as Culotte or Crush, are unattractive due to mechanical properties and strut size of currently available devices. Further research should be performed to detect the optimal bifurcation stenting procedure for this novel devices. ■

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