The Bioresorbable Stent in Perspective— How Much of an Advance is It?

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Abstract

The novel idea of bioresorbable stent technology continues to fascinate the interventional community. This article aims to provide a concise and balanced overview of the available technology and clinical evidence. Both potentially positive and negative aspects of bioresorbable stents in different lesion subsets and clinical situations are discussed.

Keywords

Bioresorbable vascular scaffold, biodegradable stent

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Terminology

When the first-in-human implantation of a bioresorbable device into the coronary artery was reported in 2007, the term 'fully bioabsorbable stent' was used.¹ Later, in 2011, Onuma and colleagues explained that the term 'bioresorbable' provides a more precise description of the complete cleavage of macromolecules to small molecules with total elimination and the term 'scaffold' was introduced.² However, the structure looks and behaves exactly like a stent, which is a commonly used term, understood by both medical professionals and patients. Thus, to prevent possible confusion we believe that the term 'bioresorbable stent' would be most fitting.

Technology

In 2014, there are many bioresorbable stents in different stages of development of which three are described in more detail below.

The most clinical literature currently available is with two generations of the balloon expandable **Absorb®** device (Abbott Vascular, Santa Clara, California, US). This is formed by a poly-L-lactic-acid polymer backbone (processed for an increased radial strength in the 1.1 version) and a thin amorphous everolimus/poly-lactic-acid matrix coating for controlled drug release. The implant is radiolucent but two platinum markers at each end allow easy visualization with angiography. The single strut thickness is 156 microns. According to preclinical studies the polymer backbone is fully resorbed in 2–3 years; the polymer coating is absorbed more quickly.³ The Absorb stent is commercially available in Europe.

The **Dreams®** device (Biotronic, Bulach, Switzerland) is a balloon expandable, paclitaxel-eluting magnesium alloy-based bioresorbable coronary stent.⁴ The implant is radiolucent with no markers and has a single strut thickness of 125 microns. The absorption process takes 9–12 months. Mechanical properties are similar to the current generation of metallic stents including safe overdistention. The Dreams stent has not yet received a CE mark.

The **DESolve®** stent (Elixir Medical, Sunnyvale, California, US) is also a balloon expandable scaffold made of a poly-L-lactic-acid-based polymer with a strut thickness of 150 microns. It provides sufficient radial strength for over 3 months and is fully bioresorbed in 1–2 years. Interestingly, self-apposing properties have been described and the stent can also be overexpanded by at least 1 mm without evidence of strut fracture in laboratory conditions. The DESolve stent received a CE mark in May 2013.

Evidence

First-in-human Studies

The **ABSORB A** study enrolled 30 stable patients with single *de novo* native short lesions of 3.0 mm calibre and tested the first generation of Absorb stent version 1.0.⁵ In-stent angiographic late lumen loss was 0.44 ± 0.35 mm at 6 months. Intravascular ultrasound (IVUS) analysis revealed a small neointimal area but also a significant reduction in stent area, probably due to recoil of the Absorb stent version 1.0. Four-year clinical results with complete follow-up are excellent with only one cardiac event (non-ST elevation acute coronary syndrome) and no stent thrombosis.⁶

The **ABSORB B** study enrolled 101 stable patients, again with single *de novo* lesions, suitable for the implantation of the Absorb stent version 1.1 sized 3.0/18 mm. Excellent clinical results were reported up to four years and, again, there was no stent thrombosis. Planned 6 month invasive assessment of cohort B1 (45 patients) revealed late lumen loss 0.19 ± 1.18 mm and optical coherence tomography (OCT) subanalysis (25 patients) demonstrated 96.8 % strut coverage.⁷ Similar invasive results were documented at 12, 24, and 36 months.^{8,9}

The **BIOSOLVE-I** study enrolled 46 patients with stable or unstable angina with one or two *de novo* short (12 mm or less) and simple lesions with a reference vessel diameter between 3.0 and 3.5 mm for implantation of Dreams stents (3.25/16 mm or 3.5/16 mm).

Late lumen loss at 6 months was 0.65 ± 0.50 mm. OCT subanalysis (seven patients) demonstrated 97.2 % of struts to be well apposed at 6 months follow-up. The 12-month rate of clinically driven target lesion revascularization was 4.6 %.⁴ No further events were reported at the 3-year follow-up, no stent thrombosis occurred.

The **DESolve Nx** study enrolled 126 patients with mostly stable coronary artery disease with a single *de novo* short lesion (12 mm or less) and reference vessel diameter between 3.0 and 3.5 mm. Angiographic late lumen loss was 0.21 ± 0.34 mm at 6 months. OCT subanalysis (38 patients) demonstrated 98.9 % of struts to be covered. The major adverse cardiac event rate at 12 months was 5.7 % and there was one case of stent thrombosis.

In summary, the first-in-man studies of selected three bioresorbable stents have included a total of 303 patients with mostly stable coronary artery disease. Patients with *de novo*, short, and 'simple' lesions were selected. Acute procedural results were excellent and the angiographic outcomes at 6 months were acceptable. Most importantly, the safety profile seems to be outstanding.

Randomized Studies

No results from randomized studies are available. ABSORB II started enrollment in 2011 and compares Absorb stent version 1.1 with the Xience Prime (Abbott Vascular, Santa Clara, California, US) stent in a 2:1 randomized fashion in patients with stable or unstable angina (myocardial infarction is an exclusion criterion). The larger ABSORB III study started enrollment in 2012 in the same fashion and should be sufficiently powered to prove clinical noninferiority. The estimated date of the primary outcome measure completion is August 2015.

Further Reported Data

Quantitative coronary angiography analysis demonstrated that the Absorb stent version 1.1 acute recoil is not different, and has better conformability, from metallic stents (Multi-Link or Xience V, Abbott Vascular, Santa Clara, California, US).^{10,11} Description of strut resorption and surrounding plaque composition by IVUS after Absorb 1.0 and Absorb 1.1 implantation has been reported.¹²⁻¹⁴ OCT provides excellent resolution but analysis of polymeric structures is different in comparison from metallic stents. The optically translucent polymeric struts appear as a black central core framed by light-scattering borders that do not shadow the vessel wall thus allowing excellent visualization of the vessel wall behind the struts and evaluation of stent apposition. Stent strut apposition was 95 % at baseline and 98 % at 6 months. A lack of tissue coverage was present in only 1.6 % of struts at 6 months.¹⁵ Normalization of local vascular compliance was demonstrated at 6 months.¹⁶ The use of online quantitative coronary angiography and especially measurement of maximal diameter of reference segment as a guide to stent size results in more favorable post implantation OCT findings.^{17,18} Absorb stent version 1.1 implantation was associated with a higher incidence of postprocedural side branch occlusion compared with the everolimus-eluting metallic stent Xience V. This effect was more pronounced with small side branches with a calibre of ≤ 0.5 mm.¹⁹

As far as expanding the use of bioresorbable stents into more challenging clinical scenarios, first case reports or small cohort studies have been reported, generally with encouraging results including: ST segment elevation myocardial infarction (STEMI),²⁰⁻²² retrograde approach to chronic total occlusion,²³ stenting of left main bifurcation,²⁴ vein graft,²⁵ or cardiac allograft vasculopathy intervention.²⁶

The metal-free struts of Absorb stent version 1.1 (and likely all other polymer-based stents) allow unrestricted coronary computed tomography angiography.²⁷

Opinions

The currently available evidence, as summarized above, does not allow us to reach definitive conclusions. By contrast, two opposing views can often be argued. We present a hypothetical structured debate between a bioresorbable enthusiast and a sceptic.

1) Overall situation. *Bioresorbable enthusiast:* Revolutionary bioresorbable stents are supported by encouraging data and will expand and dominate in the future. *Bioresorbable sceptic:* Bioresorbable stents have no proven benefit over currently available drug eluting stents (DES) and should not be routinely used yet.

2) Side branches and bifurcations. *Enthusiast:* Bioresorbable stents are optimal for interventions involving side branches as struts will be resorbed and access to branches restored.²⁸ *Sceptic:* Bioresorbable stents should not be used in bifurcations—struts may fracture during side branch dilatation and struts are thicker, i.e. more difficult to cross. More side-branch occlusions have been reported.^{19,29}

3) Long lesions. *Enthusiast:* The longer the lesion, the bigger the potential benefit of resorbable stent with possible elimination of late stent thrombosis and technically possible performance of bypass anastomosis at a later time. *Sceptic:* Overlaps with struts stacking and resulting thickness over 300 microns present a possible risk for delayed endothelialization.³⁰

4) Imaging. *Enthusiast:* Polymeric bioresorbable stents allow the evaluation of the coronary artery by computer tomography angiography at any time post implantation. *Sceptic:* The bioresorbable stent structure is not visualized and optimal expansion cannot be confirmed by angiography thus making the use of intracoronary imaging technology, such as IVUS or OCT, more frequent and thus increasing the complexity and cost of intervention.

5) Myocardial infarction. *Enthusiast:* Patients with STEMI are ideal candidates for the use of bioresorbable stents as they are typically younger and have soft thrombotic plaques. The first encouraging data have already been presented. *Sceptic:* There is not enough safety data regarding the use of bioresorbable stents in the highly thrombogenic milieu of acute coronary lesions and there is no proven clinical benefit yet.

6) Vasomotion. *Enthusiast:* Restoration of normal vasomotion is desirable and could result in a lower rate of future cardiovascular events. *Sceptic:* Restoration of normal vasomotion could increase the incidence of future vasospasm.

7) Antiplatelet therapy. *Enthusiast:* If needed, antiplatelet therapy might be safely interrupted once resorption of stent struts is complete and the risk for late stent thrombosis eliminated. *Sceptic:* Thicker struts of bioresorbable stents might mandate a longer duration of dual antiplatelet therapy than the current generation of DES (all reported studies so far have mandated 12-month dual antiplatelet therapy).

Authors' Personal View

Both authors have been actively involved in the Prague 19 study with the use of Absorb 1.1 stents in patients with STEMI and both

support the use of bioresorbable stent technology. However, there are some remaining concerns. Scientific evidence of superiority over current-generation DES might be achieved in surrogate endpoints, such as vasomotion and vessel remodeling, but evaluation of clinical superiority would require large patient cohorts and long follow-up times (significantly longer than the resorption time of the stent). This is not likely in the near future. There is no clearly established relationship between the above-mentioned surrogate endpoints and clinical outcomes. On the other hand, evidence of noninferiority could be achievable with a medium-sized randomized study and given the immensely attractive and logical idea of bioresorbable stent, this might

be enough to justify widespread use of this technology. From an even more philosophical perspective, this novel technology might lead our community to question the concept of mortality as the only valid and important endpoint. The matter of quality of life with individual patient feelings and, also, interventionalist preference might become more important and result in more diversity in our medical practice. As far as safety is concerned, it is reassuring to note that long-term (over 10 years) clinical outcomes of Igaki-Tamai poly-L-lactic acid coronary stents are excellent with no evidence of harm.³¹ This particular, first-in-human bioresorbable stent is not in clinical use anymore but paves the way for future safe clinical use. ■

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