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Review

Absorb bioresorbable vascular scaffold: What have we learned after 5 years of clinical experience?

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ABSTRACT

Bioresorbable scaffolds have the potential to introduce a paradigm shift in interventional cardiology, a true anatomical and functional "vascular restoration" instead of an artificial stiff tube encased by persistent metallic foreign body. Early clinical studies using the first commercially available drug-eluting bioresorbable vascular scaffold (BVS) reported very promising safety and efficacy outcomes, comparable to best-in-class second-generation drug-eluting metal stent. To date, more than 60,000 Absorb BVSs have been implanted with only the interim analysis of one randomized trial (ABSORB II RCT) available. Recent registries have challenged the initial claim that BVS is immune from Scaffold Thrombosis (ST). However, suboptimal device expansion and insufficient intracoronary imaging guidance can explain higher than expected ST, especially in complex lesions. The aim of this review article is to critically evaluate the results of the available Absorb BVS studies and discuss the lessons learned to optimize lesion selection and implantation technique of such devices.

1. Introduction

Several bioresorbable scaffolds have been proposed and have now reached clinical testing but only for the Absorb (Abbott Vascular, Santa Clara, CA, USA) bioresorbable vascular scaffold (BVS) a considerable amount of clinical data is available to date [1,2]. First-in-man studies on small and highly selected cohorts, using multimodality intracoronary imaging, have confirmed the timing of the reabsorption process and suggested good safety and efficacy [3,4]. These initial favorable results have been challenged by "real world" registries showing high Scaffold Thrombosis (ST) rates [5–8]. With the fast approaching milestone of 100.000 implanted Absorb BVS and the prediction that more than 50% stents will be BVS by 2017, it is essential to learn from critically reviewing the many studies and registries and the only one randomized trial available to possibly correct current pitfalls in the implantation technique of such devices [9].

2. ABSORB bioresorbable vascular scaffold

2.1. The device

The ABSORB BVS is constituted by a poly-L-lactide (PLLA) backbone covered by a 1:1 mixture of an amorphous matrix of poly-D,L-lactide (PDLLA) and the anti-proliferative drug everolimus (100 μl/cm^2) [2]. The first proof of concept study (ABSORB cohort A) used a prototype soon replaced by the 1.1 version, storable at room temperature, with the same high strut thickness of 150 μm but greater resistance to acute and early recoil [10–12] and greater conformability and flexibility provided by in-phase zigzag hoops linked by bridges [13] (Fig. 1). The longer hydrolysis rate translates in a slower mass loss; the actual duration of resorption of the second generation scaffold in vivo is approximately 18 months longer than the first generation, and its mass loss takes approximately 36 months [14]. Reabsorption time is critical for the device performance, with mechanical integrity required over a period of 6 months to avoid recoil [15]. Loss of structural integrity and radial support depends on initial focal degradation within the more amorphous regions, while significant mass loss requires much longer, with the polymer replaced by a provisional matrix of proteoglycan followed by collagen fibers [16]. The reabsorption process has also been studied with Optical Coherence Tomography (OCT) showing progressive strut degradation [17].

Abbreviations: ACS, acute coronary syndrome; BVS, bioresorbable vascular scaffold; DES, drug eluting stent; MACE, major adverse cardiovascular events; MI, myocardial infarction; ST, stent/Scaffold Thrombosis; TLF, target lesion failure; TLR, target lesion revascularization; TVF, target vessel failure; TVR, target vessel revascularization.

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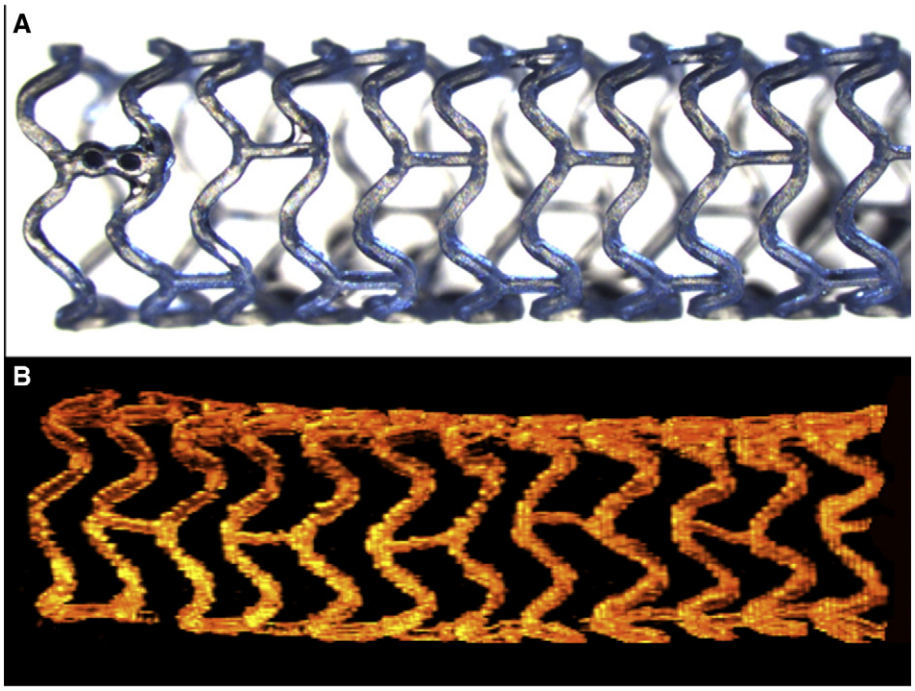

Fig. 1. Absorb BVS structure and design. High-resolution microscope image of a 3.0 mm BVS inflated at nominal pressure (panel A); BVS structure at OCT 3D reconstruction (panel B).

2.2. Landmark studies — the ABSORB program

The first-in-man study, the Absorb cohort A study, enrolled 30 patients undergoing implantation of the first generation (Absorb BVS 1.0) scaffold for the treatment of lesions shorter than 14 mm in 3.0–3.5 mm vessels [2] and showed good clinical outcomes but evidence of early scaffold recoil at 6 months. Of note, the invasive imaging (IVUS and OCT) analysis at 2 years demonstrated late lumen enlargement with restoration of vasoreactivity [2,3]; recently, excellent 5-year clinical outcomes (3.4% MACE) have been reported [18]. The improved BVS 1.1 version achieved a greater lumen area at 6 months in the larger ABSORB cohort B (n = 101) with persistently good late clinical outcomes (10.1% MACE and no ST at 3 years) [10,14]. In order to build a body of evidence to support a broader utilization of the Absorb BVS, a prospective, single-arm, open-label clinical study (the ABSORB EXTEND) was designed [19]. The one-year results were reassuring with a 4.3% MACE, 2.9% MI and 0.8% ST. To date, the three-year follow-up data of 250 patients implanted with BVS in the ABSORB EXTEND study showed 9.3% cumulative MACE, with 6.0% TLR and 1.2% definite/probable ST rate (see Table 1). Similar lesions have been treated in the ABSORB II trial, the first randomized study comparing Absorb BVS with the equivalent metallic drug-eluting stent (DES) in 501 patients [9]. The primary endpoint was nitrate induced vasomotion and in-stent late loss at 3 years. At 1-year no significant difference in the prespecified composite secondary clinical outcomes was observed, while a lower cumulative rate of recurrent or worsening angina was reported for the Absorb. However, final in-stent minimum lumen diameter and IVUS minimum lumen cross-sectional area were significantly smaller in the Absorb group than in the Xience group. Also, a trend towards a higher rate of MI and ST was observed in the Absorb-treated arm (4.5% vs 1.2% MI p = 0.06 and 0.9% vs 0.0% ST p = 0.55). Since the study included simple lesions with an average length of 20 mm, a 0.9% difference in the ST rate might represent a worrisome signal, given the catastrophic clinical consequences of ST. The B-SEARCH registry included 88 patients from the ABSORB cohorts A and B and EXTEND with a reassuringly low event rate (only one non-TVR at 1-month follow-up) [20]. New studies included in the ABSORB program (ABSORB III [NCT01751906], ABSORB FIRST [NCT01759290], etc.) are currently

Table 1
The ABSORB program — manufacturer-sponsored studies.

Study	Study design	Phase	N	Reported FU
ABSORB cohort A	Observational, prospective	Completed	30	5 years
ABSORB cohort B	Non-randomized, open label	Completed	101	3 years
ABSORB EXTEND	Observational, prospective	Active, not recruiting	1000	3 years[a]
ABSORB II	Randomized, single blind	Active, not recruiting	330	1 year
ABSORB physiology[b]	Randomized, single blind	Terminated	35	N/A
ABSORB FIRST	Observational, prospective	Recruiting	1800	1 month
ABSORB III	Randomized, single blind	Recruiting	1502	N/A
ABSORB IV	Randomized, single blind	Recruiting	3000	N/A
ABSORB Japan	Randomized, single blind	Active, not recruiting	265	N/A
ABSORB China	Randomized, open label	Active, not recruiting	200	N/A
ABSORB UK	Observational, prospective registry	Recruiting	1000	N/A

[a] Smits PC. ABSORB EXTEND: An Interim Report on the 36-month Clinical Outcomes from the First 250 Patients Enrolled. Presented at: TCT Congress; September 13, 2014; San Francisco, USA.
[b] Only 1 patient recruited; Eeckhout E. ABSORB FIRST: An interim report on baseline characteristics and acute performance on the first 1200 patients from a prospective, multi-center, global registry. Presented at: TCT 2014, San Francisco, USA. N = number of patients; FU = Follow-Up; N/A = not available.