

Bioresorbable Vascular Scaffolds: Progress and Potential

Koen Deloose, MD, discusses the potential advantages of this technology, results to date, and remaining questions to be answered.



What are the theoretical advantages of bioresorbable stents?

Absorbable stents, more appropriately termed *scaffolds* to emphasize their transient nature, potentially offer several advantages.

First of all, there is the effective scaffolding without the permanence of a metallic implant. By full resorption, these scaffolds avoid a long-term, inflammatory foreign body reaction and physical irritation. They facilitate the positive vascular remodeling by returning the vessel to its natural “uncaged” state. In this way, the physiological vessel biomechanics are preserved for the mid and long term. All these characteristics will potentially lead to a reduction in diameter stenosis and an improvement of patency rates. Finally, future endovascular or open surgical procedures are not impaired by this type of implant.

How would you characterize the initial clinical experiences using early iterations of these devices in the lower extremities?

The first bioresorbable vascular scaffold (BVS) developed for the superficial femoral artery (SFA) was the non-drug-eluting Igaki-Tamai device (Remedy, Kyoto Medical Planning, Kyoto, Japan), designed as a monofilament poly-L-lactide (PLLA) coil with a zigzag helical pattern. With diameters up to 5 mm (expandable to 7 mm) and lengths of 3.6 and 7.8 cm, the devices were self-expanding, although balloon dilatation was necessary to optimize vessel wall apposition. The initial clinical experience in the PERSEUS trial included treatment of 45 patients with SFA de novo lesions < 6 cm. A 100% technical success rate, no serious adverse events, a 30% angiographically based binary restenosis \geq 50% at 6 months, and an impressive 91% primary-assisted patency rate at 9 months were reported. However, the initially favorable results of the PERSEUS trial deteriorated with time. Larger cohorts with the Igaki-Tamai device in the SFA suggested 1-year primary patency lower than 50%.¹

Another bioresorbable scaffold tested in the lower extremity (tibial) arteries is the absorbable magnesium

stent (AMS, Biotronik, Berlin, Germany). This device is a balloon-expandable, laser-cut scaffold consisting of magnesium, zirconium, yttrium, and rare earth elements. The AMS INSIGHT trial was a randomized trial in which 117 patients with critical limb ischemia were randomized between an angioplasty-alone arm and an AMS arm. Unfortunately, after 6 months, the patency rate in the AMS group was significantly lower than in the angioplasty-alone group (32% vs 58%; $P = .013$). Early recoil and neointima formation were responsible for these disappointing results.²

What was learned from these experiences, and how has current technology improved since then?

First, all endovascular procedures create profound and circumferential stretch injuries to the target artery. This direct vascular injury and inflammatory response with smooth muscle cell activation and proliferation should be blocked by a slow release of an antiproliferative drug. Second, the artery remains from the beginning but also over a longer time susceptible to mechanical contracture and recoil from energy stored in the stretched external elastic lamina. Maintaining scaffolding and support to deal with this elastic recoil for a sufficient duration has been one of the biggest challenges of this technology.

The previously mentioned devices showed failures in providing durable arterial scaffolding. The Absorb drug-eluting Bioresorbable Vascular Scaffold (Abbott Vascular, Santa Clara, CA), which is composed of a PLLA polymer scaffold, a poly(D,L-lactide) coating, and the antiproliferative drug everolimus, can probably overcome the two problems. The everolimus effectively inhibits neointimal hyperplasia, enhances remodeling, and has been shown to be safe. The Absorb BVS is designed to maintain its structure and strength for the full 6-month postimplantation period. This is already proven in the coronaries, where optical coherence tomography images after 6 and even 12 months showed full preservation of the scaffold

area without any shrinkage. Three-year follow-up now shows very encouraging results in this field.³⁻⁶

What are your impressions of the 30-day ESPRIT I data presented by Prof. Scheinert at LINC 2013?

I was not really surprised by these amazing but very preliminary 30-day results.⁷ A 100% technical success rate and no major adverse events or scaffold thrombosis were reported at 30 days. Even more important was the fact that there were no indicators of acute scaffold recoil on angiography and no evidence for binary restenosis on duplex at 30 days. From a clinical point of view, there was a substantial improvement in functional status. Of course, we need to wait for the 6- and 12-month results to judge the application of this technology in TASC A SFA lesions definitively.

What other studies are ongoing?

Although a lot of studies with resorbable devices in the coronaries have been reported or are ongoing, the peripheral space remains wide open for this new technology. An extension of the ESPRIT I trial to a larger cohort of patients is planned. The STANCE trial, a prospective, single-arm, multicenter trial testing the Stanza bioresorbable scaffold (480 Biomedical, Watertown, MA) in the SFA is getting started.⁸ A drug-eluting version of this scaffold is in development and will be tested soon too. In the tibial arteries, several trials are on the way.

I'm really looking forward to explore tests of other devices, such as the newer generations of the AMS with modifications in the alloy that allow for slower degradation, thinner struts, an improved design, and active coating with paclitaxel or the redesigned, sirolimus-coated coronary Resolve scaffold (Reva Medical, San Diego, CA) in the challenging peripheral area.⁶

What duration of follow-up do you think we need to see before bioresorbable scaffolds can be evaluated against bare-metal and drug-eluting stent results, even if still in an apples-to-oranges, nonrandomized fashion?

Acute outcomes are important, because after all, these devices have to perform like self-expanding stents at implantation. They need to yield a good angiographic appearance and a solid luminal gain. Midterm follow-up is the most important because the anticipation of returning to the natural biomechanics of the vessel as the device degrades and resorbs is essential in this concept. Drug elution and its effect on the vessel wall will also gradually stop in this time frame. Thus, sustained symptom-free patency is important throughout this period. Polymer resorption in the long-term has been shown to cause very little inflam-

ESPRIT I KEY FACTS

- Prospective, single-arm, multicenter OUS trial evaluating the Esprit BVS in symptomatic SFA or iliac atherosclerosis
- N = 35
- One target lesion treated with a single 6- X 58-mm Esprit BVS
- Single de novo lesions; vessel diameter ≥ 5.5 and ≤ 6.5 mm, length ≤ 50 mm
- Rutherford 1 through 3
- Follow-up scheduled for 1, 6, 12 months, 2 and 3 years
- 30-day data presented at LINC 2013:
 - 100% acute procedural success
 - No clinical endpoint events or scaffold thrombosis
 - No indication of acute scaffold recoil on angiography
 - No binary restenosis on duplex
 - Rutherford 3 patients dropped from 57% to 0%

mation in preclinical models, and it is generally seen as a passive, late-term process.

Truly evaluating bioresorbable scaffolds against the current technologies will take several more years, waiting for larger cohorts and longer lesion treatment results.

Whereas existing stent platforms are engineered for long-term structural integrity, it could be said that bioresorbable scaffolds aim to break down in a controlled fashion. What might be some of the unique challenges facing these technologies (versus permanent stents)?

The basic material—the semicrystalline polymer PLLA—of the currently tested bioresorbable devices (Igaki-Tamai, Absorb BVS) can be tuned by varying the mechanical and thermal conditions of processing. This concept, besides the device design, makes differentiation in radial forces, acute recoil percentages, timing of full scaffolding before the start of disintegration, and flexibility ratios possible. If a drug is present, it must elute in a relevant time frame and at a dose rate that is effective yet relatively benign to the tissue. Creating the right properties for the right indication—the anatomic location and lesion type—is in my opinion one of the unique challenges in the development of these technologies.

Is distal embolization more of a possible concern?

Distal embolization remains a concern with this technology. However, in the coronaries (ABSORB trial)⁴ and

in the tibial vessels (INSIGHT trial),² where it has been studied extensively with intravascular ultrasound and optical coherence tomography, there have been no signs of embolization. The resorbable devices are completely imbedded into the vessel wall and covered with a neointima.

How does this fundamental design difference affect clinical trial endpoints and markers of success?

I personally prefer to use the same clinical endpoints as we have in the bare-metal and drug-eluting stent and drug-eluting balloon trials for infrainguinal occlusive arterial disease. Reporting serious adverse events, evolution of Rutherford classification, primary patency, freedom from target lesion revascularization, late lumen loss, and for critical limb ischemia patients, limb salvage, should be obligatory parameters in all well-designed trials, independent of the techniques and devices used. Of course, extra substudies can be scheduled with these types of stents to follow the resorption of the scaffold and the risk of distal embolization by intravascular ultrasound, optical coherence tomography, or multislice CT/MR (ESPRIT I, STANCE).

Is there anything particularly unique about the design, endpoints, and core lab evaluation of the ESPRIT I trial? What are the specifics of the evaluation?

Quite unique was the need for the perfect preparation of the target vessel before the implantation of the Esprit BVS. Adequate measurements of the pre-treatment diameter on quantitative vessel analysis (to avoid real oversizing) and a meticulous predilatation of the lesion to the desirable diameter were obligatory before BVS implantation. In my opinion, we also need to spend some more time on these issues during our routine angioplasties, drug-coated balloons, and bare-metal stent implantations. The core lab evaluation of the BVS is similar to other clinical trials. Only later on, resorption will force us to redefine concepts such as percentage stenosis or late lumen loss, when the frame of reference (the original device diameter) has disappeared.

Do you see bioresorbable scaffolds as having the potential to be the next step in the progression of stenting technologies, after bare-metal and drug-eluting stents?

I'm convinced this technology will gain an additional and complementary space in our endovascular armamentarium of tomorrow. Because of the already

excellent results of current endovascular technologies (bare-metal stents, drug-eluting stents, and drug-coated balloons) in short lesions, I would position bioresorbable scaffolds in the treatment of more challenging, longer lesions in the above-the-knee and below-the-knee areas, where there is still the need for a lot of improvement. They might act as a primary treatment or as a bailout, temporary scaffolding solution after atherectomy or drug-coated balloon treatments.

Any early insights into the costs, cost-effectiveness, and reimbursements of bioabsorbable stents?

It is really too early to discuss these parameters on such a nascent technology. As we learn more about its results and applicability, we can determine a strategy to deliver this to patients who really need it.

What's next in the study of bioresorbable scaffolds?

Extensions to larger controlled cohorts, more challenging (TASC C and D) lesions, and to other areas like the tibial arteries in critical limb ischemia patients are needed to truly assess the effect of biomechanical vessel restoration and full resorption of the implant in the current vascular population. I'm very encouraged by the recent data so far, but much more work is needed in the field. ■

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