Off-label indications for bioresorbable scaffolds: "Beethoven can, but you cannot"

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The pianist Carl Czerny, a pupil of Beethoven, reports in his book *On the Proper Performance of all Beethoven's Works for the Piano* an interesting anecdote. The young Anton Halm presented the master a sonata that he had just composed. Beethoven looked through it without finding anything that aroused his attention and after a few minutes gave the young composer his piece back, remarking that he had contravened several elementary rules of harmony. The young Halm protested: "But Beethoven himself also infringes the same rules of harmony!" Then the genius turned to him with a fulminating glance and declared: "Beethoven can, but you cannot".

We should remember this motto whenever we consider off-label indications for novel devices or novel therapeutic options in general: "Beethoven can, but WE cannot". The excess of self-assurance and overconfidence in our own capabilities is most likely behind the poorer-than-expected clinical performance of bioresorbable scaffolds (BRS) after becoming widely available [1], at variance with the outstanding promising results reported in pilot studies [2–4]. Therefore putting ourselves in the pupil's shoes is always the advisable starting point to face an off-label indication for BRS.

Nonetheless, potential off-label indications pop up daily in our routine clinical practice, and we are compelled to explore them if we aim to optimise the treatment of our patients and the potential of the emerging technology. The motto "Beethoven can, but you cannot" is the best possible starting point, but it can never become an excuse to brake the expansion of novel therapeutic tools into more challenging scenarios, in which they may also be convenient and useful. In a recent number of *Advances in Interventional Cardiology*, our colleagues from Katowice, namely Roleder T, Wanha W, Smolka G, Zimoch J, Ochała A and Wojakowski W publish a modest but interesting descriptive study entitled "Bioresorbable vascular scaffolds in saphenous vein graft disease. Pilot results from the OCTOPUS registry" [5]. It is just a descriptive series of 6 patients undergoing percutaneous coronary intervention (PCI) with implantation of the Absorb BRS (Abbott Vascular, Santa Clara, CA) in saphenous vein grafts, but very relevant to expand the indication of the BRS to this challenging (still off-label) scenario. To date there have been several case reports of BRS implanted in saphenous vein grafts [6, 7], some of them reported by the same authors of the current study [8], but this is the first systematic series specifically focusing on the treatment of saphenous vein grafts. The sample size is too small to draw any meaningful conclusion (n = 6 patients), but the study protocol is detailed and exhaustive, including clinical follow-up at the 12th month (n = 6), and angiographic (n = 4) and OCT (n = 3) follow-up at 6–7 months. The limitations are blatantly obvious, namely the small sample size and the irregular imaging protocol compliance, but still it is a landmark in our understanding of the performance of scaffolds in non-native cardiac vessels.

The use of BRS in saphenous vein grafts is not a trivial issue. Bioresorbable devices have narrow overexpansion margins, limited by low rupture thresholds [9, 10]. Due to this particular feature, sizing becomes a critical step in BRS implantation. The correction of undersizing always entails a risk of scaffold rupture, and beyond a 0.5 mm mismatch in diameter the correction becomes most likely impossible [9, 10]. Accurate sizing is particularly challenging in saphenous bypass grafts, because of the usually larger diameter of the venous grafts that might exceed the size of currently available BRS. Aside from the mechanical challenges during the implantation procedure, there are additional factors that might theoretically introduce some variability in the BRS outcomes in a saphenous-graft scenario: the different structure of the vessel wall, the peculiar composition of the stenotic

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lesion in the venous graft or the lower wall shear-stress. These factors might modulate the vessel response to BRS in venous grafts, eventually resulting in some nuances as compared with the results extensively described for native coronary arteries. The resorption rate should not be altered depending on the vessel in which the BRS is implanted, at least theoretically, since it is a mainly hydrolysis-dependent process, not so influenced by the flow rate or by the architecture of the underlying tissue [11]. However, empirical data are still missing.

The current study by Roleder *et al.* is obviously insufficient to answer the array of open questions [5]. It is perhaps even underpowered to provide a single solid answer to any of these questions. However, it shows for the first time that neither major mechanical complications nor grossly suboptimal acute results are expected following a simple standard implantation protocol. This is of the utmost relevance, particularly because 50% of the patients underwent optical coherence tomography (OCT) during the implantation (i.e. the sizing might have been guided by the OCT measurements), but the other 50% of patients underwent a purely angiographic-guided implantation procedure. The protocol describes anyway that the implantation was guided by angiography in all cases, irrespective of the OCT imaging: the OCT pullbacks were obtained after the BRS deployment. The hereby reported results, although modest, encourage us to proceed in this direction. Regarding the other theoretical factors that could modulate the long-term outcome (tissue/lesion structure, flow conditions, bioresorption rate, etc...), we cannot infer any conclusion from the current study, too small to detect any subtle nuance, but at least the 12-month clinical follow-up is encouraging (no death, myocardial infarction or target vessel revascularisation). Again, inconclusive but encouraging.

In summary, this preliminary report of the OCTOPUS registry is a modest but bold step forward to become Beethoven and feel confident enough to break the elementary rules of harmony if it makes sense, i.e. to move out of the safe but narrow path of the on-label indications for BRS, expanding them to the challenging scenario of saphenous vein grafts. The authors must be congratulated for their pioneering initiative and for the high-quality scientific approach to generate evidence at all the required levels. Nonetheless, it is just a first bold step forward: we are still closer to the pupil than to the master. Further results of larger and more conclusive studies are required to shape definitely the evidence about this indication and will be celebrated by the scientific community.

Conflict of interest

The authors declare no conflict of interest.

References

1. Capodanno D, Gori T, Nef H, et al. Percutaneous coronary intervention with everolimus-eluting bioresorbable vascular scaffolds in routine clinical practice: early and midterm outcomes from the European Multicentre Ghost-EU Registry. Eurointervention 2015; 10: 1144-53.
2. Serruys PW, Ormiston JA, Onuma Y, et al. A bioabsorbable everolimus-eluting coronary stent system (ABSORB): 2-year outcomes and results from multiple imaging methods. Lancet 2009; 373: 897-910.
3. Onuma Y, Serruys PW, Ormiston JA, et al. Three-year results of clinical follow-up after a bioresorbable everolimus-eluting scaffold in patients with de novo coronary artery disease: the ABSORB trial. Eurointervention 2010; 6: 447-53.
4. Dudek D, Onuma Y, Ormiston JA, et al. Four-year clinical follow-up of the absorb everolimus-eluting bioresorbable vascular scaffold in patients with de novo coronary artery disease: the ABSORB trial. Eurointervention 2012; 7: 1060-1.
5. Roleder T, Wanha W, Smolka G, et al. Bioresorbable vascular scaffolds in saphenous vein grafts (data from OCTOPUS registry). Postep Kardiol Inter 2015; 10: 323-6.
6. Ong PJ, Jafary FH, Ho HH. "First-in-man" use of bioresorbable vascular scaffold in saphenous vein graft. Eurointervention 2013; 9: 165.
7. Yew KL. Novel use of absorb bioresorbable vascular scaffold and STENTYS self-apposing coronary stent for complex saphenous vein grafts intervention. Int J Cardiol 2014; 177: e184-5.
8. Roleder T, Parma Z, Smolka G, et al. Optical coherence tomography imaging of everolimus-eluting bioresorbable vascular scaffold implanted into coronary vein graft at 3-month follow-up. Eur Heart J 2014; 35: 2207.
9. Foin N, Lee R, Mattesini A, et al. Bioabsorbable vascular scaffold overexpansion: insights from in vitro post-expansion experiments. Eurointervention 2015 Jul 8;11(3). pii: 20141213-04. doi: 10.4244/EIJY15M07_02. [Epub ahead of print].
10. Ormiston JA, Webber B, Ubod B, et al. An independent bench comparison of two bioresorbable drug-eluting coronary scaffolds (Absorb and DESolve) with a durable metallic drug-eluting stent (ML8/Xpedition). Eurointervention 2015; 11: 60-7.
11. Oberhauser JP, Hossainy S, Rapoza RJ. Design principles and performance of bioresorbable polymeric vascular scaffolds. Eurointervention 2009; 5 (Suppl. F): f15-22.