Editorial

Bioresorbable drug eluting scaffolds—are bioresorbable stents ready for today's clinical practice?

Christoph Lutter[1], Michael Joner[2]

[1]CVPath Institute Inc., Gaithersburg MD, USA; [2]German Heart Center Munich, Technische Universität Munich, Germany

Correspondence to: Michael Joner, MD. Assistant Professor Cardiology, German Heart Center Munich and Deutsches Zentrum fuer Herz-Kreislaufforschung e.V., Technische Universität Munich, Germany. Email: joner@dhm.mhn.de.

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During the course of stent development, a novel concept has recently been introduced, which is based on transient scaffolding of the coronary artery with the help of fully bioresorbable stents eventually allowing vascular restoration over time. Bioresorbable vascular scaffolds represent a landmark innovation and are designed to fully disappear from the coronary artery once their function is no longer needed. This new approach in the treatment of coronary artery disease is widely believed to be beneficial as compared to current metallic devices, especially in younger patients. In this context, recent studies have indicated potential advantages of bioresorbable scaffolds, as treated vessels seem to regain vasomotor functionality during degradation of the device (1).

Different materials and components have been investigated, where two concepts have reached the stage of clinical investigation: Magnesium-based bioresorbable stents and scaffolds consisting of lactic acid co-polymers. The development of the latter material is further advanced to date and by now two bioresorbable scaffolds based on a lactic acid polymer have received CE approval at the European market (ABSORB—Abbott Vascular, Santa Clara, California and DESolve—Elixir Medical Corporation, Sunnyvale, California).

Despite the rapid adoption of this novel technology in clinical practice soon after CE-mark approval, comparative clinical data on patient outcomes relative to current standards have been missing. Recent randomized studies and registries helped to improve our understanding of the benefits and drawbacks of this novel technology. In this regard, the most important requirement for innovative techniques or technologies is the proof of non-inferiority regarding both safety and efficacy versus the existing standards, especially in the initial phase after treatment (2). Apart from the results of the first clinical trials, the available literature on clinical outcome data after bioresorbable stent implantation has increased significantly within the last year. Although the overall clinical results reported so far look promising, a slightly higher risk of early device thrombosis seems to dampen the widespread optimism derived from bioresorbable scaffold implantation (3). One of the key pathological explanations seems to be the substantially increased thrombogenicity of current generation BRS, where strut thickness and width exceeds by far what we have been accustomed to with the use of contemporary metallic DES. It has been demonstrated in a preclinical porcine arterio-venous shunt model that bioabsorbable scaffolds reveal a significantly higher acute thrombogenicity compared with second generation DES; besides that, metallic DES showed greater re-endothelialization after 28 days and reduced inflammatory reactions after 14 days as compared with bioabsorbable scaffolds (4).

Since the introduction of BRS in clinical practice, there has been continued debate about their practical implementation, where one of the suggested indications was in the setting of acute myocardial infarction. The proposed benefit of BRS in this specific setting is thought to derive from their temporary presence since malapposition of stent struts is a frequent finding when stents are implanted in occluded vessels where appropriate sizing represents a major challenge. Furthermore, it is believed that BRS enable vascular restoration over time, which may be especially important in the healing phase of acute plaque rupture, where vascular remodeling plays an important role. Another argument favoring the implantation of BRS in the setting of acute ST-elevation myocardial infarction is that patients

are often younger than patients presenting with chronic stable CAD, where the capacity of vascular restoration might be preserved. In this respect, an interesting study which was published in *JACC Cardiovasc Interv* in 2015 has to be highlighted, in which the authors focused on the performance of fully bioresorbable scaffolds in the setting of acute myocardial infarction (5).

For their observational study, Brugaletta and colleagues combined the data from two independent studies in order to analyze differences between everolimus eluting bioresorbable scaffolds and contemporary DES and bare metal stents, respectively (5). Although the rate of stent thrombosis was higher in the biodegradable scaffold group as compared with DES within 30 days (1.4% *vs*. 0.3%) and 12 months (1.7% *vs*. 0.7%), the authors describe no statistical significant differences among the groups. To reduce the strong influence of baseline patient risk differences among the two datasets, the authors performed propensity-score matching. However, this correction cannot fully compensate differences in patient baseline characteristics and, although the propensity score matching was overall well performed and described, the customized model might have had some downsides. The main goal of this statistical matching technique is to gauge the effects of pre-treatment factors that predict receiving one treatment or the other. For this reason, only pre-treatment factors that potentially can influence the treatment should be considered for this matching whereas e.g., procedural circumstances should be disregarded (6). Furthermore, as the presented study was not randomized, other influences than the chosen stent type might affect the outcome results. Especially the fact that patients treated with biodegradable implants were enrolled in the setting of a registry study whereas the patients of the DES and BMS groups were selected from the dataset of a prospective clinical trial has to be considered critically. Furthermore, the comparison of bioresorbable stents *vs*. bare metal stents seems to be pointless, as bare metal stents are nowadays not recommended for the setting of primary angioplasty. Last but not least, the study appears to be underpowered in order to compare rarely-occurring clinical endpoints like stent-thrombosis.

Nevertheless, the study highlights promising and potentially pioneering results in regard to daily clinical use of fully biodegradable drug eluting stents in the setting of primary angioplasty. The most notable finding is the similar performance of the degradable devices as compared to the standard metallic drug eluting stents at 12 months follow-up. These findings were recently confirmed in the Absorb III trial which showed a non-inferiority of BRS compared with metallic DES in regards of target lesion failure at one year follow up (7). Furthermore, fully biodegradable scaffolds were recently investigated in the setting of acute ST-elevation myocardial infarction and compared against 2nd generation DES with regards to their performance on a multicomponent ordinal healing score (8). In this respect, the absorbable vascular scaffold was non-inferior and compared favorable to the metallic DES in the percentage of malapposed stent struts. However, this innovative imaging endpoint, even though it is promising, has important limitations since established and validated evidence for this score is missing. For that reason, skepticism regarding the safety profile of fully absorbable scaffolds in the setting of acute myocardial infarction is still indicated.

In their meta-analysis of all available randomized controlled trials, Cassese and colleagues recently highlighted the increased risk of stent thrombosis, especially within the first 30 days, as well as a greater in-device late lumen loss in BRS as compared with metallic DES (3). Therefore, we should not become too euphoric in this respect as long-term results (>1 year) are still pending. These long term results might also answer the questions whether or not the new generation of devices is capable to re-establish vasomotion and to provide a positive remodeling effect within the treated artery or whether the degradation process triggers inflammatory reactions after drug elution. The finding of slightly higher thrombosis rates, especially within the first 30 days of implantation, seems to be mainly related to the procedural results more than to the shape or chemical composition of the stent. Additional information from intravascular imaging techniques should be gathered whenever necessary to guarantee satisfying stent positioning and deployment. Further development of the bioresorbable scaffolds might solve current disadvantages with regard to radial strength.

To summarize: the available data, as well as our own experience, furnishes us with optimism that this latest technology can deliver benefits to many patients. The essential point behind the successful use of fully biodegradable stents seems to be a careful patient—as well as lesion selection combined with an optimization of the procedural results.

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Footnote

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