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Editorial

Bioresorbable scaffold -fourth revolution or failed revolution: Is low scaffold strut thickness the wrong target?

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ABSTRACT

Bioresorbable scaffold (BRS) technology has currently fallen into disrepute because of inordinately high risk of scaffold thrombosis and post-procedure myocardial infarction. Low tensile and radial strengths of polymeric BRS contributing to improper strut embedment have been identified as major correlates of poor outcomes following BRS implantation. Magnesium has a better tensile/radial strength compared with polymeric BRS but it is still far lower than cobalt-chromium. Newers innovations utilizing alteration in polymer composition and orientation or even newer polymers have focused on attempts to reduce strut thickness but may have little effect on tensile/radial strength of finished product and therefore may not impact the BRS outcome on long run. Currently, newer generation BRS usage may be restricted to suitable low risk younger patients with proper vessel preparation and application of technique.

1. Background

The prospect of leaving a metallic prosthesis in the body, especially when it is no longer required has always been a matter of concern to both physicians and patients alike. In case of metallic stents for coronary or peripheral interventions this is of particular worry because they don't remain innocuous, rather interfere with vascular remodeling and flow and serve as a nidus for accumulation of platelets (stent thrombosis) as also interfere with future interventions in the area. Bioresorbable scaffolds (BRS) were developed with a view to address some of these philosophical and practical issues particularly that of late stent thrombosis with metallic drug eluting stents (DES) and were purported to represent "Fourth Revolution" in stent technology. The trick was to match physical performance of the metallic stent but at the same time making the scaffold disappear at a variable period of 6 months to 3 years after implantation. The initial results with this technology, in simple lesions with a careful application of technique, seemed equivalent to any metallic stent with the advantage of melting away in due course of time and possible favorable remodeling of artery and a better flow. However, soon problems of late scaffold thrombosis and post-procedural myocardial infarctions started cropping up, the very reasons BRS was developed in the first instance.[1,2] Thus suddenly medical opinion moved from "Fourth Revolution" to possible "Failed Revolution." This whole fiasco demands explanation and possible learning for future.

2. What are the reasons?

The reasons for this negative evolution could be numerous and encompass histo-pathologoical, mechanical and behavioral explanations. Table 1

2.1. Histo-pathological co-relates

1. Dense distribution of incompletely embedded, thick protruding struts (which are incompletely endothelized) may disrupt the laminar flow and induce endothelial shear stress, a precursor for adherent thrombosis.[3]
2. Early structural disruption and late scaffold discontinuity, as a part of property of polymer used, with elongation and break at resorption points- an inherent component of resorption process (which in any case appears delayed in humans) could also make the site vulnerable to thrombotic events for a prolonged period of time.[4]
3. Peri-strut, low intensity area (PSLA) in absence of classical mechanical triggers has been correlated with peri-strut inflammation, mal-apposition, evagination, strut fracture, and un-endothelized struts in metallic DES and could serve as additional patho-physiological correlates with BRS as well.[5–7]

2.2. Mechanical factors

The mechanical limitations of current BVS are:

1. Low tensile and radial strength of scaffold material. Typically bio-resorbable polymers, polylactide (PLLA) and poly(d,l-lactide) have tensile strengths ranging between 45 and 70 MPa (<200 times) compared with nearly 1500 MPa with cobalt chromium. The radial strength is also around 10 times lower.[1,8,9] Thus to improve the tensile and radial strengths, typically a greater strut thickness (≥150 μ) may be required but this

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Table 1
Reasons for sub-optimal outcomes with current BRS.

Histo-pathological Factors
Incompletely embedded struts
Early structural disruption and late scaffold discontinuity
Peri-strut low intensity areas
Mechanical Factors
Low tensile and radial strength
Low ductility
Improper scaffold design
High strut thickness
Physician Factors
Faulty research
Inappropriate procedural technique
improper choice of lesion – small vessels, calcific lesions etc
sub-optimal vessel sizing
inability to achieve optimal deployment – under-dilatation or mal-apposition
inadequate post-dilatation with
non-use of imaging techniques for optimization of result – OCT/IVUS
Discontinuation of DAPT

modification may still remain inadequate to overcome the vast differences in radials and tensile strengths. Consequently, the embedding force during the deployment of scaffold may still remain deficient resulting in only partly embedded and largely exposed scaffold struts (a focal point for thrombus formation), despite high-pressure post dilatation.

2. Insufficient ductility is another mechanical aspect which affects not only the crimping ability of scaffold on the delivery balloon but also limits the range of device expansion because the polymer may easily snap during the process of deployment. The break-point for polymers occurs at only 2% to 6% of elongation compared with 40% for metallic stents.[10,11]
3. Improper design of scaffold could be another factor. The rectangular shape and excessive height compared with current generation DES, increases its foot-print within the lumen, a large part protruding from the vessel wall, contributing to blood flow disturbances with consequent at least two-fold risk of scaffold thrombosis.[12]
4. Strut thickness has been a correlate of metallic stent thrombosis and re-stenosis. However, this factor seems to play a lesser important role in context of BRS.[13]

2.3. Physician factors

Several research and operator factors are also responsible for the current scenario.

1. Research questions may not have been properly framed and device trials pushed through without properly understanding how to use the device.
2. Inappropriate procedural technique; improper choice of lesions (small vessel, diffuse disease, calcific lesions), inability to prepare proper bed, sub-optimal vessel sizing and inability to achieve optimal deployment (non use of imaging techniques like OCT and IVUS, mal-apposed struts and inadequate post-dilation – with balloon sized $\geq$1.1:1 compared with scaffold diameter) all contribute to scaffold thrombosis.[10–12,14,15]
3. Dual anti-platelet therapy discontinuation by physician or patients themselves also remains a risk factor for scaffold thrombosis.[15]

3. What lies in future?

The current crisis is certainly not end-game for BRS technology; however innovations in material science will have to be made to overcome the deficiencies. The current attempts to tinker with complex composition of polymers, mixing PLLA, poly-glycolide, and poly-caprolactone to improve radial and tensile strength and improve ductility have yielded slightly superior mechanical characteristics. Improved strength has also been attempted to be imparted by altering the polymer orientation (melt extrusion, drawing) and polymer treatment (heat annealing and blow molding to achieve a proper mix of crystalline with amorphous polymer), even using newer polymers; tyrosine based polycarbonates and poly-lactide anhydrides. Currently, the main focus of innovation from structural stand-point has been to try achieve a lower strut thickness, which was a correlate of DES outcomes. However, it is possible that all this while, this may have been a step in wrong direction because for BRS the most important predictor of thrombosis is a low tensile and radial strengths contributing to un-embedded scaffold struts, a precursor for future events. Thus lower strut thickness could actually lead to even lower tensile/radial strength, and thus even less properly embedded scaffold struts, a potential recipe for paradoxically increased scaffold thrombosis. On the other hand it is possible that while these minor modifications in polymer technology may improve the tensile strength of device it may still be still difficult to bridge the 100 fold gap in tensile strength and 10 fold gap in radial strength. Thus unless a landmark innovation happens in polymer technology it will remain a dream unfulfilled. In this context magnesium, based BRS which have a tensile strength of 220–330 MPa and elongation at break-point like cobalt chromium (of 40%) may be more useful in immediate future.[8] However, it has to be remembered that tensile strength is still 1/5th and radial strength 1/3rd of cobalt chromium, so there is still some work to do. Meanwhile the nattiness of BRS can still be utilized in suitable low risk younger patients with proper vessel preparation and application of technique utilizing some newer generation devices.

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