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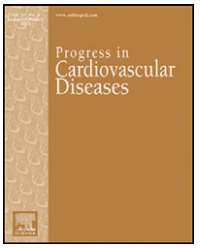

Bioresorbable Stents: Is This Where We Are Headed?

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ABSTRACT

Current drug-eluting stents (DES) have shown excellent safety and efficacy in various clinical settings. However, the presence of a permanent metallic scaffold remains an Achilles heel, with concerns for late stent thrombosis and the need for prolonged dual anti-platelet therapy. The bioresorbable vascular scaffold (BRS) has been termed the fourth revolution in interventional cardiology, with an ability to not only treat the coronary lesion, but also restore endothelial function after complete absorption. The absence of a permanent scaffold after months of implantation has the potential to overcome the shortcomings of current metallic DES and markedly impact interventional cardiology practice around the world. This review article focuses on the history, development and clinical studies on various BRS and attempts to predict how this technology could impact future cardiology practice.

Plain old balloon angioplasty (POBA) revolutionized acute cardiovascular (CV) care in the late 1970's.[1] However, this innovation was found to be associated with unacceptably high rates of non-success in acute and chronic target vessel revascularization. These weaknesses were somewhat alleviated by introduction of bare metal stents (BMS). By placing a metallic scaffold, acute and chronic arterial recoil post-angioplasty could be prevented.[2] Despite initial success, restenosis due to neo-intimal hyperplasia (NIH) was noted in 16%–44% of patients. This remained the Achilles' heel for BMS technology for a decade until drug-eluting stents (DES) were developed around the turn of the century. These stents eluted anti-proliferative drugs, showed remarkable reduction in NIH and in-stent restenosis (ISR) and were quickly adopted into practice.[3] However, operators noticed the limitations of sub-acute and delayed stent thrombosis (ST) due to inhibition of healing of the permanent metallic remnant by the anti-mitotic drug, inflammation in part from the polymer, as well as neo-atherosclerosis due to a number of processes.[4] Hence the interventional community searched for a device that provided good radial force after angioplasty, thereby preventing acute recoil, and then disappeared over a period of time. This might prevent complications of the persistent metallic scaffold and the need for prolonged dual anti-platelet therapy (DAPT) to prevent late and very late ST. Bioresorbable vascular scaffolds (BRS) present one such solution. This article summarizes the history, current status and future of this "fourth revolution" in the field of interventional cardiology. In this paper, we use the term "BRS" to refer to the generic bioresorbable device and BVS to refer to the specific Abbott® scaffold.

Rationale for BRS

Proponents of BRS technology believe that it eventually may overcome a major limitation of current stents, delayed stent/scaffold thrombosis. Stents are required only for avoiding

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Abbreviations and Acronyms

EES = everolimus-eluting stents

BMS = bare metal stent

MI = myocardial infarction

TLR = target lesion revascularization

LM = left main artery

CABG = coronary artery bypass surgery

PCI = percutaneous coronary intervention

IST = in-stent thrombosis

ISR = in-stent restenosis

RCT = randomized control trial

MACE = major adverse cardiovascular events

STEMI = ST elevation myocardial infarction

BRS = Bio-resorbable scaffold

OAC = oral anticoagulants

TIMI = Thrombolysis in Myocardial Infarction

NSTEMI = non-ST elevation myocardial infarction

ACS = acute coronary syndrome

BP = byproducts

PROGRESS AMI trial = Clinical Performance and Angiographic Results of Coronary Stenting with Absorbable Metal Stents

RESORB trial = REVA Endovascular Study of a Bioresorbable Coronary Stent

ARTDIVA FIM = Arterial Remodelling Transient Dismantling Vascular Angioplasty First in Man trial

PTD-PC = poly-tyrosine derived polycarbonate

PDLLA = poly-DL-lactic acid

PLLA = poly-L-lactic acid

AMS = absorbable metallic stent

CSA = cross sectional area

IVUS = intra-vascular ultrasound

CO_2 = carbon dioxide

early complications of angioplasty. Once healing of the vessel has been achieved, the DES was shown to instigate vascular inflammation and favor neo-atherosclerosis.[5,6] Also, permanent metallic struts led to high rates of acquired late malposition — a feature known to favor ST.[7] BRS, therefore, may obviate the need for prolonged DAPT, thereby minimizing bleeding events especially in high risk groups such as the elderly and patients on oral anti-coagulation. Additionally, complete absorption of the stent has been shown in some studies to restore vascular function (vasomotion).

Though early to comment on, it is believed that disappearance of metallic scaffolds would allow the option of repeat percutaneous or surgical myocardial revascularization in or beyond areas of previous scaffolding. This may be important in certain settings like long or bifurcating lesion. Within the latter, jailing of a side branch is an important issue that most operators face. While the peri-procedural data on current BRS may favor the metallic stents due to the large BRS "footprint", it is to be noted that BRS revolution is at a primitive stage and, further, that acute outcomes may not reflect long-term benefits. If refinement of BRS technology treads the same path as the modern metallic stents, such acute issues may not remain a weakness for BRS. In this vain, BRS technology may allow easier access to a side-branch in the future.

Some additional points in favor of BRS development include the ability to follow these stents by advanced multi-slice computed tomography (CT) techniques without causing any metallic artifacts. Further, we can expect freedom from strut fracture induced restenosis with use of BRS. Finally, the ABSORB II trial and ABSORB EXTEND trial have opened up a new avenue of future research. These trials found that compared to patients with metallic stents, BVS patients had less angina and fewer rates of nitrate utilization — a feature that drove target lesion revascularization (TLR) rates in favor of BVS. Hopefully, the ABSORB III and IV trials will shed more light on this topic.

Design of an ideal BRS

- Should be bio-compatible — before, during and after degradation
- Provide adequate radial force for acute treatment of vessel lesions
- Adequate degradation time — too fast increases inflammation and too long defeats the purpose. Radial support of the scaffold required for at least 4–6 months.
- Degradation should not aggravate/initiate a vascular inflammatory process.
- Should be compatible with DES technology and elute the drug at a pre-determined rate without affecting its radial strength/degradation properties
- Should not have thick struts and should be easily deliverable
- Easy to store — no need for refrigeration
- Enhanced visualization under fluoroscopy — at least comparable to current DES/BMS
- Deployed with currently available equipment (5Fr/6Fr compatible)
- Improved dwell time before deployment. Current Absorb® and Elixir® stents require prompt delivery after they are inserted into the vascular system. Ideally, like the current metallic scaffolds, performance should not be a function of dwell time.

BRS — current data on safety and efficacy

Table 1 describes the past, current and future BRS, their specifications, and clinical evidence supporting their use in clinical practice.

Expectations vs accomplishments — evidence-based analysis

Scaffolding

The objective of any stent is to overcome the limitations of angioplasty, i.e., acute recoil, NIH, and late constrictive