

dure was also associated with edge-related complications and a high recurrence of ISR (> 50%) (1, 4). In regards to treatment strategy, nonetheless, observational studies and randomised trials have consistently shown that DCB and DES have relatively superior outcomes than POBA in ISR (29, 30).

## Cutting/Scoring Balloon

Cutting or Scoring balloons (CB or SB) were introduced to minimise barotraumas to the vessel wall and slippage of a conventional balloon when inflated over fibrotic scar tissue. They prevent balloon slippage-related complications using the lateral blades that anchor the balloon within the target lesion. In the treatment of ISR, cutting and scoring balloons may play an important role in lesion preparation preceding DES or DCB (1).

Neointimal modification with a scoring or cutting balloon has possible advantages over standard balloon pre-dilatation (31). Neointimal change of ISR with CB plus DCB vs. standard DCB lowers the 5-year rate of TLR, even though not statistically significantly. The benefit seems to be persistent in ISR after implantation of BMS and DES (32). In the ISAR-DESIRE 4 trial, neointimal modification with scoring balloon before DCB compared with DCB standard therapy showed superior results concerning angiographic outcomes at follow-up. However, at 1-year follow-up, there were no differences when the clinical events or TLR were assessed (16.2% vs. 21.8%;  $P = 0.26$ ) (33). Both technologies are interfered with their inability to hinder neointimal proliferation and have limitations similar to balloon angioplasty (BA) (5).

## Bare Metal Stent (BMS)

During the BMS era, conventional balloon angioplasty or repeated BMS implantation was mostly used as the treatment for ISR. Recurring event rates after BA were approximately 20% by 1 to 2 years. The RIBS I (Restenosis Intra-stent Balloon Angioplasty Versus Elective Stenting) trial randomised 450 patients with BMS-ISR to undergo either BA or repeat BMS implantation. After 4 years of follow-up, target vessel revascularisation was as high as 25% and 29% ( $P = 0.35$ ), and the major adverse cardiac event (MACE) rates

were 31% and 37% for the BMS implantation and balloon angioplasty groups, respectively. Currently, BMSs have been replaced by DESs, and BMSs are only used in specific situations (eg, in patients with an extremely high bleeding risk, when short-duration antiplatelet therapy is required, or for economic reasons), and studies assessing the value of BMS in patients with DES-ISR are lacking and unlikely to be undertaken (31, 34).

## Bioresorbable Vascular Scaffolds (BVS)

BVS has also been proposed as a treatment for patients with ISR. The main advantages are that the device eventually disappears from the vessel wall, avoids the presence of multiple stent layers, and prevents early lumen loss associated with tissue retraction seen in balloon angioplasty (4). Some studies suggest that the use of BVS implantation for the treatment of complex drug-eluting stent and bare-metal stent ISR lesions might be associated with acceptable long-term clinical outcomes (35, 36).

Based on Restenosis Intrastent: Bioresorbable Vascular Scaffolds Treatment (RIBS VI), target lesion revascularisation rates following BVS were similar to those seen with DEB (10.4%) but higher than with EES (3.2%;  $p < 0.001$ ). After potential confounders in baseline characteristics were adjusted, results remained unchanged. It can be concluded that BVS yielded late angiographic and clinical results similar to DEB, but inferior to EES (37).

Potential limitations of BVS include lumen crowding due to thickness (particularly in small vessels), device flexibility that may influence access to restenotic lesions, and questions concerning radial strength and recoil, which may be particularly crucial in the management of ISR (34).

## Intravascular Brachytherapy (IVBT)

Intravascular brachytherapy is a technique that is intended to suppress cellular proliferation and migration by directing radiation at the site of the vascular intervention. It allows a localised delivery of radiation to inhibit the proliferative response seen after angioplasty (38). Condado et al conducted the first trial of

coronary IVBT. They treated 21 participants with gamma irradiation after balloon angioplasty. The result was that 19 of 21 participants showed evidence of late occlusion at two-year angiographic follow-up (39). The final pathway of DES-ISR includes the formation of neointima with an accumulation of lipid macrophages within the neointima and subsequent calcification. IVBT inhibits neoatherosclerosis in DES-ISR. It impedes neointimal growth without affecting the surrounding healthy tissue. In a previous retrospective study, IVBT showed good outcomes for patients with DES-ISR. The incidence of target lesion failure (TLF) occurred in one in three patients at 2 years (40). In a systematic review and meta-analysis conducted by Megaly et al., the incidence of target vessel revascularisation occurred in approximately one in four patients at two-year follow-up, with an incidence rate of 29.2% (95% CI 18.0–40.4%) (41). Nowadays, the popularity of brachytherapy decreased after the introduction of DES because of logistic difficulties and lower restenosis events in the newer stents (42).

## Intravascular Lithotripsy (IVL)

Intravascular lithotripsy is a procedure for treating severely calcified plaques in the coronary and peripheral arteries. It generates sonic pressure waves through the vessel wall and produces calcium modification. This acoustic wave selectively fractures the intimal and medial calcium. This increases vessel compliance and optimises stent expansion (43). Some reports showed the safety and efficacy of IVL in treating in-stent restenosis. IVL can be promising to optimise the outcome of ISR in heavily calcified coronary artery disease (44–46).

## Ablative Strategies

### Excimer Laser Coronary Atherectomy (ELCA)

ELCA is a long-established adjunctive therapy that can be applied during PCI. Excimer laser generates pulses of short-wavelength, high-energy ultraviolet light that uses an active medium containing gas and halogen (47). It has been useful to facilitate stent ex-