Interventional cardiology was born in the late ’70s thanks to the pioneering efforts of Andreas Gruntzig and colleagues [1]. The limitations of the original Gruntzig balloon were however severalfold, including the lack of a steerable wire, the early risks of recoil and abrupt vessel closure, and the late risk of restenosis [2]. The introduction of stents revolutionized the invasive management of coronary artery disease, by virtually eliminating the need for emergency bypass and delaying the process of restenosis [3]. However, stents created two main and novel iatrogenic diseases: stent thrombosis and in-stent restenosis. The risk of stent thrombosis was tackled by improving stenting technique, [4] and intensifying antiplatelet therapy, [5] whereas in-stent restenosis lead to several attempts at modulating in-stent neointimal hyperplasia. Intracoronary radiation, while theoretically promising, proved too aggressive and with risks that clearly outweighed its benefits [6]. Conversely, the concept of a metallic stent platform covered by a drug inhibiting neointimal hyperplasia soon proved remarkably effective and reasonably safe, leading to the worldwide success of drug-eluting stents [7]. This viewpoint provides a concise yet comprehensive overview of USA Food and Drug Administration approved drug-eluting stents, emphasizing pros, cons and unmet needs still requiring further development.

**First-generation Drug-eluting Stents**

After the initial setbacks of very early devices,[8-9] sirolimus-eluting stents (Cypher, Cordis, Miami, FL, USA) and paclitaxel-eluting stents (Taxus, Boston Scientific, Natick, MA, USA) proved extremely successful and acceptably safe in comparison to the corresponding bare-metal stents [10-11]. Whereas no significant reductions in the risk of death or myocardial infarction could be inferred, both sirolimus- and paclitaxel-eluting stents showed substantial reductions in angiographic end-points such as late lumen loss and binary restenosis [12], as well as clinical end-points such as target lesion revascularization, and major adverse cardiac events [13]. However, the safety of such first-generation drug-eluting stents was questioned repeatedly, given the increased risk of protocol-defined stent thrombosis and the occasionally reported raised risk of death in studies with short-term dual antiplatelet therapy [14].

**Second-generation Drug-eluting Stents**

The limitations of first-generation drug-eluting stents and the competition among medical device manufacturers lead to the development of several second-generation drug-eluting stents, including zotarolimus-eluting stents and everolimus-eluting stents. These two novel device classes should however be further distinguished into fast-elution (Endeavor, Medtronic, Fridley, MN, USA) and slow-elution zotarolimus-eluting stents (Resolute, Medtronic), and into cobalt-chromium (Xience, Abbott Vascular, Temecula, CA, USA and Promus, Boston Scientific) and platinum-chromium everolimus-eluting stents (Promus Element, Boston Scientific).

Fast-elution zotarolimus-eluting stents appeared significantly superior to the corresponding bare-metal stents [15], but the inhibition of neointimal hyperplasia achieved by these stents was inferior to those associated with other second-generation drug-eluting stents as well as with first-generation devices [16-17]. In particular, angiographic late lumen loss was 0.61±0.46 mm with Endeavor in comparison to 1.03±0.58 mm with its bare-metal stent equivalent in the ENDEAVOR 2 trial [15]. This appears as a suboptimal effect on neointimal hyperplasia given that Cypher and Taxus were associated with late loss of, respectively, 0.24±0.47 mm in the SIRIUS trial and 0.23±0.44 mm in the TAXUS 4 trial [10-11].

Everolimus-eluting stents have shown so far very favorable results in the SPIRIT clinical trial program as well as in other independent studies [18-20], with outstanding reductions in neointimal hyperplasia and ensuing risks of binary restenosis, target lesion revascularization, target vessel revascularization, and major adverse cardiac events. Such inhibitory effects on smooth muscle cells appear associated with a very favorable impact on endothelial function and strut coverage, at least in light of the risk of stent thrombosis associated with these devices. Indeed, recent data suggest everolimus-eluting stents may be superior to other drug-eluting stents as well as bare-metal stents in terms of risk of stent thrombosis, but further analyses, including those based on mixed treatment comparisons techniques, are awaited [21]. In addition, while most of the data on these devices stem from studies relying on a cobalt-chromium platform (Xience or Promus), recently a platinum-chromium platform has been developed (Promus Element), which seems associated with higher flexibility and similar clinical results [22].

Slow-elution zotarolimus-eluting stents represent another significant breakthrough in drug-eluting stent technology, as extensively shown in the Resolute All Comers trial, a non-inferiority study which compared such stents with everolimus-eluting stents, finding similar outcomes in the two groups, with the notable exception of an increased risk of stent thrombosis with zotarolimus-eluting stents [23]. Nonetheless, in general these devices appear associated with a very favorable risk-benefit profile.

**Future Perspectives**

Current second-generation drug-eluting stents provide such beneficial results in terms of repeat revascularization and major adverse cardiac events that it is difficult to envision substantial improvements when these devices can be safely implanted. Thus, in most patients with proximal and mid-tract lesions, we believe that drug-eluting stents will remain the dominating technology for several years. Unmet needs are however still there. In particular, we miss devices which can be delivered very distally or in very tortuous segments [24], dedicated bifurcation devices [25], and we still need to rely on permanent metallic platforms to ensure mechanical support and drug elution [26].
The Sparrow stent (Biosensors, Singapore, Singapore) is ideally posed to become a useful adjunct to the interventionist’s armamentarium aiming to treat distal and tortuous lesions [27], whereas bioabsorbable endoprostheses (Absorb, Abbott Vascular) appear as very promising alternatives to standard metallic stents when permanence of the metallic platform is called into question [26]. Finally, drug-eluting balloons might become a routine means to revascularize patients with coronary artery disease as they may represent a suitable middle man between standard balloons and drug-eluting stents [28,29].

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