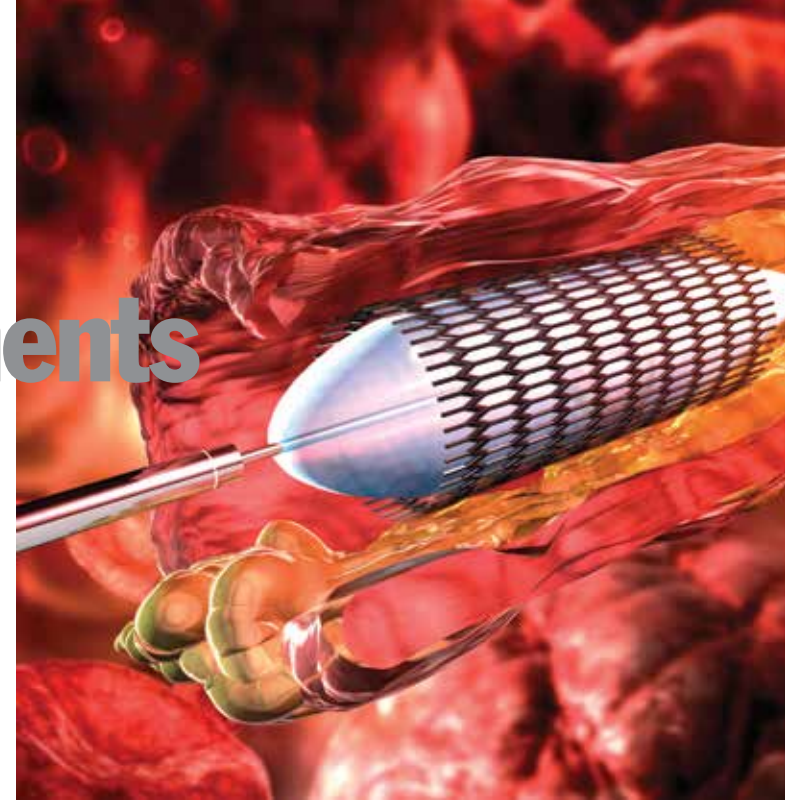
PERSPECTIVE

New developments in coronary stent technology



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Coronary artery disease is the leading cause of death and morbidity in the world. Significant coronary artery lesions may be treated by percutaneous coronary intervention, typically balloon angioplasty and stent implantation. A new generation of drug-eluting coronary stents are undergoing clinical trial evaluation and are being introduced into clinical practice. Out of all emerging stent technologies, fully bioresorbable scaffolds hold promise as being the most debated, ambitious and intuitive concept.

Key points

- **Percutaneous coronary intervention has revolutionised the treatment of coronary artery disease.**
- **Metallic coronary stents provide a vascular scaffold to maintain luminal patency after coronary artery dilation.**
- **Traditional coronary stents are associated with a small but significant risk of stent thrombosis.**
- **Bioresorbable stents provide temporary scaffolding after angioplasty but are subsequently fully resorbed with multiple theoretical benefits. Their safety and efficacy are yet unproven in large randomised clinical trials.**

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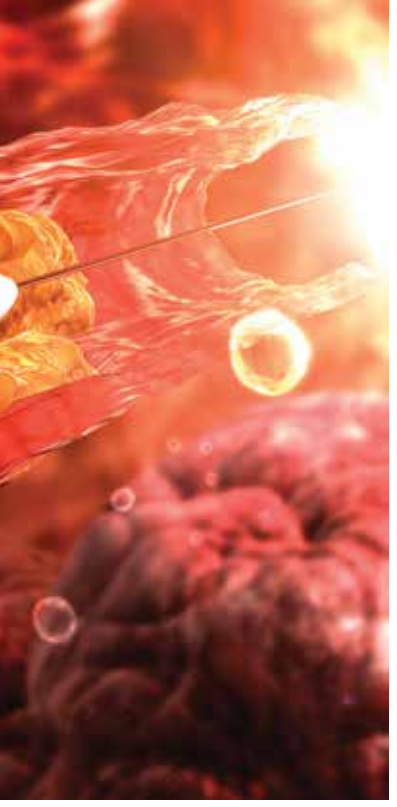
About 35 years ago, Andreas Gruntzig pioneered coronary angioplasty, in which a small balloon is threaded over a wire and inflated at the site of a stenosis.[1] This 'plain old balloon angioplasty' is a minimally invasive way of managing symptomatic coronary artery disease; however, significant numbers of patients experience rebound artery occlusion from vessel dissection and restenosis.

Bare metal stents were developed in the mid 1980s, providing a vascular scaffold to maintain short- and longer-term luminal patency following balloon dilation. However, the process of implanting a stent in a coronary artery causes mechanical injury to the vessel wall triggering an inflammatory healing response. This may cause in-stent restenosis (target lesion failure) necessitating further treatment. To avoid this, drug-eluting stents incorporating antiproliferative agents within a polymer coated over a metallic stent were introduced (Figure 1).

Drug-eluting stents and acute stent thrombosis

Drug-eluting stents reduce the need for repeat intervention without reducing rates of death or myocardial infarction.[2] Nevertheless, the use of drug-eluting stents is linked with an increased risk of late sudden stent thrombosis after insertion.[3,4] Pathological studies associate the polymer coating of first-generation drug-eluting stents with poor endothelial coverage of stent struts and chronic inflammation increasing the propensity to thrombosis and subsequent occlusion.[5]

Second-generation drug-eluting stents with improved durable polymer mounted on thinner struts maintain efficacy while improving safety compared with their first-generation counterparts.[6] Nevertheless, 'real-world' data demonstrate appreciable rates of very late stent thrombosis and the need for repeat revascularisation in the years following implantation (in approximately 2% of patients over four-years' follow up).[7] Stent thrombosis is a feared and potentially fatal complication with a 30-day mortality of up to 33%.[8]



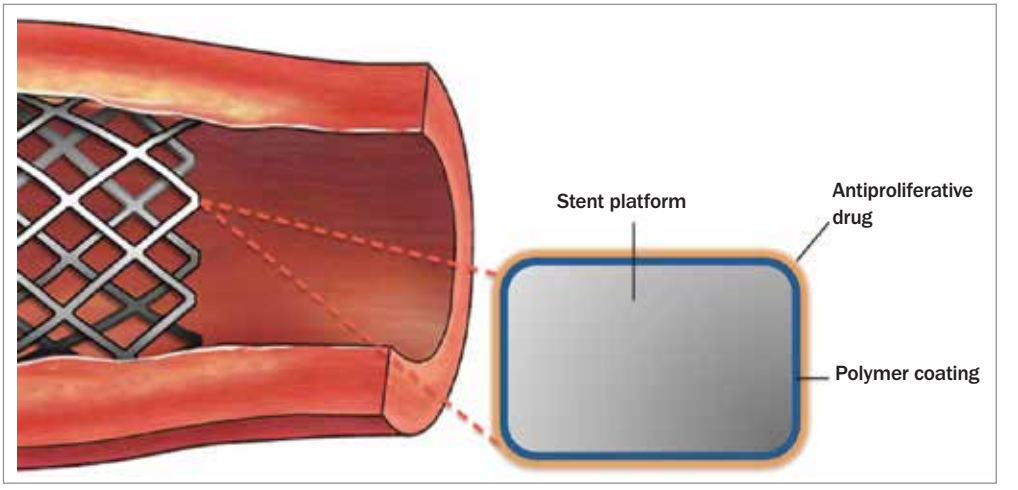


Figure 1. Schematic diagram of a drug-eluting stent.

Desire for better long-term safety and efficacy has catalysed the evolving third-generation of drug-eluting stents. These technologies comprise a broad range of innovations and include polymer-free stents, biodegradable polymer coated stents and fully biodegradable scaffolds (see Box 1 for a brief description of these third-generation drug-eluting stents).

Out of all emerging stent technologies, fully bioresorbable scaffolds hold promise as being the most debated, ambitious and intuitive concept.[9] They provide temporary scaffolding for a defined period after angioplasty but are subsequently fully resorbed.

1. Types of third-generation drug-eluting stents

Biodegradable polymers
Biodegradable polymers leave a bare metal stent in situ after the polymer and drug matrix has served its short-term purpose of reducing vessel restenosis.

Polymer-free drug-eluting stents
Bare metal stent scaffolds incorporate antiproliferative drug delivery via micro or nanoporous channels on the abluminal surface eliminating the need for the polymer.

Bioresorbable scaffolds
Bioresorbable scaffolds provide temporary scaffolding for a defined period after angioplasty but are subsequently fully resorbed.

Bioresorbable scaffolds

Liberation of the metallic cage

The presence of a permanent metallic foreign body and polymer within a coronary artery may cause inflammation and

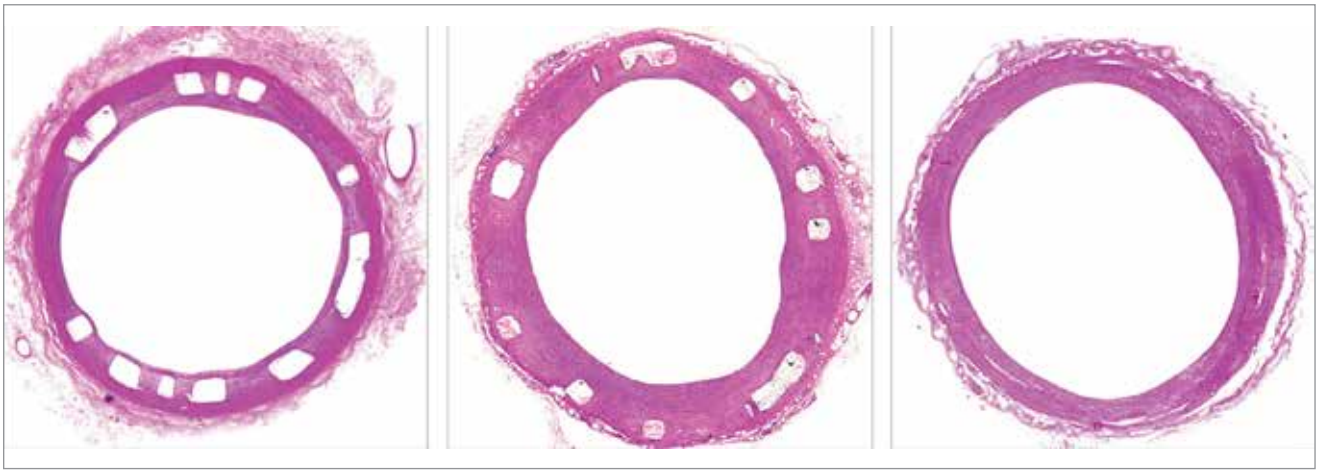


Figure 2. Biodegradation of Absorb bioresorbable scaffold struts in a porcine coronary artery model. Histopathology with haematocylin and eosin staining.
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2. Potential advantages of bioresorbable scaffolds over other stent technologies

- Reduction in late target lesion failure and very late stent thrombosis
- Restoration of physiological arterial vasomotion
- Expansive vessel remodelling (late luminal loss expected with permanent stents)
- More conducive to imaging with computed tomography or magnetic resonance
- Facilitates future revascularisation (percutaneous or bypass grafting)
- Preservation of vessel geometry

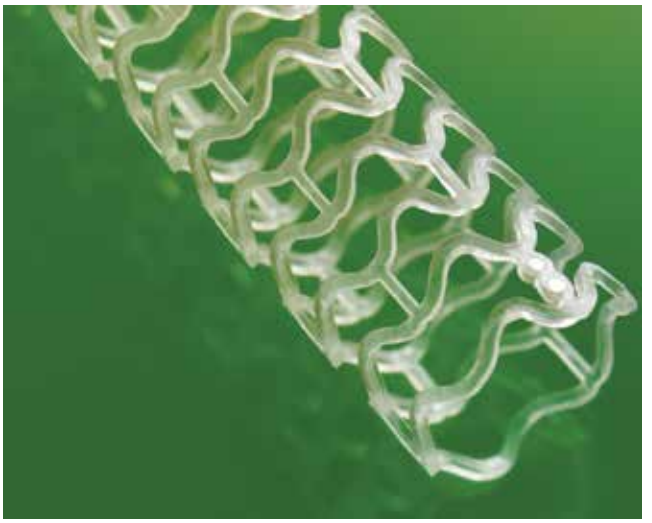
neoatherosclerosis potentially predisposing to thrombosis and restenosis.[10,11] This may be responsible for the small but accumulating requirement for repeat revascularisation in the years following contemporary drug-eluting stent implantation.[12] The ultimate goal is temporary scaffolding with sealing of the atheromatous plaque before full stent resorption occurs. Endothelial coverage of the bioresorbable scaffolds may be enhanced hence reducing the risk of (very late) stent thrombosis and, importantly, the need for long-term dual antiplatelet therapy (Figure 2). Liberation of the metallic cage also allows restoration of physiological arterial vasomotion together with other theoretical advantages (Box 2).

Polymeric or metallic bioresorbable scaffolds

Bioresorbable scaffolds are composed of polymers or metallic alloys (Figures 3a and b).

Absorb bioresorbable vascular scafford (1.1) is the sole bioresorbable scaffold available for clinical use in Australia and New Zealand and is the most widely investigated bioresorbable scaffold at present.[13,14] It is composed of two polymers (poly-L-lactic acid and poly-D,L-lactide acid) that provide short-term radial strength before the polymeric scaffold is metabolised via the Krebs cycle into carbon dioxide and water. There is increasing evidence of both safety and efficacy extending beyond three years.[15,16] Results from randomised trials on these gold-standard contemporary drug-eluting stent are eagerly awaited.[17,18] Caveats include radiological visibility, thicker polymer stent struts leading to increased crossing profile, and reduced deliverability compared with contemporary drug-eluting stents. In addition, they are less expandable and therefore require more quantitative sizing otherwise strut fracture may ensue.[19]

Dreams magnesium-based bioresorbable metal scaffold has recently reported a first-in-man study showing feasibility with a good safety and efficacy profile at 12 months.[20] This is a dynamic area with many more types of bioresorbable scaffolds in clinical trials and preclinical development.[11]



Figures 3a and b. Examples of two leading bioresorbable scaffolds in clinical use and development. a, top. Absorb vascular scaffold (1.1). b, bottom. Dreams magnesium-based scaffold.

Conclusion

With contemporary drug-eluting stents proving increasingly safe and effective, some clinicians question the need for bioresorbable scaffolds as 'a solution without a clinical problem'.[21] Nonetheless, the goal of a temporary vascular scaffold liberating the treated vessel from a metal cage is intuitive: bioresorbable scaffolds are the most promising avenue in emerging stent technology. Long-term safety and efficacy data from large randomised controlled trials are needed to propel its use into the mainstream. **CT**

References

A list of references is included in the website version (www.medicinetoday.com.au) of this article.

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References

1. Gruntzig A. Transluminal dilatation of coronary artery stenosis. Lancet 1978; 1: 263.
2. Kastrati A, Mehilli J, Pache J, et al. Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents. N Engl J Med 2007; 356: 1030-1039.
3. Ong AT, McFadden EP, Regar E, de Jaegere PP, van Domburg RT, Serruys PW. Late angiographic stent thrombosis (LAST) events with drug-eluting stents. J Am Coll Cardiol 2005; 45: 2088-2092.
4. Camenzind E, Steg PG, Wijns W. Stent thrombosis late after implantation of first-generation drug-eluting stents: a cause for concern. Circulation 2007; 115: 1440-1455.
5. Finn AV, Nakazawa G, Joner M, et al. Vascular responses to drug eluting stents: importance of delayed healing. Arterioscler Thromb Vasc Biol 2007; 27: 1500-1510.
6. Stefanini GG, Holmes DR. Drug-eluting coronary-artery stents. N Engl J Med 2013; 368: 254-265.
7. Raber L, Magro M, Stefanini GG, et al. Very late coronary stent thrombosis of a newer-generation everolimus-eluting stent compared with early-generation drug-eluting stents: a prospective cohort study. Circulation 2012; 125: 1110-1121.
8. Mauri L, Hsieh WH, Massaro JM, Ho KK, D'Agostino R, Cutlip DE. Stent thrombosis in randomized clinical trials of drug-eluting stents. N Engl J Med 2007; 356: 1020-1029.
9. Sammel AM, Chen D, Jepson N. New generation coronary stent technology – Is the future biodegradable? Heart Lung Circ 2013; 22: 495-506.
10. Iqbal J, Onuma Y, Ormiston J, Abizaid A, Waksman R, Serruys P. Bioresorbable scaffolds: rationale, current status, challenges, and future. Eur Heart J 2014; doi:10.1093/eurheartj/eht542.
11. Di Mario C, Borgia F. Assimilating the current clinical data of fully bioabsorbable stents. EuroIntervention 2009;5: F103-F108.
12. Stone G, Midei M, Newman W, et al. Randomized comparison of everolimus-eluting and paclitaxel- eluting stents: two-year clinical follow-up from the clinical evaluation of the Xience V everolimus eluting coronary stent system in the treatment of patients with de novo native coronary artery. Circulation 2009; 119: 680-686.
13. Somaratne JB, Whitbourn RJ. Bioresorbable vascular scaffolds: the promise of transience. Intern Med J 2013; 43: 615-618.
14. Patel N, Banning AP. Bioabsorbable scaffolds for the treatment of obstructive coronary artery disease: the next revolution in coronary intervention? Heart 2013; 99: 1236-1243.
15. Dudek D, Onuma Y, Ormiston JA, Thuesen L, Miquel-Hebert K, Serruys PW. Four-year clinical follow-up of the ABSORB everolimus-eluting bioresorbable vascular scaffold in patients with de novo coronary artery disease: the ABSORB trial. EuroIntervention 2012; 7: 1060-1061.
16. Jepson N, Arnott C, Back L, Ooi S, Pitney M. Real-world experience with absorb bioresorbable scaffold technology – early Australian registry results. Presented at Transcatheter Cardiovascular Therapeutics October, 2013.
17. Diletti R, Serruys PW, Farooq V, et al. ABSORB II randomized controlled trial: a clinical evaluation to compare the safety, efficacy, and performance of the Absorb everolimus-eluting bioresorbable vascular scaffold system against the XIENCE everolimus-eluting coronary stent system in the treatment of subjects with ischemic heart disease caused by de novo native coronary artery lesions: rationale and study design. Am Heart J 2012; 164: 654-663.
18. Woudstra P, Grundeken MJ, Kraak RP, et al. Amsterdam Investigator-initiateD Absorb strategy all-comers trial (AIDA trial): a clinical evaluation comparing the efficacy and performance of ABSORB everolimus-eluting bioresorbable vascular scaffold strategy vs the XIENCE family (XIENCE PRIME or XIENCE Xpedition) everolimus-eluting coronary stent strategy in the treatment of coronary lesions in consecutive all-comers: rationale and study design. Am Heart J 2014; 167: 133-140.
19. Onuma Y, Serruys PW, Ormiston JA, et al. Three-year results of clinical follow-up after a bioresorbable everolimus-eluting scaffold in patients with de novo coronary artery disease: the ABSORB trial. Euro Intervention 2010; 6: 447-453.
20. Haude M, Erbel R, Erne P, et al. Safety and performance of the drug-eluting absorbable metal scaffold (Dreams) in patients with de-novo coronary lesions: 12 month results of the prospective, multicentre, first-in-man biosolve-i trial. Lancet 2013; 381: 836-844.
21. Palmerini T, Biondi-Zoccai G, Della Riva D, et al. Stent thrombosis with drug eluting stents. Is the paradigm shifting? J Am Coll Cardiol 2013; 62: 1915-1921.