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Bioabsorbable coronary stents

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Introduction

Placing a coronary stent during angioplasty minimizes reduces of acute vessel occlusion [1] and restenosis [2]. Although permanent metallic stents are effective in preventing recoil and late restenosis after coronary angioplasty, they continue to have limitations such as stent thrombosis and mismatch of the stent to the vessel size. In-stent restenosis is the major shortcoming of conventional (permanent-implant) stent therapy. To mitigate the adverse effects of metallic stents, drug-eluting stents have been developed. These also act as time-released delivery mechanisms for antiproliferative agents, thus further reducing restenosis.

There is no clear advantage, however, of having stents remaining in the coronaries after they are endothelized. On the contrary, there are documented disadvantages since incomplete healing can induce a chronic inflammatory state increasing the risk for thrombosis [3]. Permanently implanted stents can also impair endothelial function [4], prevent late favourable remodelling [5], and hamper future imaging and reintervention.

Thus, the concept of bioabsorbable stents has emerged as a viable alternative to permanent stents. The idea behind the bioabsorbable stents is to develop a device that provides scaffolding in the periprocedural phase and during short-term follow-up.

Bioabsorbable stents, once they are bioabsorbed, leave behind only the healed natural vessel, allowing restoration of vasoreactivity with the potential of vessel remodelling. Late stent thrombosis is unlikely since the stent is gone, and prolonged antiplatelet therapy is not necessary in this instance. Bioabsorbable stents can also be suitable for complex anatomy where stents impede on vessel geometry and morphology and are prone to crushing and fractures, such as is seen in saphenous femoral and tibial arteries. Bioabsorbable implant stents can be used as a delivery device for agents such as drugs and genes, and will perhaps play a role in the treatment of vulnerable plaque [6].

In addition, drug-eluting bioabsorbable stents can deliver antiproliferative agents to reduce restenosis and then dissolve over time, thereby eliminating the disadvantages associated with permanent stents.

In this paper we will briefly review the technology, preclinical, and initial clinical experimental studies regarding bioabsorbable stents.

Bioabsorbable stent technology

A number of technologies suitable for bioabsorbable stents have been investigated so far. Magnesium and poly-L-lactic acid (PLLA) have been the most widely used materials for construction of bioabsorbable stents (Table 1).

Magnesium alloy bioabsorbable stents

The **bioabsorbable** magnesium stent is constructed from a **magnesium** alloy also containing zirconium (< 5%), yttrium (< 5%), and rare earth elements (< 5%). The struts disappear over time, but their position can still be identified because of the fact that the strut material is absorbed and the space filled in by calcium apatite complex, accompanied by a phosphorous compound. These **stents** are compatible with cardiac magnetic resonance imaging and multi-slice computed tomography and can be used as vehicles for possible drug and gene delivery [7].

The magnesium alloy elements are well tolerated by the body, the degradation rate of the

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Table 1. Materials applied for development of biodegradable stents.

	Material	Stent	Status	References
Polymers				
	PLA	Thermal ballon expandable, ring (Igaki-Tamai)	4-year clinical data	Tamai H et al., CCT 2004
	PLA	Ballon expandable, tubular (Abbott Vascular, Inc.)	Phase I Clinical trial (Absorb)	Stack RS, TCT 2005 Ormiston J, TCT 2006
	Tyrosine-polycarbonate	Ballon expandable (REVA Medical)	Pre-clinical	Kaluza G, TCT 2006
	PAE-Salicylate	Ballon expandable, tubular	Pre-clinical	Robinson KA, TCT 2006
Metalic				
	Magnesium	Ballon expandable, tubular (Biotronik)	Phase I Clinical	Haublein B et al., Heart 2003; 89: 651–656
	Iron	Ballon expandable, tubular	Pre-clinical	Peuster M et al., Heart 2001; 86: 563–569

PLA — polylactide; PAE — poly(anhydride esters)

material can be adjusted, and the material is easily deformable yet very rigid so it can support the blood vessel.

Polymer bioabsorbable stents

The earliest polymeric bioabsorbable stent is known as an "IGAKI-TAMAI" stent. This bioabsorbable stent is formed from biodegradable polymer PLLA. The stent has the characteristics of being dissolved into water and carbon dioxide and absorbed into vessel tissue within a few years after implantation. It is also possible to use it for patients who cannot receive stents because they are still growing or due to metal allergies. Even though stented segments become narrow again, implanted PLLA stents, which do not remain in the body permanently, will not interfere with other procedures such as restenting. Furthermore, PLLA stents are more useful for containing drugs compared to metal stents, and thus have been intended as a platform for drug eluting stents (Table 2).

A magnesium bioabsorbable stent was evaluated in the PROGRESS-AMS study and had restenosis and target lesion revascularization (TLR) rates similar to those seen for balloon-only angioplasty [2, 9] (Table 3).

Another promising bioabsorbable drug-eluting stent was developed by Abott Laboratories. Its bioabsorbable everolimus-eluting coronary stent is made of polylactic acid, said to be used in medical implants such as dissolvable sutures. As with a metallic stent,

Table 2. Initial and 6-month results of biodegradable poly-L-lactic acid (Igaki-Tamai) coronary stents in humans [n = 15 patients, 25 stents, 18 *de novo* and 1 restenotic lesion(s)] [8].

Outcome	Before stenting	After stenting	6 months
TLR			10.5%
Minimal lumen diameter [mm]	1.02 ± 0.36	2.59 ± 0.35	1.84 ± 0.66
Diameter stenosis (%)	64 ± 11	12 ± 8	33 ± 18
Loss index*			0.48 ± 0.32

*Late loss + initial gain, TLR — target lesion revascularization

Table 3. Results of the PROGRESS AMS Study [n = 63 patients, 71 stents, 63 *de novo* lesions at 8 centres] [9].

Outcome	4 months	1 year
TLR	25 (38%)	27 (45%)
Ischemia-driven TLR	15 (24%)	16 (27%)
MACE (cardiac death, MI, TLR)	15 (24%)	16 (27%)
Outcome (mean)	**After stenting**	**4 months**
In-stent diameter stenosis	12.7%	48.4%
In-stent acute gain [mm]	1.41	
In-stent late loss [mm]		1.08

TLR — target lesion revascularization; MACE — major adverse cardiac events; MI — myocardial infarction

Abbott's bioabsorbable stent is designed to restore blood flow by propping a clogged vessel open, and to provide support until the blood vessel heals.

Data from ABSORB, the world's first clinical trial of Abott's fully bioabsorbable drug eluting stent for the treatment of coronary artery disease, demonstrated no stent thrombosis, no clinically driven target lesion revascularizations (retreatment of a diseased lesion), and a low (3.3%) rate of major adverse cardiac events (MACE) in 30 patients out to one year. Abbott's prospective, non-randomized ABSORB clinical trial is designed to evaluate the overall safety and performance of a fully bioabsorbable everolimus eluting stent out to 5 years.

Abbott's bioabsorbable everolimus eluting stent has demonstrated excellent clinical safety out to one year in patients with coronary artery disease.

The positive results from this clinical trial form a strong basis for the development of additional bioabsorbable stent platforms with the potential to eliminate some of the restrictions posed by non-absorbable metallic stents in areas such as vessel imaging and vessel remodelling.

At 6 months, the overall MACE rate in the ABSORB trial was 3.3% (1 patient, n = 30), and late loss (a measure of reduction in vessel lumen diameter after stenting) was 0.44 mm. At one year, the overall MACE rate in the ABSORB trial was consistent with results at 6 months (1 patient, 3.3%, n = 30; 3.4% adjusted for one patient who withdrew from follow-up, known to be event free at 1 year, n = 29). MACE was a composite measure of cardiac death, heart attack, and re-treatment of a diseased lesion (ischemia-driven TLR) in the ABSORB trial. Abbott's bioabsorbable everolimus eluting stent also demonstrated 100% procedural success and 94% device success in the ABSORB trial (Table 4).

Table 4. Results of the ABSORB Study [n = 30 patients with single *de novo* lesion] [10].

Outcome		1 year
MACE (cardiac death, MI, ischemia-driven TLR, 1 NQWMI and no TLR)		3.3%
Outcome (mean)	**After stenting**	**180 days**
In-stent diameter stenosis	16%	27%
In-stent acute gain [mm]		1.24
In-stent late loss [mm]		0.44

MACE — major adverse cardiac events; TLR — target lesion revascularization; MI — myocardial infarction; NQWMI — non-Q-wave myocardial infarction

Conclusions

Drug eluting bioabsorbable stents have the potential to revolutionize interventional cardiology. The greatest challenge, however, remains the control of the bioabsorption rate.

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