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Review article

Bioabsorbable stents – Has the concept really translated to clinical benefits? – Concept to clinical – Update: 2012

P. Divya [a], N. Rama [a], S. Prashanth [b,*], N. Senthil Kumar [c], J. Vidya Sagar [d]

[a] Clinical Research Associate, Relisys Medical Devices LTD, India
[b] Scientist, Research and Development, Relisys Medical Devices LTD, India
[c] Head, Stent Division, Relisys Medical Devices LTD, India
[d] Chief Scientist, Research and Development, Relisys Medical Devices LTD, India

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ABSTRACT

Bioabsorbable stents have altogether opened a new perceptive in coronary interventions and a debate on benefits over bare metallic stents and drug eluting stents. There had been difference of opinion from experts in this state of art over the technology, indications of usage, clinical benefits and economics. The review enumerates material and technical related issues of so for developed bioabsorbable stents and the players involved. Unbiased, categorical information on the clinical trials of the stents – till date are also discussed.

1. Introduction

Coronary stents are used as a mechanical means to overcome the major limitations of balloon angioplasty with adequate scaffolding, preventing early recoil and late vascular remodeling.[1,2] Bare Metal Stents (BMS) have been associated with relatively high rates of restenosis requiring additional procedures for target vessel revascularization. This lead to the development of the Drug Eluting Stents (DES) composed of a polymer layer and an anti-proliferative drug to prevent restenosis.[3] However DES were reported to be associated with delayed healing, inflammation, hypersensitivity due to drug/polymer and endothelial dysfunction which have contributed to late thrombosis and prolonged dual antiplatelet therapy.[4–7]

Bioabsorbable stents came in to the arena to offer several potential advantages over BMS or DES. These include abolished late stent thrombosis, improved lesion imaging, reduction in revascularization procedures, restoration of vasomotion, freedom from side-branch obstruction and strut fracture-induced restenosis.[8,9]

2. Materials and technical specifications

There are several polymeric bioabsorbable stents that have been tested. One of the first bioabsorbable stent tested was the Igaki-Tamai (Igaki Medical Planning Co.Ltd., Kyoto, Japan) made of a high-molecular-weight poly L-lactic acid, without any drug.[10] Two other companies, Bioabsorbable Therapeutics

* Corresponding author.
E-mail address: prashanth.srirangam@gmail.com (S. Prashanth).
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Table 1 – Comparative – technical specifications of bioabsorbable stents.

Company	Stent name	Stent material	Drug	Strut thickness (μm)	Absorption time (months)	Stent radio-opacity	Design	Current status of development
Kyoto Medical	Igaki tamai	PLLA	None	170	24	Gold markers	Zig-zag helical coils with straight bridges	Stopped
Biotronik	AMS	Magnesium alloy	None	165	<4	Nil	Sinusoidal in-phase hoops linked by straight bridges	Ongoing clinical trials
REVA Medical	REVA DES	Tyrosine derived polycarbonate	Paclitaxel/ Sirolimus	200	36	Covalently bound iodine	Slide and lock	Ongoing clinical trials
BTI	IDEAL	Polyanhydride ester	Sirolimus/ Salicylicacid	200	6	Nil	Tube with laser cut voids	Under development
Abbott	BVS	PLLA	Everolimus	156	24	Platinum markers	Out-of-phase/in-phase hoops with straight and direct links	Ongoing clinical trials

AMS-absorbable metallic stent; BTI-Bioabsorbable Therapeutics Inc; BVS-bioabsorbable vascular solutions.

Inc (BTI) and Reva Medical *Inc* have tested bioabsorbable stents, coated with sirolimus and paclitaxel respectively. The BTI sirolimus-eluting stent uses a poly (anhydride ester) salicylic acid polymer that gives the stent physical structure and a polymer coating that controls release of sirolimus. During absorption, the bonds between salicylic acid and linker molecules are hydrolyzed releasing the anti-inflammatory drug, salicylic acid.[11] While REVA paclitaxel stent uses an absorbable tyrosine-derived polycarbonate polymer that metabolizes to amino acids, ethanol and carbon dioxide. The stent possesses high radial strength and negligible recoil with standard balloon deployment.[12] Biotronik's magnesium-alloy stent without drug had been tested in the PROGRESS-AMS study.[13]

Till now the most successful bioabsorbable stent was the BVS stent from Abbott Vascular and it was originally developed by Bioabsorbable Vascular Solutions *Inc*. The device claimed to be fully absorbed over 2 years, has a backbone of PLLA, which was subsequently coated with a thin layer of amorphous matrix of poly-D,L-lactide (PDLLA) and 8.2 μg/mm^2 of the anti-proliferative drug everolimus in equal ratios. The PLLA enables controlled release of everolimus, such that 80% is eluted in 30 days.[14] Comparative technical specifications of bioabsorbable stents so for developed and evaluated were summarized in Table 1.

3. Clinical issues

Comparative clinical data of bioabsorbable stents is mentioned in Table 2. The Igaki-Tamai stent was implanted in 15 patients (25 stents), had re-stenosis rate of 10.5% at 6 months.[15] A second, larger study of 50 elective patients (63 lesions, 84 stents) at 4 years showed promising results with the absence of late stent thrombosis. The clinical outcomes showed MACE-free survival rates of 82.0%, but these stents promoted a thick rim of intimal thickening separating struts from lumen, a result very different from the strut protrusion or malapposition.[16] At 10-year clinical follow-up, freedom from cardiac death, non-cardiac death, and MACE were 98%, 87%, and 48%, respectively. Despite impressive results, failure of the stent for further progress was related primarily to heat induced self-expansion. There were concerns that this could cause necrosis of the arterial wall, leading to excessive intimal hyperplasia or increase platelet adhesion, leading to sub-acute stent thrombosis.[17,18]

In the FIM WHISPER trial, BTI stent was implanted in 11 patients. After 12 months there was no evidence of acute or chronic recoil, but IVUS data showed insufficient neointimal suppression,[19] and further improvisations on the BTI stent was not reported.

Table 2 – Comparative clinical data of bioabsorbable stents.

Stent	Trial	Clinical outcomes			
		MACE	TLR	Binary restenosis	Late loss (mm)
Igaki-tamai	Igaki-Tamai Coronary	–	10.5%(6M)	10.5%(6M)	0.48(6M)
Biotronik	PROGRESS AMS	26.7%(1Y)	45%(1Y)	–	0.44(1Y)
BTI	WHISPER	–	–	–	–
REVA	RESORB	–	66.7%(6M)	–	
Abbott	ABSORB	3.4%(3Y)	0%	7.7%(6M)	0.48(3Y)

MACE: Major adverse cardiac events; TLR: Target lesion revascularization, M–months, Y – years.