The Egyptian Heart Journal 70 (2018) 409–414

HOSTED BY

Contents lists available at ScienceDirect

The Egyptian Heart Journal

journal homepage: www.elsevier.com/locate/ehj

REVIEW

Bioresorbable scaffold technology: The yet unfulfilled promise of becoming the workhorse stent in the cardiac catherization laboratory

Wael Elabbassi [a,*], Mohammed Andaleeb Chowdhury [b], Robert Hatala [c]

[a] Slovak Medical University in Bratislava, Slovakia
[b] Vanderbilt University Medical Center, Nashville, TN, United States
[c] The National Institute of Cardiovascular Diseases, Bratislava NÚSCH, Slovakia

ARTICLE INFO

Article history:
Received 21 January 2018
Accepted 14 July 2018
Available online 14 September 2018

Contents

1. Introduction

In 1977, Andreas Gruntzig performed the first human balloon angioplasty and ushered in the era of percutaneous treatment for coronary artery disease. Initial enthusiasm was tampered down by reports of acute vessel occlusion due to dissections[1] and late constrictive remodeling. Next large leap was the introduction of bare metal stents. The BENESTENT trial[2] reported reduced vessel restenosis (22% vs. 32%, P = 0.02) and the need for repeat coronary angioplasty (RR, 0.58; P = 0.005) in BMS treated patients. The rate of sub-acute vessel occlusion decreased to 1.5%; reducing the need for emergency bypass surgery.

In 1996 Schömig et al.[3] introduced dual anti-platelet instead of anticoagulant therapy, resulting in 82% lower risk of MI and 78% reduction in need for repeat interventions (RR 0.25(0.06–0.77).

In 2001 Surreys et al.[4] reported the first use of Drug Eluting Stents in 45 patients, who were treated with Sirolimus eluting Bx VELOCITY stents with negligible neo-intimal hyperplasia at one-year follow-up. The RAVEL trial[5] reported lower mean late luminal loss (−0.01 mm vs. 0.80 mm, P < 0.001) and no recurrent revascularization attempts (vs. 26% in control). However, reports on late stent thrombosis surfaced,[6] which increased to 3.5% at 4 years.[7]

2. The promise of bioresorbable scaffolds

Initially, Tamai et al.[9] examined the feasibility of a bio-absorbable poly-L-lactic acid (PLLA) Igaki-Tamai stents (Igakl Medical, Kyoto, Japan) with a thickness of 0.17 mm and a zigzag helical coil pattern (not drug eluted). They reported 18% repeat revascularization at 4 years[10] and 28% target vessel revascularization at 10 years. One case of definite stent thrombosis was reported.[26,29] Di Mario et al.[11] used magnesium stents in de-novo coronary lesions, with modest results (1-year Target Lesion Revascularization (TLR) rate 45%).

The Bioresorbable Vascular Scaffold (BVS) (Abbott Vascular, California) consists of processed Poly-L-Lactic acid (PLLA) backbone covered with amorphous Everolimus/PLA matrix coating for controlled drug release. The use of polylactic acid is widespread in clinical practice, ranging from absorbable sutures to orthopedic screws and dermatology fillers. Safety of PLLA is supported by the benign vascular response to its use in Angioseal closure devices. PDLLA (poly(D,L-lactide), the polymer used for controlled release of Everolimus, has also been used previously.[14] Everolimus

Peer review under responsibility of Egyptian Society of Cardiology.
* Corresponding author at: Slovak Medical University, Limbová 12, 833 03 Bratislava, Slovakia.
E-mail address: welabbassi@yahoo.com (W. Elabbassi).

https://doi.org/10.1016/j.ehj.2018.07.004

(Novartis, Switzerland) is a semi-synthetic macrolide immunosuppressant which blocks cell proliferation by arresting cell division in G1-S phase. BVS contains 8.2 mcg/mm of Everolimus, 80% of which is released within 30 days; similar to Xience V stent. Safety and efficacy of Everolimus eluting stents were attested in SPIRIT and FUTURE trials.[14–16]

The BVS stent strives to perform comparably to others: its crossing profile is comparable to that of BX Velocity stent (1.4 mm). At room temperature, its radial strength is similar to MULTILINK stent.[12] Its balloon delivery system is the same as for MULTI LINK, VISION and XIENCE V stents. BVS also shows higher conformability to vessel structure.[31]

Its initial version (Revision 1.0) had to be stored at low temperatures in order to avoid device instability and cracks upon deployment. The second generation (Revision 1.1) can be stored at room temperature.[24] Its previous polymer treatment and scaffold design were replaced with in-phase zigzag hoops linked by bridges, allowing for more uniform strut distribution, higher radial support, less vessel recoil and uniform drug distribution.[30]

The BVS is composed of repeating units of PLLA/PDLLA. After implantation, bonds between repeating units get hydrolyzed producing lactic acid, which is metabolized via Krebs cycle and residual small particles (<2 μm) are phagocytosed by macrophages.

Chemically, scaffold resorption takes place in three phases; initially water starts hydrolysis of ester bonds, resulting in decline of stent's molecular weight. In the second stage there is scission of chains linking regions, causing decline in the radial strength. At third stage, remaining short polymer chains diffuse out of the device to get reabsorbed into blood.

Degradation of scaffold governs mechanical performance, which divides into three phases: during initial "revascularization phase" it acts like mainstream drug eluting stents (comparable deliverability, minimal acute recoil and high radial strength). At the restoration phase there is hydrolysis of amorphous regions and connecting points, causing a decline in radial strength. In studied cases it took three months after implantation for the process to start. During the last "resorption phase" the BVS becomes discontinuous and ceases to act as a scaffold while hydrolysis continues and generates L- and D-lactate into the body,[22] meanwhile the stent strut sites become occupied with proteoglycan material and strut outline becomes surrounded by calcification.[23] In most cases this process may take up to 24 months. In animal studies there were complete luminal endothelialization and minimal Inflammatory response, which is comparable to earlier reports with Cypher stents (J&J, Miami,Fl).[12] At 6 months these arteries were still splinted; and at 12 months the vessel became capable of autovasomotion.[12,24]

In 2006, Ormiston et al. reported the first BVS in man implantation.[13] In 2008 the ABBSORB FIRST[17] reported 94% device success rate in 30 patients with single de-novo coronary lesions who underwent BVS implantation (Table 1). At one year, only one patient needed target vessel revascularization. IVUS showed post-procedural incomplete strut apposition in 6 patients and no late stent thrombosis was reported. At 6 months, the OCT substudy showed 99% of struts where covered with tissue. At 2 years there was 34.5% decrease in strut thickness.[24] These patients showed higher acute stent recoil than EES stents (percent recoil 6.9% % vs. 4.3% historical data from SPIRIT FIRST and SPIRIT II; P = 0.25).[18] IVUS data also noted significant late stent recoil (7.6%[19] vs. 0.03% Xience V.[15,17] This translated into 0.44 mmlate lumen loss at six months. Partly, this is due to neointimal hyperplasia and the rest is due to reduction inside stent area. Hyperplasia was comparable to that observed in SPIRIT FIRST with Xience and was better than BMS.[15] Reduction in inside stent area was due to acute stent recoil, non-uniform vessel wall support and loss of radial strength through scaffold resorption. In-stent restenosis rate was 11.5%, which did not necessitate re-intervention.

From 6 months to 2 years there was a reduction in plaque area,[24] while the vessel size remained same, leading to gain in lumen area, with no scaffold mal-apposition noted.[25] At 3 and 5 years,[26,32] the ischemia-driven major adverse cardiac event rate was 3.4%. Scaffold thrombosis was not observed.

The ABSORB II trial enrolled 501 patients with one or two de-novo native vessel disease to receive BRS or Xience (Abbott Vascular, Santa Clara, CA, USA). Although acute recoil was similar, acute lumen gain was less for BVS (IVUS: 2.85 mm^2 vs. 3.60 mm2, $p < 0.0001$). Composite device orientated endpoint at 1-year was similar (5% vs.3%, p = 0.35), myocardial infarction (MI) (4% vs. 1%) and TLR (1% vs. 2%).[48] Three BVS patients had definite or probable scaffold thrombosis. At three years[57] BVS showed no difference in vasomotor reactivity (BVS 0.047 mm vs. Xience 0.056 mm; $p_{superiority}$ 0.49). Late luminal loss was larger for BVS (0.37 mm vs. 0.25 mm; $p_{non\text{-}inferiority}$ 0.78). This was confirmed by IVUS (BVS MLA 4.32 mm^2 vs. 5.38 mm^2 Xience; $p < 0.0001$). There was a higher rate of device-oriented composite endpoint in the BVS group (10% vs 5%, hazard ratio 2·17 [95% CI 1.01–4.70]; log-rank test p = 0·0425), mainly due to target vessel MI (6% vs. 1%; p = 0.0108).

The ABSORB III[50] is a multicenter trial where 2008 patients undergoing PCI for one or two new native coronary lesions were randomly assigned to BRS or Xience. High-pressure post-dilatation was enforced to achieve <10% residual stenosis. Acute segmental gain was less for BVS. At 1 year, target-lesion failure occurred in 7.8% of BVS and 6.1% in Xience ($p_{non\text{-}inferiority} = 0.007$, $p_{superiority} = 0.15$). Sub-acute thrombosis up to 30 days was more common with BVS, similar to findings noted from GHOST EU (1.4% 30 days, 1.9% 180 days, 2.0% 360 days). The primary end point remained similar between years 1 and 2.[58] At the end of year 2, BVS arm had a higher risk of target lesion failure (10.9% vs. 7.8% for DES; $p < 0.05$). This was driven by target vessel MI (7.3% vs. 4.9% for DES; $p < 0.05$).

The ABSORB IV[59] trial avoided small vessels, while aggressive pre-dilatation and routine high-pressure post-dilatation were encouraged. 3000 patients were randomized 1:1 to Absorb BVS or XIENCE. Post-dilatation was at pressures 16–18 atmospheres, and with a balloon-to-scaffold ratio of 1.1–1. At 30 days, target lesion failure occurred in 5.1% of BVS patients and 3.7% of XIENCE patients (p = 0.07). The composite of death, MI, and revascularization occurred in 5.2% of BVS and 4.1% of XIENCE patients (p = 0.17). Device thrombosis occurred in 0.6% of BVS vs. 0.2% of XIENCE patients (p = 0.06).[60]

The EVERBIO II[49] randomly assigned 240 patients to EES, Biolimus Eluting Stents (BES), or BVS. Nine months in-stent lumen loss was similar (BVS: 0.28 mm vs. EES/BES: 0.25 mm; p = 0.30). Patient-oriented MACE was similar (27% in BVS; 26% in EES/BES group; p = 0.83) as was device-oriented MACE rate (12% in BVS; 9% in the EES/BES group; p = 0.6).

In the largest metanalysis of BVS trials[51] (3389 patients with stable CAD or stabilized ACS assigned to BVS: n = 2164) or Xience: n = 1225). BVS implantation took longer (43.7 vs.39.7, $p < 0.05$), attained a smaller reference vessel diameter (2.37 vs. 2.58; $p < 0.05$) despite a higher post-dilatation rate (66% vs. 55%; $p < 0.05$) and required a higher IVUS/OCT use (23.9 vs. 20; p = 0.02). At 1 year, rates of patient-oriented and device-oriented composite endpoints were similar (RR] 1.09 [0.89–1.34], p = 0.38 for earlier and 1.22;0.91-1.64, p = 0.17 for later), the rate of Target vessel MI was increased with BVS due to increased peri-procedural myocardial infarction and device thrombosis with BVS (TVMI RR 1.45; 1.02–2.07, p = 0.04; BVS thrombosis 1.3% vs. 0.6%; RR

Table 1

Study	Design	Result
ABSORB Ormiston et al.[17] 2008	Prospective, open-label 30 patients with single de-novo lesion treated with BRS	100% procedural success 94% Device success At 1 yr follow up: MACE was 33%
ABSORB II Serruys et al.[15] 2015	Single-blind, multicenter, randomized trial 501 pts with evidence of myocardial ischemia and one or two de-novo native lesions treated with BVS versus metallic stent	1-yr report: Composite device orientated endpoint was similar between BRS and metallic stent groups (5% vs 3%, p = 0.35)
ABSORB II Serruys et al.[57] 2017		3 yrs follow up report: Vasomotor reactivity at 3 years was not statistically different (Absorb group 0.047 mm [SD 0.109] vs Xience group 0·056 mm [0.117]; psuperiority = 0.49) Late luminal loss was larger in the Absorb group than in the Xience group (0.37 mm [0.45] vs 0.25 mm [0.25]; pnon-inferiority = 0.78) Secondary endpoints of patient-oriented composite endpoint, Seattle Angina Questionnaire score, and exercise testing were not statistically different in both groups
ABSORB III Ellis et al.[50] 2015	Multicenter, randomized trial including 2008 patients with stable or unstable angina Randomly assigned in 2:1 ratio to receive Absorb (1322 patients) or Xience stent (686 patients)	Target-lesion failure at 1 year: Absorb (7.8%) vs Xience (6.1%) (P = 0.007 for noninferiority) No difference between groups in cardiac death, target-vessel MI, ischemia-driven target-lesion revascularization or device thrombosis at 1 yr
EVERBIO II Puricel et al.[49] 2015	Single-center, assessor-blinded study of 240 patients randomly assigned in a 1:1:1 ratio to EES, BES, or BVS Patients followed for 9 months	In-Stent Late lumen loss and clinical outcomes were similar among groups
Stone et al.[51] 2016	Pooled meta-analysis of four randomized trials Included 3389 patients	1-year relative rates of the patient-oriented composite endpoint, device-oriented composite endpoint and all-cause and cardiac mortality did not differ between BVS and EES. Increased target vessel-related myocardial infarction observed in BVS group (RR 1.45 [95% CI 1.02–2.07], p = 0.04)
GHOST-EU registry Capodanno et al.[34] 2015	Included 1189 patients who underwent percutaneous coronary intervention with one or more BVS at 10 European centers	Technical success was achieved in 99.7% of cases TLF was 2.2% at 30 days and 4.4% at six months At 6 months rate of cardiac death was 1.0%, target vessel myocardial infarction was 2.0%, TLR was 2.5%, and target vessel revascularization was 4.0% Diabetes mellitus was the only independent predictor of TLF (hazard ratio 2.41, 95% confidence interval: 1.28–4.53; p = 0.006) Incidence of definite/probable scaffold thrombosis was 1.5% at 30 days and 2.1% at six months
Naganuma et al.[43] 2017	1189 patients underwent PCI with BVS at 10 European centers (GHOST EU registry). Of these, 289 consecutive patients (302 bifurcation lesions) were treated with either single-stenting (n = 260) or double-stenting (n = 42)	At 360 days rate of target lesion failure was 6.4% rate of scaffold thrombosis was 2.5% Independent predictors for TLF: ACS and diabetes mellitus (HR 4.67; 95% CI: 1.78–12.3; P = 0.002 and HR 3.37; 95% CI: 1.38–8.26; P = 0.008, respectively)

MACE: Major adverse cardiac events.
BRS: Bioresorbable Scaffold.
EES: Everolimus-eluting stents.
BES: Biolimus-eluting stents.
TLF: Target lesion failure.
TLR: Target lesion revascularization.

2.09:0.92–4.75, p = 0.08), highlighting the issue of BVS thrombosis and sheding light on the need for attention to details required when implanting BVS.

3. Evidence from real life registries

The large GHOST-EU registry[34] in 11 European centers looked at target lesion failure among 1549 lesion in 1304 real life patients. It was an "all-comer" registry, including patients with ostial lesions, in-stent restenosis (ISR), bifurcations, chronic total occlusions and left main disease. 53% of patients were treated for stable angina, while rest presented with an acute coronary syndrome. Acute technical success was 99.7%. Target Lesion Failure was 2.2% at 30 days; 4.4% at six months. At six months cardiac death was 1.0%, target vessel infarction was 2.0%, and Target Lesion Revascularization was 2.5%. Procedural-related myocardial injury was higher in the BVS group (25% vs. 12%, p = 0.001). Diabetes mellitus was an independent predictor of TLF (HR 2.41; 1.28–4.53; p < 0.05). The incidence of definite/probable scaffold thrombosis was 1.5% at 30 days and 2.1% at six months. Diabetes mellitus and the treatment of ostial lesions were independent risk factors.[35] Patients with ostial lesions had higher incidence of prior revascularization and less post-dilation (43% vs. 58% in non-ostial group, p = 0.008) and higher residual stenosis (30% vs. 26%, p = 0.035). 12-month rates of scaffold thrombosis were 4.9% vs. 2.0% (ostial vs. non-ostial lesion, p = 0.005; HR 2.65; 1.41–4.97; p = 0.0025[36]). Sizing was another important issue. Quantitative coronary angiography (QCA) showed that BVS patients with under-sizing had more MACE (7.9% vs. 4.6%; p = 0.015; HR 2.65;95% CI: 1.27–5.53, p = 0.009). This was true for the number of implanted scaffolds too (HR

1.33;1.04–1.70, p = 0.024). BVS overlap did not increase MACE (HR 1.05,0.48–2.20; *P* = 0.904),[45] as confirmed by another group.[46]

Another analysis of the GHOST-EU registry looked at BVS use in diffusely diseased vessels.[38] Patients were divided into 3 groups (short: <30 mm, intermediate: 30–60 mm, and long scaffold length: ≥60 mm). Patients with longer BRS were mostly diabetic (24% vs. 30.8% vs. 34.6%, p = 0.01) with higher SYNTAX scores (10.4 ± 7.2 vs. 14.6 ± 8.6 vs. 16.4 ± 7.8, p < 0.001). Despite higher use of Intravascular ultrasound and post-dilatation, there was higher incidence of peri-procedural myocardial infarction (MI) in longer BVS group (6.5% vs. 7.5% vs. 11.3%, p = 0.45). Target lesion failure was higher at 1-year (14.3% long vs. 4.8% in short and 4.5% in intermediate group; p = 0.001). This lead to a higher rate of repeat revascularization (HR = 1.962; 95% CI: 1.25–3.08; p = 0.0034).[38] Incidence of scaffold thrombosis was higher in the long stent group (3.8% vs. 2.1% in short, 1.1% in intermediate group; p = 0.29).[37] Mode of presentation was a significant determinant too (one-year MACE 3.7% in stable vs. 6.9% in ACS patients; p < 0.05). BVS restenosis was observed in 15.6% among diffusely diseased lesions (median follow-up 192 days), compared to 3.4% ISR in the whole GHOST EU registry.[41] Overall, restenosis patients had a higher prevalence of diabetes (20% vs. 7%, p = 0.03), longer implanted BVS (33.4 ± 26 mm vs. 28.0 ± 18 mm, p = 0.33), more residual stenosis >20% (56% vs. 9%, p < 0.001) despite higher post-dilation rate (55% vs. 30%, p = 0.02). BVS restenosis was mostly focal (body in 47%, margin in 35%) and rarely diffuse (3% of lesions). Total occlusion was observed in 6% of lesions and aneurysm formation was seen in 6% of lesions. Percent residual stenosis post implantation was the only independent predictor for restenosis.[39,41]

In another registry, 302 bifurcation lesions were treated using BVS (provisional single-stenting 86%; elective double-stenting 14%). True bifurcation (Medina 1,1,1/1,0,1/0,1,1) were observed in 45%. Pre-dilation and post-dilation of the main branch were performed in 96% and 61%. Final kissing inflation with small protrusion of a side branch balloon into main branch was performed in 19%. At 356 days follow up rates of target lesion failure and scaffold thrombosis were high at 6.4% and 2.5%. Independent predictors for TLF were ACS presentation and diabetes (HR 4.67; 1.78–12.3; P = 0.002 and HR 3.37; 95%:1.38–8.26; P = 0.008, respectively). Majority of patients with scaffold thrombosis occurred within 35 days from index PCI (75%) and lacked use of intravascular imaging.[40,43]

Acute coronary syndrome presentation once again showed poorer outcomes[45] (MACE 9.3% vs. 4.7%, p < 0.001; TLR 6.1% vs. 1.9%, p < 0.001) with increased stent thrombosis (BVS 2.8% vs. 0.9% EES group, p = 0.01). Here post-dilatation resulted in lower MACE (BVS with post-dilatation 6.0% vs. 12.6% BVS without post-dilatation vs. 4.7% EES group, p < 0.001). Post dilatation did not alter the rate of stent thrombosis (post-dilatation: 2.6% vs. no post-dilatation: 3.2% vs. 0.9%: EES patients, p = 0.045).[45]

Review of real world registries shows an increasing trend for post-dilation. We note a change from 52.3% rate in GHOST EU,[36] to 68% in GABI-R,[52] 72% in FRANCE ABSORB,[53] to 96.8% in IT-DISAPPEAR;[54,55] which also enrolled the most complicated patients (59%, diabetics 23.7%, bifurcation lesions 22.3%). This is accompanied by a concomitant decline in BVS thrombosis, initially observed at 3.4% in GHOST EU (least post-dilatation rate) to 0.6% in IT-DISAPPEAR.

Recent emphasis on implantation technique formulated the nomenclature of four P's: Prepare the lesion with non-compliant balloon, Proper sizing with use of intracoronary nitroglycerin and imaging as necessary; Pay attention to expansion limits; staying within nominal limits of 0.5 mm and expanding the scaffold at 2 mm every five seconds while implanting, then staying 30 s when fully expanded before deflating. Finally Post-dilating with a non-compliant balloon at high pressure aiming at <10% residual stenosis after implantation. By using this protocol and avoiding small vessels with lumen diameters <2.5; BVS thrombosis rates can be reduced by 70%.[56]

In order to clarify the issues concerning BVS use for clinicians, the FDA issued a "Dear Doctor" letter noting it that the higher risk of stent-related thrombosis and other major cardiac events among patients who got Absorb GT1 BVS is under investigation. It reminds operators using BVS to follow instructions in FDA labeling, avoiding its use in small vessels and to adhere to the label's recommended implantation technique.

In 14th September 2017, Abbott decided to voluntarily withdraw its product from market except for patients in the setting of a registry or study, citing low market penetration. Abbott promised to come back with a new improved scaffold of 92 μm thickness.

To summarize, despite having only a fraction of the tensile strength of metallic stents (30–45 compared to 820–1200 MPA); the BVS showed favorable 1 year results in large studies despite a possible small but statistically significant increased risk of peri-procedural MI. Longer term follow up showed higher BVS late thrombosis rates and higher target lesion failure. This may be due to numerous factors. For example, 19% of patients in ABSORB III[60] were treated for vessels which were smaller than the size advised by the FDA. Clinicians tend to use visual assessment to in estimating vessel size rather than quantitative analysis. This may result in underestimating vessel size. Moreover, techniques of implantation have been largely suboptimal (only 63% of BVS recipients had post-dilatation in ABSORB III[60]). Diligent attention to choosing vessels of appropriate diameter and paying attention to technique of implantation, more frequent use of imaging for vessel sizing should result in improved outcomes. This needs to be shown in long-term follow up of Absorb III and IV studies which could then open the door for introduction of newer generation of scaffolds. Other scaffolds are also already in clinical use,[61,62] though to a lesser extent and their long term clinical efficacy remains to be shown too.

Conflict of interest

None.

References

1. Meier B, Rutishauser W. Transluminal coronary angioplasty-state of the art 1984. *Acta Med Scand Suppl*. 1985;701:142–147.
2. Surreys PW, Dejeaggere P, Keimeneij F, et al.. A comparison of Balloon expandable stent implantation with balloon angioplasty in patients with coronary artery disease. Benestent Group. *N Engl J Med*. 1994;331:489–495.
3. Schomig A, Neumann FJ, Kastrati A, et al.. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary artery stents. *N Engl J Med*. 1996;334:1084–1089.
4. Sousa JE, Costa MA, Abizaid AC, Rensing BJ, Abizaid AS, Serruys PW. Sustained suppression of neointimal proliferation by sirolimus-eluting stents: one-year angiographic and intravascular ultrasound follow-up. *Circulation*. 2001;104:2007–2011.
5. Morice MC, Serruys PW, Sousa JE, et al.. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med*. 2002;346:1773–1780.
6. Daemen J, Wenaweser P, Tsuchida K, et al.. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. *Lancet*. 2007;369:667–678.
7. Serruys PW, Onuma Y, Garg S, et al.. 5-year clinical outcomes of the ARTS II (Arterial Revascularization Therapies Study II) of the sirolimus-eluting stent in the treatment of patients with multi-vessel de novo coronary artery lesions. *JACC*. 2010;11:1093–1101.
9. Tamai H, Igaki K, Kyo E, et al.. Initial and 6-month results of biodegradable poly-l-lactic acid coronary stents in humans. *Circulation*. 2000;102:399–404.
10. Tamai H. *Biodegradable stents. Four year follow up*. Washington DC: TCT; 2004.
11. Erbel R, Di Mario C, Bartunek J, et al.. PROGRESS-AMS (Clinical Performance and Angiographic Results of Coronary Stenting with Absorbable Metal Stents) Investigators. Temporary scaffolding of coronary arteries with bioabsorbable magnesium stents: a prospective, non-randomised multicentre trial. *Lancet*. 2007;369:1869–1875.

12. Absorb Trial Investigator Brochur. Abbott Vascular, Santa Clara, Ca.
13. Ormiston JA, Webster MW, Armstrong G. First-in-human implantation of a fully bioabsorbable drug-eluting stent: the BVS poly-L-lactic acid everolimus-eluting coronary stent. *Catheter Cardiovasc Interv*. 2007;69:128–131.
14. Grube E, Sonoda S, Ikeno F, et al.. Six- and twelve-month results from first human experience using everolimus-eluting stents with bioabsorbable polymer. *Circulation*. 2004;109:2168–2171. Epub 2004.
15. Serruys PW, Ong AT, Piek JJ, et al.. A randomized comparison of a durable polymer Everolimus-eluting stent with a bare metal coronary stent: The SPIRIT first trial. *Eurointervention*. 2005;1:58–65.
16. Tsuchida K, Piek JJ, Neumann FJ, et al.. One-year results of a durable polymer everolimus-eluting stent in de novo coronary narrowings (The SPIRIT FIRST Trial). *EuroIntervention*. 2005;1:266–272.
17. Ormiston JA, Serruys PW, Regar E, et al.. A bioabsorbable everolimus-eluting coronary stent system for patients with single de-novo coronary artery lesions (ABSORB): a prospective open-label trial. *Lancet*. 2008;371:899–907.
18. Tanimoto S, Serruys PW, Thuesen L, et al.. Comparison of in vivo acute stent recoil between the bioabsorbable everolimus-eluting coronary stent and the everolimus-eluting cobalt chromium coronary stent: insights from the ABSORB and SPIRIT trials. *Catheter Cardiovasc Interv*. 2007;70:515–523.
19. Tanimoto S, Bruining N, van Domburg RT, et al.. Late stent recoil of the bioabsorbable everolimus-eluting coronary stent and its relationship with plaque morphology. *J Am Coll Cardiol*. 2008;52:1616–1620.
22. Oberhauser JP, Hossainy S, Rapoza RJ. Design principles and performance of bioresorbable polymeric vascular scaffolds. *EuroIntervention*. 2009;5(Suppl F): F15–F22.
23. Vorpahl M, Finn AV, Nakano M, Virmani R. The bioabsorption process: tissue and cellular mechanisms and outcomes. *EuroIntervention*. 2009;5(Suppl F): F28–F35.
24. Garg S, Serruys P. Biodegradable stents and non-biodegradable stents. *Minerva Cardioangiol*. 2009;57:537–565.
26. Onuma Y, Thuesen L, Webster M, Nieman K, Serruys PW. Five-year clinical and functional multislice computed tomography angiographic results after coronary implantation of the fully resorbable polymeric everolimus-eluting scaffold in patients with de novo coronary artery disease: the ABSORB cohort A trial. *JACC Cardiovasc Interv*. 2013;6:999–1009.
29. Kimura T, Abe K, Shizuta S, et al.. Long-term clinical and angiographic follow-up after coronary stent placement in native coronary arteries. *Circulation*. 2002;105:2986–2991.
30. Werner M, Micari A, Cioppa A, et al.. Evaluation of the biodegradable peripheral Igaki-Tamai stent in the treatment of de novo lesions in the superficial femoral artery: the GAIA study. *JACC Cardiovasc Interv*. 2014;7:305–312.
31. Okamura T, Garg S, Gutiérrez-Chico JL, et al.. In vivo evaluation of stent strut distribution patterns in the bioabsorbable everolimus-elutingdevice: an OCT ad hoc analysis of the revision 1.0 and revision1.1 stent design in the ABSORB clinical trial. *EuroIntervention*. 2010;5:932–938.
32. Gomez-Lara J, Garcia-Garcia HM, Onuma Y, Ormiston JA, Serruys PW. A comparison of the conformability of everolimus-eluting bioresorbable vascular scaffolds to metal platform coronary stents. *JACC Cardiovasc Interv*. 2010;3:1190–1198.
34. Serruys PW, Onuma Y, Garcia-Garcia HM, et al.. Dynamics of vessel wall changes following the implantation of the absorb everolimus-eluting bioresorbable vascular scaffold: a multi-imaging modality study at 6, 12, 24 and 36 months. *EuroIntervention*. 2014;9:1271–1284.
35. Capodanno D, Gori T, Nef H, et al.. Percutaneous coronary intervention with everolimus-eluting bioresorbable vascular scaffolds in routine clinical practice: early and midterm outcomes from the European multicentre GHOST-EU registry. *EuroIntervention*. 2015;10:1144–1153.
36. Ruparelia N, Kawamoto H, Capodanno D, et al. BRS and thrombosis: insights from the GHOST-EU registry. Published in Abstracts EuroPCR; May 2016.
37. Gori T, Wiebe J, Capodanno D, et al.. Early and midterm outcomes of bioresorbable vascular scaffolds for ostial coronary lesions: insights from the GHOST-EU registry. *EuroIntervention*. 2016;12:e550–e556, published online ahead of print September 2015 published online e-edition August 2016;12 (5);2016.
38. Kawamoto H, Latib A, Geraci S, et al. One-year clinical outcomes following BRS implantation for diffuse coronary lesions: a sub-study from the GHOST-EU registry. Published in Abstracts EuroPCR; May 2016.
39. Schnorbus B, Capodanno D, Nef H, et al. Comparison of the outcomes of patients undergoing percutaneous coronary intervention with Bioresorbable Vascular Scaffolds (BVS) with acute coronary syndrome and stable coronary artery disease (S-CAD). In: 6 months data from the European multi-centre GHOST-EU registry. Published in Abstracts EuroPCR; May 2015.
40. Baquet M, Nef H, Grujic K, et al. Pattern of restenosis after bioresorbable vascular scaffold implantation: angiographic substudy of the European multicentre GHOST-EU Registry. Published in Abstracts EuroPCR; May 2015.
41. Latib A. Naganuma T. Capodanno et al. Expansion of bioresorbable vascular scaffold use to coronary bifurcation lesions: a substudy of the European multicentre GHOST-EU registry. Published in Abstracts EuroPCR; May 2015.
43. Pyxaras S, Capodanno D, Gori, et al. Impact of device sizing on outcome in patients undergoing percutaneous coronary intervention with bioresorbable scaffolds: insights from the GHOST-EU registry. Published in Abstracts EuroPCR, May 2015.
45. Ortega-Paz L, Capodanno D, Giacchi G, et al.. Impact of overlapping on 1-year clinical outcomes in patients undergoing everolimus-eluting bioresorbable scaffolds implantation in routine clinical practice: Insights from the European multicenter GHOST-EU registry. *Catheter Cardiovasc Interv*. 2016 August 12.
46. Imori Y, D'Ascenzo F, Gori T, et al.. Impact of postdilatation on performance of bioresorbable vascular scaffolds in patients with acute coronary syndrome compared with everolimus-eluting stents: A propensity score-matched analysis from a multicenter "real-world" registry. *Cardiol J*. 2016;23:374–383. Epub 2016 Aug 12.
48. Serruys PW, Chevalier B, Dudek D, Cequier A, Carrié D. A bioresorbable everolimus-eluting scaffold versus a metallic everolimus-eluting stent for ischemic heart disease caused by de-novo native coronary artery lesions (ABSORB II): an interim 1-year analysis of clinical and procedural secondary outcomes from a randomized controlled trial. *Lancet*. 2015;385:43–54.
49. Puricel S, Arroyo D, Corpataux N, et al.. Comparison of everolimus- and biolimus-eluting coronary stents with everolimus-eluting bioresorbable vascular scaffolds. *J Am Coll Cardiol*.. 2015;65:791–801.
50. Ellis SG, Kereiakes DJ, Metzger DC, et al.. Everolimus-eluting bioresorbable scaffolds for coronary artery disease. *N Engl J Med*. 2015;373:1905–1915.
51. Stone GW, Gao R, Kimura T, Onuma Y, Serruys PW. 1-year outcomes with the Absorb bioresorbable scaffold in patients with coronary artery disease: a patient-level, pooled meta-analysis. *Lancet*. 2016;387:1277–1289.
52. Nef H, Wiebe J, Achenbach S, et al.. Evaluation of the short- and long-term safety and therapy outcomes of the everolimus-eluting bioresorbable vascular scaffold system in patients with coronary artery stenosis: Rationale and design of the German-Austrian ABSORB RegIstRy (GABI-R). *Cardiovasc Revasc Med*. 2016;17:34–37.
53. France ABSORB registry-In-hospital and one-month results in 2,000 patients, presentation in Congress: EUROPCR; 2016.
54. Testa L, Biondi Zoccai G, Tomai F, Bedogni F, De Carlo M. Italian diffuse/multivessel disease ABSORB prospective registry (IT-DISAPPEARS). Study design and rationale. *J Cardiovasc Med (Hagerstown)*. 2015;16:253–258.
55. Italian Diffuse/Multivessel Disease ABSORB Prospective Registry (IT-DISAPPEARS); Lecture in Theatre Boardeu; EUROPCR; 2016.
56. Puricel S, Cuculi F, Weissner M, et al.. Bioresorbable coronary scaffold thrombosis multicenter comprehensive analysis of clinical presentation, mechanisms, and predictors. *J Am Coll Cardiol*. 2016;67:921–931.
57. Serruys PW, Chevalier B, Sotomi Y, et al.. Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II): a 3 year, randomised, controlled, single-blind, multicentre clinical trial. *Lancet*. 2017 Feb 25;389:804.
58. Tamai H, Igaki K, Tsuji T, et al.. A Biodegradable poly(lactic acid) coronary stent in the porcine coronary artery. *J Interven Cardiol*. 1999;12:443–450.
59. Personal communication Tamborino C et al; EUROPCR; 2015.
60. http://www.acc.org/latest-in-cardiology/articles/2017/10/26/12/56/tues-2pm-absorbii-tct-2017.
61. Haude M, Ince H, Abizaid A, et al.. Safety and performance of the second-generation drug-eluting absorbable metal scaffold in patients with de-novo coronary artery lesions (BIOSOLVE-II): 6 month results of a prospective, multicenter, non-randomized, first-in-man trial. *Lancet*. 2016;387:31–39.
62. Wijns W, Vrolix M, Verheye S, et al.. Randomised study of a bioabsorbable polymer-coated sirolimus-eluting stent: results of the DESSOLVE II trial. *EuroIntervention*. 2015;12:1383–1390.

Further reading

8. Ormiston JA, Serruys PW, Regar E, et al.. A bioabsorbable everolimus-eluting coronary stent system for patients with single de-novo coronary artery lesions (ABSORB): a prospective open-label trial. *Lancet*. 2008;371:899–907.
20. García-García HM, Gonzalo N, Thuesen L, Ormiston JA, Serruys PW. Assessment of the absorption process following bioabsorbable everolimus-eluting stent implantation: temporal changes in strain values and tissue composition using intravascular ultrasound radiofrequency data analysis. A substudy of the ABSORB clinical trial. *EuroIntervention*. 2009;4:443–448.
21. García-García HM, Schultz C, Duckers E, Ligthart J, van Geuns RJ. Five-year follow-up of the ABSORB bioresorbable everolimus-eluting vascular scaffold system: multimodality imaging assessment. *EuroIntervention*. 2013;8:1126–1127.
25. Serruys PW, Ormiston JA, Onuma Y, et al.. A bioabsorbable everolimus-eluting coronary stent system (ABSORB): 2-year outcomes and results from multiple imaging methods. *Lancet*. 2009;373:897–910.
27. Nishio S, Kosuga K, Igaki K, et al.. Long-Term (>10 Years) clinical outcomes of first-in-human biodegradable poly-l-lactic acid coronary stents: Igaki-Tamai stents. *Circulation*. 2012;125:2343–2353.
28. Okamura T, Onuma Y, García-García HM, et al.. 3-Dimensional optical coherence tomography assessment of jailed side branches by bioresorbable vascular scaffolds: a proposal for classification. *J Am Coll Cardiol Intv*. 2010;3:836–844.
33. 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. *EuroIntervention*. 2010;6:447–453.
42. Wiebe J, Capodanno D, Gori T, et al. Everolimus-eluting bioresorbable scaffold as a treatment option for patients with in-stent restenosis: insights from the multicentre GHOST-EU registry. Published in Abstracts EuroPCR, May 2015.
44. Naganuma T, Colombo A, Lesiak M, et al. Bioresorbable vascular scaffold use for coronary bifurcation lesions: A substudy from GHOST EU registry. Catheter Cardiovasc Interv 10.1002/ccd.26634.

47. Biscaglia S, Ugo F, Ielasi A, Secco GG, Durante A, D'Ascenzo F. Bioresorbable scaffold vs. second generation drug eluting stent in long coronary lesions requiring overlap: a propensity-matched comparison (the UNDERDOGS study). *Int J Cardiol*. 2016;1:40–45.

63. Kawamoto H, Panoulas VF, Sato K, et al.. Impact of strut width in periprocedural myocardial infarction: a propensity-matched comparison between bioresorbable scaffolds and the first-generation sirolimus-eluting stent. *JACC Cardiovasc Interv*. 2015 Jun;8:900–909.