Device specificity of vascular healing following implantation of bioresorbable vascular scaffolds and bioabsorbable polymer metallic drug-eluting stents in human coronary arteries: the ESTROFA OCT BVS vs. BP-DES study

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KEYWORDS

- bioresorbable scaffolds
- drug-eluting stent
- optical coherence tomography

Abstract

Aims: We sought to compare vascular healing with bioresorbable everolimus-eluting vascular scaffolds (BVS) and drug-eluting stents with bioabsorbable polymers (BP-DES) at six and 12 months both implanted in the same patients.

Methods and results: This was a multicentre and prospective study including patients with at least two comparable lesions to treat. In every patient both BVS and BP-DES (SYNERGY, Orsiro or BioMatrix Flex) were implanted by lesion randomisation. Patients included were evaluated with optical coherence tomography at six or 12 months (2:1). Finally, 68 patients had an examination at six months and 27 patients at 12 months. The rates of uncovered struts at six months were 1.7±3.2% for BVS and 5.3±5.6% for BP-DES (p=0.0001), and at 12 months 0.48±0.72% and 4.8±5%, respectively (p=0.001). Rates of strut malapposition were significantly lower with BVS. There was no significant intra-patient correlation with BP-DES/BVS for endpoints. Evaginations were more frequent and larger with BVS. Discontinuities in BVS were observed in 19.4% at six months and 14.3% at 12 months.

Conclusions: Vascular healing with BVS and BP-DES could be more device-specific than patient-specific. At follow-up, BVS presented fewer uncovered or non-apposed struts than BP-DES but more frequent and larger evaginations. Discontinuities in BVS were relatively frequent at both time points.

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Abbreviations

BP-DES bioabsorbable polymer drug-eluting stents
BVS bioresorbable vascular scaffolds
EES everolimus-eluting stents
MLA minimum lumen area
MSA minimum stent area
OCT optical coherence tomography

Introduction

Drug-eluting stents with bioabsorbable polymers (BP-DES) were designed to decrease polymer-triggered unfavourable vascular responses and, ultimately, the risk of very late stent thrombosis. The development of bioresorbable vascular scaffolds (BVS) was aimed at preventing long-term stent-related events. Nonetheless, recent data show that their use is associated with a higher rate of thrombosis[1,2].

The arterial healing process depends on device features, but it could be influenced by biological factors that are highly variable among individuals. Accordingly, we designed a study in which both BVS and BP-DES were implanted randomly in selected lesions of the same patient, enhancing the comparability with respect to a per-patient randomised design.

We sought to evaluate and compare the vascular healing process using optical coherence tomography (OCT) at six and 12 months with BVS and different models of BP-DES. The study was supported by the research agency of the Spanish Society of Cardiology.

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Methods

The ESTROFA (grupo de EStudio de la TROmbosis de stents FArmacoactivos) OCT BVS vs. BP-DES study was a multicentre prospective study conducted in 15 centres, designed to compare the healing process at six and 12 months between BP-DES and BVS.

STUDY POPULATION

Patients were eligible for the study if they met all of the following clinical and angiographic criteria.

Clinical inclusion criteria: a) indication for percutaneous revascularisation out of the setting of primary angioplasty; b) adequate candidates for a dual antiplatelet therapy period of at least 12 months.

Angiographic inclusion criteria: a) patients should have at least two lesions to be treated. If in the same vessel, it should be feasible to treat both lesions without overlapping of stents and leaving a gap >20 mm; b) lesions should be suitable to be treated with stents >8 mm in length and ≥2.5 mm in diameter.

Angiographic exclusion criteria: a) restenosis; b) left main disease; c) chronic total occlusion; d) bifurcation; e) ostial location; f) presence of clear angiographic signs of complication (rupture, dissection, ulceration or thrombus).

The study protocol was approved by the local research ethics committee of all participating centres. A specific informed consent was obtained in all patients included in this study. The study was promoted by the Spanish Society of Cardiology.

STUDY DEVICES

The BVS used was the Absorb GT1™ (Abbott Vascular, Santa Clara, CA, USA) and the BP-DES group comprised the BioMatrix Flex™ stent (Biosensors Interventional Technologies, Singapore), the SYNERGY™ stent (Boston Scientific, Marlborough, MA, USA) and the Orsiro™ stent (Biotronik, Berlin, Germany). Technical details are provided in **Supplementary Appendix 1**.

PROCEDURE

In every patient the first target lesion to treat was by protocol randomly allocated to BVS or BP-DES treatment through an on-site system, treating the second target lesion with the other study device so that every patient had both types of study device implanted. In case of the presence of three or more lesions to treat, all of these additional lesions were treated with BP-DES. Among lesions assigned to treatment with BP-DES, subtype selection was carried out following an on-site alternate sequence, 2:1:1 for SYNERGY, Orsiro and BioMatrix, respectively.

Adequate lesion preparation, device sizing and post-dilatation were highly recommended, especially for BVS. Dual antiplatelet therapy was indicated for a minimum period of 12 months. Angiographic and OCT examination at follow-up was scheduled at six or 12 months (2:1) using an alternate sequence.

ANGIOGRAPHIC ANALYSIS

Serial angiographic studies were obtained after intracoronary administration of nitroglycerine in two well selected orthogonal matching views at baseline, post-procedure, and follow-up. Quantitative analysis was performed with validated 2D software for QCA analysis (QAngio XA version 7.3; Medis, Leiden, the Netherlands).

OCT ACQUISITION AT FOLLOW-UP

Per protocol OCT acquisition was planned at six-month or 12-month angiographic follow-up with a variation of ±15 days. All OCT recordings were collected for analysis in a centralised core lab (Hospital Clinico San Carlos, Madrid, Spain). A more detailed description of the OCT acquisition procedure is provided in **Supplementary Appendix 1**.

OCT ANALYSIS AND STUDY ENDPOINTS

Co-primary endpoints were: a) rate of uncovered struts at six months for BVS and BP-DES; b) rate of uncovered struts at 12 months for BVS and BP-DES.

Off-line analysis of the stented segment was performed at 1 mm intervals with a dedicated analysis system (QIvus®; Medis, Leiden, the Netherlands) in a core lab.

ASSESSMENT OF COVERAGE

The struts of the BP-DES were classified as uncovered if any part of the strut was visibly exposed to the lumen and the struts of the BVS were classified as uncovered if the thickness of the coverage from the endoluminal border of the black box to the lumen contour was <30 μm[3,4].

Assessment methods for other findings are fully described in **Supplementary Appendix 1**. Investigators in the core lab were obviously not blinded to the type of stent (BVS or BP-DES) but they were blinded for the time of examination.

STATISTICAL ANALYSIS

The sample size calculation was based at the initiation of the study on the limited available data at that time[5-8]. A detailed description of the sample calculation and the statistics applied is provided in **Supplementary Appendix 1**.

Results

A total of 120 patients were enrolled in the study. Clinical and procedural characteristics are shown in **Supplementary Table 1**. The study flow diagram is shown in **Figure 1**. Clinical outcomes at 12 months are presented in **Supplementary Table 2**. The quantitative angiographic analysis at baseline, six- and 12-month follow-up did not show significant differences **(Supplementary Table 3)**. Findings in planimetric OCT analysis are presented in **Supplementary Table 4**. In the BVS group, a smaller minimum lumen area was noted at six months, as well as a lower BVS area than expected from the nominal stent area ratio at both time points.

The OCT analysis at strut level is shown in **Table 1**. The kappa statistic for the interobserver agreement was 0.86 for strut uncoverage and 1 for strut malapposition. A significantly lower rate of uncovered and/or malapposed struts was observed with BVS at six and 12 months. However, significant heterogeneity was found for uncoverage. Notably, only 4-10% of uncovered struts with BVS or BP-DES either at six or 12 months had concomitant malapposition. Among BP-DES, uncoverage was significantly lower with SYNERGY and Orsiro. The clusters for uncoverage and malapposition are shown in **Supplementary Table 5**. Overall, the independent predictors for an uncoverage rate over 1% were the BVS (OR 0.13, 95% CI: 0.05 to 0.29; p<0.0001) and stent length >18 mm (OR 2.34, 95% CI: 1.04 to 5.25; p=0.039).

The relationship between uncoverage or non-apposition with BVS and BP-DES within the same patient is illustrated in **Figure 2** and **Figure 3**. No significant correlation was found for any strut-level endpoint. The correlative graphics for uncovered strut rates at six months with BVS vs. each model of BP-DES are shown in **Supplementary Figure 1**. The strut-level endpoints at six and 12 months for BVS and BP-DES groups are presented in **Figure 4**.

Analysis of discontinuities in BVS and qualitative analysis of the neointimal tissue are presented in **Table 2**. Peri-strut low-intensity areas were found similarly at six months but were significantly more prevalent with BVS at 12 months. BVS discontinuities were relatively frequent, even at six months, and mostly evident as overhanging and stacked struts.

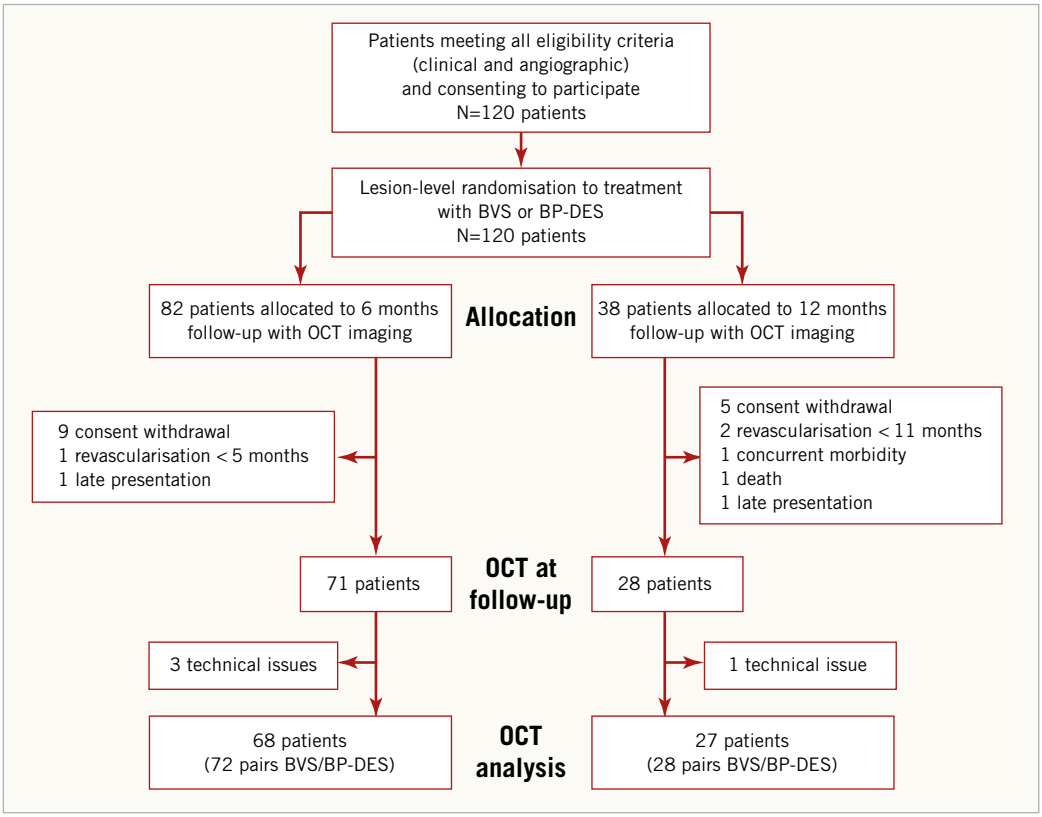

Figure 1. *Flow diagram of the study.*

Table 1. OCT findings at strut-level analysis at 6 and 12 months.

	BVS		BP-DES			
	Mean SD	Median (IQR)	Mean SD	Median (IQR)	*p*	I^2
6 months OCT	**n=72**					
Uncovered, %	1.70±3.21	0.53 (0-1.62)	5.31±5.65	3.90 (0.9-7)	0.0001	77%
				RR 0.28, 95% CI 0.17 to 0.45		
Malapposed, %	0.82±2.15	0 (0-0.35)	1.30±2.12	0 (0-1.81)	0.024	55%
				RR 0.51, 95% CI 0.30 to 0.87		
Uncov.+Malapp., %	0.12±0.63	0 (0-0)	0.45±1.13	0 (0-0)	0.054	21%
				RR 0.47, 95% CI 0.22 to 1.01		
12 months OCT	**n=28**					
Uncovered, %	0.48±0.72	0.33 (0-0.63)	4.80±5	3.31 (0.80-7.82)	0.001	41%
				RR 0.14, 95% CI 0.07 to 0.25		
Malapposed, %	0.24±0.83	0 (0-0)	0.91±1.51	0 (0-0.98)	0.013	6%
				RR 0.31, 95% CI 0.14 to 0.68		
Uncov.+Malapp., %	0.02±0.12	0 (0-0)	0.50±1	0 (0-0.82)	0.004	0%
				RR 0.21, 95% CI 0.08 to 0.55		
6 months OCT	**SYNERGY n=32**	**Orsiro n=20**	**BioMatrix Flex n=20**	***p****	**BVS n=72**	***p**#*
Uncovered, %	4.5±5.2	4.7±4.9	6.9±6	0.01	1.7±3.2	<0.001
Malapposed, %	1.5±2.2	1.2±2	1.1±1.8	0.2	0.8±2.1	0.006
Uncov.+Malapp., %	0.2±0.5	0.6±1.5	0.2±0.6	0.2	0.1±0.6	0.005

Values are presented as mean±SD or median and interquartile range (IQR). The risk ratios (RR) are derived from a pooled analysis under a fixed effects model. I^2 is the percentage of observed total variation across cases that is due to real heterogeneity rather than chance. *p** for the comparison between BP-DES types. *p#* for comparison of BP-DES with BVS. BP-DES: bioabsorbable polymer drug-eluting stents; BVS: bioresorbable vascular scaffolds

Evaginations were observed more frequently and resulted in being larger with BVS, especially at six months **(Supplementary Table 6)**. The overall rate of evaginations in BVS was comparable between those patients showing or not showing evaginations in BP-DES (83% vs. 73%, p=0.1). The rate of evaginations was comparable between BP-DES types but the magnitude was smaller with SYNERGY. In both groups, the evaginations did not appear to be related to underexpansion of the devices but to a lower degree of intimal proliferation and more malapposition in BP-DES **(Supplementary Table 7)**.

Discussion

We found that impaired vascular healing after BP-DES and BVS implantation appears to be predominantly device-specific. We documented that strut uncoverage is less frequent in BVS and that it is influenced by BP-DES design. Of note, the rates of strut uncoverage and malapposition were not significantly different at six- and 12-month follow-up. Discontinuities were relatively frequent with BVS, even at six months, and peri-stent vascular evaginations were more frequently observed with BVS.

VASCULAR HEALING AFTER IMPLANTATION OF BVS AND METALLIC DES

At six months, the proportion of uncovered struts with BVS in series of 12-25 patients has been 2-5.3%[5-7], at 12 months 3.3%[4], at 24 months 1% and at 36 months 1.7%[7,9]. In a *post hoc* analysis of 44 unmatched patients, comparable rates of uncovered struts at 12 months were found for BVS and second-generation DES[10]. In the EVERBIO II trial, BVS showed a lower uncoverage rate at nine months compared with BP biolimus-eluting stents[11]. In the recently published TROFI II trial[12], a better healing score was observed with BVS at six months compared with a durable polymer everolimus-eluting stent, implanted in primary angioplasty.

The proportion of uncovered struts with a BP biolimus-eluting stent ranges from 17% at six to eight months to 9% at eight to 12 months[13,14]. Uncoverage rates in small series treated with the Orsiro stent were 1.3% at three months and 1.8% at six months[15], and with the SYNERGY stent 5.5% and 3.4% at three and six months, respectively[16].

A more complete extension of coverage could have been expected in our study with the thin-strut BP-DES than with BVS. However, the degree of BVS coverage was in the range of that previously reported. Nonetheless, strictly speaking, vascular healing cannot be accurately assessed by means of OCT since no distinction can be made between endothelial and fibrin strut-covering layers. A recent investigation, using OCT-derived light property analysis, showed that tissue maturation was comparable but lipidic change of neointima was less prominent after BVS implantation compared to metallic everolimus-eluting stents, suggesting a more stable superficial neointima on the BVS[17]. On the other hand, the thicker BVS struts could promote a more extensive peri-strut deposition of fibrin, explaining the higher early strut coverage[18,19]. Moreover, the higher prevalence of peri-strut low-intensity area

observed with BVS at 12 months could be related to more fibrin deposition and inflammatory activity.

EVAGINATIONS AND DISCONTINUITIES

In a recent publication, the incidence of evaginations in 102 BVS at 12 months was high (54%) but major evaginations were infrequent (0.9%)[20]. The presence of evaginations was strongly associated with malapposition but not with uncoverage and these were related with more fractures and more peri-stent low-intensity area. In our study, in agreement with the data mentioned above, evaginations were more frequently seen with BVS and were present in scaffolds showing more fractures and peri-stent low-intensity area. Regarding the mechanisms involved, evaginations in BP-DES were related to less intimal proliferation and higher rates of strut uncoverage and malapposition. In BVS, these were related to the right coronary artery location and a smaller lumen area stenosis. Nonetheless, the absence of baseline OCT prevents drawing any conclusions about their mechanisms.

Late strut discontinuity of the polymeric struts has been observed in up to 40% of patients at three years[21]. In our study, discontinuities were less common but not infrequent even at six months. The different rates between studies could be related mainly to the different times of assessment. The prognostic relevance of discontinuities was inferred in the previously mentioned study from a small sample size (51 patients) of the ABSORB cohort B. Nonetheless, the recently published INVEST registry, including 36 patients with very late BVS thrombosis at a median time of 20 months, demonstrated that the leading mechanism underlying

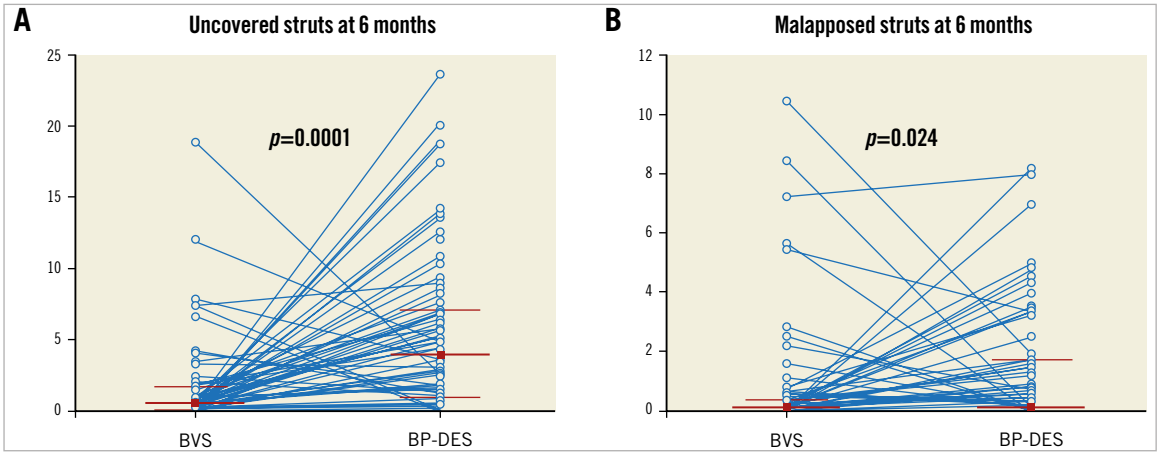

Figure 2. *Strut-level endpoints in paired BVS and BP-DES at six months. A) Rates of uncovered struts at six months, correlation coefficient –0.21 (95% CI: –0.43 to 0.016). B) Rates of malapposed struts at six months, correlation coefficient 0.098 (95% CI: –0.14 to 0.32). Blue lines connect values from the same patient. Median and interquartile range is shown for BVS and BP-DES cohorts.*

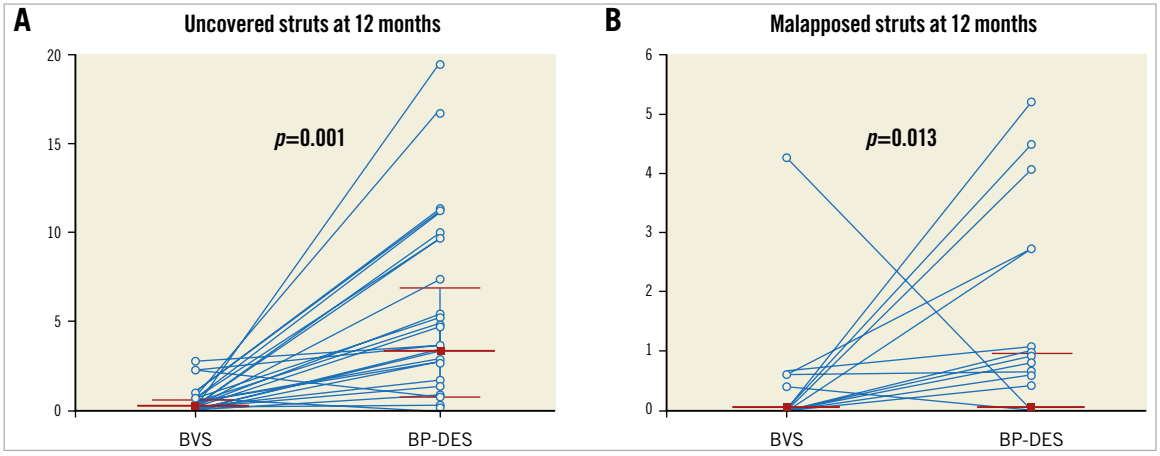

Figure 3. *Strut-level endpoints in paired BVS and BP-DES at 12 months. A) Rates of uncovered struts at 12 months, correlation coefficient 0.14 (95% CI: –0.25 to 0.49). B) Rates of malapposed struts at 12 months, correlation coefficient 0.11 (95% CI: –0.27 to 0.47). Blue lines connect values from the same patient. Median and interquartile range is shown for BVS and BP-DES cohorts.*

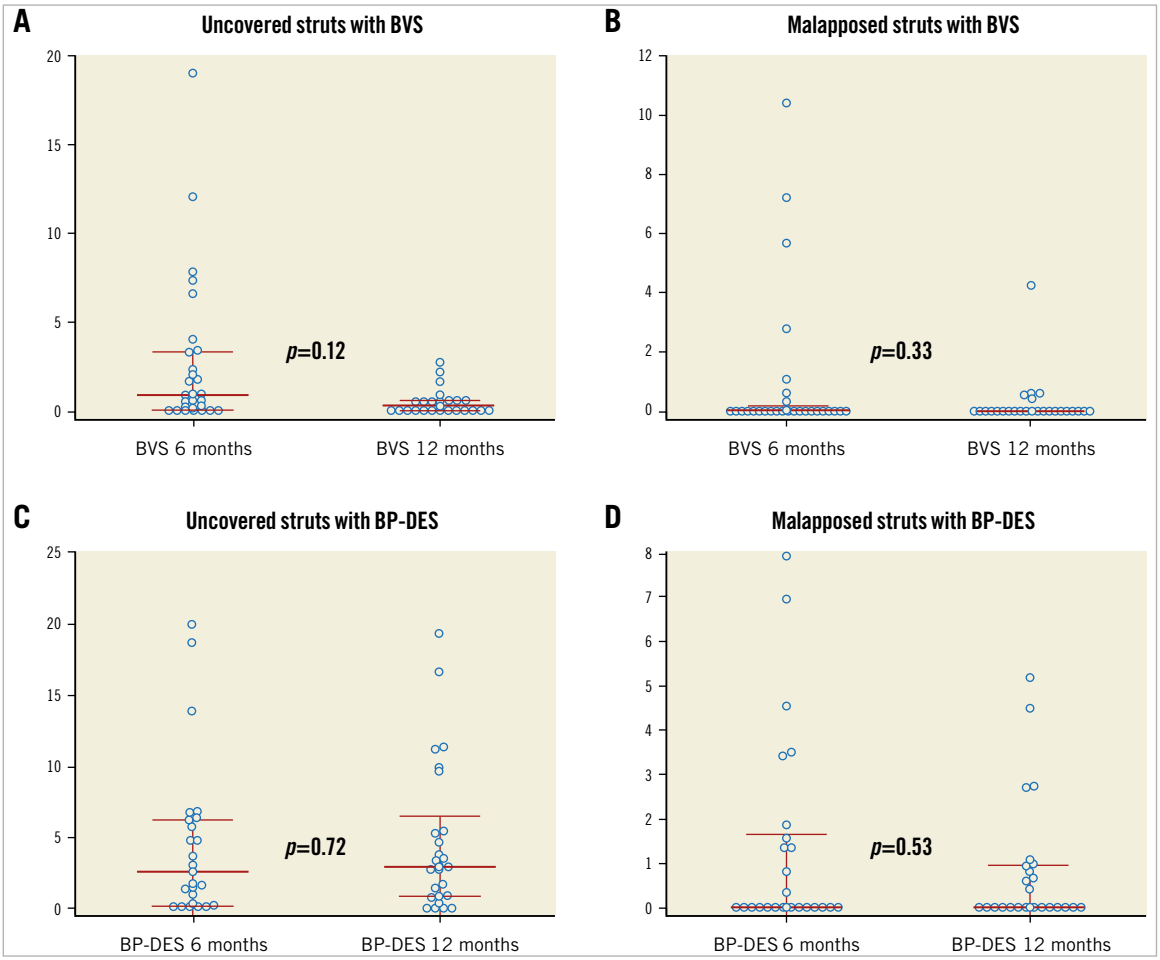

Figure 4. *Strut-level endpoints from six to 12 months. A) Rates of uncovered struts with BVS. B) Rates of malapposed struts with BVS. C) Rates of uncovered struts with BP-DES. D) Rates of malapposed struts with BP-DES. Median and interquartile range is shown for the six- and 12-month cohorts.*

Table 2. Discontinuities in BVS and qualitative analysis of neointimal tissue in BVS and BP-DES.

	BVS at 6 months (N=72)			BVS at 12 months (N=28)		
	n	CS	mean	n	CS	mean
Discontinuities	14 (19.4%)	39	0.57±2.27	4 (14.3%)	14	0.5±1.5
Isolated struts	1 (1.4%)	2	0.03±0.24	0	0	0
Overhanging struts	6 (8.3%)	27	0.40±2.23	4 (14.3%)	8	0.29±0.85
Stacked struts	8 (11.1%)	15	0.22±0.67	2 (7.1%)	10	0.36±1.42
No significant differences in either rates or means between 6 and 12 months.						
	6 months			12 months		
	BVS (N=72)	BP-DES (N=72)	*p*	BVS (N=28)	BP-DES (N=28)	*p*
Peri-stent low-intensity	40 (55%)	33 (45.8%)	0.34	20 (71.4%)	10 (35.7%)	<0.01
Neoatheroma	0	1 (1.4%)	0.98	0	0	
Lipid neointima	0	1 (1.4%)	0.98	0	0	
Calcific neointima	0	0		0	0	
Signal-rich bands	11 (15.2%)	2 (2.8%)	0.02	4 (14.2%)	1 (3.6%)	0.05
Microvessels	5 (7%)	3 (4.2%)	0.71	4 (14.2%)	3 (10.7%)	0.70
BP-DES: bioabsorbable polymer drug-eluting stents; BVS: bioresorbable vascular scaffolds						

very late thrombosis with BVS was scaffold discontinuity, which could suggest an unfavourable resorption-related process[22].

BVS STRUT COVERAGE AND RISK OF LATE/VERY LATE THROMBOSIS

The endpoint of strut coverage by OCT has thus far been considered an adequate surrogate for the risk of late thrombosis with metallic DES. The high rates of coverage for BVS struts reported herein and in previous studies and, on the other hand, the increased risk of late thrombosis reported with BVS could be seen as contradictory. However, these are not necessarily in contradiction with clinical evidence regarding BVS thrombosis. As clearly shown in patient-level meta-analysis of the ABSORB trials, the risk of BVS thrombosis is concentrated in two periods, the first 30 days and between 18 and 36 months[23]. As previously mentioned, factors other than coverage could account for the increased late/very late thrombosis risk with BVS[22].

The reported findings regarding discontinuities and evaginations could most probably count as risk factors for very late thrombosis events. Therefore, the endpoint of strut coverage by OCT might not be as valid as a surrogate for late/very late thrombosis risk with bioresorbable scaffolds as it is for metallic DES.

Limitations

The lack of baseline OCT examination precluded any definitive conclusion regarding the cause of the incomplete stent apposition and evaginations found at follow-up. The absence of mandatory post-procedural OCT was mainly due to the intention to assess vascular healing in conditions closer to real practice where no systematic use of imaging is carried out.

We acknowledge the limitations of the methodology employed to evaluate tissue coverage in BVS, and it is plausible that there may have been a certain rate of false positive findings; nonetheless, we used the most accepted technique (OCT) and we followed the most established standards. Assessment of coverage with OCT portends certain limitations that could be overcome to some extent with the use of coronary angioscopy; however, this technique is affected by relevant limitations which notably restrain its use in trials. The study design isolates quite well the device-specific effects on vascular healing but it does not permit establishing the relative contribution of the patient-specific vs. device-specific effects.

Conclusions

We found that vascular healing after BP-DES and BVS implantation could be predominantly device-specific. BVS showed a lower rate of uncovered and/or non-apposed struts at six months and 12 months. No intra-patient correlation for endpoints was found between BVS and BP-DES. Evaginations were more frequent and larger with BVS, particularly at six months. Discontinuities in BVS were relatively frequent at both time points. These results suggest that we should focus on specific imaging risk features in specific devices rather than evaluating the same features in all of them.

Impact on daily practice

The study provides new insights into the vascular healing process after implantation of BVS and BP-DES, proposing a study model which allows a more accurate device comparison. The study casts doubt on the validity of the commonly used endpoint of strut coverage as determined by OCT to inform about the risk of late/very late thrombosis with bioresorbable devices, pointing out the value of other findings such as evaginations or discontinuities. It is crucial to achieve a deep knowledge about the bioresorbable coronary devices if we want this promising technology to succeed.

Acknowledgements

(Supplementary Appendix 2).

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Conflict of interest statement

J.M. de la Torre Hernandez has received unrestricted grants for research from Boston Scientific, Abbott Vascular, St. Jude Medical, Biotronik and Biosensors, and consulting fees from Medtronic and Philips Volcano Inc. N. Gonzalo has received personal fees from Abbott Vascular for educational events. J. Escaned has received personal fees from Boston Scientific and Abbott Vascular for educational events. The other authors have no conflicts of interest to declare.

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Supplementary data

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The supplementary data are published online at: http://www.pcronline.com/eurointervention/145th_issue/234

Supplementary data

Supplementary Appendix 1. Methods

Study devices, technical details

The Absorb vascular scaffold BVS is a 150-μm thick bioresorbable PLLA scaffold with a 7-μm thick bioresorbable PDLLA coating, which elutes everolimus. The BioMatrix Flex™ stent has a stainless steel frame of 120 μm thickness with an abluminal 10 μm coating of PLA as a carrier of Biolimus A9. The SYNERGY™ stent has a Pt-Cr alloy backbone with 74 μm strut thickness with a thin abluminal polymer coat of 4 μm of PLGA, eluting everolimus. The Orsiro stent has a Co-Cr platform with strut thickness of 71 μm and a coating of 7.5 μm (abluminal) and 3.5 μm (luminal) thickness, coated with a layer of amorphous hydrogen-rich silicon carbide and a matrix consisting of the carrier PLLA and the active substance sirolimus.

OCT acquisition at follow-up

Investigators used the currently available optical frequency domain imaging systems (ILUMIEN™ or Optis™ Imaging System; St. Jude Medical, St. Paul, MN, USA, or the Lunawave® Imaging System; Terumo, Tokyo, Japan) with a pullback speed ranging from 18 to 20 mm/s. The monorail imaging catheter was advanced distal to the stented segment. Images were acquired using a non-occlusive technique with a contrast infusion. The optimal volume/time intracoronary infusion of contrast was tested to achieve a complete blood clearance in the vessel lumen. In case of restenosis, the examination with OCT was performed first and then treatment or not was applied according to the operator's decision.

OCT analysis

Assessment of apposition

For BP-DES, strut malapposition was defined when the distance from the luminal edge of strut reflection and the vessel wall was higher than the corresponding strut thickness. For BVS, incomplete strut apposition was defined as a clear separation between the abluminal side of the strut and the vessel wall.

Assessment of evaginations

The area and maximal depth of evaginations were measured. Major evagination was considered major when extending >3 mm with depth >10% of the stent diameter.

Scaffold discontinuities

Strut discontinuities were diagnosed by at least 1 of the following: 1) if 2 struts overhung each other in the same angular sector of the lumen perimeter, without close contact (overhung strut) or with contact (stacked strut) in at least 1 cross-section; or 2) if there were isolated (malapposed) struts that could not be integrated in the expected circularity of the device in at least 1 cross-section. "Isolated strut" was defined as a strut located at a distance from the vessel wall (>1/3 of span between the centre of gravity and the luminal border).

Qualitative analysis of the neointimal tissue

a) Peri-strut low-intensity area (region around stent struts with homogenous lower intensity than surrounding tissue on OCT images without signal attenuation); b) signal-rich bands with linear shadows (suggestive of the presence of macrophages); c) microvessels, defined as well delineated low-backscattering structures less than 200 micron in diameter that show a trajectory within the vessel wall; d) neoatherosclerosis, defined as presence of calcification or diffuse low reflectivity regions with intense attenuation within the neointima region.

Statistics

The sample size calculation was based at the initiation of the study on the limited available data at that time [5-8]. Uncoverage rate in BVS at 6 months was 2% in 23 patients, 3.2% in 25 patients and 5.3% in 12 patients [5-7]. Uncoverage rate in BioMatrix at 9 months was 1.8% in 20 patients [8].

With 200-240 struts to be analysed per device (BP-DES and BVS) and assuming a 3% uncoverage rate for BVS at 6 months (average of previous data), the number of struts to have per group in order to detect a 1% lower uncoverage with BP-DES, with an 80% statistical power at a two-sided alpha level of 0.05, was 4,023 struts per group (roughly 20 devices). Since three types of BP-DES will be included and in order to allow a respective separate analysis vs. BVS at 6 months, then 60 patients would be required with OCT examination at 6 months. For the 12-month endpoint (with no separate analysis by BP-DES

type) the sample would be 20 patients. Assuming an expected attrition rate of up to 20%, a final sample size of 100-120 patients was estimated to be necessary in order to have at least 60 patients examined at 6 months and at least 20 patients evaluated at 12 months.

Continuous variables are presented as mean±standard deviation or median and interquartile range. Categorical variables are expressed as percentages. Categorical variables were compared with the χ^2 test or the Fisher's exact test, where indicated. The Wilcoxon signed-rank test was applied for paired samples (BVS vs. BP-DES in same patients at 6 or 12 months), the Wilcoxon rank-sum test for two independent samples (BVS or BP-DES at 6 months vs. 12 months) and the Kruskal-Wallis test for four independent samples (BVS vs. SYNERGY vs. Orsiro vs. BioMatrix, all at 6 months).

Given the specific design of this study, with both BVS and BP-DES implanted in the same patient, the degree of association between strut-level endpoints for both stents was calculated using rank correlation. Based again on the particular design, comparison of strut coverage and apposition at 6 and 12 months between BVS and BP-DES was carried out under a paired approach by means of a pooled analysis using an inverse variance random effects model, taking into account the between-clusters and within-the-cluster variability, using each pair of matched stents (BVS and BP-DES were paired by corresponding patient) as an independent unit of clustering. Heterogeneity was estimated by I^2 (proportion of the effect attributable to heterogeneity). Risk ratios and confidence intervals were calculated.

A multivariate logistic regression analysis was conducted entering as covariates all lesion-/procedure-related variables and as dependent variables the uncoverage rates over 1% and over 5% separately. The kappa statistic was calculated to estimate the interobserver agreement for main strut-level OCT-derived endpoints in 10 patients. All probability values were two-sided and values of $p<0.05$ were considered statistically significant. The statistical packages SPSS 19.0 and Medcalc 12.0 were used throughout.

Supplementary Appendix 2. Acknowledgements

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Supplementary Table 1. Clinical and procedural characteristics.

Patients	**n=120**		
Age, years	61.8±9.8		
Females	20 (16.6%)		
Family history of coronary artery disease	11 (9.2%)		
Smoker	33 (27.5%)		
High blood pressure	74 (61.6%)		
Hypercholesterolaemia	78 (65%)		
Diabetes	36 (30%)		
Insulin-treated diabetes	12 (10%)		
Previous myocardial infarction	23 (19.2%)		
Previous coronary angioplasty	24 (20%)		
Stable angina	58 (48.3%)		
Unstable angina	30 (25%)		
Non-ST-elevation myocardial infarction	32 (26.6%)		
Left ventricular ejection fraction, %	57.4±8.2		
Devices implanted	**127 BVS**	**134 BP-DES**	***p*-value**
Devices/patient	1.06±0.31	1.11±0.50	0.28
Coronary artery treated			0.65
Left anterior descending artery	50 (39.3%)	50 (37.3%)	
Right coronary artery	45 (35.4%)	49 (36.5%)	
Left circumflex artery	32 (25.2%)	35 (26.1%)	
Mild-moderate calcification	20 (15.7%)	23 (17.1%)	0.79
Device diameter	3.09±0.42	3.05±0.45	0.41
Device length	18.8±5.1	19.7±6.8	0.22
Intravascular imaging	12 (9.5%)	10 (7.5%)	0.71
Peak pressure, atm	16.1±2	15.8±2	0.22
Predilatation	117 (92.1%)	113 (84.3%)	0.10
Post-dilatation	105 (82.6%)	100 (74.6%)	0.11
Post-dilatation balloon diameter, mm	3.28±0.50	3.35±0.55	0.26
Device success∗	125 (98.4%)	134 (100%)	0.43

∗Device success was defined as the attainment of <25% residual stenosis at the target lesion and TIMI 3 flow using only the protocol assigned device.
BP-DES: bioabsorbable polymer drug-eluting stents; BVS: bioresorbable vascular scaffolds

Supplementary Table 2. Major adverse cardiac events at 12 months.

Patient-oriented events	**N=120**
Death	1 (0.8%)
Cardiac death	0
Myocardial infarction	1 (0.8%)
Revascularisation	10 (8.3%)

Device-oriented events	**BVS N=120**	**BP-DES N=120**	***p*-value**
Device-related death	0	0	
Device-related infarction	0	0	
Device thrombosis	0	0	
Target lesion revascularisation	5 (4.2%)	1 (0.8%)	0.19

BP-DES: bioabsorbable polymer drug-eluting stents; BVS: bioresorbable vascular scaffolds

Supplementary Table 3. Quantitative angiographic data.

	BVS	BP-DES	
Devices in 6-month follow-up cohort	**n=72**	**n=72**	
Baseline			
Reference vessel diameter, mm	2.80±0.5	2.76±0.5	0.63
Minimum lumen diameter, mm	0.98±0.5	0.95±0.5	0.72
Diameter stenosis, %	64.5±18	66±16	0.59
Lesion length, mm	13.62±6	14.38±8.6	0.57
Post procedure			
Minimum lumen diameter, mm	2.41±0.5	2.54±0.5	0.12
Diameter stenosis, %	13.22±9	11.40±8	0.20
Follow-up			
In-device late lumen loss, mm	0.20±0.3	0.18±0.3	0.68
In-segment late lumen loss, mm	0.18±0.4	0.16±0.4	0.76
Devices in 12-month follow-up cohort	**n=28**	**n=28**	
Baseline			
Reference vessel diameter, mm	2.80±0.6	2.81±0.6	0.95
Minimum lumen diameter, mm	0.86±0.6	0.90±0.4	0.77
Diameter stenosis, %	67±20	64±16	0.54
Lesion length, mm	14.91±5	14.57±9	0.83
Post procedure			
Minimum lumen diameter, mm	2.51±0.7	2.68±0.6	0.33
Diameter stenosis, %	9±10	6.7±6.4	0.30
Follow-up			
In-device late lumen loss, mm	0.28±0.6	0.24±0.3	0.75
In-segment lumen late loss, mm	0.32±0.5	0.30±0.4	0.86

BP-DES: bioabsorbable polymer drug-eluting stents; BVS: bioresorbable vascular scaffolds

Supplementary Table 4. OCT planimetric findings at 6- and 12-month follow-up.

6-month OCT	**BVS**	**BP-DES**	***p*-value**
	n=72	**n=72**	
Stent diameter, mm	3.11±0.4	3.07±0.4	0.55
Stent length, mm	19.80±4.8	20.91±6.8	0.30
Struts analysed	202±87	234±107	0.05
Maximal neointimal area, mm^2	1.67±1.1	1.59±0.76	0.61
Minimum lumen area, mm^2	4.77±1.8	5.50±2.4	0.04
Minimum stent area, mm^2	5.66±1.7	6.19±2.2	0.10
Lumen area stenosis*, %	19.80±13.3	18±15	0.24
MSA/nominal stent area**, %	73.32±14	82.52±16	0.001
Maximal MA area, mm^2	0.61±1.3	0.59±1	0.80
12-month OCT	**BVS**	**BP-DES**	***p*-value**
	n=28	**n=28**	
Stent diameter, mm	3.07±0.4	2.90±0.4	0.12
Stent length, mm	22±9	19.51±7.8	0.27
Struts analysed	226±98	215±97	0.63
Maximal neointimal area, mm^2	2±1.2	2±1.6	0.90
Minimum lumen area, mm^2	4.35±1.8	4.92±2.2	0.31
Minimum stent area, mm^2	5.41±1.5	5.80±2.6	0.47
Lumen area stenosis, %	24.40±19	20.58±14	0.38
MSA/nominal stent area, %	73.10±15	88±20	0.002
Maximal MA area, mm^2	0.48±0.9	0.54±0.9	0.70

*Lumen area stenosis was defined as: reference (average) lumen CSA minus minimum lumen CSA divided by reference lumen CSA.
**Nominal stent area was defined as the area of the stent at nominal diameter expansion.
BP-DES: bioabsorbable polymer drug-eluting stents; BVS: bioresorbable vascular scaffolds; MA: malapposed: MSA: minimum stent area

Supplementary Table 5. Clusters for uncoverage and malapposition in OCT.

	6 months			12 months		
	BVS n=72	**BP-DES n=72**	***p*-value**	**BVS n=28**	**BP-DES n=28**	***p*-value**
Uncovered struts						
>0%	46 (64%)	61 (84.7%)	0.008	15 (53.5%)	23 (82%)	0.046
>5%	8 (11%)	29 (40%)	0.001	0	9 (32%)	0.003
>10%	2 (2.8%)	12 (16.6%)	0.015	0	4 (14%)	0.13
Malapposed struts						
>0%	18 (25%)	36 (50%)	0.003	5 (17.8%)	12 (42.8%)	0.08
>5%	6 (8.3%)	4 (5.5%)	0.70	0	1 (3.6%)	0.98
>10%	1 (1.4%)	0	0.98	0	0	
Uncovered + Malapposed struts						
>0%	5 (7%)	17 (23.6%)	0.014	1 (3.6%)	10 (35.7%)	0.007
>5%	0	1 (1.4%)	0.98	0	0	
>10%	0	0		0	0	

BP-DES: bioabsorbable polymer drug-eluting stents; BVS: bioresorbable vascular scaffolds

Supplementary Table 6. Evaginations in OCT.

At 6 months	**BVS**	**BP-DES**	
	N=72	**n=72**	***p*-value**
Presence of evaginations	56 (77.7%)	39 (54.1%)	0.004
Maximal evagination area, mm^2	0.28±0.13	0.24±0.22	0.18
Maximal evagination area over upper quartile*	21 (29.2%)	7 (9.7%)	0.006
Maximal evagination depth, mm	0.29±0.13	0.26±0.12	0.16
Major evaginations **	3 (4.1%)	0	0.23
Maximal evagination depth/stent diameter, %	8.75±4	8.60±4.3	0.82
SA at evagination/MSA, %	125±26	127.5±22	0.53
SA at evagination/reference stent area***, %	95±9	103±22	0.0049

At 12 months	**BVS**	**BP-DES**	
	N=28	**n=28**	***p*-value**
Presence of evaginations	23 (82.1%)	17 (60.7%)	0.14
Maximal evagination area, mm^2	0.18±0.16	0.26±0.36	0.28
Maximal evagination area over upper quartile	2 (7.1%)	3 (10.7%)	0.95
Maximal evagination depth, mm	0.23±0.13	0.25±0.14	0.58
Major evaginations	1 (3.5%)	1 (3.5%)	0.46
Maximal evagination depth/stent diameter, %	7.63±4	8.91±4.9	0.28
SA at evagination/MSA, %	131±25	124±19	0.24
SA at evagination/reference stent area, %	98±6.5	102±5.8	0.018

* The upper quartile was 0.3 mm^2.

** Major evagination when extending >3 mm with a depth >10% of the stent diameter.

*** Reference stent area was the average of proximal and distal (to evagination site) stent areas.

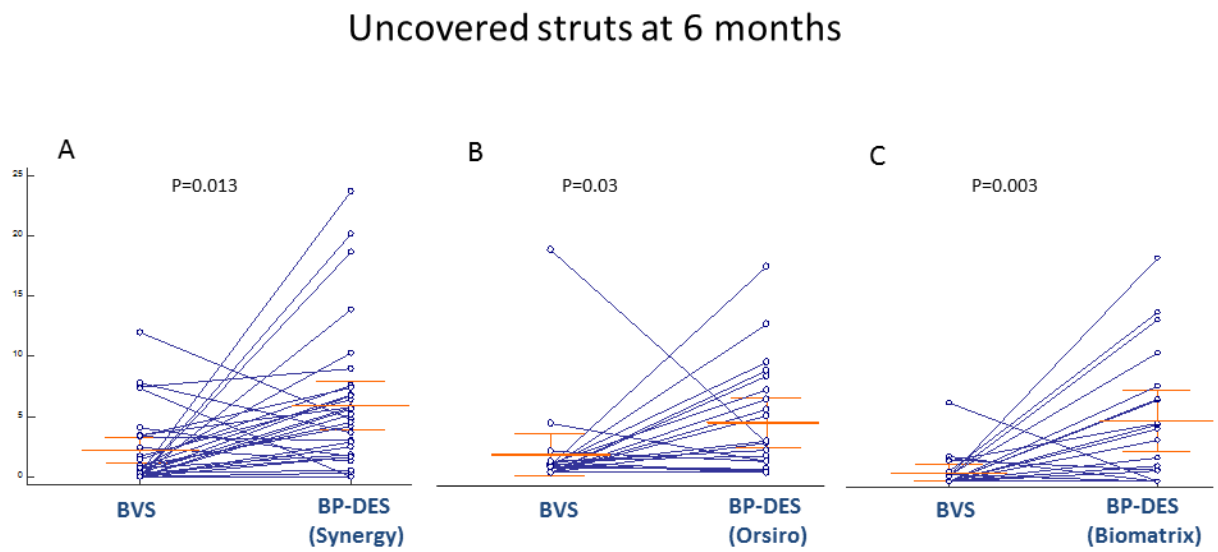
BP-DES: bioabsorbable polymer drug-eluting stents; BVS: bioresorbable vascular scaffolds; LA: lumen area; MLA: minimum lumen area; MSA: minimum stent area; SA: stent area

Supplementary Table 7. OCT findings in devices with and without evaginations.

BVS	**Evaginations N=79**	**No evaginations n=21**	***p*-value**
Right coronary artery	33 (41.7%)	3 (14.2%)	0.037
MSA, mm^2	5.74±1.6	5±1.6	0.062
MSA/nominal stent area, %	74±15	70±13	0.26
MLA, mm^2	4.91±1.7	3.74±1.7	0.005
Lumen area stenosis, %	18.50±14.9	31±13.5	0.0007
Maximal neointimal area, mm^2	1.72±1.2	1.88±0.58	0.50
Maximal MA area, mm^2	0.66±1.2	0.24±0.72	0.13
NC struts, %	1.49±3	0.69±1.4	0.26
MA struts, %	0.80±2	0.14±0.56	0.09
NC+MA struts, %	0.11±0.6	0.03±0.13	0.70

BP-DES	**Evaginations N=56**	**No evaginations n=44**	***p*-value**
Right coronary artery	21 (37.5%)	16 (36.3%)	0.93
MSA, mm^2	5.99±2.1	6.20±2.7	0.66
MSA/nominal stent area, %	84.73±21	81.80±27	0.54
MLA, mm^2	5.38±2.1	5.24±2.6	0.70
Lumen area stenosis, %	15±12	24±17	0.002
Maximal neointimal area, mm^2	1.46±0.97	2.12±1.1	0.002
Maximal MA area, mm^2	0.82±1	0.31±0.7	0.007
NC struts, %	7±6	2.7±3	0.001
MA struts, %	1.82±2.3	0.39±0.9	0.0001
NC+MA struts, %	0.59±1.3	0.16±0.6	0.0045

BP-DES: bioabsorbable polymer drug-eluting stents; BVS: bioresorbable vascular scaffolds; MLA: minimum lumen area; MSA: minimum stent area; MA: malapposed; NC: non-covered



Supplementary Figure 1. Uncoverage in BVS and different types of BP-DES at 6 months.

A) Rates of uncovered struts at 6 months in BVS and BP-DES (SYNERGY), correlation coefficient -0.14 (95% CI: -0.44 to 0.18).

B) Rates of uncovered struts at 6 months in BVS and BP-DES (Orsiro), correlation coefficient -0.35 (95% CI: -0.67 to 0.081).

C) Rates of uncovered struts at 6 months in BVS and BP-DES (BioMatrix), correlation coefficient -0.14 (95% CI: -0.58 to 0.35).

Blue lines connect values from same patient. Median and interquartile range is shown for BVS and BP-DES cohorts.