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Vascular response to bioresorbable polymer sirolimus-eluting stent vs. permanent polymer everolimus-eluting stent at 9-month follow-up: an optical coherence tomography sub-study from the CENTURY II trial

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Aims The Ultimaster bioresorbable polymer sirolimus-eluting stent (BP-SES) is a newly developed drug-eluting stent (DES) that consists of a thin-strut, cobalt chromium with bioresorbable polymer coated only albuminally. We sought to compare tissue coverage in coronary lesions treated with BP-SES with the XIENCE permanent polymer everolimus-eluting stent (PP-EES) using optical coherence tomography (OCT).

Methods and results A total of 36 patients participated in the CENTURY II trial in our institution and were randomly assigned to BP-SES ($n = 15$) and PP-EES ($n = 21$). Of these, 27 patients (13 BP-SES and 14 PP-EES) underwent OCT at 9-month follow-up. Tissue coverage and apposition were assessed on each strut, and the results in both groups were compared using multilevel logistic or linear regression models with random effects at three levels: patient, lesion, and struts. A total of 6450 struts (BP-SES, $n = 2951$; PP-EES, $n = 3499$) were analysed. Thirty and 79 uncovered struts (1.02 and 2.26%, $P = 0.35$), and 3 and 4 malapposed struts (0.10 and 0.11%, $P = 0.94$) were found in BP-SES and PP-EES groups, respectively. Mean neointimal thickness did not significantly differ between both groups (110 ± 10 vs. 93 ± 10 μm, $P = 0.22$). No significant differences in per cent neointimal volume obstruction (13.2 ± 4.6 vs. 10.5 ± 4.9%, $P = 0.14$) or other areas-volumetric parameters were detected between both groups.

Conclusion BP-SES shows an excellent vascular healing response at 9-month follow-up, which is similar to PP-EES.

Keywords Bioresorbable polymer • Sirolimus-eluting stent • Optical coherence tomography • Coronary artery disease

Introduction

Drug-eluting stents (DESs) have dramatically reduced the rate of in-stent restenosis and target revascularization by inhibiting neointimal hyperplasia.[1] However, delayed neointimal healing and incomplete endothelialization have gained attention as a cause for late stent thrombosis (LST) with first-generation DESs.[2–4] Newer generation DES is designed to overcome these limitations of first-generation DES by the improvement in stent platform, the use of alternative anti-proliferative limus analogues, and the development of biocompatible and biodegradable polymers.[5,6]

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Bioresorbable polymer sirolimus-eluting stent (BP-SES) (Ultimaster™, Terumo Corporation, Tokyo, Japan) is a newly developed DES that consists of a thin-strut (80 μm), cobalt chromium, sirolimus-eluting stent with bioresorbable polymer (resorbed within 3–4 months) coated only albuminally by applying special gradient technology. CENTURY (Clinical Evaluation of New Terumo Drug-Eluting Coronary Stent System in the Treatment of Patients with Coronary Artery Disease) study demonstrated good performance of BP-SES, including high procedural success, strong suppression of neointimal proliferation at 6 months, and a low rate of target lesion failure at 2 years.[7] Recently, CENTURY II trial showed that BP-SES has the similar safety and efficacy to permanent polymer everolimus-eluting stent (PP-EES) (Xience V™, Xience Prime™, Abbott Vascular, Santa Clara, CA, USA) at 9 months.[8]

Optical coherence tomography (OCT) is a high resolution intravascular imaging modality to evaluate neointimal tissue adequately *in vivo*. In the CENTURY study, an OCT analysis at 6-month follow-up showed that the percentage of mean strut coverage and malapposed struts were 96.2 ± 5.0 and 1.66 ± 4.02%, respectively.[7] To date, however, there has been no data investigating coronary arterial response to BP-SES at late phase (≥6 months). Therefore, we sought to evaluate the neointimal tissue coverage of BP-SES at 9 months after stent implantation using OCT compared with that of PP-EES.

Methods

Study population and procedural protocol

From March and October 2012, a total of 36 patients participated in the CENTURY II trial in our institution and were randomly assigned to BP-SES ($n = 15$) and PP-EES ($n = 21$). The design and main results from the CENTURY II trial have been published elsewhere.[8] It was an international, multicentre, randomized (1:1), single-blind, controlled, non-inferiority, two-arm clinical trial comparing BP-SES with PP-EES. In cohort Japanese requirements, patients with unstable angina pectoris and stable angina pectoris were eligible for inclusion. Patients with acute myocardial infarction within 48 h before baseline procedure were excluded. For the purpose of the present study, 9-month follow-up OCT examination was prospectively attempted in 36 patients between December 2012 and June 2013.

All initial interventions were performed using standard techniques. Pre-dilatation, post-dilatation, and intravascular ultrasound or OCT uses were left to the operator's discretion. After the procedure, all patients were advised to continue on aspirin (81–162 mg daily) for life unless there were contraindications. Either ticlopidine (200 mg daily) or clopidogrel (75 mg daily) was also prescribed for at least 1 year after stent implantation. Written informed consent to participation was obtained from all patients in accordance with the Declaration of Helsinki, and this study was approved by the ethics committee of Kokura Memorial Hospital.

Study endpoints

The study primary endpoint was neointimal tissue coverage at 9-month follow-up, which was evaluated as the percentage of uncovered struts and the mean neointimal thickness (NIT). Secondary endpoints included apposition and standard areas and volumes.

Quantitative coronary angiography

Coronary angiography was performed after the intracoronary administration of 0.2 mg nitroglycerin. Quantitative coronary angiographic analysis was performed before and after stenting and 6–9 months after index procedure, using a guiding catheter to calibrate the magnification and a validated automated edge detection algorithm (CASS 5.9, Pie Medical Imaging, Eindhoven, The Netherlands). The analyses were performed independently by two experienced independent observers in an independent core laboratory (Kokura Memorial Hospital, Kitakyushu, Japan) blinded to the clinical information. ISR was defined as a per cent diameter stenosis of >50% within the stent at the time of follow-up.

OCT imaging acquisition

The OCT imaging was performed with an OCT system (C7XR Fourier-Domain System, St Jude Medical, St Paul, MN, USA). The C7XR system used a conventional wire to cross the segment of interest. The OCT imaging catheter (Dragonfly, St Jude Medical, St Paul, MN, USA) was then advanced distally to the stented lesion. Pullback was performed during continuous injection of contrast medium through the guide catheter with an injection pump. Automatic pullback rate was 20 mm/s, and the frame rate was 100 frames/s.

OCT analysis

OCT pullback was analysed offline in a core laboratory (Cardiolysis BV, Rotterdam, The Netherlands) by independent analysts blinded to clinical and procedural characteristics of the patients, using Qlvus software (Medis Medical Imaging Systems BV, Leiden, The Netherlands). Cross-sectional OCT images were analysed at 1-mm intervals within the stented segment and 5-mm proximal and distal to the stent edges. Cross-sections with side branches or poor quality of OCT images were excluded from this analysis. Lumen and stent areas were drawn in each analysed cross-section, and the derived incomplete stent apposition or neointimal hyperplasia (NIH) areas were calculated as appropriate. The NIT was determined based on automated measurements performed from the centre of the luminal surface of each strut blooming and its distance to the lumen contour.[9] An uncovered strut was defined as having an NIT of 0 μm.[9] A malapposed strut was defined as a distance between the centre reflection of the strut and the vessel wall (BP-SES >80 μm and PP-EES >89 μm).[10] An intraluminal mass was defined as an irregular mass in the lumen accompanied by shadow or mass not connected with the lumen.

Statistical analysis

Data are presented as values and percentages, mean ± SD, or median [inter-quartile range (IQR)]. Categorical variables were compared between groups with the χ^2 test or Fisher exact test, as appropriate. Continuous variables were compared between groups using the Student's unpaired *t*-test or the Mann–Whitney *U* test, based on the distribution. In per strut analysis, apposition was estimated through the categorical variable (well-apposed or malapposed). Tissue coverage was estimated through the percentage of uncovered struts (dichotomous variable) and through the mean thickness of coverage (continuous). Dichotomous or categorical variables were analysed using multilevel logistic regression models with random effects at three levels: (i) patient, (ii) lesion, and (iii) stent. Similarly, continuous variables were analysed using multilevel linear regression models with random effects at the same three levels.

All statistical analyses were performed using the use of JMP version 10.0.2 (SAS Institute Inc., Cary, NC, USA) for data description and baseline comparisons; and SAS version 9.4 (SAS Institute Inc.) for multilevel

modelling. A two-sided *P*-value of <0.05 was considered statistically significant.

Results

Study population

Of 36 patients, a total of nine patients (two BP-SES and seven PP-EES) were excluded in the present study because of the following reasons: seven refused to participate in the present study and two failed to perform the OCT examination due to technical reasons. Finally, 13 BP-SES and 14 PP-EES patients were enrolled in the present study (*Figure 1*).

Baseline patient characteristics

Baseline patient characteristics of the study population are summarized in *Table 1* and were similar between the two groups.

Baseline lesion characteristics and quantitative coronary angiography findings

Table 2 shows baseline lesion characteristics and quantitative coronary angiography (QCA) findings of the two groups. There were no significant differences between both groups. At 9-month follow-up, late lumen loss was comparable between groups (0.29 ± 0.22 vs. 0.24 ± 0.17 mm, $P = 0.44$).

OCT findings

Figure 2 shows representative OCT images of BP-SES and PP-EES. *Table 3* shows the results of tissue coverage and apposition between BP-SES and PP-EES groups at 9-month follow-up. Mean NIT did not differ significantly between the two groups (difference 17.0 μm, 95% confidence interval, CI: −11.3 to 45.0 μm, $P = 0.22$). The distribution of NIT is shown in *Figure 3*. The percentage of uncovered struts was comparable between both groups (odds ratio, OR 0.61, 95% CI: 0.21–1.74, $P = 0.35$). The percentage of malapposed struts was very low in both groups (OR 1.09, 95% CI: 0.07–15.53, $P = 0.94$). *Table 4* shows mean in-stent areas and volumes between two groups. No significant differences in per cent neointimal volume obstruction (13.2 ± 4.6 vs. $10.5 \pm 4.9\%$, $P = 0.14$) or other areas-volumetric parameters were detected between both groups.

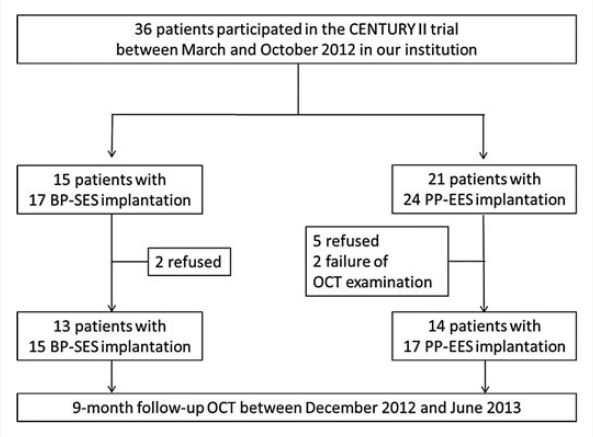

Figure 1 Study chart flow. BP-SES, bioresorbable polymer sirolimus-eluting stent; PP-EES, permanent polymer everolimus-eluting stent.

Clinical outcomes through 9 months

Clinical adverse events such as any revascularization, myocardial infarction, and stent thrombosis did not occur in both groups during 9-month follow-up.

Discussion

At 9-month follow-up, the present OCT sub-study of CENTURY II trial showed excellent tissue coverage and apposition of both BP-SES and PP-EES. The main findings of this study are as follows: (i) the percentage of uncovered and malapposed struts was very low in both BP-SES and PP-EES; (ii) the mean NIT did not differ significantly between BP-SES and PP-EES.

Histopathological studies of first-generation DES have revealed that a chronic inflammatory reaction to components of the permanent polymer matrix may lead to the delayed arterial healing, which was associated with increased risks of late DES failure such as LST

Table 1 Baseline patient characteristics

	BP-SES (*n* = 13)	PP-EES (*n* = 14)	*P*
Age, years	75.0 ± 7.2	71.2 ± 9.0	0.24
Male	8 (61.5)	12 (85.7)	0.20
Hypertension	10 (76.9)	10 (71.4)	>0.99
Dyslipidaemia	11 (84.6)	13 (92.8)	0.59
Diabetes mellitus	3 (23.0)	6 (42.8)	0.41
Current smoker	1 (7.6)	1 (7.1)	>0.99
Previous MI	1 (7.6)	2 (14.2)	>0.99
Prior PCI	2 (15.3)	5 (35.7)	0.38
LVEF, %	65.4 ± 6.3	60.7 ± 9.9	0.15
Clinical presentation			
Stable angina	13 (100.0)	14 (100.0)	–
Acute coronary syndrome	0 (0.0)	0 (0.0)	–
Medication			
Aspirin	13 (100.0)	14 (100.0)	–
Clopidogrel	13 (100.0)	14 (100.0)	–
ACEI/ARB	9 (69.2)	9 (64.2)	>0.99
β-Blocker	4 (30.7)	3 (21.4)	0.67
Statin	12 (92.3)	11 (78.5)	0.59
OHA	3 (23.0)	5 (35.7)	0.67
Insulin	2 (15.3)	1 (7.1)	0.59

Data are presented as mean ± SD or *n* (%).
ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP-SES, bioresorbable polymer sirolimus-eluting stent; LVEF, left ventricular ejection fraction; MI, myocardial infarction; OHA, oral hypoglycaemia agent; PCI, percutaneous coronary intervention; PP-EES, permanent polymer everolimus-eluting stent.

Table 2 Baseline lesion characteristics and quantitative coronary angiography findings

	BP-SES (n = 13)	PP-EES (n = 15)	P
Location of target lesion			0.67
RCA	3 (23.1)	2 (13.3)	
LAD	8 (61.5)	9 (60.0)	
LCX	2 (15.4)	4 (26.7)	
Lesion type			0.99
A/B1/B2/C	1/7/3/2	1/8/3/3	
Bifurcation	2 (15.4)	1 (6.7)	0.58
Stent diameter, mm	2.88 ± 0.42	2.90 ± 0.34	0.91
Stent length, mm	17.4 ± 4.3	19.7 ± 5.0	0.21
Total stent length, mm	20.8 ± 8.8	24.4 ± 10.5	0.35
No. of stents per lesion			>0.99
1	11 (84.6)	13 (86.7)	
2	2 (15.4)	2 (13.3)	
Maximal inflation pressure, atm	13.4 ± 2.8	14.3 ± 4.7	0.53
Post-dilatation	6 (46.2)	5 (33.3)	0.70
Use of IVUS	9 (69.2)	11 (73.3)	>0.99
Use of OCT	4 (30.8)	4 (26.7)	>0.99
Quantitative coronary angiography			
Baseline			
RVD, mm	2.93 ± 0.44	2.91 ± 0.39	0.91
MLD, pre, mm	0.57 ± 0.30	0.75 ± 0.42	0.21
%DS, pre, %	80.4 ± 8.1	73.2 ± 17.4	0.31
MLD, post, mm	2.65 ± 0.39	2.59 ± 0.33	0.66
%DS, post, %	9.4 ± 4.5	10.5 ± 5.1	0.54
Lesion length, mm	18.3 ± 8.2	19.8 ± 9.6	0.68
9-month follow-up			
RVD, mm	2.92 ± 0.46	2.81 ± 0.38	0.53
MLD, mm	2.34 ± 0.42	2.35 ± 0.44	0.96
%DS, %	20.0 ± 9.1	16.8 ± 5.4	0.26
Late loss, mm	0.29 ± 0.22	0.24 ± 0.17	0.44
In-stent restenosis	1 (7.7)	0 (0.0)	0.46

Data are presented as mean ± SD or n (%).
BP-SES, bioresorbable polymer sirolimus-eluting stent; DS, diameter stenosis; LAD, left coronary artery; LCX, left circumflex artery; MLD, minimal lumen diameter; PP-EES, permanent polymer everolimus-eluting stent; RCA, right coronary artery; RVD, reference vessel diameter.

and late restenosis.[2–4] To overcome this limitation, biocompatible and biodegradable polymers have been developed and equipped with newer generation DES. BP-SES has an albuminally coated bioresorbable polymer, which is resorbed within 3–4 months. These features are expected to reduce inflammatory reaction for the vessel and translate into the positive clinical outcome.[11,12] In the present study, uncovered and malapposed struts were observed in 1.02 and 0.10% of BP-SES struts and 2.26 and 0.11% of PP-EES struts, respectively. Although there is no data regarding OCT results of BP-SES at 9-month follow-up, the percentage of uncovered and malapposed struts at 8–12 months after PP-EES implantation was reported to be 1.6–2.4 and 0.22–1.76%, respectively.[13,14] These findings supported that both BP-SES and PP-EES showed an excellent vascular healing response at 9 months after implantation. Furthermore, the percentage of uncovered and malapposed struts in both groups was surprisingly lower compared with previous studies.[13,14] In the present study, we performed IVUS- or OCT-guided PCI to obtain the optimal stent expansion and apposition in all patients, which may lead to better vascular healing.

The shorter polymer resorption time is one of the unique features of BP-SES. On the other hand, it has gained attention as a cause for concern due to a potential inflammatory response to polymer degradation products.[15] Interestingly, an angiographic sub-study of the CENTURY II trial showed that in-stent late loss was significantly lower in PP-EES than in BP-SES, although the rate of TLR was similar between the two groups. This discrepancy caused a little concern regarding the efficacy and safety of BP-SES. As reported previously, OCT is useful to evaluate the *in vivo* vascular healing comparing different types of DESs.[10,13,14,16] In the present study, the percentage of uncovered and malapposed struts was not significantly different between BP-SES and PP-EES. Furthermore, mean NIT of BP-SES was 110 μm and did not significantly differ from that of PP-EES (93 μm). Previous OCT studies showed the mean NIT of newer generation DES as follows: 100–142 μm in PP-EES;[10,13,14] 91 μm in biodegradable polymer biolimus-eluting stent (BP-BES) (Nobori™, Terumo, Tokyo, Japan);[14] 116 μm in zotalolimus-eluting stent (Resolute Integrity™, Medtronic Inc., Santa Rosa, CA, USA).[10] These findings support that the mean NIT of BP-SES is similar to that of other newer generation DES and might dispel the concerns regarding the shorter polymer resorption time of BP-SES.

Biodegradable polymer is designed to improve long-term safety and efficacy compared with first-generation DES.[11] Recently, BP-BES (Nobori™) showed clinical non-inferiority to PP-EES in NEXT and COMPARE II trial.[17,18] To date, however, it remains unclear whether biodegradable polymer leads to better long-term safety and efficacy compared with newer generation permanent polymer. A network meta-analysis demonstrated that BP-BES was associated with a higher risk of definite or probable stent thrombosis than PP-EES.[19] Furthermore, OCT studies showed that the percentage of uncovered struts was significantly higher in BP-BES than in PP-EES at 6- to 9-month follow-up.[14,20] These findings did not support a preferential use of biodegradable polymer DES over newer generation permanent polymer DES. In the present study, vascular healing characterized by the presence of uncovered and malapposed struts was similar between BP-SES and PP-EES at 9-month follow-up. Compared with BP-BES, BP-SES has lots of different features in terms of stent alloy (cobalt chromium vs. stainless steel), strut thickness (80 vs. 120 μm), and eluting drug (sirolimus vs. biolimus). These differences may translate into the results in the present study. Although biodegradable polymer may become one of the important DES components, the optimal combination of stent design, strut thickness, polymer, and eluting drug may play a pivotal role in newly developed DESs.

CENTURY II trial demonstrated non-inferiority of BP-SES to PP-EES with respect to the target lesion failure within 9 months, regardless of significant differences in in-stent late loss.[8] Moreover, the present OCT study showed comparable vascular healing response between BP-SES and PP-EES at 9-month follow-up. Theoretically,

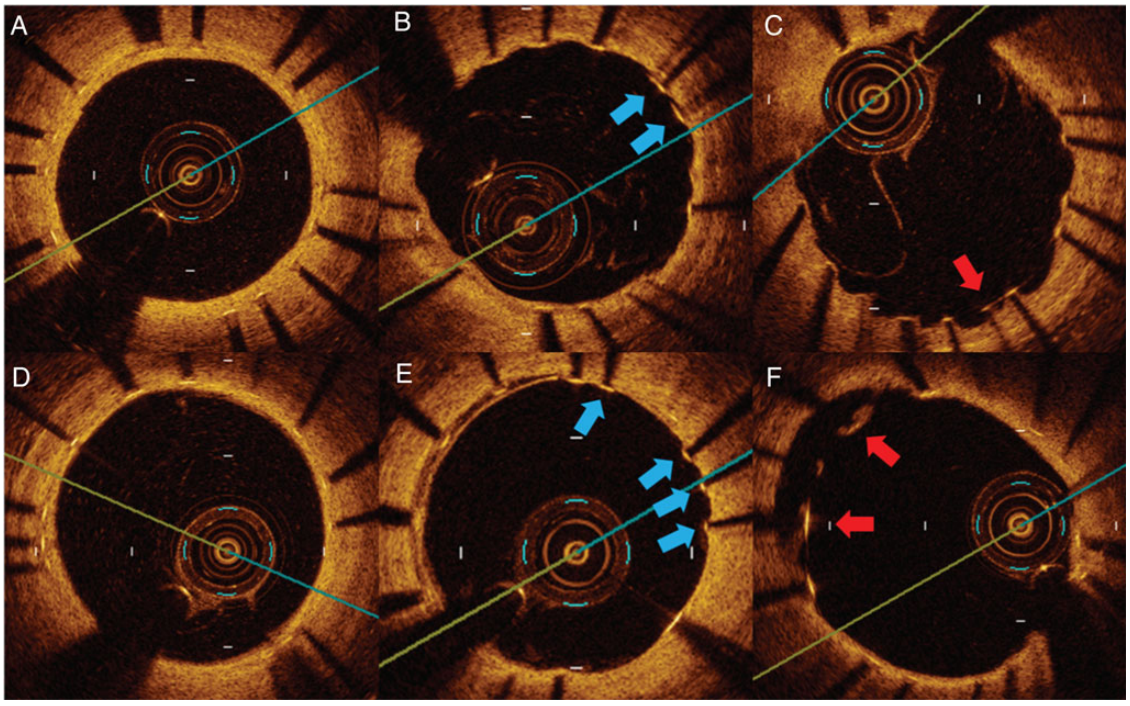

Figure 2 Representative optical coherence tomographic images of BP-SES (*A*–*C*) and permanent polymer everolimus-eluting stent (*D*–*F*) at 9-month follow-up. Images shown are (*A* and *D*) covered struts, (*B* and *E*) uncovered struts (blue arrows), and (*C* and *F*) malapposed struts (red arrows).

Table 3 Analysis of tissue coverage and apposition per stent strut

	BP-SES	PP-EES	Difference or odds ratio (95% CI)	*P*
Total of stent struts	2951	3499		
Tissue coverage				
Mean NIT, μm	110 ± 10	93 ± 9	17.0 (−11.3 to 45.0)	0.22
Covered struts	2921 (98.98)	3420 (97.74)	1.64 (0.57 to 4.70)	0.35
Uncovered struts	30 (1.02)	79 (2.26)	0.61 (0.21 to 1.74)	0.35
Apposition				
Well-apposed struts	2935 (99.46)	3484 (99.56)	0.75 (0.30 to 1.85)	0.53
Malapposed struts	3 (0.10)	4 (0.11)	1.09 (0.07 to 15.53)	0.94

Data are presented as mean ± SD or *n* (%).
BP-SES, bioresorbable polymer sirolimus-eluting stent; CI, confidence intervals; NIT, neointimal thickness; PP-EES, permanent polymer everolimus-eluting stent.

however, potential benefits related to biodegradable polymer may appear during long-term follow-up. Indeed, 5-year follow-up of LEADERS trial demonstrated the safety benefit of BP-BES compared with durable polymer SES (DP-SES) (Cypher™, Cordis, Johnson & Johnson, Warren, NJ, USA) due to a significant reduction in very LST.[11] Furthermore, we previously reported 5-year OCT study that BP-BES (Nobori™) showed a favourable vascular response compared with DP-SES (Cypher™) and the frequency of in-stent neoatherosclerosis tended to be lower in BP-BES than in DP-SES.[21] However, there is no data regarding long-term clinical outcome and vascular response after BP-SES implantation. Therefore, further long-term follow-up study is required to validate the safety and efficacy of BP-SES. Moreover, OCT study may be able to provide more insights into the long-term vascular response of BP-SES as previously reported in other DESs.[21,22]

Study limitations

There are several limitations in the present study. First, this study included a small study population. Therefore, selection bias may exist in the present study and have biased the conclusion. Nevertheless,

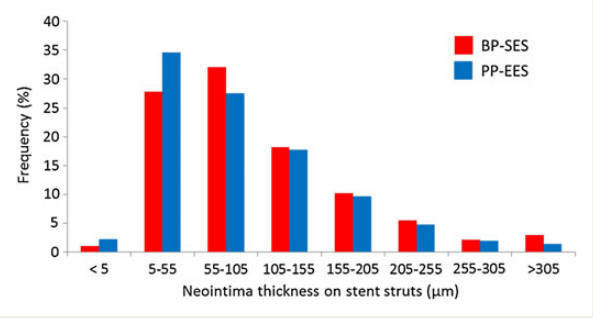

Figure 3 Neointimal thickness at intervals of 50 μm. In BP-SES, the percentage of stent struts with a neointimal thickness of <5, 5–55, 55–105, 105–155, 155–205, 205–255, 255–305, and >305 μm was 1.1, 27.8, 32.1, 18.2, 10.2, 5.5, 2.2, and 3%, respectively. That for permanent polymer everolimus-eluting stent was 2.3, 34.6, 27.6, 17.7, 9.7, 4.8, 2.0, and 1.4%, respectively. BP-SES, bioresorbable polymer sirolimus-eluting stent; PP-EES, permanent polymer everolimus-eluting stent.

Table 4 Area and volumetric analysis per stent

	BP-SES	PP-EES	*P*
Mean lumen area, mm^2	5.79 ± 1.69	6.19 ± 1.89	0.57
Minimal lumen area, mm^2	4.28 ± 1.60	4.72 ± 1.86	0.51
Lumen volume, mm^3	114.7 ± 44.2	140.2 ± 55.1	0.19
Mean stent area, mm^2	6.58 ± 1.79	6.90 ± 1.87	0.65
Minimal stent area, mm^2	5.57 ± 1.64	5.45 ± 1.97	0.87
Stent volume, mm^3	131.2 ± 48.7	156.7 ± 61.7	0.24
Mean NIH area, mm^2	0.83 ± 0.30	0.70 ± 0.31	0.28
NIH volume, mm^3	17.0 ± 7.4	16.5 ± 11.2	0.90
NIH volume obstruction, %	13.2 ± 4.6	10.5 ± 4.9	0.14
% frames with ISA	0.33 ± 1.21	0.38 ± 1.48	0.93
Mean ISA area, mm^2	0.01 ± 0.02	0.00 ± 0.01	0.83
ISA volume, mm^3	0.07 ± 0.26	0.10 ± 0.38	0.83
ISA volume, % of stent volume	0.04 ± 0.14	0.05 ± 0.20	0.84
Mean intraluminal mass area, mm^2	0.00 ± 0.00	0.00 ± 0.01	0.36
Mean intraluminal mass volume, mm^3	0.00 ± 0.00	0.01 ± 0.05	0.36

Data are presented as mean ± SD.
BP-SES, bioresorbable polymer sirolimus-eluting stent; ISA, incomplete stent apposition; NIH, neointimal hyperplasia; PP-EES, permanent polymer everolimus-eluting stent.

to the best of our knowledge, this is the first study to assess the neointimal tissue coverage of BP-SES at 9 months after stent implantation using OCT. Second, OCT evaluation immediately after stent implantation was not available in the present study. Therefore, it was not possible to distinguish between persistent and late-acquired stent malapposition. Finally, the present study was not powered or designed to assess the relationship between OCT suboptimal results and future clinical events. Additionally, it is difficult to draw conclusions on changes in clinical treatment such as the optimal duration of dual antiplatelet therapy based on the results of current study. Further studies are required to investigate the clinical implication of OCT findings at 9-month follow-up.

Conclusion

The percentage of uncovered and malapposed struts is very low in both BP-SES and PP-EES at 9-month follow-up. Additionally, NIT is similar between BP-SES and PP-EES. Our findings support that BP-SES shows an excellent vascular healing response at 9-month follow-up, which is similar to PP-EES.

Conflict of interest: S.S. reports grants from Terumo Corporation during the conduct of CENTURY II trial.

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References

1. Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C *et al.* Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med* 2003;**349**:1315–23.
2. Joner M, Finn AV, Farb A, Mont EK, Kolodgie FD, Ladich E *et al.* Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol* 2006;**48**:193–202.
3. Virmani R, Guagliumi G, Farb A, Musumeci G, Grieco N, Motta T *et al.* Localized hypersensitivity and late coronary thrombosis secondary to a sirolimus-eluting stent: should we be cautious? *Circulation* 2004;**109**:701–5.
4. Finn AV, Joner M, Nakazawa G, Kolodgie F, Newell J, John MC *et al.* Pathological correlates of late drug-eluting stent thrombosis: Strut coverage as a marker of endothelialization. *Circulation* 2007;**115**:2435–41.
5. Sarno G, Lagerqvist B, Fröbert O, Nilsson J, Olivecrona G, Omerovic E *et al.* Lower risk of stent thrombosis and restenosis with unrestricted use of 'new-generation' drug-eluting stents: a report from the nationwide Swedish Coronary Angiography and Angioplasty Registry (SCAAR). *Eur Heart J* 2012;**33**:606–13.
6. Abizaid A, Costa JR Jr. New drug-eluting stents: an overview on biodegradable and polymer-free next-generation stent systems. *Circ Cardiovasc Interv* 2010;**3**:384–93.
7. Barbato E, Salinger-Martinovic S, Sagic D, Beleslin B, Vrolix M, Neskovic AN *et al.* A first-in-man clinical evaluation of Ultimaster, a new drug-eluting coronary stent system:CENTURY study. *EuroIntervention* 2014. doi: 10.4244/EIJY14M08_06.
8. Saito S, Valdes-Chavarri M, Richardt G, Moreno R, Iniguez Romo A, Barbato E *et al.* A randomized, prospective, intercontinental evaluation of a bioresorbable polymer sirolimus-eluting coronary stent system: the CENTURY II (Clinical Evaluation of New Terumo Drug-Eluting CoronaryStent System in the Treatment of Patients with Coronary Artery Disease) trial. *Eur Heart J* 2014;**35**:2021–31.
9. Tanigawa J, Barlis P, Di Mario C. Intravascular optical coherence tomography: optimisation of image acquisition and quantitative assessment of stent strut apposition. *EuroIntervention* 2007;**3**:128–36.
10. Gutiérrez-Chico JL, van Geuns RJ, Regar E, van der Giessen WJ, Kelbæk H, Saunamäki K *et al.* Tissue coverage of a hydrophilic polymer-coated zotarolimus-eluting stent vs. a fluoropolymer-coated everolimus-eluting stent at 13-month follow-up: an optical coherence tomography substudy from the RESOLUTE All Comers trial. *Eur Heart J* 2011;**32**:2454–63.
11. Serruys PW, Farooq V, Kalesan B, de Vries T, Buszman P, Linke A *et al.* Improved safety and reduction in stent thrombosis associated with biodegradable polymer-based biolimus-eluting stents versus durable polymer-based sirolimus-eluting stents in patients with coronary artery disease: final 5-year report of the LEADERS (Limus Eluted From A Durable Versus ERodable Stent Coating) Randomized, Non-inferiority Trial. *JACC Cardiovasc Interv* 2013;**6**:777–89.
12. Stefanini GG, Byrne RA, Serruys PW, de Waha A, Meier B, Massberg S *et al.* Biodegradable polymer drug-eluting stents reduce the risk of stent thrombosis at 4 years in patients undergoing percutaneous coronary intervention: a pooled analysis of individual patient data from the ISAR-TEST 3, ISAR-TEST 4, and LEADERS randomized trials. *Eur Heart J* 2012;**33**:1214–22.
13. Inoue T, Shite J, Yoon J, Shinke T, Otake H, Sawada T *et al.* Optical coherence evaluation of everolimus-eluting stents 8 months after implantation. *Heart* 2011;**97**:1379–84.

14. Kubo T, Akasaka T, Kozuma K, Kimura K, Fusazaki T, Okura H *et al.* Vascular response to drug-eluting stent with biodegradable vs. durable polymer. Optical coherence tomography substudy of the NEXT. *Circ J* 2014;**78**:2408–14.
15. van der Giessen WJ, Lincoff AM, Schwartz RS, van Beusekom HM, Serruys PW, Holmes DR Jr *et al.* Marked inflammatory sequelae to implantation of biodegradable and nonbiodegradable polymers in porcine coronary arteries. *Circulation* 1996; **94**:1690–7.
16. Barlis P, Regar E, Serruys PW, Dimopoulos K, van der Giessen WJ, van Geuns RJ *et al.* An optical coherence tomography study of a biodegradable vs. durable polymer-coated limus-eluting stent: a LEADERS trial sub-study. *Eur Heart J* 2010; **31**:165–76.
17. Natsuaki M, Kozuma K, Morimoto T, Shiomi H, Kimura T. Two-year outcome of a randomized trial comparing second-generation drug-eluting stents using biodegradable or durable polymer. *JAMA* 2014;**311**:2125–7.
18. Smits PC, Hofma S, Togni M, Vázquez N, Valdés M, Voudris V *et al.* Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent (COMPARE II): a randomised, controlled, non-inferiority trial. *Lancet* 2013;**381**:651–60.
19. Kang SH, Park KW, Kang DY, Lim WH, Park KT, Han JK *et al.* Biodegradable-polymer drug-eluting stents vs. bare metal stents vs. durable-polymer drug-elutingstents: a systematic review and Bayesian approach network meta-analysis. *Eur Heart J* 2014;**35**:1147–58.
20. Adriaenssens T, Ughi GJ, Dubois C, De Cock D, Onsea K, Bennett J *et al.* STACCATO (Assessment of Stent sTrut Apposition and Coverage in Coronary ArTeries with Optical coherence tomography in patients with STEMI, NSTEMI and stable/unstable angina undergoing everolimus vs. biolimus A9-eluting stent implantation): a randomised controlled trial. *EuroIntervention* 2014. doi: 10.4244/EIJY14M11_11.
21. Kuramitsu S, Sonoda S, Yokoi H, Iwabuchi M, Nishizaki Y, Shinozaki T *et al.* Long-term coronary arterial response to biodegradable polymer biolimus-eluting stents in comparison with durable polymer sirolimus-eluting stents and bare-metal stents: Five-year follow-up optical coherence tomography study. *Atherosclerosis* 2014;**237**: 23–9.
22. Räber L, Baumgartner S, Garcia-Garcia HM, Kalesan B, Justiz J, Pilgrim T *et al.* Long-term vascular healing in response to sirolimus- and paclitaxel-eluting stents: an optical coherence tomography study. *JACC Cardiovasc Interv* 2012;**5**:946–57.

IMAGE FOCUS

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Left ventricular asynchrony in early isolated cardiac sarcoidosis

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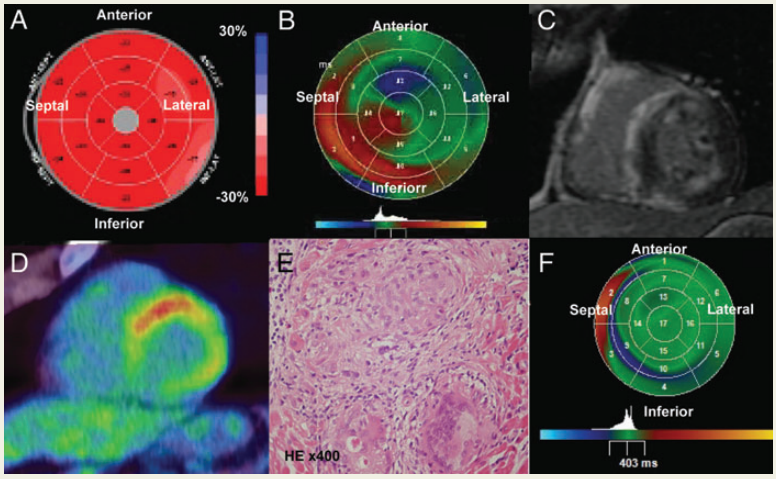

A 43-year-old asymptomatic man was screened for premature ventricular contractions on electrocardiography during an annual health check-up. Echocardiography demonstrated preserved left ventricular function with a normal radial strain profile (*Panel A*). However, three-dimensional analysis revealed left ventricular asynchrony with delayed peak excursion in the septal to inferior wall (*Panel B*). No abnormalities were detected on coronary computed tomographic angiography. Cardiac magnetic resonance imaging revealed late gadolinium enhancement in the septal to inferior wall (*Panel C*). Fluorodeoxyglucose-positron emission tomography/computed tomography demonstrated high uptake in the interventricular septum (*Panel D*). Endomyocardial biopsy of the interventricular septum demonstrated non-caseating granuloma (*Panel E*) with negative Ziehl–Neelsen staining results. Although the patient was in the early stage of cardiac sarcoidosis without major cardiac symptoms and other organ involvement, with positive tuberculin and negative laboratory test results (serum/urinary calcium and angiotensin-converting enzyme), he was successfully diagnosed using modern cardiac imaging modalities. Thus, the patient was treated with corticosteroids for 9 months, which improved the septal asynchrony (*Panel F*).

The prognosis of cardiac sarcoidosis is poor if untreated and immunosuppressive therapy is needed at the time of diagnosis. In our patient with early isolated cardiac sarcoidosis, the polar map of the peak excursion time on three-dimensional echocardiography enabled us to easily recognize asynchronically contracting sites of the left ventricle, which is one of the regions most commonly affected by cardiac sarcoidosis. This diagnostic tool has a potential to precisely screen for subclinical left ventricular dysfunction in early cardiac sarcoidosis.

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