Long-term tissue coverage of a biodegradable polylactide polymer–coated biolimus-eluting stent: Comparative sequential assessment with optical coherence tomography until complete resorption of the polymer

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Background Biolimus-eluting stents (BESs) with a biodegradable polymer in abluminal coating achieve more complete coverage at 9 months compared with sirolimus-eluting stents (SESs) with a durable polymer, as assessed by optical coherence tomography (OCT). Whether this advantage persists or augments after complete resorption of the polymer (>12 months) is unknown.

Methods The LEADERS trial compared the performance of BES with that of SES. Patients were randomly allocated to a sequential angiographic follow-up, including OCT in selected sites, at 9 and 24 months. Struts coverage was compared using Bayesian hierarchical models as the primary outcome for the OCT substudy.

Results Fifty-six patients (26 BES, 30 SES) were enrolled in the OCT substudy. Twenty-one patients (10 BES, 11 SES) agreed to perform a second OCT follow-up at 24 months. Eleven lesions and 12 stents were analyzed sequentially in the BES group (2,455 struts at 9 months, 2,131 struts at 24 months) and 11 lesions and 18 stents in the SES group (3,421 struts at 9 months, 4,170 struts at 24 months). The previously reported advantage of BES over SES in terms of better strut coverage at 9 months was followed by improvement in coverage of the SES, resulting in identical coverage in both BES and SES at 24 months: 1.5% versus 1.8% uncovered struts, difference –0.2%, 95% credibility interval, –3.2% to 2.6%, $P = .84$.

Conclusions More complete strut coverage of BES as compared with SES at 9 months was followed by improvement of coverage in SES between 9 and 24 months and a similar long-term coverage in both stent types at 24 months. (Am Heart J 2011;162:922-31.)

Drug-eluting stents (DESs) have reduced restenosis rates to approximately 9%,[1] but they might pose a higher risk of late and very late stent thrombosis,[1] with the common pathological finding of delayed neointimal healing and incomplete endothelialization.[2,3] In first-generation DES, the mechanism for incomplete neointimal coverage seems to go beyond the antiproliferative potency of the drug and also involve an inflammatory reaction.[3-6] The presence of intense eosinophilic infiltrates in the vessel wall[3] and in the thrombus harvested from patients with very late stent thrombosis[4] suggests that inflammation might be mediated by delayed type IVb hypersensitivity. Hypersensitivity is likely triggered by the polymer rather than by other components of the device,[6] given the timing of onset (later than 90 days, when the drug is no longer detectable in the vessel wall) and the presence of polymer fragments surrounded by giant cells.[3,5] An interesting approach to minimize polymer-induced inflammation consists of coating the metallic backbone of the stent with a biodegradable polymer

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that is fully resorbed after elution of the drug.[7] The risk of delayed hypersensitivity disappears together with the potential allergens, and complete neointimal healing is no longer in jeopardy.

The LEADERS trial was the first published randomized study to use optical coherence tomography (OCT) for the evaluation of tissue coverage in 2 different types of DES.[8,9] It compared a new-generation biolimus-eluting stent (BES) with a biodegradable polymer in abluminal coating versus a first-generation sirolimus-eluting stent (SES) with a durable polymer in conformal coating. At 9 months, BES showed a lower proportion of uncovered struts compared with SES (weighted estimate 0.6% vs 2.1%, $P = .04$).[9] The aim of this study was to assess whether this difference persists after complete resorption of the BES polymer.

Methods

Study population and design

The design and main results from the LEADERS trial have been published elsewhere.[8] It was an international randomized multicenter noninferiority trial comparing the BES BioMatrix Flex stent (Biosensors International, Morges, Switzerland) with the SES Cypher SELECT stent (Cordis, Miami Lakes, FL), following an all-comers approach with minimal exclusion criteria: patients with symptomatic coronary heart disease or silent ischemia were eligible if they had at least one coronary lesion of ≥50% diameter stenosis in vessels with 2.25- to 3.50-mm reference diameters, amenable for percutaneous treatment. The primary end point was a composite of cardiac death, myocardial infarction, and clinically indicated target vessel revascularization at 9 months of follow-up.

Patients were randomly allocated on a 1:1 basis to receive either BES or SES using random computer-generated sequences, stratified according to center. In a factorial design, they were additionally randomized on a 1:3 basis to angiographic and clinical follow-up at 9 months or clinical follow-up alone. Patients allocated to angiographic follow-up in 2 of the study sites (Royal Brompton Hospital [London, UK], and Erasmus MC [Rotterdam, the Netherlands]) were also included in the OCT substudy. Serum creatinine ≥200 mol/L and left ventricular ejection fraction <30% were the exclusion criteria for the OCT substudy. The primary end point for the OCT substudy was the proportion of uncovered struts at 9 and 24 months. The study complied with the Declaration of Helsinki, was approved by all institutional ethics committees, and was registered at clinicaltrials.gov (NCT00389220). All patients provided written informed consent for participation.

Intervention and study stents

Direct stenting was allowed, and full lesion coverage was pursued by implanting one or several stents, as required. Only 1 type of DES was used per patient.

The BioMatrix Flex stent (Biosensors International) consists of a stainless-steel platform (Juno; Biosensors International) coated by an abluminal 11-μm layer of polylactide polymer. The polymer contains Biolimus-A9 (Biosensors International, Morges, Switzerland) at a concentration of 15.6 μg/mm of stent length. Polylactide is linearly degraded by surface hydrolysis to lactide during a period of 6 to 12 months, resulting in simultaneous release of the drug.[7] The Cypher SELECT stent (Cordis) consists of a stainless-steel platform coated by a durable blend of poly(ethylene-vinyl-acetate) and poly(butyl-methacrylate) containing sirolimus at a concentration of 8.3 to 10.4 μg/mm, depending on the stent nominal diameter. The drug elution period is estimated to be 90 days. After the intervention, the patients received at least 75 mg of acetylsalicylic acid indefinitely and dual-antiplatelet therapy with 75 mg of clopidogrel for 12 months.

Table I. Characteristics of the different OCT systems* in the study

		M3	C7
Domain		Time	Fourier
Catheter*		ImageWire	Dragonfly
Rotation speed (Hz)		20	100
Pullback speed (mm/s)		3	20
Patients with SES	9 mo	11	0
	24 mo	3	8
Patients with BES	9 mo	10	0
	24 mo	3	7

* All systems and catheters were obtained from Lightlab Imaging.

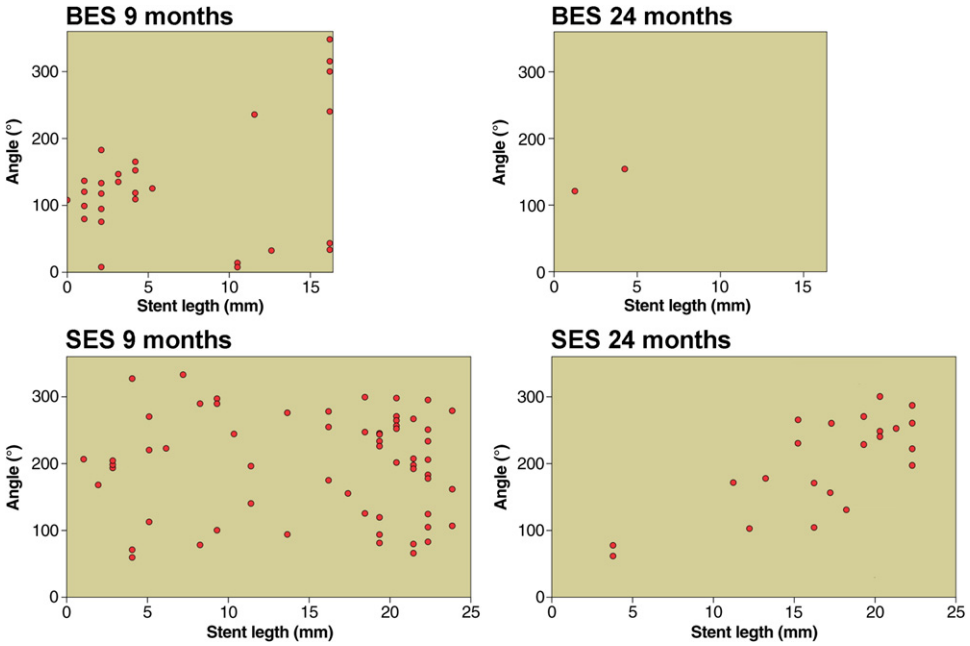
OCT study and analysis

Optical coherence tomography pullbacks were obtained at 9 and 24 months of follow-up with M3 or C7 systems (Lightlab Imaging, Westford, MA), depending on availability, using a nonocclusive technique[10] (Table I). Optical coherence tomography pullbacks were analyzed offline in a core laboratory (Cardialysis BV, Rotterdam, the Netherlands) by independent staff blinded to allocation and to clinical or procedural characteristics of the patients using proprietary software (Lightlab Imaging). Cross sections at 1-mm intervals within the stented segment were analyzed. Lumen and stent areas were drawn in each cross section, and incomplete stent apposition (ISA) or neointimal hyperplasia (NIH) areas were calculated, as appropriate.[11] Apposition was assessed per strut by placing a marker at the adluminal leading edge, in the midpoint of the strut's long axis, and by measuring the distance between this marker and the lumen contour, following a straight line directed to the center of gravity of the vessel.[12] Struts were considered malapposed if the distance was ≥170 μm (for SES) or ≥140 μm (for BES), the thresholds resulting from rounding up the sum of the strut-polymer thickness of each stent (SES 153 μm, BES 120 μm) plus the axial resolution of OCT (14 μm). Struts located at the ostium of side branches, with no vessel wall behind, were labeled as nonapposed side-branch struts and excluded from the analysis of apposition.[13,14]

Struts were classified as uncovered if any part of the strut was visibly exposed to the lumen, or as covered if a layer of tissue was visible over all the reflecting surfaces. In covered struts, thickness of coverage was measured from the strut marker to the adluminal edge of the tissue, following a straight line connecting the strut marker with the center of gravity of the vessel.[11,13–15]

The clustering and spatial distribution of uncovered struts were summarized in "spread-out vessel graphics"[13] (Figure 1).

Figure 1



Examples of spatial distributions of uncovered struts in spread-out-vessel graphs. Examples of 1 BES (upper panel) and 1 SES (lower panel) studied with OCT at 9 and 24 months. The *x*-axis represents the distance from the distal edge of the stent to the strut; the *y*-axis represents the angle where the strut is located in the circular cross section with respect to the center of gravity of the vessel. The result is a graph representing the spatial distribution of the noncovered struts (red spots) along the stent, as if it had been cut along the reference angle (0°) and spread out on a flat surface.

Statistical analysis

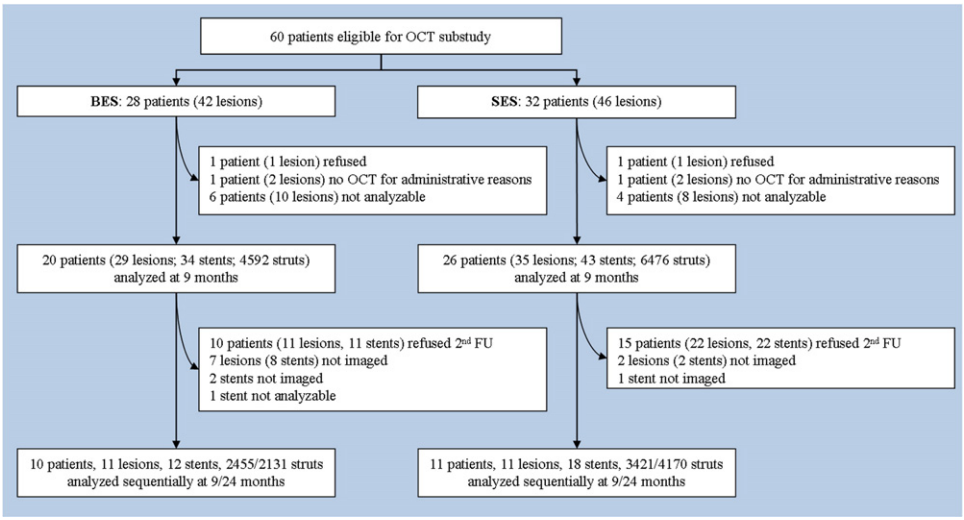
Prespecified primary outcome was the difference in percentage of uncovered struts at 24 months. Assuming an average number of 1.5 lesions per patient and 180 struts per lesion, an intracluster correlation coefficient of 0.04 for binary coverage of struts within lesions, and a design factor of 1.3, we estimated that the inclusion of 22 patients (with 33 lesions and 5,940 struts) per group would yield a greater than 90% power to detect a difference in uncovered struts of 4% at 9 months between BESs and SESs at a 2-sided type I error of 0.05. Secondary outcomes comprised other variables assessing coverage, ISA, and the geometric mean thickness of coverage. To estimate the differences between BES and SES, we used a Bayesian hierarchical random-effects model based on Markov chain Monte Carlo simulations with minimally informative priors.[9] The model included random effects at the level of lesions and patients, fully accounting for the correlation of lesion characteristics within patients and their variation between patients. We used the Wilcoxon test for continuous variables and the Pearson χ^2 or Fisher exact test as appropriate for dichotomous variables to compare baseline characteristics as well as areas and volumetric parameters per stent. Statistical analyses were performed using WinBUGS version 1.4.3 (Imperial College and Medical Research Council, London, UK) and Stata release 11 (StataCorp, College Station, TX).

The LEADERS trial (NCT00389220) and this OCT substudy have been sponsored by Biosensors International. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

Results

Eighty-eight patients (43 BES, 45 SES) were allocated to angiographic follow-up in the OCT study centers. Optical coherence tomography studies from 46 patients were finally analyzed at 9 months (Figure 2). All 46 patients were contacted at 24 months, but 25 refused to participate in a second invasive follow-up (20 BES, 26 SES). Sequential OCT follow-up was analyzed in 10 patients, 11 lesions, and 12 stents in the BES group (2,455 struts at 9 months, 2,131 struts at 24 months) and in 10 patients, 11 lesions, and 18 stents in the SES group (3,421 struts at 9 months, 4,170 struts at 24 months). All 9-month studies were performed with a time-domain M3 system, whereas 15 studies at 24 months (71%) were performed with a Fourier-domain C7 system (Table I).

Figure 2



Flowchart of the OCT study and sequential follow-up.

Table II. Patients' characteristics

	BES (n = 10)	SES (n = 11)	*P*
Age (y), mean (SD)	61.3 (6.6)	60.3 (10.8)	.78
Male	7 (70)	7 (64)	1.00
Diabetes mellitus	2 (20)	2 (18)	1.00
Hypertension	3 (30)	6 (55)	.39
Hypercholesterolemia	5 (50)	9 (82)	.18
Smoking	3 (30)	7 (64)	.20
Previous MI	4 (40)	5 (45)	1.00
Previous PCI	2 (20)	3 (27)	1.00
Previous CABG	1 (10)	1 (9)	1.00
Clinical presentation			
Stable angina	6 (60)	6 (55)	1.00
Acute coronary syndrome	4 (40)	5 (45)	1.00
Unstable angina	0 (0)	2 (18)	
NSTEMI	1 (10)	2 (18)	
STEMI	3 (30)	1 (9)	
Angiographic characteristics			
No. of lesions per patient, mean (SD)	1.8 (0.9)	1.2 (0.4)	.09
Multivessel disease	4 (40)	0 (0)	.035
Long lesions (>20 mm)	3 (30)	6 (55)	.39
Small-vessel disease (RVD < 2.75mm)	6 (60)	8 (73)	.66

Results are expressed as n (%) unless otherwise indicated. *MI* indicates myocardial infarction; *PCI*, percutaneous coronary intervention; *CABG*, coronary artery bypass graft; *NSTEMI*, non–ST elevation myocardial infarction; *STEMI*, ST elevation myocardial infarction; *RVD*, reference vessel diameter.

Table III. Angiographic and procedural characteristics of the lesions

	BES (n = 11)	SES (n = 11)	*P*
Coronary artery of the target lesion			.51
LAD	6 (55)	3 (27)	
LCX	1 (9)	1 (9)	
RCA	4 (36)	7 (64)	
De novo lesions	10 (91)	11 (100)	
Bifurcation	2 (18)	2 (18)	1.00
Total occlusion	5 (45)	4 (36)	1.00
Severe calcification	1 (9)	2 (18)	1.00
QCA (in-stent)			
Lesion length (mm), mean (SD)	18.4 (14.6)	30.0 (29.0)	.53
RVD (mm), mean (SD)			
Pre-stenting	2.8 (0.5)	2.7 (0.6)	.81
Post-stenting	2.5 (0.5)	2.7 (0.6)	.45
9 mo	2.5 (0.4)	2.8 (0.6)	.19
MLD (mm), mean (SD)			
Pre-stenting	0.7 (0.8)	0.7 (0.6)	.94
Post-stenting	2.3 (0.4)	2.3 (0.5)	.87
9 mo	2.1 (0.8)	2.1 (0.6)	.68
Late lumen loss (mm)	1.4 (0.8)	1.3 (0.4)	.65
Procedural characteristics, mean (SD)			
No. of study stents per lesion	1.5 (0.7)	2.0 (1.2)	.33
Maximal stent diameter per lesion	3.1 (0.3)	3.1 (0.5)	.87
Total stent length per lesion	28.6 (21.2)	45.5 (34.7)	.18
Direct stenting	5 (45)	4 (36)	1.00

Results are expressed as n (%) unless otherwise indicated. *LAD* indicates left anterior descending; *LCX*, left circumflex; *RCA*, right coronary artery; *QCA*, quantitative coronary angiography; *RVD*, reference vessel diameter; *MLD*, minimal lumen diameter.

The baseline characteristics of the patients and lesions were comparable between both groups (Tables II and III). Table IV shows the mean areas and volumes per stent. At 9 months, corrected ISA volume was higher in

Table IV. Areas and volumetric analysis per stent (excluding overlap segments) at 24-month follow-up

	9 mo			24 mo		
21 patients, 22 lesions, 30 stents	**BES: 10 patients, 11 lesions, 12 stents**	**SES: 11 patients, 11 lesions, 18 stents**	***P***	**BES: 10 patients, 11 lesions, 12 stents**	**SES: 11 patients, 11 lesions, 18 stents**	***P***
Stented length (mm)	23.43 (13.87)	35.84 (24.78)	.193	23.05 (13.13)	35.82 (26.20)	.401
MLA (mm^2)	4.86 (2.40)	4.58 (2.46)	.748	4.89 (1.73)	4.96 (2.30)	.898
Lumen volume (mm^3)	144.69 (69.37)	252.92 (189.96)	.438	145.91 (77.34)	260.44 (176.21)	.300
Minimum stent area (mm^2)	5.38 (2.11)	5.03 (2.18)	.606	5.87 (1.52)	5.68 (2.42)	.949
Stent volume (mm^3)	158.79 (73.43)	263.02 (197.75)	.562	170.13 (87.40)	287.54 (196.02)	.365
ISA volume (mm^3)	0.24 (0.45)	4.28 (10.09)	**.040**	0.13 (0.44)	1.48 (2.11)	.151
Corrected by stent volume (%)	0.15 (0.24)	1.76 (3.52)	**.047**	0.11 (0.35)	0.78 (1.34)	.171
NIH volume (mm^3)	14.33 (18.57)	14.50 (18.17)	1.000	24.35 (18.86)	28.58 (29.12)	.949
Percent NIH volume obstruction (%)	9.02 (10.02)	5.76 (5.03)	.606	14.53 (9.57)	9.43 (5.37)	.171

MLA, Minimal lumen area.
P-values ≤ 0.05 in bold.

SES than in BES ($P \leq .047$), decreasing in both groups at 24 months and making the difference no longer significant ($P \leq .171$).

Figure 3 shows the evolution of coverage between 9 and 24 months in representative cross sections, matched using fiduciary landmarks. A total of 121 of 2,455 and 69 of 2,131 struts were uncovered in the BES group at 9 and 24 months, respectively; 286 of 3,421 and 109 of 4,170 struts were uncovered in the SES group at 9 and 24 months, respectively. At 9 months, the overall proportion of uncovered struts tended to be higher in SES than in BES, although it did not reach conventional levels of statistical significance (Table V). At 24 months, the proportion of uncovered struts decreased to similar levels in both groups (weighted percentage 2%) (Table V, Figure 4). The spread-out-vessel charts present the results for individual patients, showing the spatial distribution and temporal evolution of uncovered struts in 30 stents (Figure 5). There was little evidence for the differences in thickness of coverage or in the variables estimating apposition between the treatment groups at 9 or 24 months (Table V, Figure 6).

Discussion

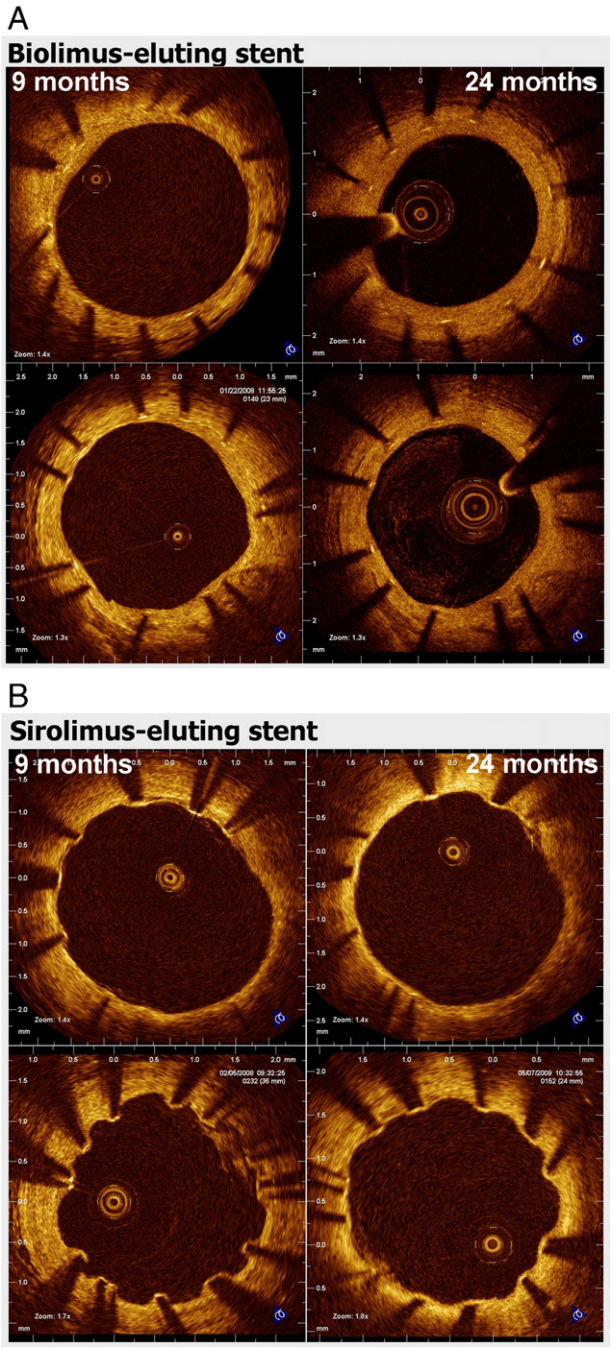
In this sequential OCT study nested in a randomized comparison of 2 different DESs, we found that the advantage of a BES with a biodegradable polymer in abluminal coating over an SES with a durable polymer in terms of strut coverage at 9 months[9] was followed by improvement of the SES coverage between 9 and 24 months, resulting in similar coverage in BES and SES at 24 months. Both types of stent converged at a maximum plateau around 98% strut coverage. Taken together, our results suggest that BES, indeed, is associated with faster healing compared with SES, achieving a percentage of coverage close to the maximum plateau (97%) at 9 months, whereas SES is catching up subsequently.

To our knowledge, this is the first clinical in vivo study using sequential OCT to compare the coverage of 2 different types of DES. Previous sequential studies had reported SES coverage at 6 to 12 months[16] and at 24 to 48 months[17] using OCT, or at 4-11-21 months using angioscopy[18]; the latter was compared with a control bare metal stent.

"Very late healing" phenomenon

The improvement in coverage observed in SES between 9 and 24 months challenges the currently accepted evidence about the healing process after stenting and compels us to reconsider the initial interpretation of the 9-month results.[9] Experimental studies suggested that the reendothelialization process ensuing a vessel injury, for example, stenting, was limited in time.[19-21] Endothelial denudation of carotid arteries is followed by reendothelialization that stops after 2 weeks (in the rabbit) or after 6 weeks (in the rat), although endothelial continuity has not been restored.[22,23] This experimental evidence seemed consistent with the results of sequential angioscopic studies in SES, showing no improvement in the minimum coverage between 6 and 24 months, with an increase in the maximum[24] and only slight improvement in the predominant score at 4-11-21 months,[18] eventually suggesting an arrested healing process undergoing phenomena of intima maturation or plaque progression. Our results question this static time-limited model of neointimal healing, suggesting a more dynamic process, still evolving between 9 and 24 months. Previous noncomparative studies using OCT suggested also this possibility: improvement of SES coverage has been reported at 3-24-48 months[17,25,26] or between 6 and 12 months.[16] Because of its high resolution (10-20 μm) and ability for detailed analysis, OCT could detect subtle changes in neointimal coverage, which are unnoticed for angioscopy or other imaging techniques. The evolution of neointimal volumes,

Figure 3



A, Representative examples of matched cross sections at 9 and 24 months in BESs showing the pattern of coverage. **B**, Representative examples of matched cross sections at 9 and 24 months in SESs showing the pattern of coverage.

increasing similarly in both stent groups between 9 and 24 months (Table IV), might indicate an actively repairing neointima but can also be the consequence of intima maturation or plaque progression. The ISA reduction between 9 and 24 months is more specific as an indicator of very late healing. Higher incidence of ISA in the SES group had been reported at 9 months[9] and interpreted in terms of late-acquired ISA. This interpretation now becomes unlikely because the most pronounced reduction in ISA between 9 and 24 months is observed in SES. This is in disagreement with previous sequential studies reporting an increase in ISA areas and ISA struts between 24 and 48 months in SES.[17] This discrepancy deserves further clarification in the future.

Different healing rates in different types of stent

The design of our study does not permit to elucidate the mechanism for the different healing rates observed between the devices. Although inflammation was the driving hypothesis for this study and was advocated to explain the differences reported at 9 months,[9] it cannot satisfactorily explain the very late healing. Why does the initial advantage in coverage not persist after the proinflammatory polymer has completely disappeared in one of the devices? The role played by polymer-induced inflammation[6] in the neointimal healing after stenting should be revisited: its deleterious effect might be not as sustained in time as currently assumed, with the exception of infrequent delayed hypersensitivity reactions.[3,4] The kinetics of release differ from the coverage rates observed: the elution periods for SES and BES are 90 days and 6 to 9 months, respectively. The different inhibitory potency, lipophilicity, concentration, or pleiotropic effects of biolimus and sirolimus have played a role: the effective neointimal inhibition could be more intense in SES than in BES. Likewise, the design and geometry of the stent platforms could have promoted faster healing in the BES, especially the strut thickness. Both platforms are made of stainless steel, hence requiring thick struts (>100 μm) to provide enough radial strength for vessel scaffolding; but BES struts are slightly thinner (120 μm) than SES struts (140 and 154 μm if we add the polymer thickness), which is associated with faster healing.[27] The selective abluminal coating of BES appears to be a more plausible explanation: the abluminal release of the drug might modulate the proliferation of smooth muscle cells in the media that minimally interferes with the reendothelialization of the adluminal side, thus promoting a faster reendothelialization.

Clinical implications

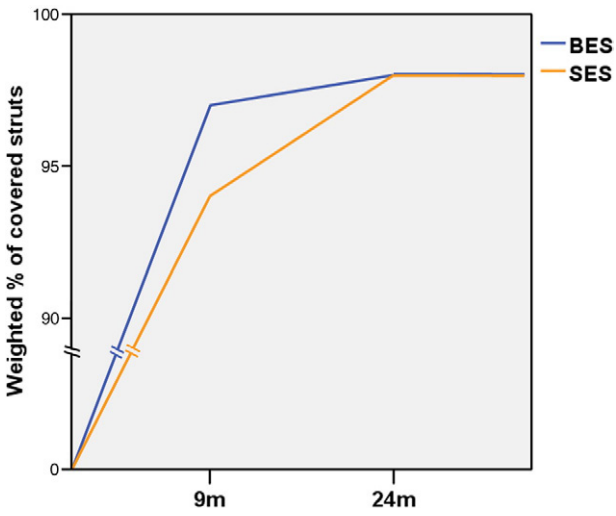
Very late healing could be key to understanding why clinical studies have failed to demonstrate higher rates of stent thrombosis in SES,[28] although angioscopy[18,24] or OCT[16,17,25,26] have reported suboptimal coverage between 3 and 48 months. As suggested by our results and also by other studies,[18,26] longer follow-up intervals

Table V. Analysis of apposition and coverage per strut at 9 and 24 months

21 patients, 22 lesions, 30 stents			BES: 10 patients, 11 lesions, 12 stents; weighted % (95% CrI)	SES: 11 patients, 11 lesions, 18 stents; weighted % (95% CrI)	Comparison	
					Difference (95% CrI)	*P*
9 mo	Struts	6226	2640	3586		
	Coverage	Uncovered struts*	2.8 (0.9-7.3)	5.7 (2.0-14.3)	−2.9 (−11.6 to 2.9)	.31
		Lesions with				
		≥10% uncovered struts	18.6 (2.2-60.3)	29.8 (5.2-71.7)	−9.6 (−57.2 to 37.8)	.66
		≥5% uncovered struts	42.9 (9.8-82.9)	58.0 (17.7-90.6)	−14.0 (−65.3 to 43.2)	.63
		Any uncovered struts	91.6 (59.5-99.4)	100.0 (92.6-100.0)	−7.9 (−40.0 to 0.2)	.054
		Thickness of coverage (μm)†	56.7 (32.5-101.9)	41.6 (23.4-70.2)	14 (−21 to 64)	.41
	Apposition	ISA struts	0.5 (0.2-1.5)	1.4 (0.5-3.5)	−0.8 (−3.0 to 0.4)	.18
		Lesions with				
		≥10% ISA struts	0.0 (0.0-1.3)	3.2 (0.1-27.2)	−3.1 (−27.2 to −0.0)	.035
		≥5% ISA struts	0.0 (0.0-1.3)	3.2 (0.1-27.2)	−3.1 (−27.2 to −0.0)	.035
		Any ISA struts	73.2 (29.9-96.1)	91.6 (56.2-99.3)	−16.2 (−61.8 to 22.5)	.34
24 mo	Struts	6490	2337	4153		
	Coverage	Uncovered struts*	1.5 (0.5-4.2)	1.8 (0.6-4.5)	−0.2 (−3.2 to 2.6)	.84
		Lesions with				
		≥10% uncovered struts	2.9 (0.1-25.4)	0.0 (0.0 to −)‡	2.9 (0.0-25.4)	.012
		≥5% uncovered struts	31.2 (5.5-74.3)	8.2 (0.6-41.4)	20.2 (−18.1 to 66.7)	.27
		Any uncovered struts	73.1 (30.1-96.0)	97.2 (74.7-100.0)	−21.9 (−65.7 to 6.0)	.12
		Thickness of coverage (μm)†	86.4 (60.2-121.4)	62.2 (44.5-87.7)	24 (−15 to 62)	.17
	Apposition	ISA struts	0.1 (0.0 to −)‡	0.4 (0.1-1.4)	−0.3 (−1.3 to 0.1)	.15
		Lesions with				
		≥10% ISA struts	0.0 (0.0-0.7)	0.0 (0.0-0.7)	−0.0 (−0.7 to 0.6)	.49
		≥5% ISA struts	0.0 (0.0-1.1)	2.7 (0.0-25.0)	−2.6 (−24.9 to −0.0)	.042
		Any ISA struts	18.6 (2.3-60.3)	71.3 (27.0-95.1)	−48.7 (−85.1 to 5.2)	.08

Weighted percentages and differences are derived from medians and 25th and 97th percentiles of the corresponding posterior distributions in WinBugs. *CrI* indicates credibility interval.
* Prespecified primary outcome of OCT substudy.
† Averages are geometric means and differences in geometric means derived from posterior distributions in WinBugs (Imperial College and Medical Research Council, London, UK).
‡ Note that the upper limit of the 95% CrI could not be estimated.

Figure 4



Trend graph showing the weighted percentage of covered struts at 9 and 24 months for both types of stent.

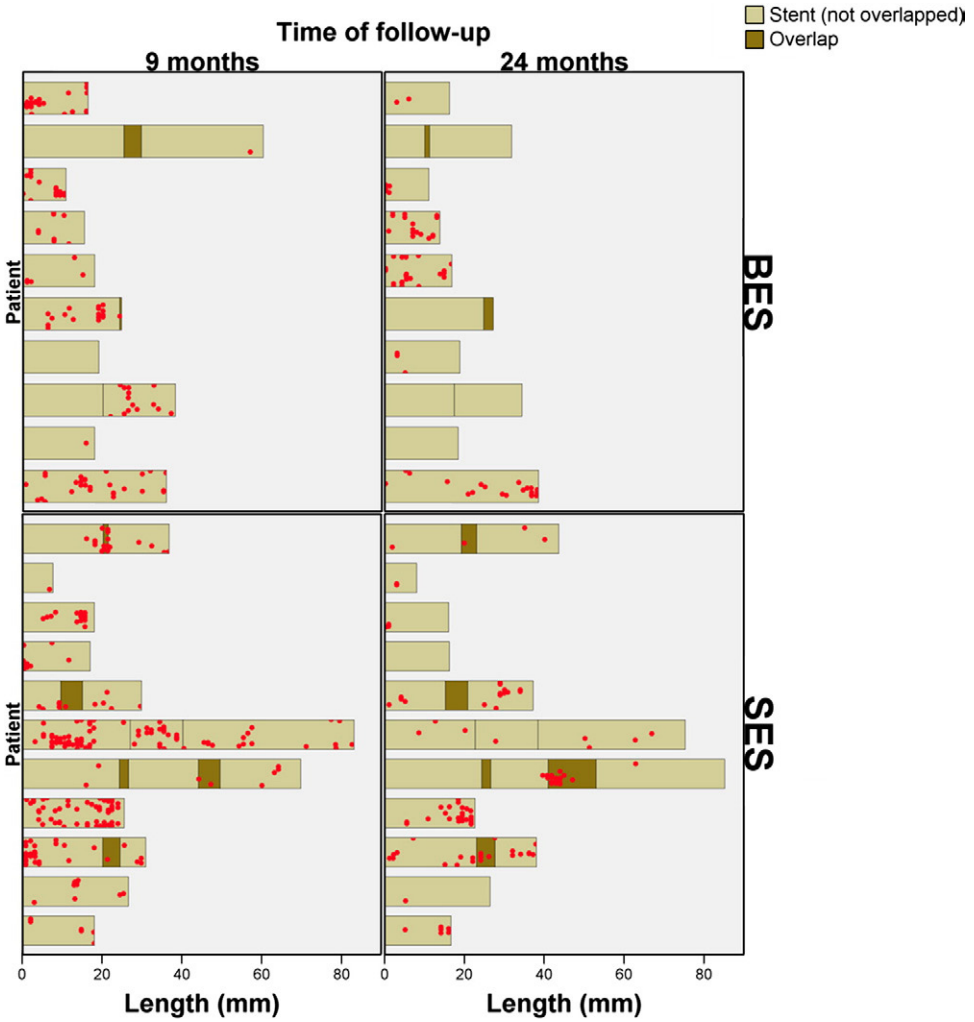
would be required to assess the final neointimal coverage achieved.

To our knowledge, this is the first sequential OCT study suggesting that different types of stent can promote different healing rates. This may be relevant for tailoring the duration of dual-antiplatelet therapy after stenting.

Limitations

The refusal of some patients to undergo the 24-month OCT follow-up is the main limitation of this study. It might have induced some selection bias because the patients with more favorable outcome might have been more prone to refuse a second invasive follow-up. The lack of statistical significance at 9 months in this second analysis is also explained by the substantial loss of statistical precision resulting from the restricted sample size and not contradictory with the previously published results.[9] The high percentage of refusals turned this study underpowered to detect the difference of the same magnitude.

Figure 5



Spread-out-vessel charts showing the spatial distribution of uncovered struts at 9 and 24 months in the matched stents.

Conclusion

Better strut coverage of a BES with a biodegradable polymer and abluminal coating as compared with a first-generation SES with a durable polymer at 9 months was followed by improvement in coverage of the latter stent and similar long-term OCT outcomes in both stent types at 24 months.

Disclosures

Conflict of interest: This trial has been sponsored by Biosensors International. The participating centers (Royal Brompton, Erasmus MC, and Bern University Hospitals) and the core laboratory (Cardialysis BV) have received grants from Biosensors to conduct the LEADERS trial and this substudy. Windecker, Serruys, and di Mario have received speaker's fees from the sponsor. Susanne Meis is a full-time employee in Biosensors International.

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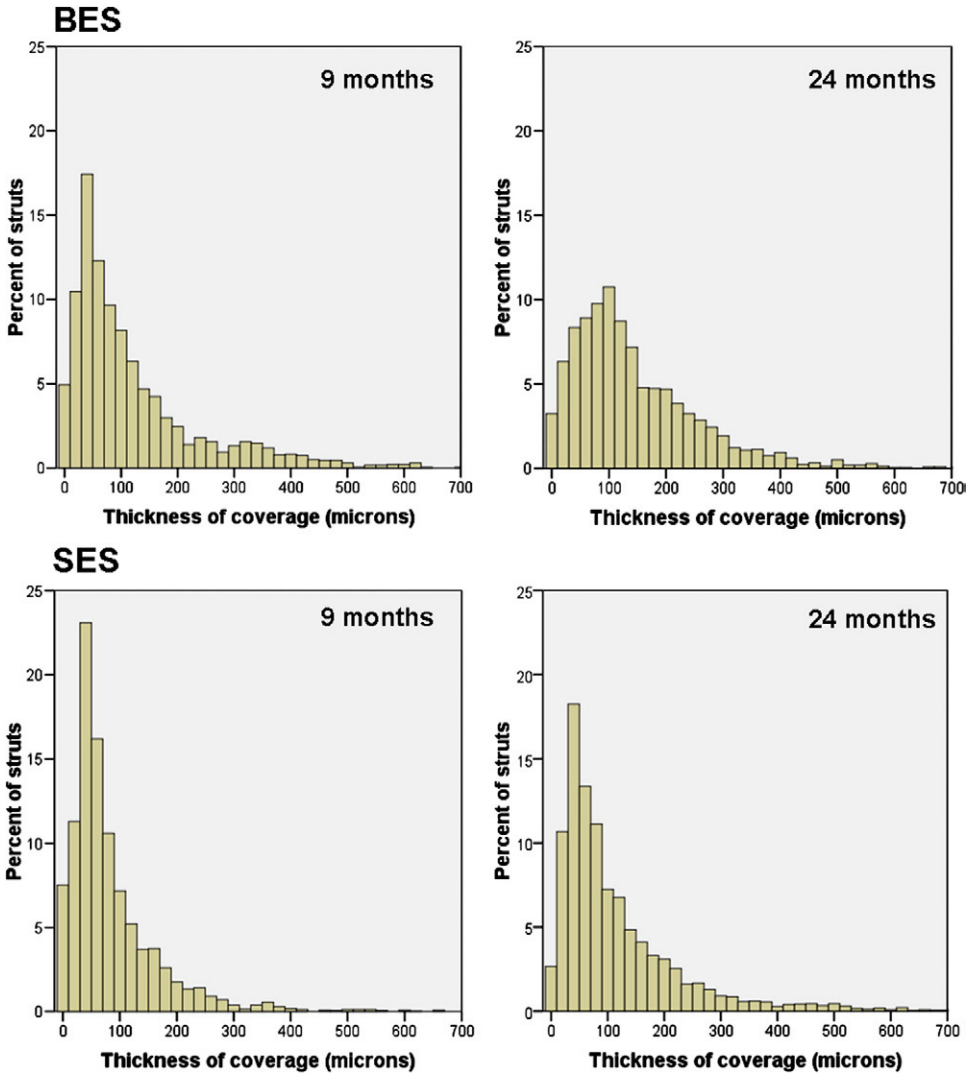
Figure 6



Histograms showing the distribution of the thickness of coverage at 9 and 24 months in the 2 types of stent.

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