Established in 1871

Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • www.smw.ch

Original article | Published 14 January 2016, doi:10.4414/smw.2016.14274

Cite this as: Swiss Med Wkly. 2016;146:w14274

Vascular response to everolimus- and biolimus-eluting coronary stents versus everolimus-eluting bioresorbable scaffolds – an optical coherence tomography substudy of the EVERBIO II trial

Zacharenia Kallinikou, Diego Arroyo, Mario Togni, Sonja Lehmann, Noé Corpataux, Malica Cook, Olivier Müller, Gérard Baeriswyl, Jean-Christophe Stauffer, Jean-Jacques Goy, Serban Puricel, Stéphane Cook

Hospital and University Fribourg, Fribourg, Switzerland

Summary

QUESTIONS UNDER STUDY: Head-to-head optical coherence tomography (OCT) data comparing metallic stents with bioresorbable vascular scaffolds (BVS) are lacking. This study assessed vascular healing at 9-month follow-up after implantation of everolimus- and biolimus-eluting stents (EES; BES) and everolimus-eluting BVS.

METHODS: OCT was performed in 74 patients enrolled in the EVERBIO II (NCT01711931) trial (23 with EES: 26 lesions, 7 625 struts; 23 with BES: 26 lesions, 6 140 struts; 28 with BVS: 33 lesions, 10 891 struts). OCT images were acquired using the pullback and nonocclusive flushing technique and analysed offline.

RESULTS: BVS demonstrated fewer uncovered struts per patient (12 ± 27 [3.8 ± 8.4%] vs 59 ± 55 [21.8 ± 13.7%] in the EES&BES group, p <0.001), and thicker neointimal hyperplasia (BVS 102 ± 44 µm vs EES&BES 66 ± 36 µm, p <0.01). There was no significant difference with regard to malapposed struts (2.1 ± 2.7% in the BVS vs 4.4 ± 8.8% in the EES&BES group, p = 0.41). In a predefined signal intensity scale, quantitative analysis of the "key component" (black) revealed lower intensity in BVS than EES&BES (14 ± 23% vs 13 ± 12%, p = 0.007). Intensity was lower in polylactide-containing stents (BVS&BES) than in EES (15 ± 19% vs 10 ± 10%, p <0.001).

CONCLUSIONS: BVS has fewer uncovered struts and presents with a thicker neointimal coverage compared with EES&BES. It is not known whether this improved capping correlates with superior vascular healing. Polylactide-containing stents (BVS and BES) demonstrate lower peristrut intensity compared with EES.

Clinicaltrials.gov registration: NCT01711931

Key words: *coronary artery disease; drug-eluting stent; bioresorbable vascular scaffold; optical coherence tomography*

Introduction

The development of drug-eluting stents (DES) has been associated with a significant reduction in the rate of target lesion revascularisation [1]. Early generation DES however, suffered a significant rate of late complications (stent thrombosis and/or neoatherosclerosis) [2, 3]. Newer generations of DES have improved short- and long-term safety. Of these, second-generation everolimus-eluting stents (EES) using a biocompatible durable polymer (fluorinated copolymer) with thin strut (81 µm) and third generation biolimus-eluting stents (BES) using an abluminally coated biodegradable polymer (polylactide) with relatively thick struts (112 µm) are currently considered the safest DES [4–13]. The issue of neointimal proliferation and very late stent thrombosis from lingering polymers and vascular scaffolds has led to the development of completely resorbable stents, among which are the everolimus-eluting bioresorbable vascular scaffolds (BVS).

Several optical coherence tomography (OCT) studies have evaluated the vascular healing response to EES, BES [14–16] and BVS [17, 18]. To date, head-to-head OCT data comparing BVS with EES and/or BES are scarce. We therefore sought to assess vascular healing in BVS compared with EES&BES using OCT, 9 months after stent implantation.

Methods

Patient population

This study was a substudy of the EVERBIO II trial (Comparison of Everolimus- and Biolimus-Eluting Coronary Stents with Everolimus-Eluting Bioresorbable Vascular Scaffold), a prospective, single centre, assessor-blinded, randomised, superiority trial comparing EES&BES with BVS, the results of which have previously been published [19, 20]. A total of 240 patients with coronary artery disease were recruited between November 2012 and November 2013 at the University and Hospital Fribourg (Switzer-

land). The only exclusion criterion was a reference vessel size of >4.0 mm which precluded BVS implantation.
The inclusion period of the substudy extended from January 2013 to June 2014. The first 25–30 consecutive patients in each treatment group willing to undergo additional intracoronary imaging were included in the present substudy. Assessment of OCT outcomes was not blinded.
The study complied with the Declaration of Helsinki and was approved by the local ethics committee and all patients gave written, informed consent. The trial is registered in ClinicalTrials.gov, number NCT01711931.

OCT acquisition and analysis

Per protocol OCT acquisition was planned at 9-month angiographic follow-up. After the diagnostic angiography, 200 µg of i.c. nitroglycerin and 2 500–5 000 IU of unfractionated heparin were administrated. OCT was performed with the Optis Illumen system (St. Jude Medical) according to manufacturer guidelines using the Dragonfly™ Duo OCT Imaging Catheter with "54 mm high resolution mode" pullback, the nonocclusive flushing technique and a pullback speed of 25 mm/s. OCT pullbacks were assessed offline using a proprietary software (Lightlab Imaging, St. Jude Medical). Lesions were analysed at cross-sectional level with an interval of 0.5 mm and assessed for strut coverage, malapposition and protrusion by a single analyst (ZK) blinded to patient and lesion presentation. All frames were reviewed by a second analyst (SC) with the final decision based on consensus. Pullbacks were excluded in cases where >30% of the total stent length was not analysable. Thickness of strut coverage was assessed for each individual strut and was measured as the distance between the endoluminal side of the strut in the midpoint of its long axis and the intersection of the lumen contour with the straight line between the endoluminal side of the strut and the gravitational centre of the vessel. Struts were considered uncovered in the case of a partial or complete absence of tissue coverage (<10 µm, minimal axial resolution of OCT). Strut malapposition was defined as a distance ≥163 µm for BVS (strut thickness 153 µm), ≥122 µm for BES (strut thickness 112 µm) and ≥91 µm for EES (strut thickness 81 µm) based on the consensus derived from the strut thickness plus the minimal axial resolution of OCT. Strut protrusion was defined as strut extension into the lumen for more than 160 µm but with no obvious separation from the vessel wall. Cross-sectional areas of lumen, stent and neointima were measured at intervals of 0.5mm in the stented segment, as well as the luminal areas of the proximal and distal nonstented reference segments. Neointima area was defined as stent area minus lumen area; volumes were calculated using Simpson's rule. Representative images of OCT analyses for both BVS and DES are provided on figure 1. The peristrut low intensity area (PLIA) was analysed quantitavely by measuring the intensity of the "key" component of the CMYK colour model based on raw cross-sectional images, with an interval of 1/10 of the lesion length at the mid-strut depth and at equal distance between two contiguous struts. This quantitative measure reflects the "darkness of the pixels". Peristrut intensity was reported as percentage decrease of intensity units of the "key" component of the CMYK colour model. Further definitions with regard to OCT analysis can be found in the appendix to this article.

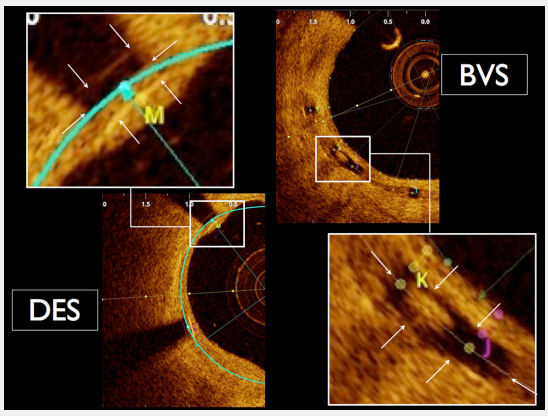


Figure 1

Representative images of OCT analysis of BVS and DES. This image shows the analysis of stent/scaffold area. After identifying all struts in a cross-section, stent/scaffold area was delineated by a curvilinear interpolation connecting the middle points of the struts at mid-strut depth.
BVS = bioresorbable vascular scaffold; DES = drug-eluting stent; OCT = optical coherence tomography

Statistical analysis

The sample size calculation can be accessed in the appendix. The substudy is powered on superiority assuming 1% fewer uncovered struts for BVS than for EES&BES (power: 90%, 2-sided alpha: 0.05).
Variables were compared between patients treated with ESS or BES (EES&BES) and BVS. Categorical variables are reported as counts and percentages, continuous variables are reported as means and standard deviations. Normality was assessed by means of visual inspection of histograms, computation of QQ-plots and the Shapiro-Wilk test. Categorical variables were compared using chi-square or Fisher's exact tests. Continuous variables were analysed using the Student's t-test or the Wilcoxon rank-sum test according to their distribution. All statistical analyses were performed using dedicated software (Stata version 13, StataCorp LP, College Station, Texas) at a two-tailed significance level of $\alpha = 0.05$. In the case of multiple testing, the Bonferroni method was employed. A multilevel linear mixed effects model with random effects at patient and lesion level was employed to compare strut coverage and apposition between patients treated with EES/BES and patients treated with BVS. Univariate comparison at strut level was carried out and is provided for illustrative purposes as an appendix (table S3).
Hypothesis testing of EES versus BVS and BES versus BVS is provided in the appendix (tables S1–S4) for illustrative purposes.

Results

Baseline patient characteristics

The patient flow chart is depicted in figure 2. A total of 74 patients, 23 patients with 26 EES-treated lesions, 23 patients with 26 BES-treated lesions and 28 patients with 33 BVS-treated lesions, were included in the final OCT analysis.

Baseline clinical characteristics among patients undergoing OCT were generally well balanced between the EES&BES and the BVS group and are summarised in table 1. Baseline characteristics of included patients were similar to those of the overall trial population (table S1a; see appendix).

Baseline angiographic and procedural characteristics

Implanted devices were longer in the BVS group (26 ± 12 mm) compared with the EES&BES group (23 ± 15 mm, p = 0.04) (table 2). At 9 months, BVS demonstrated a higher percentage of in-stent diameter stenosis (17 ± 11% vs 11 ± 8%, p <0.01) and in-segment late lumen loss (0.40 ± 0.45 vs 0.19 ± 0.40 mm, p <0.01) compared with EES&BES.

OCT findings

Morphometry

Quantitative analysis of lumen and stent areas at cross-sectional level showed no differences between the groups, whereas neointimal area was greater in the BVS compared with the EES&BES group (1.19 ± 0.62 vs 0.60 ± 0.52 mm^2, p <0.001) (table 3).

At lesion level, mean neointima thickness (102 ± 44 vs 66 ± 36 µm, p <0.01; fig. 3) and mean neointima volume (29.2 ± 19.2 vs 11.0 ± 11.0 mm^3, p <0.001; fig. 4) were significantly greater in BVS- than in EES&BES-treated patients.

Strut coverage

A mean of 335 ± 144 BVS struts and 265 ± 131 EES&BES struts were analysed per patient. In the BVS group 12 ± 27 (3.8 ± 8.4%) struts were uncovered compared with 59 ± 55 (21.8 ± 13.7%) in the EES&BES group (p <0.001, fig. 5).

Incomplete stent apposition

Protruding struts were significantly less frequent in BVS than EES&BES (1.6 ± 2.7% vs 4.4 ± 6.3%. There was no significant difference with regard to malapposed struts, although the percentage was higher in EES&BES than BVS (4.4 ± 8.8% vs 2.1 ± 2.7%, p = 0.41).

Peristrut intensity

A total of 9 370 peristrut intensity measurements were carried out (EES 2 591, BES 2 880, BVS 3 899). At peristrut level, BVS showed significantly decreased intensity when compared with EES&BES (14 ± 23% vs 13 ± 12%, p = 0.007). However, this difference was dependent on the relatively smallest intensity loss in EES-treated patients (EES 10 ± 10%, BES 16 ± 13%, BVS 14 ± 23%). Comparing bioresorbable polymer coated devices (BES&BVS) to EES showed a marked and significant difference in peristrut intensity (EES 10 ± 10% vs BES&BVS 15 ± 19%, p <0.001).

Discussion

This first direct comparative OCT analysis comparing BVS with DES had the following findings: (a) At 9-month OCT

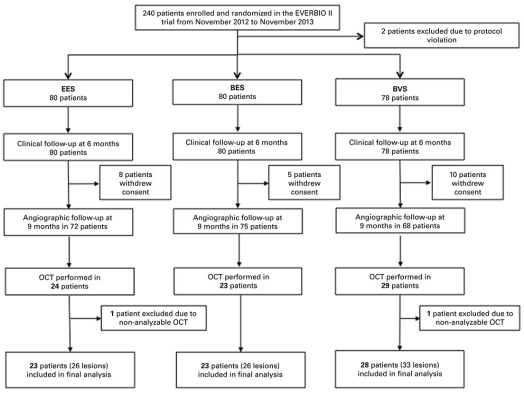


Figure 2

Patient flow chart.

BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; EES = everolimus-eluting stent; OCT = optical coherence tomography

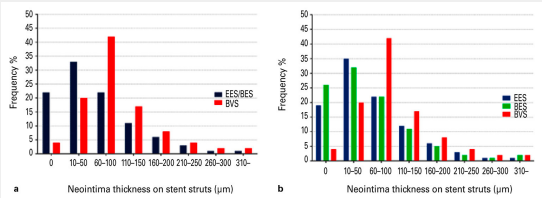
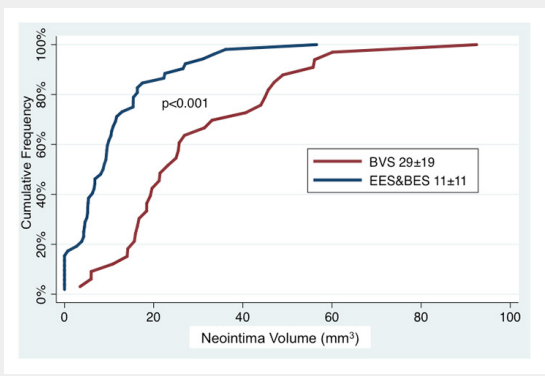


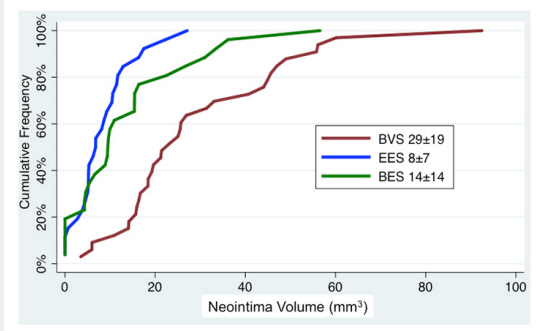
Figure 3a and b

Frequency distribution of mean neointima thickness at intervals of 50 µm.

BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; EES = everolimus-eluting stent.



a



b

Figure 4a and b

Cumulative frequency distribution of mean neointima volume at 9 months.

The numbers provided are mean ± standard deviation. BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; EES = everolimus-eluting stent.

follow-up, BVS demonstrated a higher "capping" effect with fewer uncovered and/or malapposed struts and thicker neointimal hyperplasia, (b) peristrut intensity was, however, significantly lower in BVS than EES&BES.

Several trials have previously investigated strut coverage of EES and BES by use of OCT [14–16] but only a few subtrials of the ABSORB Cohort B are available for the second-generation everolimus-eluting BVS [17, 21, 22]. To date, there is no reported trial in humans that directly compared OCT findings of BVS to any of the available DES. Gomez-Lara and colleagues compared vascular response to EES and BVS at 1 year by performing a *post-hoc* analysis in 44 unmatched patients from RESOLUTE All Comers and ABSORB Cohort B2 for whom OCT imaging was available. They found no difference in neointimal response as assessed from mean neointimal thickness over stent struts (EES 126 vs BVS 136 µm). They further reported a low number of uncovered struts (EES 5.3% vs BVS 4.5%) or malapposed struts (EES 1.1% vs BVS 2.2%, p <0.01) with both devices. In our study, BVS achieved high lesion capping with a low percentage of uncovered struts at 9-month follow-up. These results are in line with OCT findings by Gomez-Lara et al. and other studies assessing strut coverage of BVS [17, 21, 22]; the ABSORB Cohort B trial reported a mean of 2% uncovered struts at 6 months and 1% uncovered struts at 24 months.

When compared with EES&BES, BVS presented significantly fewer uncovered struts in our study. This finding contradicts the results by Gomez-Lara and colleagues and is most likely driven by the high rate of uncovered struts found with EES and BES, which is very different from the available literature. In the *post-hoc* analysis from RESOLUTE and ABSORB Cohort B, EES was associated with 5.3% uncovered struts. The NEXT OCT substudy reported 3 ± 7% uncovered struts in EES-treated and 9 ± 10% in BES-treated patients at 8–12 months (p <0.001) [16]. Tada et al. recently reported no difference in uncovered struts between EES and BES at 6–8 months (588 [15%] vs 479 [17%] unadjusted respectively, p = 0.34) [15]. However,, this improved capping does not necessarily reflect better vascular healing. Indeed, the visible covering layer can be formed by loosely organised and possibly prothrombotic elements such as fibrin.

Incomplete stent apposition and lack of neointimal strut coverage are thought to be correlated with an increased risk of late stent or scaffold thrombosis and myocardial infarction [23, 24]. In this trial, the rate of malapposed struts was not significantly different in EES&BES compared with BVS. BVS rates of malapposed struts seen in our study were similar to previously reported data, but

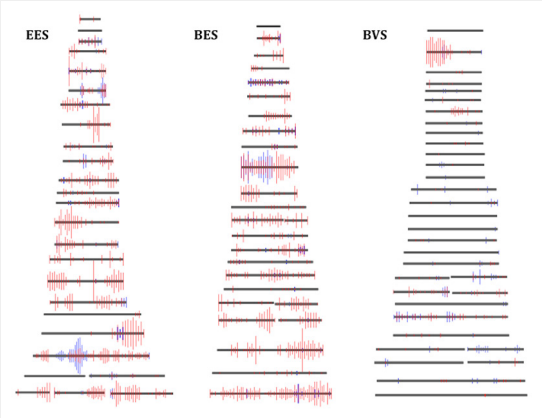


Figure 5

Graphical representation of strut coverage and malapposition in lesions.

Lesions = horizontal gray bars, uncovered struts = red lines, malapposed struts = blue lines, according to geographical location on stent/scaffold.

BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; EES = everolimus-eluting stent

Table 1: Baseline patient characteristics.

	EES	BES	EES&BES	BVS	p-value
	n = 23	n = 23	n = 46	n = 28	EES&BES vs BVS
Male, n (%)	20 (87)	19 (83)	39 (85)	26 (93)	0.47
Age, years ± SD	67 ± 7	67 ± 10	67 ± 8	62 ± 11	<0.05
Hypertension, n (%)	17 (74)	18 (78)	35 (76)	10 (36)	<0.01
Obesity (BMI >30 kg/m^2), n (%)	3 (13)	5 (22)	8 (17)	6 (21)	0.76
Diabetes, n (%)	3 (13)	11 (48)	14 (30)	6 (21)	0.43
Smoking, n (%)	3 (13)	6 (26)	9 (20)	11 (39)	0.1
Dyslipidaemia, n (%)	14 (61)	16 (70)	30 (65)	14 (46)	0.15
Family History of CAD, n (%)	4 (17)	10 (44)	14 (30)	9 (32)	1
Previous PCI, n (%)	8 (35)	9 (39)	17 (37)	10 (36)	1
Previous CABG, n (%)	4 (17)	5 (22)	9 (20)	0 (0)	0.01
Previous MI, n (%)	4 (17)	5 (22)	9 (20)	8 (29)	0.4
Indication for index procedure					0.99
Acute coronary syndrome					
Unstable angina, n (%)	1 (4)	1 (4)	2 (4)	1 (4)	
NSTEMI, n (%)	4 (17)	8 (35)	12 (26)	7 (25)	
STEMI, n (%)	4 (17)	2 (9)	6 (13)	3 (11)	
Stable angina, n (%)	13(57)	9 (39)	22 (48)	14 (50)	
Silent ischaemia, n (%)	1 (4)	3 (13)	4 (9)	3 (11)	
Left ventricular ejection fraction, %, median (IQR)	57 (45–65)	58 (42–65)	58 (44–65)	58 (50–65)	0.58

BES = biolimus-eluting stent; BMI = body mass index; BVS = bioresorbable vascular scaffold; CABG = coronary artery bypass graft; CAD = coronary artery disease; EES = everolimus-eluting stent; MI = myocardial infarction; NSTEMI = non-ST segment elevation myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation; STEMI = ST segment elevation myocardial infarction

EES&BES rates of malapposed struts were considerably higher than reported in the literature [14–17, 21].

OCT assessment of neointimal coverage is a useful surrogate for risk stratification of very late DES thrombosis [25]. The current study showed better neointimal coverage in BVS-treated than in EES&BES-treated lesions. Whether neointimal coverage is equally important in stratifying the risk for very late scaffold thrombosis is uncertain. It may be that a distinctive pathophysiology and/or different mechanistic phenomena, not yet identified, lead to scaffold thrombosis.

The current study is the first to compare PLIA between BVS, EES and BES and to address this issue with quantitative OCT assessment. In a comparative histological observation Teramoto et al. suggested that these areas of low intensity may represent fibrin accumulations surrounded by

Table 2: Procedural characteristics.

	EES	BES	EES&BES	BVS	p-value
	n = 26	n = 26	n = 52	n = 33	EES&BES vs BVS
Target vessel					0.17
LM, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	
LAD, n (%)	12 (48)	7 (27)	19 (37)	20 (61)	
LCX, n (%)	6 (24)	2 (8)	8 (16)	4 (12)	
RCA, n (%)	7 (28)	15 (58)	22 (43)	9 (27)	
SVG, n (%)	0 (0)	2 (8)	2 (4)	0 (0)	
Lesion type					0.21
De novo, n (%)	22 (85)	23 (88)	45 (87)	32 (97)	
Restenosis, n (%)	2 (8)	1 (4)	3 (6)	1 (3)	
CTO, n (%)	2 (8)	2 (8)	4 (8)	0 (0)	
Calcific lesions, n (%)	4 (15)	4 (15)	8 (15)	7 (21)	0.57
Bifurcation lesion, n (%)	3 (12)	2 (8)	5 (10)	2 (6)	0.70
Aorto-ostial lesion, n (%)	2 (8)	5 (19)	7 (13)	1 (3)	0.14
Baseline TIMI flow					0.75
TIMI 0, n (%)	5 (19)	3 (12)	8 (15)	5 (15)	
TIMI 1, n (%)	2 (8)	1 (4)	3 (6)	0 (0)	
TIMI 2, n (%)	3 (12)	6 (23)	9 (17)	6 (18)	
TIMI 3, n (%)	16 (61)	16 (61)	32 (62)	22 (67)	
Postprocedural TIMI flow					0.61
TIMI 0, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	
TIMI 1, n (%)	0 (0)	0 (0)	0 (0)	0 (0)	
TIMI 2, n (%)	1 (4)	0 (0)	1 (2)	0 (0)	
TIMI 3, n (%)	25 (96)	26 (100)	51 (98)	33 (100)	
Thrombus aspiration, n (%)	3 (12)	3 (12)	6 (12)	2 (6)	0.48
Direct stenting, n (%)	3 (12)	6 (23)	9 (17)	1 (3)	0.08
Number of stents per lesion, mean ± SD	1.2 ± 0.5	1.1 ± 0.2	1.1 ± 0.4	1.2 ± 0.4	0.30
Total stent length, mm ± SD	23 ± 15	24 ± 14	23 ± 15	26 ± 12	0.04
Maximum stent diameter, mm ± SD	2.91 ± 0.44	3.34 ± 0.56	3.13 ± 0.54	3.12 ± 0.38	0.95
Minimum stent diameter, mm ± SD	2.76 ± 0.41	3.19 ± 0.54	2.98 ± 0.52	3.02 ± 0.39	0.39
Maximum inflation pressure, atm ± SD	16 ± 3	13 ± 2	14 ± 3	13 ± 3	0.12
Postdilatation, n (%)	8 (31)	12 (46)	20 (38)	14 (42)	0.82
QCA measurements					
Preprocedure					
RVD, mm ± SD	2.51 ± 0.60	2.70 ± 1.12	2.61 ± 0.89	2.79 ± 0.55	0.52
MLD, mm ± SD	0.46 ± 0.44	0.66 ± 0.63	0.56 ± 0.55	0.38 ± 0.31	0.46
Diameter stenosis, % ± SD	84 ± 15	80 ± 19	81 ± 17	86 ± 12	0.52
Postprocedure					
MLD, in-stent, mm ± SD	2.67 ± 0.44	2.96 ± 0.48	2.82 ± 0.48	2.56 ± 0.40	0.01
MLD, in-segment, mm ± SD	2.20 ± 0.53	2.55 ± 0.59	2.37 ± 0.58	2.35 ± 0.52	0.85
Diameter stenosis, in-stent, % ± SD	10 ± 7	8 ± 7	9 ± 7	10 ± 6	0.23
Diameter stenosis, in-segment, % ± SD	10 ± 11	11 ± 10	11 ± 11	11 ± 7	0.46
9 months					
MLD, in-stent, mm ± SD	2.42 ± 0.55	2.87 ± 0.56	2.65 ± 0.59	2.22 ± 0.44	<0.001
MLD, in-segment, mm ± SD	1.86 ± 0.55	2.50 ± 0.56	2.18 ± 0.64	1.97 ± 0.48	0.12
Diameter stenosis, in-stent, % ± SD	12 ± 9	10 ± 6	11 ± 8	17 ± 11	<0.01
Diameter stenosis, in-segment, % ± SD	18 ± 13	9 ± 6	14 ± 11	20 ± 15	0.09
Late lumen loss, in-stent, mm ± SD	0.25 ± 0.28	0.09 ± 0.30	0.17 ± 0.30	0.33 ± 0.43	0.1
Late lumen loss, in-segment, mm ± SD	0.33 ± 0.38	0.05 ± 0.36	0.19 ± 0.40	0.40 ± 0.45	0.04

BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; CTO = chronic total occlusion; EES = everolimus-eluting stent; LAD = left anterior descending; LCX = left circumflex; LM = left main; MLD = minimal lumen diameter; QCA = quantitative coronary angiography; RCA = right coronary artery; RVD = reference vessel diameter; SD = standard deviation; SVG = saphenous vein graft; TIMI = Thrombolysis in Myocardial Infarction study group.

proteoglycan extracellular matrix and inflammatory cell infiltration, indicating delayed arterial healing [26]. In the same preclinical study using a porcine model, they reported a 3-fold higher rate of PLIA for early-generation DES than for bare metal stents [26]. Tada et al. reported similar rates of PLIA for EES and BES [15]. In the present study, peristrut intensity significantly differed between the three platforms studied. There was a significantly lower peristrut intensity found in BVS- and BES- compared with EES-treated lesions. The lower intensity in devices with a degradable polymer coating compared with a durable polymer coating might suggest a prolonged inflammatory process around the degradable polymer coating, which could be a marker of delayed vascular healing.

The present study is limited in size with inevitable uncertainty around point estimations. Another issue is the lack of baseline OCT examination precluding any definitive conclusion regarding the cause of the incomplete stent apposition found at 9-month follow-up. A systematic bias might have been introduced by the differences in assessment of malapposition between the metallic stents (estimation of the abluminal border by adding the strut and polymer thickness to the endoluminal border) and the BVS (direct visualisation of the abluminal border and the lumen contour behind it). Furthermore, neointimal hyperplasia may have been overestimated in patients treated with BVS. Due to the reduction of the black box signal (by filling of the strut voids with connective tissue) that induces an abluminal displacement of the endoluminal scaffold strut border, measurement of neointimal hyperplasia becomes systematically larger in BVS than in metallic stents.

Finally, the study was neither powered nor designed to assess the impact of suboptimal stent coverage by neointima, incomplete stent apposition and PLIA on subsequent late clinical events, particularly late stent thrombosis.

Notwithstanding, specific strengths include meticulous OCT measurements at longitudinal intervals of 0.5 mm while standard intervals used by OCT investigators to date was 1 mm. Moreover, this was a substudy with a representative sample of the EVERBIO II trial population, an investigator-initiated and funded randomised controlled trial in all-comers.

Conclusions

BVS has fewer uncovered struts and presents with a thicker neointimal coverage compared with EES&BES. It is not known whether this improved capping correlates with superior vascular healing. Polylactide-containing stents (BVS&BES) demonstrated lower peristrut intensity compared with EES. The clinical significance of these findings needs further assessment.

Disclosure statement: The trial was an investigator-initiated study supported by an unrestricted grant from the Fonds Scientifique Cardiovasculaire (Fribourg, Switzerland). The funding source had no role in the design of the study, data collection, data monitoring, data analysis, data interpretation, or writing of the report.

Dr. Cook has received speaker fees/honoraria from Abbott Vascular, Biosensors Int., and Boston Scientific. Dr. Cook receives support from the Swiss National Science Foundation

Table 3: OCT analysis at 9-month follow-up.

	EES	BES	EES&BES	BVS	p-value
	N = 23	N = 23	N = 46	N = 28	EES&BES vs BVS
Number of analysed frames	**748**	**682**	**1430**	**1103**	
Analysis at strut level					
Number of struts per patient	**293 ± 133**	**245 ± 128**	**265 ± 131**	**335 ± 144**	
Number of uncovered struts, n ± SD	57 ± 44	61 ± 64	59 ± 55	12 ± 27	<0.001
Percent of uncovered struts, % ± SD	20.3 ± 12.1	23.4 ± 14.8	21.8 ± 13.7	3.8 ± 8.4	<0.001
Number of malapposed struts, n ± SD	13 ± 25	10 ± 24	11 ± 23	6 ± 9	0.31
Percent of malapposed struts, % ± SD	4.4 ± 6.7	4.2 ± 9.2	4.4 ± 8.8	2.1 ± 2.7	0.41
Number of malapposed and uncovered struts, n ± SD	5 ± 8	6 ± 14	5 ± 11	1 ± 2	0.07
Percent of malapposed and uncovered struts, % ± SD	1.8 ± 2.9	2.1 ± 4.6	1.9 ± 3.8	0.3 ± 0.7	0.11
Number of protruding struts, n ± SD	5 ± 6	21 ± 35	13 ± 27	5 ± 8	0.13
Percent of protruding struts, % ± SD	2.0 ± 2.4	6.9 ± 7.9	4.4 ± 6.3	1.6 ± 2.7	0.03
Neointimal thickness, mm ± SD	64 ± 33	68 ± 40	66 ± 36	102 ± 44	<0.01
Morphometry					
Reference segment					
EEM CSA, mm^2 ± SD	11.7 ± 4.1	14.1 ± 4.2	12.9 ± 4.3	11.7 ± 3.7	0.27
Lumen CSA, mm^2 ± SD	6.2 ± 2.6	8.4 ± 3.5	7.3 ± 3.2	6.8 ± 2.6	0.69
In-stent					
EEM CSA, mm^2 ± SD	11.2 ± 2.3	15.5 ± 5.2	13.3 ± 4.5	11.9 ± 2.5	0.28
Lumen CSA, mm^2 ± SD	5.6 ± 1.5	8.5 ± 2.9	7.1 ± 2.7	6.3 ± 1.7	0.34
Stent CSA, mm^2 ± SD	6.0 ± 2.0	9.0 ± 3.1	7.4 ± 2.9	7.4 ± 1.8	0.56
Stent length, mm ± SD	18.7 ± 9.7	20.3 ± 10.5	19.5 ± 10.3	24.2 ± 8.4	<0.01
Neointima CSA, mm^2 ± SD	0.52 ± 0.41	0.68 ± 0.60	0.60 ± 0.52	1.19 ± 0.62	<0.001
Lumen volume, mm^3 ± SD	105 ± 64	170 ± 96	138 ± 87	147 ± 51	0.08
Stent volume, mm^3 ± SD	112 ± 62	180 ± 105	146 ± 92	176 ± 60	<0.01
Neointima volume, mm^3 ± SD	8.4 ± 6.7	13.6 ± 13.7	11.0 ± 11.0	29.2 ± 19.2	<0.001

BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; CSA = cross-sectional area; EEM = external elastic membrane; EES = everolimus-eluting stent; OCT = optical coherence tomography

(SNSF) - CR32I3_150271 / 1. All other authors have no conflict of interest to declare.
Authors' contribution: SP and SC contributed equally and should be considered shared senior authors.

Correspondence: *Professor Stéphane Cook, MD, Department of Cardiology, University and Hospital Fribourg, CH-1708 Fribourg, stephane.cook[at]unifr.ch*

References

1 Dibra A, Kastrati A, Alfonso F, Seyfarth M, Perez-Vizcayno MJ, Mehilli J, Schomig A. Effectiveness of drug-eluting stents in patients with bare-metal in-stent restenosis: meta-analysis of randomized trials. J Am Coll Cardiol. 2007;49(5):616–23.

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(1):193–202.

3 Nakazawa G. Stent thrombosis of drug eluting stent: pathological perspective. J Cardiol. 2011;58(2):84–91.

4 Kedhi E, Joesoef KS, McFadden E, Wassing J, van Mieghem C, Goedhart D, Smits PC. Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice (COMPARE): a randomised trial. Lancet. 2010;375(9710):201–9.

5 Park KW, Chae IH, Lim DS, Han KR, Yang HM, Lee HY, et al. Everolimus-eluting versus sirolimus-eluting stents in patients undergoing percutaneous coronary intervention: the EXCELLENT (Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting) randomized trial. J Am Coll Cardiol. 2011;58(18):1844–54.

6 Stone GW, Rizvi A, Newman W, Mastali K, Wang JC, Caputo R, et al. Everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease. N Engl J Med. 2010;362(18):1663–74.

7 Byrne RA, Kastrati A, Massberg S, Wieczorek A, Laugwitz KL, Hadamitzky M, et al. Biodegradable polymer versus permanent polymer drug-eluting stents and everolimus- versus sirolimus-eluting stents in patients with coronary artery disease: 3-year outcomes from a randomized clinical trial. J Am Coll Cardiol. 2011;58(13):1325–31.

8 Raber L, Juni P, Nuesch E, Kalesan B, Wenaweser P, Moschovitis A, et al. Long-term comparison of everolimus-eluting and sirolimus-eluting stents for coronary revascularization. J Am Coll Cardiol. 2011;57(21):2143–51.

9 Chevalier B, Silber S, Park SJ, Garcia E, Schuler G, Suryapranata H, et al. Randomized comparison of the Nobori Biolimus A9-eluting coronary stent with the Taxus Liberte paclitaxel-eluting coronary stent in patients with stenosis in native coronary arteries: the NOBORI 1 trial –Phase 2. Circ Cardiovasc Interv. 2009;2(3):188–95.

10 Stefanini GG, Kalesan B, Serruys PW, Heg D, Buszman P, Linke A, et al. Long-term clinical outcomes of biodegradable polymer biolimus-eluting stents versus durable polymer sirolimus-eluting stents in patients with coronary artery disease (LEADERS): 4 year follow-up of a randomised non-inferiority trial. Lancet. 2011;378(9807):1940–8.

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, noninferiority trial. JACC Cardiovasc Interv. 2013;6(8):777–89.

12 Smits PC, Hofma S, Togni M, Vazquez N, Valdes 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(9867):651–60.

13 Puricel S, Oberhansli M, Guntern P, Lehmann S, Goy JJ, Arroyo D, et al. Long-term comparison of everolimus-eluting and biolimus-eluting stents. EuroIntervention. 2013;9(3):336–44.

14 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(2):165–76.

15 Tada T, Kastrati A, Byrne RA, Schuster T, Cuni R, King LA, et al. Randomized comparison of biolimus-eluting stents with biodegradable polymer versus everolimus-eluting stents with permanent polymer coatings assessed by optical coherence tomography. Int J Cardiovasc Imaging. 2014;30(3):495–504.

16 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. Circ J. 2014;78(10):2408–14.

17 Gomez-Lara J, Radu M, Brugaletta S, Farooq V, Diletti R, Onuma Y, et al. Serial analysis of the malapposed and uncovered struts of the new generation of everolimus-eluting bioresorbable scaffold with optical coherence tomography. JACC Cardiovasc Interv. 2011;4(9):992–1001.

18 Gogas BD, Radu M, Onuma Y, Perkins L, Powers JC, Gomez-Lara J, et al. Evaluation with in vivo optical coherence tomography and histology of the vascular effects of the everolimus-eluting bioresorbable vascular scaffold at two years following implantation in a healthy porcine coronary artery model: implications of pilot results for future pre-clinical studies. Int J Cardiovasc Imaging. 2012;28(3):499–511.

19 Arroyo D, Togni M, Puricel S, Gerard B, Sonja L, Corpataux N, et al. Comparison of everolimus-eluting and biolimus-eluting coronary stents with everolimus-eluting bioresorbable scaffold: study protocol of the randomized controlled EVERBIO II trial. Trials. 2014;15:9.

20 Puricel S, Arroyo D, Corpataux N, Baeriswyl G, Lehmann S, Kallinikou Z, et al. Comparison of everolimus- and biolimus-eluting coronary stents with everolimus-eluting bioresorbable vascular scaffolds. J Am Coll Cardiol. 2015;65(8):791–801.

21 Serruys PW, Onuma Y, Ormiston JA, de Bruyne B, Regar E, Dudek D, et al. Evaluation of the second generation of a bioresorbable everolimus drug-eluting vascular scaffold for treatment of de novo coronary artery stenosis: six-month clinical and imaging outcomes. Circulation. 2010;122(22):2301–12.

22 Serruys PW, Onuma Y, Dudek D, Smits PC, Koolen J, Chevalier B, et al. Evaluation of the second generation of a bioresorbable everolimus-eluting vascular scaffold for the treatment of de novo coronary artery stenosis: 12-month clinical and imaging outcomes. J Am Coll Cardiol. 2011;58(15):1578–88.

23 Cook S, Eshtehardi P, Kalesan B, Raber L, Wenaweser P, Togni M, et al. Impact of incomplete stent apposition on long-term clinical outcome after drug-eluting stent implantation. Eur Heart J. 2012;33(11):1334–43.

24 Cook S, Wenaweser P, Togni M, Billinger M, Morger C, Seiler C, et al. Incomplete stent apposition and very late stent thrombosis after drug-eluting stent implantation. Circulation. 2007;115(18):2426–34.

25 Guagliumi G, Sirbu V, Musumeci G, Gerber R, Biondi-Zoccai G, Ikejima H, et al. Examination of the in vivo mechanisms of late drug-eluting stent thrombosis: findings from optical coherence tomography and intravascular ultrasound imaging. JACC Cardiovasc Interv. 2012;5(1):12–20.

26 Teramoto T, Ikeno F, Otake H, Lyons JK, van Beusekom HM, Fearon WF, Yeung AC. Intriguing peri-strut low-intensity area detected by optical coherence tomography after coronary stent deployment. Circ J. 2010;74(6):1257–9.

Appendix

Supplemental information about the methods

OCT acquisition and analysis

Each stent strut condition was classified into one of the following categories: (a) well-apposed to the vessel wall with neointimal coverage over the strut, (b) well-apposed to the vessel wall without neointimal coverage, (c) malapposed to the vessel wall with neointimal coverage, (d) mal-apposed to the vessel wall without neointimal coverage, (e) protruding to the vessel wall with neointimal coverage and (f) protruding to the vessel wall without neointimal coverage. The maximum length of a segment with uncovered struts and strut malapposition was estimated as the number of consecutive frames of 0.2 mm of uncovered and malapposed struts, respectively.

Statistical analysis

At the time of study initiation and based on available data from ABSORB Cohort B [1] (2% uncovered struts at 6 months; 1% at 24 months) and data from studies assessing EES and BES (3–4% uncovered struts at 9 months), [2–4] we estimated a difference of 1% uncovered struts in favour of BVS. The analysis of 3 889 struts in the BVS and 7 778 in the EES&BES group would yield 90% statistical power at a two-sided alpha level of 0.05 to detect that difference accounting for the unequal allocation ratio. Therefore, 39 patients in the EES/BES and 19 patients in the BVS-group were needed (200 struts expected per patient). In order to account for unreadable pullbacks and underestimation of struts per patient, we increased the number of patients to 47 in the EES&BES group and 29 in the BVS group.

Supplementary tables

Table S1a: Baseline characteristics of patients included compared with patients not included in the OCT substudy.

	OCT	**No OCT**	**p-value**
	n = 74	**n = 164**	
Male, n (%)	65 (88)	124 (76)	0.04
Age, years ± SD	65 ± 9	65 ± 11	0.85
Hypertension, n (%)	45 (61)	99 (60)	0.95
BMI, kg/m^2 ± SD	27 ± 3	27 ± 4	0.86
Diabetes, n (%)	20 (27)	36 (22)	0.39
Smoking, n (%)	20 (27)	63 (38)	0.09
Dyslipidaemia, n (%)	43 (58)	103 (63)	0.49
Family history of CAD, n (%)	23 (31)	46 (28)	0.63
Previous PCI, n (%)	27 (36)	46 (28)	0.19
Previous CABG, n (%)	9 (12)	24 (15)	0.61
Previous MI, n (%)	17 (23)	24 (15)	0.12
Indication for index procedure			0.33
Acute coronary syndrome			
Unstable angina, n(%)	3 (4)	17 (10)	
NSTEMI, n (%)	18 (24)	32 (20)	
STEMI, n (%)	9 (12)	14 (9)	
Stable angina, n (%)	37 (50)	78 (48)	
Silent ischaemia, n (%)	7 (9)	23 (14)	
Left ventricular ejection fraction, %, median (IQR)	58 (45–65)	60 (50–66)	0.11

BMI = body mass index; CABG = coronary artery bypass graft; CAD = coronary artery disease; MI = myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; OCT = optical coherence tomography; PCI = percutaneous coronary intervention; SD = standard deviation; STEMI = ST elevation myocardial infarction

Table S1b: Baseline patient characteristics.

	EES	BES	EES&BES	BVS	p-value		
	n = 23	n = 23	n = 46	n = 28	EES vs BVS	BES vs BVS	EES&BES vs BVS
Male, n (%)	20 (87)	19 (83)	39 (85)	26 (93)	0.64	0.39	0.47
Age, years ± SD	67 ± 7	67 ± 10	67 ± 8	62 ± 11	0.07	0.12	<0.05
Hypertension, n (%)	17 (74)	18 (78)	35 (76)	10 (36)	0.01	<0.01	<0.01
Obesity (BMI >30 kg/m^2), n (%)	3 (13)	5 (22)	8 (17)	6 (21)	0.49	1	0.76
Diabetes, n (%)	3 (13)	11 (48)	14 (30)	6 (21)	0.49	0.07	0.43
Smoking, n (%)	3 (13)	6 (26)	9 (20)	11 (39)	0.06	0.38	0.1
Dyslipidaemia, n (%)	14 (61)	16 (70)	30 (65)	14 (46)	0.4	0.16	0.15
Family history of CAD, n (%)	4 (17)	10 (44)	14 (30)	9 (32)	0.34	0.56	1
Previous PCI, n (%)	8 (35)	9 (39)	17 (37)	10 (36)	1	1	1
Previous CABG, n (%)	4 (17)	5 (22)	9 (20)	0 (0)	0.04	0.01	0.01
Previous MI, n (%)	4 (17)	5 (22)	9 (20)	8 (29)	0.51	0.75	0.4
Indication for index procedure					0.82	0.92	0.99
Acute coronary syndrome							
Unstable angina, n (%)	1 (4)	1 (4)	2 (4)	1 (4)			
NSTEMI, n (%)	4 (17)	8 (35)	12 (26)	7 (25)			
STEMI, n (%)	4 (17)	2 (9)	6 (13)	3 (11)			
Stable angina, n (%)	13 (57)	9 (39)	22 (48)	14 (50)			
Silent ischaemia, n (%)	1 (4)	3 (13)	4 (9)	3 (11)			
Left ventricular ejection fraction, %, median (IQR)	57 (45–65)	58 (42–65)	58 (44–65)	58 (50–65)	0.68	0.59	0.58

BES = biolimus-eluting stent; BMI = body mass index; BVS = bioresorbable vascular scaffold; CABG = coronary artery bypass graft; CAD = coronary artery disease; EES = everolimus-eluting stent; MI = myocardial infarction; NSTEMI = non-ST segment elevation myocardial infarction; PCI = percutaneous coronary intervention; SD = standard deviation; STEMI = ST segment elevation myocardial infarction.

Table S2: Procedural characteristics.

	EES	BES	EES&BES	BVS	p-value		
	n = 26	n = 26	n = 52	n = 33	EES vs BVS	BES vs BVS	EES&BES vs BVS
Target vessel					0.46	0.02	0.17
LM, n (%)	0 (0)	0 (0)	0 (0)	0 (0)			
LAD, n (%)	12 (48)	7 (27)	19 (37)	20 (61)			
LCX, n (%)	6 (24)	2 (8)	8 (16)	4 (12)			
RCA, n (%)	7 (28)	15 (58)	22 (43)	9 (27)			
SVG, n (%)	0 (0)	2 (8)	2 (4)	0 (0)			
Lesion type					0.18	0.26	0.21
De novo, n (%)	22 (85)	23 (88)	45 (87)	32 (97)			
Restenosis, n (%)	2 (8)	1 (4)	3 (6)	1 (3)			
CTO, n (%)	2 (8)	2 (8)	4 (8)	0 (0)			
TIMI flow postintervention per lesion							
Baseline, n ± SD	2.8 ± 0.8	2.9 ± 0.6	2.8 ± 0.7	3.0 ± 0.2	0.4	0.85	0.54
Postprocedure, n ± SD	2.9 ± 0.2	3.0 ± 0	3.0 ± 0.1	3.0 ± 0	0.26	0.85	0.43
Thrombus aspiration, n (%)	3 (12)	3 (12)	6 (12)	2 (6)	0.65	0.65	0.48
Direct stenting, n (%)	3 (12)	6 (23)	9 (17)	1 (3)	0.31	0.64	0.08
Total stent length, mm ± SD	23 ± 15	24 ± 14	23 ± 15	26 ± 12	0.12	0.06	0.04
Maximum stent diameter, mm ± SD	2.91 ± 0.44	3.34 ± 0.56	3.13 ± 0.54	3.12 ± 0.38	0.06	0.09	0.95
Maximum inflation pressure, atm ± SD	16 ± 3	13 ± 2	14 ± 3	13 ± 3	<0.01	0.06	0.12
Postdilatation, n (%)	8 (31)	12 (46)	20 (38)	14 (42)	0.42	0.80	0.82
QCA measurements							
Preprocedure							
RVD, mm ± SD	2.51 ± 0.60	2.70 ± 1.12	2.61 ± 0.89	2.79 ± 0.55	0.13	0.63	0.52
MLD, mm ± SD	0.46 ± 0.44	0.66 ± 0.63	0.56 ± 0.55	0.38 ± 0.31	0.31	0.80	0.46
Diameter stenosis, % ± SD	84 ± 15	80 ± 19	81 ± 17	86 ± 12	0.74	0.44	0.52
Postprocedure							
MLD, in-stent, mm ± SD	2.67 ± 0.44	2.96 ± 0.48	2.82 ± 0.48	2.56 ± 0.40	0.61	<0.001	0.01
MLD, in-segment, mm ± SD	2.20 ± 0.53	2.55 ± 0.59	2.37 ± 0.58	2.35 ± 0.52	0.28	0.18	0.85
Diameter stenosis, in-stent, % ± SD	10 ± 7	8 ± 7	9 ± 7	10 ± 6	0.99	0.04	0.23
Diameter stenosis, in-segment, % ± SD	10 ± 11	11 ± 10	11 ± 11	11 ± 7	0.33	0.80	0.46
Acute gain, in-stent, % ± SD	2.21 ± 0.48	2.29 ± 0.57	2.25 ± 0.52	2.19 ± 0.47	0.61	0.84	0.67
Acute gain, in-segment, % ± SD	1.74 ± 0.43	1.90 ± 0.53	1.82 ± 0.49	1.98 ± 0.61	0.08	0.64	0.18
Acute recoil, % ± SD	7 ± 5	10 ± 5	8 ± 5	10 ± 8	0.14	0.99	0.39
9 months							
MLD, in-stent, mm ± SD	2.42 ± 0.55	2.87 ± 0.56	2.65 ± 0.59	2.22 ± 0.44	0.14	<0.001	<0.001
MLD, in-segment, mm ± SD	1.86 ± 0.55	2.50 ± 0.56	2.18 ± 0.64	1.97 ± 0.48	0.41	<0.001	0.12
Diameter stenosis, in-stent, % ± SD	12 ± 9	10 ± 6	11 ± 8	17 ± 11	0.01	<0.01	<0.01
Diameter stenosis, in-segment, % ± SD	18 ± 13	9 ± 6	14 ± 11	20 ± 15	0.74	<0.01	0.09
Late lumen loss, in-stent, mm ± SD	0.25 ± 0.28	0.09 ± 0.30	0.17 ± 0.30	0.33 ± 0.43	0.49	0.04	0.10
Late lumen loss, in-segment, mm ± SD	0.33 ± 0.38	0.05 ± 0.36	0.19 ± 0.40	0.40 ± 0.45	0.61	<0.01	0.04

BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; CTO = chronic total occlusion; EES = everolimus-eluting stent; LAD = left anterior descending; LCX = left circumflex; LM = left main; MLD = minimal lumen diameter; QCA =quantitative coronary angiography; RCA = right coronary artery; RVD = reference vessel diameter; SD = standard deviation; SVG = saphenous vein graft; TIMI = Thrombolysis in Myocardial Infarction study group.

Table S3: OCT analysis at 9-month follow-up

	EES	BES	EES&BES	BVS	p-value		
	n = 23	n = 23	n = 46	n = 28	EES vs BVS	BES vs BVS	EES&BES vs BVS
Analysis at strut level							
Number of struts	7 625	6 140	13 765	10 891			
Well apposed and covered struts, n (%)	5 876 (77.0)	4 203 (68.5)	10 079 (73.2)	10 197 (93.6)	<0.001	<0.001	<0.001
Well apposed and uncovered struts, n (%)	1 286 (16.9)	1 168 (19.0)	2 454 (17.8)	332 (3.1)	<0.001	<0.001	<0.001
Malapposed and covered struts, n (%)	197 (2.6)	132 (2.1)	329 (2.4)	181 (1.7)	<0.001	0.02	<0.001
Malapposed and uncovered struts, n (%)	119 (1.6)	135 (2.2)	254 (1.9)	32 (0.3)	<0.001	<0.001	<0.001
Protruding and covered struts, n (%)	77 (1.0)	241 (3.9)	318 (2.3)	147 (1.3)	0.04	<0.001	<0.001
Protruding and uncovered struts, n (%)	70 (0.9)	261 (4.3)	331 (2.4)	2 (0.02)	<0.001	<0.001	<0.001
Analysis at lesion level							
Number of stent-treated lesions	26	26	52	33			
Neointimal coverage over stent struts							
Percent uncovered struts, % ± SD	20 ± 12	24 ± 16	22 ± 14	4 ± 8	<0.001	<0.001	<0.001
Lesions with any uncovered struts, n (%)	24 (92)	25 (96)	49 (94)	26 (79)	0.27	0.07	0.04
Lesions with at least 30% uncovered struts, n (%)	5 (19)	11 (42)	16 (31)	1 (3)	0.08	<0.001	0.002
Lesions with at least 10% uncovered struts, n (%)	19 (73)	20 (77)	39 (75)	5 (15)	<0.001	<0.001	<0.001
Maximum length of segments with uncovered struts, mm ± SD	4.2 ± 2.9	6.8 ± 6.0	5.5 ± 4.9	1.6 ± 1.9	<0.001	<0.001	<0.001
Stent malapposition							
Percent malapposed and protruding struts, % ± SD	6.1 ± 7.4	10.6 ± 13.6	8.4 ± 11.1	3.6 ± 4.8	0.11	0.02	0.02
Percent malapposed struts, % ± SD	4.1 ± 6.6	4.2 ± 10.2	4.1 ± 8.5	2.1 ± 3.3	0.33	0.93	0.60
Percent protruding struts, % ± SD	2.1 ± 2.3	6.4 ± 8.1	4.2 ± 6.3	1.5 ± 2.7	0.14	<0.001	<0.01
Lesions with any malapposed struts, n (%)	18 (69)	18 (69)	36 (69)	25 (76)	0.77	0.77	0.62
Lesions with at least 10% malapposed struts, n (%)	3 (12)	2 (8)	5 (10)	2 (6)	0.65	1	0.7
Lesions with at least 5% malapposed struts, n (%)	4 (15)	3 (12)	7 (13)	4 (12)	0.72	1	0.86
Lesions with any protruding struts, n (%)	18 (69)	21 (81)	39 (75)	22 (67)	0.83	0.23	0.41
Lesions with at least 10% protruding struts, n (%)	1 (4)	4 (15)	5 (10)	1 (3)	1	0.14	0.40
Lesions with at least 5% protruding struts, n (%)	1 (4)	12 (46)	13 (25)	2 (6)	0.7	<0.001	0.03
Maximum length of segments with stent malapposition, mm ± SD	1.8 ± 2.0	3.2 ± 4.0	2.5 ± 3.2	1.7 ± 1.9	0.79	0.22	0.56
Number of struts per pullback, n ± SD	293 ± 141	236 ± 134	265 ± 139	330 ± 147	0.25	<0.01	0.02
Mean thickness of strut coverage, μm ± SD	66 ± 34	65 ± 42	65 ± 38	100 ± 45	<0.001	<0.001	<0.001
Number of uncovered struts, n ± SD	66 ± 34	60 ± 66	59 ± 56	11 ± 26	<0.001	<0.001	<0.001
Morphometry							
Reference segment							
EEM CSA, mm^2 ± SD	11.7 ± 4.1	14.1 ± 4.2	12.9 ± 4.3	11.7 ± 3.7	0.92	<0.05	0.27
Lumen CSA, mm^2 ± SD	6.2 ± 2.6	8.4 ± 3.5	7.3 ± 3.2	6.8 ± 2.6	0.43	0.14	0.69
In-stent							
EEM CSA, mm^2 ± SD	11.2 ± 2.3	15.5 ± 5.2	13.3 ± 4.5	11.9 ± 2.5	0.38	<0.01	0.28
Lumen CSA, mm^2 ± SD	5.6 ± 1.5	8.5 ± 2.9	7.1 ± 2.7	6.3 ± 1.7	0.13	<0.01	0.34
Stent CSA, mm^2 ± SD	6.0 ± 2.0	9.0 ± 3.1	7.4 ± 2.9	7.4 ± 1.8	<0.01	0.07	0.56
Neointima CSA, mm^2 ± SD	0.52 ± 0.41	0.68 ± 0.60	0.60 ± 0.52	1.19 ± 0.62	<0.001	0.001	<0.001
Lumen volume, mm^3 ± SD	105 ± 64	170 ± 96	138 ± 87	147 ± 51	0.001	0.78	0.08
Stent volume, mm^3 ± SD	112 ± 62	180 ± 105	146 ± 92	176 ± 60	<0.001	0.42	<0.01
Neointima volume, mm^3 ± SD	8.4 ± 6.7	13.6 ± 13.7	11.0 ± 11.0	29.2 ± 19.2	<0.001	<0.001	<0.001

BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; CSA = cross-sectional area; EEM = external elastic membrane; EES = everolimus-eluting stent; OCT = optical coherence tomography; SD = standard deviation

Supplementary references

1 Ormiston JA, Serruys PW, Onuma Y, van Geuns RJ, de Bruyne B, Dudek D, et al. First serial assessment at 6 months and 2 years of the second generation of absorb everolimus-eluting bioresorbable vascular scaffold: a multi-imaging modality study. Circ Cardiovasc Interv 2012;5(5):620–32.

2 Barlis P, Regar E, Serruys PW, Dimopoulos K, van der Giessen WJ, 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(2):165–76.

3 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(17):1379–84.

4 Choi HH, Kim JS, Yoon DH, Hong KS, Kim TH, Kim BK, et al. Favorable neointimal coverage in everolimus-eluting stent at 9 months after stent implantation: comparison with sirolimus-eluting stent using optical coherence tomography. Int J Cardiovasc Imaging 2012;28(3):491–7.

Figures (large format)

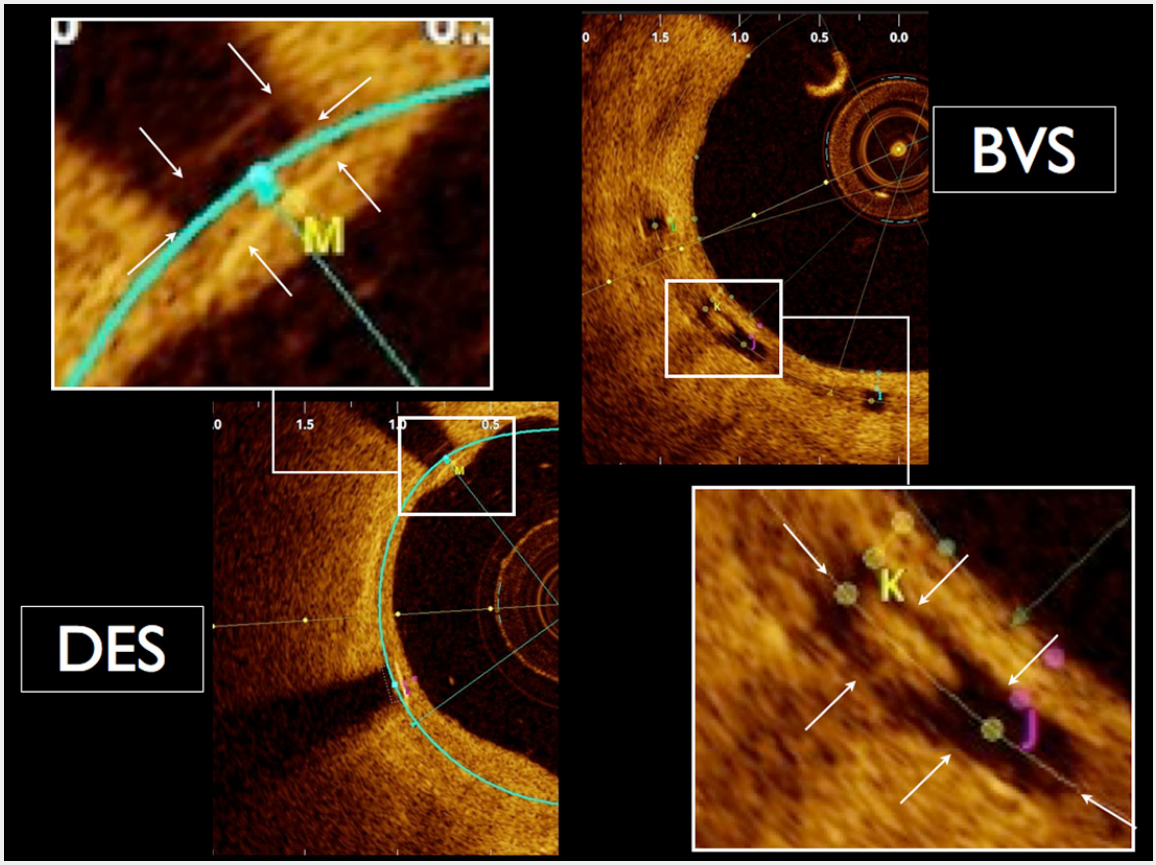


Figure 1

Representative images of OCT analysis of BVS and DES. This image shows the analysis of stent/scaffold area. After identifying all struts in a cross-section, stent/scaffold area was delineated by a curvilinear interpolation connecting the middle points of the struts at mid-strut depth. BVS = bioresorbable vascular scaffold; DES = drug-eluting stent; OCT = optical coherence tomography

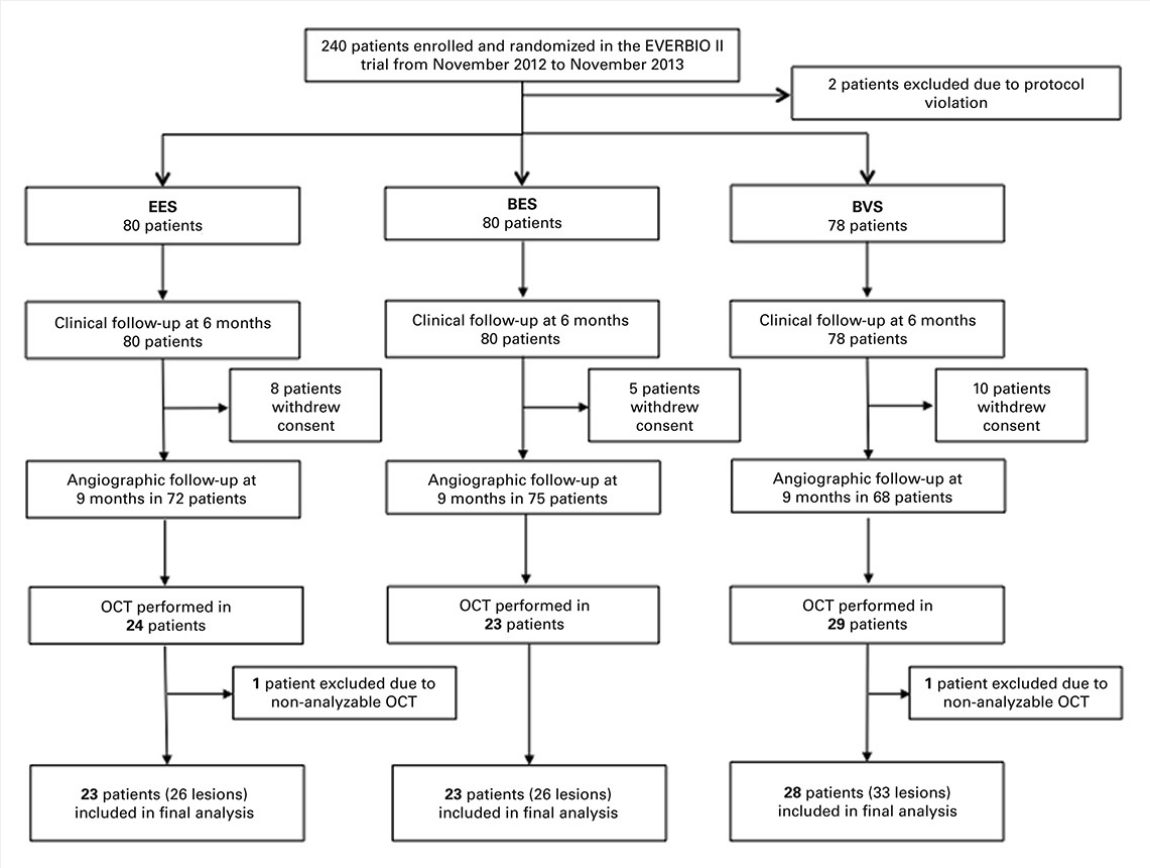


Figure 2

Patient flow chart.
BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; EES = everolimus-eluting stent; OCT = optical coherence tomography

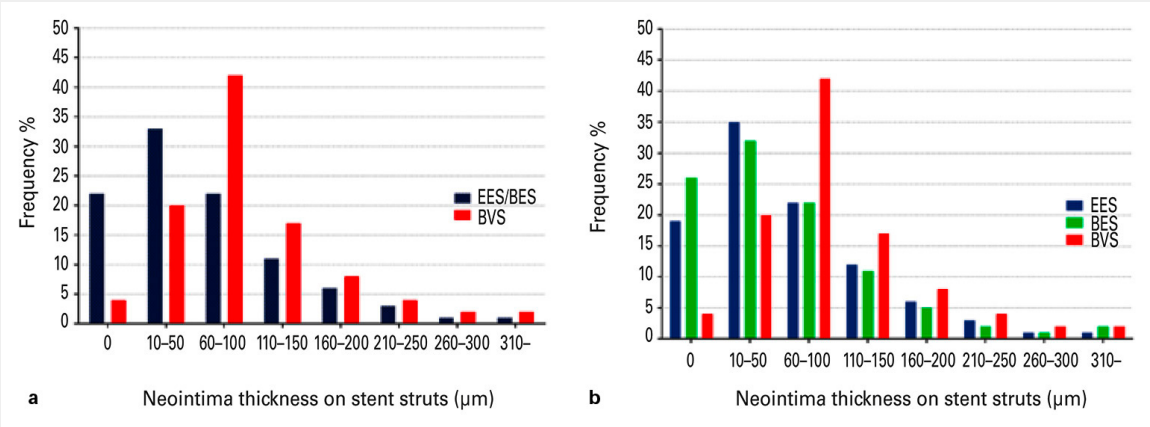
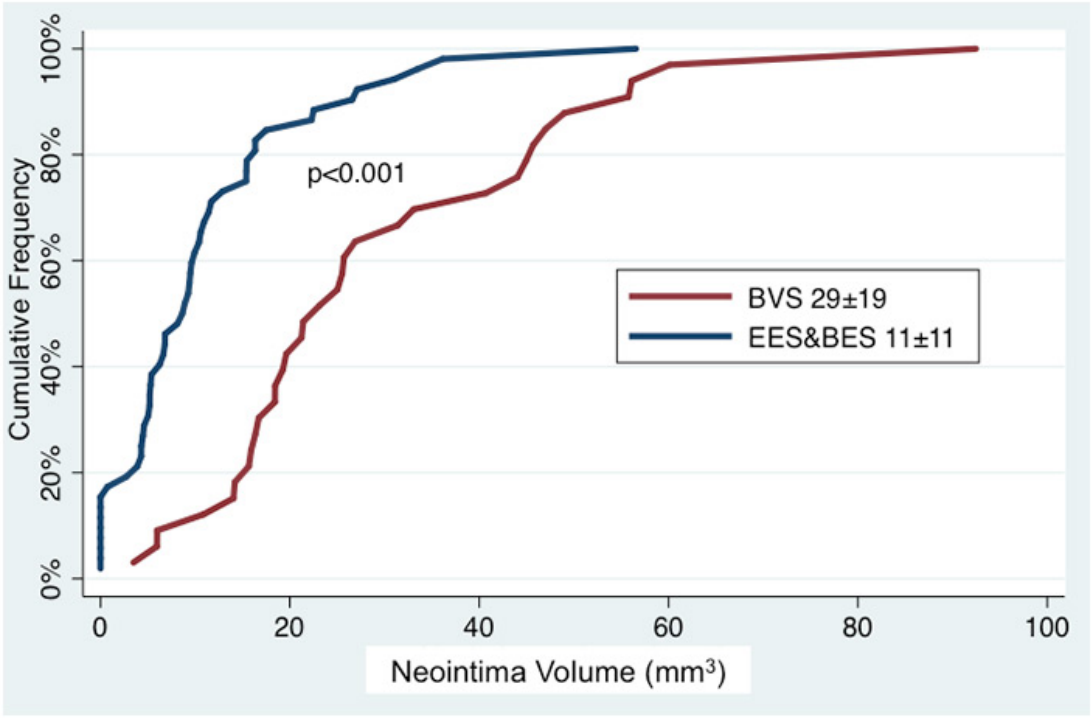
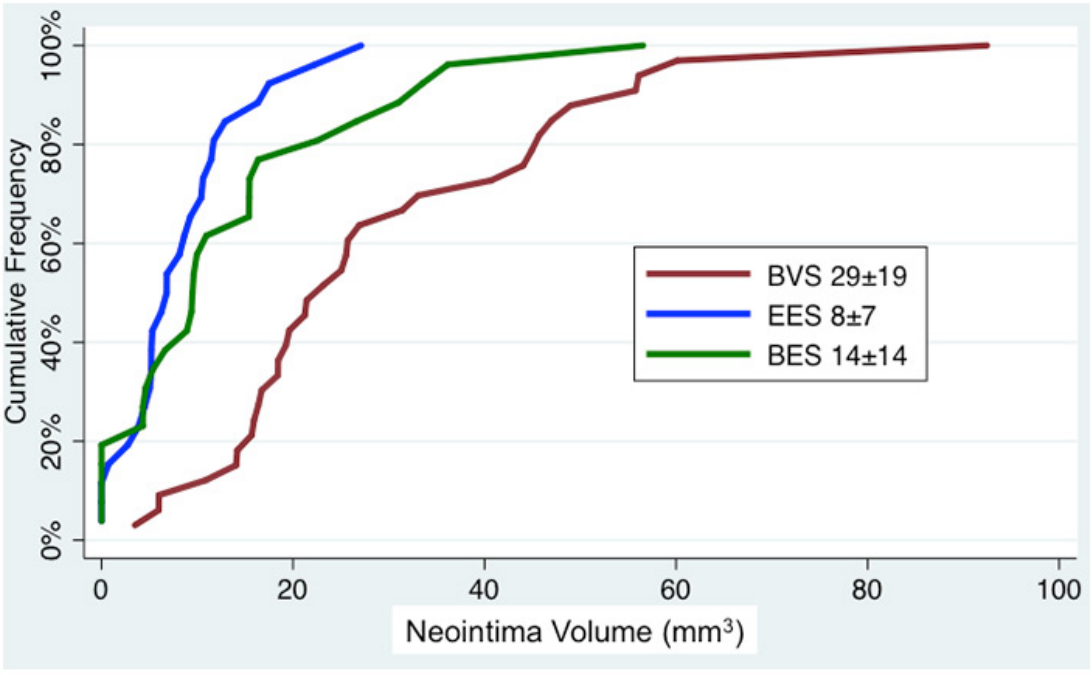


Figure 3a and b

Frequency distribution of mean neointima thickness at intervals of 50 µm.
BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; EES = everolimus-eluting stent.



a



b

Figure 4a and b

Cumulative frequency distribution of mean neointima volume at 9 months.
The numbers provided are mean ± standard deviation. BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; EES = everolimus-eluting stent.

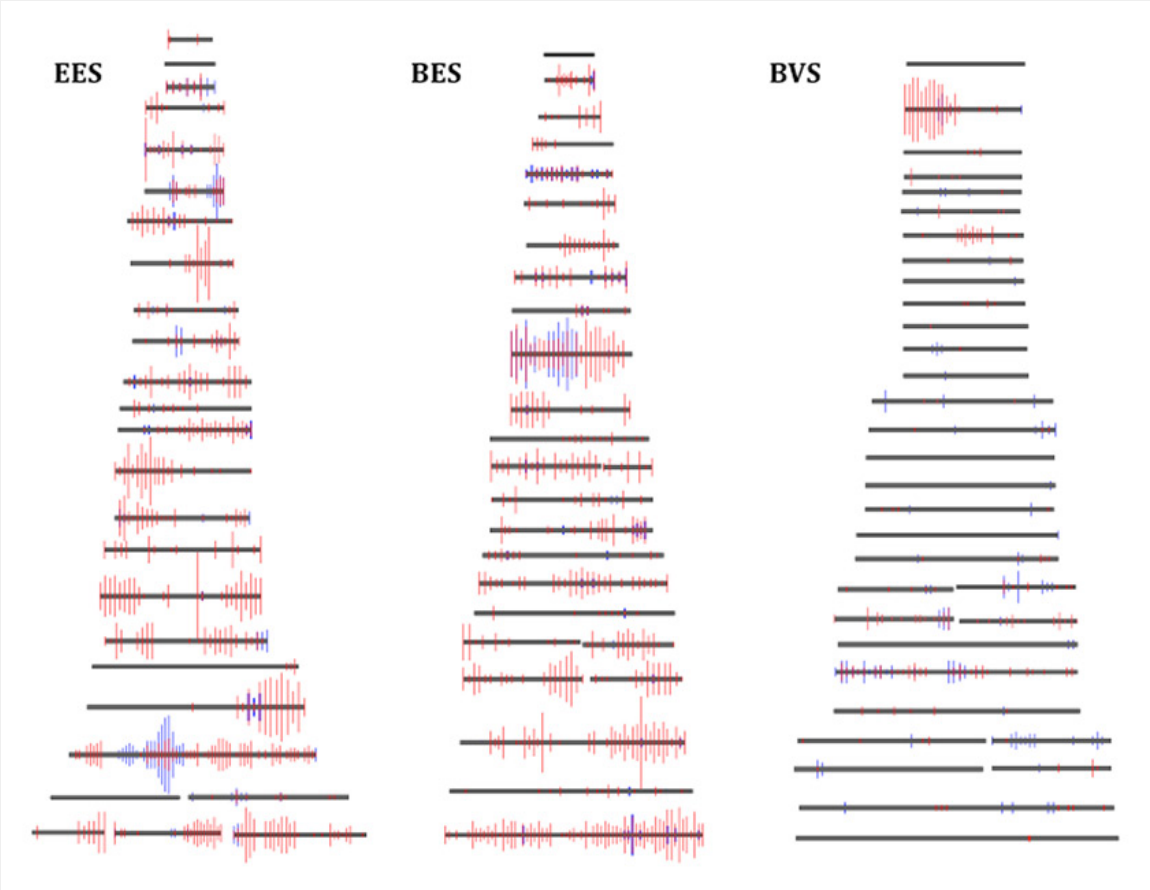


Figure 5

Graphical representation of strut coverage and malapposition in lesions.
Lesions = horizontal gray bars, uncovered struts = red lines, malapposed struts = blue lines, according to geographical location on stent/scaffold.
BES = biolimus-eluting stent; BVS = bioresorbable vascular scaffold; EES = everolimus-eluting stent