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Optical coherence tomography analysis of neointimal tissue in drug-eluting stents with biodegradable and durable polymer coatings: the ALSTER-OCT registry

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KEYWORDS

- biodegradable polymer
- drug-eluting-stents
- optical coherence tomography

Abstract

Aims: Optical coherence tomography (OCT) for follow-up after drug-eluting stent implantation permits detection of strut coverage, apposition and neointimal tissue. We aimed to compare OCT follow-up data and clinical outcome of two new-generation drug-eluting stents, Orsiro sirolimus-eluting stents (O-SES) and zotarolimus-eluting stents (ZES).

Methods and results: Eighty patients underwent OCT following implantation of O-SES (n=34) or ZES (n=46). Imaging was performed after three (n=39), six (n=28) or nine months (n=13). OCT data were acquired (coverage, apposition, neointimal thickness) and neointimal maturation was assessed by novel greyscale signal intensity analysis. Image analysis revealed increased strut coverage, tissue maturation and neointima formation over the three time points. There were no significant differences between O-SES and ZES in terms of coverage and apposition at any time. We also found no differences for neointimal thickness, maturation and rate of major adverse cardiac events (a composite of cardiac death, myocardial infarction and ischaemia-driven target lesion revascularisation within 12 months, O-SES 9.4% vs. ZES 6.8%, p=0.69).

Conclusions: No statistical differences were observed between O-SES and ZES concerning stent healing as well as one-year clinical outcome. Although preliminary, our findings may support the hypothesis that OCT-based analyses in small patient cohorts sensitively detect stent healing and could possibly be regarded as surrogates for DES healing and closely correlated to clinical outcome.

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Introduction

Since the introduction of second-generation drug-eluting stents (DES), event rates for target lesion failure (TLF) and late stent thrombosis (LST) have been remarkably low. Yet, these events are potentially fatal complications of percutaneous coronary interventions (PCI) and contribute to the long-term outcome[1]. Recent findings suggest that inflammatory reactions caused by durable polymers play an important role in neoatherosclerosis, delayed DES healing, LST and stent restenosis[2]. New technologies combine thinner struts, biocompatible polymers and different drug release kinetics to tackle these remaining problems. New-generation DES showed similar effectiveness compared to second-generation DES after one year[3,4]; however, improved safety may become apparent in larger sample sizes or expanded follow-up. Validated parameters for stent healing may allow judgement on the safety and efficacy of a particular stent in small patient cohorts prior to large studies with clinical outcome parameters. While post-mortem and *in vivo* studies have presented a significant relation of LST and uncovered and malapposed struts, optical coherence tomography (OCT) allows highly detailed *in vivo* imaging and has become a useful tool to evaluate stent coverage and apposition[5-7]. Therefore, quantitative parameters such as coverage and malapposition assessed by OCT have been proposed as surrogate parameters for stent biocompatibility and possibly clinical outcome in DES[8,9]. The ALSTER-OCT (AskLepios ST. GEoRg's Hospital-Optical Coherence Tomography) registry used quantitative OCT analyses to compare healing characteristics to clinical outcome of patients receiving new-generation Orsiro Hybrid sirolimus-eluting stents with biodegradable polymer (O-SES) (Biotronik AG, Bülach, Switzerland) to zotarolimus-eluting-stents with durable polymer (ZES) (Resolute Integrity® and Endeavor® Resolute; Medtronic, Santa Rosa, CA, USA).

Methods

DESIGN AND PATIENT ENROLMENT

The ALSTER-OCT registry **(Figure 1)** was a prospective, all-comers, single-centre registry to investigate DES healing at three (90±30 days), six (180±30 days) and nine-month (270±30 days) follow-up. Between June 2010 and January 2014, clinically indicated surveillance angiography was performed with OCT in 110 patients (121 lesions). The type of DES and the time point of angiography were determined by the initial operator or the referring physician. Patients with complex lesions (ostial stenosis, stenosis of the left main trunk, lesions ≥10 mm length in vessels ≤3.5 mm diameter) treated with ZES (n=46) or O-SES (n=34) were eligible. Written informed consent was obtained from all patients.

STUDY DEVICES

Detailed device characteristics have been previously reported[10,11]. Concerning ZES, two different types were analysed. The Endeavor Resolute ZES comprises a cobalt-chromium alloy (same CoCr alloy as used in the Driver® BMS; Medtronic) coated by the polymer combined with zotarolimus. The Resolute Integrity ZES is the latest version of the ZES. It uses the same drug and polymer mounted on an altered cobalt-chromium alloy platform (Integrity™; Medtronic). Both bare metal stent backbones (Driver/Integrity) have a strut thickness of 91 µm; therefore, we did not differentiate between these platforms.

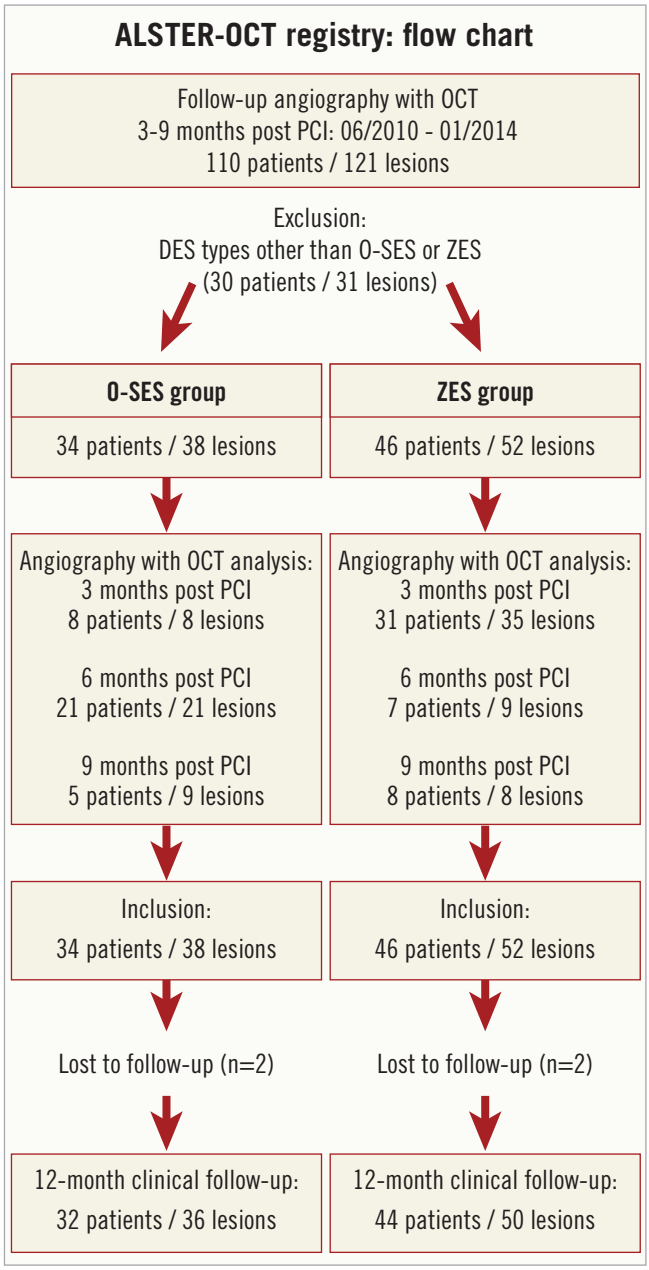

Figure 1. *ALSTER-OCT registry - flow chart. Flow chart of patients included in this prospective registry.*

OCT IMAGING AND ANALYSIS

As recently described by our group, frequency-domain OCT was performed according to the latest consensus documents and obtained with the ILUMIEN™ system (St. Jude Medical, St. Paul, MN, USA) combined with the C7 Dragonfly™ imaging catheter (St. Jude)[5,12]. Acquired data were analysed using LightLab software (OCT system software B.0.1; LightLab Imaging [now St. Jude])[5]. All images were initially screened for quality assessments and

excluded from analysis if any portion of the image was out of the screen or the image had poor quality due to artefacts[13]. In case of ostial lesions, the proximal part of the stent was excluded from the analysis. Struts located at the ostium of coronary artery side branches were designated as non-apposed side branch struts and were excluded from the analysis[7,12]. A strut was considered suitable for analysis only if it had a well-defined, bright "blooming" and a characteristic shadow perpendicular to the light source[12]. Image assessments were performed in every third cross-section. According to previously described methods, stents were analysed strut by strut and classified into four categories. Struts covered by tissue and not interfering with the lumen contour were defined as "covered embedded". Struts covered by tissue protruding into the vessel lumen were defined as "covered protruding". If no evidence of tissue was visualised above the struts and the struts were abutting the vessel wall they were defined as "uncovered apposed". Struts not covered by tissue and separated abluminally from the luminal contour of the vessel wall were defined as "uncovered malapposed"[12]. If neointimal tissue was observed, its average thickness was measured[12]. Two independent expert observers (blinded to the clinical and procedural characteristics) performed the analysis and intra- and inter-observer reproducibility was calculated[8].

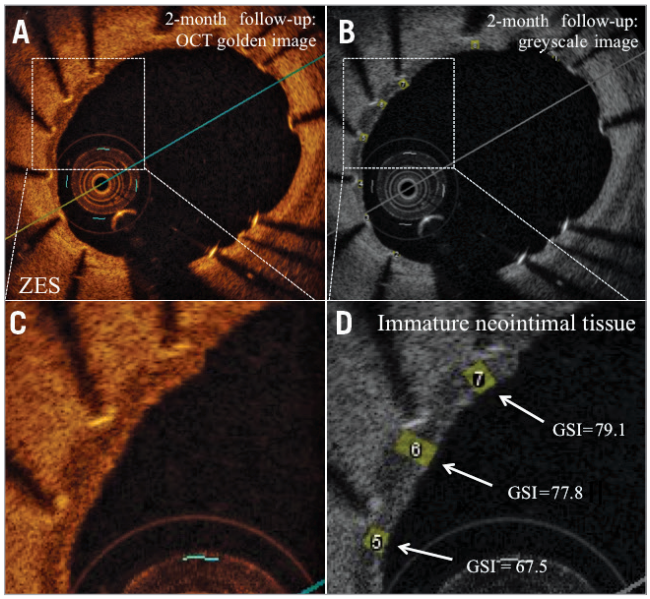

Figure 2. *OCT-based GSI analysis - immature neointimal tissue. A) Representative OCT golden image at two-month follow-up and corresponding GSI image (B) as well as magnification (C & D). GSI values presenting evidence for immature neointimal tissue.*

GREYSCALE SIGNAL INTENSITY MEASUREMENTS

To discriminate between mature and immature neointimal tissue, OCT-based greyscale signal intensity (GSI) analysis was assessed previously[9]. Exemplary figures are presented in **Figure 2** and **Figure 3**. In brief, analysis of cross-sections was assessed at every fifth cross-section. In each section 10 to 12 regions of interest (ROI) luminal to each covered strut were chosen (every 30°±10° of 360° cross-section) and each width was predefined to 0.1 mm. To normalise the brightness level (GSI=256), the guidewire was set as a reference in each analysed frame, while the darkest level (GSI=0) of the vessel lumen was set as the minimum value. A 256-level GSI was measured for every pixel within the given ROI. The previously validated histology-based GSI cut-off value (GSI=109.7) was used for the differentiation between mature and immature neointimal tissue[9].

CLINICAL FOLLOW-UP

The patients were followed up with telephone interviews at 12 months after PCI. TLF was defined as a composite of cardiac death, target vessel myocardial infarction (MI), ischaemia-driven target lesion revascularisation within 12 months[3]. Target vessel revascularisation (TVR) was defined as non-target lesion revascularisation of the target vessel[14]. The composite of cardiac death, MI and ischaemia-driven target lesion revascularisation within 12 months was considered as a major adverse cardiac event (MACE)[15].

STATISTICAL ANALYSIS

Continuous data were summarised as means and standard deviations or as medians and 25th and 75th percentiles, as appropriate. Categorical data are presented as N (%). We examined strut coverage, cross-section and GSI data between the two stent groups. As recently reported by our group, to account for the clustered nature of OCT data, multilevel regression analyses on lesion level, cross-section level and strut level were realised[13,16]. For intra-group analysis within each group, an analysis of variance was performed.

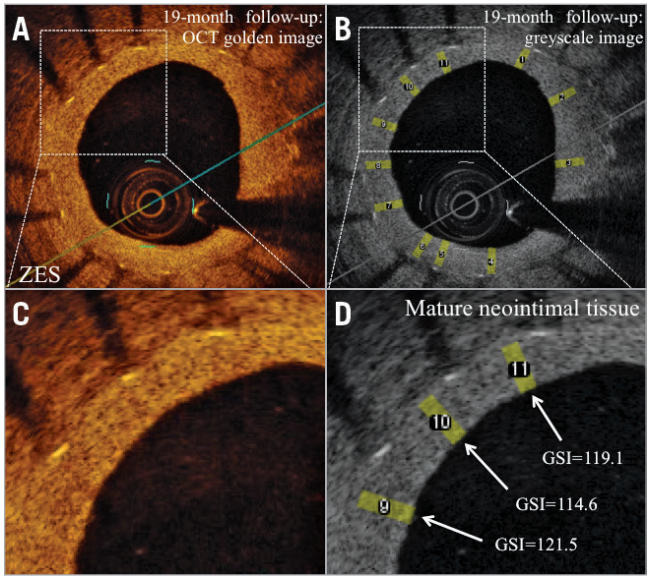

Figure 3. *OCT-based GSI analysis - mature neointimal tissue. A) Representative OCT golden image at 19-month follow-up and corresponding GSI image (B) as well as magnification (C & D). GSI values presenting evidence for mature neointimal tissue. White arrows show GSI values of respective region of interest. Yellow marked area indicates region of interest. GSI: greyscale signal intensity*

A p-value <0.05 was considered to be statistically significant and all analyses were two-tailed. Intra-observer and inter-observer reproducibility was assessed using the intraclass correlation coefficient. Statistical analysis was performed using GraphPad Prism, version 6 (GraphPad Software, Inc., San Diego, CA, USA).

Results

PATIENT BASELINE CHARACTERISTICS

Table 1 summarises patient baseline characteristics and procedural details. The two groups showed no statistical differences concerning baseline characteristics. Concerning ZES, 33 patients with Endeavor Resolute (71.7%) and 13 patients with Resolute Integrity (28.3%) were analysed.

QUANTITATIVE OCT IMAGE ANALYSIS

Results of OCT analysis are shown in **Table 2**. As expected with stent healing, the percentage of uncovered struts decreased over time while GSI parameters of tissue maturation increased. Interestingly, mean neointima thickness did not change in the O-SES group (0.5 mm), while it significantly increased between six and nine months in the ZES group (0.5-1.3 mm). No differences were found concerning coverage and apposition. One subclinical intra-stent thrombus formation of a ZES at three-month follow-up was detected while the patient was under DAPT. In this specific patient the rate of uncovered malapposed struts was remarkably high (10.7%).

Intra-group analyses between different time points showed no differences for coverage and apposition. The qualitative assessments were reproducible and comparable to findings of other groups. The measurements of five randomly chosen patients (n=2,124 struts) were repeated and the intra-observer and inter-observer reproducibility was calculated as 0.87 and 0.89, respectively[17].

OCT-BASED GSI ANALYSES

Findings of GSI analyses are presented in **Figure 4** and **Table 2**. We found no differences for the intra-group comparison of GSI values and percentage of mature neointimal tissue concerning the O-SES and no differences within the inter-group analysis compared to the ZES. Nevertheless, ZES had increased neointima maturation over time (p=0.0001), while O-SES showed stable measurements at all three time points (p=0.532), again possibly reflecting the different release kinetics of polymer and drug.

CLINICAL FOLLOW-UP

Clinical follow-up is shown in **Table 3**. Concerning O-SES, no TVR and MI were reported but one patient died due to major cerebral bleeding while she was on DAPT seven months after PCI. One further patient died due to respiratory insufficiency related to pneumonia after ten months. Four patients of the ZES group were readmitted requiring TVR (9.1%). Although not reaching statistical significance, this observation is in line with the observed increase of neointimal formation between six and nine months when ZES already equals a bare metal stent, while O-SES (TVR=0%) still releases drug and the polymer is slowly degraded. One patient experienced a transient ischaemic attack, most likely due to a cardiac embolic event caused by unknown atrial fibrillation without intake of oral anticoagulation. He recovered totally after 24 hours. The 12-month rates of cardiac death, MACE (O-SES 9.4% vs. ZES 6.8%, p=0.69) and TLF (O-SES 9.4% vs. ZES 6.8%, p=0.69) were not significantly different. Additionally, no differences were found for the duration of DAPT.

Table 1. Patient baseline characteristics and procedural data.

Characteristics	O-SES (n=34 patients)	ZES (n=46 patients)	*p*-value
Clinical features			
Age (years)	66.5±1.3	65.3±1.5	0.89
Male sex	25 (73.5)	36 (78.3)	0.79
Obesity	22 (64.7)	28 (50)	0.82
Hypertension	31 (91.2)	39 (84.8)	0.51
Hyperlipidaemia	19 (55.9)	30 (65.2)	0.49
Diabetes mellitus type 2	11 (32.4)	12 (26.1)	0.62
Smoking	14 (41.2)	23 (50.0)	0.50
Prior PCI	15 (44.1)	23 (50.0)	0.66
Prior MI	14 (41.2)	14 (30.4)	0.35
Prior CABG	3 (8.8)	5 (10.9)	>0.99
Multivessel disease	23 (73.5)	33 (71.7)	>0.99
Left ventricular ejection fraction	50.3±1.8	51.5±1.0	0.51
Antiplatelet therapy at baseline			
Acetylsalicylic acid	33 (97.1)	46 (100)	0.43
$P2Y_{12}$ inhibitors	34 (100)	46 (100)	>0.99
Clinical presentation at baseline			
Stable angina pectoris	5 (14.7)	6 (13.0)	>0.99
Unstable angina pectoris	19 (55.9)	31 (67.4)	0.35
NSTE-ACS	8 (23.5)	6 (13.0)	0.25
STEMI	2 (5.9)	3 (6.5)	>0.99
Treatment			
Number of treated lesions	38	52	
Left anterior descending artery	14 (36.8)	18 (34.6)	0.83
Left circumflex artery	6 (15.8)	7 (13.5)	0.77
Right coronary artery	18 (47.4)	27 (51.9)	0.83
Chronic total occlusions	5 (13.2)	9 (17.3)	0.77
Ostial lesions	1 (2.6)	3 (5.7)	0.64
Bifurcations	8 (21.1)	11 (21.2)	>0.99
Drug-eluting stents/lesion	1.4±0.1	1.2±0.1	0.13
Total stent length (mm)	24.7±2.7	25.0±1.8	0.33
Mean stent diameter (mm)	2.9±0.06	2.9±0.06	0.92
Stent overlap	15 (39.5)	13 (25.5)	0.18

Values are mean±SEM or n (%) as appropriate.

Discussion

This registry aimed to compare OCT data regarding coverage, apposition, neointimal formation and maturation as well as clinical outcome of two specific DES designs.

Table 2. OCT findings.

	O-SES				ZES				*p*-value O-SES vs. ZES		
	3 months	6 months	9 months	*p*-value	3 months	6 months	9 months	*p*-value	3 months	6 months	9 months
Time to follow-up (days)	104.6±15.8	182.1±14.4	267.3±13.8	–	92.9±15.3	174.3±16.0	278.9±21.3	–	0.68	0.15	0.13
Lesion level											
Analysed patients	8	21	5	–	31	7	8	–	–	–	–
Analysed lesions	8	21	9	–	35	9	8	–	–	–	–
Lesions with ≥10% uncovered struts	2 (25.0)	8 (38.1)	1 (11.1)	0.33	19 (54.3)	4 (44.4)	3 (37.5)	0.66	0.40	>0.99	0.29
Lesions with ≥30% uncovered struts	1 (12.5)	1 (4.8)	0 (0.0)	0.53	12 (34.3)	2 (22.2)	1 (12.5)	0.44	0.40	0.21	0.47
Lesions with ≥5% malapposed struts	1 (12.5)	7 (33.3)	1 (11.1)	0.32	12 (34.3)	3 (16.7)	1 (12.5)	0.49	0.40	>0.99	>0.99
Cross-section level											
Analysed cross-sections	367	663	343	–	1,064	263	240	–	–	–	–
Analysed cross-sections per patient	45.9±11.2	31.6±3.4	38.1±5.8	0.23	30.4±2.2	29.2±4.8	30.0±6.9	0.98	0.41	0.90	0.15
Struts analysed per cross-section	6.9±0.6	6.7±0.2	6.9±0.4	0.74	10.1±0.4	9.9±0.7	8.9±0.8	0.44	0.0003	<0.0001	<0.0001
Cross-sections with ≥10% uncovered struts, %	15.5 [12.2, 33.1]	10.5 [1.2, 37.4]	3.8 [0, 11.5]	0.16	41.5 [8.5, 83.3]	17.1 [6.8, 64.4]	13.9 [2.6, 46.4]	0.37	0.51	0.30	0.13
Cross-sections with ≥30% uncovered struts, %	5.1 [1.0, 9.9]	8.7 [0, 20.1]	0 [0, 1.3]	0.25	10.7 [0, 43]	9.1 [0, 27.1]	3.3 [0, 12.5]	0.43	0.71	0.85	0.08
Cross-sections with ≥5% malapposed struts, %	4.8 [0, 14.6]	5.1 [0, 21.8]	0 [0, 1.4]	0.17	9.4 [0, 31]	4.5 [1.2, 37.6]	0.8 [0, 7]	0.28	0.43	0.81	0.19
Vessel diameter, mm	2.7±0.2	2.8±0.1	2.6±0.1	0.69	2.9±0.1	2.6±0.1	2.8±0.3	0.33	0.23	0.09	0.72
Vessel area, mm^2	5.9±0.9	6.4±0.6	5.3±0.5	0.56	6.8±0.4	5.4±0.5	6.9±1.3	0.30	0.23	0.30	0.41
Stent diameter, mm	2.7±0.1	2.9±0.1	2.7±0.1	0.61	2.9±0.7	2.7±0.1	3.0±0.2	0.18	0.08	0.32	0.36
Stent area, mm^2	5.9±0.4	6.8±0.6	5.9±0.5	0.49	7.0±0.3	5.7±0.4	8.0±1.2	0.10	0.16	0.32	0.23
Neointimal area, mm^2	0.5±0.1	0.5±0.1	0.6±0.1	0.46	0.5±0.1	0.4±0.1	1.3±0.3	<0.001	0.37	0.18	0.19
Area of malapposition, mm^2	0 [0, 2.6]	0 [0, 0.3]	0 [0, 0]	0.13	0 [0, 2]	0 [0, 0.1]	0.03 [0, 0.9]	0.67	0.97	0.69	0.09
Strut level											
Analysed struts	2,671	4,307	2,458	–	10,817	2,774	2,109	–	–	–	–
Struts analysed/patient	307 [102, 583]	187 [142, 242]	258 [162, 358]	0.10	276 [176, 399]	225 [143, 458]	224 [114, 449]	0.80	0.99	0.27	0.79
Covered embedded struts, %	56.8±9.5	63.8±5.0	68.9±8.1	0.59	58.3±4.6	61.1±8.1	75.7±7.2	0.24	0.99	0.67	0.53
Covered protruding struts, %	27.2 [15.7, 38.4]	29.3 [13.7, 38.6]	18.9 [14.5, 43.4]	0.90	17.1 [7.2, 27.1]	19.6 [6.2, 42.7]	18.0 [6, 23.8]	0.50	0.08	0.80	0.41
Uncovered apposed struts, %	4.5 [3.7, 7.7]	1.4 [0.4, 8.5]	0.6 [0.1, 2.9]	0.15	9.9 [1.4, 28.8]	5.0 [1.9, 17]	2.0 [0.7, 9.9]	0.20	0.63	0.07	0.19
Uncovered malapposed struts, %	2.7 [0, 3.7]	1.9 [0.2, 6.5]	0.0 [0, 3]	0.37	1.4 [0, 9.9]	0.6 [0.1, 7.8]	0.8 [0, 2.2]	0.30	0.98	0.63	0.75
Neointimal thickness of covered struts, µm	92.7 [68, 101]	100.0 [85, 115]	91.0 [81, 106]	0.82	90.0 [70, 110]	80.0 [60, 120]	145.0 [103, 233]	0.002	0.98	0.26	0.07
GSI analysis											
Analysed ROIs, n	803	2,366	1,153	–	3,402	1,326	1,594	–	–	–	–
ROI lengths, µm	64.3 [49, 75]	67.7 [57, 89]	65.0 [54, 70]	0.39	67.5 [49, 87]	51.9 [43, 73]	109.4 [79, 145]	0.0001	0.71	0.06	0.01
GSI value	96.2±2.3	98.9±1.6	99.0±1.8	0.47	91.9±1.2	96.1±2.8	104.0±2.2	0.0001	0.16	0.52	0.07
Mature neointimal tissue, %	51.4±6.4	59.3±3.8	58.0±4.1	0.532	42.5±2.9	50.1±6.1	68.9±4.8	0.0001	0.284	0.189	0.069

Values are mean±SEM or n (%) as appropriate. GSI: greyscale signal intensity; ROI: region of interest

The main findings are:

1. No differences were found in intra- and inter-group comparisons for coverage and apposition.
2. The inter-group comparison showed no differences for neointimal thickness and maturation.
3. The O-SES showed no differences over time, while the ZES presented an increased neointimal thickness and tissue maturation between three, six and nine months.
4. Strut coverage was already nearly complete after three months in both DES.

CLINICAL IMPLICATIONS

The O-SES has shown promising results in TLF and LST at nine-month follow-up (BIOFLOW-I)[10]. The BIOFLOW-II trial compared the nine-month late lumen loss of O-SES with everolimus-eluting-stents (EES). The first results showed a comparable late lumen loss, non-inferiority and comparable clinical safety and efficacy[18]. The combination of sirolimus and poly-L-lactic acid used in O-SES seems to reduce neointimal hyperplasia effectively without decreasing neointimal coverage. The present registry found no differences for neointimal thickness,

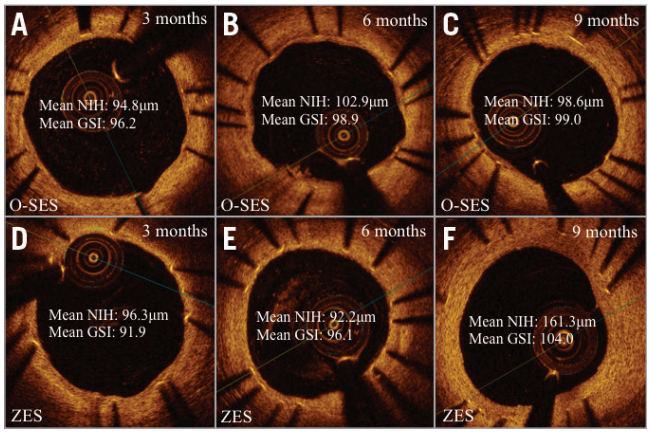

Figure 4. *OCT images at three, six and nine-month follow-up. Representative OCT images at three, six and nine-month follow-up after implantation of O-SES (A, B, & C) and ZES (D, E, & F). The figure presents the comparable healing pattern of the two DES. In the case of nine-month follow-up of ZES, an increased neointimal thickness and maturation was observed. GSI: greyscale signal intensity; NIH: neointimal hyperplasia*

maturation or coverage. ZES showed a significantly increased neointimal formation after nine months when analysed over time; yet, this increase did not reach clinical significance in an intergroup analysis to O-SES. These results possibly reflect the different drug release kinetics. While zotarolimus is released over about three months, the drug release and polymer degradation of O-SES occur within 12 to 24 months. We therefore suggest that OCT should be able to measure even small differences between different DES. If any differences exist, our OCT data suggest that they occur later than nine to 12 months.

Guidelines for DAPT duration after PCI depend on the underlying disease. If DAPT is prescribed only for DES healing in non-ACS patients, current instructions for use allow interrupting DAPT after even one month (ZES) and six months (O-SES). DAPT reduces the risk of stent thrombosis, but long-term use increases the rate of bleeding events. Balancing these risks remains a challenge; therefore, reliable detection of DES coverage with mature tissue may allow stopping DAPT early in individual patients. We found both DES to be almost completely covered after three months, with no differences in coverage, apposition and clinical outcome, suggesting a reduction of DAPT to three months for O-SES in non-ACS patients to be possibly safe.

OCT-BASED GSI ANALYSIS FOR THE ASSESSMENT OF NEOINTIMAL MATURATION

Although OCT analysis has improved our capability to distinguish covered from uncovered struts, not all covered struts are covered by mature neointimal tissue[9]. Coverage by immature tissue was previously shown as an important risk factor for LST[13]. An OCT-based GSI analysis was previously introduced to assess tissue characterisation and discriminate mature and immature tissue[9]. This may have important implications for clinical practice.

Table 3. Clinical follow-up.

Characteristics	O-SES (n=34 patients)	ZES (n=46 patients)	*p*-value
12-month follow-up			
Lost to follow-up	2 (5.9)	2 (4.3)	>0.99
Completed 12-month follow-up	32 (94.1)	44 (95.7)	>0.99
MACE	3 (9.4)	3 (6.8)	0.69
All-cause death	2 (6.3)	0 (0)	0.17
Cardiac death	0 (0)	0 (0)	>0.99
Unstable angina pectoris	6 (18.8)	7 (15.9)	0.77
NSTE-ACS	0 (0)	0 (0)	>0.99
STEMI	0 (0)	0 (0)	>0.99
Target vessel revascularisation	0 (0)	4 (9.1)	0.13
Target lesion failure	3 (9.4)	3 (6.8)	0.69
Target lesion revascularisation	3 (9.4)	3 (6.8)	0.69
In-stent restenosis	3 (9.4)	3 (6.8)	0.69
Late stent thrombosis	0 (0)	0 (0)	>0.99
Major bleeding events	1 (3.1)	0 (0)	0.42
Minor bleeding events	1 (3.1)	0 (0)	0.42
Cerebrovascular events	1 (3.1)	1 (2.3)	>0.99
Antiplatelet therapy			
Patients following MI	9	8	
Dual at 3 months	9 (100)	8 (100)	>0.99
Dual at 6 months	8 (88.9)	8 (100)	>0.99
Dual at 12 months	8 (88.9)	7 (87.5)	>0.99
Patients following non-MI	23	36	
Dual at 3 months	21 (91.3)	35 (97.2)	0.63
Dual at 6 months	19 (82.6)	30 (83.3)	>0.99
Dual at 12 months	13 (56.5)	23 (63.9)	0.60

The data are presented as number of events (n) and percentage of total number (%). No differences were found concerning the observed parameters.

To determine the quality of neointimal tissue, GSI analyses were performed in the present registry. While no differences were found between the two DES, ZES demonstrated significant maturation over time, which was not observed in O-SES. The six- and nine-month data showed no additional maturation compared to three-month data. This may be explained by the higher effectiveness of sirolimus concerning suppression of smooth muscle cell proliferation compared to zotarolimus[19]. Furthermore, these results again reflect the different drug release kinetics. Interestingly, O-SES did not exhibit more malapposition despite less neointimal tissue. This may support the concept of biocompatible polymers.

OCT - A SURROGATE FOR CLINICAL OUTCOME?

Although event rates after PCI with new-generation DES are remarkably low, no plateau is reached over time[1]. Therefore, there is an unmet need to improve current PCI strategies. Due to the low event rates, clinical studies with large numbers are necessary to compare

clinical endpoints of upcoming DES generations. Surrogate markers could be able to predict clinical outcome even in smaller populations[7]. Detailed OCT analysis may allow judgement on safety and efficacy in a much smaller cohort and give surrogates until data from large clinical trials are available. In addition, OCT may be hypothesis-generating, as recently executed with biolimus-eluting stents (BES)[4]. After encouraging OCT data this DES has now been tested in a randomised trial for one month of DAPT (LEADERS FREE)[20]. Furthermore, an OCT substudy of the LEADERS trial presented evidence for 0.6% of uncovered struts after nine months[21]. Although we present only a limited number of patients, our findings regarding clinical outcome are similar to the findings of multicentre trials. The BIOFLOW-III registry aimed to test O-SES in clinical practice and found a low 12-month TLF rate of 5.1%[14]. Additionally, the RESOLUTE All-Comers trial compared the 12-month TLF rates of ZES (8.2%) and EES (8.3%)[22]. Recently published data from the BIOSCIENCE trial found no significant differences in TLF for O-SES (6.5%) and EES (6.6%)[3]. The clinical outcome of O-SES and ZES have not been evaluated head-to-head to date. Since our results show comparable findings of OCT data and clinical outcome, our findings may suggest a similar clinical performance.

Limitations

A limitation of this registry was the absence of a baseline OCT analysis. A primary stent-vessel mismatch, as a reason for late malapposition, may therefore be an issue, and the results of the intra-group comparison have to be interpreted with caution. The MACE rate is in the range of current studies and supports the PCI techniques used as being the best available standard. Additionally, the time point of OCT analysis was determined by chance at the index procedure. Therefore, the groups differed in size, which limits our findings. A further limitation is OCT accuracy. Due to its resolution, a precise analysis of neointimal cellular tissue cannot be distinguished and a misclassification of struts could be possible. Cut-off values regarding tissue maturation are arbitrary and should be further validated. Nevertheless, the characterisation of neointimal maturation by OCT-based GSI analyses may be an important step towards the assessment of vascular healing. The fact that no randomisation was performed also limits our results. Although there was no LST or recurrent MI, the small number of patients involved in this registry limits the validity of our findings. Furthermore, we cannot exclude type II error in the detection of adverse events and further complications.

Conclusions

Neointimal coverage was nearly complete at three-month follow-up in both DES. Between three and nine months, stent healing had progressed with no significant differences concerning strut coverage and apposition between the DES. Furthermore, no difference in clinical outcome was found in this OCT analysis, as in large clinical trials comparing these two DES to the current standard, namely the EES. We propose OCT-based follow-up of DES as a potential surrogate parameter to predict a patient's clinical outcome.

Impact on daily practice

No differences were found concerning OCT-based assessments as well as clinical follow-up between the two DES. Our findings may support the hypothesis that OCT-based analyses in small patient cohorts sensitively detect stent healing and could possibly be regarded as surrogates for DES healing and clinical outcome.

Conflict of interest statement

C-H. Heeger has received travel grants from St. Jude and Biotronik. R. A. Byrne reports receiving lecture fees from B. Braun Melsungen AG, Biotronik and Boston Scientific and research grants to the institution from Boston Scientific and Heartflow. M. Joner reports the following financial decision-making role: Biotronik, Medtronic and Terumo Corporation. K-H. Kuck has received research contracts/grants from Medtronic, St. Jude and Boston Scientific as well as consulting fees from St. Jude and Edwards Lifesciences. M. Bergmann has received travel grants, research grants and speaker honoraria from Medtronic, Biotronik and St. Jude. The other authors have no conflicts of interest to declare.

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