Early healing after treatment of coronary lesions by thin strut everolimus, or thicker strut biolimus eluting bioabsorbable polymer stents: the SORT-OUT VIII OCT study

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Early healing after treatment of coronary lesions by thin strut everolimus, or thicker strut biolimus eluting bioabsorbable polymer stents: The SORT-OUT VIII OCT study

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Abstract

Aims: Early healing after drug-eluting stent (DES) implantation may reduce the risk of stent thrombosis. The aim of this study was to compare patterns of early healing after implantation of the thin strut everolimus-eluting Synergy DES (Boston Scientific) or the biolimus-eluting Biomatix Neoflex DES (Biosensors).

Methods and Results: A total of 160 patients with the chronic or acute coronary syndrome were randomized 1:1 to Synergy or Biomatrix DES. Optical coherence tomography (OCT) was performed at baseline and at either 1- or 3-month follow-up. The primary endpoint was a coronary stent healing index (CSHI), a weighted index of strut coverage, neointimal hyperplasia, malapposition, and extrastent lumen. A total of 133 cases had OCT follow-up and 119 qualified for matched OCT analysis. The median CSHI score did neither differ significantly between the groups at 1 month: Synergy 8.0 (interquartile range [IQR]: 3.0; 14.0) versus Biomatrix 8.5 (IQR: 4.0; 15.0) ($p = 0.47$) nor at 3 months: Synergy 6.5 (IQR: 2.0; 13.0) versus Biomatrix 6.0 (IQR: 4.0; 11.0) ($p = 0.83$). Strut coverage was 84.6% (IQR: 72.0; 97.9) for Synergy versus 77.6% (IQR: 70.1; 90.3) for Biomatrix ($p = 0.15$) at 1 month and 90.3% (IQR 79.0; 98.8) (Synergy) versus 83.9% (IQR: 77.5; 92.6) (Biomatrix) ($p = 0.068$) at 3 months. Pooled 1- and 3-month coverage was 88.6% (IQR: 74.4; 98.4) for Synergy compared with 80.7% (IQR: 73.2; 90.8) for Biomatrix ($p = 0.02$).

Conclusions: The early healing response after treatment with the Synergy or Biomatrix DES did not differ significantly as determined by a healing index. The Synergy DES showed overall better early stent strut coverage.

KEYWORDS
drug-eluting stent, optical coherence tomography, stent enhancement

1 | INTRODUCTION

First-generation drug-eluting stents (DES) reduced the incidence of restenosis when compared to bare metal stents but were associated with an increased risk of late stent thrombosis (ST).[1–3] The drug-eluting polymer coating caused local inflammation and induced heterogeneous healing patterns with delayed endothelialisation, stent malapposition, evaginations of the vessel wall, and neoatherosclerosis. As these patterns were associated with increased rates of ST[4,5] newer generation DES were introduced with more biocompatible and bioabsorbable polymers to reduce inflammation and subsequently the risk of ST. The development improved clinical outcomes compared with first-generation DES.[6,7] However, the differences in design for DES with bioabsorbable polymers may have important implications for early healing patterns. The risk of stopping platelet inhibition drugs at early time points is a major concern if healing is incomplete. In particular, patients with higher bleeding risk selected for short dual antiplatelet therapy (DAPT) duration might have a lower risk of early stent-related events if the stent design facilitates a fast and balanced healing response. Thinner stent struts may reduce the risk of ST as they have been shown to induce less flow disturbance, reduce platelet activation,[8] and facilitate faster endothelialization compared with thicker struts.[9]

The aim of this study was to compare early coronary vessel healing detected by optical coherence tomography (OCT) 1 or 3 months after implantation of two different bioabsorbable polymer DES in patients randomized to the thin strut (74–84 μm), everolimus-eluting Synergy DES with an abluminal polymer that degrades within 4 months,[10] and the thick strut (112 μm), biolimus-eluting Biomatrix Neoflex DES with a polymer degradation within 6–9 months.[11]

2 | METHODS

2.1 | Study design

The SORT-OUT VIII OCT study was a prospective, open-label, single-blind, active treatment-controlled randomized trial, comparing stent healing response after 1 and 3 months in patients treated with either the 74–84-μm-thick Synergy DES or the 120 μm Biomatrix DES at two Danish tertiary heart centers (Aarhus University Hospital and Odense University Hospital). A detailed description of the study stents is given in the Supporting Information File. Randomization (1:1) was performed using a web-based, concealed, randomization system (TrialPartner; Aarhus University) and was stratified by diabetes and ST-elevation myocardial infarction (STEMI). The inclusion of 160 patients was planned to have a follow-up with OCT after 1 (Cohort A; 80 patients) or 3 months (Cohort B; 80 patients). The study complies with the Declaration of Helsinki and was approved by the Central Denmark Region Committees on Health Research Ethics and The Danish Data Protection Agency. Public registration was made to clinicaltrails.gov (NCT02253108). All patients provided written informed consent for participation in the trial.

2.2 | Study population

Inclusion criteria were chronic—or acute coronary syndrome, age >18 years, a de novo coronary lesion with an indication for percutaneous coronary intervention (PCI), and the ability to provide signed informed consent. Exclusion criteria were expected survival of less than 1 year, severe heart failure (New York Heart Association ≥ III), s-creatinine > 120 μmol/L, ostial left main coronary artery—, ostial right coronary artery—or true bifurcation lesions with a high risk of side branch failure, lesions to be treated by a planned two-stent technique, or allergy to contrast media, aspirin, clopidogrel, ticagrelor, prasugrel, everolimus, or biolimus.

2.3 | Study procedure

PCI was performed by the radial or femoral approach. Patients received aspirin (300 mg), unfractionated heparin (5000–10,000 IU), and either clopidogrel (300–600 mg), ticagrelor (180 mg), or prasugrel (60 mg) before or immediately after the intervention. PCI was performed by standard implantation techniques. OCT findings were used at the physician's discretion for guiding the procedure. Predilatation of the lesion, direct stenting, and postdilatation of the stent was performed at the discretion of the treating physician. Post-PCI OCT scans were performed as the last step before wire removal. In patients with more than one lesion requiring treatment, the allocated study stent was used in all lesions. Bivalirudin or glycoprotein IIb/IIIa inhibitor was administrated at the physician's discretion. DAPT with clopidogrel, ticagrelor, or prasugrel was used for 12 months in patients after myocardial infarction (MI) and for 6 months in stable patients. Statins were prescribed to all patients after PCI.

2.4 | OCT acquisition

OCT scans were performed using the Lunawave intracoronary optical frequency domain imaging system (Terumo) after intracoronary administration of nitroglycerine. Scans were recorded at 158 frames/s with a catheter pullback speed of 20 or 40 mm/s in cases with long stented segments.

2.5 | Clinical follow-up

Clinical endpoints were obtained during 1- or 3-month angiographic follow-up and at 3-year using Danish registry data as described in the SORT-OUT VIII trial.[12] All clinical endpoints were adjudicated by an independent event committee. Register-based clinical follow-up will continue until 5 years for all enrolled patients.

2.6 | Clinical endpoints

The composite endpoint of target lesion failure (TLF) included cardiac death, acute MI not clearly attributed to a nontarget lesion, and target lesion revascularization. Further individual endpoints were all-cause mortality, target vessel failure, and ST. Clinical endpoint definitions follow those described in the SORT-OUT VIII trial.[12]

2.7 | Healing endpoints

The primary endpoint was a coronary stent healing index (CSHI), a weighted index including six healing parameters assessed by OCT: (1) percentage (%) of uncovered struts, (2) % uncovered jailing and two-dimensional (2D)-OCT malapposed struts, (3) total length of persisting 3D-OCT malapposed struts and (4) acquired 3D-OCT malapposed struts, (5) maximal neointimal thickness (NIT), and (6) extrastent lumen enlargement from baseline to follow-up (Figure 1). A high cumulated index score represents a combination of more incomplete healing and a higher degree of adverse vessel wall findings in the stented segment. Secondary OCT endpoints included stent strut coverage, malapposition, NIT, average and minimal stent area (MSA), average and minimal lumen area (MLA), percent area stenosis (AS%), stent recoil, lumen late loss (LLL), extrastent lumen, evaginations, 3D-OCT verified stent fracture, and thrombus on struts.

2.8 | OCT analysis

Baseline and follow-up OCT were matched at frame level and analysed by blinded observers using semiautomated analysis software (QCU-CMS Research, Leiden University Medical Center). Qualitative as well as quantitative OCT analyses were performed using the same definitions as in the SORT OUT VII OCT study[13] with the following additions: quantitative OCT analysis was performed with a sampling frequency of 0.65 mm, malapposed clusters of struts were identified in 3D reconstructions using the QangioOCT RE software (Medis Medical Imaging). For every cluster of malapposed struts, multiple reconstructed measurement planes were fitted, and the cumulated malapposed strut length was measured. Stent fracture was defined as discontinuity of struts confirmed in a 3D reconstruction. The reference area was found within 2–10 mm from the stent edge. If a reliable reference area was not detectable by OCT, the 3D quantitative coronary angiography (QCA) reference in the same segment was used. MSA was reported as an absolute value and in the percentage of interpolated reference area (stent AS%). Stent recoil was assessed as loss in the mean stent area at follow-up. LLL was loss in MLA from baseline to follow-up. AS% was calculated as 1−(MLA/interpolated reference area at the site of MLA). Please

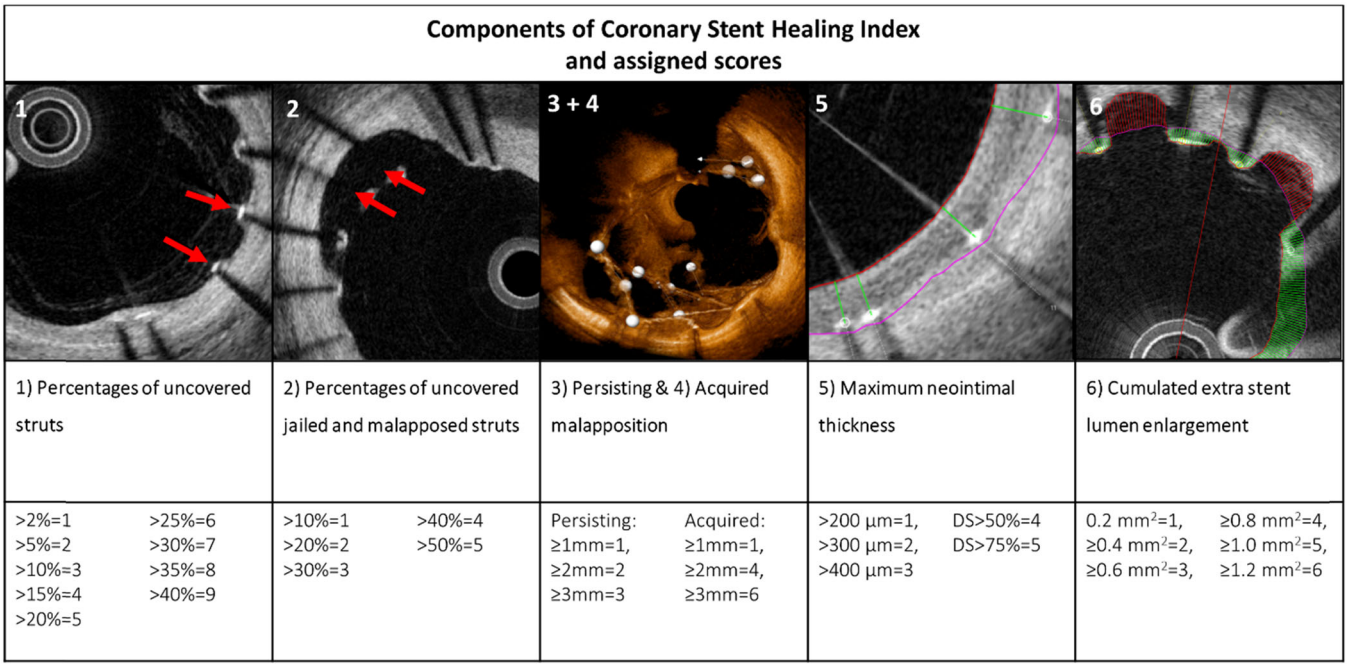

FIGURE 1 Components of the coronary stent healing index and the weighted scores. DS, diameter stenosis; mm, millimeter. [Color figure can be viewed at wileyonlinelibrary.com]

see the Supporting Information for the description of the QCA analysis.

2.9 | Sample size

The assigned values in the weighted index were estimates based on limited available evidence on early healing after implantation of the Biomatrix Neoflex DES and earlier generation DES[14,15] as well as internal Core Lab data.[14,16] Estimates on coverage for Synergy were based on animal experiments by the manufacture and preliminary findings.[14,15]

For the Biomatrix DES, the expected mean healing index score at 1 month was 23, standard deviation (SD) = 7. For the Synergy DES, the expected score was 18, SD = 5 (see Supporting Information: Table 1 for values on each index component). Power calculation assumptions were $\alpha = 0.05$ and power = 0.90. A sample size of 64 patients was needed in both Cohorts A and B. We decided to include 160 patients in total taking into account possible loss to follow-up.

2.10 | Statistical analysis

Categorical variables are presented as counts and % and were compared using the χ^2 test, or Fisher's exact test if a cell value was below 5. Continuous variables are presented as mean ± SD and were compared using a *t* test if following a Gaussian distribution. If non-Gaussian distributed, data are presented as median and interquartile range and were compared by the Wilcoxon Mann–Whitney *U* test. Multiple linear regression analysis was performed for the pooled population to assess for independent predictors of high CSHI scores or uncovered struts. Variables included in the model were age, stent length, stent type, diabetes, stent area, STEMI, calcified plaque in the lesion, and lipid plaque in the lesion. Analysis was performed using STATA 16.0.

3 | RESULTS

3.1 | Study population

A total of 160 patients were included in the study; 133 (83.1%) patients had an angiographic follow-up with OCT and 119 (74.4%) entered the matched OCT analysis; 62 patients in Cohort A and 57 in Cohort B. Detailed patient flowchart is presented in Figure 2. Baseline characteristics were well balanced between treatment groups for both cohorts (Table 1). Study lesions and procedural characteristics were comparable between stent groups for both Cohorts A and B (Supporting Information: Table 2).

3.2 | Primary endpoint, the CSHI

The CSHI score for both cohorts is presented in Figure 3. At 1-month follow-up, the median index score was 8 (3.0; 14.0) in the Synergy group and 8.5 (4.0; 15.0) in the Biomatrix group ($p = 0.47$). At 3 months, the CSHI score was 6.5 (2.0; 13.0) in the Synergy group versus 6 (4.0; 11.0) in the Biomatrix group ($p = 0.83$). By pooled 1- and 3-month analysis, the median cumulated CSHI score was 7.0 (3.0; 13.0) for the Synergy DES and 7.0 (4.0; 12.0) for the Biomatrix

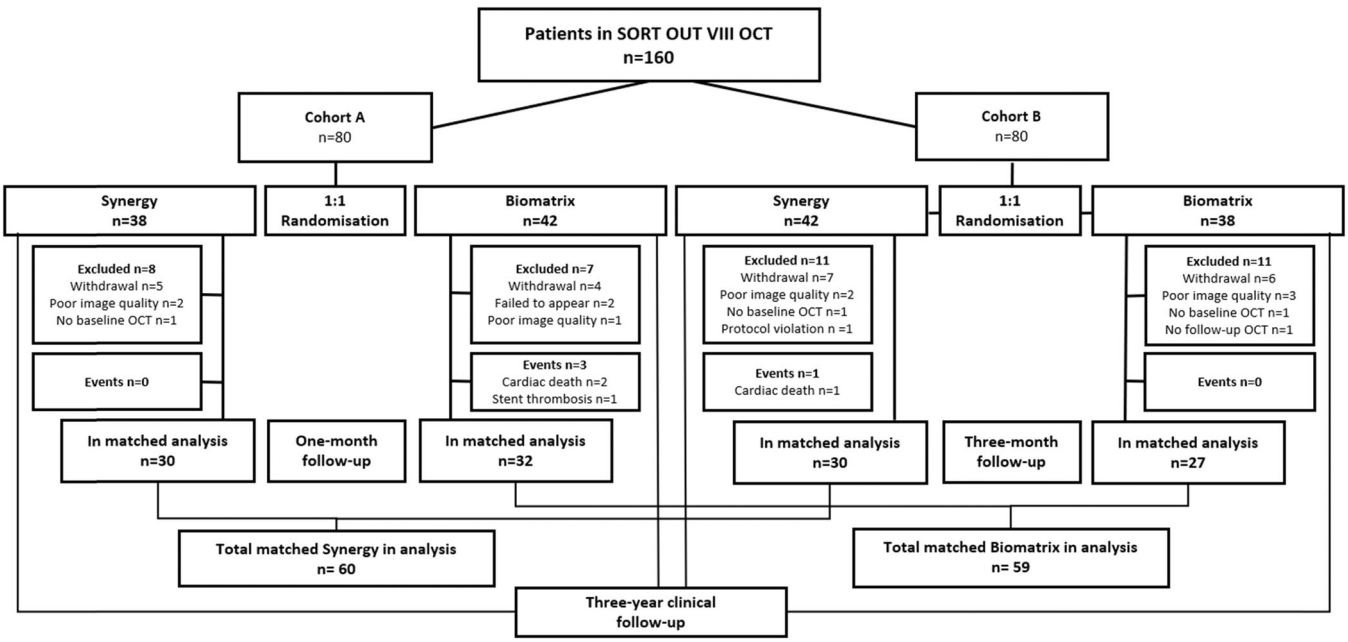

FIGURE 2 Patient flowchart. Patients flowchart. *n*, number; OCT, optical coherence tomography.

TABLE 1 Patient baseline characteristics.

	Cohort A, 1-month follow-up, *n* = 62			Cohort B, 3-month follow-up, *n* = 57		
	Synergy *n* = 30	Biomatrix *n* = 32	*p* Value	Synergy *n* = 30	Biomatrix *n* = 27	*p* Value
Age (years)	63.4 ± 8.3	65.0 ± 8.7	0.46	60.4 ± 9.5	61.3 ± 8.9	0.72
Male gender, *n* (%)	23 (76.7)	25 (78.1)	0.89	24 (80.0)	19 (70.4)	0.40
BMI (kg/m^2)	27.5 ± 4.6	27.5 ± 4.2	0.97	28.1 ± 3.5	27.4 ± 4.9	0.54
Diabetes, *n* (%)	3 (10.0)	4 (12.5)	1.00	4 (13.3)	6 (22.2)	0.49
Current smoking, *n* (%)	8 (28.6)	8 (25.0)	0.87	11 (36.7)	7 (25.9)	0.50
Family history of IHD, *n* (%)	11 (36.7)	15 (46.9)	0.59	16 (53.3)	10 (37.0)	0.43
Creatinine (mmol/L)	82.7 ± 15.4	90.0 ± 28.5	0.29	82.3 ± 18.9	79.3 ± 19.5	0.60
Antihypertensive treatment, *n* (%)	16 (53.3)	16 (50.0)	0.54	13 (43.3)	13 (48.1)	0.26
Statin treatment, *n* (%)	12 (40.0)	16 (50.0)	0.46	12 (40.0)	12 (44.4)	0.70
Systolic blood pressure (mmHg)	133.7 ± 20.6	137.6 ± 22.7	0.50	134 ± 23.9	139 ± 22.8	0.41
Diastolic blood pressure (mmHg)	78.7 ± 13.5	75.9 ± 15.4	0.48	80.3 ± 13.4	76.6 ± 6	0.27
Previous PCI, *n* (%)	3 (10.0)	4 (12.5)	0.56	5 (16.7)	3 (11.1)	0.55
Previous AMI, *n* (%)	3 (10.0)	5 (15.6)	0.48	4 (13.3)	3 (11.1)	0.80
Previous CABG, *n* (%)	2 (6.7)	0 (0.0)	0.14	0 (0.0)	2 (7.41)	0.13
LVEF, %	60 [50; 60]	60 [55; 65]	0.80	60 [60; 60]	60 [55; 60]	0.36
Indications for PCI, *n* (%)						
SAP	15	13	0.46	14	14	0.70
UAP	0	0	–	2	2	1.00
Non-STEMI	7	10	0.49	6	6	0.84
STEMI	8	9	0.90	8	5	0.46

Abbreviations: AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass grafting; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; SAP, stable angina pectoris; STEMI, ST-elevated myocardial infarction; UAP, unstable angina pectoris.

TABLE 2 Baseline OCT characteristics.

	Cohort A, 1-month follow-up, *n* = 62			Cohort B, 3-month follow-up, *n* = 57		
	Synergy *n* = 30	Biomatrix *n* = 32	*p* Value	Synergy *n* = 30	Biomatrix *n* = 27	*p* Value
Mean stent area (mm^2)	8.4 ± 2.4	9.4 ± 2.7	0.12	9.4 ± 0.4	9.3 ± 2.4	0.87
Min. stent area (mm^2)	6.6 ± 1.9	7.5 ± 2.2	0.09	7.6 ± 2.2	7.3 ± 2.0	0.58
Stent area stenosis %	32.0 ± 16.3	36.3 ± 11.2	0.23	34.2 ± 14.4	35.0 ± 16.4	0.85
Mean lumen area (mm^2)	7.8 ± 2.3	8.7 ± 2.4	0.15	8.7 ± 2.2	8.5 ± 7.6	0.66
Min. lumen area (mm^2)	6.0 ± 1.8	6.8 ± 2.0	0.15	7.0 ± 2.0	6.4 ± 1.8	0.25
Lumen area stenosis %	40.0 ± 13.5	42.8 ± 9.7	0.36	40.5 ± 13.4	43.8 ± 26.2	0.46
Calcified plaque in lesion, *n* (%)	21 (70.0)	20 (62.5)	0.53	3 (10.0)	6 (22.2)	0.28
Lipid plaque in a lesion, *n* (%)	14 (46.7)	16 (50.0)	0.79	26 (86.7)	24 (88.9)	0.80

Abbreviation: OCT, optical coherence tomography.

DES ($p = 0.44$). Few patients in both stent groups received points for persisting and acquired malapposition (Parameters 3 and 4) or extrastent lumen enlargement (Parameter 6). Dot plots of measured values for uncovered struts (Parameter 1), uncovered jailed—and 2D malapposed struts (Parameter 2) and maximum NIT (Parameter 5) are provided in Figure 4. When using multiple linear regression analysis, we were unable to identify independent predictors of a high CSHI score.

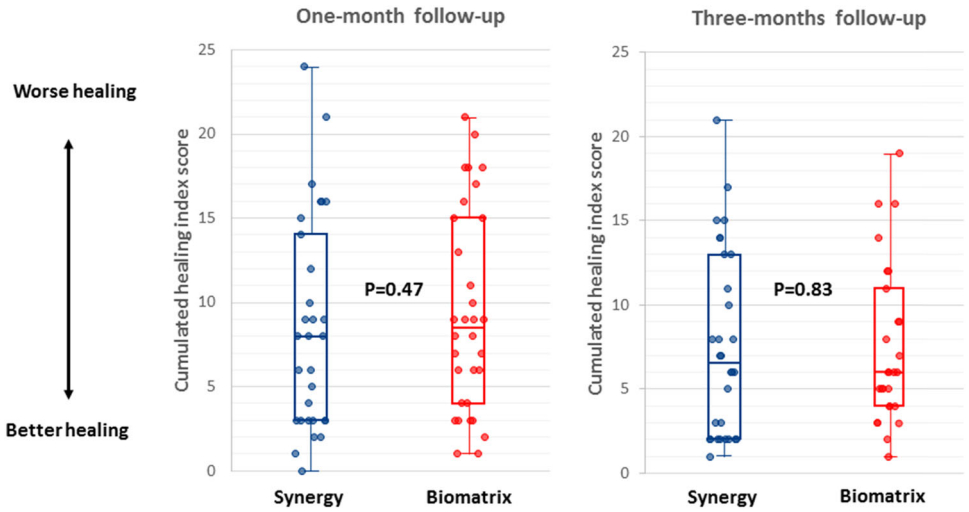

FIGURE 3 Primary endpoint of coronary stent healing index (CSHI). CSHI for each patient 1 and 3 months after implantation of the Synergy or the Biomatrx drug-eluting stent. Medians Q1 and Q3 are indicated by the boxes. [Color figure can be viewed at wileyonlinelibrary.com]

3.3 | Secondary OCT endpoint

3.3.1 | Strut coverages

Strut coverage for each cohort and the pooled population are plotted in Figure 5A. In the pooled analysis, strut coverage was significantly more complete in the Synergy group with a median of 88.6% (74.4%; 98.4%) compared with 80.7% (73.2%; 90.8%) in the Biomatrix group ($p = 0.02$). Wide interpatient ranges in coverages were seen in both stent groups (1 month: Synergy: 44.6%–100.0%; Biomatrix: 61.5%–98.7%; 3 months: Synergy: 61.5%–100.0%; Biomatrix: 62.5%–98.4%) and for all treatment indication groups (Table 3 and Supporting Information: Figure 1). Age and the presence of lipid plaque in lesions were independent predictors of uncovered struts. An increase in age by 1 year resulted in an increase in uncovered struts of 0.28 percentage points (95% confidence interval [CI]: 0.02–0.55). The presence of lipid plaque in the treated lesion was associated with an increase in uncovered struts by a factor of 6.0 (95% CI: 1.08–10.8). Stent length and type, diabetes, mean stent area, and STEMI as indication or presence of calcified plaque were not independent predictors of uncovered struts.

3.3.2 | Malapposition

Results of baseline and follow-up malapposition are found in Figure 5B. Acquired malapposed clusters were shown in the Synergy group; 1/30 at 1 month and 2/30 at 3 months (Supporting Information: Table 4). Two of these patients had STEMI as an indication and buildup of thrombus at baseline. The third patient showed coronary bending motion identified at 3 months. Examples of abolished, persisting and acquired malapposition are illustrated in Supporting Information: Figure 2.

Additional secondary endpoints are presented in Table 2 and 3.

3.4 | Clinical outcome

Three STEMI patients suffered sudden cardiac death (Biomatrix; $n = 2$, Synergy; $n = 1$) before the planned OCT follow-up. One patient in the Biomatrix group had ST within 24 h post-PCI, the patient had no follow-up OCT performed. Three years of clinical follow-up are presented in Table 4 and Supporting Information: Figure 3.

4 | DISCUSSION

The SORT OUT VIII OCT study aimed to identify possible advantages in early healing patterns after treatment with the thin strut, everolimus-eluting Synergy stent compared with the thicker strut biolimus eluting Biomatrix DES. The main findings were: (1) the Synergy DES did not show improved early coronary vessel healing compared with the Biomatrix DES as determined by the CSHI, (2) the Synergy DES demonstrated better early strut coverage, (3) neither the Synergy nor the Biomatrix DES showed excessive neointimal hyperplasia or cases with substantial enlargement of the lumen outside the stent, and (4) major interpatient variation in early healing patterns was seen both in the Synergy and the Biomatrix groups.

The use of combined index endpoints for OCT-evaluated healing was introduced in the TROFI II study in 2015.[17] The rationale for the combined healing index is to combine multiple OCT parameters associated with impaired clinical outcomes in a single endpoint. In autopsy and imaging studies (intravascular ultrasound or OCT)[18,19] uncovered and malapposed struts correlated with ST and malapposition was associated with flow disturbances and ST.[20] Furthermore, neointimal hyperplasia predisposed to restenosis.[21] Extrastent lumen enlargement may indicate the presence of positive remodeling, evaginations, and in severe cases, aneurysms possibly caused by mechanical forces and hypersensitivity reactions against the device as with the first-generation DES.[4]

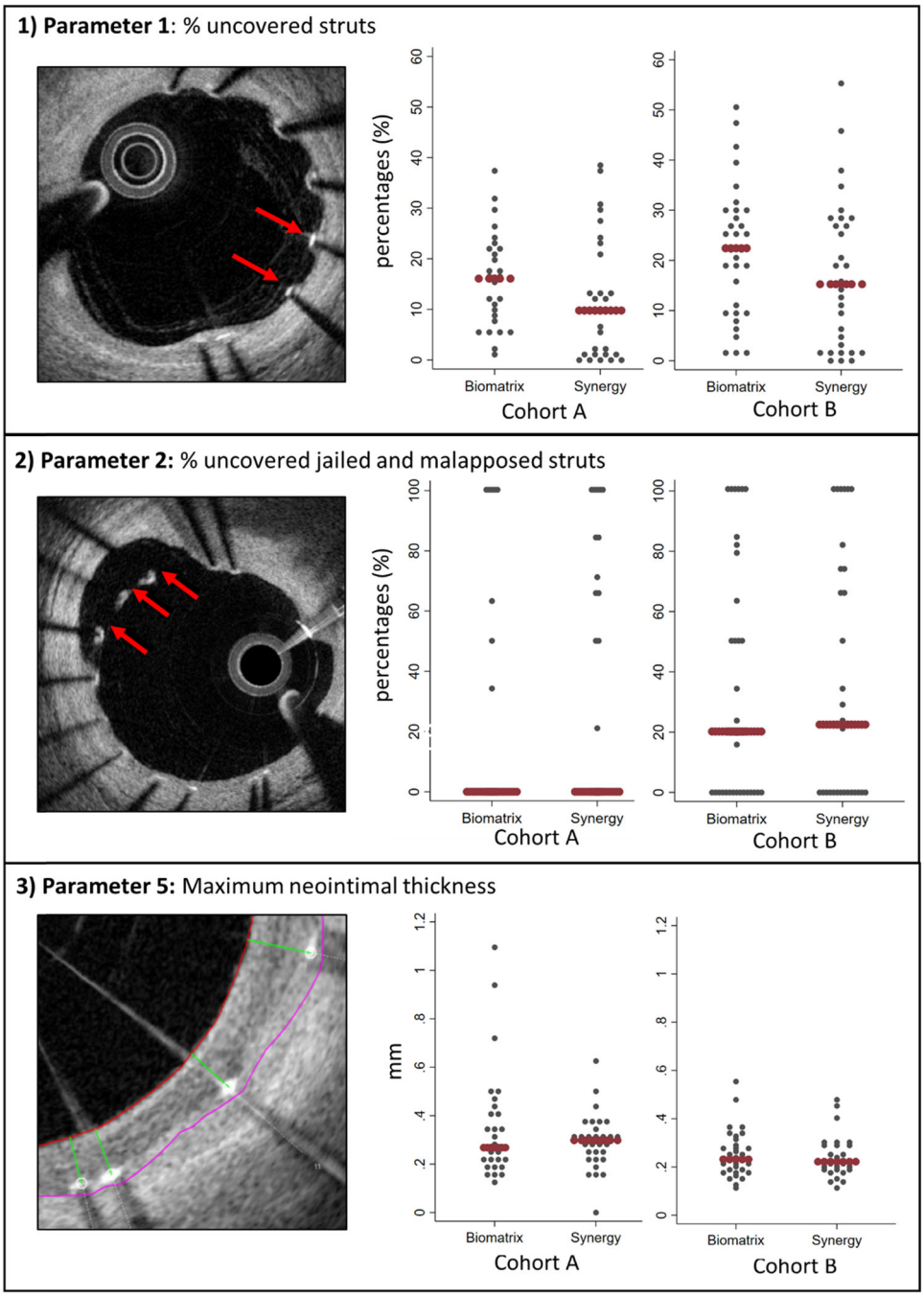

FIGURE 4 Selected parameters in coronary stent healing index. [Color figure can be viewed at wileyonlinelibrary.com]

Our follow-up study showed that the thinner strut Synergy DES was not associated with a more favorable early healing pattern than the Biomatrix DES as determined by the healing index although strut coverage was more complete with Synergy. Both stents showed excellent ability to heal in presence of malapposition at baseline. We did not identify excessive neointimal hyperplasia or cases with the substantial extrastent lumen.

A favorable early healing response after stent implantation could be important in patients with higher bleeding risk as it may allow for safe early discontinuation of antiplatelet drugs. In a histopathological study, Finn et al. reported that a frame level ratio of uncovered struts >30% was associated with ST[22] and a cutoff value of 6% of uncovered struts was found to be associated with major safety events.[23] At 1 month, the OCT-EROS study found mean strut coverages of 78.5% in patients with NSTEMI[24] and Won et al. found mean strut coverage of 91.5% at 3 months in a pooled analysis of different newer generation DES.[25] The Synergy DES was previously shown to cover 94.5 ± 4.4% of struts in 22 patients after 3 months whereas Biomatrix had 3-month coverages of 83.9%[15] (n = 30). This difference corresponds well with the findings in our study. Our study

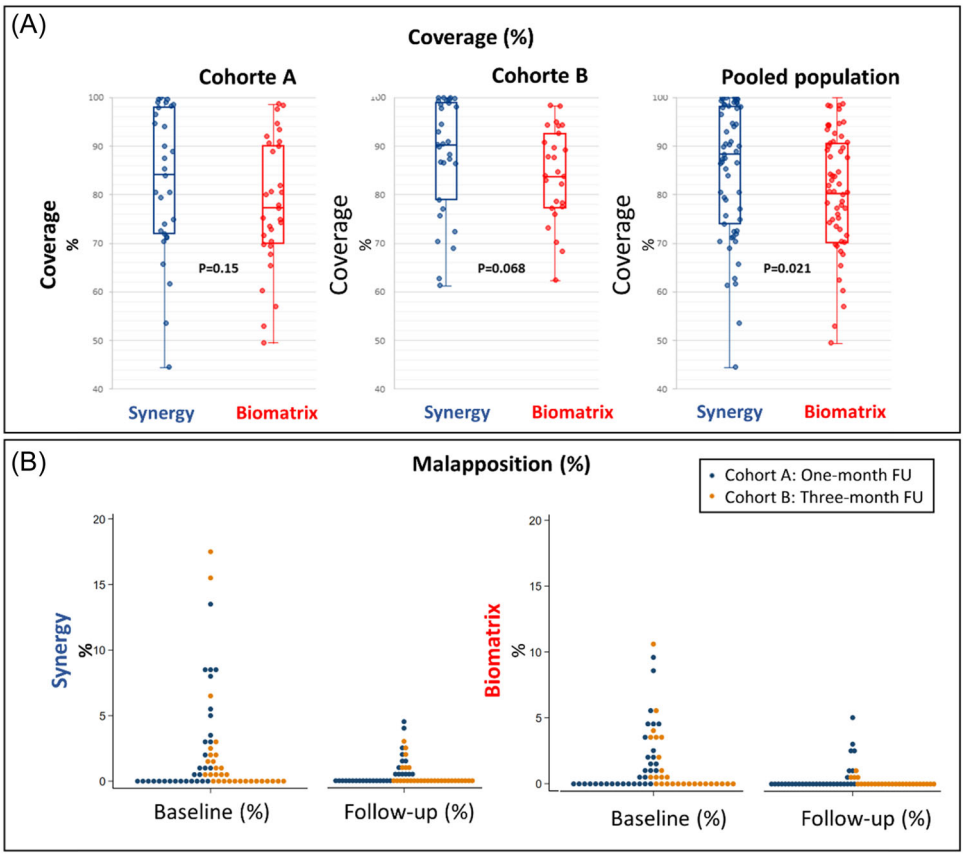

FIGURE 5 Strut coverage and malapposition by cohort. (A) Patient level coverage for each patient for the Synergy and the Biomatrix groups after 1- and 3-month follow-up (FU). Medians Q1 and Q3 are indicated by the boxes. (B) Malapposition by cohort and stent at baseline and follow-up. [Color figure can be viewed at wileyonlinelibrary.com]

population included a large proportion of patients with the acute coronary syndrome as well as high numbers of calcified and lipid-rich lesions. Interestingly, we found that the presence of lipid plaque in the treated lesion was an independent predictor of uncovered struts. Others have reported that both calcified and lipid plaques were associated with incomplete healing.[26]

A concerning finding in our study was the large interpatient variation in healing patterns shown in Figures 4 and 5. Incomplete stent apposition and delayed coverage have been shown to be more frequent in DES implanted in STEMI patients.[27,28] We observed a large variation in coverage, both among stable and acute coronary syndrome patients (Supporting Information: Figure 2). Routine measures to facilitate early healing and reduce interpatient variation patterns may be important to reduce risk, particularly in patients with a higher risk for bleeding. Such measures could include sufficient plaque preparation, routine post dilatation, and image-guided optimization.

Overall rates of malapposed struts were low in both groups at the early follow-up time points; however, persistent malapposed struts tended also to be uncovered at follow-up in both groups. The extent of delayed healing of malapposed struts is in line with previously published data.[29] It has been shown that reducing malapposition at index PCI results in better strut healing after 6 months,[30] and thus malapposition is an important factor in the early healing response.

The SORT-OUT VIII trial, including 2764 patients, concluded that the Synergy DES was noninferior to the Biomatrix DES for the primary composite TLF endpoint at 1 year (Synergy 4.0%, Biomatrix 4.4%, [$p = 0.57$]),[12] confirmed at long-term 5 years (Synergy 10.8%, Biomatrix 12%).[31] The 3-year clinical outcome in this study of 160 patients indicated a better safety profile with Synergy DES, although not significantly and the trial was not powered for comparison of clinical event rates (Supporting Information: Figure 3). The CASTLE trial with imaging optimization and 1440 patients randomized to the ultra-thin strut, biodegradable polymer Orsiro DES or the thin strut permanent polymer Xience DES also did not show any difference in outcome at 1 year.[32]

4.1 | Study limitations

OCT studies provide valuable insights into vessel healing and stent performance. A limitation is the follow-up selection of healthy survivors due to a low rate of patients with clinical events investigated by OCT. Although being one of the largest randomized and matched OCT studies on stent performance, our sample size is modest. With the most

TABLE 3 One- and three-month OCT results.

	Cohort A, 1-month follow-up, *n* = 62			Cohort B, 3-month follow-up, *n* = 57		
	Synergy *n* = 30	Biomatrix *n* = 32	*p* Value	Synergy *n* = 30	Biomatrix *n* = 27	*p* Value
Mean stent area (mm^2)	8.9 ± 2.6	9.7 ± 2.8	0.21	9.6 ± 2.4	9.8 ± 2.6	0.79
Min. stent area (mm^2)	6.8 ± 2.1	7.6 ± 2.3	0.21	7.7 ± 2.2	7.6 ± 2.3	0.71
Stent area stenosis %	30.7 ± 14.7	33.4 ± 14.2	0.46	27.4 ± 14.4	30.7 ± 16.9	0.49
Stent recoil (mm^2)	0.4 ± 0.7	0.3 ± 0.5	0.40	0.2 ± 0.6	0.4 ± 1.0	0.21
Mean lumen area (mm^2)	8.0 ± 2.6	8.7 ± 2.6	0.29	8.5 ± 2.3	8.5 ± 2.2	0.88
Min. lumen area (mm^2)	6.2 ± 2.2	6.7 ± 2.3	0.45	6.8 ± 2.1	6.2 ± 2.1	0.27
Lumen late loss (mm^2)	0.3 ± 0.8	0.005 ± 0.6	0.13	−0.2 ± 0.7	−0.03 ± 1.1	0.58
Area stenosis percentage (%)	36.7 ± 15.1	42.6 ± 12.5	0.09	38.1 ± 11.7	45.1 ± 14.1	0.08
Coverage by indication (%)						
SAP	84.0 [72.6; 98.6]	77.2 [73.5; 84.2]	0.32	91.9 [79.0; 98.5]	83.8 [78.3; 94.2]	0.20
UAP	–	–	–	85.9 [72.3; 99.4]	79.9 [70.2; 89.6]	0.44
Non-STEMI	87.5 [71.3; 97.9]	77.2 [67.7; 90.0]	0.33	89.3 [75.7; 98.1]	90.2 [87.6; 94.4]	0.87
STEMI	79.6 [66.9; 96.4]	80.5 [70.4; 90.6]	0.77	88.8 [86.6; 99.6]	77.2 [73.2; 82.9]	0.057
Neointimal thickness (μm)	51.0 [40.8; 88.2]	52.6 [41.9; 68.8]	0.96	81.1 [52.4; 125.6]	59.5 [46.2; 83.9]	0.06
Cumulated ESL stent lumen (mm^2)	0.04 [0.006; 0.1]	0.04 [0.01; 0.1]	1.0	0.03 [0.007; 0.1]	0.01 [0.005; 0.1]	0.55

Note: Values are *n* (%) or median [Q1; Q3].

Abbreviations: ESL, extrastent lumen; OCT, optical coherence tomography; SAP, stable angina pectoris; STEMI, ST-elevated myocardial infarction; UAP, unstable angina pectoris.

TABLE 4 Three-year clinical outcome.

	Synergy *n* = 80 (%)	Biomatrix *n* = 80 (%)
Target lesion failure	4 (5.0)	11 (13.8)
Cardiac death	1 (1.3)	3 (3.8)
AMI	1 (1.3)	5 (6.3)
Target lesion revascularization	2 (2.5)	7 (8.8)
Target vessel revascularization	2 (2.5)	6 (7.5)
Any revascularization	2 (2.5)	8 (10.0)
Noncardiac death	1 (1.3)	0 (0)
Stent thrombosis		
Definite	0 (0.0)	2 (2.5)
Probable	0 (0.0)	0 (0.0)
Possible	1 (1.3)	2 (2.5)

Abbreviation: AMI, acute myocardial infarction.

severely diseased cases lost to OCT follow-up, there is a risk of type-1 and -2 errors. At last, baseline optimization in some cases based on OCT findings might have resulted in improved post-PCI results and hence better follow-up healing results as compared with a solely angiographic-guided population.

5 | CONCLUSION

The CSHI score did not differ significantly between the Synergy and the Biomatrix DES. There was a large interpatient variation in early healing for both stents. However, the Synergy DES demonstrated overall better early strut coverage compared to the Biomatrix DES.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

Data are not available for external reanalysis. Reasonable requests for on-site reanalysis will be considered.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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