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ORIGINAL STUDIES

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Three- and 6-month optical coherence tomographic surveillance following percutaneous coronary intervention with the Angiolite® drug-eluting stent: The ANCHOR study

Rishi Puri, MBBS, PhD[1,2,3] | Imanol Otaegui, MD[4] | Manel Sabaté, MD, PhD[5] | Antonio Serra-Peñaranda, MD[6] | Marti Puigfel, MD[7] | Armando Perez de Prado, MD, PhD[8] | Luis Nombela-Franco, MD, PhD[9] | Jose M. de la Torre Hernandez, MD, PhD[10] | Rosario Ortas Nadal, MD[11] | Andres Iniguez-Romo, MD[12] | Gustavo Jiménez, MD[5] | Felipe Fernandez-Vazquez, MD, PhD[8] | Carlos Cuellas-Ramon, MD, PhD[8] | Nieves Gonzalo, MD, PhD[9] | Victor Alfonso Jiménez Diaz, MD[12] | Lluis Duocastella, PhD[13] | Maria Molina, MSc[13] | Marc Amoros, PhD[13] | Isabel Perez, MSc[13] | Alberto Barria Perez, MD[1] | Emilie Pelletier Beaumont, MSc[1] | Stephen J. Nicholls, MBBS, PhD[14] | Bruno Garcia del Blanco, MD[4] | Josep Rodés-Cabau, MD[1]

[1]Department of Cardiology, Quebec Heart and Lung Institute, Laval University, Quebec City, Canada

[2]Cleveland Clinic Coordinating Center for Clinical Research (C5R), Cleveland, Ohio

[3]Department of Medicine, University of Adelaide, Adelaide, Australia

[4]Hospital Universitari Vall d'Hebron, Barcelona, Spain

[5]Hospital Clinic de Barcelona, Barcelona, Spain

[6]Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

[7]Hospital Universitari de Girona Dr. Josep Trueta, Girona, Spain

[8]Hospital Universitario de León, Léon, Spain

[9]Hospital Clinico San Carlos, Madrid, Spain

[10]Hospital Universitario Marqués de Valdecilla, Santander, Spain

[11]Hospital Universitario Miguel Servet, Zaragoza, Spain

[12]Hospital Álvaro Cunqueiro, Vigo, Spain

[13]iVascular, Barcelona, Spain

[14]South Australian Health and Medical Research Institute (SAHMRI), University of Adelaide, Adelaide, Australia

Abstract

Background: Pre-clinical results of a novel open-cell, thin strut, durable polymer, laser cut cobalt chromium sirolimus-eluting stent (Angiolite) were promising. Using quantitative optical coherence tomographic (OCT) analyses, we explored the healing characteristics of the Angiolite DES system at 3- and 6-months post implantation.

Methods: A total of 103 patients with *de novo* coronary lesions underwent percutaneous coronary intervention with the Angiolite DES and were randomized 1:3 into two cohorts for angiographic and OCT follow-up, with 28 and 70 patients returning for 3- or 6-month post-PCI surveillance, respectively. The primary endpoints were the 6-month rates of OCT-derived neointimal proliferation, strut coverage and incomplete strut apposition (ISA), whilst the secondary endpoints were 3-month OCT-derived measures of strut coverage and ISA, as well as 6-month quantitative coronary angiographic-derived measures [late lumen loss (LLL), binary restenosis].

Results: The Angiolite stent was successfully implanted in all patients, without periprocedural complications. At 3- and 6-months follow-up, OCT strut coverage was evident in 86.3% and 83.3% of struts, mean neointimal thickness was 73.7 ± 46.5 μm and 73.9 ± 54.3 μm, mean neointimal area obstruction of 5.8% ±10.3% and 4.4% ± 11.3%, and ISA rates were 1.3% ± 7.3% and 1.1% ± 6.2%, respectively. In-stent LLL at 6 months was 0.07 ± 0.37 mm, with a binary in-stent angiographic restenosis rate of 0% without any stent thrombosis, myocardial infarction or cardiovascular death, with 1 patient undergoing ischemia-driven target-lesion revascularization.

Conclusions: At 6 months, the Angiolite DES was safe with high rates of strut coverage, modest degrees of neointimal hyperplasia and very low rates of strut malapposition. These data coupled

Correspondence
Josep Rodés-Cabau, MD, Quebec Heart and Lung Institute, 2725 chemin Ste-Foy, Québec City, Québec, Canada.
Email: josep.rodes@criucpq.ulaval.ca

Funding information
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with the absence of in-stent binary restenosis and a very low 6-month in-stent LLL point towards an efficacious DES. Future studies are required to evaluate its efficacy in broader lesion subsets with longer follow-up.

KEYWORDS
drug-eluting stent, OCT, stent restenosis

1 | INTRODUCTION

Although drug-eluting stents (DES) revolutionized the management of coronary artery disease [1], early (1st) generation DES were hampered by stent thrombosis confirmed both pathologically and in large clinical series [2–4]. These findings led to changes in clinical guidelines that now recommend a more prolonged dual anti-platelet therapy (DAPT) regimen post-percutaneous coronary intervention (PCI) with DES [5]. In parallel, these observations sparked intense interest in all aspects of DES manufacturing, including cell design, strut thickness, biocompatibility of the adhesive polymer as well as the pharmacology and elution kinetics of antiproliferative agents. Furthermore, despite initial enthusiasm with the advent of bioabsorbable vascular scaffolds, their recently reported higher-than-expected thrombosis rates have sparked renewed interest in refining the design and performance of DES with metallic backbones [6,7]. The Angiolite® DES (iVascular, Barcelona, Spain) is a thin-strut cobalt-chromium sirolimus-eluting stent with an open-cell design containing a durable fluroacrylate-based biostable polymer. A preclinical trial comparing the Angiolite DES against other contemporary DES demonstrated its superior healing properties and lower restenosis rates [8], supporting further prospective in vivo investigations in humans.

Optical coherence tomography (OCT) offers exquisite imaging resolution in vivo. OCT-derived measures of neointimal healing correlate well with histological findings in preclinical models of stent healing [9–11], and have been used in human studies for evaluating the healing properties of currently approved and investigational stent platforms [12]. Yet there is a paucity of systematic, strut-level data comparing healing rates at certain time intervals post-PCI. Using OCT, the ANCHOR (ANgiolite drug-eluting stent: an optical CoHerence TOmogRaphy study; NCT02776267) study was designed to prospectively explore the 3- and 6-month healing properties of the Angiolite DES. Safety and clinical efficacy of the Angiolite stent were also evaluated.

2 | MATERIALS & METHODS

2.1 | Patient population

Patients at least 18 years of age with ischemic heart disease scheduled for a clinically indicated PCI of a de novo epicardial lesion, including those presenting with stable angina, acute coronary syndrome (ACS: defined as non ST-segment elevation myocardial infarction or ACS with negative cardiac enzymes), or in the setting of elective PCI of a preplanned lesion were eligible. Angiographic inclusion criteria included the need for the target lesion to contain a visually estimated stenosis $\geq$50% with evidence of ischemia or a stenosis $\geq$70% severity. Major exclusion criteria included age >85 years, ST segment elevation myocardial infarction, cardiogenic shock, known left ventricular ejection fraction <30%, renal impairment with serum creatinine >2/0 g dL^{-1}, inability to take $\geq$6 months of DAPT, and life expectancy <12 months. The main angiographic exclusion criteria included the presence of a chronic total occlusion, bifurcation lesions requiring a 2-stent strategy, in-stent restenosis, severe lesion calcification or tortuosity, stent lenght requirement >24 mm, stent diameter $\leq$2.5 mm or >4.0 mm, unprotected left main coronary artery disease, and lesion/vessel poorly suited for OCT imaging.

Patients were enrolled across 9 medical centers from May 2015 till April 2016. The study was conducted per the Declaration of Helsinki, Good Clinical Practice, ISO 14155. The protocol was approved by the ethics committees of each participating center, and written informed consent was obtained from each patient prior to study enrolment. ANCHOR was sponsored by iVascular.

2.2 | The Angiolite DES

The Angiolite® stent (iVascular, Barcelona, Spain, CE Mark reference number: 2014 12 0833 ED) is made from a cobalt-chromium alloy backbone, with a strut thickness of 75–85 μm. The stent is manufactured from a metal tube that is laser cut and subjected to various treatments providing a smooth, glossy surface finish (Figure 1). The stent structure has been modified to consist of eight crowns linked by three rows of nonconcatenated connectors in a non-continuous sinusoid fashion. This feature confers a slightly higher metal-to-artery ratio, enabling improved drug distribution to the vessel wall. The metallic backbone is coated with a biostable, durable fluoroacrylate-based polymer. The stent is coated with sirolimus at a dose of 1.4 μg mm^{-2}, with >75% elution within the first month, followed by complete sirolimus elution by the end of the 2nd month. The % recoil is <4%, the degree of shortening during expansion is <3%, and there is a 10–20% stent surface contact with the intima. Table 1 summarizes the characteristics of the Angiolite stent system.

2.3 | Coronary stenting procedure

Index PCI was performed per local standards and practice. Predilation of the lesion was strongly suggested, prior to Angiolite stent deployment. Investigators were encouraged to use a single Angiolite stent to treat the index lesion, however additional Angiolite stent deployment was permissible to treat edge dissections or sub-optimal results.

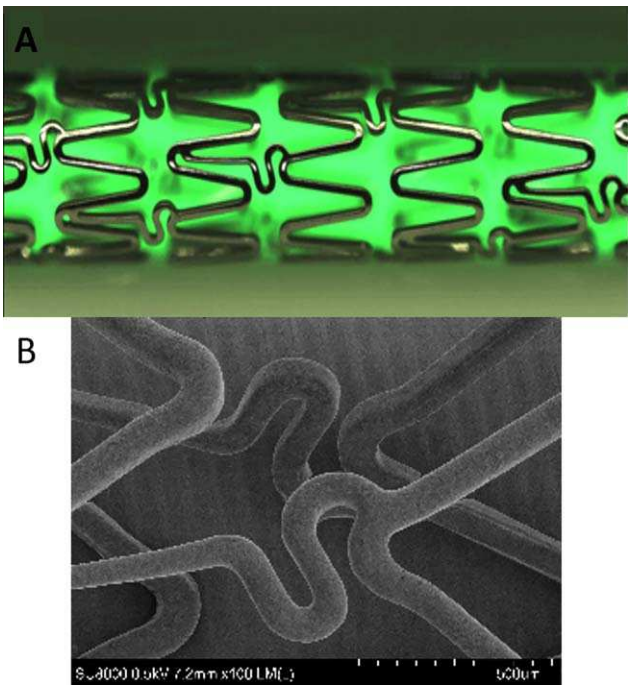

FIGURE 1 Characteristic features of the Angiolite DES. (A) The Angiolite drug-eluting stent, comprised of a laser cut cobalt chromium (L605), thin strut (80 μm) backbone, featuring an open-cell design consisting eight crowns linked by three rows on noncontinuous connectors in a noncontinuous sinusoidal fashion. (B) Micro-CT of the Angiolite DES showing the result of an innovative coating technology providing a smooth glossy surface finish. [Color figure can be viewed at wileyonlinelibrary.com]

Postdilation was left to the operators' discretion. Pre- and post-PCI electrocardiograms were obtained and cardiac enzymes were measured at baseline and post-PCI per institution protocol. Following Angiolite DES implantation, all patients were required to receive dual antiplatelet therapy for a minimum of 6-months duration. Investigators were also strongly advised to prescribe empirical high-intensity statin therapy (defined as rosuvastatin 20–40 mg or atorvastatin 40–80 mg), forming the central component of optimal medical therapy.

2.4 | Randomization and patient follow-up

Following informed consent and assessment for clinical and angiographic suitability, patients who underwent PCI with the Angiolite DES were randomized (≈1:3) to undergo scheduled repeat coronary angiogram and OCT at either 3- or 6-months post index PCI. Random block sizes were used to randomly assign patients to the 3- or 6-month angio/OCT follow-up periods. Also, following index PCI, patients were followed via scheduled clinic and/or phone contact at 1-, 3-, 6-months.

2.5 | Quantitative coronary angiography and OCT evaluation

An independent core laboratory (Atherosclerosis Imaging Core Laboratory, Cleveland Clinic Coordinating Center for Clinical Research, C5R) conducted the angiographic analysis. A separate independent core laboratory (South Australian Health & Medical Research Institute, SAHMRI) undertook the OCT analysis. Intracoronary OCT was performed using the C7XR Fourier-Domain OCT system (St. Jude Medical, St. Paul, MN) or the Terumo Lunaway™ OCT system (Terumo Medical Corporation, Tokyo, Japan) at the time of scheduled angiographic follow-up. Intracoronary nitrates (100–200 μg) were administered prior to OCT catheter intubation. Automated OCT pullback was performed at a speed of 20 mm sec^{-1} at a frame rate of 100 frames sec^{-1}. Frequency-domain OCT images were calibrated by adjusting for the Z-offset. All OCT frames were digitally stored and cross-sectional OCT images of stented segments were analyzed at 0.4/0.6 mm alternative

TABLE 1 Characteristics of the Angiolite drug-eluting stent

Characteristic	ANGIOLITE stent system
Available stent lengths (mm)	9, 14, 16, 19, 24, 29, 34, 39
Available stent diameters (mm)	2, 2.25, 2.50, 2.75, 3.00, 3.50, 4.00, 4.50*; *not available with length 9 mm
Stent material	Cobalt chromium alloy
Drug product	Sirolimus 1.4 μg mm^{-2}
Polymer	Biostable, durable fluoroacrylate-based polymer
Delivery system effective length	142 cm
Stent delivery balloon	Semi-compliant, with two radiopaque markers on the catheter delimiting the stent
Balloon inflation pressure	Nominal inflation pressure: 9–12 atm Rated burst pressure (RBP): 16 atm Average burst pressure (ABP): 22 atm
Recommended guide wire	0.014 inch
Catheter shaft outer diameter	Proximal: 2F Mid: 2.6F Distal:2.2F
Stent strut thickness	75–85 μm

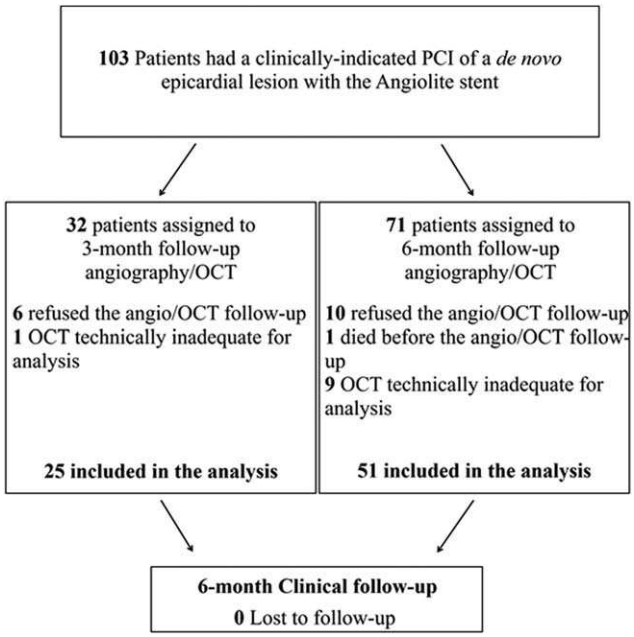

FIGURE 2 Flowchart of the study population

stepping intervals (yielding an average inter-slice distance of 0.5 mm) by the SAHMRI core laboratory.

2.6 | Endpoints

The coprimary endpoints were the OCT-derived strut-level neointimal proliferation, including strut coverage [measured by the % of uncovered stent struts and the number of cross-sections with RUTTS (rate of uncovered to total number of struts) score >30%] and rates of incomplete stent apposition (ISA; rate of nonapposed struts on OCT) at the 6-month post-PCI period. Secondary endpoints included OCT-derived measures of neointimal proliferation and ISA at 3-months post-PCI, and the angiographic-derived measures of in-stent late lumen loss (LLL) and in-stent binary restenosis. The % diameter stenosis (%DS), minimum lumen diameter (MLD), and major adverse clinical events (MACE) at 6-months (defined as cardiovascular death, nonfatal myocardial infarction, ischemia-driven target lesion revascularization, and stent thrombosis) were additional endpoints collected. These endpoints were defined per standardized definitions and criteria [13].

2.7 | Sample size calculation and statistical analysis

Sample size calculation of this single arm study was based on the predefined hypothesis of the Angiolite DES demonstrating endothelial coverage and healing characteristics similar in nature to those historically demonstrated by OCT evaluations of contemporary and novel DES platforms at 3- and 6-month post-index PCI. With the assumption of an average Angiolite stent length of 20 mm, a mean number of eight struts per analyzed cross-sectional frame, and a 0.5 mm stepping interval for OCT analysis, we estimated to have 8,000 analyzable struts for 3-month analysis and a further 8,000 struts analyzable at 6-month analysis if $n = 75$ patients were to be enrolled (25 patients and 50 patients scheduled for 3- and 6-month OCT follow-up, respectively). On the basis of the recent published OCT data evaluating stent healing characteristics [14–19], we empirically chosed to enroll 75 patients (potentially yielding 24,000 struts for analysis). Assuming a 20% loss to imaging follow-up rate, we thus planned to enroll a minimum of 100 patients.

For continuous variables, results are presented as mean ± standard deviation for normally distributed variables or median ± inter-quartile range for variables that failed the normal distribution test. Categorical variables are presented as counts and percentages. Statistical analyses were performed using SAS V.9.4 software (SAS Institute, Cary, NC).

We undertook a strut-level sensitivity analysis to ascertain stent healing in diabetic versus non-diabetic patients. For strut-level analysis of clinical OCT parameters, mixed effect modelling was used to investigate group differences between diabetic and non-diabetic individuals. Within this model, the number of struts per stent was the covariate. Categorical variables were compared with chi-square statistics of Fisher's exact test.

3 | RESULTS

3.1 | Clinical characteristics

A total of 103 patients were enrolled, and the flow chart of patient participation throughout the trial is shown in Figure 2. Table 2 describes the clinical and procedural characteristics of the patients enrolled in ANCHOR. Mean age was 65 ± 10 years, with a male preponderance (76%), 30% with diabetes, and 69% with an ACS. The left anterior descending artery was most often the culprit vessel (48%), with most lesions being either type A (35%) or B1 (45%) in classification.

3.2 | Quantitative angiographic characteristics

Table 3 summarizes quantitative angiographic criteria of the overall ANCHOR population, as well as those enrolled for 3- or 6-month follow-up. Overall, the baseline reference vessel diameter (RVD), minimal lumen diameter (MLD) and mean percent diameter stenosis (DS) were 3.05 ± 0.63 mm, 0.87 ± 0.36 mm, and 70.9% ± 11.9%, respectively. Corresponding follow-up values immediately post-PCI were 2.92 ± 0.53 mm, 2.67 ± 0.46 mm, and 6.7% ± 12.1%, respectively.

In those who underwent follow-up at 3-months post-PCI, the in-stent MLD, in-stent %DS, in-stent LLL and in-stent binary restenosis rate were 2.67 ± 0.42 mm, 3.0% ± 14.3%, 0.03 ± 0.24 mm and 0%, respectively. In those who underwent follow-up at 6-months post-PCI, the in-stent MLD, in-stent %DS, in-stent LLL and in-stent binary restenosis rate were 2.56 ± 0.53 mm, 8.8% ± 9.1%, 0.07 ± 0.37 mm and 0%, respectively.

3.3 | Optical coherence tomographic findings

Table 4 summarizes the OCT findings of the 3- and 6-month patient cohorts. At the 3-month follow-up period, 25 patients had analyzable

TABLE 2 Clinical and procedural characteristics

	N = 103
Age (years)	65 ± 10
Men	78 (76)
Weight (kg)	82 ± 17
Diabetes mellitus	31 (30)
Hypertension	71 (69)
Dyslipidemia	67 (65)
Smoking (prior or current)	68 (66)
Prior PCI	26 (25)
Prior myocardial infarction	22 (21)
Clinical indication for PCI	
Stable angina	31 (30)
Acute coronary syndrome	71 (69)
Silent ischemia	1 (1)
Culprit artery	
Left anterior descending artery	49 (48)
Left circumflex artery	21 (20)
Right coronary artery	33 (32)
Modified ACC/AHA classification	
Type A lesion	36 (35)
Type B1 lesion	46 (45)
Type B2 lesion	20 (19)
Type C lesion	1 (1)
Stent diameter (mm)	3.0 (3.0–3.5)
Stent length (mm)	19 (14–19)
Stent inflation pressure (atmospheres)	14 ± 3
Need for a second stent	7 (7)
Number of stents per patient	1.1 ± 0.4
Predilation	81 (79)
Postdilatation	40 (39)
Postdilatation maximal inflation pressure (atm)	17 ± 4
Postprocedural anti-platelet therapy	103 (100)
Aspirin	102 (99)
Clopidogrel	65 (63)
Ticagrelor	30 (29)
Prasugrel	8 (8)

PCI = percutaneous coronary intervention.
Data are presented as mean ± SD or *n* (%).

OCT images. The number of analyzable struts totaled 11,401, with 9837 (86.3%) displaying OCT strut coverage and the RUTTS score of >30% was apparent in 7.5% of analyzed cross sections. Mean neointimal thickness was 73.7 ± 46.5 μm and the ISA rate was 1.3% ± 7.3%. At the 6-month follow-up period, 51 patients had analyzable OCT images. The number of analyzable struts totaled 24,672, with 20,542 (83.3%) displaying OCT strut coverage and the RUTTS score of >30% was apparent in 8.9% of analyzed cross sections. Mean neointimal thickness was 73.9 ± 54.3 μm and the ISA rate was 1.1% ± 6.2%.

A strut-level sensitivity analysis was performed examining the Angiolite's healing characteristics in diabetic versus nondiabetic individuals (Supporting Information Table). Across both the 3- and 6-month time points, no significant differences were noted in strut coverage, neointimal nor apposition rates.

3.4 | 6-month clinical outcomes

Table 5 describes MACE rates at 6-months post-PCI of all enrolled patients. Target lesion failure occurred in 1 patient (1%) (ischemia-driven target target-lesion revascularization), yet there were no target-vessel-related MIs or stent-thromboses. One patient died from noncardiac-related death. A total of eight patients underwent coronary revascularization, of which two were ischemia-driven non-target vessel related, two were nonischemia target-lesion driven, and four were non-ischemic driven target vessel related. Two patients experienced an OCT-derived coronary artery dissection, promptly treated with stent insertion.

4 | DISCUSSION

We evaluated the healing properties of the Angiolite DES at 3- and 6-months post-PCI, including its clinical performance. The chief findings of ANCHOR are as follows:

i The majority of stent struts at 3- to 6-months post-PCI with the Angiolite DES displayed OCT evidence of strut coverage, with a

TABLE 3 Quantitative coronary angiographic characteristics

Preprocedure (*n* = 98)	
RVD (mm)	3.05 ± 0.63
MLD (mm)	0.87 ± 0.36
DS (%)	70.9 ± 11.9
Lesion length (mm)	13.2 ± 5.4
Postprocedure (*n* = 98)	
RVD (mm)	2.92 ± 0.53
MLD (mm)	2.67 ± 0.46
DS (%)	6.7 ± 12.1
Acute gain (mm)	1.81 ± 0.52
3 months (*n* = 21)	
In-stent MLD (mm)	2.67 ± 0.42
In-segment MLD (mm)	2.07 ± 0.45
In-stent DS (%)	3.0 ± 14.3
In-stent late lumen loss (mm)	0.03 ± 0.24
In-stent binary restenosis, *n* (%)	0 (0)
In-segment binary restenosis, *n* (%)	1 (4.7)
6 months (*n* = 56)	
In-stent MLD (mm)	2.56 ± 0.53
In-segment MLD (mm)	2.28 ± 0.59
In-stent DS (%)	8.8 ± 9.1
In-stent late lumen loss (mm)	0.07± 0.37
In-stent binary restenosis, *n* (%)	0 (0)
In-segment binary restenosis, *n* (%)	0 (0)

RVD = reference vessel diameter; MLD = minimal lumen diameter; DS = diameter stenosis.
Data are presented as mean ± SD or *n* (%).

TABLE 4 Strut-based optical coherence tomographic characteristics

	3-month N = 25	6-month N = 51
Neointimal coverage		
Total number of struts analyzed	11,401	24,672
Number of covered struts	9837 (86.3)	20,542 (83.3)
Total number of cross sections analyzed	2,684	5,410
Cross sections with RUTTS score >30%	200 (7.5)	483 (8.9)
Neointimal obstruction		
Mean neo-intimal thickness (μm)	73.7 ± 46.5	73.9 ± 54.3
Neo-intimal area obstruction (%)	5.8 ± 10.3	4.4 ± 11.3
Apposition		
Incomplete strut apposition (ISA) rate (%)	1.3 ± 7.3	1.1 ± 6.2
Number of frames with ISA	59 (2.2)	104 (1.9)

Data are presented as mean ± SD or *n* (%).
RUTTS = rate of uncovered to total number of struts.

relatively low mean strut thickness suggesting highly effective neo-intimal suppression

ii A low rate of ISA was observed at both time points

iii The very low angiographic LLL dimensions at 3- and 6-months post-PCI respectively with absence of a binary 6-month re-stenosis demonstrated excellent stent performance

iv These OCT and angiographic outcomes translated into only 1 ischemia-driven TLR, without any patient experiencing an MI, stent thrombosis or cardiovascular death

Despite there being several published analyses utilizing OCT to quantitatively characterize stent healing performance, limited data currently exist outlining the temporal healing properties of DES relatively early postimplantation as a means of understanding implications for the duration of anti-thrombotic therapies post-PCI. A recent strut-level meta-analysis involving >2,770 patients who underwent OCT surveillance post-PCI revealed strut coverage rates to correspond with the type of stent, with the greatest degrees of coverage found in bare metal stents (BMS), followed in decreasing order by zotarolimus-eluting stents (ZES-E), everolimus-eluting stents (EES), Resolute zotarolimus-eluting stents (ZES-R), paclitaxel-eluting stents (PES), and sirolimus-eluting stents (SES) [12]. Most newer (2nd) generation DES demonstrated >90% OCT strut coverage rates at 6- to 12-month intervals post-PCI, reflecting in part, the enhanced elution kinetics and potencies of newer limus-based compounds (everolimus, zotarolimus). In fact, a more rapid (2 weeks) elution of zotarolimus following implantation of the ZES-E associated with greater degrees of lumen loss compared with SES [20]. Optimizing these elution kinetics led to lesser strut coverage and slightly greater neointimal hyperplasia with the ZES-R, but improved clinical outcomes, compared with the ZES-E [12,21]. These data highlight the delicate balance between achieving adequate OCT strut coverage rates (for minimizing stent thromboses) versus under-suppressing neointimal hyperplasia and ultimately allowing restenosis to occur.

TABLE 5 6-month clinical outcomes

Target lesion failure	1 (1)
Cardiac death	0
Target-vessel related myocardial infarction	0
Ischemia-driven target lesion revascularization	1 (1)
Stent thrombosis (definite or probable)	0
Death from any cause	1 (1)
Any myocardial infarction	0
Any other revascularization	8 (8)
Ischemia-driven	
Target vessel	0
Nontarget vessel	2 (1.9)
Not ischemia-driven	
Target lesion	2 (1.9)
Target vessel	4 (3.9)
Nontarget vessel	0

Data are presented as *n* (%).

An in vivo preclinical study (in porcine coronary arteries) evaluated Angiolite's performance against the Architect® cobalt-chromium BMS (iVascular, Barelona, Spain), as well as the 1st generation Cypher® DES (J & J Cordis, Miami Lakes, FL) and 2nd generation Xience® (Abbott Vascular, Santa Clara, CA) DES [8]. Quantitative coronary angiographic and histological analyses were performed 28 days following stent insertion. In these preclinical experiments, the Angiolite stent demonstrated numerically lower LLL, percent diameter restenosis, and inflammation scores compared with its Cypher and Xience contemporaries. Re-endothelialization rates were significantly higher in the BMS group compared with all DES groups, however the comparison between the BMS and Angiolite groups were not statistically significant. No significant differences across groups were noted for histological injury scores. The totality of these preclinical data supported the rationale to evaluate in humans the Angiolite stent performance in vivo.

The comparative performance of the Angiolite DES at 3- to 6-months post-PCI is broadly in keeping with the performance with most 2nd generation DES systems. Strut coverage rates of circa 85% at 3- to 6-months post-PCI are numerically slightly lower than some (but not all) comparator 2nd generation DES systems [17,22–24], however the mean strut-based neointimal thickness of 74 μm coupled with an ISA rate of ≈1% are amongst the lowest reported for contemporary DES systems. To place these data into perspective, a novel (3rd) generation polymer free cobalt chromium sirolimus (drug) filled stent (DFS, Medtronic, Santa Rosa, CA) with an 81-μm strut thickness and drug density of ≈1.1 μm mm^{-2} demonstrated OCT strut coverage rates at 1-, 3-, and 9-months post-PCI of 89.3, 92.9, and 98.5%, respectively. The mean neointimal thickness at 3- and 9-months post-PCI was 70 and 160 μm, respectively, with a mean neointimal obstruction at 3-months of 7.6% [25].

Despite the widespread use of OCT for assessing stent healing parameters, the correlation of histopathological findings following stent implantation with imaging findings regarding strut coverage on OCT

may not however be completely transferable. Histopathological evidence of endothelium upon stent struts poorly visualized with contemporary OCT imaging suggests that current generation OCT imaging systems could underestimate, or recognize with less accuracy, true stent strut endothelialization [26]. Although recently reported by some [27], "partial" strut coverage was not part of the OCT core laboratory's routine imaging protocol for evaluating stent performance. Moreover, preclinical evaluation of the Angiolite DES yielded numerically greater degrees of endothelialized stent surfaces compared with the 2nd generation Xience® DES and the 1st generation Cypher® DES systems [8]. Furthermore, ISA rates of <1.5% are also one of the lowest reported in the literature, commensurate with the absence of an inflammatory reaction [8] and subsequent outward remodeling that was seen with 1st generation DES systems, which created a milieu for late stent thrombosis [3]. Although limited in the duration of follow-up coupled with relatively low overall patient numbers, the absence of stent thrombosis and myocardial infarction in ANCHOR could underscore the clinical efficacy of the Angiolite DES as a function of its quantitative OCT findings and design features.

The angiographic LLL has long been regarded as a more reliable means of discriminating DES efficacy compared with simply assessing crude restenosis rates, particularly in small trials [28,29]. The angiographic LLL of 0.03 and 0.07 mm at 3- and 6-months, respectively post-PCI with the Angiolite DES are amongst the lowest reported within contemporary benchmark 2nd generation DES trials [30–33], and arguably superior to the recent results of a 3rd generation metallic DES which demonstrated an in-stent LLL at 9-months post-PCI of 0.26 mm with a corresponding %DS of 13.7% [25]. The fact that the incidence of diabetic patients was 30% in ANCHOR, a population known to harbor accelerated atherosclerosis and greater restenosis rates, further outlines the anti-proliferative effects and safety of the Angiolite DES. The strut-based sensitivity analysis, albeit underpowered to truly evaluate efficacy in diabetic versus nondiabetic patients, suggests efficacy in diabetic individuals without notable differences in coverage and neointimal obstruction. A longer duration of follow-up (>1 year, preferably out to 3- to 5-years) will be required to truly understand the Angiolite DES durability and performance characteristics, as well as systematic comparisons of its healing performance against 2nd-generation DES systems. Nevertheless, the 0% in-stent binary restenosis rate is an early, yet additional positive signal of its performance.

Several caveats of the present study warrant consideration. ANCHOR was a modest-sized study not powered for MACE. Nevertheless, the sample size was adequately powered to elucidate its quantitative healing characteristics on OCT and QCA. ANCHOR was designed chiefly to evaluate healing performance at 3- and 6-month post-PCI intervals, thus no extrapolation or interpolation can be made of its performance before or beyond these time points. The 3- and 6-month patient cohorts were mutually exclusive populations, therefore no direct inference can be made of the serial healing response of the Angiolite DES. ANCHOR precluded enrolling patients presenting with the highest-risk lesion subsets (i.e., left main stem disease, chronic total occlusions, bifurcation lesions, culprit lesions causing ST segment elevation myocardial infarction). Hence demonstrating safety and efficacy in larger-scale "real-world" clinical scenarios and in more complex lesions will be needed to better understand the safety and efficacy of the Angiolite DES system.

5 | CONCLUSIONS

In conclusion, within de novo coronary lesions of modest angiographic complexity, a novel thin-strut, open cell designed, laser-cut, cobalt-chromium sirolimus-eluting stent with a durable fluroacrylate-based biostable polymer demonstrated a favorable early healing profile assessed with OCT at 3- and 6-months post-PCI. This was characterized by high rates of strut coverage, a very mild degree of neointimal hyperplasia, minimal ISA, very low rates of in-stent LLL coupled with the absence of binary in-stent restenosis, stent thrombosis, myocardial infarction or cardiac death. Larger scale "real-world" registries are required to assess the longer-term efficacy of the Angiolite DES, and the comparative efficacy of Angiolite's healing performance against the 2nd-generation Xience DES is currently being evaluated (NCT03049657).

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CONFLICT OF INTEREST

Drs Lluis Duocastella and Marc Amoros, and Mrs Maria Molina and Isabel Perez are full-time paid employees of iVascular. Dr Armando Perez de Prado received honoraria for consulting for iVascular. Dr Luis Nombela-Franco was reimbursed for traveling to a congress. Dr Rodés-Cabau is a consultant for and received research grant support from iVascular. All other authors report no disclosures with respect to this work.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

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