JACC: CARDIOVASCULAR INTERVENTIONS VOL. 2, NO. 5, 2009

ISSN 1936-8798/09/$36.00
PUBLISHED BY ELSEVIER INC. DOI: 10.1016/j.jcin.2009.01.010

MINI-FOCUS: STENT STRUT COVERAGE

A Randomized Optical Coherence Tomography Study of Coronary Stent Strut Coverage and Luminal Protrusion With Rapamycin-Eluting Stents

Philip Moore, MD,* Peter Barlis, MD,* Jonathan Spiro, MD,* Gopal Ghimire, MD,* Michael Roughton, MSc,* Carlo Di Mario, MD,* William Wallis, MD,* Charles Ilsley, MD,* Andrew Mitchell, MD,* Mark Mason, MD,* Rajesh Kharbanda, MD,* Peter Vincent, BSc,† Spencer Sherwin, PhD,† Miles Dalby, MD*

Middlesex and London, United Kingdom

Objectives We used optical coherence tomography, which has a resolution of <20 μm, to analyze thin layers of neointima in rapamycin-eluting coronary stents.

Background Lack of neointimal coverage has been implicated in the pathogenesis of drug-eluting coronary stent thrombosis. Angiography and intracoronary ultrasound lack the resolution to examine this.

Methods We conducted a randomized trial in patients receiving polymer-coated rapamycin-eluting stents (Cypher, Cordis, Johnson & Johnson, Miami, Florida) and nonpolymer rapamycin-eluting stents (Yukon, Translumina, Hechingen, Germany) to examine neointimal thickness, stent strut coverage, and protrusion at 90 days. Twenty-four patients (n = 12 for each group) underwent stent deployment and invasive follow-up at 90 days with optical coherence tomography. The primary end point was binary stent strut coverage. Coprimary end points were neointimal thickness and stent strut luminal protrusion.

Results No patient had angiographic restenosis. For polymer-coated and nonpolymer rapamycin-eluting stents, respectively, mean (SD), neointimal thickness was 77.2 (25.6) μm versus 191.2 (86.7) μm (p < 0.001). Binary stent strut coverage was 88.3% (11.8) versus 97.2% (6.1) (p = 0.030). Binary stent strut protrusion was 26.5% (17.5) versus 4.8% (8.6) (p = 0.001).

Conclusions Mean neointimal thickness for the polymer-coated rapamycin-eluting stent was significantly less than the nonpolymer rapamycin-eluting stent but as a result coverage was not homogenous, with >10% of struts being uncovered. High-resolution imaging allowed development of the concept of the protrusion index, and >25% of struts protruded into the vessel lumen with the polymer-coated rapamycin-eluting stent compared with <5% with the nonpolymer rapamycin-eluting stent. These findings may have important implications for the risk of stent thrombosis and, therefore, future stent design. (An optical coherence tomography study to determine stent coverage in polymer coated versus bare metal rapamycin eluting stents. ORCA 1, from the Optimal Revascularization of the Coronary Arteries group; ISRCTN42475919) (J Am Coll Cardiol Intv 2009;2:437–44) © 2009 by the American College of Cardiology Foundation

From the *Royal Brompton & Harefield NHS Trust, Middlesex, United Kingdom; and the †Department of Aeronautics, Imperial College, London, United Kingdom. This trial was supported through an unrestricted educational grant from Translumina, Germany. Dr. Dalby has received honoraria from Translumina, Germany. Drs. Moore and Barlis contributed equally to this work and are joint first authors.

Manuscript received December 1, 2008, accepted January 7, 2009.

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 2, NO. 5, 2009
MAY 2009:437–44

Polymer-coated drug-eluting coronary stents reduce restenosis and repeat revascularization (1,2). Lack of endothelial coverage, however, has been reported as the most powerful predictor of stent thrombosis in post-mortem series (3), which, in turn, carries a high mortality (4–6). Coronary angiography and intravascular ultrasound lack the resolution to assess thin layers of coverage. In contrast, optical coherence tomography (OCT) is safe, feasible, has a resolution of <20 μm, and has been correlated well with histological analysis of neointima making it suitable for this application (7–9).

Methods

We undertook a randomized study comparing a polymer-coated rapamycin-eluting stent (Cypher, Cordis, Johnson & Johnson, Miami, Florida) with a nonpolymer rapamycin-eluting stent (Yukon, Translumina, Hechingen, Germany) to examine whether 1 device was superior to the other with regard to the primary and coprimary end points of binary stent strut coverage, neointimal thickness, and luminal strut protrusion. Approximately 200 patients were screened for trial participation between October 2006 and July 2007, and 51 were randomized and underwent stent deployment as part of the study. Twenty-four patients completed the trial with 90-day angiography and OCT. Relatively slow recruitment and significant drop out were due in large part to patient concerns about the risks and inconvenience associated with follow-up catheterization and, in particular, the fact that OCT was a relatively new technology. Blocked randomization was carried out by the use of sealed envelopes, with patients per block allocated in a 1:1 ratio between the polymer-coated and nonpolymer rapamycin-eluting stents. Follow-up used 90-day angiography with quantitative coronary angiography and OCT. Inclusion criteria were age 18 to 75 years, stable angina pectoris, or acute coronary syndrome pain-free for 24 h. Exclusion criteria were ST-segment elevation myocardial infarction, cardiogenic shock, chronic total occlusion, bifurcation procedure, left ventricular ejection fraction $<30\%$, and renal impairment (serum creatinine >200 μmol^{-1}). Stent deployment was performed using angiography but without intracoronary imaging. Patients received loading doses of aspirin (300 mg) and clopidogrel (600 mg) at least 2 h before the index procedure if they were not on maintenance therapy, followed by planned lifelong aspirin 75 mg daily and clopidogrel 75 mg daily for a minimum of 1 year. Ninety days was used as the study end point for 2 reasons. First, early reports of OCT in a nonrandomized series had presented data from 2-month follow-up demonstrating a large and significant difference between stent strut coverage with bare-metal stents (BMS) and sirolimus-eluting polymer-coated stents on which the power calculation was based (10), and secondly there was a clinical desire to gain mechanistic insight into the potential safety of the withdrawal of clopidogrel at this relatively early time in nonpolymer rapamycin-eluting stents, as compared with the usually recommended 1 year for polymer-coated rapamycin-eluting stents.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
OCT = optical coherence tomography
3D = three-dimensional

OCT image acquisition. OCT was performed with the M2 system (LightLab Imaging Inc., Westford, Massachusetts) as previously described (11). Briefly, an over-the-wire proximal occlusion balloon catheter (Helios, Goodman Inc., Nagoya, Japan) was deployed and the imaging catheter advanced (ImageWire, LightLab Imaging Inc.) with the light source distal to the stent. The occlusion balloon was inflated to a maximum of 0.7 atms for a maximum of 30 s with continual electrocardiographic monitoring while the coronary artery was infused with Ringer's lactate at 0.5 to 1.0 ml/s using a power injector (Mark V ProVis, Medrad, Inc., Indianola, Pennsylvania). A motorized pullback at 1 mm/s was performed acquiring cross-sectional images at 15.6 frames/s. Frames analyzed were those occurring at every 1 mm (15 frames). In addition, the 2 adjacent frames both proximal and distal to the frame were also assessed to confirm tissue coverage or absence of tissue and apposition. If the stent could not be visualized with a single pullback (due to a long stent or patient intolerance), scanning was prematurely terminated and the pull-back stopped with a second pull-back started from the site where it was interrupted. Anatomical landmarks such as side branches, calcifications, or stent overlap segments were used for longitudinal orientation.

OCT analysis. OCT data analysis was performed offline using proprietary software (LightLab Imaging Inc.). Analysis of angiographic images, quantitative coronary angiography (Medis, Leiden, the Netherlands), and OCT was performed by experienced investigators (P.B. and P.M.). Regarding blinding, the very different presentation of the 2 stent types (including, in particular, the hub of the devices and the angiographic appearances of the markers) made it impractical to blind the operators; however, for the angiographic and OCT analysis, investigators were blinded to the randomization arm. The analyst was blinded to all clinical and procedural variables and thus, did not have any knowledge of stent sizes or stent type. When a strut was felt to be 'malapposed,' the distance from the strut to lumen surface was recorded. Only after completion of the analysis was the stent type used to then confirm the presence or absence of malapposition by incorporating the actual strut thickness for the 2 stents used. This is required as OCT is unable to penetrate through metal and thus can only visualize the luminal aspect of the stent strut.

A blooming effect can result from hyperdense signals arising from metal struts. It is an optical property of the inferometer and, hence, an inevitable part of OCT. We did observe this, and, on the few occasions it was apparent, a frame immediately proximal or distal was selected without this effect. Although we

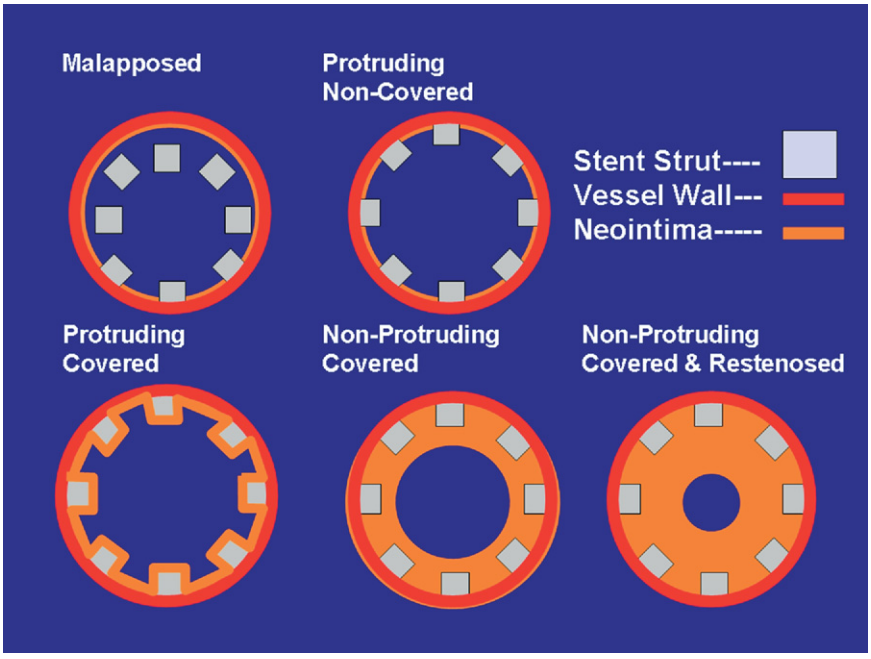

Figure 1. Schematic Diagram of Stent Strut Apposition, Coverage, Protrusion, and Restenosis

are aware of such an effect, this was not an issue observed in the few stent struts malapposed (12).

Neointimal thickness (μm) on the luminal side of each strut section was measured. Neointimal area (mm^2) was calculated by manually tracing and subtracting the stent and luminal areas. Percentage neointimal area was calculated as: ([stent area − lumen area]/stent area) × 100. *Binary strut coverage* (%) was calculated as: (number of strut sections covered/total number of strut sections examined) × 100. Apposition: strut sections in contact with the vessel wall were defined as apposed. Strut sections were malapposed if protruding into the lumen at a distance greater to the strut thickness (154 μm for the polymer-coated rapamycin-eluting stent and 90 μm for the nonpolymer rapamycin-eluting stent). *Protrusion* was defined as projection of the luminal surface of the strut section (whether covered or not) into the lumen, relative to the intima between the adjacent strut sections. The protrusion ratio (%) was calculated as: (number of protruding strut sections/total number of strut sections) × 100. In the text, all parameters quoted are for the group level analysis of total number of strut sections studied in each stent type cohort. The terms apposition, protrusion, and coverage are demonstrated in Figure 1.

Three-dimensional (3D) reconstruction. Representative OCT sections appearing to show protruding stent struts were subjected to 3D reconstruction for comparison with the known stent geometry to support validation of OCT for

Table 1. Baseline Clinical and Procedural Characteristics

Variable	Polymer-Coated Rapamycin Stent	Nonpolymer Rapamycin Stent
Number	12	12
Age (yrs)	61.6	62.3
Male sex, n (%)	11 (92)	10 (83)
Follow-up, days (SD)	91 (6.7)	91 (6.6)
Hypertension, n (%)	8 (67)	8 (67)
Diabetes mellitus, n (%)	4 (42)	3 (25)
Hypercholesterolemia, n (%)	10 (83)	11 (92)
Current or ex-smoker, n (%)	6 (50)	7 (58)
Acute coronary syndrome, n (%)	4 (33)	3 (25)
Chronic stable angina, n (%)	6 (67)	9 (75)

Table 2. Procedural Characteristics and Angiographic Follow-Up

Variable	Polymer-Coated Rapamycin Stent	Nonpolymer Rapamycin Stent
Vessel treated	LAD 9/Cx 1/RCA 1	LAD 6/Cx 4/RCA 2
Stent diameter (mm)	2.88 (0.20)	2.88 (0.38)
Stent length (mm)	18.0 (3.0)	20.2 (2.9)
Post-dilation, n (%)	5 (41.7)	1 (8.3)
Maximal inflation pressure (atm)	17.0 (3.1)	16.7 (2.8)
Inflation duration (s)	18.9 (6.2)	15.4 (7.2)
1 stent, n (%)	8 (66.7)	6 (50.0)
2 stents, n (%)	3 (25.0)	6 (50.0)
3 stents, n (%)	1 (8.3)	0 (0)
Stent:artery ratio	1.14 (0.09)	1.06 (0.09)
90-day restenosis, n (%)	0 (0)	0 (0)
Late loss (mm)	0.06 (0.29)	0.16 (0.33)

Cx = circumflex artery; LAD = left anterior descending coronary artery; RCA = right coronary artery.

Table 3. OCT Follow-Up

Variable	Polymer-Coated Rapamycin Stent Mean (SD)	Nonpolymer Rapamycin Stent Mean (SD)	Difference (95% CI)	p Value
Neointimal thickness (um)	72.7 (25.6)	191.2 (86.7)	118.6 (64.4 to 172.7)	<0.001
Strut coverage (%)	88.3 (11.8)	97.2 (6.1)	8.9 (0.9 to 16.8)	0.030
Protruding struts (%)	26.5 (17.5)	4.8 (8.6)	−21.7 (−33.34 to −10.0)	0.001
Struts counted per frame (n)	8.2 (1.3)	8.4 (1.3)	0.2 (−0.9 to 1.3)	0.700
Apposed and uncovered struts (%)	8.9 (12.4)	2.4 (6.0)	−6.6 (−16.0 to 3.0)	0.170
Malapposed struts (%)	2.2 (2.1)	1.2 (1.1)	−0.9 (−3.2 to 1.3)	0.380
Uncovered and malapposed struts (%)	1.7 (1.6)	0.4 (0.8)	−1.3 (−2.5 to −0.1)	0.049
Covered and malapposed struts (%)	0.4 (0.8)	0.2 (0.4)	−0.2 (−0.8 to 0.3)	0.410
Stent area (mm^2)	8.8 (2.0)	8.0 (1.9)	−0.8 (−2.5 to 0.8)	0.310
Lumen area (mm^2)	8.0 (2.0)	6.1 (1.7)	−1.9 (−3.5 to −0.4)	0.020
Neointimal area (mm^2)	0.3 (0.2)	1.2 (0.8)	0.9 (0.3 to 1.4)	0.002

CI = confidence interval; OCT = optical coherence tomography; SD = standard deviation.

quantifying this characteristic. Intensity iso-contours delineating the lumen-wall interface were extracted from the OCT data. Points on the extracted iso-contours were then used to reconstruct a triangulation of the lumen-wall interface (13). Image coloration gives a qualitative indication of the local curvature of the surface and highlights particular features of the lumen-wall interface.

Ethics and trial registration. The study was approved by the Brompton, Harefield, and National Heart and Lung Institute ethics committees, United Kingdom (06/Q0404/61). All patients enrolled gave written informed consent (International Randomized Controlled Trial Registration number ISRCTN42475919).

End points and statistical methods. The primary end point was binary stent strut coverage (%). Coprimary end points were neointimal thickness (μm) and luminal strut protrusion (%). Secondary end points were malapposition and stent, lumen, and neointimal areas.

The power calculation was based upon limited presented nonrandomized data available at the time suggesting a significant difference in stent strut coverage between BMS (n = 5) and polymer-coated rapamycin-eluting stents (n =

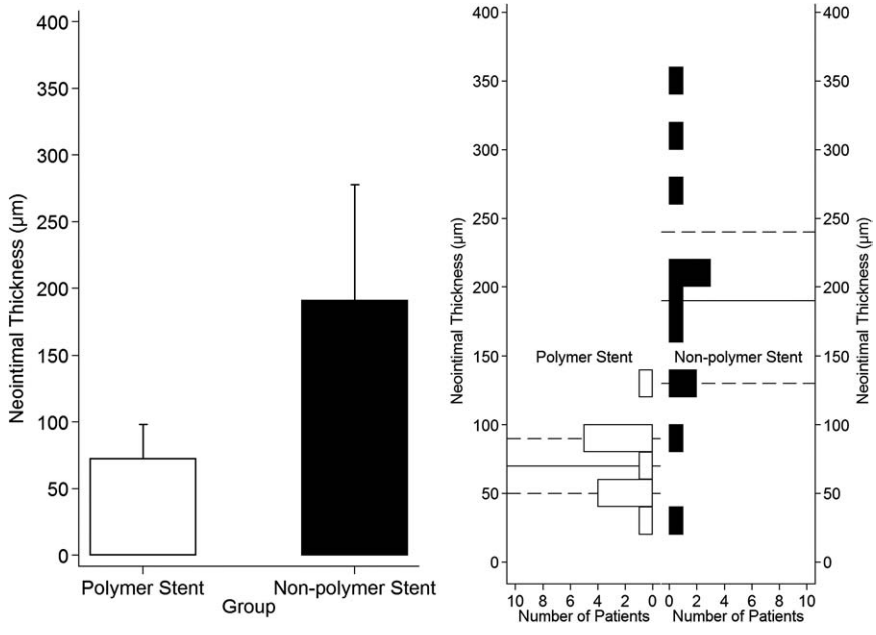

Figure 2. Neointimal Thickness by Stent Group and by Patient

Combined results of neointimal thickness by the randomized stent groups (bar chart n = 5,330 strut sections presented as mean [SD]) and by patient (histogram n = 24 patients presented as median [interquartile range]).

12) with 2-month OCT follow-up (10). In this study there was a large (>2-fold) difference in strut coverage between the 2 stent types, and we estimated that 12 patients in each group would be adequate to demonstrate a difference in coverage between the 2 stent types in our study based on the premise that the nonpolymer rapamycin-eluting stent would probably yield a coverage intermediate between that of a BMS and the polymer-coated rapamycin-eluting stent.

To account for the repeated measurements within each patient, the values for each end point were derived for each individual frame (n = 623), and then the average of all that patient's frames was calculated to give a final summary value for each patient. Comparisons between the polymer-coated and polymer-free rapamycin-eluting stent groups were made using *t* tests. For the main outcomes, the results are presented as mean (SD) along with the mean difference and the associated 95% confidence interval. A 2-sided p value of <0.05 was considered to be statistically significant. In order for this trial to be considered as having a positive outcome, the primary end point had to achieve a value of $p < 0.05$. Other p values are exploratory in nature. Analysis was carried out using STATA 9.2 (StataCorp, College Station, Texas).

Results

Patient characteristics and procedural details are summarized in Tables 1 and 2. There were no significant complications of stent implantation. At follow-up angiography and OCT analysis, chest pain or ST-segment elevation on continuous electrocardiogram (ECG) recording mandated balloon deflation, and in all cases this resulted in prompt resolution of pain and return of the ECG to baseline. There were no incidences of ventricular fibrillation or visible thrombus during the OCT. All study stents were patent at follow-up with no cases of angiographic restenosis (defined as >50% diameter angiographic stenosis relative to the proximal reference segment).

A total of 5,330 strut sections were analyzed (polymer-coated rapamycin-eluting stent: 2,465; and nonpolymer rapamycin-eluting stent: 2,865). The OCT outcome data are shown in Table 3, and summarized in Figures 2 through 4 at both group and patient levels. The primary end point of binary stent strut coverage indicated significantly greater binary coverage with the nonpolymer rapamycin-eluting stent than the polymer-coated rapamycin-eluting stent.

A representative 3D reconstruction of a polymer-coated rapamycin-eluting stent with evidence of protruding struts matched closely with the known strut geometry of the bare in vitro stent and is compared with a nonprotruding, nonpolymer rapamycin-eluting stent (Fig. 5).

Discussion

These data demonstrate that although the polymer-coated rapamycin-eluting stent shows reduced neointimal thick-

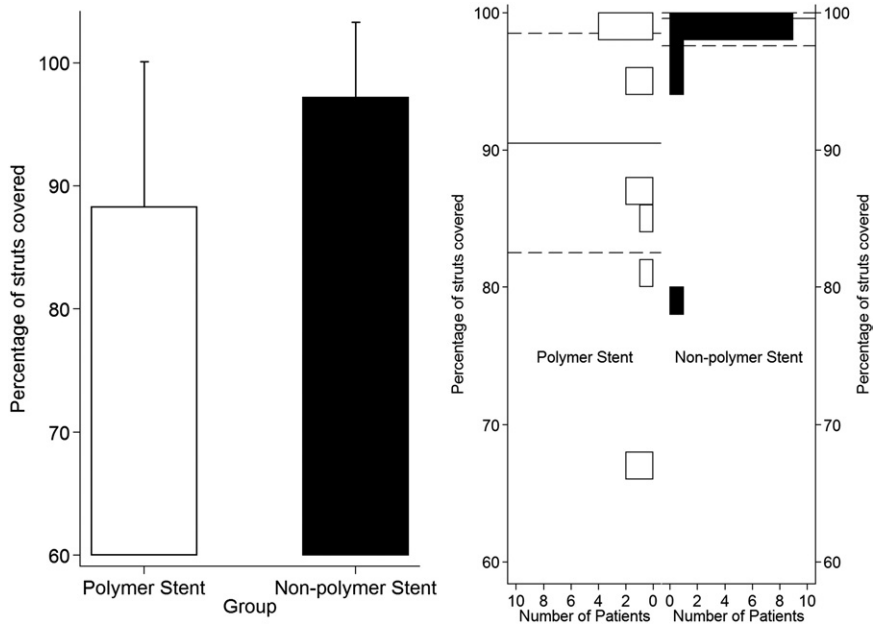

Figure 3. Binary Strut Coverage by Stent Group and by Patient

Combined results of binary strut coverage by the randomized stent groups (bar chart n = 5,330 strut sections presented as mean [SD]) and by patient (histogram n = 24 patients presented as median [interquartile range]).

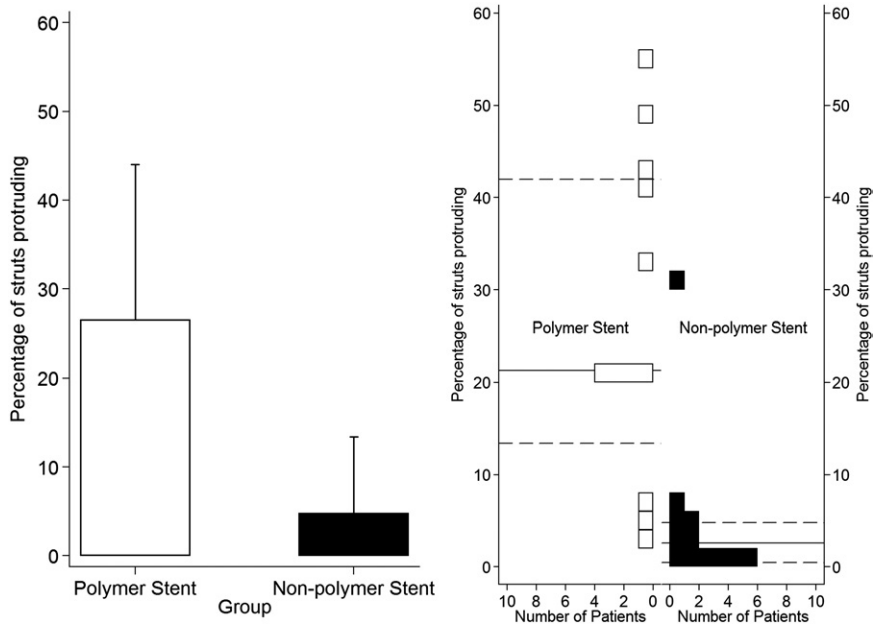

Figure 4. Binary Luminal Strut Protrusion by Stent Group and by Patient

Combined results of binary luminal strut protrusion by the randomized stent groups (bar chart n = 5,330 strut sections presented as mean [SD]) and by patient (histogram n = 24 patients presented as median [interquartile range]).

ness compared with the nonpolymer rapamycin-eluting stent, this is associated with a significantly higher number of uncovered and luminally protruding struts. Experimental data suggest these may be adverse features. Importantly, angiographic late loss is a parameter based focally upon the point of maximum neointimal hyperplasia, and therefore relevant when considering flow limitation. In contrast, this methodology provides a more global picture of stent strut neointimal growth, coverage, and protrusion, which is often nonuniform and is likely therefore to be more representative when considering potential predictors of thrombotic risk. Regarding the polymer coat as a system for drug delivery, evidence suggests that this may be pro-inflammatory in its own right and may retard healing and therefore coverage (14). The etched porous surface of the nonpolymer rapamycin-eluting stent as a drug delivery system in contrast has no potentially pro-inflammatory coating.

A number of OCT series have been reported (15–17); however, investigators are still working toward consensus with regard to which parameters are the most pathophysiologically relevant, what precise methodology should be used to analyze the images, and, as yet, have reported no randomized trial data.

Observational studies using OCT have examined neointimal thickness in the polymer-coated rapamycin-eluting stent. Tatsuya et al. (10) undertook OCT examination at 3 months and 2 years after polymer-coated rapamycin-eluting stent implantation in 21 patients. The neointimal thickness at 2 years was greater than that at 3 months (71 ± 93 μm vs. 29 ± 41 μm, respectively; $p < 0.001$). The frequency of uncovered struts was lower in the 2-year group compared with that in the 3-month group (5% vs. 15%, respectively; $p < 0.001$). However, the prevalence of patients with uncovered struts did not differ between the 3-month and the 2-year group (95% vs. 81%, respectively). Matsumoto et al. (17) examined 57 polymer-coated rapamycin-eluting stents in 34 patients at 6 months after implantation and found the median neointimal thickness to be 52.5 μm with 89% of struts covered and 11% exposed. This compares with our findings at 3 months post-implantation, with a mean neointimal thickness of 77 μm and 89% of struts covered.

Neointimal thickness. In the present study, the neointimal thickness seen with the nonpolymer rapamycin-eluting stent was significantly greater than with the polymer-coated rapamycin-eluting stent. Dose-ranging studies, when compared with a BMS, have indicated significant angiographic antirestenotic efficacy for the nonpolymer rapamycin-eluting stent (18) although it has not been formally compared with the polymer-coated rapamycin-eluting stent in a clinical trial. In the randomized ISAR-Test study, the nonpolymer rapamycin-eluting stent, however, was seen to be noninferior to a polymer-coated paclitaxel-eluting stent (Taxus, Boston Scientific Inc., Natick, Massachusetts) (mean difference in angiographic late loss between the groups was 0.002 mm, $p = 0.02$), with no significant differences between angiographic restenosis rates or target vessel revascularization

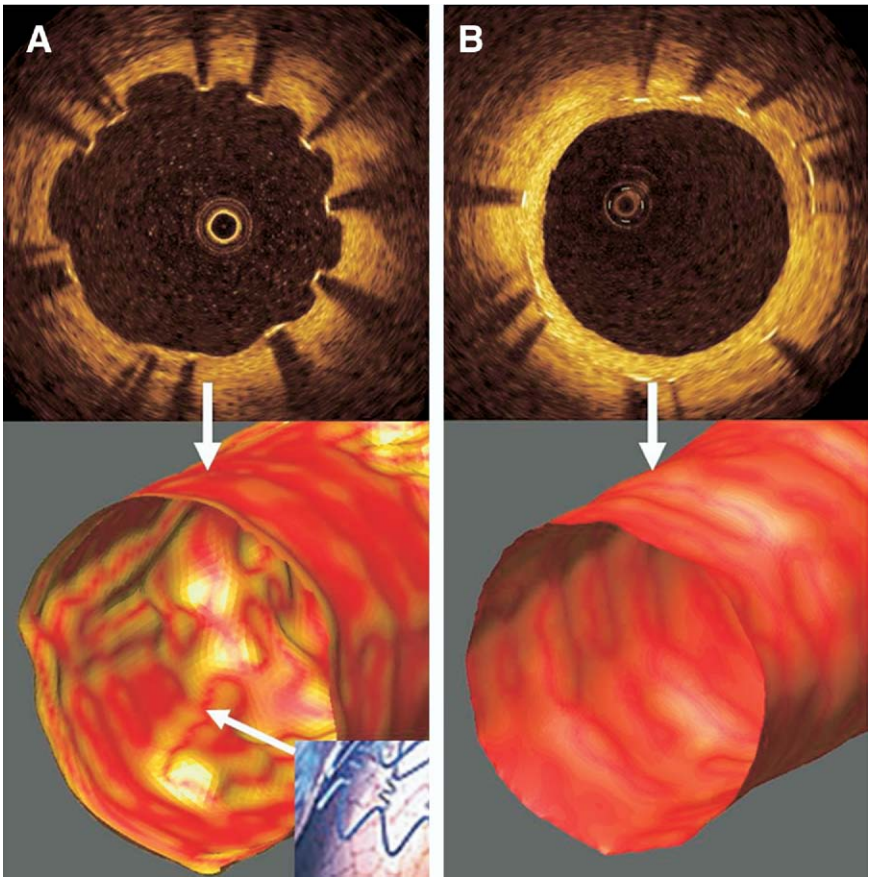

Figure 5. Representative OCT Image and 3D Reconstruction for Different Stent Types

Representative 3-dimensional optical coherence tomography (OCT) image of stent strut sections of an uncovered polymer rapamycin-eluting stent **(A)** and a covered nonpolymer rapamycin-eluting stent **(B)** with paired 3-dimensional (3D) reconstructions and reference photograph of a polymer-coated rapamycin-eluting stent.

(19). Furthermore, a recently published registry series of patients treated with more than 200 nonpolymer rapamycin stents and the paclitaxel stent indicated no difference in major adverse cardiac event rates at 6 months (20).

Strut protrusion. Although the concept of stent strut protrusion and flow disturbance as a potential contributor to stent thrombosis is not widely recognized, the protrusion of a foreign body into the coronary lumen will disturb flow at the blood-intima interface, potentially inducing complex flow patterns, which may be thrombogenic in their own right. We suggest that the stent strut protrusion ratio may potentially be an important parameter when considering the safety of intracoronary stents.

Regarding the 3D reconstruction, this was an exploratory technique that was applied to some representative OCT 2D images and is being further developed, but was not used quantitatively in this study.

Study limitations. Stent strut coverage is not a clinical outcome, but an important potential surrogate for thrombosis and, therefore, stent safety. The presence or absence of neointimal coverage is clearly as defined by the resolution of OCT and struts reported as bare could have had a thin covering of tissue (<10 μm), though at this level the biological protection of the coverage has been debated (21). The trial was small in terms of patient numbers; however, more than 5,000 strut sections were analyzed with, on average, more that 150 per patient driving the statistical power. From a statistical standpoint, there were some unequal variances; however, the *t* test remains robust when variances are not equal, and, furthermore, reanalyzing all outcomes in Table 3 using the Mann-Whitney *U* test, which makes no distributional assumptions, gave extremely similar results in all cases. OCT was performed at a single, relatively early time point. This was considered appropriate in the light of the drive to develop drug-eluting stents in which dual antiplatelet therapy can potentially be stopped relatively early to reduce bleeding risk, allow noncardiac surgery, and reduce cost. Neointimal heterogeneity of optical signal in different stent types has been described; however, neointimal compositional analysis was beyond the

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 2, NO. 5, 2009
MAY 2009:437–44

scope of this study, which focused upon anatomical coverage. Finally, OCT was not performed immediately after stent deployment. Although this may have provided some useful comparative information, it was judged that at this point in the evolution of the technique 2 OCT procedures were excessive from an ethical standpoint.

Conclusions

This trial demonstrated that the polymer-coated rapamycin-eluting stent exhibited low neointimal thickness; however, this was at the expense of >10% of the struts being uncovered and >25% protruding into the lumen at 90 days by OCT criteria. The nonpolymer rapamycin-eluting stent in contrast exhibited greater neointimal thickness (with no angiographic or clinical restenosis) with <3% of struts uncovered and <5% protruding. These findings have to be interpreted in the context of reduced neointimal thickness being the very mechanism by which the efficacy of polymer-coated rapamycin-eluting stents is achieved, with a proven reduction in subsequent target vessel revascularization. Nevertheless, uncovered and protruding struts may be surrogates for thrombotic risk with the former indicating delayed healing, exposing the stent strut to the blood and the latter resulting in flow disturbance.

These findings challenge the paradigm that less in-stent restenosis is better within a coronary stent, and we hypothesize that at least enough neointima to cover the stent struts and prevent protrusion may be important for safety. In addition, it raises the possibility of earlier clopidogrel withdrawal in patients treated with nonpolymer rapamycin-eluting stents than with polymer-coated rapamycin-eluting stents. Proving these concepts will need clinical outcome trials; however, stent coverage and protrusion are logical parameters that can be employed in small scale trials to investigate the potential safety of new and existing coronary stent technologies.

Reprint requests and correspondence: Dr. Miles Dalby, Harefield University Hospital, Hill End Road, Harefield, Middlesex, UB9 6JH, United Kingdom. E-mail: m.dalby@rbht.nhs.uk.

REFERENCES

1. Moses JW, Leon MB, Popma JJ, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med 2003;349:1315–23.
2. Weisz G, Leon MB, Holmes DR Jr., et al. Two-year outcomes after sirolimus-eluting stent implantation: results from the Sirolimus-Eluting Stent in de Novo Native Coronary Lesions (SIRIUS) trial. J Am Coll Cardiol 2006;47:1350–5.
3. Finn AV, Joner M, Nakazawa G, et al. Pathological correlates of late drug-eluting stent thrombosis: strut coverage as a marker of endothelialization. Circulation 2007;115:2435–41.
4. Daemen J, Wenaweser P, Tsuchida K, et al. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. Lancet 2007;369:667–78.
5. Bavry AA, Kumbhani DJ, Helton TJ, Borek PP, Mood GR, Bhatt DL. Late thrombosis of drug-eluting stents: a meta-analysis of randomized clinical trials. Am J Med 2006;119:1056–61.
6. Pfisterer M, Brunner-La Rocca HP, Buser PT, et al. Late clinical events after clopidogrel discontinuation may limit the benefit of drug-eluting stents: an observational study of drug-eluting versus bare-metal stents. J Am Coll Cardiol 2006;48:2584–91.
7. Yamaguci T, Terashima M, Akasaka T, et al. Safety and feasibility of an intravascular optical coherence tomography image wire system in the clinical setting. Am J Cardiol 2008;101:562–7.
8. Suzuki Y, Ikeno F, Koizumi T, et al. In vivo comparison between optical coherence tomography and intravascular ultrasound for detecting small degrees of in-stent neointima after stent implantation. J Am Coll Cardiol Intv 2008;1:168–73.
9. Matsumoto D, Shite J, Shinke T, et al. Neointimal coverage of sirolimus-eluting stents at 6-month follow-up: evaluated by optical coherence tomography. Eur Heart J 2007;8:961–7.
10. Tatsuya I, Mitsuyasu T, Yoshihiro T. Optical coherence tomography analysis of neointimal stent coverage in sirolimus eluting stents compared with bare metal stents. American College of Cardiology Scientific Sessions 2006. J Am Coll Cardiol 2006;47 Suppl:A2906–73.
11. Tanigawa J, Barlis P, Di Mario C. Intravascular optical coherence tomography: optimisation of image acquisition and quantitative assessment of stent strut apposition. EuroIntervention 2007;3:128–36.
12. Tanigawa J, Barlis P, Dimopoulos K, Dalby M, Moore P, Di Mario C. The influence of strut thickness and cell design on immediate apposition of drug-eluting stents assessed by optical coherence tomography. Int J Cardiol 2008 Sep 3 [Epub ahead of print].
13. Giordana S, Sherwin SJ, Peiro J, et al. Automated classification of peripheral distal by-pass geometries reconstructed from medical data. J Biomech 2005;38:47–62.
14. Joner M, Finn AV, Farb A, et al. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. J Am Coll Cardiol 2006;48:193–202.
15. Chen BX, Ma FY, Wei L, et al. Neointimal coverage of bare metal and sirolimus-eluting stents evaluated with optical coherence tomography. Heart 2008;94:566–70.
16. Takano M, Inami S, Jang IK, et al. Evaluation by optical coherence tomography of neointimal coverage of sirolimus-eluting stent three months after implantation. Am J Cardiol 2007;99:1033–8.
17. Matsumoto D, Shite J, Shinke T, et al. Neointimal coverage of sirolimus-eluting stents at 6-month follow-up: evaluated by optical coherence tomography. Eur Heart J 2007;28:961–7.
18. Hausleiter J, Kastrati A, Wessely R, et al. Prevention of restenosis by a novel drug-eluting stent system with a dose-adjustable, polymer-free on-site stent coating. Eur Heart J 2005;26:1475–81.
19. Mehilli J, Kastrati A, Wessely R, et al. Randomized trial of a nonpolymer-based rapamycin-eluting stent versus a polymer-based paclitaxel-eluting stent for the reduction of late lumen loss. Circulation 2006;113:273–9.
20. Ruef J, Storger H, Schwarz F, et al. Comparison of a polymer-free rapamycin-eluting stent (Yukon) with a polymer-based paclitaxel-eluting stent (Taxus) in real-world coronary artery lesions. Catheter Cardiovasc Interv 2008;71:333–9.
21. Finn A, Nakazawa G, Joner M, et al. Vascular responses to drug eluting stents: importance of delayed healing. Arterioslcer Thromb Vasc Biol 2007;27:1500–10.

Key Words: stents ■ optical coherence tomography ■ stent thrombosis.