

# Paclitaxel-eluting stents reduce neointimal hyperplasia compared to bare metal stents in saphenous vein grafts: intravascular ultrasonography analysis of the SOS (Stenting of Saphenous Vein Grafts) trial

Omar M. Jeroudi<sup>1,2</sup>, BA; Abdul-Rahman R. Abdel-Karim<sup>1,2</sup>, MD; Tesfaldet T. Michael<sup>1,2</sup>, MD; Christopher Lichtenwalter<sup>1,2</sup>, MD; James A. de Lemos<sup>1,2</sup>, MD; Owen Obel<sup>1,2</sup>, MD; Tayo Addo<sup>1,2</sup>, MD; Michele Roesle<sup>1</sup>, RN; Donald Haagen<sup>1</sup>, RCIS; Bavana V. Rangan<sup>1</sup>, BDS, MPH; Deepa Raghunathan<sup>1,2</sup>; Monica DaSilva<sup>1,2</sup>; Bilal Saeed<sup>3</sup>, MD; Joseph K. Bissett<sup>4</sup>, MD; Rajesh Sachdeva<sup>4</sup>, MD; Vassilios V. Voudris<sup>5</sup>, MD, PhD; Panagiotis Karyofyllis<sup>5</sup>, MD; Biswajit Kar<sup>6</sup>, MD; James Rossen<sup>7</sup>, MD; Panayotis Fasseas<sup>8</sup>, MD; Peter Berger<sup>9</sup>, MD; Subhash Banerjee<sup>1,2</sup>, MD; Emmanouil S. Brilakis<sup>1,2\*</sup>, MD, PhD

1. Veteran Affairs North Texas Healthcare System, Dallas, TX, USA; 2. University of Texas Southwestern Medical Center, Dallas, TX, USA; 3. Department of Internal Medicine, University of Toledo, Toledo, OH, USA; 4. Central Arkansas Veterans Healthcare System and University of Arkansas for Medical Sciences, Little Rock, AR, USA; 5. Onassis Cardiac Surgery Center, Athens, Greece; 6. Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX, USA; 7. Iowa City Veteran Affairs Medical Center, Iowa City, IA, USA; 8. Medical College of Wisconsin, Milwaukee, WI, USA; 9. Geisinger Clinic, Danville, PA, USA

## KEYWORDS:

- saphenous vein graft
- intravascular ultrasonography
- paclitaxel-eluting stent
- neointimal hyperplasia

## Abstract

**Aims:** To compare the intravascular ultrasonography (IVUS) findings between saphenous vein grafts (SVG) treated with paclitaxel-eluting stents (PES) vs. bare metal stents (BMS) in the Stenting Of Saphenous Vein Grafts (SOS) trial.

**Methods and results:** Of the 80 SOS trial patients, 38 had both baseline and follow-up IVUS examination and were included in this substudy: 17 patients received 28 BMS in 26 lesions and 21 patients received 30 PES in 28 lesions. Quantitative IVUS analysis was performed to determine the volume of in-stent neointimal hyperplasia (NIH) - defined as the difference between stent volume and lumen volume in the stented segments. Baseline characteristics were similar between patients who did and did not undergo baseline and follow-up IVUS. Patients receiving BMS and PES had similar stent and lumen volumes immediately after stenting. At 12-month follow-up, compared to BMS, PES-treated lesions had significantly less NIH volume (3.4 vs. 21.9 mm<sup>3</sup>, p<0.001) and neointima hyperplasia progression (1.6 vs. 17.1 mm<sup>3</sup>, p<0.001). No significant differences were seen in the 5 mm segment proximal and distal to the stent.

**Conclusions:** Compared to BMS, use of PES in SVG lesions is associated with significantly lower NIH formation, which may help explain the improved clinical outcomes with PES in these lesions.

\* Corresponding author: Dallas VA Medical Center (111A), 4500 South Lancaster Road, Dallas, TX 75216, USA  
E-mail: esbrilakis@yahoo.com

## Introduction

Drug-eluting stents (DES) are currently used in the majority of saphenous vein graft (SVG) interventions,<sup>1</sup> despite limited and conflicting data on their safety and efficacy in this lesion subset<sup>2-10</sup>. The SOS (Stenting of Saphenous Vein Grafts) trial (NCT00247208) demonstrated improved angiographic and clinical outcomes with the use of paclitaxel-eluting stents (PES) compared to bare metal stents (BMS) in SVG lesions<sup>11-14</sup>. The objective of the present study was to report the intravascular ultrasonography (IVUS) findings of the SOS study.

## Methods

### PATIENTS

The SOS study design and primary results have been published<sup>11</sup>. Briefly, 80 patients undergoing SVG stenting were randomised to a PES (TAXUS; Boston Scientific, Natick, MA, USA) (n=41) or a similar BMS (Express2; Boston Scientific) (n=39). For patients with >1 lesion, the same stent type was used in all lesions. Patients were asked to return after 12 months for follow-up coronary angiography and were also followed clinically. Intravascular ultrasonography was strongly recommended (but not mandated) after initial stent deployment and at the time of follow-up angiography.

### INTRAVASCULAR ULTRASONOGRAPHY

Intravascular ultrasonography imaging was performed after intracoronary administration of 100-200 mcg of nitroglycerine using motorised pullback (0.5 or 1 mm/s) with a 20 MHz or a 40 MHz commercially available scanner. The stented SVG was imaged starting at least 10 mm distal to the stent, imaging proximally to the SVG ostium. Images were recorded in CDs and were analysed at the Dallas VA Medical Centre Core Laboratory. All IVUS analyses were performed blinded to stent allocation using CAAS QIVA software (Pie Medical, Maastricht, The Netherlands).

The primary endpoint of the IVUS substudy was in-stent neointimal hyperplasia (NIH) volume, calculated as the difference between stent volume and lumen volume in the stented segments. To correct for slight differences in stent length between the baseline and follow-up IVUS examination (likely related to altered catheter movement within the stent), a NIH index was calculated as the NIH volume divided by the stent length in each IVUS pullback. Baseline and follow-up NIH indices for each stent were then multiplied by the actual known stent length to calculate a corrected NIH volume. NIH progression was calculated as the difference between the corrected NIH volume between the follow-up IVUS and the baseline IVUS.

Secondary IVUS endpoints were: 1) in-stent lumen and stent volume; 2) in-stent lumen, stent, and NIH cross-sectional areas and diameters; 3) in-stent percent area and diameter stenosis; 4) in-stent percent obstruction volume, calculated as corrected neointimal volume divided by corrected stent volume at follow up multiplied by 100; 5) incomplete stent apposition defined as greater than one stent strut separated from the vessel wall with blood speckling behind the strut; and 6) proximal and distal reference segment lumen volume,

cross-sectional area and percent area and diameter stenosis, measured 5 mm from the stent border. We were unable to analyse overlapping stent segments due to small numbers (only two such lesions were included in the BMS and two lesions in the PES arm).

### STATISTICAL ANALYSIS

Statistical analyses were performed using JMP 8.0 software (SAS Institute, Cary, NC, USA). Continuous parameters are presented as mean±standard deviation or median with interquartile range and were compared using the Wilcoxon rank-sum test. Nominal parameters were presented as percentages and compared with the chi-square test. A p value <0.05 was considered statistically significant.

## Results

### PATIENTS

Of the 80 patients (with 124 stents in 112 SVG lesions) enrolled in the SOS study, 38 patients (with 58 stents in 54 SVG lesions) underwent both baseline and follow-up IVUS and were included in the IVUS substudy (**Figure 1**). The remaining 42 patients were not included because they died prior to follow-up angiography (n=5), follow-up angiography was not performed (n=8), IVUS was not performed at the time of follow-up angiography (n=24), emergent CABG surgery was performed (n=1), or because of suboptimal IVUS image quality (n=4). The baseline characteristics of the patients who did and those who did not have follow-up IVUS were similar (data not presented), although patients with TIMI 2 flow after the initial stent procedure and those with SVGs to the right coronary artery were less likely to undergo follow-up IVUS.

Of the 38 patients included in the IVUS substudy, 17 (with 28 stents in 26 lesions) received a BMS and 21 (with 30 stents in 28 lesions) received a PES. Both groups had similar baseline characteristics (**Table 1**). The average follow up time in the BMS and PES group was 306±98 days and 316±92 days, respectively (p=0.75).

### INTRAVASCULAR ULTRASONOGRAPHY

The baseline IVUS measurements within the stent and in the proximal and distal 5 mm segments were similar between the BMS and PES patients (data not presented). On the follow-up IVUS, PES patients had less in-stent NIH volume, NIH area, area stenosis, NIH progression, and percent volume obstruction (**Figure 2, Table 2**). NIH volume <15, 15 to 30, and >30 mm<sup>3</sup> was found in 42%, 27%, and 31% of BMS patients compared to 93%, 7%, and 0% for PES patients, respectively (**Figure 3**) (p=0.0002). NIH progression <3 mm<sup>3</sup> between baseline and follow-up IVUS was seen in 15% of BMS patients vs. 61% of PES patients (p=0.0006). Follow-up IVUS measurements in the 5 mm proximal and distal to the stent were similar between the two groups (data not presented).

Incomplete stent apposition was documented in six lesions (11.1% of lesions treated): three with BMS (11.5%) and three with PES (10.7%) (p=0.92). In two of the BMS lesions, stent malapposition was located within the stent, while in the remaining BMS and all PES lesions the incomplete stent apposition was located at the proximal or distal edges of the stent.

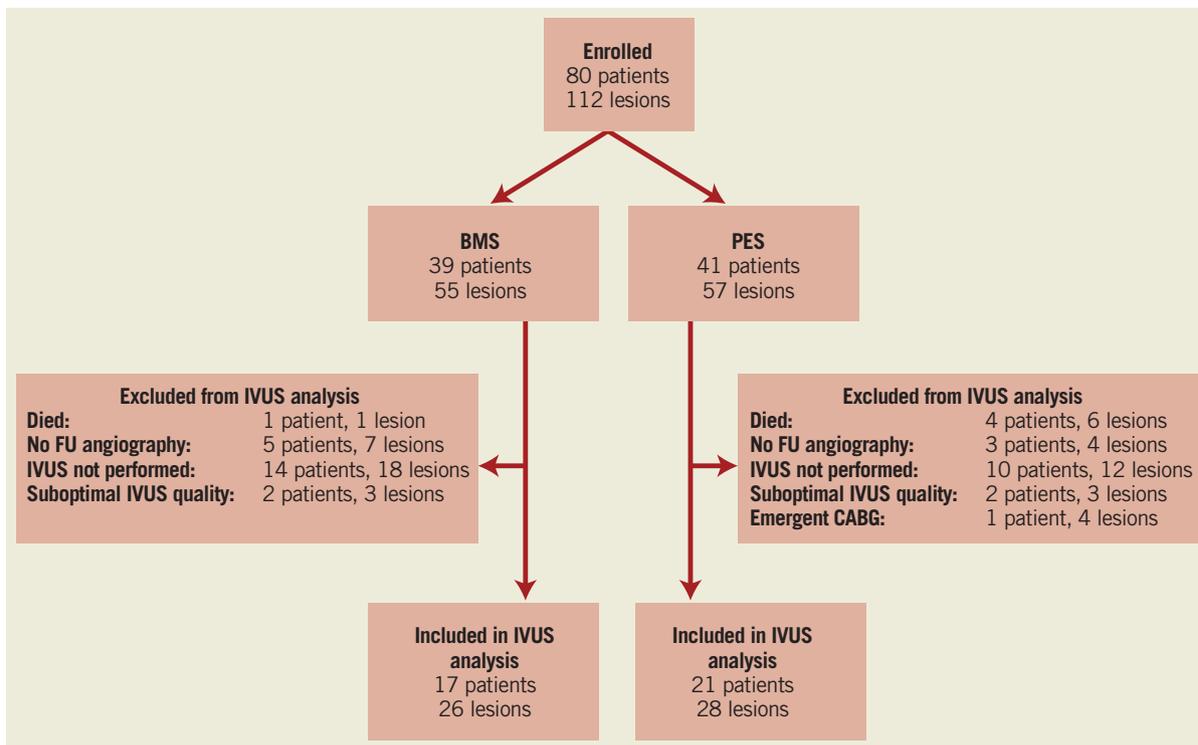


Figure 1. Flow chart describing which patients were included in the IVUS substudy of the SOS Trial.

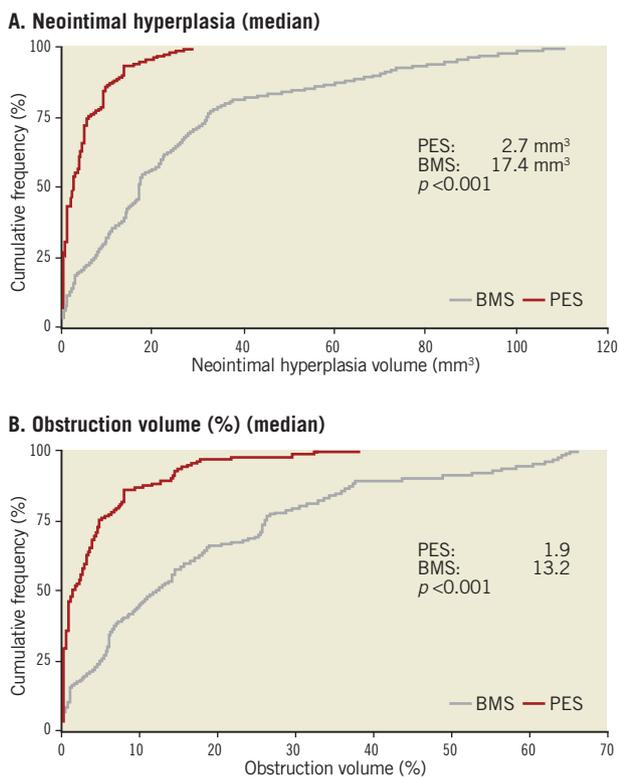


Figure 2. Cumulative frequency distribution curves of in-stent neointimal hyperplasia volume (Panel A) and percent obstruction volume (Panel B) at follow-up intravascular ultrasonography in lesions treated with paclitaxel-eluting stents (red line) or bare metal stents (grey line).

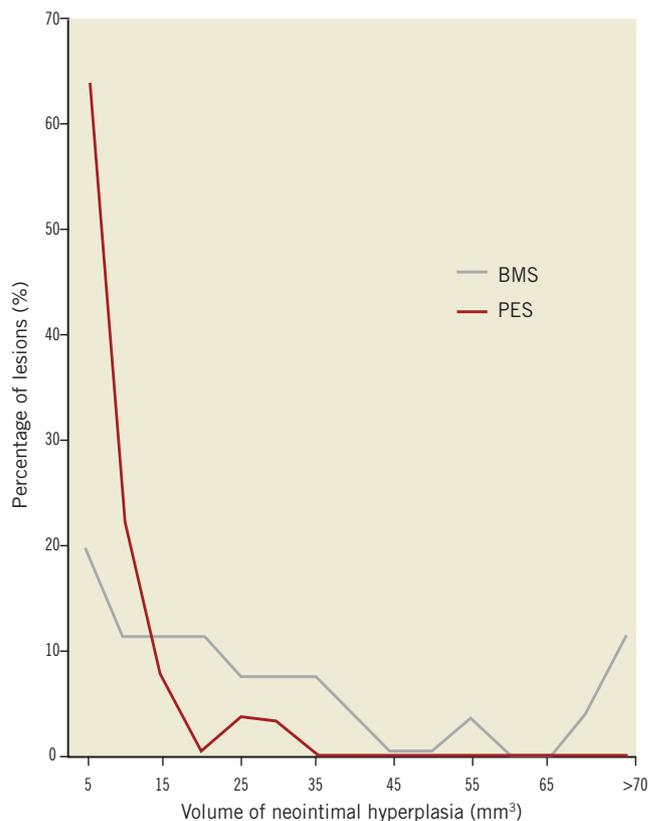


Figure 3. Distribution of neointimal hyperplasia (NIH) volume within paclitaxel-eluting stents (red) and bare metal stents (grey).

**Table 1. Baseline characteristics of the patients included in the intravascular ultrasonography substudy of the SOS trial.**

Variable	BMS (n=17 patients, 26 lesions, 28 stents)	PES (n=21 patients, 28 lesions, 30 stents)	p
Age (years)	67±9	66±10	0.63
Men	17 (100%)	21 (100%)	1.00
Hypertension	16 (94%)	20 (95%)	0.88
Hyperlipidaemia	16 (94%)	21 (100%)	0.26
Prior MI	11 (65%)	14 (67%)	0.90
Smoking status			0.10
Never	3 (18%)	4 (19%)	
Past	13 (76%)	10 (48%)	
Current	1 (6%)	7 (33%)	
Diabetes mellitus	8 (47%)	9 (43%)	0.80
Clinical presentation			0.82
Stable angina	5 (29%)	6 (29%)	
Unstable angina	6 (35%)	7 (33%)	
Non-ST-elevation acute MI	4 (24%)	7 (33%)	
Other	2 (12%)	1 (5%)	
Ejection fraction (%)	51±7	45±11	0.10
Age of grafts (yrs)	12±7	11±6	0.53
No. lesions treated per patient			0.63
1	10 (59%)	15 (71%)	
2	5 (29%)	5 (24%)	
3	2 (12%)	1 (5%)	
Recipient native coronary vessel territory			0.15
LAD/Diagonal	9 (35%)	7 (25%)	
Obtuse marginal	4 (15%)	11 (39%)	
RCA/PDA	13 (50%)	10 (36%)	
Lesion location in graft			0.21
Aortic anastomosis	9 (35%)	7 (25%)	
Proximal	4 (15%)	12 (43%)	
Mid	10 (38%)	6 (21%)	
Distal	1 (4%)	2 (7%)	
Coronary anastomosis	2 (8%)	1 (4%)	
TIMI flow grade before procedure			0.26
1	0	2 (7%)	
2	4 (15%)	2 (7%)	
3	22 (85%)	24 (86%)	
TIMI flow grade after procedure			1.00
3	26 (100%)	28 (100%)	
Percent stenosis before stenting (%)	82±14	81±11	0.60
Percent stenosis following stenting (%)	0.4±2	2.5±4.4	0.03
Total stent length per patient (mm)	31.5±14.8	27.4±13	0.29
Total stent length per lesion (mm)	20.6±6.5	20.1±7.4	0.62
Use of distal protection device per lesion	17 (65%)	16 (57%)	0.53
Stent diameter (mm)	3.15±0.42	3.15±0.36	0.99
Post-dilated	4 (15%)	4 (14%)	0.91

LAD: left anterior descending artery; MI: myocardial infarction; PDA: posterior descending artery; RCA: right coronary artery; TIMI: Thrombolysis In Myocardial Infarction

**Table 2. Follow-up in-stent intravascular ultrasonography findings in lesions treated with bare metal stents (BMS) vs. those treated with paclitaxel-eluting stents (PES).**

Variable	BMS (n = 26 lesions)	PES (n = 28 lesions)	p
Actual stent length (mm)	20.0 (16.0 - 24.0)	20.0 (16.0 - 27.0)	0.62
IVUS perceived stent length (mm)	22.8 (17.1 - 30.5)	21.9 (16.9 - 28.9)	0.82
Luminal volume (mm <sup>3</sup> )	163.5 (83.5 - 208.9)	152.8 (101.3 - 277.5)	0.67
Stent volume (mm <sup>3</sup> )	190.6 (146.0 - 259.7)	153.1 (114.3 - 287.7)	0.51
Mean lumen area (mm <sup>2</sup> )	6.4 (3.9 - 8.5)	7.1 (5.8 - 9.3)	0.32
Maximum lumen area (mm <sup>2</sup> )	8.6 (5.3 - 11.3)	9.2 (6.9 - 12.1)	0.34
Minimum lumen area (mm <sup>2</sup> )	4.1 (2.5 - 6.6)	5.2 (4.0 - 7.6)	0.19
Mean stent area (mm <sup>2</sup> )	7.5 (6.3 - 9.3)	7.4 (6.0 - 9.3)	0.61
Maximum stent area (mm <sup>2</sup> )	9.3 (8.1 - 11.3)	9.3 (7.4 - 12.1)	0.80
Minimum stent area (mm <sup>2</sup> )	6.2 (4.9 - 7.6)	5.3 (4.5 - 7.6)	0.45
Mean NIH area (mm <sup>2</sup> )	0.9 (0.5 - 1.7)	0.2 (0 - 0.4)	<0.001
Maximum NIH area (mm <sup>2</sup> )	3.1 (1.5 - 4.6)	1.0 (0.6 - 1.9)	<0.001
Minimum NIH area (mm <sup>2</sup> )	0 (0 - 0.2)	0 (0 - 0)	0.01
Mean area stenosis (%)	12.5 (5.4 - 27.0)	2.1 (0.4 - 6.3)	<0.001
Maximum area stenosis (%)	34.5 (17.4 - 65.2)	14.5 (7.3 - 25.9)	<0.001
Minimum area stenosis (%)	0 (0 - 6.0)	0 (0 - 0)	0.01
NIH volume (mm <sup>3</sup> )	21.9 (9.2 - 45.4)	3.4 (0.6 - 9.0)	<0.001
NIH index	0.9 (0.5 - 1.7)	0.1 (0 - 0.4)	<0.001
Corrected NIH volume (mm <sup>3</sup> )	17.4 (7.6 - 33.8)	2.7 (0.6 - 8.4)	<0.001
Corrected luminal volume (mm <sup>3</sup> )	138.1±72.5	154.8±83.6	0.48
Corrected stent volume (mm <sup>3</sup> )	165.5±66.3	160.1±83.5	0.53
NIH progression (mm <sup>3</sup> )	17.1 (7.5 - 31.6)	1.6 (0.2 - 6.7)	<0.001
Percentage of obstruction Volume (%)	13.2 (5.3 - 27.9)	1.9 (0.4 - 6.4)	<0.001

Data is presented as median (interquartile range) or mean±standard deviation; BMS: bare metal stent; IVUS: intravascular ultrasonography; MLD: minimum lumen diameter; NIH: neointimal hyperplasia; PES: paclitaxel-eluting stent

## Discussion

The main finding of the IVUS substudy of the SOS trial is that compared to BMS, PES-treated lesions had significantly less in-stent NIH formation, without increase in the frequency of late stent malapposition and without any difference in the measurements within 5 mm proximal and distal to the stent.

Drug-eluting stents have been shown to reduce neointimal hyperplasia formation in native coronary arteries by preventing smooth muscle cell proliferation<sup>15,16</sup>. Whether DES have similar efficacy in SVGs has been debated<sup>2</sup>, in part because SVG atherosclerosis has different pathological features compared to native coronary atherosclerosis and in part because once a SVG has a severe enough lesion to require PCI, it is likely to re-narrow or occlude elsewhere in the graft within the relatively near future. SVG atherosclerosis is usually diffuse, concentric, and friable with a poorly developed fibrous cap and little evidence of calcification, whereas native vessel plaques tend to be proximal, focal, eccentric, and non-friable with a well-developed fibrous cap and frequent calcification<sup>17</sup>. SVG atheromas tend to have more foam cells and inflammatory cells, including multinucleated giant cells, than native coronary

atheromas<sup>17</sup>, express elevated inflammatory cytokine levels<sup>18</sup>, and may be more prone to thrombus formation<sup>19</sup>. Finally, the SVGs' intimal layer has fewer cells compared to native coronary arteries<sup>20</sup>, which may have implications for ISR, that appears to be largely mediated by smooth muscle cells. Although the histologic response of SVGs to DES implantation has been poorly studied<sup>18</sup>, the response to BMS implantation is different in SVGs compared to native coronary arteries<sup>21</sup>. First, the media layer of the SVG is thinner than that of native coronary arteries and is more likely to fracture post stenting leading to aggressive neointimal proliferation. Second, there is more plaque protrusion through stent struts in SVGs, possibly predisposing to stent thrombosis. Third SVGs are more likely to form circular calcification around the stent struts. Fourth, SVGs may be more likely to have persistent inflammation around the stent struts, even long after implantation. These differences could lead to different histologic responses to DES implantation in SVGs.

A recent systematic review of published studies comparing DES and BMS in SVGs demonstrated that DES had lower angiographic late loss compared to BMS in all seven comparative studies<sup>2</sup>, five of which were retrospective comparative studies<sup>22-26</sup>, and two of which were prospective randomised-controlled trials. However, only one IVUS study of DES in SVGs has been published, the IVUS substudy of the RRISC (Reduction of Restenosis In Saphenous vein grafts with Cypher sirolimus-eluting stent) trial<sup>27,28</sup>. RRISC and SOS are the only two, randomised-controlled trial comparing DES with BMS in SVGs. In RRISC a sirolimus-eluting stent (SES, Cypher; Cordis, Warren, NJ, USA) was compared with a similar BMS in 75 patients (96 lesions in 80 SVGs); there was less angiographic restenosis at six month follow-up angiography with SES<sup>27</sup>, but significantly higher mortality after a median follow-up of 32 months<sup>29</sup>. In the RRISC trial, IVUS was performed in 59 patients (73 lesions) at six months post-stent implantation and revealed significantly less NIH volume in the SES group<sup>28</sup> (1.3 mm<sup>3</sup> vs. 24.5 mm<sup>3</sup> in the BMS group,  $p < 0.001$ )<sup>28</sup>. As in RRISC, the SOS trial also identified a significant reduction of NIH volume in the drug-eluting stent arm (3.4 mm<sup>3</sup> vs. 21.9 mm<sup>3</sup> in the BMS group,  $p < 0.001$ ), although follow-up angiography and IVUS was done at 12, rather than six months and different drug-eluting stents were used. A reduction of NIH with PES in SVGs was also demonstrated in native coronary arteries at nine months in the TAXUS IV trial<sup>16</sup> (18 mm<sup>3</sup> with PES vs. 41 mm<sup>3</sup> with BMS,  $p < 0.0001$ ). It is of interest that both absolute and relative effects of PES on suppression of NIH appear to be greater in SVG than native coronary arteries. This may be due to the smaller smooth muscle cell layer in SVG, or a differential injury response.

Our study findings have important implications. First, they suggest that PES effectively suppress neointima formation in SVGs, similar to native coronary arteries, supporting the recently proposed use of undersized DES in SVG lesions to decrease the risk of periprocedural myocardial infarction<sup>30</sup>. Second, although the number of patients in the IVUS substudy of SOS was small, PES appeared to be safe with no increase in edge stenosis ("candy wrapper" phenomenon), as was seen in the Taxus IV trial<sup>16</sup>.

However, greater suppression of NIH in SVGs compared to native coronary arteries could result in incomplete stent strut coverage. This, in turn, could lead to increased risk for DES thrombosis in SVGs, that could explain the adverse long-term outcomes observed in the RRISC trial<sup>29</sup>. Novel, high resolution intracoronary imaging modalities, such as optical coherence tomography, may soon provide improved insights on DES strut coverage in SVGs<sup>19</sup>.

Our study has important limitations. The SOS protocol strongly encouraged (but did not mandate) intravascular ultrasonography (IVUS) after initial stent implantation and during follow-up angiography. Accordingly, only approximately half of the SOS study patients had good quality baseline and follow-up IVUS and were included in the IVUS substudy; however the characteristics of the patients who were and those who were not included were similar. Many patients (especially in the BMS group) had occluded SVGs at follow-up<sup>12</sup> and therefore follow-up IVUS could not be performed; this would bias the results in favour of BMS, yet PES were still found to have significantly less NIH. Therefore, the reduction in NIH with PES may well be greater than what we report. Finally, NIH is a surrogate endpoint; its suppression with DES may not necessarily translate into improved clinical outcomes in SVGs, as was demonstrated in the RRISC trial. However, PES were associated with improved clinical outcomes in SOS<sup>11</sup>, as well as the Moderate VEin Graft LESion Stenting With the TAXUS Stent and Intravascular Ultrasound (VELETI) Pilot trial<sup>31</sup>, the ARRIVE (TAXUS Peri-Approval Registry: A Multicentre Safety Surveillance) registries<sup>32</sup> and the recently published Is Drug-Eluting Stenting Associated With Improved Results in Coronary Artery Bypass Grafts (ISAR-CABG) trial.<sup>33</sup>

In summary, PES significantly reduced NIH formation in SVG lesions compared to bare metal stents in the SOS trial with no increase in late malapposition, supporting their superior efficacy in this challenging lesion subset.

## Funding

The SOS trial was funded by the Department of Veterans Affairs VISN-17 Startup Award and by the Clark R. Gregg grant of the Harris Methodist Foundation to Dr. Brilakis.

## Conflict of interest statement

O. Jeroudi received support from NIH/LBI grant T35-HL086346. J. de Lemos has received speaker honoraria from Bristol-Myers Squibb/Sanofi-Aventis and consulting income from Johnson and Johnson (<\$10,000). O. Obel works predominantly with cardiac rhythm devices and has speaker agreements with St. Jude, Medtronic, and Boston Scientific. T. Addo has served on the Speakers Bureau for Sanofi-Aventis, Merck-Schering, Eli Lilly and Dai-ichi-Sankyo. J. Rossen participated in multicentre clinical studies supported by Boston Scientific. P. Berger owns equity in Lumen, Inc. S. Banerjee has served on the Speakers' Bureau for St. Jude Medical Center, Medtronic Corp., and Johnson & Johnson and has received a research grant from Boston Scientific. E. Brilakis has

received speaker honoraria from St. Jude Medical and Terumo, research support from Abbott Vascular and Infraredx, and his spouse is an employee of Medtronic. The other authors have no conflicts of interest to declare.

## References

1. Brilakis ES, Wang TY, Rao SV, Banerjee S, Dai D, Chin CT, Harding TM, Roe MT. Frequency and Predictors of Drug-Eluting Stent Use in Saphenous Vein Bypass Graft Percutaneous Coronary Interventions: A Report from the American College of Cardiology National Cardiovascular Data CathPCI Registry®. *JACC Cardiovasc Interv.* 2010;10:1068-73.
2. Brilakis ES, Saeed B, Banerjee S. Drug-eluting stents in saphenous vein graft interventions: a systematic review. *EuroIntervention.* 2010;5:722-30.
3. Lee MS, Yang T, Kandzari DE, Tobis JM, Liao H, Mahmud E. Comparison by meta-analysis of drug-eluting stents and bare metal stents for saphenous vein graft intervention. *Am J Cardiol.* 2010;105:1076-82.
4. Meier P, Brilakis ES, Conti R, Knapp G, Shishehbor MH, Gurm HS. Drug-eluting versus bare-metal stent for treatment of saphenous vein grafts: a meta-analysis. *Plos One.* 2010;5:e11040.
5. Joyal D, Filion KB, Eisenberg MJ. Effectiveness and safety of drug-eluting stents in vein grafts: a meta-analysis. *Am Heart J.* 2010;159:159-69 e4.
6. Sanchez-Recalde A, Valero SJ, Moreno R, Barreales L, Lozano I, Galeote G, Reyes RM, Calvo L, Lopez-Sendon JL. Safety and efficacy of drug-eluting stents versus bare-metal stents in saphenous vein grafts lesions: a meta-analysis. *EuroIntervention.* 2010;6:149-60.
7. Testa L, Agostoni P, Vermeersch P, Biondi-Zoccai G, Van Gaal W, Bhindi R, Brilakis E, Latini RA, Laudisa ML, Pizzocri S, Lanotte S, Brambilla N, Banning A, Bedogni F. Drug eluting stent versus bare metal stent in the treatment of saphenous vein graft disease. A systematic review and meta-analysis. *EuroIntervention.* 2010;6:527-536.
8. Brilakis ES, Berger PB. Should Bare Metal or Drug-Eluting Stents Be Used During PCI of Saphenous Vein Graft Lesions: Waiting For Godot? *Catheter Cardiovasc Interv.* 2008;72:815-8.
9. Hakeem A, Helmy T, Munsif S, Bhatti S, Mazraeshahi R, Cilingiroglu M, Effat M, Leesar M, Arif I. Safety and efficacy of drug eluting stents compared with bare metal stents for saphenous vein graft interventions: A comprehensive meta-analysis of randomized trials and observational studies comprising 7,994 patients. *Catheter Cardiovasc Interv.* 2010;published online before print.
10. Paradis J-M, Bélisle P, Joseph L, Bertrand OF, DeLarochelière R, Déry J-P, Larose E, Rodés-Cabau J, Rinfret S. Drug-Eluting or Bare Metal Stents for the Treatment of Saphenous Vein Graft Disease. *Circ Cardiovasc Interv.* 2010;3:565-76.
11. Brilakis ES, Lichtenwalter C, de Lemos JA, Roesle M, Obel O, Haagen D, Saeed B, Gadiparthi C, Bissett JK, Sachdeva R, Voudris VV, Karyofillis P, Kar B, Rossen J, Fasseas P, Berger P, Banerjee S. A randomized controlled trial of a paclitaxel-eluting stent versus a similar bare-metal stent in saphenous vein graft lesions the SOS (Stenting of Saphenous Vein Grafts) trial. *J Am Coll Cardiol.* 2009;53:919-28.
12. Lichtenwalter C, de Lemos JA, Roesle M, Obel O, Holper EM, Haagen D, Saeed B, Iturbe JM, Shunk K, Bissett JK, Sachdeva R, Voudris VV, Karyofillis P, Kar B, Rossen J, Fasseas P, Berger P, Banerjee S, Brilakis ES. Clinical presentation and angiographic characteristics of saphenous vein graft failure after stenting: insights from the SOS (stenting of saphenous vein grafts) trial. *JACC Cardiovasc Interv.* 2009;2:855-60.
13. Badhey N, Lichtenwalter C, de Lemos JA, Roesle M, Obel O, Addo TA, Haagen D, Abdel-Karim, A, Saeed B, Bissett JK, Sachdeva R, Voudris VV, Karyofillis P, Kar B, Rossen J, Fasseas P, Berger PB, Banerjee S, Brilakis ES. Contemporary Use of Embolic Protection Devices in Saphenous Vein Graft Interventions: Insights from the SOS (Stenting Of Saphenous vein grafts) Trial. *Catheter Cardiovasc Interv.* 2010;76:263-9.
14. Brilakis ES, Lichtenwalter C, Abdel-karim AR, de Lemos JA, Roesle M, Obel OO, Addo TA, Haagen D, Rangan BV, Saeed B, Bissett JK, Sachdeva R, Voudris VV, Karyofillis P, Kar B, Rossen J, Fasseas P, Berger PB, Banerjee S. Continued Benefit from Paclitaxel-Eluting Compared to Bare Metal Stent Implantation in Saphenous Vein Graft Lesions During Long-Term Follow-Up of the SOS (Stenting Of Saphenous vein grafts) Trial. *JACC Cardiovasc Interv.* 2011;in press.
15. Serruys PW, Degertekin M, Tanabe K, Abizaid A, Sousa JE, Colombo A, Guagliumi G, Wijns W, Lindeboom WK, Ligthart J, de Feyter PJ, Morice MC, RAVEL Study Group. Intravascular Ultrasound Findings in the Multicenter, Randomized, Double-Blind RAVEL (RAnomized study with the sirolimus-eluting VELOCITY balloon-expandable stent in the treatment of patients with de novo native coronary artery Lesions) Trial. *Circulation.* 2002;106:798-803.
16. Weissman NJ, Koglin J, Cox DA, Hermiller J, O'Shaughnessy C, Mann JT, Turco M, Caputo R, Bergin P, Greenberg J, Kutcher M, Wong SC, Strickland W, Mooney M, Russell ME, Ellis SG, Stone GW. Polymer-based paclitaxel-eluting stents reduce in-stent neointimal tissue proliferation: A serial volumetric intravascular ultrasound analysis from the TAXUS-IV trial. *J Am Coll Cardiol.* 2005;45:1201-5.
17. Motwani JG, Topol EJ. Aortocoronary saphenous vein graft disease: pathogenesis, predisposition, and prevention. *Circulation.* 1998;97:916-31.
18. Rittersma SZ, van der Wal AC, de Winter RJ. Eosinophilic tissue response several weeks after sirolimus-eluting cypher stent implantation within a bare metal stent in a coronary saphenous vein graft. *Catheter Cardiovasc Interv.* 2006;67:38-40.
19. Fusazaki T, Itoh T, Koeda T, Kimura T, Ogino Y, Matsui H, Sugawara S, Nakamura M. Angioscopy and OCT in Repeated In-Stent Restenosis in Saphenous Vein Graft. *JACC Cardiovasc Imaging.* 2010;3:785-6.20.
20. Klima T, Beard EF, Milam JD, Reul GJ, Jr., Cooley DA. Atherosclerosis of Aortocoronary Artery Saphenous Vein Bypass Grafts. *Cardiovasc Dis.* 1979;6:318-23.

21. Ribichini F, Pugno F, Ferrero V, Wijns W, Vacca G, Vassanelli C, Virmani R. Long-term histologic and immunohistochemical findings in human venous aorto-coronary bypass grafts. *Clin Sci (Lond)*. 2008;114:211-20.
22. Ge L, Iakovou I, Sangiorgi GM, Chieffo A, Melzi G, Cosgrave J, Montorfano M, Michev I, Airoldi F, Carlino M, Corvaja N, Colombo A. Treatment of saphenous vein graft lesions with drug-eluting stents: immediate and midterm outcome. *J Am Coll Cardiol*. 2005;45:989-94.
23. Lee MS, Shah AP, Aragon J, Jamali A, Dohad S, Kar S, Makkar RR. Drug-eluting stenting is superior to bare metal stenting in saphenous vein grafts. *Catheter Cardiovasc Interv*. 2005;66:507-11.
24. Hoffmann R, Pohl T, Koster R, Blindt R, Boeckstegers P, Heitzer T. Implantation of paclitaxel-eluting stents in saphenous vein grafts: clinical and angiographic follow-up results from a multicentre study. *Heart*. 2007;93:331-4.
25. Wohrle J, Nusser T, Kestler HA, Kochs M, Hombach V. Comparison of the slow-release polymerbased paclitaxel-eluting Taxus-Express stent with the bare-metal Express stent for saphenous vein graft interventions. *Clin Res Cardiol*. 2007;96:70-6.
26. Guo JC, Xu M, Wang GZ, Ma CS. Late lumen loss of drug eluting stents versus bare metal stents for saphenous vein graft intervention. *Journal of Clinical Rehabilitative Tissue Engineering Research*. 2008;12:6971-5.
27. Vermeersch P, Agostoni P, Verheye S, Van den Heuvel P, Convens C, Bruining N, Van den Branden F, Van Langenhove G. Randomized double-blind comparison of sirolimus-eluting stent versus bare-metal stent implantation in diseased saphenous vein grafts: six-month angiographic, intravascular ultrasound, and clinical follow-up of the RRISC Trial. *J Am Coll Cardiol*. 2006;48: 2423-31.
28. Agostoni P, Vermeersch P, Semeraro O, Verheye S, Van Langenhove G, Van den Heuvel P, Convens C, Van den Branden F, Bruining N. Intravascular ultrasound comparison of sirolimus-eluting stent versus bare metal stent implantation in diseased saphenous vein grafts (from the RRISC [Reduction of Restenosis In Saphenous Vein Grafts With Cypher Sirolimus-Eluting Stent] trial). *Am J Cardiol*. 2007;100:52-8.
29. Vermeersch P, Agostoni P, Verheye S, Van den Heuvel P, Convens C, Van den Branden F, Van Langenhove G. Increased late mortality after sirolimus-eluting stents versus bare-metal stents in diseased saphenous vein grafts: results from the randomized DELAYED RRISC Trial. *J Am Coll Cardiol*. 2007;50:261-7.
30. Hong YJ, Pichard AD, Mintz GS, Kim SW, Lee SY, Kim SY, Ahn Y, Jeong MH, Satler LF, Kent KM, Suddath WO, Weissman JK, Kang JC, Waksman R. Outcome of undersized drug-eluting stents for percutaneous coronary intervention of saphenous vein graft lesions. *Am J Cardiol*. 2010;105:179-85.
31. Rodes-Cabau J, Bertrand OF, Larose E, Dery J, Rinfret S, Bagur R, Proulx G, Nguyen CM, Cote M, Landcop M, Boudreault J, Rouleau J, Roy L, Gleeton O, Barbeau G, Noel B, Curtis J, Dagenais GR, Despres J, DeLarochelliere R. Comparison of Plaque Sealing With Paclitaxel-Eluting Stents Versus Medical Therapy for the Treatment of Moderate Nonsignificant Saphenous Vein Graft Lesions. The Moderate VEin Graft LESion Stenting With the Taxus Stent and Intravascular Ultrasound (VELETI) Pilot Trial. *Circulation*. 2009;120:1978-86.
32. Brilakis ES, Lasala JM, Cox DA, Berger PB, Bowman TS, Starzyk, RM, Dawkins KD. Outcomes After Implantation of the TAXUS Paclitaxel-Eluting Stent in Saphenous Vein Graft Lesions: Results From the ARRIVE (TAXUS Peri-Approval Registry: A Multicenter Safety Surveillance) Program. *JACC Cardiovasc Interv*. 2010;3:742-50.
33. Mehilli J, Pache J, Abdel-Wahab M, Schulz S, Byrne RA, Tiroch K, Hausleiter J, Seyfarth M, Ott I, Ibrahim T, Fusaro M, Laugwitz KL, Massberg S, Neumann FJ, Richardt G, Schomig A, Kastrati A. Drug-eluting versus bare-metal stents in saphenous vein graft lesions (ISAR-CABG): a randomised controlled superiority trial. *Lancet* 2011;378:1071-8.