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Dedicated everolimus-eluting side branch access system: XIENCE SBA

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Background

Coronary atherosclerotic lesions often develop at branching points, presumably dictated by altered shear stress profiles.[1] Percutaneous treatment of coronary bifurcation lesions is challenging due to technical difficulties and suboptimal long-term clinical results. There are different techniques currently used for the treatment of coronary bifurcation lesions, depending on the lesion type.[2] With the one-stent technique only the main branch (MB) is stented, while a second stent is only used when the side branch (SB) perfusion is jeopardised (provisional SB stenting). Using the multiple-stent technique, the intended stenting strategy is that both the MB and SB receive a separate stent. Current consensus is that provisional SB stenting is the best strategy for the treatment of bifurcation lesions with conventional stents.[3-5] This consists of stenting the main vessel across the SB, followed by the opening of a stent cell with a kissing balloon inflation in the SB and if deemed necessary followed by stent implantation in the proximal SB. However, this strategy is technically limited by the inability to cross the "jailed" SB with the guidewire or balloon. Even in case of successful SB stenting, inadequate coverage of the SB ostium often occurs.

Furthermore, the use of the multiple-stent technique was associated with long procedural times and high contrast utilisation, contributing to a higher incidence of periprocedural complications and adverse clinical events.[6] The introduction of bare metal dedicated side-branch access systems, designed to reduce most technical difficulties of treating such lesions, did not translate into an improvement in the long-term clinical results, mainly due to restenosis at the SB ostium.[7-9] Moreover, while for non-bifurcation lesions the introduction of drug-eluting stents has reduced the incidence of restenosis as compared to bare metal stents, the treatment of bifurcation lesions with conventional DES proved less effective.[10] Thus the combination of drug-elution and a dedicated system for the complex geometry of the bifurcation seems a useful approach.

The new everolimus-coated dedicated side branch access (XIENCE SBA) system is one of the first platforms combining these two advantages. The present study evaluated in a preclinical setting the procedural difficulty and short-term (acute and seven days follow-up) implantation efficacy of the SBA stent in coronary bifurcations of swine.

Device description

Stent

XIENCE SBA is a modified XIENCE V stent (Abbott Vascular, Santa Clara, CA, USA) designed with an open portal for side branch access (Figure 1A). It is a double balloon (single shaft, single inflation) delivery system, the stent having identical strut thickness (0.0032 in), stent material (CoCr), drug (everolimus), dose (100 µg/cm^2) and biocompatible fluorinated copolymer coating (PVDF-HFP) as the XIENCE V DES. XIENCE SBA exhibits similar stent pattern and surface area (87.57 mm^2 for XIENCE V and 86.35 mm^2 for XIENCE SBA). The SBA access portal is similar to the FRONTIER stent. The XIENCE SBA stent is 18 mm in length and 2.5 and 3.0 mm in diameter. The 2.5 mm main branch

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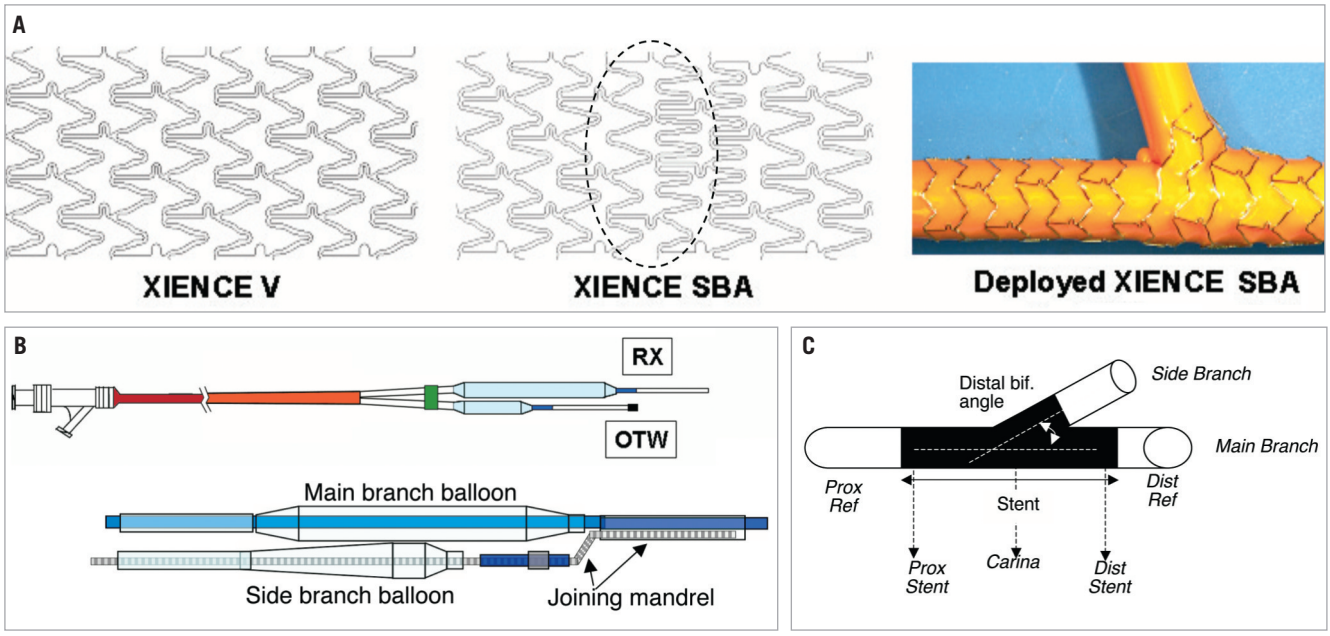

Figure 1. A) Details of the XIENCE SBA stent system. The system is based on the XIENCE V platform (left image). The SBA stent is provided with a side portal (dotted line) which opens to the side branch during the inflation of the double balloon. B) XIENCE SBA Delivery System Design. C) Schematic representation of a stented bifurcation indicating the stent segments considered for analysis.

includes a 2.0 mm side branch balloon and the 3.0 mm device includes a 2.5 mm side branch balloon.

SBA is placed in a single procedure after wiring both the MB and SB. During the simultaneous double balloon inflation the side portal is opened to the SB. Following deployment and pull-back of the delivery system, both MB and SB are easily accessible for additional treatment, when needed.

Delivery procedure

The XIENCE SBA (side branch access) system consists of both a main branch (MB) and a side branch (SB) balloon, with the two tips joined together, and a common inflation lumen for simultaneous balloon inflation during stent deployment, (Figure 1B). The system is delivered to the target site in rapid exchange fashion over a single wire placed in the MB vessel. Delivering to the target lesion with the joined tips is intended to reduce the instance of wire wrap. As the system approaches the bifurcation, the tip is positioned just proximal to the SB origin. Or to ensure that the lesion can be crossed successfully, the system may be advanced to a point just beyond the SB.

Once the device is in the desired position, the joining mandrel, which runs the entire length of the OTW lumen of the SB balloon, is removed completely from the proximal adaptor hub. At this point, the two catheter tips which were previously joined via the mandrel become two separate tips. The operator's wire of choice for the SB is introduced into the OTW lumen and exits the SB tip. We typically recommend an extra supportive wire. If the wire is proximal to the SB origin, it is advanced into the daughter vessel. If the wire is distal to the SB, then the entire device is pulled back slowly in order to allow the SB wire to fall into the SB vessel ostium. This will occur easily if the device is "in phase", that is, if the SB tip is oriented toward the daughter vessel. The extra supportive wire often facilitates self-rotation of the device as the XSBA device is advanced into the bifurcation. Both wires are held with tension as the operator advances the device until resistance is felt and the mid (carina) radio-opaque marker on the MB balloon is visible at the level of the carina. Once the operator confirms that the device is in the proper position, forward tension is held to ensure the position is maintained while the device is being deployed. Both the MB and SB balloons are pressurised and inflated through a single inflation lumen.

Following deployment and deflation of the balloons, the delivery system is withdrawn slightly from the bifurcation, while guide wire access is maintained to both branch vessels. In order to maintain SB guide wire access during removal of the XSBA delivery system, an exchange length (300 cm) or DOC-extended wire of equal length is required. After angiographic assessment, further treatment of all branch segments is facilitated with the existing guide wires in place. The parent branch vessel has been stented, and access is maintained to the daughter vessel by means of the wire through the SB portal. The degree of scaffold coverage in the SB ostium is dependent on the angle of the bifurcation (Figure 1C).

Pre-clinical experience

We evaluated the procedural difficulty and short-term (acute and seven days follow-up) implantation efficacy of the SBA stent in coronary bifurcations of swine.

Animal model and preparation

Experiments were performed in farm-bred swine (Yorkshire-Landrace). The study was approved by the animal ethics committee of the Erasmus University Rotterdam, The Netherlands and complied with the "Guide for the care and use of laboratory animals" (NIH publication 85-23, updated 1996).

After a loading dose of 300 mg, 75 mg clopidogrel and 100 mg acetylsalicylic acid were administered daily, orally for the follow-up period. The animals were anesthetised, and stents placed under sterile conditions. After intracoronary administration of 2 mg isosorbide dinitrate, coronary angiography was performed. Two orthogonal views were used in order to visualise the vascular architecture. MB segments of 2.5-3.2 mm in diameter were selected in each of the coronary arteries in order to contain a coronary bifurcation with a SB diameter ≥1.8 mm. Stents were placed (balloon/artery ratio of 1.1, guided by QCA using a CAAS 5.5 system; Pie Medical, Maastricht, The Netherlands) at the qualifying segments. After stent implantation and repeat angiography, *in vivo* imaging by IVUS and OCT was performed.

Study groups and time-points

Acute: N=6 SBA implants were analysed acutely for assessment of the deployment procedure.

Seven days: N=7 SBA implants were analysed both at implantation (baseline) and at seven days follow-up.

The stent segments (proximal, distal, carina) considered in all analyses are schematically presented in Figure 1B.

In vivo imaging

In vivo imaging was performed by angiography, intravascular ultrasound (IVUS) gray scale (IVUS analysis was performed using the Boston Scientific (Natick, MA, USA) Atlantis SR pro system, 40 MHz, pullback rate 0.5 mm/s), and optical coherence tomography (OCT; LightLab Imaging Inc., Westford, MA, USA).

Ex vivo imaging

Hearts were flushed with saline, and pressure-fixed in situ (±100 mmHg) with buffered formaldehyde. The stented arterial segments including 0.5-1 cm proximal and distal to the stent were excised and studied by micro computed tomography (microCT). Thereafter, vessels were embedded in methyl methacrylate (MMA) for histology.

MicroCT imaging: The three-dimensional (3D) reconstruction of the stented bifurcation was performed following scanning with a computer tomography micro-scanner (35 µm resolution). A fly-through 3D reconstruction of the vessel could be computed in order to assess the stent deployment parameters (symmetrical deployment and proximal and distal stent tapering and positioning of the SB opening in relation to the stent length). Tapering and symmetry was calculated as a ratio of vascular area at rings A/B and C/D, respective minimal/maximal diameters proximal, at the carina and distal, as indicated on Figure 3. A symmetry coefficient cut-off value of 0.8 was considered acceptable. The positioning of the SB opening was considered proximal if the opening was in the first seven strut rings (the total stent had 13-14 rings) of the stent.

Histology: En-block toluidine blue staining was performed on both longitudinal and perpendicular (cross-) sections through the branching point (carina) for the assessment of the MB and SB coverage with struts, presence of struts in the lumen, malapposition and distal branching angle.

Results

QCA analysis

The angiographic images analysed using standard two-dimensional (2D) software indicate no differences between groups in MB or SB diameters pre- or post- stent implantation (Table 1). No differences in acute gain or late loss of the MB and SB were seen between the groups. More importantly, no differences were seen in the distal branching angles pre- or post- stent implantation.

Table 1. QCA measurements of SBA (N=7 at 7 days FU)

XIENCE SBA		
Pre	MBprox (mm)	3.21±0.22
	MBdist (mm)	2.69±0.24
	SB (mm)	1.91±0.33
	Distal branching angle (°)	51±28
Post	MBprox (mm)	3.53±0.45
	MBdist (mm)	3.08±0.45
	SB (mm)	2.02±0.29
	Distal branching angle (°)	49±18
	Acute gain MB prox	0.33±0.35
	Acute gain MB dist	0.39±0.31
	Acute gain SB	0.13±0.09
FU	MBprox (mm)	3.33±0.37
	MBdist (mm)	2.93±0.31
	SB (mm)	1.70±0.32
	Distal branching angle (°)	48±19
	LL MB prox	0.21±0.14
	LL MB dist	0.14±0.18
	LL SB	0.32±0.18

IVUS analysis

IVUS analysis indicates similar vascular diameters of both the MB and SB between groups at baseline (Table 2). The symmetry indices were above 0.8 both in the MB and SB for the SBA.

Table 2. IVUS data obtained at baseline.

			XIENCE SBA
MB	Stent diameter (mm)	prox	3.46±0.50
		carina	3.73±0.74
		dist	3.04±0.55
	Stent symmetry index	prox	0.81±0.08
		carina	0.79±0.02
		dist	0.89±0.05
SB	Lumen diameter (mm)		2.22±0.23
	Lumen symmetry		0.90±0.00

OCT analysis

Examples of the OCT images including normal strut coverage, presence of intraluminal tissue (possibly thrombus) on the struts and media dissection are presented in Figure 2.

The data are presented in Table 3. Three of 13 stents showed proximal dissection, one showed dissection in the carina and one showed a distal dissection at implantation. One dissection in the proximal reference segment was still present at seven days follow-up. All other dissections seen in the chronic group were repaired at follow-up.

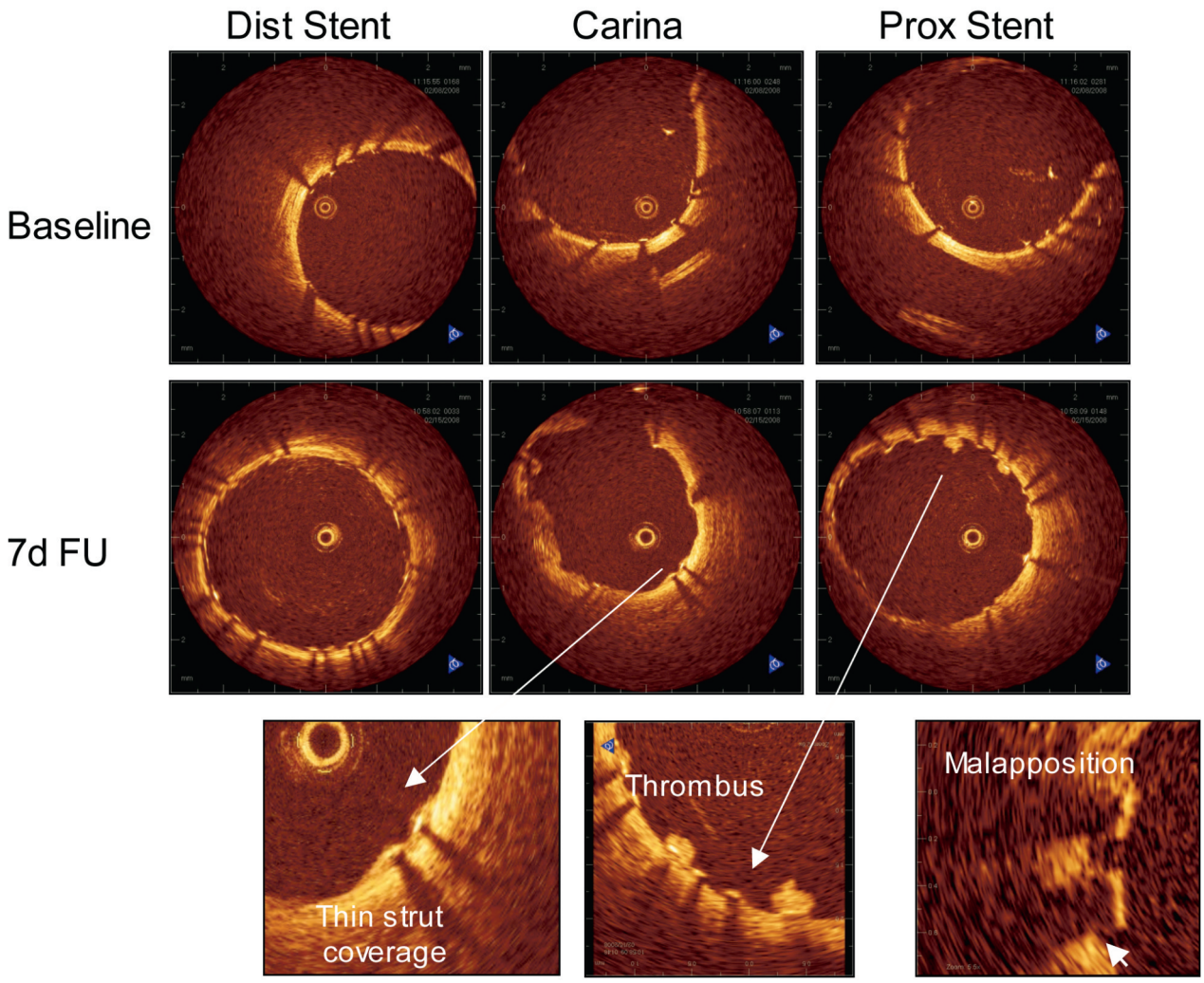

Figure 2. Typical example of images obtained during the OCT pullback In a XIENCE SBA system. Thin strut coverage, presence of tissue on the struts and malapposition of the stent struts against the vascular wall are shown (arrows).

Table 3. OCT data obtained at baseline and FU.

	Acute group	7 days FU group	
	Baseline	Baseline	7 days
Struts coverage with tissue carina (% struts)	–	–	32±46
Thrombus carina (% stents)	17%	0%	33%

MicroCT analysis

3D reconstruction of the stented segments was used for the assessment of the symmetry of the stent cells (longitudinal view, Figure 3), tapering and symmetry of the proximal and distal segments of the MB (cross-sectional view, Figure 3) as well as the positioning of the branching point in relation to the total stent length (longitudinal view, Figure 3). Data from both follow-up times were pooled and are summarised in Table 4. No proximal or distal tapering was seen in either stent group. The data also indicated symmetric deployment in all stents, as the ratio between the min and max diameter was close to one in all groups. SB positioning in the SBA stents was always at ring eight (counted from distal to proximal, 14 rings in total), thus 100% proximal.

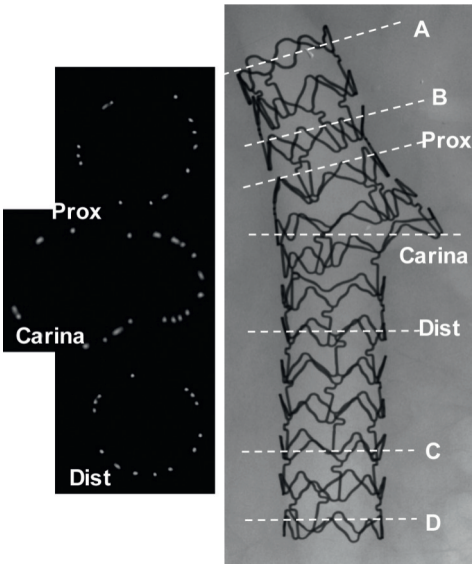

Figure 3. Longitudinal and cross-sectional proximal, carina, and distal images obtained with microCT in a XIENCE SBA stent. The coverage of both the MB and SB (cross-section through the carina) with stent struts is visible.

Table 4. Assessment of proximal and distal tapering and symmetry as well as the positioning of the opening towards the SB using microCT.

	XIENCE SBA
Prox. tapering	0.96±0.12
Dist. tapering	1.00±0.08
Prox. symmetry	0.96±0.05
Dist. symmetry	0.95±0.04
SB positioning prox.	100%

Histology

The presence of thrombus around the stent struts, (Figure 4), assessed in the animals sacrificed acutely showed that 10-15% of the struts showed signs of thrombus formation, no differences being seen between MB and SB. In the seven days group, slightly higher percentages of thrombus were seen (40-50% of the struts) although the differences did not reach statistical significance due to the small sample size. 5±2 struts covering a length of 1.89±0.39 mm were counted in SB of arteries receiving a SBA stent, being positioned mostly opposite to the flow divider. Most vessels had an intact media.

The measurement of distal bifurcation angles on the longitudinal en-block sections correlated with the same measurements by QCA as indicated both by linear correlation plots and Pearson's correlation test (p=0.002 versus QCA).

Discussion

The present study shows that the new XIENCE SBA stent can be safely deployed with good procedural outcome. The main findings are that the SBA stent shows good preservation of luminal diameter both in the MB and SB, and of the vascular branching angles. The side branch was accessible and most of the stent struts were well apposed to the luminal surface without major modification of the stent pattern during deployment. All stents were uniformly deployed, while the SBA stent supported the ostium as shown by the coverage of the SB with stent struts, mainly opposite to the flow divider.

However, the results indicate that bifurcation stenting remains accompanied by vascular damage as shown by the presence of thrombus and vascular dissections. Longitudinal studies are required in order to assess the neointimal response to the stents.

Implantation technique

Percutaneous coronary interventions on ostial lesions carry technical challenges related to the size of the SB and its orientation relative to the MB (bifurcation angle)[11,12], as well as the position of the plaque and possible obstruction of the SB due to plaque shift. Provisional stenting of the MB across the branching point confers an additional level of complexity to the percutaneous treatment of the SB since the stent struts may jail the SB and impede the access of the guidewire or balloon to the SB. Moreover, potential complications of balloon dilatation of side branches through stent

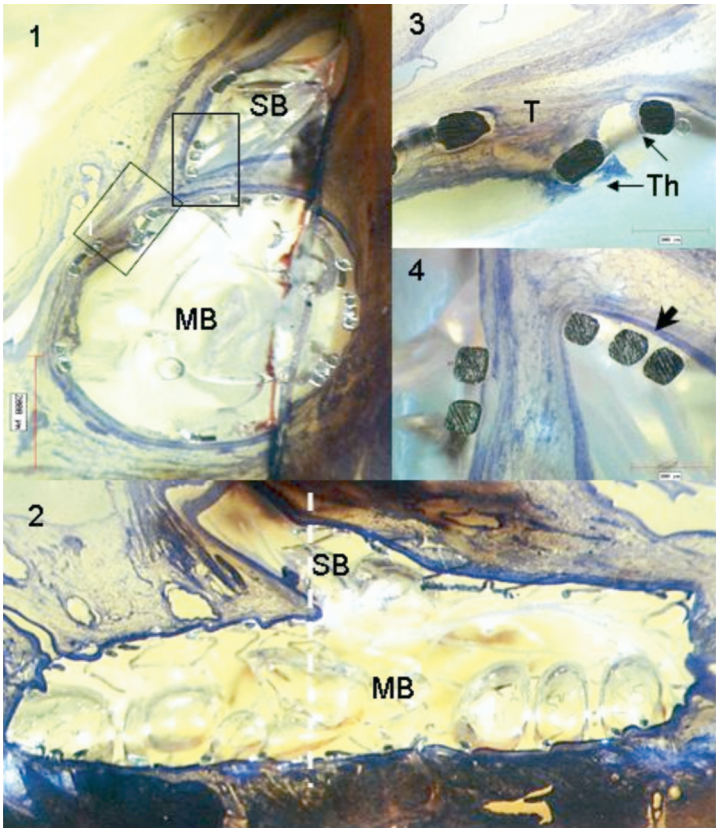

Figure 4. Overview and detail of cross- and longitudinal sections of coronaries receiving a XIENCE SBA stent. The dotted line in the longitudinal view (Figure 4.2) indicate the location of the cross section, showing the MB and SB. While a good coverage of the SB with struts is seen (Figure 4.1) medial tearing by the stent struts (T) with adherent thrombus (Th) are also visible (Figure 4.3). Figure 4.4 indicates malapposition of stent struts in the SB.

struts include device entrapment as well as deformation of the stent cells in the parent vessel, resulting in additional vessel trauma. Most of these problems are overcome by the SBA stent since its deployment requires a single inflation of a double balloon opening both the MB and SB at the same time without the need of rewiring the SB. Furthermore, the SB was easy accessible for extra treatment when necessary. The stent cells remained uniform in size and stent deformation or tapering was seen in very limited cases, suggesting good uniform deployment of the SBA stents.

In conclusion, the new XIENCE SBA dedicated bifurcation stent is safe, and shows a good preservation of the vascular architecture. Whether it is superior, due to it-s easy implantation procedure and good SB coverage, to the clinical DES on the long term will have to be studied in a clinical trial.

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