PHILIPS

AngioSculpt Evo

RX PTCA scoring balloon catheter

Instructions for use

English- en

RX PTCA scoring balloon catheter with hydrophilic coating

REF Catalog number	LOT Lot number	 Balloon outer diameter
 Balloon length	NOM Nominal pressure	RBP Rated burst pressure
 Max guidewire compatibility	Min guide catheter ID (MGCID)	 Caution: Do not exceed rated burst pressure

English- en

RX PTCA scoring balloon catheter with hydrophilic coating

Use by date

Packaging unit

Pressure atm (kPa)

Non-pyrogenic

Rx
ONLY

Caution: Federal (USA) law restricts this device sale by or on the order of a physician.

Consult Instructions for use (IFU)

Upper limit of temperature

Keep dry

Sterilized using ethylene oxide

English- en

RX PTCA scoring balloon catheter with hydrophilic coating

 **Do not use if package is damaged**	 **Single use**	 **Manufacturer**
 **Medical device**	 **Date of manufacture**	**Made in USA**

English- en

RX PTCA scoring balloon catheter with hydrophilic coating

Caution: Federal (USA) law restricts this device to sale by or on the order of a physician.

Carefully read all instructions prior to use. Failure to observe all warnings and precautions may result in complications.

Note: These instructions apply to all balloon diameters and lengths.

Sterile: Sterilized with ethylene oxide gas. Non-pyrogenic. **Do not use if the package is open or damaged.**

Contents: One (1) AngioSculpt Evo scoring balloon catheter.

Storage: Store in a dry, dark, cool place.

Device name

The device name is the AngioSculpt Evo scoring balloon catheter; the generic name is scoring percutaneous transluminal coronary angioplasty (PTCA) catheter.

Device description

The AngioSculpt Evo scoring balloon catheter is a standard PTCA catheter with a scoring balloon near the distal tip. The balloon is designed to expand to a specified diameter and length at a specified pressure. The distal end of the catheter has a conventional nylon-blend balloon and a nitinol scoring element with three spiral struts that wrap around the balloon. The struts create focal concentrations of dilating force, which minimizes balloon slippage and assists in the luminal expansion of stenotic arteries. Conventional radiopaque markers aid in positioning the balloon in the stenosis.

Figure 1 shows the distal section of the catheter with the scoring balloon. The proximal end of the balloon is connected to a balloon inflation channel.

Figure 1: Distal section of AngioSculpt Evo scoring balloon catheter

The product is offered on a rapid exchange (RX) delivery platform, and is available in balloon diameters of 2.0 – 3.5 mm in 0.5 mm increments, and in scoring balloon lengths of 6, 10, 15 and 20 mm. The catheter length is approximately 139 cm and is compatible with 0.014-inch guide wires and 5F guide catheters. The catheter is supplied sterile and is intended for a single use. As shown in Figure 2 below, the catheter has a segment that is coated with a hydrophilic coating.

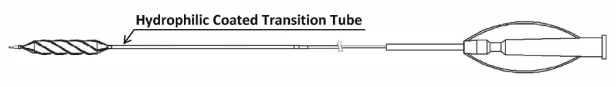

Figure 2: AngioSculpt Evo scoring balloon catheter with hydrophilic coating

Indications

The AngioSculpt Evo scoring balloon catheter is indicated for use in the treatment of hemodynamically significant coronary artery stenosis, including in-stent restenosis and complex type C lesions, for the purpose of improving myocardial perfusion.

Contraindications

The AngioSculpt Evo catheter should not be used for the following:

- Coronary artery lesions unsuitable for treatment by percutaneous revascularization.
- Coronary artery spasm in the absence of a significant stenosis.

Warnings

- The AngioSculpt Evo catheter is indicated for use in coronary arteries. The safety and effectiveness of the device has not been established, or is unknown, in vascular regions other than those specifically indicated.
- The AngioSculpt Evo catheter is coated with a hydrophilic coating on the transition tube at the distal end of the catheter for a length of 53mm; see Figure 2. Please refer to Directions for Use, Step 16 for further information on how to prepare and use this catheter to ensure it performs as intended. Failure to abide by the warnings in this labeling might result in damage to the device coating, which may necessitate intervention or result in serious adverse events.

- Administer appropriate antiplatelet, anticoagulant and coronary vasodilator therapy, consistent with institutional practice for coronary stent procedures, during and after the procedure.
- This device is intended for single (one patient) use only. Do not resterilize and/or reuse, as this can potentially result in compromised device performance and increased risk of inappropriate resterilization and cross contamination.
- For use in de novo or in-stent restenosis (ISR) lesions, the inflated diameter size of the balloon should approximate the vessel diameter size just proximal and distal to the stenosis, in order to reduce potential vessel damage. When used to pre-dilate the lesion prior to pre-planned stenting, the catheter should be one size smaller than the estimated vessel diameter (e.g., a 2.5mm diameter device should be used in a vessel estimated to have a 3.0mm diameter).
- PTCA in patients who are not acceptable candidates for coronary artery bypass graft surgery require careful consideration, including possible hemodynamic support during PTCA, as treatment of this patient population carries special risk.
- When the catheter is exposed to the vascular system, it should be manipulated while under high quality fluoroscopic observation. Do not advance or retract the catheter unless the balloon is fully deflated under vacuum. If resistance is met during manipulation, determine the cause of the resistance before proceeding.
- Do not exceed the rated burst pressure (RBP) during balloon inflation. The RBP is based on results of in-vitro testing. At least 99.9% of the balloons (with 95% confidence) will not burst at or below their RBP. Use of a pressure monitoring device is recommended to prevent over-pressurization.
- PTCA should only be performed at hospitals where emergency coronary artery bypass graft surgery can be quickly performed in the event of a potential cardiovascular injury or life-threatening complication.
- Use only the recommended balloon inflation medium. Never use air or any gaseous medium to inflate the balloon.
- Use the device prior to the expiration date specified on the package.

Precautions

- Take extra care when using the AngioSculpt Evo catheter to treat a lesion distal to a freshly deployed stent. This precaution is particularly applicable to a drug-eluting stent so as to minimize the risk of damage to the stent coating.
- Prior to angioplasty, examine the catheter to verify functionality, catheter integrity and to ensure that its size and length are suitable for the specific procedure for which it is to be used.
- Only physicians trained in the performance of percutaneous transluminal coronary angioplasty should use the AngioSculpt Evo catheter.
- Do not rotate the catheter shaft in excess of 180 degrees when the tip is constrained.
- Do not rotate the catheter luer/hub in excess of five (5) turns during use.
- Do not advance or retract the AngioSculpt Evo catheter over the floppy portion of the guide wire.
- Catheter manipulation, including advancement and retraction, should be performed by grasping the catheter shaft.
- If unusual resistance is felt when the catheter is being manipulated or if it is suspected that the guide wire has become kinked, carefully remove the entire catheter system (AngioSculpt Evo catheter and steerable guide wire) as a unit.
- If fluoroscopic guidance indicates that the AngioSculpt Evo catheter has advanced beyond the end of the guide wire, withdraw the catheter and reload the wire before advancing again.

Adverse effects

Possible adverse effects include, but are not limited to, the following:

• Death • Heart attack (acute myocardial infarction) • Embolism • Total occlusion of the treated coronary artery • Coronary artery dissection, perforation, rupture, or injury • Pericardial tamponade • No/slow reflow of treated vessel • Emergency coronary artery bypass (CABG) • Emergency percutaneous coronary intervention • CVA/stroke/embolic stroke • Pseudoaneurysm • Restenosis of the dilated vessel • Unstable angina • Thromboembolism or retained device components	• Irregular heart rhythm (arrhythmias, including life-threatening ventricular arrhythmias) • Severe low (hypotension)/high (hypertension) blood pressure • Coronary artery spasm • Hemorrhage or hematoma • Need for blood transfusion • Surgical repair of vascular access site • Creation of a pathway for blood flow between the artery and the vein in the groin (arteriovenous fistula) • Drug reactions, allergic reactions to x-ray dye (contrast medium) • Infection

Observed adverse events

A total of 200 patients were enrolled in the AngioSculpt catheter pivotal IDE clinical trial, a prospective, multi-center, non-randomized, single-arm study. The primary objective of the study was to evaluate safety and efficacy of the AngioSculpt catheter in a wide range of coronary artery lesions in both native vessels and following in-stent restenosis (ISR).

Table 1 provides a summary of the Major Adverse Cardiac Events (MACE) observed in the AngioSculpt catheter multi-center IDE study, as determined by the Clinical Events Committee (CEC). MACE was defined as death, Q wave or non-Q wave myocardial infarction (MI) or target lesion revascularization (TLR).

Table 1: Summary of principal adverse event rates observed in the IDE study

	Aggregate	95% C.I.
In-hospital complications	**% of patients (number of events)**	
MACE (Death, MI, TLR)	1.5% (3/200)	(0.3%, 4.3%)
Death	0.0% (0/200)	(0.0%, 1.8%)
MI (Q or Non-Q wave)	1.5% (3/200)	(0.3%, 4.3%)
Q wave MI	0.5% (1/200)	(0.0%, 2.8%)
Non-Q wave MI*	1.0% (2/200)	(0.1%, 3.6%)
Target lesions		
Revascularization (TLR)	0.0% (0/200)	(0.0%, 1.8%)
TLR PTCA	0.0% (0/200)	(0.0%, 1.8%)
TLR CABG	0.0% (0/200)	(0.0%, 1.8%)
Target vessel		
Revascularization(TVR)	0.0% (0/200)	(0.0%, 1.8%)
TVR PTCA	0.0% (0/200)	(0.0%, 1.8%)
TVR CABG	0.0% (0/200)	(0.0%, 1.8%)
Thrombosis	0.5% (1/200)	(0.0%, 2.8%)
Acute thrombosis	0.5% (1/200)	(0.0%, 2.8%)
Confirmed	0.0% (0/200)	(0.0%, 1.8%)
Presumed	0.5% (1/200)	(0.0%, 2.8%)
Sub-acute thrombosis	0.0% (0/200)	(0.0%, 1.8%)
Confirmed	0.0% (0/200)	(0.0%, 1.8%)
Presumed	0.0% (0/200)	(0.0%, 1.8%)
Out-of hospital complications	**% of patients (number of events)**	
MACE (Death, MI, TLR)	1.0% (2/200)	(0.1%, 3.6%)
Death	0.0% (0/200)	(0.0%, 1.8%)
MI (Q or Non-Q)	1.0% (2/200)	(0.1%, 3.6%)
Q wave MI	1.0% (2/200)	(0.1%, 3.6%)
Non-Q wave MI	0.0% (0/200)	(0.0%, 1.8%)
TLR	1.0% (2/200)	(0.1%, 3.6%)
TLR PTCA	0.5% (1/200)	(0.0%, 2.8%)
TLR CABG	0.5% (1/200)	(0.0%, 2.8%)
Target vessel		
Revascularization(TVR)	1.0% (2/200)	(0.1%, 3.6%)
TVR PTCA	0.5% (1/200)	(0.0%, 2.8%)
TVR CABG	0.5% (1/200)	(0.0%, 2.8%)
Sub-acute thrombosis	1.0% (2/200)	(0.1%, 3.6%)
Confirmed	1.0% (2/200)	(0.1%, 3.6%)
Presumed	0.0% (0/200)	(0.0%, 1.8%)

Table 1: Summary of principal adverse event rates observed in the IDE study *(continued)*		
	Aggregate	**95% C.I.**
Cumulative complications	**% of patients (number of events)**	
MACE (Death, MI, TLR)	2.5% (5/200)	(0.8%, 5.7%)
Death	0.0% (0/200)	(0.0%, 1.8%)
MI (Q or Non-Q)	2.5% (5/200)	(0.8%, 5.7%)
Q wave MI	1.5% (3/200)	(0.3%, 4.3%)
Non-Q wave MI	1.0% (2/200)	(0.1%, 3.6%)
TLR	1.0% (2/200)	(0.1%, 3.6%)
TLR PTCA	0.5% (1/200)	(0.0%, 2.8%)
TLR CABG	0.5% (1/200)	(0.0%, 2.8%)
Target vessel Revascularization (TVR)	1.0% (2/200)	(0.1%, 3.6%)
TVR PTCA	0.5% (1/200)	(0.0%, 2.8%)
TVR CABG	0.5% (1/200)	(0.0%, 2.8%)
Thrombosis	1.5% (3/200)	(0.3%, 4.3%)
Confirmed	1.0% (2/200)	(0.1%, 3.6%)
Presumed	0.5% (1/200)	(0.0%, 2.8%)
* Non-Q wave MI is defined as elevation of the CPK to >3x the upper limit of normal (associated with an abnormally elevated Troponin-I) without the development of new pathologic Q-waves.		

In addition to MACE, a total of 23 patients experienced a non-MACE cardiovascular event and 37 patients experienced a non-cardiovascular event, as reported by the clinical sites. Among these events, the principal cardiovascular events were classified as unstable angina (3%), coronary artery injury (1.5%), hypotension (1.5%), and hematoma or excessive blood loss/hemorrhage requiring transfusion (1.5%). The coronary artery injuries consisted of 2 residual post-stenting dissections, 1 non-device related perforation, and 0 ruptures. These events have been associated with the use of other PTCA catheters.

Summary of clinical studies

European multi-center clinical investigation

An initial AngioSculpt catheter clinical study was performed at two clinical sites outside the United States. This was a nonrandomized registry which enrolled 45 patients with a wide range of de novo lesions and in-stent restenosis (ISR). The primary safety objective was to demonstrate that the incidence and severity of device-related complications (MACE: death, Q wave/non-Q wave myocardial infarction (MI), target lesion revascularization (TLR)) at one month follow-up were acceptably low. The primary performance objective was to demonstrate successful percutaneous revascularization (defined as a reduction in target lesion diameter stenosis to ≤ 50% following completion of all interventions and the absence of in-hospital MACE).

Forty-six lesions were treated with 100% procedural success. All patients completed the final 14-28 day clinical follow-up post procedure and experienced no MACE in-hospital or post discharge related to the study device. Additional six month follow-up beyond that required by the study protocol was performed at one clinical site. Six month angiographic and IVUS evaluations were performed on 11 patients treated with the AngioSculpt catheter for ISR. Only one patient (9%) demonstrated recurrent restenosis.

United States clinical investigation (pivotal study)

Objective

The primary objective of this study was to determine the safety and effectiveness of the AngioSculpt catheter in patients with single or multiple vessel coronary artery disease, in both de novo lesions and in-stent restenosis lesions.

Study design

This study was conducted as a multi-center, non-randomized, single-arm prospective clinical study in patients with single or multiple vessel coronary artery disease scheduled to undergo percutaneous coronary intervention because of symptoms of stable or unstable angina pectoris. No more than two lesions were to be treated during the index procedure. The investigation was conducted at nine clinical sites and enrolled 200 patients. A subset of patients was evaluated with IVUS. All patients enrolled in this study were followed for 14-21 days post-procedure for any evidence of MACE (death, Q wave or non-Q wave MI, or TLR).

The study hypotheses stated that the procedural success rate and clinical success rate for the AngioSculpt catheter will meet the objective performance criteria for conventional coronary angioplasty balloons based on contemporary published literature. The primary effectiveness endpoint was procedural success, defined as ≤ 50% final diameter stenosis in at least one of the AngioSculpt-attempted lesions following completion of the interventional procedure, including adjunctive stenting when used, without death, Q wave or non-Q wave MI, or emergency CABG surgery during the hospital stay. The primary safety endpoint was clinical success rate, defined as freedom from MACE (death, Q wave or non-Q wave MI, or TLR) at 14-day follow-up.

Demographics

Following informed consent, 200 patients (age 63.5 ± 11.3 years, males 72%) referred for percutaneous coronary intervention underwent treatment with the AngioSculpt catheter. Of these patients, 27% (54/200) had a history of diabetes mellitus. Unstable angina was present in 31.5% (63/200) of patients. Other relevant clinical characteristics are described in Table 2, and are consistent with that of the general population of patients in whom the AngioSculpt catheter is likely to be used.

Table 2: Baseline patient demographics and clinical characteristics

	Aggregate
Age	63.45 ± 11.32 (200)
Male	71.5% (143/200)
Female	28.5% (57/200)
Stable angina	53.5% (107/200)
Unstable angina	31.5% (63/200)
History of diabetes	27.0% (54/200)
History of MI	26.0% (52/200)
History of smoking	58.0% (116/200)
History of CHF	6.0% (12/200)
History of hypertension	78.0% (156/200)
History of hyperlipidemia	85.0% (170/200)
Patients with only 1 lesion treated with ASC	84.5% (169/200)
Patients with 2 lesions treated with ASC	15.5% (31/200)

ASC = AngioSculpt

Baseline qualitative and quantitative angiographic characteristics are summarized in Table 3 below. Of the 219 lesions, 184 (84.0%) were de novo and 35 (16.0%) were treated for in-stent restenosis. The AngioSculpt catheter was used in combination with stenting in 97.7% of cases.

Table 3: Baseline angiographic characteristics

	Aggregate
ACC[1] score A	4.1% (9/219)
ACC score B1	19.6% (43/219)
ACC score B2	28.3% (62/219)
ACC score C	47.9% (105/219)
Lesion length	17.79 ± 8.94 (219)
Pre-procedure RVD	2.72 ± 0.39 (219)
Pre-procedure MLD	0.78 ± 0.31 (219)
Pre-procedure %DS	71.61 ± 10.16 (219)
Lesion angulation (degrees)	15.48 ± 17.62 (218)
Eccentric lesion	26.9% (59/219)
Bifurcation lesion	28.8% (63/219)
Visible thrombus	2.7% (6/219)
Lesion location	
Proximal	35.6% (78/219)
Mid	37.0% (81/219)
Distal	14.6% (32/219)
Ostial	12.8% (28/219)
LAD	37.9% (83/219)
RCA	37.0% (81/219)
LCX	23.3% (51/219)
LM	1.4% (3/219)
SVG	0.5% (1/219)
Lesion calcification*	35.3% (73/207)
Moderate	29.0% (60/207)
Severe	6.3% (13/207)
TIMI flow	
TIMI flow 0	1.4% (3/219)
TIMI flow 1	0.9% (2/219)
TIMI flow 2	5.0% (11/219)
TIMI flow 3	92.7% (203/219)

RVD = reference vessel diameter (mm), MLD = minimal lumen diameter (mm), %DS = percent diameter stenosis (%), LAD = left anterior descending, RCA = right coronary artery, LCX = left circumflex, LM = left main, SVG = saphenous vein graft

*Pre-procedure calcification was not able to be assessed for 12 lesions in 11 patients.

[1]ACC/AHA Lesion Class #: Smith, et al ACC/AHA Percutaneous Coronary Intervention Guidelines. JACC 2001;37:2239i-xvi

Methods

The AngioSculpt catheter was prepped according to standard procedures consistent with those described in the Directions for Use section below. When used to pre-dilate the lesion prior to pre-planned stenting, physicians were instructed to select a catheter that was one size smaller relative to the estimated reference vessel diameter (RVD). For example, for a RVD of 3.0 mm by visual estimation, a 2.5 mm diameter device was used. When used for in-stent restenosis, catheters were selected to closely approximate the RVD (≤ 1.0 x RVD). Additional clinically indicated procedures (e.g., stent placement) were performed at the discretion of the investigator. Anticoagulation and antiplatelet medications were prescribed per institutional protocol f or procedures involving stents. Baseline clinical and angiographic data were collected on standardized case report forms. QCA, ECG, and IVUS outcomes were assessed by quantitative analysis at designated core laboratories. All suspected MACE and device failures/malfunctions were adjudicated by an independent Clinical Events Committee.

Results

Data analysis was performed on an intent-to-treat basis. The study met its primary safety and efficacy endpoints as described and summarized in Table 4.

All patients and all lesions had a final diameter stenosis that were ≤ 50% in at least one AngioSculpt-attempted lesion following completion of the interventional procedure. Three patients experienced an in-hospital MACE (two non-Q wave MI, one Q wave MI) contributing to a procedural success rate of 98.5% (197/200). Additionally, two patients experienced MACE post-hospital discharge (one Q wave MI with TLR-PCI and one Q wave MI with TLR-CABG). This led to a clinical success rate of 97.5% (195/200).

Table 4: Summary of primary endpoints

	Aggregate	Lower bound of 1-sided 95% C.I.
Procedural success	98.5%(197/200)	96.2%
Clinical success	97.5% (195/200)	94.8%

Procedural success = ≤50% final diameter stenosis in at least one AngioSculpt-attempted lesion following completion of the interventional procedure, including adjunctive stenting when used, without death, Q-wave or non-Q-wave MI, or emergency CABG during the hospital stay.
Clinical success = freedom from MACE (death, Q wave or non-Q wave MI, or TLR) at 14-day follow-up.

In all 219 lesions (100%) the angiographic component of the primary efficacy endpoint (reduction of the lesion diameter stenosis to ≤ 50% at the completion of the interventional procedure) was successfully achieved. Table 5 summarizes the angiographic results following AngioSculpt treatment and following adjunctive stenting which was reported as performed in 97.7% (211/216) of lesions.

In all treated lesions the AngioSculpt catheter demonstrated stable position during deployment without slippage, as reported by the investigator and independently analyzed by the angiographic core laboratory.

The post-AngioSculpt dissection rate was 13.6% with the majority of these rated as low grade (A-C) utilizing the NHLBI classification.

Table 5: QCA and lesion morphology characteristics (post-procedure/in-hospital)

	Aggregate	Range	95% C.I.
Post ASC in-lesion MLD	1.55 ± 0.45 (190)	(0.51, 2.74)	(1.48, 1.61)
Post ASC in-lesion %DS	43.48 ± 14.66 (190)	(13.36, 79.84)	(41.38, 45.58)
Post ASC dissection	13.6% (26/191)		(9.1%, 19.3%)
Type A	0.5% (1/191)		(0.0%, 2.9%)
Type B	6.3% (12/191)		(3.3%, 10.7%)
Type C	5.8% (11/191)		(2.9%, 10.1%)
Type D	1.0% (2/191)		(0.1%, 3.7%)
Type E	0.0% (0/191)		(0.0%, 1.9%)
Type F	0.0% (0/191)		(0.0%, 1.9%)
Final in-lesion MLD	2.34 ± 0.42 (219)	(1.31, 3.45)	(2.29, 2.40)
Final in-lesion %DS	17.73 ± 7.18 (219)	(3.65, 39.84)	(16.78, 18.69)
Final thrombus	0.5% (1/219)		(0.0%, 2.5%)
Final dissection	0.5% (1/218)		(0.0%, 2.5%)
Type A	0.0% (0/218)		(0.0%, 1.7%)
Type B	0.5% (1/218)		(0.0%, 2.5%)
Type C	0.0% (0/218)		(0.0%, 1.7%)
Type D	0.0% (0/218)		(0.0%, 1.7%)
Type E	0.0% (0/218)		(0.0%, 1.7%)
Type F	0.0% (0/218)		(0.0%, 1.7%)

Table 5: QCA and lesion morphology characteristics (post-procedure/in-hospital) *(continued)*			
	Aggregate	**Range**	**95% C.I.**
Post ASC acute gain	0.77 ± 0.43 (190)	(-0.28, 1.93)	(0.71, 0.83)
Final in-lesion acute gain	1.57 ± 0.41 (219)	(0.18, 2.73)	(1.51, 1.62)
Slippage	0.0% (0/206)		(0.0%, 1.8%)
Slippage - slight	0.0% (0/206)		(0.0%, 1.8%)
Slippage - moderate	0.0% (0/206)		(0.0%, 1.8%)
Slippage - severe	0.0% (0/206)		(0.0%, 1.8%)
Balloon to artery ratio	0.99 ± 0.14 (201)	(0.67, 1.43)	(0.97, 1.00)

ASC = AngioSculpt, MLD = Minimal lumen diameter (mm),
%DS = percent diameter stenosis (%)
In a small number of cases, post-AngioSculpt angiograms were not performed and only the final angiograms were available.
All data were determined by Core Lab QCA evaluation.

A summary of CEC adjudicated MACE is provided in Table 6. The cumulative MACE rate was calculated by including only one event per patient. Two patients experienced more than one MACE (Q wave MI with TLR-PTCA and Q wave MI with TLR-CABG). Thus, there were a total of seven MACE among five patients. The events included two (1%) non-Q wave MI, three (1.5%) Q wave MI, one (0.5%) TLR-PTCA and one (0.5%) TLR-CABG).

MACE was defined as 'major adverse cardiac event' (i.e., major complication) and includes: death, Q wave or non-Q wave MI, or target lesion revascularization (TLR).

Non-Q wave myocardial infarction (MI) was defined as elevation of the CPK to >3x the upper limit of normal (associated with an abnormally elevated Troponin-I) without the development of new pathologic Q-waves.

Q wave myocardial infarction (MI) was defined as the development of new pathologic Q-waves in two or more contiguous leads associated with an elevation of the CPK to >3x the upper limit of normal (associated with an abnormally elevated Troponin-I).

TLR was defined as target lesion revascularization including CABG or re-intervention to the treated target area.

"Confirmed" thrombosis was defined as angiographically documented thrombus or subacute closure within or adjacent to a previously successfully treated lesion at the time of clinically-driven (due to chest pain and/or ECG changes) angiographic restudy for ischemia. Thrombosis is "presumed" in the absence of angiography.

Table 6: Cumulative MACE rates (through 14 days follow-up)		
	Aggregate	**95% C.I.**
Cumulative complications		
MACE (Death, MI, TLR)	2.5% (5/200)	(0.8%, 5.7%)
Death	0.0% (0/200)	(0.0%, 1.8%)
MI (Q or Non-Q)	2.5% (5/200)	(0.8%, 5.7%)
Q wave MI	1.5% (3/200)	(0.3%, 4.3%)
Non-Q wave MI	1.0% (2/200)	(0.1%, 3.6%)
TLR	1.0% (2/200)	(0.1%, 3.6%)
TLR PTCA	0.5% (1/200)	(0.0%, 2.8%)
TLR CABG	0.5% (1/200)	(0.0%, 2.8%)
Target Vessel Revascularization(TVR)	1.0% (2/200)	(0.1%, 3.6%)
TVR PTCA	0.5% (1/200)	(0.0%, 2.8%)
TVR CABG	0.5% (1/200)	(0.0%, 2.8%)
Thrombosis	1.5% (3/200)	(0.3%, 4.3%)
Confirmed	1.0% (2/200)	(0.1%, 3.6%)
Presumed	0.5% (1/200)	(0.0%, 2.8%)

Further analysis of the data for the 35 ISR lesions treated compared to the de novo lesions demonstrated no significant difference in primary efficacy and safety endpoints or in any of the MACE components between the two groups. The results are summarized in Table 7.

Table 7: Comparison of outcomes in patients with ISR vs. *de novo* lesions

Efficacy Measures	ISR	*de novo*	Aggregate	p-value
Procedural Success	100.0% (33/33)	98.2% (164/167)	98.5% (197/200)	1.0000
Clinical Success	100.0% (33/33)	97.0% (162/167)	97.5% (195/200)	0.5932
In-Hospital MACE Free	100.0% (33/33)	98.2% (164/167)	98.5% (197/200)	1.0000
Out-of-Hospital MACE Free	100.0% (33/33)	98.8% (165/167)	99.0% (198/200)	1.0000
Death Free	100.0% (33/33)	100.0% (167/167)	100.0% (200/200)	N/A
MI Free	100.0% (33/33)	97.0% (162/167)	97.5% (195/200)	0.5932
Q-Wave MI Free	100.0% (33/33)	98.2% (164/167)	98.5% (197/200)	1.0000
Non Q-Wave MI Free	100.0% (33/33)	98.8% (165/167)	99.0% (198/200)	1.0000
TLR Free	100.0% (33/33)	98.8% (165/167)	99.0% (198/200)	1.0000
TLR CABG Free	100.0% (33/33)	99.4% (166/167)	99.5% (199/200)	1.0000
TLR PTCA Free	100.0% (33/33)	99.4% (166/167)	99.5% (199/200)	1.0000

IVUS Sub-study

IVUS was performed in a subset of 80 patients pre- and post-treatment with the AngioSculpt catheter to evaluate the morphologic effects of the device on the plaque and to further confirm device safety. Of these, 72 IVUS images were evaluable post-treatment, and showed an increase in minimal lumen area from 2.42 ± 0.98 mm^2 at baseline to 3.05 ± 1.04 mm^2 post-AngioSculpt treatment. There were no adventitial dissections or intramural hematomas, and there was no thrombus formation or any other evidence of unanticipated vessel injury following AngioSculpt treatment at the lesion site or in the adjacent reference vessel segments.

Observed device failures/malfunctions

In total, there were 16 reported failures to cross the lesion with the AngioSculpt catheter. Fifteen of these failures were adjudicated as device-related. There was one failure to cross the lesion which was adjudicated by the Clinical Events Committee as procedure-related but unrelated to the study device. All sixteen lesions were subsequently successfully pre-dilated with a commercially available balloon followed by stent placement.

There were two reported cases of device malfunction due to loss of balloon pressure below the rated burst pressure. These device malfunctions were unassociated with any adverse event.

AGILITY Coronary bifurcation study

The AngioSculpt scoring balloon catheter was also studied in the AGILITY study, which was designed to evaluate patients with significant (> 50% diameter stenosis) disease involving both the main branch vessel and ostium of the side branch vessel in a native coronary artery bifurcation [Medina class (x, x, 1)].

Study design

The AGILITY study was a U.S. based multi-center, non-randomized, single-arm prospective clinical investigation designed to evaluate the acute procedural success, device performance and long term safety of the AngioSculpt catheter in patients who were scheduled to undergo percutaneous coronary intervention of their bifurcation lesion because of symptoms of stable or unstable angina pectoris or silent myocardial ischemia.

Following informed consent, a total of 93 patients were enrolled at 9 clinical sites and evaluated through their index hospitalization. All patients were followed at 30 days and 9 months post-procedure by office visit or telephone interview. All study data were analyzed according to the intention-to-treat principle.

Demographics

93 patients (age 61.5 ± 11.6 years, males 72%) participated in the AGILITY study. Of these patients, 24.7% (23/93) had a history of diabetes mellitus. Unstable angina was present in 40.9% (38/93) of patients. Other relevant clinical characteristics are described in Table 8, and are consistent with that of the general population of patients in whom the AngioSculpt catheter is likely to be used.

Table 8: Baseline patient demographics and clinical characteristics

Patient characteristic	Aggregate
Age	
Mean ± SD(n)	61.54 ± 11.60 (93)
Gender	
Male	72.0% (67/93)
Female	28.0% (26/93)
History of diabetes	24.7% (23/93)
History of PTCA	52.7% (49/93)
History of CABG	7.5% (7/93)
History of CVA/TIA	5.4% (5/93)
History of MI	36.6% (34/93)
History of smoking	57.0% (53/93)
History of congestive heart failure	6.7% (6/90)
History of hypertension requiring medication	81.7% (76/93)
History of hyperlipidemia requiring medication	79.6% (74/93)
History of peripheral vascular disease	14.8% (13/88)
History of renal insufficiency	4.4% (4/91)
Family history of CAD	60.9% (53/87)
Angina	67.7% (63/93)
CCS III	29.0% (27/93)
CCS IV	9.7% (9/93)
Patients with 1 lesion treated with ASC - MB	72.0% (67/93)
Patients with 1 lesion treated with ASC - SB	98.9% (92/93)
Patients with 2 lesions treated with ASC - MB	0.0% (0/93)
Patients with 2 lesions treated with ASC - SB	0.0% (0/93)
Medina classification	
1,0,0	1.1% (1/93)
1,1,0	4.3% (4/93)
1,1,1*	73.1% (68/93)
0,1,1*	17.2% (16/93)
0,1,0	2.2% (2/93)
0,0,1*	1.1% (1/93)
1,0,1*	1.1% (1/93)

* Denotes Medina class (x, x, 1) ASC = AngioSculpt
SB= Side Branch MB= Main Branch

Table 9: Pre-procedure quantitative measurements				
	Main Branch, n = 93		Side Branch, n = 93	
	Mean ± SD	Range (min,max)	Mean ± SD	Range (min,max)
Pre-procedure percent diameter stenosis (%DS)	67.32 ± 11.69	(16.59,88.89)	61.29 ± 17.73	(4.02,95.71)

Results

The AGILITY study primary effectiveness endpoint and main secondary endpoint results are summarized in Table 10. Procedural success was defined as ≤ 30% diameter stenosis of the main branch vessel and ≤ 70% diameter stenosis of the side branch vessel with TIMI-3 flow at the conclusion of the procedure (including adjunctive stenting) in the absence of in-hospital MACE.

Table 10: Summary of primary and secondary endpoint results		
	Aggregate	95% Confidence interval
Procedural success	91.4% (85/93)	[83.8%, 96.2%]
Side-branch "bailout" stenting	10.9% (10/92)	[5.3%,19.1%]
Final kissing balloon	16.3% (15/92)	[9.4%,25.5%]

The angiographic success rate was 93.5% (87/93).

The Clinical Events Committee (CEC) adjudicated MACE and major complications are listed in Table 11.

Table 11: CEC adjudicated cumulative MACE, stent thrombosis and other complications						
	In-hospital		30 day		9 month	
Complications	Aggregate	95% Confidence interval	Aggregate	95% Confidence interval	Aggregate	95% Confidence interval
MACE (Cardiac death, MI, Clinically driven TLR)	3.2% (3/93)	[0.7%, 9.1%]	4.3% (4)	(0.2%, 8.4%)	5.4% (5)	(0.8%, 10.0%)
Cardiac death	0.0% (0/93)	[0.0%, 3.9%]	1.1% (1)	(0.0%, 3.2%)	1.1% (1)	(0.0%, 3.2%)
Myocardial infarction	2.2% (2/93)	[0.3%, 7.6%]	2.2% (2)	(0.0%, 5.1%)	2.2% (2)	(0.0%, 5.1%)
Q-Wave MI	0.0% (0/93)	[0.0%, 3.9%]	0.0% (0)		0.0% (0)	
Non Q-Wave MI	2.2% (2/93)	[0.3%, 7.6%]	2.2% (2)	(0.0%, 5.1%)	2.2% (2)	(0.0%, 5.1%)
Clinically driven target Lesion revascularization (TLR)	2.2% (2/93)	[0.3%, 7.6%]	2.2% (2)	(0.0%, 5.1%)	3.3% (3)	(0.0%, 6.9%)
PTCA	1.1% (1/93)	[0.0%, 5.9%]	1.1% (1)	(0.0%, 3.2%)	2.2% (2)	(0.0%, 5.2%)
CABG	1.1% (1/93)	[0.0%, 5.9%]	1.1% (1)	(0.0%, 3.2%)	1.1% (1)	(0.0%, 3.2%)

Table 11: CEC adjudicated cumulative MACE, stent thrombosis and other complications *(continued)*						
	In-hospital		30 day		9 month	
Complications	**Aggregate**	**95% Confidence interval**	**Aggregate**	**95% Confidence interval**	**Aggregate**	**95% Confidence interval**
Clinically driven target vessel revascularization (TVR)	2.2% (2/93)	[0.3%, 7.6%]	3.2% (3)	(0.0%, 6.9%)	4.4% (4)	(0.2%, 8.5%)
PTCA	1.1% (1/93)	[0.0%, 5.9%]	2.2% (2)	(0.0%, 5.2%)	3.3% (3)	(0.0%, 6.9%)
CABG	1.1% (1/93)	[0.0%, 5.9%]	1.1% (1)	(0.0%, 3.2%)	1.1% (1)	(0.0%, 3.2%)
Any stent thrombosis	1.1% (1/93)	[0.0%, 5.9%]	2.2% (2)	(0.0%, 5.1%)	2.2% (2)	(0.0%, 5.1%)
Definite	1.1% (1/93)	[0.0%, 5.9%]	1.1% (1)	(0.0%, 3.2%)	1.1% (1)	(0.0%, 3.2%)
Probable	0.0% (0/93)	[0.0%, 3.9%]	1.1% (1)	(0.0%, 3.2%)	1.1% (1)	(0.0%, 3.2%)
Possible	0.0% (0/93)	[0.0%, 3.9%]	0.0% (0)		0.0% (0)	
Definite/Probable	1.1% (1/93)	[0.0%, 5.9%]	2.2% (2)	(0.0%, 5.1%)	2.2% (2)	(0.0%, 5.1%)

The primary and main secondary endpoints and MACE events in the patients with true bifurcations were similar to the entire study population, as shown in Table 12.

The patients who were classified as Medina (x, x, 0) did not require side-branch stenting or a kissing balloon procedure (by definition they had no significant side-branch vessel disease).

Table 12: Clinical outcomes by Medina classification cohort						
	Procedural success	**Rate of SBS**	**Rate of FKB without SBS**	**MACE in-hospital**	**Cumulative MACE 30-days**	**Cumulative MACE 9-months**
All AGILITY patients, n=93	91.4% (85/93)	10.9% (10/92)	16.3% (15/92)	3.2% (3/93)	4.3% (4/93)	5.4% (5/93)
AGILITY cohort (X,X,1), "true bifurcations," n=86	90.69% (78/86)	11.62% (10/86)	17.4% (15/86)	3.48% (3/86)	3.48% (3/86)	4.65% (4/86)
AGILITY cohort (x,x,0), n=7	100% (7/7)	0% (0/7)	0% (0/7)	0% (0/7)	14.28% (1/7)	14.28% (1/7)

The protocol definition of peri-procedural MI was CPK > 3x ULN. Using a more rigorous definition for peri-procedural MI (CPK >2x ULN) resulted in the inclusion of only one additional patient, as shown in Table 13. The cumulative rates of MACE for the protocol definition of MI and for the more rigorous definition are shown in the table below.

Table 13: Cumulative MACE rates associated with MI definitions

Post-procedure CPK	MACE in-hospital	MACE 30 days	MACE 9 months
CPK > 3x normal	3.2% (3/93)	4.3% (4/93)	5.4% (5)
CPK > 2x normal	4.3% (4/93)	5.4% (5/93)	6.5% (6)

Observed device failures/malfunctions

During the AGILITY trial, there were only two patients (2.2%) with reported failure-to-cross the target lesion with the AngioSculpt catheter. Pre-dilatation with POBA (conventional balloons) was required in 9.1% (6/66) of main branch lesions and 9.9% (9/91) of side branch lesions and resulted in subsequent successful delivery of the AngioSculpt catheter.

Materials required for use with the AngioSculpt Evo catheter

Warning- Use single use items only. Do not resterilize or reuse

- Femoral, brachial or radial guiding catheter (≥ 5F)
- Hemostatic valve
- Contrast medium diluted 1:1 with normal saline
- Sterile heparinized normal saline
- 10cc and 20cc syringes for flushing and balloon prep
- Stopcock for balloon prep
- Inflation device (indeflator)
- 0.014" coronary guide wire
- Guide wire introducer
- Guide wire torque device
- Radiographic contrast
- Manifold (for pressure monitoring and contrast injection), extension pressure tubing
- Sterile gauze

Directions for use

Prior to use of the AngioSculpt Evo catheter, examine carefully for damage and catheter integrity. Do not use if the catheter has bends, kinks, missing components or other damage. Do not use if inner package is open or damaged.

1. Pre-medicate patients with ASA, Clopidogrel/Ticlopidine, intravenous anti-coagulants, coronary vasodilators and GP2b/3a blockers according to institutional protocol for percutaneous coronary interventions involving stents.
2. Perform coronary angiogram in at least 2 orthogonal views of the target lesion prior to device deployment with online QCA.
3. Position 0.014" coronary guide wire of choice beyond the target lesion.

4. In the case of pre-planned stenting, select a catheter that is one size smaller relative to the estimated reference vessel diameter (RVD). For example, if the RVD by visual "estimation" during the procedure is 3.0 mm, use a 2.5 mm diameter AngioSculpt Evo catheter. For in-stent restenosis, select a catheter that closely approximates the RVD (≤ 1.0 x RVD).
5. Using sterile technique, remove the appropriately sized AngioSculpt Evo catheter from the sterile package and place on the sterile field.
6. Remove the stylet from the catheter.
7. Remove the protective tubing from the balloon.
8. Inspect the catheter to ensure that all components are intact.
9. Flush the guide wire lumen with saline by carefully inserting the distal catheter tip into the distal end of a 10 cc syringe and injecting saline until droplets emerge from the proximal guide wire lumen.
10. Attach a stopcock to the catheter's balloon inflation port.
11. Attach 20 cc syringe filled with 2-3 cc of 1:1 mixture of radiographic contrast and normal saline to the stopcock.
12. Open the stopcock to the syringe, aspirate/remove air from the catheter balloon lumen using the 20 cc syringe filled with 2-3 cc of radiographic contrast and leave on vacuum for 30 seconds.
13. Close the stopcock to the catheter balloon inflation port and remove the syringe.
14. Attach inflation device (indeflator), filled with 1:1 mixture of radiographic contrast and normal saline, to the stopcock by creating a meniscus. Avoid introducing air bubbles into the catheter balloon lumen.
15. Open the stopcock to the inflation device and aspirate using the inflation device, locking in vacuum.
    Note: All air must be removed from the balloon and displaced with contrast medium prior to inserting into the body (repeat steps 11-14 if necessary).
16. To activate the hydrophilic coating, wet the catheter's coated area with saline or wipe a wet sterile gauze over the coated area immediately prior to insertion into the guide catheter (see Figure 2).

    Note: Avoid using alcohol, antiseptic solutions, or other solvents to wet the hydrophilic coating, because this may cause unpredictable changes in the coating which could affect the device safety and performance.

17. Advance the AngioSculpt Evo catheter over the coronary guide wire (through a previously placed guiding catheter) and position at the target lesion utilizing standard fluoroscopic technique. If there is difficulty advancing the catheter through the hemostatic valve of the introducer sheath due to lubricity, gently grasp the catheter with a wet sterile gauze.

    Note: When back loading the catheter onto the guide wire, the catheter should be supported, ensuring that the guide wire does not come in contact with the balloon. Do not advance or retract the AngioSculpt Evo catheter over the floppy portion of the guide wire. Do not advance or retract the catheter unless the balloon is fully deflated under vacuum. If resistance is met during manipulation, determine the cause of the resistance before proceeding.

18. Inflate the AngioSculpt Evo balloon per the following recommended protocol:
    - Increase the inflation pressure by 2 atmospheres every 10-15 seconds until full device inflation is achieved
    - Do not exceed the rated burst pressure (RBP) printed on the package label
19. Perform coronary angiogram in at least 2 orthogonal views (same views as step 2) of the target lesion following completion of each device treatment.
20. Apply negative pressure to the inflation device, confirm that the balloon is fully deflated, and remove the AngioSculpt Evo catheter. The catheter should be retracted only by grasping the catheter shaft. If there is difficulty removing the catheter through the hemostatic valve of the guide catheter due to lubricity, gently grasp the catheter with a wet sterile gauze.

    Note: Do not rotate the catheter shaft in excess of 180 degrees when the tip is constrained. Do not rotate the catheter luer hub in excess of five (5) turns during use. Catheter manipulation, including advancement and retraction, should be performed by grasping the catheter shaft.

21. Inspect all components to ensure that the catheter is intact. Follow institutional procedures for disposal of biohazards. If device malfunction occurs or any defects are noted on inspection, flush the guide wire lumen and clean the outer surface of the catheter with saline, store the catheter in a sealed biohazard bag, and contact the manufacturer for further instructions.
22. Complete any additional interventions as clinically indicated (e.g. stent placement).
23. Remove the coronary guide wire and perform coronary angiography in at least 2 orthogonal views (same views as step 2) of the target lesion following completion of all interventions.
24. Remove all catheters and manage the arterial access site according to institutional protocol.
25. Continue treatment with aspirin, Clopidogrel/Ticlopidine, and GP2b/3a blockers according to institutional protocol for percutaneous coronary interventions involving stents.

References

The physician should consult recent literature on current medical practice regarding balloon dilatation and PTCA procedures.

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