



INSTRUCTIONS FOR USE

BioMimics 3D® Vascular Stent System

Carefully read all instructions prior to use. Observe all warnings and precautions noted throughout these instructions. Failure to do so may result in complications.

CAUTION: Federal law restricts this device to sale by or on the order of a physician.

BioMimics 3D is a trademark of Veryan Medical



Contents

Description	3
Indications.....	3
Contraindications.....	3
Warnings	3
Precautions	4
Magnetic Resonance Imaging (MRI) Safety Information	5
Potential Adverse Events	5
Instructions for Use.....	6
Patient Preparation and Stent System Selection.....	7
Preparation of Stent Delivery System (SDS)	7
Delivery Procedure	8
Stent Deployment Procedure	9
Post stent deployment.....	10
Summary of clinical studies	11
The MIMICS-2 Study	11
Mimics Study.....	Error! Bookmark not defined.
WARRANTY DISCLAIMER.....	20

How the System Is Supplied:

STERILE: The BioMimics 3D® Vascular Stent System is supplied sterile inside a pouch. The device is sterilized with ethylene oxide gas. It is intended for single use only. The device is non-pyrogenic. Do not use if the package is opened or damaged. Store in a dry location away from direct sunlight.

BioMimics 3D® Vascular Stent System.

Rx only

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

DESCRIPTION

The BioMimics 3D Vascular Stent System is comprised of two components: (i) a Nitinol stent with a three dimensional (3D) helical profile in a range of lengths and diameters and (ii) an over-the-wire stent delivery system.

The BioMimics 3D stent is a peripheral self-expanding nickel-titanium alloy (Nitinol) stent with 3D helical centerline geometry. The stent is laser cut from a straight Nitinol tube and 3D helical geometry is stored in the Nitinol shape memory. Three tantalum radiopaque markers are located at both ends of the stent to increase visibility of the stent to aid in placement.

The BioMimics 3D stent is mounted on a 6F over-the-wire stent delivery system (SDS) for use with a 0.035" guidewire.

INDICATIONS

The BioMimics 3D Vascular Stent System is indicated to improve luminal diameter in the treatment of symptomatic de novo or restenotic lesions in the native superficial femoral artery and/or proximal popliteal artery, with reference vessel diameters ranging from 4.0 - 6.0 mm and lesion lengths up to 140 mm.

CONTRAINDICATIONS

All customary contraindications for angioplasty must be considered when using the BioMimics 3D Vascular Stent System.

There are additional contraindications:

- Patients whose lesions cannot be crossed with a wire and/or balloon catheter and cannot be dilated sufficiently to allow passage of the delivery system.
- Patients with known intolerance to antiplatelet and/or anticoagulation therapies.
- Patients who are judged to have a lesion that prevents proper placement or deployment of the stent.
- A lesion that is within an aneurysm or an aneurysm with a proximal or distal segment to the lesion.
- Patients with a known hypersensitivity to nickel, titanium or tantalum.

WARNINGS

General Warnings

- DO NOT use after the "use by" date specified on the label.
- DO NOT use if the sterile package is opened or damaged or any information provided is obscured.
- DO NOT use if the device is damaged or if the stent is partially deployed.

- DO NOT reuse the BioMimics 3D Stent Delivery System (SDS) – this may lead to infection, contamination and non-performance.
- DO NOT re-sterilize the BioMimics 3D Vascular Stent System.

Deployment Warnings

- DO NOT force passage if resistance is encountered at any time during delivery of the SDS. This may cause damage to the stent, the SDS, or vessel or may lead to partial deployment. If the stent cannot be deployed, remove the entire delivery system (a partially deployed stent may require surgical removal).
- DO NOT push or advance the SDS forward (distally) once stent deployment has commenced.
- DO NOT attempt to recapture a partially deployed stent using the stent delivery system.
- DO NOT force removal of the delivery system if resistance is encountered at any time during withdrawal (post stent deployment); instead hold the bifurcated Luer stationary and retract the inner shaft until the SDS tip contacts the outer sheath marker and withdraw the system as one unit. Applying excessive force could result in loss of delivery system components or damage to the stent, delivery system, or vessel.

PRECAUTIONS

- The SDS is not designed for use with power injection systems.
- Always use an introducer or guide sheath for the implant procedure, to protect the access site.
- Never post-dilate the stent using a balloon that is larger in diameter than the nominal (labeled) diameter of the stent.
- The minimally acceptable introducer or guide sheath size is printed on the package label. Do not attempt to pass the stent delivery system through a smaller size introducer or guide sheath than indicated on the label.
- Prior to deployment, ensure adequate distance between the proximal end of stent and the introducer/guide sheath to prevent deployment within introducer/guide sheath.
- This device has not been tested in patients who are pregnant or patients who may be pregnant.
- Take caution when considering whether to use this device in a vessel in which there may be a residual stenosis of 50% diameter or larger in the target vessel after the planned intervention.
- In patients with poor kidney function, contrast agents may precipitate kidney failure.
- The stent is intended for use by physicians who have received appropriate training in endovascular intervention and placement of vascular stents.
- Failure to hold the Luer hub in a fixed position during stent deployment may result in partial or inaccurate deployment, incorrect deployed stent length or increased deployment forces.
- The reference vessel diameter should be measured accurately to reduce the possibility of stent migration or vessel damage due to incorrect sizing.
- The SDS is not intended for repositioning or recapturing a partially or completely deployed stent.
- If a second BioMimics 3D stent is required, deliver the most distal stent first to minimize the risk of stent dislodgement/damage or unsuccessful delivery of the second stent.
- If a second BioMimics 3D stent is placed in sequence and overlapped, the overlap should be less than 10mm. Overlapping more than two stents has not been evaluated.
- If the procedure requires additional non-BioMimics 3D stent placement, a Nitinol stent should be selected. The risk of corrosion increases if stents of differing metals contact one another.
- Caution should be used when crossing the deployed stent with any ancillary devices.

- The BioMimics 3D SDS is not designed for guidewire exchanges. If a guidewire exchange is needed or desired, remove the delivery system first.
- Carefully inspect the sterile package and device prior to use to verify that neither has been damaged during shipment.
- The BioMimics 3D SDS is provided sterile for single use only and should be used by the end of the month of the “Use By” date printed on the package.
- After use the BioMimics 3D SDS is a potential biohazard. Handling and disposal should be in accordance with medical practice and local regulations.

MAGNETIC RESONANCE IMAGING (MRI) SAFETY INFORMATION

Non-clinical testing has demonstrated that the BioMimics 3D stent is MR Conditional in single and overlapped configurations. A patient with the BioMimics 3D stent can be scanned safely under the following conditions:



- Static magnetic field of 1.5 or 3 Tesla
- Spatial gradient field of 4,000 Gauss/cm (40 T/m) or less
- Maximum whole body averaged specific absorption rate (SAR) of 2 W/kg (Normal Operating Mode)

Under the scan conditions defined above, the BioMimics 3D stent is expected to produce a maximum temperature rise of 6°C after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends approximately 12.8 mm from the BioMimics 3D stent when imaged with a spin echo pulse sequence and a 3 Tesla MRI System. The artifact partially obscures the device lumen.

POTENTIAL ADVERSE EVENTS

Possible complications associated with any endovascular procedure or stenting procedure include:

- **Stent system events:** device embolization; device malfunction; serious injury or surgical intervention; stent strut fracture(s); stent migration; stent misplacement/jumping.
- **Vascular events:** aneurysm; arterial dissection; arterial perforation; arterial rupture; arterial spasm; arteriovenous fistula; embolism and/or arterial thrombosis; hematoma; hypotension; ischemia; vascular complications which may arise during placement of a bailout stent; pseudoaneurysm; restenosis of the treated segment; stenosis; total occlusion of the peripheral artery; abrupt occlusion of the peripheral artery; vascular complications which may require surgical repair (conversion to open surgery) or endovascular intervention; worsening of peripheral arterial disease leading to additional surgical intervention, endovascular intervention or amputation, vasospasm.
- **Bleeding events:** access site complications including bleeding or hemorrhage; gastrointestinal bleed; bleeding complications requiring transfusion.
- **Procedural events:** allergic reaction to contrast media / medications; extravasation of contrast media; fracture of the guide wire or any component of the BioMimics 3D Vascular Stent System that may or may not lead to device embolism; radiation exposure.
- Angina
- Bradycardia

- Cardiac arrest
- Cardiac arrhythmia
- Death
- Emergency or non-emergency arterial bypass surgery
- Infection or fever
- Leg pain/ Claudication
- Myocardial infarction or coronary ischemia
- Nausea/vomiting
- Neurological deficit
- Renal insufficiency or failure
- Respiratory distress or failure
- Serious injury requiring surgical intervention
- Stroke or transient ischemic attack

INSTRUCTIONS FOR USE

Standard of care practice should be followed for preparing a subject for endovascular intervention, including medication and vascular access.

The BioMimics 3D Vascular Stent System is shown in Figure 1 and consists of the inner shaft (2) and outer shaft (5) secured together via the Tuohy Borst valve (3). The operating length of the stent delivery system (SDS) is 113 cm.

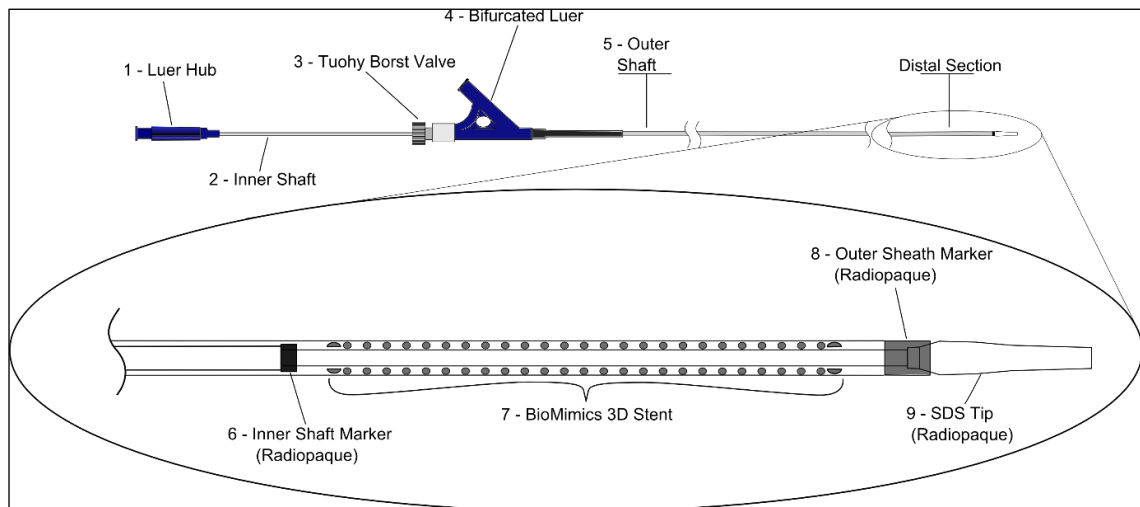


Figure 1: BioMimics 3D Stent Delivery System

The inner shaft (2) and Luer hub (1) act as the guidewire lumen.

The outer shaft includes a bifurcated Luer (4) with Tuohy Borst valve (3). The bifurcated Luer allows for flushing through the system while the valve is opened to facilitate deployment.

The stent (7) is crimped and loaded into the space between the inner shaft and the outer sheath at the distal end of the SDS. Radiopaque markers are positioned proximal (6) and distal (8) to the stent to facilitate stent placement.

Patient Preparation and Stent System Selection

- Using standard techniques, gain access to the vessel and insert a vascular introducer sheath.
- To determine the appropriate stent size, measure the vessel diameter and lesion length using standard imaging techniques.

Measure the diameter of the reference vessel proximal and distal to the lesion and, with reference to Table 1 below, use the larger reference diameter to determine the appropriate stent size.

Table 1: BioMimics 3D Stent Diameter Selection

Unconstrained stent diameter (mm)	Reference Vessel Diameter (mm)	Stent Delivery System Outer Diameter	Guide Wire Diameter
5.0	4.0	6 French (0.079", 2 mm)	0.035" (0.889 mm)
6.0	4.0 - 5.0		
7.0	5.0 - 6.0		

- Choose a stent length that will extend to normal vessel, proximal and distal to the targeted lesion, taking the information in Table 2 into account.

Table 2: BioMimics 3D Stent Length Selection

Labeled Stent Length (mm)	Nominal Length of Stent in the Delivery System (mm)	Typical Deployed Length of Stent within the Reference Vessel Diameter (mm)
60	67	62 - 66
80	86	80 - 85
100	104	97 - 103
125	129	120 - 128
150	154	143 - 152

- It is recommended to pre-dilate the lesion using standard PTA techniques before stenting.

Preparation of Stent Delivery System (SDS)

- Open the outer box to reveal the pouch containing the SDS.
- After careful inspection of the pouch for damage to the sterile barrier, carefully peel open the pouch at the chevron end and extract the stent delivery system tray. Remove the SDS and place it onto the sterile field.
- Examine the SDS for damage. Examine the distal section to ensure that the stent is contained within the outer sheath.
- Conduct three (3) system flushes as follows:
 - Attach a 5-10 cc syringe filled with heparinized saline to the Luer hub (1). Flush saline solution through the guidewire lumen until it comes out of the SDS tip.
 - Attach the syringe to the bifurcated Luer (4) and flush heparinized saline solution through the outer sheath lumen until it comes out of the distal end.
 - Release the Tuohy Borst valve (3) by turning the thumbscrew counter-clockwise and flush the proximal portion of the bifurcated Luer (4) and Tuohy Borst valve (3). Verify the heparinized saline solution comes out of the valve cap.

- After flushing, confirm the inner shaft is secure by tightening the Tuohy Borst valve (3) clockwise.
- Ensure that there is no gap between the SDS tip (9) and distal end of the outer sheath marker (8). If a gap exists, loosen the Tuohy Borst valve (3) and retract the Luer hub (1) until the proximal edge of the SDS tip is flush with the outer sheath marker (8). Tighten the Tuohy Borst valve (3) once the adjustment is complete.

Delivery Procedure

Note: The BioMimics 3D stent is suitable for deployment in an overlapping configuration. Should a second stent be required to cover the target lesion or lesions, place the most distal stent first followed by the proximal stent. The length of stent overlapping regions should be no more than 10 mm, which is equivalent to the length of three stent crowns, as indicated by dimension 1 in Figure 2.

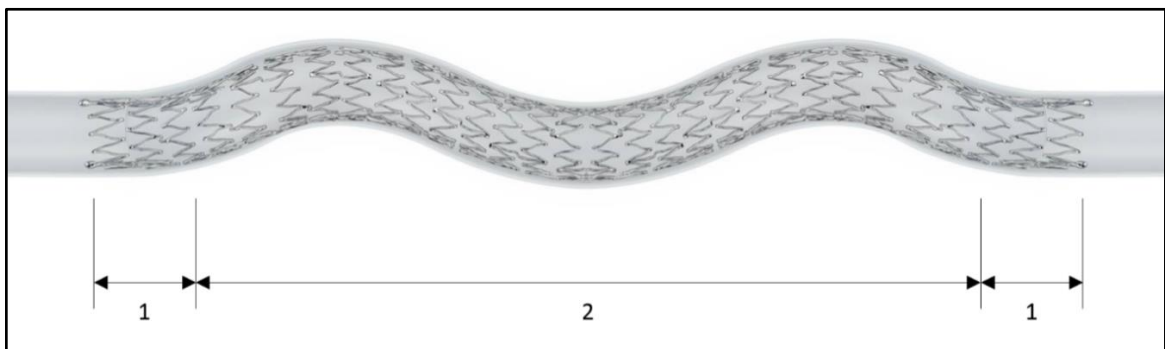


Figure 2: Stent overlapping region is indicated by dimension 1.

- Advance the SDS over the guidewire through the sheath/guide catheter.

WARNING: If resistance is encountered at any time during the insertion procedure, do not force passage. Resistance may cause damage to the stent, the SDS, or the vessel. Carefully withdraw the SDS without deploying the stent.

WARNING: For cases involving a contralateral approach, it is important to observe and prevent the prolapse of the introducer sheath into the aorta during insertion of the stent delivery system as this can result in the kinking of the device and/or introducer sheath. If sheath prolapse does occur, the delivery system should be withdrawn and inspected. If a kink is present, it should not be reinserted.

- Continue to advance the SDS over the guidewire until the radiopaque tip and distal stent marker are both distal to the target lesion site.
- Before stent deployment it is important to ensure that there is no excess slack in the delivery system (Figure 3). If excess slack is apparent in the delivery system prior to deployment, slightly retract the SDS while ensuring that the distal stent tantalum markers remain distal to the target lesion and the proximal tantalum markers remain proximal to the target lesion (Figure 4).

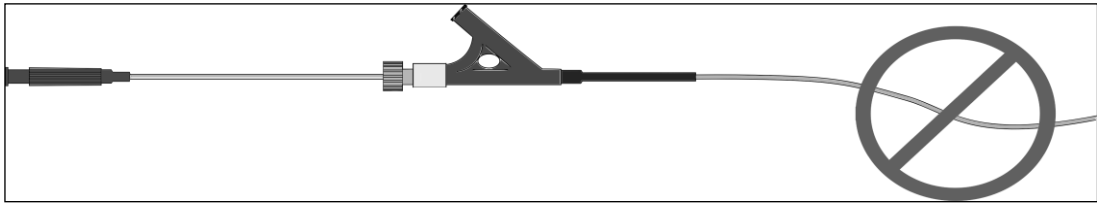


Figure 3: Remove excess slack from the delivery system prior to stent deployment

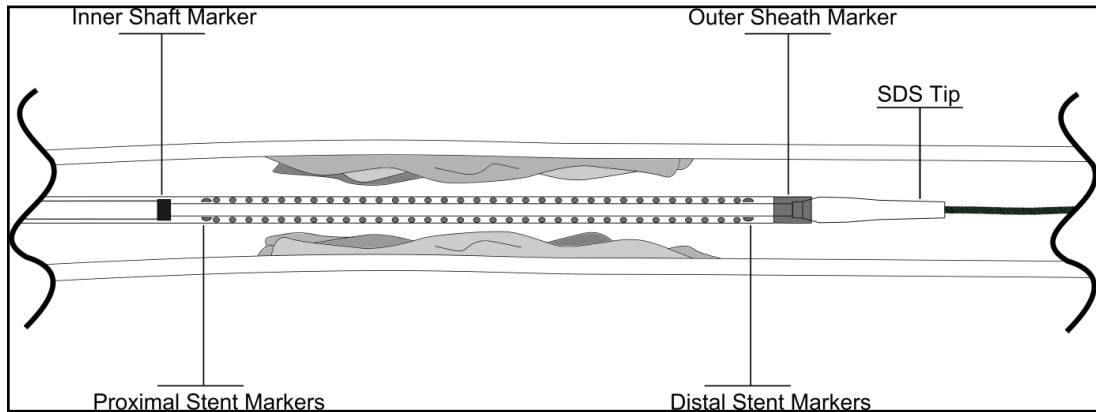


Figure 4: Intended position of all radiopaque markers relative to target lesion prior to deployment

Stent Deployment Procedure

- Open the Tuohy Borst valve (3) by holding the bifurcated Luer (4) in a fixed position and rotate the Tuohy Borst valve (3) counter-clockwise.
- Initiate stent deployment by holding the Luer hub (1) in a fixed position and move the bifurcated Luer (4) towards the fixed Luer hub, which will retract the outer sheath over the inner shaft (Figure 5).

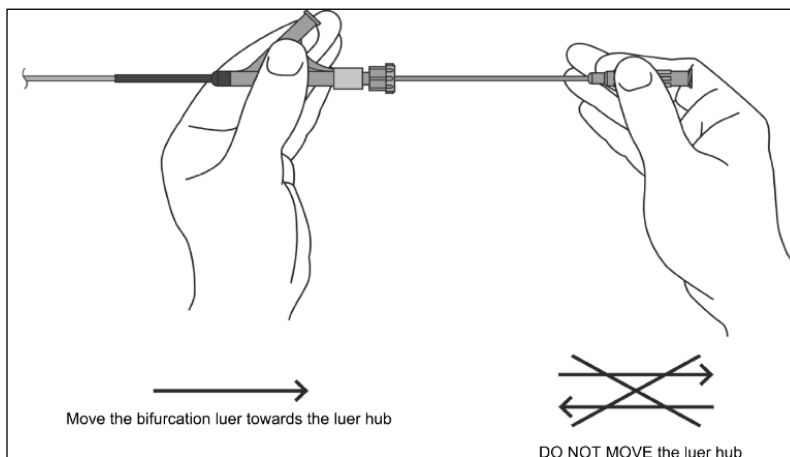


Figure 5: BioMimics 3D Stent Deployment Illustration

WARNING: If unexpected resistance is felt at the start of deployment, do not force the movement of the bifurcation Luer; instead carefully withdraw the SDS without deploying the stent.

WARNING: Do not push or advance the SDS forward (distally) once stent deployment has commenced.

CAUTION: Failure to hold the Luer hub (1) in a fixed position during stent deployment may result in partial or inaccurate deployment, incorrect deployed stent length or increased deployment forces.

- As soon as initial stent deployment is visible (emergence of distal tantalum markers), prior to the stent struts achieving vessel apposition, it is possible to reposition the stent closer to the target vessel/lesion as needed.

Note: It is recommended that the Tuohy Borst valve (3) is secured during stent repositioning in order to prevent accidental deployment.

CAUTION: The stent is not designed for repositioning once the stent struts contact the vessel wall. The stent delivery system is not designed for reloading/recapturing a partially or fully deployed stent.

- Full deployment of the stent is achieved by holding the Luer hub (1) in a fixed position and moving the bifurcated Luer (4) toward the Luer hub (1) until the outer sheath marker (8) passes proximal to the inner shaft marker band (6) and the stent is released and expands to appose the vessel wall.

Post stent deployment

- Under fluoroscopic guidance, holding the bifurcated Luer (4), withdraw the entire delivery system, over the guidewire.

WARNING: If resistance is encountered at any time during withdrawal, do not force removal of the delivery system; instead hold the bifurcated Luer stationary and retract the inner shaft until the SDS tip contacts the outer sheath marker and withdraw the system as one unit. Applying excessive force could result in loss of delivery system components or damage to the stent, delivery system, or vessel.

- Using fluoroscopy, visualize the stent to verify full deployment.
- Standard PTA post-dilatation should be used following stent placement at the physician's discretion.

CAUTION: Use caution when crossing a deployed stent with any ancillary device.

WARNING: Never expand the stent using a balloon that is larger in diameter than the labelled nominal diameter of the stent.

- If a second stent needs to be deployed, it should be placed proximal to the first with no more than 10mm overlapped and following the same procedural instructions.

SUMMARY OF CLINICAL STUDIES

The MIMICS-2 Study

MIMICS-2 is a prospective, single-arm, multicenter clinical trial conducted under FDA-approved Investigational Device Exemption to evaluate the safety and effectiveness of the BioMimics 3D Vascular Stent System in the treatment of patients with intermittent claudication due to atherosclerotic disease of the femoropopliteal artery. MIMICS-2 performance goals were based on those defined by VIVA Physicians, Inc. for Nitinol stents. The Study investigated the use of the BioMimics 3D Stent to improve luminal diameter in the endovascular treatment of de-novo lesions from 40 - 140 mm in length in native superficial femoral (SFA) and/or proximal popliteal arteries with reference vessel diameters ranging from 4.0 – 6.0 mm. Stent sizes of 5.0 – 7.0 mm (diameter) and 60 – 125 mm (length) were available throughout the Study, with the mid-study addition of a 150 mm stent.

Clinical Endpoints

The *primary safety endpoint* of MIMICS-2 was measured as a composite of independently adjudicated major adverse events (MAE) comprising death, any major amputation performed on the target limb or clinically-driven target lesion revascularization (CDTLR) through 30 days. The primary safety objective is achieved if the one-sided lower 97.5% Agresti-Coull confidence limit for the proportion of subjects treated with BioMimics 3D who are free from MAE through 30 days, is greater than the VIVA Physicians' performance goal of 88%.

The *primary effectiveness endpoint* was primary stent patency rate at 12 months. Patency was defined as no significant reduction in luminal diameter (i.e. < 50% diameter stenosis) since the index procedure or an intervening CDTLR. The primary effectiveness endpoint is achieved if the one-sided, lower 97.5% Agresti-Coull confidence limit for the proportion of subjects treated with BioMimics 3D that continue to have primary stent patency through 12 months is greater than the VIVA Physicians' performance goal of 66%.

The sample size for the primary effectiveness objective in MIMICS-2 was determined by the method of Agresti-Coull taking account of the 12-month, 75% primary stent patency performance of BioMimics 3D observed in the first Mimics Study (summary below). To statistically power the primary endpoint at the 85% level, 230 subjects were required, evaluable at 12 months. Providing for attrition, a total of 271 subjects were enrolled at 43 investigational sites in US, Germany and Japan. The first subject was enrolled in June 2015 and enrollment was completed in October 2016. Subject follow-up continued through 3 years from stent placement.

A range of secondary outcome measures were defined in the MIMICS-2 Study Protocol including longer-term assessment of safety and stent patency, together with clinical and functional outcomes. Independent core laboratories conducted reviews of duplex ultrasound, X-ray and angiographic images from index procedure and follow-up visits. In addition, all adverse events potentially contributing to determination of primary outcome measurement, were reviewed by an independent and experienced Clinical Events Committee (CEC). Events were evaluated as to a relationship with the BioMimics 3D stent placement procedure and/or the BioMimics 3D stent and delivery system, and whether any revascularization events during follow-up were clinically-driven.

Total number of subjects studied, schedule of follow-up visits and numbers completing each follow-up.

Two hundred and seventy-one (271) subjects were enrolled in the MIMICS-2 Study and the number of subjects completing each follow-up visit is detailed in Table 3.

Table 3: Study time points and number of subjects completing each follow-up visit

Follow-up visit timepoint	No. of subjects completing follow-up visit
Enrolment	271
12-month	256
24-month	225
36-month	208

Study subjects' follow-up visits were scheduled at Day-30, Month-12, Month-24 and Month-36. The post-approval study schedule of Month-24 and Month-36 is summarised in Table 4. The final visit at Month-36 was completed either as a clinic visit or telephone visit.

Table 4: MIMICS-2 post-approval study schedule

Assessment	Month-24 (730 days \pm 60 days)	Month-36 (1095 days \pm 60 days)
Physical Exam	x	
Ankle Brachial Index (ABI) [or Toe Brachial Index (TBI), if indicated]	x	
Rutherford Clinical Category (RCC)	x	
Walking Impairment Questionnaire (WIQ)	x	
Six-Minute Walk Test (6MWT) (subgroup only)	x	
Medications	x	x
Duplex Scan	x	x ¹
X-ray imaging of treatment area	x	x ²
Adverse event assessment	x	x

¹ Duplex ultrasound at 36 months only if clinical signs or symptoms were present suggestive of worsening claudication.

² The requirement for X-ray imaging may have been fulfilled at a facility remote to the investigational site.

Demographics and Medical History

Table 5 provides a summary of the demographics and medical history at the enrolment/baseline visit for all enrolled subjects in the MIMICS-2 Study.

Table 5: MIMICS-2 Study Baseline Demographics and Medical History

Parameter (n)	ITT Subjects; N=271
Age: Years mean \pm SD [Range: Min,Max]	68.4 \pm 9.5 [45,94] (271)
Sex: Male	66.4% (180)
Race:	
White	79.3% (215)
Asian	11.4% (31)
Black or African American	5.9% (16)
Other	0.4% (1)
Refuse to disclose	3.0% (8)
Ethnicity:	
Not Hispanic or Latino	93.4% (253)
Hispanic or Latino	3.7% (10)
Refuse to disclose	3.0% (8)
Relevant Medical History:	
Hypertension	90.0% (244)
Hypercholesterolemia / dyslipidemia	81.9% (222)
Unstable angina	3.3% (9)
Previous myocardial infarction	18.5% (50)
Previous percutaneous coronary intervention	33.6% (91)
Previous coronary artery bypass graft	20.7% (56)
Congestive heart failure	6.6% (18)
Cerebrovascular accident or stroke	7.7% (21)
Renal insufficiency	0.7% (2)
Diabetes mellitus	45.4% (123)
Previous revascularization (endovascular or surgery) in leg(s) other than to Target Lesion	36.2% (98)
Smoking:	80.8% (219)
Current	40.2% (109)
Former	40.6% (110)
ABI (Target Limb):	
Mean \pm SD; Range (Min, Max)	0.70 \pm 0.20; (0.00, 1.73) (257)
> 0.9	11.3% (29)
> 0.4 - \leq 0.9	85.6% (220)
\leq 0.4	3.1% (8)
Rutherford Clinical Category:	
Mean \pm SD; Range (Min, Max)	2.8 \pm 0.5; (2.0, 5.0) (271)
0	0% (0)
1	0% (0)
2	26.9% (73)
3	67.5% (183)
4	5.2% (14)
5	0.4% (1)
6	0% (0)

Lesion Characteristics

Table 6 summarizes the baseline quantitative vascular angiographic data derived by the core laboratory for all enrolled subjects at the index procedure.

Table 6: MIMICS-2 Study Population Baseline Angiographic Data

Lesion Characteristic ¹ (n)	Category	ITT Subjects; N=271
Lesion type ²	<i>De novo</i>	100% (271/271)
Location of treated lesion within the superficial femoral and proximal popliteal arteries	Proximal Mid Distal	11.5% (31/270) 48.1% (130/270) 40.4% (109/270)
Reference vessel diameter (mm)	Mean ± SD	5.2 ± 0.9 (269)
Pre-procedure minimum lumen diameter (MLD) (mm)	Mean ± SD	1.1 ± 1.0 (270)
Pre-procedure diameter stenosis %	Mean ± SD	77.8 ± 18.3 (269)
Lesion length (mm)	Mean ± SD Median [IQR ³] Range	81.2 ± 38.4 (269) 73.8 [54.4,108.6] 9.3, 217.2
Calcification % (moderate + severe)		45.9 (124/270)
Total occlusion %		30.0 (81/270)
Tibial vessel runoff % (<50% stenosis in 1 or more vessel)		98.8 (237/240)
Pre-stent MLD (mm)	Mean ± SD	4.5 ± 0.8 (269)
Pre-stent diameter stenosis %	Mean ± SD	18.0 ± 7.3 (269)
Stent luminal diameter (mm)	Mean ± SD	5.7 ± 0.8 (269)
Post-stent diameter stenosis %	Mean ± SD	12.6 ± 7.5 (269)
Deployed stent length (mm)	Mean ± SD Median [IQR] Range	112.3 ± 36.3 (269) 104.0 [82.8, 146.8] 54.3, 238.7
Technical Success %		100% (269/269)
¹ Core laboratory reported data, unless indicated		
² Investigator reported		
³ IQR: Interquartile Range		

Safety and Effectiveness Results

a. Primary safety and effectiveness endpoints

The primary outcome measures for safety (freedom from MAE through 30 days) and effectiveness (primary stent patency rate at 12 months) in the MIMICS-2 Study are presented in Table 7.

Table 7: MIMICS-2 Study Primary Safety and Effectiveness Endpoint Results

	Rate (n/N) [95% CI]	Endpoint target per Protocol
Rate of freedom from MAE through 30 days	99.6% (268/269) [97.7%, 100%]	Lower bound of confidence interval >88% - Endpoint achieved
Primary stent patency at 12 months	73.1% (182/249) [67.3%, 78.2%]	Lower bound of confidence interval >66% - Endpoint achieved

b. Post-approval primary endpoint

The primary outcome measure of the MIMICS-2 Continued Follow-up (Post-Approval) Study is freedom from CDTLR at 36 months with events independently adjudicated by the CEC. CDTLR is defined in the MIMICS-2 Protocol as revascularization of the target lesion with objective evidence of recurrent symptoms associated with an angiographic determination of $\geq 50\%$ stenosis and new distal ischemic signs (worsening ABI or worsening Rutherford Category associated with the index limb), or $\geq 70\%$ diameter stenosis in the absence of objective evidence of recurrent symptoms.

The definition of success for the Primary Endpoint of the Post-Approval Study is for the lower bound of the KM-estimated rate of freedom from CDTLR at 36 months to exceed 55%. Figure 6 indicates that the KM-estimated rate of 3-Year CDTLR in the MIMICS-2 study is 79.9% [74.8%, 84.9%] – thus the Post-Approval Study primary endpoint was met.

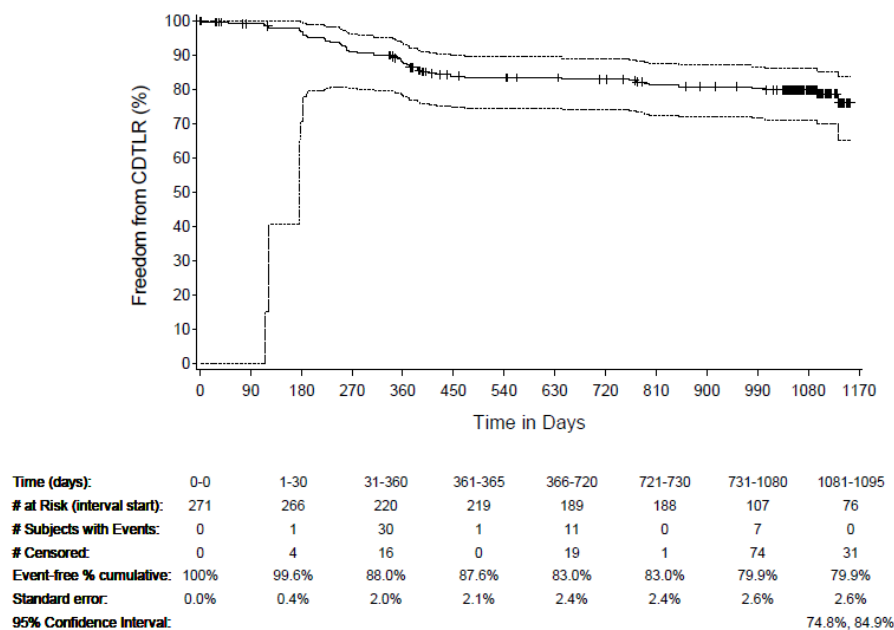


Figure 6: Kaplan-Meier Survival Estimate for CEC-Adjudicated CDTLR through 36 months.

c. Summary of Secondary Endpoints

Rutherford Clinical Category

Rutherford Clinical Category was measured at Baseline, Day-30, Months-12 and 24 to assess clinical outcome. Worsening of Rutherford Clinical Category is defined as an increase by one or more categories compared to baseline, or unexpected major amputation of the target limb.

At 24 months, for the 221 subjects with matched assessments, there was a maintained mean improvement over baseline of -1.9 ± 1.2 . An improvement of ≥ 1 Category was reported in 86.9% (233/268) of subjects at 30 days, in 85.0% (216/254) at 12 months and in 88.2% (195/221) at 24 months. An improvement of 2 or more Categories was observed in 65.2% of subjects (144/221), with more than one-third, 37.6% (83/221), achieving an improvement of 3 or more Categories. At 24 months, only 7 subjects (3.2% 7/221) had deteriorated compared to baseline; four of those due to worsening of both the treated (index) leg and the non-treated leg.

These data show a sustained clinical benefit with the use of the BioMimics 3D Stent.

Fracture resistance

The angiographic core laboratory conducted a review of all Study X-ray imaging. No fracture was reported in any Study stent at any timepoint, validating the biomechanical performance of the BioMimics 3D stent in this stented segment.

d. Subgroup Analysis

Although the MIMICS-2 Study was not statistically powered to detect differences between prospectively defined subgroups, the following observations are made:

Gender: The observed 30-day MAE free rate was 99.4% (178/179) for males and 100.0% (90/90) for females, with only one MAE reported for any subject during this assessment window. The observed 12-month primary patency rate was 76.9% (130/169) for males and 65.0% (52/80) for females.

Cilostazol: The observed 30-day MAE free rate was 100.0% (18/18) for subjects taking cilostazol and 99.6% (250/251) for those not taking cilostazol. The observed 12-month primary patency rate was 87.5% (14/16) for subjects taking cilostazol and 72.1% (168/233) for those not taking cilostazol.

Country of investigational site location: The observed 30-day MAE free rate was 100% (31/31) in Japan, 99.4% (159/160) for US and 100% (78/78) for Germany. The observed 12-month primary patency rate was 67.7% (21/31) in Japan, 71.5% (103/144) for US and 78.4% (58/74) for Germany.

5 mm Stent: The number of subjects evaluable at 12-months that were treated with 5 mm diameter BioMimics 3D stents was small (n=33), relative to those treated with 6 mm or 7 mm stents (n=216). The observed 12-month primary patency rate was 72.7% (24/33) for subjects treated with 5 mm stents and 73.1% (158/216) for those treated with 6 mm or 7 mm stents.

Overlapping Stents: A relatively small number of subjects in the MIMICS-2 Study (12.5%; 34/271) required placement of a second BioMimics 3D stent and the observed 30-day MAE

free rate was 99.6% (235/236) for subjects treated with single and 100.0% (33/33) for those treated with overlapped stents. The use of overlapped stents was primarily (65%; 22/34) to treat longer lesions \geq 120 mm, prior to the mid-study introduction of the 150 mm BioMimics 3D stent. The core laboratory reported mean stented segment lengths of 105.1 mm for single stents and 162.2 mm for overlapping stents. Across all stented segment lengths, the observed primary patency in subjects evaluable at 12 months, was higher for single stent (76.0%; 165/217) than in overlap stented segments (53.1%; 17/32). It is of interest that among 55 subjects with long stented segments \geq 150 mm, where poorer outcomes are typically expected, the observed 12-month primary patency was 63.6% (21/33) when a single stent was used and 59.1% (13/22) when overlapped stents were used.

e. Summary of Serious Adverse Events in MIMICS-2 Study

A summary of the number (n) and rates of site-reported Serious Adverse Events through database lock 11th February 2020 are presented in Table 8.

Table 8: Site-Reported Serious Adverse Events (ITT cohort; N=271)

AE Category	Event Description	Events at \leq 1 month (% (n/N))	Events at \leq 12 months (% (n/N))	Events at \leq 24 months (% (n/N))	Events at \leq 36 months (% (n/N))
All SAE	All SAE	9.6% (26/271)	42.1% (114/271)	53.9% (146/271)	60.5% (164/271)
Vascular disorders	Restenosis of treated segment	0.0% (0/271)	12.2% (33/271)	16.6% (45/271)	17.3% (47/271)
	Dissection	0.7% (2/271)	0.7% (2/271)	0.7% (2/271)	0.7% (2/271)
	Dissection (\geq Grade C) in target vessel requiring intervention	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)
	Arterial stenosis (non-target)	1.5% (4/271)	9.2% (25/271)	11.4% (31/271)	14.0% (38/271)
	Restenosis	0.0% (0/271)	2.2% (6/271)	4.4% (12/271)	5.2% (14/271)
	Restenosis of treated vessel	0.0% (0/271)	1.5% (4/271)	3.0% (8/271)	4.4% (12/271)
	Thrombosis	0.0% (0/271)	1.5% (4/271)	1.5% (4/271)	1.5% (4/271)
	Limb ischemia	0.4% (1/271)	0.7% (2/271)	1.5% (4/271)	1.5% (4/271)
	Pseudoaneurysm	0.4% (1/271)	0.7% (2/271)	0.7% (2/271)	0.7% (2/271)
	Abrupt occlusion	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)
	Amputation (unplanned, spontaneous)	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)
	Aneurysm	0.0% (0/271)	0.4% (1/271)	0.4% (1/271)	0.7% (2/271)
	Embolization, distal	0.0% (0/271)	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)
	Total occlusion of the peripheral artery	0.0% (0/271)	0.4% (1/271)	0.4% (1/271)	1.5% (4/271)
Amputation (planned)	0.0% (0/271)	0.0% (0/271)	0.4% (1/271)	0.4% (1/271)	
Cardiac disorders	Angina	0.0% (0/271)	2.2% (6/271)	3.3% (9/271)	3.7% (10/271)
	Congestive heart failure (CHF)	0.0% (0/271)	2.2% (6/271)	3.0% (8/271)	3.7% (10/271)
	Atrial fibrillation	0.4% (1/271)	1.8% (5/271)	3.7% (10/271)	3.7% (10/271)
	Myocardial infarction	0.0% (0/271)	1.1% (3/271)	4.1% (11/271)	4.8% (13/271)
	Myocardial ischemia	0.0% (0/271)	1.1% (3/271)	1.5% (4/271)	1.8% (5/271)
	Cardiac arrhythmia	0.0% (0/271)	0.4% (1/271)	1.5% (4/271)	1.5% (4/271)
	Ventricular tachycardia	0.0% (0/271)	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)
	Hypotension	0.0% (0/271)	0.7% (2/271)	0.7% (2/271)	0.7% (2/271)
Hypertension	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)	

AE Category	Event Description	Events at ≤ 1 month (% (n/N))	Events at ≤ 12 months (% (n/N))	Events at ≤ 24 months (% (n/N))	Events at ≤ 36 months (% (n/N))
Death	Death (MAE if cardiovascular-related)	0.0% (0/271)	0.0% (0/271)	0.0% (0/271)	1.8% (5/271)
Blood & lymphatic system disorders	Anemia	0.0% (0/271)	0.4% (1/271)	0.7% (2/271)	0.7% (2/271)
	Bleeding from anticoagulant or antiplatelet meds	0.0% (0/271)	0.0% (0/271)	0.4% (1/271)	0.4% (1/271)
	Hemorrhage, with or without transfusion	0.0% (0/271)	0.0% (0/271)	0.4% (1/271)	0.4% (1/271)
Gastrointestinal disorders	Gastro-intestinal bleeding	0.0% (0/271)	0.7% (2/271)	1.1% (3/271)	1.1% (3/271)
Immune system disorders	Allergic reaction (medication, contrast media, device, etc.)	0.0% (0/271)	0.0% (0/271)	0.0% (0/271)	0.4% (1/271)
Infections & infestations	Sepsis	0.4% (1/271)	1.1% (3/271)	2.2% (6/271)	2.2% (6/271)
	Infected peripheral wound	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)
	Urinary tract infection	0.0% (0/271)	0.4% (1/271)	1.1% (3/271)	1.1% (3/271)
Injury, poisoning & procedural complications	Arterial occlusion/thrombus at puncture site	0.7% (2/271)	0.7% (2/271)	0.7% (2/271)	0.7% (2/271)
	Vascular access complications	0.7% (2/271)	0.7% (2/271)	0.7% (2/271)	0.7% (2/271)
	Groin hematoma ≥ 5 cm, with or without surgical repair	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)
Nervous system disorders	Seizure	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)	0.4% (1/271)
	Stroke or other neurological complications	0.0% (0/271)	0.4% (1/271)	1.1% (3/271)	1.8% (5/271)
	Transient ischemic attack	0.0% (0/271)	0.0% (0/271)	0.0% (0/271)	0.4% (1/271)
Renal & urinary disorders	Renal failure/renal insufficiency	0.4% (1/271)	0.7% (2/271)	2.6% (7/271)	2.6% (7/271)
Respiratory, thoracic & mediastinal disorders	Respiratory distress	0.4% (1/271)	0.7% (2/271)	1.1% (3/271)	1.1% (3/271)
	Pneumonia	0.4% (1/271)	0.4% (1/271)	1.8% (5/271)	2.2% (6/271)
	Pulmonary embolism	0.0% (0/271)	0.0% (0/271)	0.4% (1/271)	0.4% (1/271)
Other events	Other	2.6% (7/271)	16.6% (45/271)	26.9% (73/271)	35.1% (95/271)

The MIMICS-2 Study utilized an independent Clinical Events Committee (CEC) to adjudicate safety events occurring during the study. Through 36 months (1095 days): 69 subjects had 87 CEC-adjudicated MAE, giving an overall MAE rate of 29.1% (69/237). This includes death in 22 subjects (9.5%; 22/232), none of these deaths were related to the procedure or the device. CDTLR was reported in 50 subjects (22.8%; 50/219). No major amputations were reported through study close-out at 3 years.

Conclusion

Long term data from the MIMICS-2 study through 3 years support the continued safety and effectiveness of the BioMimics 3D Vascular Stent System for the treatment of femoropopliteal lesions.

Core laboratory review of X-ray imaging of the treated area concluded that there was no evidence of any BioMimics 3D stent fracture in any image reviewed from patients at 12, 24 or 36-month visits

Mimics Study

The Mimics Study was a prospective, multicenter, randomized (2:1 BioMimics 3D vs. a commercially-available, straight, laser-cut Nitinol control stent), evaluation of safety and effectiveness in patients with symptomatic peripheral arterial disease undergoing femoropopliteal intervention, conducted in Germany. The study was completed prior to the MIMICS-2 Study and investigated the safety and performance of the BioMimics 3D Stent in improving luminal diameter in the treatment of symptomatic de-novo or restenotic lesions up to 100 mm in length in native superficial femoral (SFA) and/or proximal popliteal arteries with reference vessel diameters ranging from 3.5 – 7.0 mm.

Following a Phase I lead-in cohort of 10 subjects, 76 Phase II subjects were enrolled with 2:1 randomization to either BioMimics 3D or the Control stent, such that 50 subjects received treatment with BioMimics 3D stents. In total, in both Phase I and II studies, 61 BioMimics 3D stents were placed in 60 subjects. The Mimics study was not powered to detect a difference between the two Phase II cohorts with respect to either safety or performance. The comparator arm was enrolled specifically to provide a point of anatomical, mechanical and hemodynamic reference for analysis of supplementary outcome measures, including X-ray imaging of the treated area with the limb flexed and extended at the knee. Mean, core laboratory reported, lesion length and stented segment length for the 60 subjects treated with BioMimics 3D stents were: 69.5 mm \pm 28.5 mm and 103.4 mm \pm 30.3 mm, respectively.

The *primary safety endpoint* was defined as a composite of MAE comprising death, any major amputation performed on the target limb or CDTLR through 30 days. The performance goal (PG) specified that 88% of subjects should be free from MAE through 30 days. All 60 subjects remained free from MAE at 30-days.

The *primary performance endpoint* specified a PG of 67% freedom from CDTLR at 6-months post index procedure. All Phase I (10 subjects) and Phase II (50 subjects) treated with the BioMimics 3D Stent System were free from CDTLR at 6 months.



















Mimics Phase II Study subjects were followed up to 24 months. Analysis of data from the extended follow-up period showed that the proportion of patients treated with BioMimics 3D who maintained stent patency (PSVR \leq 2.0) at 12 and 24 months was 75% and 72% respectively. A Kaplan-Meier survival analysis estimated freedom from loss of primary stent patency for subjects treated with BioMimics 3D at 80% at Year 1 and 72% at Year 2, compared with 71% and 55% for the Control stent. Kaplan-Meier analysis of independently adjudicated clinical events showed that freedom from CDTLR was 91% for BioMimics 3D vs. 92% for the Control stent at 12 months and 91% versus 76% at 24 months, i.e. there was no need for re-intervention for CDTLR in the BioMimics 3D stent cohort between the 1 Year and 2 Year time points. Core laboratory review of X-ray imaging of the treated area revealed no stent fracture in any BioMimics 3D stent through 24 months of follow-up.

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Legend of symbols

	Use-by date
	Do not re-use
	Batch code
	Sterilized using ethylene oxide
	Catalogue number
	Manufacturer
	Date of Manufacture
	Consult instructions for use
	Do not use if package is damaged
	Do not re-sterilize
	MR Conditional
	Diameter
	Length
	Working Length
	Over the Wire
	Keep dry
	Keep away from sunlight
	Guide catheter/sheath internal diameter

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