Veryan
AN OTSUKA MEDICAL DEVICES COMPANY

BioMimics 3D®

Value Analysis Committee Packet

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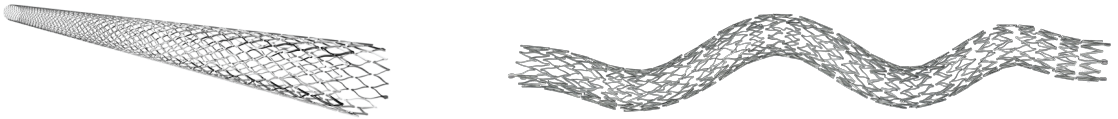
Introduction

BioMimics 3D
The Swirling Flow® Stent

Veryan Medical is an Otsuka Medical Devices company which is a division of Otsuka Holdings, a leading global healthcare group with operations in pharmaceuticals, nutraceuticals and medical devices generating annual worldwide sales of more than $13B.

Veryan is focused on developing innovative devices for use in peripheral interventional procedures. The BioMimics 3D® Vascular Stent system is intended for the treatment of peripheral arterial disease (PAD) in the femoropopliteal arteries. PAD affects 12-14% of the general population[1] and impacts the quality of life of many. Critical limb threatening ischemia (CLTI) patients in particular experience high amputation and mortality rates[2]. The cost burden on healthcare systems is significant and of particular concern are the revascularization rates up to 90 days post-intervention due to the use of sub-optimal therapies.[3]

The distal superficial femoral and proximal popliteal artery segment (DSFA/PPA) presents a particular challenge for traditional straight nitinol stents. The unique biomechanical forces generated by walking, sitting, and kneeling are not well accommodated by straight stents[4] which are not able to shorten as the artery shortens. The BioMimics 3D stent, however has a unique 3D helical geometry which imparts a gentle helical shape to the stented artery[5] and enables the stent to shorten with the vessel, improving its biomechanical compatibility (biomimetic design).

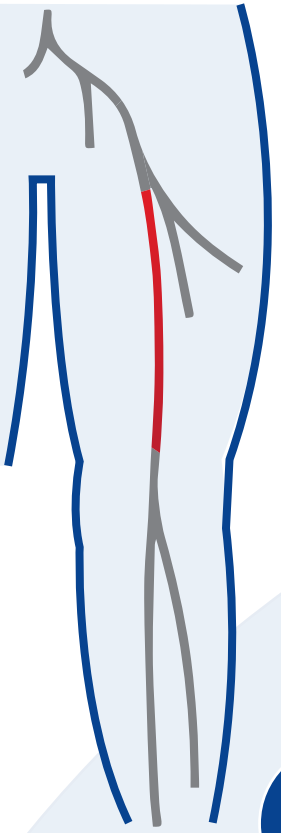


Straight Stent Helical Stent (BioMimics3D®)

The biomimetic design of the BioMimics 3D® stent helps the stented femoropopliteal artery move more naturally, reducing the risk of stent fracture and trauma to the vessel.[5]

In addition to its biomechanical compatibility advantages, BioMimics 3D's helical centerline generates laminar swirling flow which has an antiproliferative effect without the need for drug elution.[6,7] This unique mechanism of action reduces thrombus formation, the inflammatory response to injury and the proliferation and migration of smooth muscle cells, all of which lead to a reduction of neointimal hyperplasia and restenosis.[7]

Veryan Medical has amassed a significant body of clinical evidence that supports the hypothesis that BioMimics 3D's helical design impacts outcomes. This Value Analysis Committee Packet contains a comprehensive review of clinical data from the MIMICS Clinical Program which includes a randomized controlled trial, an IDE study and a real-world registry. BioMimics 3D demonstrates superior, long-lasting clinical outcomes comparable to those of drug eluting stents.



The incidence of peripheral arterial disease in the femoropopliteal segment

Burden of Illness

PAD affects 12% - 14% of the general population[1]

1 in 6
More than one in six patients with PAD are **readmitted within 30 days after revascularization[2].**

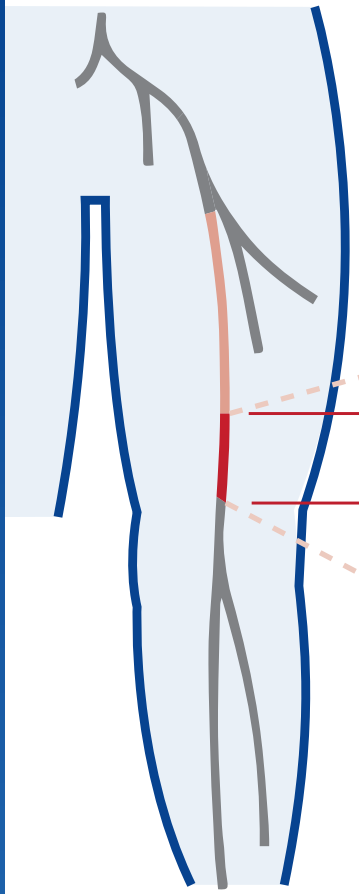
1 in 5
The prevalence of peripheral artery disease in adults >60 years of age. >8.5 million adults have PAD in the U.S. and >200 million worldwide.[3]

1 in 4
At one year, 25% of CLTI patients have undergone amputation and 25% died from a cardiovascular cause. Only 50% are alive with both limbs at one year.[4]

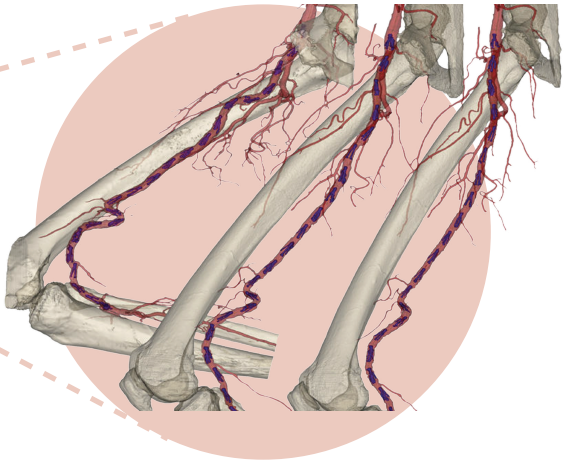
1 in 3
Relative 5-year mortality rate of 33.2% When all outcome events and cardiovascular deaths are evaluated together, it is estimated that 16% of patients had an event by the end of the first year after diagnosis which rose to about one-third after three years.[5]

Critical Risk Factors ▶

Critical Risk Factors



Stenting in the distal SFA and proximal popliteal.



Not only is the anatomy in this region challenging leading to compression, elongation, and torsion, stent performance research is limited in current data.[1]

Cadaver study examining native artery shortening under flexion[3]

TABLE 1. BARE ARTERIES DURING HIP FLEXION AND KNEE BENDING

- No elongation
- Torsion was not critically evaluated - not observed
- Shortening and bending - major changes

	Mid- SFA	Distal SFA	Popliteal	Popliteal Bending Radius/Angle
70/20 (Shortening)	5%	14%	9%	
90/90 (Shortening)	10%	23%	14%	13 mm 63°

Average values based on seven cadaver, 14 limb study

The distal SFA and proximal popliteal segment demonstrated the most significant compression under flexion

- 9-14% compression while in walking position
- 14-23% compression during seated position

Limited representation in contemporary data[2]:

Study	Stent	12M Primary Patency	12M Fracture %	D. SFA/ Prox Pop %	3yr fracture rate %
DURABILITY II	Everflex	77.9	0.4	2.1	0.9
RESILIENT	Lifestent	81.3	3.1	4.6	NA
ZILVER-PTX	Zilver PTX	83.1	0.9	7.2	1.9
SUPERB	Supera	86.3	0.0	12.8	NA
IMPERIAL RCT	Eluvia	86.8	0.9	12.7	NA
SUPERNOVA	Innova	76.7	1.9	15.1	NA
MIMICS 2	BioMimics3D	83.1	0.0	40.4	0
MIMICS3D EU	BioMimics3D	88.3	0.2	34.9	0.6

Stenting the distal SFA and proximal popliteal is traditionally associated with increased risk of reintervention and stent fracture

Value Proposition

Value Proposition

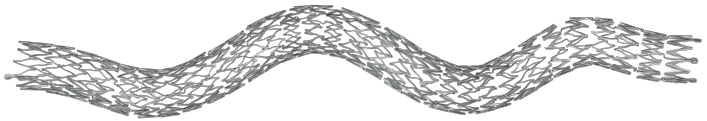
IFU

BioMimics 3D®

What makes BioMimics 3D® unique?

Unlike straight stents, BioMimics 3D has a 3D helical centerline which imparts a gentle helical shape to the stented artery.[1]

Straight Stent

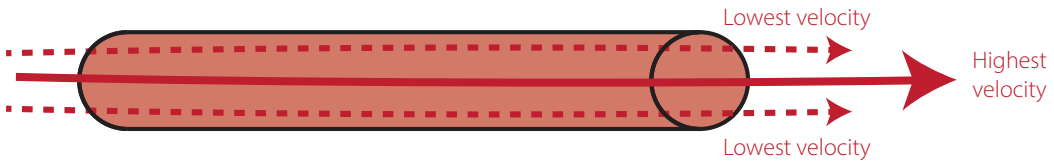


Helical Stent

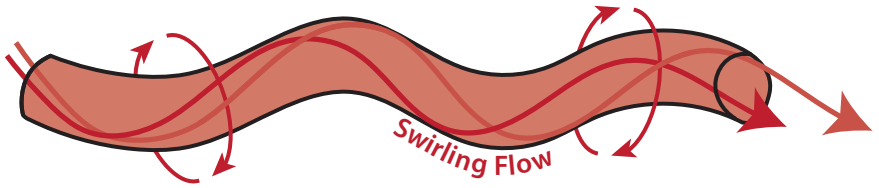
Improved Flow By Design

The hemodynamic impact of our helical stent and its benefits.

Straight Stent Flow



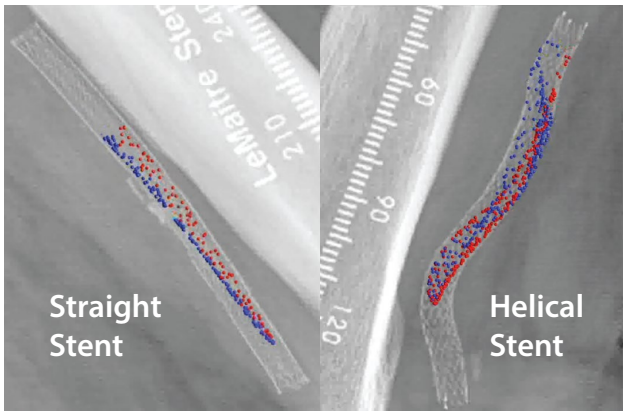
Helical Stent Flow (BioMimics 3D)



BioMimics 3D imparts non-planar curvature to the stented femoropopliteal segment intended to generate swirling flow and provide an antiproliferative effect without the need for drug elution.[1,2]

Swirling flow increases wall shear stress on endothelial cells.[3]

Elevated wall shear stress has been shown to[4]



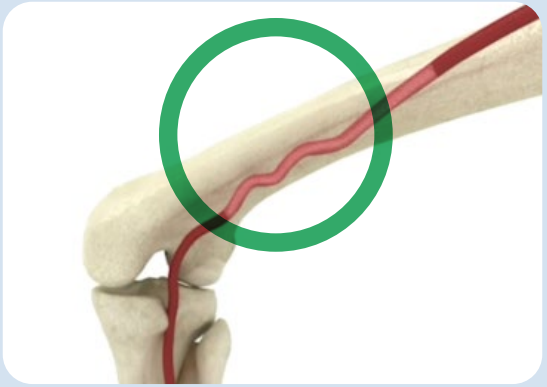
Click the image to view the computational fluid dynamic comparison between a straight stent and a helical stent. If printed, use your phone camera and access with the QR Code. (Just aim camera at image)

Reduce RESTENOSIS through

Reduced thrombus formation and inflammation
Reduced smooth muscle cell proliferation
Reduced neointimal hyperplasia

Biomechanical Compatibility[1]

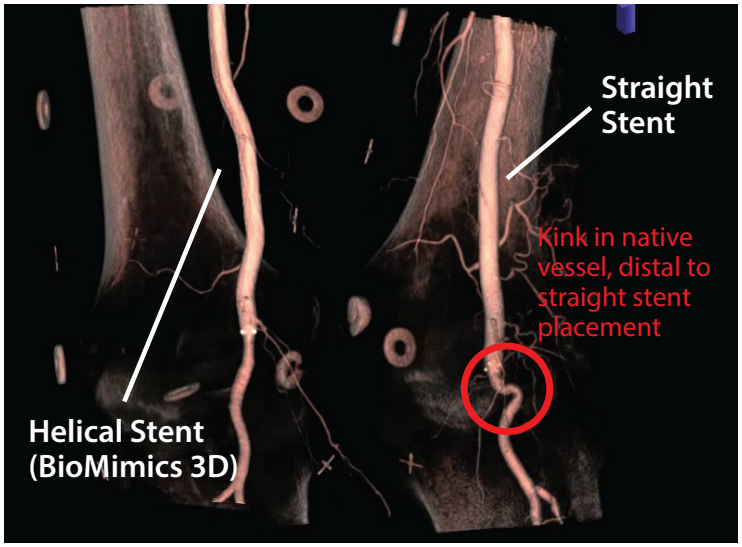
Conventional straight stents do not allow the physiological compensation required when the knee bends and the femoropopliteal artery shortens



3D helical geometry of the BioMimics 3D stent is designed to adapt to the morphological changes during knee flexion/extension and reduce the risk of buckling/kinking

Click an image to view the in-artery comparison between a straight stent and a helical stent. If printed, use your phone camera and access with the QR Code. (Just aim camera at image)

Bent-Knee Cadaver Study



Mimics natural movement of the femoropopliteal segment

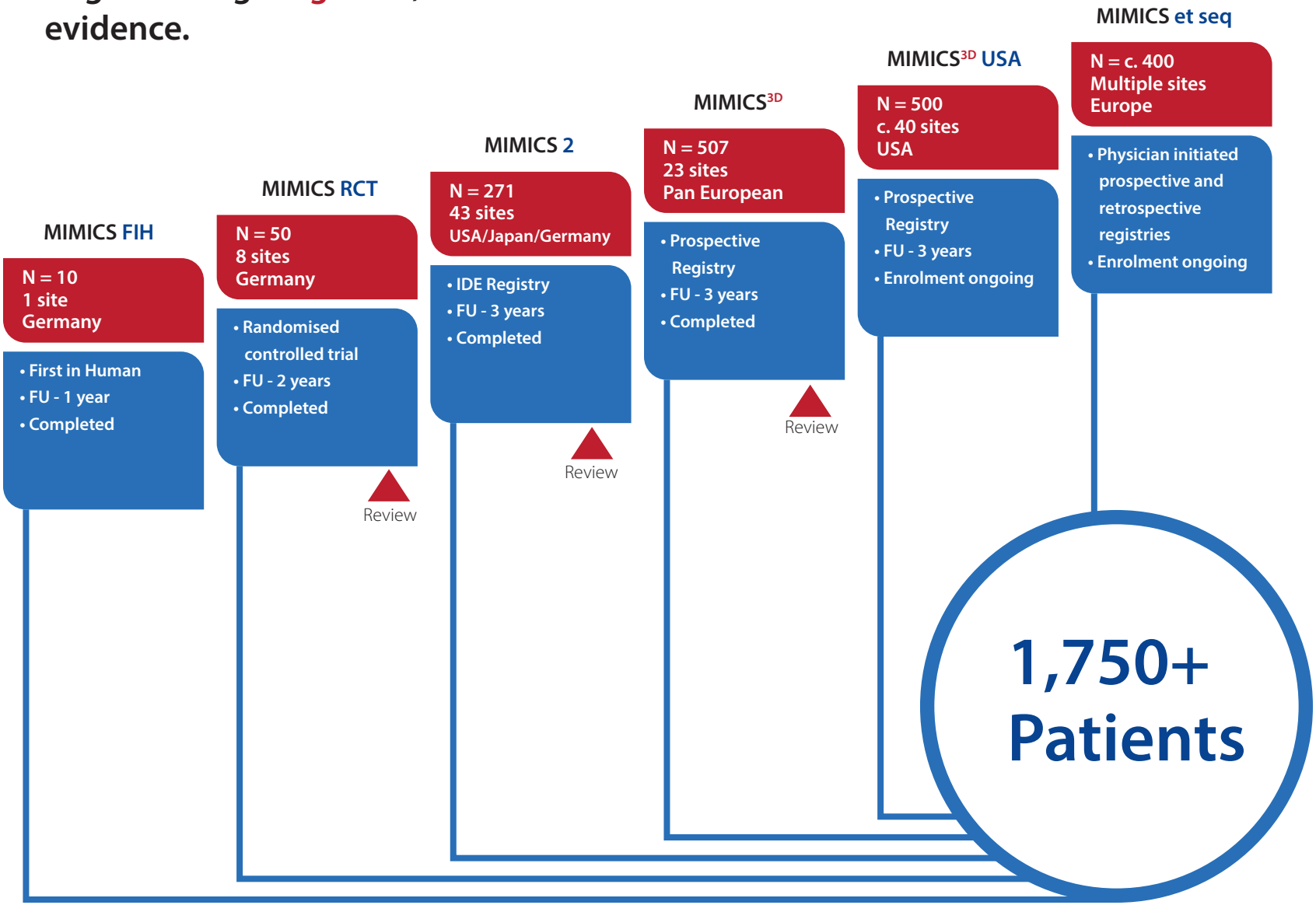
Helps reduce risk of stent fracture in dynamic artery

Aids in reducing localized trauma

Click an image to review the in-cadaver, bent-knee comparison between a straight stent and a helical stent. If printed, use your phone camera and access with the QR Code. (Just aim camera at image)

Quality, Efficacy, and Outcomes

BioMimics 3D® Clinical Program: Dedicated to generating long-term, real-world clinical evidence.



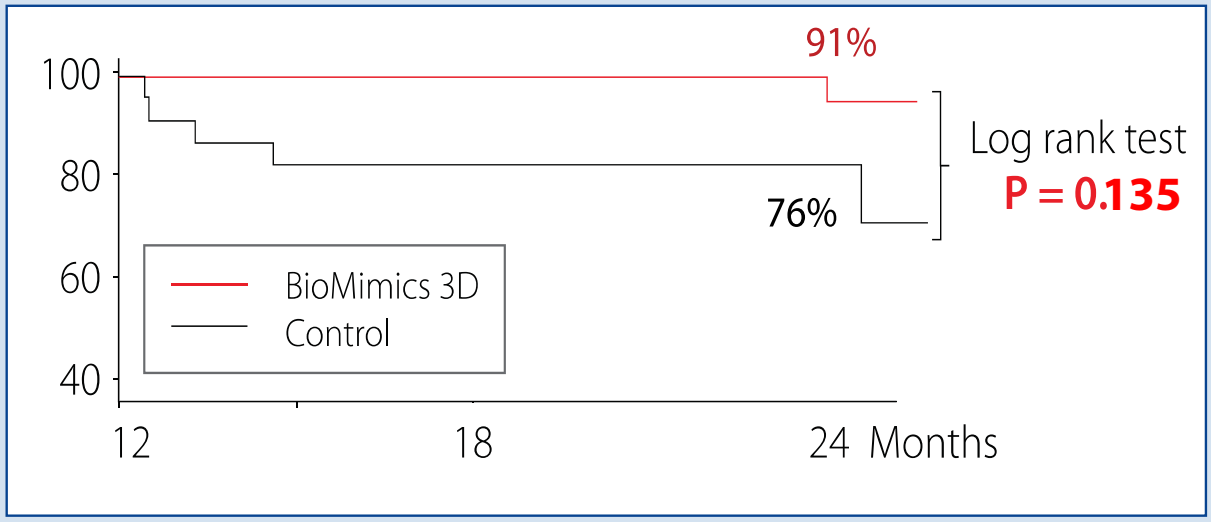
N = 50
8 sites
Germany

- Randomised controlled trial
- FU - 2 years
- Completed

MIMICS RCT

Provided the first clinical proof supporting the durable outcome benefit arising from the BioMimics 3D® stent compared to a straight nitinol stent[1,2]

FIM LEAD-IN	N=10 BioMimics 3D®	
Prospective Randomization	BioMimics 3D® N=50	Straight nitinol stent N=26
24-Month Primary Patency (p=0.05)	72%	55%
FF CDTLR 12-24 months (p=0.03)	91%	76%



Core lab X-ray imaging review confirmed 0% stent fractures at 2 years.

N = 271
43 sites
USA/Japan/Germany

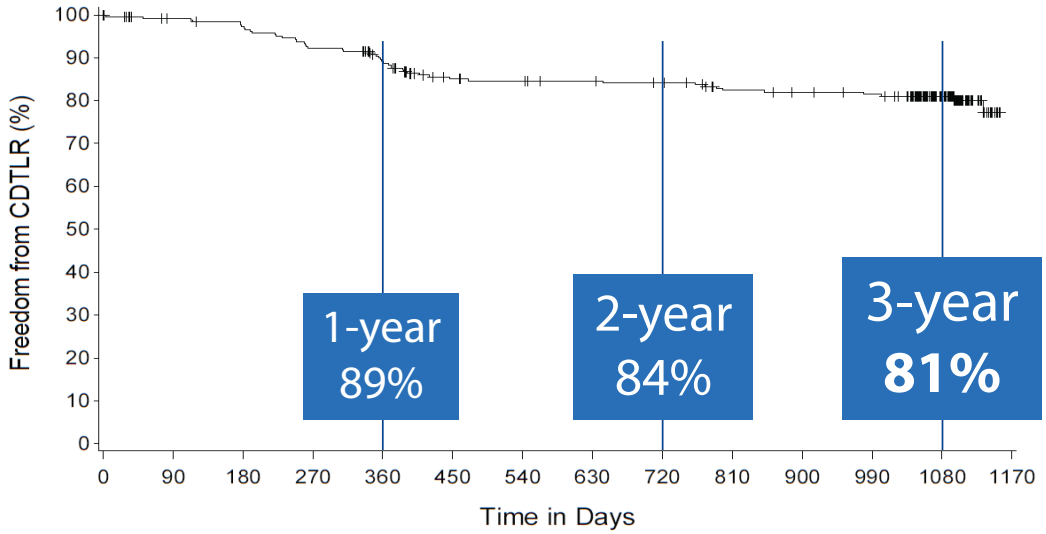
- IDE Registry
- FU - 3 years
- Completed

MIMICS 2

The MIMICS-2 study validated the outcomes of the randomized study by providing clinical proof in a larger, more challenging cohort[1]

12-Month KM Freedom from Loss of Primary Patency	83%
Core Lab X-ray imaging review of stent fracture at 3 years[2]	0%
36-Month KM Freedom from CDTLR*	81%

KM survival estimates of FFCDTL at 3-years



Kaplan Meier survival estimates from Clinically-Driven TLR at three years

*Core Lab adjudicated, clinically-driven TLR with objective evidence
Subjects are censored at their last known follow-up, or at time of study exit (withdrawal or lost to follow-up) or death

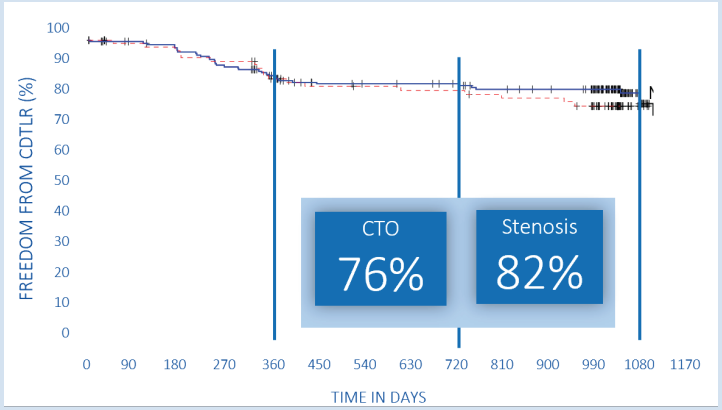
N = 271
43 sites
USA/Japan/Germany

- IDE Registry
- FU - 3 years
- Completed

MIMICS 2

The MIMICS-2 study validated the outcomes of the randomized study by providing clinical proof in a larger, more challenging cohort[1]

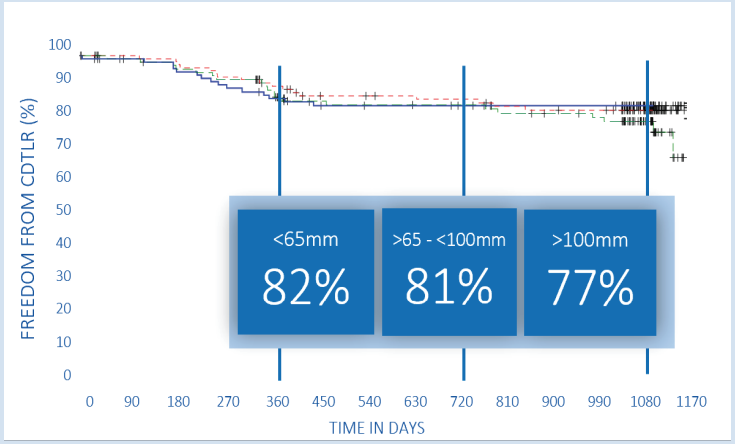
CTO vs Stenosis



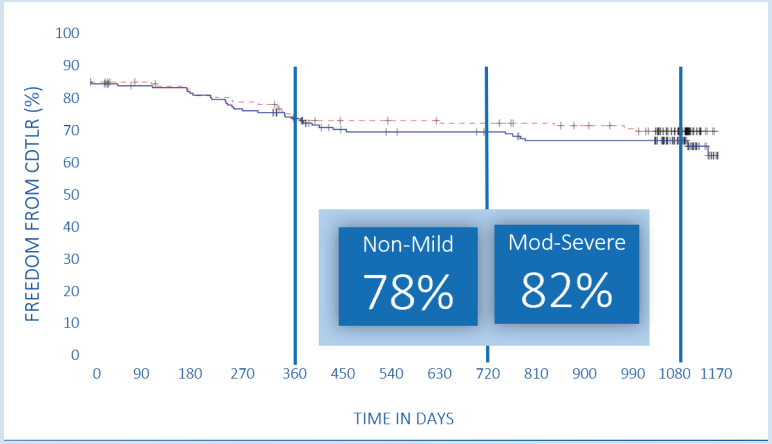
No statistical difference, even in complex lesions

*CEC adjudicated, clinically-driven TLR
Subjects are censored at their last DUS follow-up, or at time of study exit (withdrawal or lost to follow-up) or death. Subjects who are patent at DUS follow-up are censored at the end of the follow-up window

Lesion Length



Calcified Vessels



N = 507
23 sites
Pan European

- Prospective Registry
- FU - 3 years
- Completed

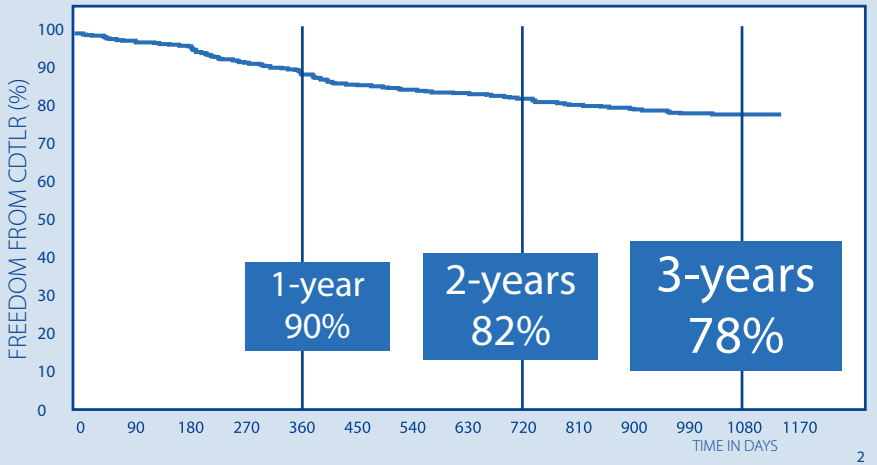
MIMICS 3D

MIMICS-3D data contribute real-world experience to the evolving database supporting the therapeutic value of swirling flow in the BioMimics 3D® stent.[1]

Key baseline and procedural data

Mean lesion length	126 mm +/-91mm
% CTO	57%
% Mod/Severe Ca++	38%
% CLTI	24%
3-yr Primary Patency*	71%

*ITT population. KM FF Loss of Patency at 36 mos. PSVR>2.4
Patency is defined as the composite of:
(1) freedom from more than 50% restenosis within the stented segment as observed by DUS or angiography and
(2) freedom from clinically-driven target lesion revascularization (TLR)



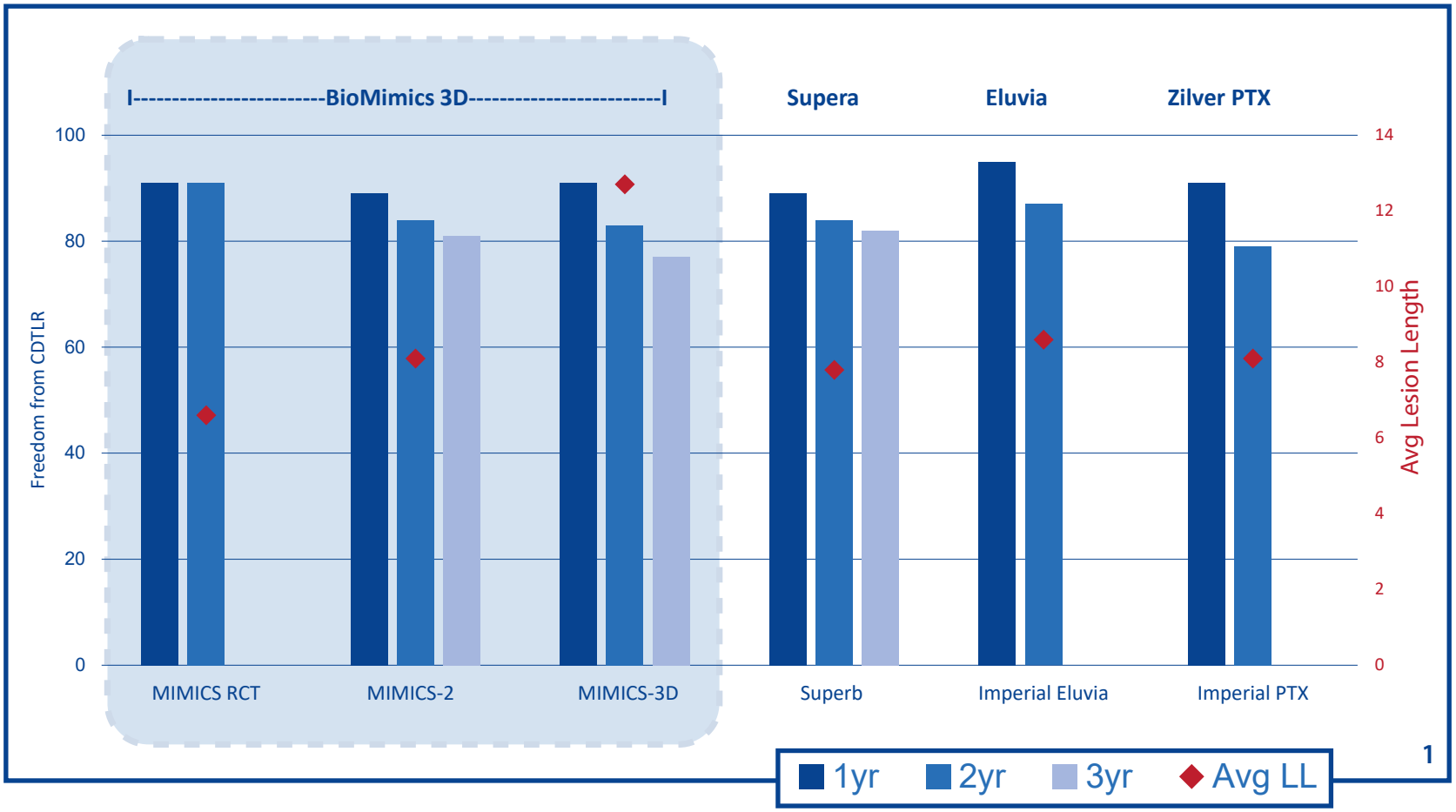
2

More challenging population than typically enrolled in registry studies

- 24% CLTI; longer, more complex lesions; >50% with DCB
- 78% Freedom from CDTLR at three years
- No statistically significant difference in freedom from CDTLR or patency between claudicants and CLTI patients through three years.
- Rate of CDTLR was independent of concomitant DCB use, lesion calcification and stent length
- 0.4% fracture rate at three years (investigation confirmed)[2]

MIMICS RCT	MIMICS 2	MIMICS[3D]
N = 50 8 sites Germany	N = 271 43 sites USA/Japan/Germany	N = 507 23 sites Pan European
• Randomised controlled trial • FU - 2 years • Completed	• IDE Registry • FU - 3 years • Completed	• Prospective Registry • FU - 3 years • Completed

Industry Study Comparisons: Freedom from CDTLR



Comparable outcomes to DES despite more challenging lesions and without the need for drug elution.[2,3]

Payment Codes

BioMimics 3D
The Swirling Flow® Stent

Hospital Outpatient

CPT	Description	APC	CY 2021 National Average Payment
37226	Femoral/Popliteal PTA + Stent	**5193**	$10,043
37227	Femoral/Popliteal PTA, Atherectomy + Stent	**5194**	$16,064

Hospital Inpatient

MS-DRG	Description	CY 2021 National Average Payment
252	Other Vascular Procedures with MCC	$21,931
253	Other Vascular Procedures with CC	$17,499
254	Other Vascular Procedures without CC/MCC	$11,975

Ordering Information

BioMimics 3D
The Swirling Flow® Stent

Quick order reference	Catalog number	Stent diameter (mm)	Reference vessel diameter (mm)	Stent length (mm)	Sheath compatibility*: Fr/Minimum ID (mm)	Guidewire compatibility (inch)
5x60	142122-01	5	4.0	60	6 / 2.2	0.035
5x80	142122-05	5	4.0	80	6 / 2.2	0.035
5x100	142122-09	5	4.0	100	6 / 2.2	0.035
5x125	142122-13	5	4.0	125	6 / 2.2	0.035
5x150	144700-05	5	4.0	150	6 / 2.2	0.035
6x60	142122-02	6	4.0-5.0	60	6 / 2.2	0.035
6x80	142122-06	6	4.0-5.0	80	6 / 2.2	0.035
6x100	142122-10	6	4.0-5.0	100	6 / 2.2	0.035
6x125	142122-14	6	4.0-5.0	125	6 / 2.2	0.035
6x150	144700-12	6	4.0-5.0	150	6 / 2.2	0.035
7x60	142122-03	7	5.0-6.0	60	6 / 2.2	0.035
7x80	142122-07	7	5.0-6.0	80	6 / 2.2	0.035
7x100	142122-11	7	5.0-6.0	100	6 / 2.2	0.035
7x125	142122-15	7	5.0-6.0	125	6 / 2.2	0.035
7x150	144700-19	7	5.0-6.0	150	6 / 2.2	0.035

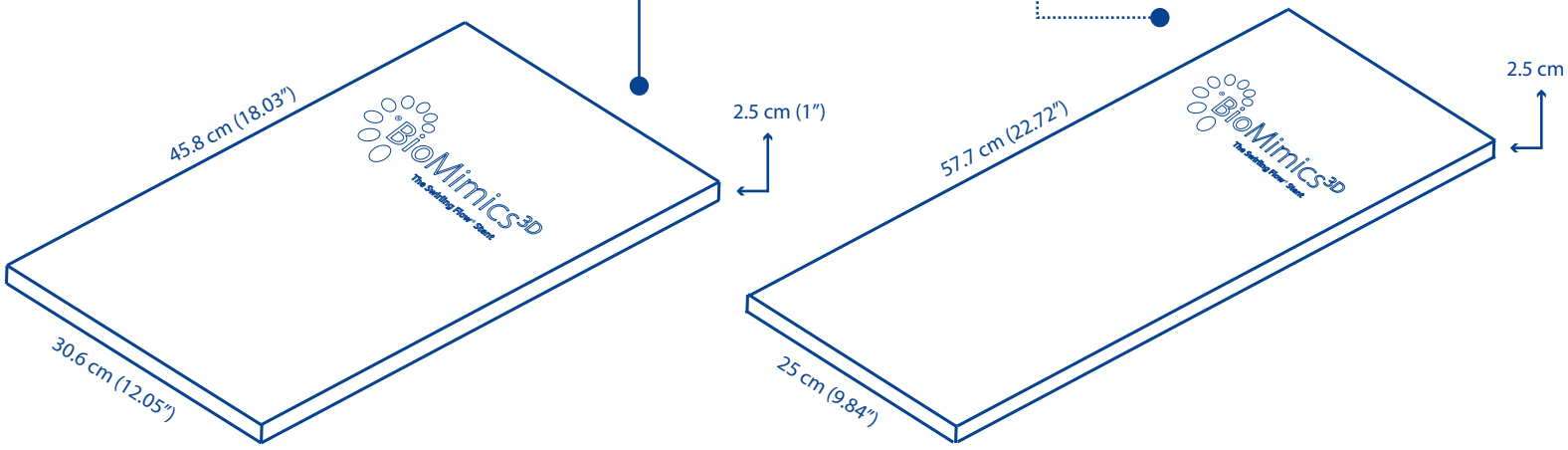
BioMimics 3D Delivery System

Recommended guidewire	0.035"
6F introducer compatible/Minimum ID	2.2 mm
Delivery catheter working length	113 cm

Packaging and Storage

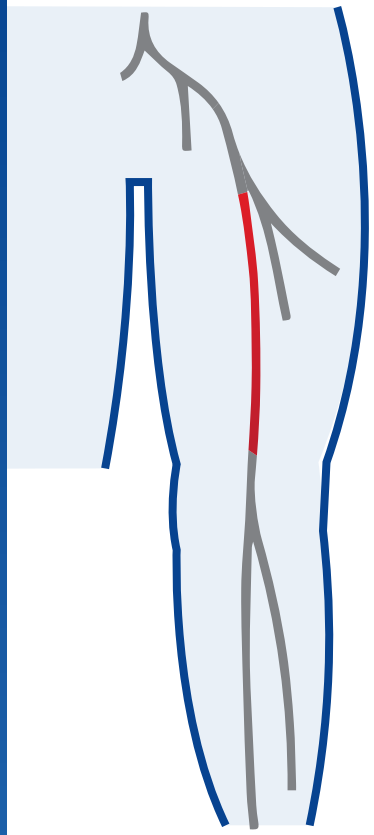
BioMimics 3D
The Swirling Flow® Stent

Shelf / Pallet / Cool storage	Product classification	Description (maximum of 60 characters)	UOM	Qty per UOM	Width (CM)	Length (CM)	Height (CM)	Weight (KG)	Country of manufacture (Origin)	Expiring date capture (Y/N)	Shelf life (days)
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 5mm x 60mm	BX	1	30.6 cm	45.8cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 6mm x 60mm	BX	1	30.6 cm	45.8 cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 7mm x 60mm	BX	1	30.6 cm	45.8cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 5mm x 80mm	BX	1	30.6 cm	45.8cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 6mm x 80mm	BX	1	30.6 cm	45.8cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 7mm x 80mm	BX	1	30.6 cm	45.8 cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 5mm x 100mm	BX	1	30.6 cm	45.8cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 6mm x 100mm	BX	1	30.6 cm	45.8 cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 7mm x 100mm	BX	1	30.6 cm	45.8 cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 5mm x 125mm	BX	1	30.6 cm	45.8 cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 6mm x 125mm	BX	1	30.6 cm	45.8 cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 7mm x 125mm	BX	1	30.6 cm	45.8 cm	2.5 cm	0.35 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 5mm x 150mm	BX	1	25 cm	57.7 cm	2.5 cm	0.375 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 6mm x 150mm	BX	1	25 cm	57.7 cm	2.5 cm	0.375 kg	Ireland	Y	540
Shelf	***Class III***	BioMimics 3D Self expanding Nitinol bare metal stent 7mm x 150mm	BX	1	25 cm	57.5 cm	2.5 cm	0.375 kg	Ireland	Y	540



Indication and Resources

BioMimics 3D®
The Swirling Flow® Stent



BioMimics 3D® Indications for Use

- **The BioMimics 3D Stent System** is indicated for the improvement of luminal diameter in the treatment of symptomatic de-novo or restenotic lesions in the native femoropopliteal arteries with reference vessel diameters ranging from 4.0 - 6.0mm and lesion lengths up to 140 mm

- **Indicated Location**
  Entire SFA and proximal popliteal: all of P1 and the proximal portion of P2

- **Angiographic Reference**
  1 cm distal to the origin of the deep femoral artery/profunda femoris and 3 cm above the bottom of the femur

Access PDF IFU here:
Click on QR Code or scan with your camera phone.

Resources

Click on QR code to visit site; if printed, use camera phone to scan QR code

Clinical Data | **FDA Approval** | **References**

Contacts

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Conclusions

BioMimics 3D
The Swirling Flow® Stent

PAD impacts more than 20% of people over 60 and represents a significant burden to the patient and global healthcare systems[1]

Despite technology advancements, acute and long-term durable outcomes remain sub-optimal for this patient population

BioMimics 3D's unique design is purpose built to help address the challenges of the femoropopliteal segment.[2]

A robust clinical program with 3-year follow-up confirms the clinical benefits of BioMimics 3D for this patient population.

BioMimics 3D has demonstrated superior patency and CDTLR compared to a bare metal stent in a head-to-head randomized controlled trial[3]

BioMimics 3D® continues to show comparable outcomes to drug eluting devices in multiple studies, without the need for drug elution and without the associated costs.[3]

Contraindications, warnings and precautions

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 adeq uate 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 rish 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.