SE34X101-03

2020-02

TERUMO

Misago®

RX Self-expanding Peripheral Stent

Instructions For Use

CAUTION

Federal law restricts this device to sale by or on the order of a Physician

Read These Instructions Before Use

CONTENTS

PM-06676

DESCRIPTION

The Misago RX Self-expanding Peripheral Stent ("stent system") consists of a self-expanding nitinol stent ("stent") pre-mounted on the distal portion of a rapid exchange delivery catheter system ("delivery catheter"). The stent is made of a nickel-titanium alloy with three (3) gold radiopaque markers located at each end for a total of six (6) markers. The delivery catheter is available in 135 cm and 200 cm usable lengths. The distal part of the delivery catheter has a coaxial construction and is constructed to allow coaxial passage of a guide wire that doesn't exceed 0.89 mm (0.035″) in diameter. The distal tip and sheath are coated with hydrophilic polymer which makes them lubricious by wetting. The intermediate shaft is blue to clearly distinguish the non-sliding part from the sliding part. The delivery catheter with 200 cm usable length has two depth markers, approximately 120 cm and 150 cm from the distal end of the catheter, which help to confirm how far the stent system has been advanced. Two inner shaft markers (radiopaque markers) are attached next to each end of the stent and allow confirmation under high-resolution fluoroscopy of the stent's position while in the patient's vessel before deployment. Stent deployment is initiated by pushing down and rolling back a thumbwheel in the deployment handle while holding the handle in place (see Fig. 1-3).

Fig. 1 Diagram of Stent System

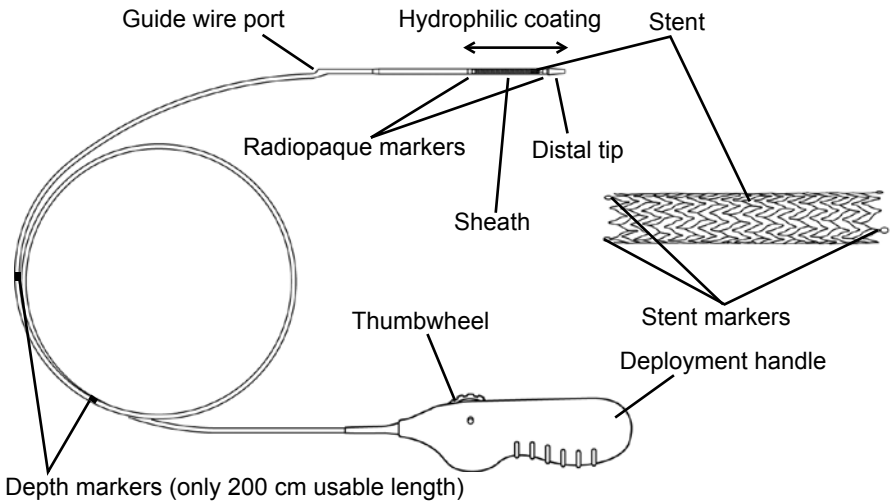


Fig. 2 Flushing Procedure

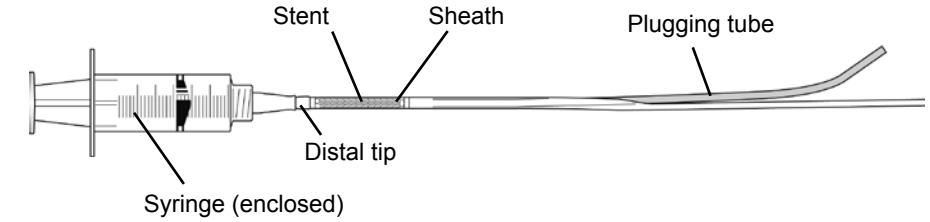
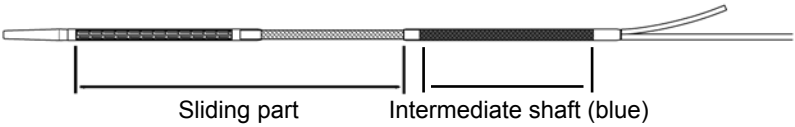


Fig. 3 The Sliding Part and the Intermediate Shaft of the Delivery Catheter



<Specifications>
• Usable length of delivery catheter: 135 cm and 200 cm
• Outer diameter of delivery catheter: 6Fr. (2.06 mm)/3Fr. (1.02 mm)
• Length of coaxial part (from distal tip to guide wire port):
Approximately 45 cm for 40 mm length stent
Approximately 47 cm for 60 mm length stent
Approximately 49 cm for 80 mm length stent
Approximately 52 cm for 100 mm length stent
Approximately 64 cm for 120 mm length stent
Approximately 67 cm for 150 mm length stent

<Specifications of Medical Devices Used Together>
• Maximum guide wire outer diameter: 0.89 mm (0.035″)
• Recommended introducer sheath: 6Fr.
• Minimum guiding catheter inner diameter: 2.16 mm

<Stent Size Selection Table>

Unconstrained stent diameter (mm)	Reference vessel diameter (mm)
6.0	4.0 - 5.0
7.0	5.0 - 6.0
8.0	6.0 - 7.0

<Stent Configurations>

Length / Diameter	40 mm	60 mm	80 mm	100 mm	120 mm	150 mm
6.0 mm	X	X	X	X	X	X
7.0 mm	X	X	X	X	X	X
8.0 mm	X	X	X	X		

INDICATIONS

The Misago RX Self-expanding Peripheral Stent is indicated to improve luminal diameter in symptomatic patients with de novo or restenotic native lesions or occlusions of the superficial femoral artery (SFA) and/or proximal popliteal artery with reference vessel diameters ranging from 4 mm to 7 mm and lesion length up to 150 mm.

CONTRAINDICATIONS

- Patients who exhibit angiographic evidence of severe thrombus in the target vessel or lesion site before/after undergoing Percutaneous Transluminal Angioplasty PTA procedure.
- Patients with contraindication to antiplatelet and/or anticoagulation therapy.
- 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.
- A lesion through which a guide wire **cannot** pass.

TRANSRADIAL DELIVERY CONTRAINDICATIONS

- Patients with known upper extremity vascular disease, extreme tortuosity, anomalous radial artery take off, severe subclavian stenosis or severe atherosclerosis.
- Patients with known Buerger's disease or Raynaud's phenomenon.
- Presence of Arterio-venous Fistula.
- Patients with known anatomical abnormalities of the upper extremity / aorta.
- Patients who are exceptionally tall with a radial artery (RA) to iliac artery (IA) length greater than 150 cm.
- Patients with known dissecting thoracoabdominal aortic aneurysm.

WARNINGS

- The stent system has been sterilized by ethylene oxide gas, and is for single use only. Do **not** reuse. Do **not** resterilize. Do **not** reprocess as reprocessing may compromise the sterility, biocompatibility and functional integrity of this product.
- The stent system is sterile and non-pyrogenic in an unopened and undamaged unit package. Do **not** use if the unit package or the product has been damaged or soiled.
- Use this device prior to the expiry date indicated on the package.
- The stent should **not** come in contact with a previously placed non-nitinol stent. Contact of stents made from two dissimilar materials could possibly result in corrosion of the stents.
- Do **not** use in patients with known allergy to nickel-titanium alloy, gold or contrast media as this may result in an allergic reaction.
- Perform appropriate antiplatelet and/or anticoagulation therapy pre- and post- procedure.
- Insert the device into a guiding sheath or guiding catheter of adequate length to guide the device from the puncture site to the treatment site, failure to do so may cause thrombus on the vessel wall and/or plaque to flow through the blood stream, which may cause severe embolization and/or stroke especially in trans-brachial approach or trans-radial approach.

PRECAUTIONS

- Do **not** use on pregnant patients or patients who may become pregnant.
- Patients for a peripheral intervention should be selected carefully. Operators should bear in mind that complications including (but **not** limited to) subacute thrombosis, vessel complication and hemorrhagic complications may result from peripheral intervention.
- This device should be used only at institutions where emergency surgery can be performed due to the risk of severe complications.
- This device should only be used by a physician who is familiar with, and well trained in, Percutaneous Transluminal Angioplasty (PTA) techniques, stent implantations, and transradial access.
- Confirm that the design of the stent system meets the criteria of the procedure and the technique to be used.
- If delivering stent from a transradial approach, standard departmental radial artery protocol should be followed to prevent radial artery occlusion, injury or spasm.
- Prior to beginning radial artery access, conduct a screening test such as an Allen test to ensure the radial access is appropriate for the patient.
- Choose the appropriate stent size by considering the regions in which diagnosis is performed, and the anatomical aspects.
- Use delivery system of adequate usable length for patient anatomy to deliver the device from the puncture site to the treatment site.
- Do **not** use in highly tortuous or highly calcified lesions and/or vessels proximal to the lesion which could prevent proper pre-dilatation.
- To avoid resistance while inserting the guide wire into the delivery system, wipe off any foreign material (including blood) on the guide wire before delivering the stent system.
- Do **not** use agents containing organic solvent (e.g. alcohol) or oil-based contrast agents (e.g. fatty acid of poppy seed oil ethyl ester iodide "Lipiodol®"), as this may cause the device to break or lose lubricity.
- Pre-dilatation of the target vessel is recommended.
- To assure optimal stent delivery, confirm that the pre-dilation is properly done before stenting patients who have highly tortuous or calcified lesions and/or vessels proximal to the lesion.
- To maintain sterility, the stent system should be used immediately after opening the package and be disposed of safely and properly after use.
- The entire operation should be carried out aseptically.
- Due to the diameter of the delivery system, buddy wire technique **cannot** be performed with a 6 Fr. introducer sheath or guiding catheter. Choose the introducer sheath or guiding catheter with sufficient inner lumen.
- Manipulate the stent system carefully within the artery. If you feel any resistance, stop manipulating the stent system and under high-resolution fluoroscopy try to determine the cause of the problem. Continuing to manipulate the stent system may result in damage to the vessel and/or damage of the stent system. This may necessitate retrieval of fragments of the stent system.
- Stenting across a major vessel branch may lead to compromised future diagnostic or therapeutic procedures.
- Care should be taken when advancing the stent system through a previously placed stent. The stent system may be caught in the previously placed stent, and may cause deformation and/or dislodgement of the stent, damage to the blood vessel, and/or thrombo-embolism.
- A partially deployed stent **cannot** be repositioned or retracted into the sheath. Retraction, or repositioning of a stent by force, could cause deformation of the stent, damage to the blood vessel and/or to the delivery catheter. The stent **cannot** be removed after implantation.
- If you feel any resistance during withdrawal of the delivery catheter after stent implantation, stop the procedure and determine the cause of resistance in order to alleviate the risk of damaging the delivery catheter.
- Care should be given when additional devices and wires are delivered through a previously placed stent in order to prevent damage or dislodgement.

PRECAUTION FOR STORAGE

• Avoid exposure to water, direct sunlight, extreme temperature, or high humidity during storage.

MRI SAFETY INFORMATION

MR Conditional

Non-clinical testing has demonstrated Misago is MR Conditional. A patient with this device can be safely scanned in an MR system meeting the following conditions:

- Static magnetic field of 1.5 T or 3 T
- Maximum spatial field gradient of 4,000 gauss/cm (40 T/m)
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2 W/kg for Normal Operating Mode

Under the scan conditions defined above, Misago is expected to produce a maximum temperature rise of 3.2 ºC after 15 minutes of continuous scanning.

Artifact Information

In non-clinical testing, the image artifact caused by the device extends approximately 2 mm from Misago when imaged with a gradient echo pulse sequence and a 3.0 T MRI system.

POTENTIAL ADVERSE EVENTS

Generally, complications to PTA are also complications for stent placement. Complications include, but are **not** be limited to:

- Allergic reaction
- Amputation of treated limb
- Arrhythmia
- Arterial dissection/perforation/rupture/injury
- Arterial embolism/thrombosis/occlusion
- Arterial spasm
- Arteriovenous fistula
- Bleeding/Hematoma
- Bradycardia/Palpitation
- Cerebral vascular accident
- Death
- Distal embolization
- Femoral pseudoaneurysm/ Pseudoaneurysm formation
- Fever
- Hemorrhage
- Hypotension/Hypertension
- Infection and pain at puncture site
- Leg Pain/Claudication
- Myocardial Infarction
- Renal failure
- Restenosis
- Sepsis
- Stent fracture
- Stroke
- Target lesion revascularization
- Thrombosis of target vessel

SUMMARY OF CLINICAL STUDIES

Following the CE Mark approval of Misago, several European registries were developed (MISAGO 1 and MISAGO 2) and are briefly reviewed below. This was later followed by a pivotal study (OSPREY) performed in both the US and Asia. The results of the OSPREY, MISAGO 1, and MISAGO 2 trials are based on clinical data using the femoral artery access route and are not based on data specifically related to transradial access.

Pivotal Study:
The OSPREY: Occlusive/Stenotic Peripheral artery REvascularization studY: A US/Japan Multi-center trial of Misago for Superficial Femoral Artery evaluated the clinical effectiveness and safety of Misago for the treatment of narrowed or occluded superficial femoral arteries with comparison to historical study outcomes.

In the US, this was a multi-center, single-arm, non-randomized, prospective clinical trial to investigate the safety and effectiveness of the flexible Misago delivered via a rapid-exchange (RX) delivery system for the treatment of focal atherosclerotic disease in the superficial femoral artery (SFA). In Japan, there were two arms of the study: 50 subjects received Misago (stent arm) and 51 subjects received percutaneous transluminal angioplasty (PTA) with potential bailout stent implantation. This US/Japan pivotal study enrolled a total of 261 subjects who were implanted with Misago: 201 in the U.S., 50 in Japan (stent arm), as well as 10 additional subjects in Taiwan and South Korea.

Demographics:

The target population included men and women, ≥ 18 years of age, having symptomatic leg ischemia without tissue loss (Rutherford category 2, 3 or 4) and a resting ABI of < 0.9 arising from one or multiple de novo SFA lesion(s) with > 50% stenosis or occlusion with a total lesion length of ≥ 40 mm and ≤ 150 mm at least 3 cm above-the-knee. Baseline demographics and clinical characteristics are summarized in Table 1. It was determined that the data was poolable between sites in the US and outside the US (Japan, Taiwan and Korea) when including out-of-window DUS patency.

Table 1: Baseline Demographics and Clinical Characteristics

Characteristic	Mean±SD
Age at implant (years)	69.3 ± 10.0
Gender (% Male)	64.8% (169/261)
Race/Ethnicity	
Caucasian	69.0% (180/261)
Asian	23.0% (60/261)
Black	6.9% (18/261)
Hispanic	1.1% (3/261)
Diabetes Mellitus	47.9% (125/261)
Smoking history	
Yes, Current	42.1% (110/261)
Yes, Previous	40.6% (106/261)
BMI (kg/m^2)	28.2 ± 5.8
Rutherford score	
Rutherford – 2	48.3%(126/261)
Rutherford – 3	47.1%(123/261)
Rutherford – 4	4.6% (12/261)
ABI	0.7 ± 0.1
Percent of diameter stenosis (angiography)	86.5 ± 12.1
Lesion length (mm)	83.8 ± 41.3

Method:

The target lesion was to be predilated utilizing standard techniques if deemed necessary. Subjects underwent SFA stent placement according to the Instructions for Use. Following deployment of the stent, dilatation of the target lesion was required. Aspirin (81 to 325 mg) intake was required to be started within 24 hrs of the procedure. During the stenting procedure, use of supplemental anticoagulation was administered according to the investigator's discretion. Following the stenting procedure, subjects were prescribed daily aspirin (81 to 325 mg) and recommended daily Plavix® (75 mg) or Ticlid® (250 mg) for 1 month following the procedure. Table 2 presents baseline lesion characteristics assessed by the angiographic core laboratory.

Table 2: Baseline Lesion Characteristics (Core Lab Reported)

Parameter	Mean±SD or % (n/N)
Location	
Left	49% (128/261)
Right	51% (133/261)
Arterial segment	
Proximal SFA	12.3% (32/261)
Middle SFA	53.6% (140/261)
Distal SFA	33.3% (87/261)
Other	0.8% (2/261)
Lesion length (mm)	83.8 ± 41.3
Proximal Reference Vessel Diameter (mm)	5.1 ± 1.0
Distal Reference Vessel Diameter (mm)	5.1 ± 1.0
Segment Minimum Lumen Diameter (mm)	1.1 ± 0.9
Bend	80.1% (209/261)
Eccentricity	
Concentric	59.8% (156/261)
Eccentric	40.2% (105/261)

Parameter	Mean±SD or % (n/N)
Thrombus	
None	98.5% (257/261)
Possible	0.4% (1/261)
Small	0.0% (0/261)
Moderate	0.8% (2/261)
Large	0.4% (1/261)
Total occlusion	0.0% (0/261)
Calcification	
None	33.3% (87/261)
Moderate	35.2% (92/261)
Severe	31.4% (82/261)
Tortuosity	
None	100.0% (261/261)
Moderate	0.0% (0/261)
Severe	0.0% (0/261)
Ulceration	20.7% (54/261)
Aneurysm	1.1% (3/261)
Pre-TIMI flow	
0	24.1% (63/261)
1	1.9% (5/261)
2	0.8% (2/261)
3	67.8% (177/261)
NA	5.4% (14/261)
TASC II Classification	
TASC II type A lesions	55.6% (145/261)
TASC II type B lesions	37.5% (98/261)
TASC II type C lesions	6.9% (18/261)
TASC II type D lesions	0.0% (0/261)
Inflow tract stenosis	
< 50%	60.9% (159/261)
> 50%	8.8% (23/261)
NA	30.3% (79/261)
Distal runoff vessels	
1	27.2% (71/261)
2	32.2% (84/261)
3	20.3% (53/261)
NA	13.4% (35/261)
Patency of anterior tibial artery	46.5% (105/226)
Patency of posterior tibial artery	61.1% (140/229)
Patency of peroneal artery	69.0% (156/226)

Primary Endpoint Analysis:
Overall, the OSPREY data provide reasonable assurance of safety and effectiveness of Misago for use in the intended population.

The primary safety endpoint for this study was freedom from major adverse events (MAE) at 30 days post-procedure. MAE was defined as TLR, amputation of the treated limb, or death. Study success was based on the proportion of patients with freedom from MAE at 30 days post-procedure when tested against a performance goal of 88% using the lower bound of the 95% confidence interval. In both cohorts, the lower confidence interval exceeded the prespecified performance goal indicating the study met its primary safety endpoint. Table 3 summarizes the primary endpoints.

The primary effectiveness endpoint was defined as stent patency at 12 months as evidenced by a peak systolic velocity ratio < 2.0 from DUS obtained within the 12 months visit window. Because patency beyond the 12 months visit window may be considered as patency at 12 months, the out-of-window patency is imputed as treatment success. It also regarded missing data as loss of patency under the intention to treat (ITT) analysis. The ITT cohort included all 261 subjects, the modified intention to treat (mITT) cohort had 226 subjects (excluded subjects with unknown primary effectiveness endpoint) and the per protocol (PP) cohort had 222 subjects (excluded subjects that failed to meet all eligibility criteria).

In the ITT analysis 54.0% (141/261) of subjects met the primary effectiveness endpoint and were noted to have patent stents at 12 months as evidenced by peak systolic velocity ratio < 2.0 and freedom from TLR event. The primary effectiveness endpoint was met in 141/226 subjects (62.4%) in the mITT cohort and in 139/222 subjects (62.6%) in the PP cohort. The lower bound of the two-sided 95% confidence interval was 48.0% in the ITT cohort. The primary effectiveness objective was not met and a 12 month patency rate of 66% or less could not be ruled out.

Supplementary Primary Endpoint Analysis:
A supporting analysis conforming to FDA guidance using Kaplan-Meier methods avoided this issue by evaluating all available data in a time-to-event format and censoring subjects with missing data at the appropriate times. Kaplan-Meier freedom from loss of patency had a 12-month (360 day) estimate of 78.9% (see Fig. 4 and Table 4). Furthermore, Kaplan-Meier freedom from Target Lesion Revascularization (TLR) had a 12-month (360 day) estimate of 88.6% (see Fig. 5 and Table 5).

Although the primary effectiveness endpoint was not met by the protocol-defined analysis, when analyzed using the Kaplan-Meier method, the freedom from loss of patency at 12 months was 78.9%. Additional considerations may also be made using a more contemporary approach to evaluate stent patency using a peak systolic velocity ratio (PSVR) ≤ 2.4 (modified VIVA criteria). The freedom from loss of patency at 12 months was 60.5% and 69.9% in the ITT and mITT cohort, respectively. Furthermore, the Kaplan-Meier freedom from loss of patency at 12 months (360 days) estimate was 82.9%.

Table 3: Primary Endpoint (Including DUS data collected outside the 12 months visit window)

Primary Endpoint	% (n/N)	95% Confidence Interval	Performance Goal
Safety:			
Freedom from MAE at 30 Days post-enrollment (ITT)	99.2% (259/261)	97.1%, 100.0%	88%
Effectiveness (based on peak systolic velocity ratio < 2.0):			
Stent patent at 12 months (ITT)[1]	54.0% (141/261)	48.0%, 60.0%	66%
US - Stent patent at 12 months (ITT)	51.7% (104/201)		
OUS - Stent patent at 12 months (ITT)	61.7% (37/60)		
Stent patent at 12 months (mITT)	62.4% (141/226)		
Stent patent at 12 months (PP)	62.6% (139/222)		
Modified Effectiveness (based on peak systolic velocity ratio ≤ 2.4):			
Stent patent at 12 months (ITT)[1]	60.5% (158/261)		
Stent patent at 12 months (mITT)	69.9% (158/226)		
Stent patent at 12 months (PP)	69.8% (155/222)		

[1] Includes DUS data collected outside the 12 months visit window

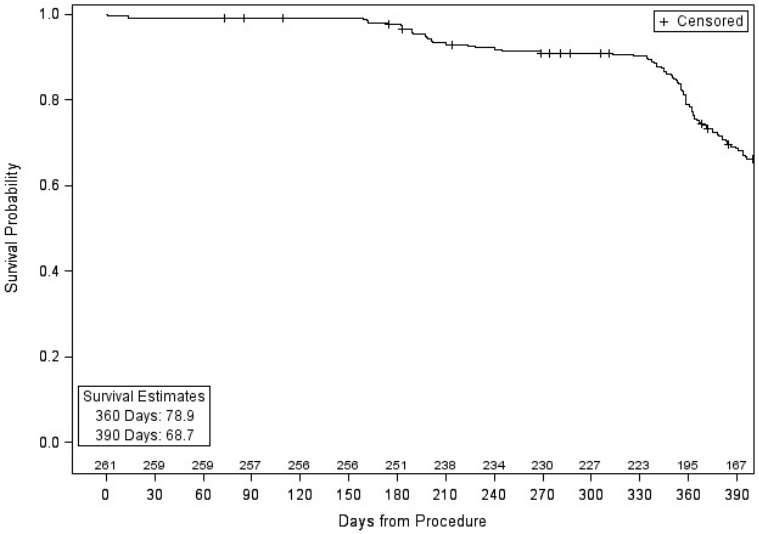


Fig. 4 Kaplan-Meier Freedom from Loss of Patency within 12 Months (PSVR ≥ 2.0 or TLR)

Table 4: Freedom from Loss of Patency (PSVR ≥ 2.0 or TLR)

Timepoint	[0, 90]	[90, 180]	[180, 270]	[270, 360]	[360, 390]
# At Risk[1]	261	257	251	230	195
# Events[2]	2	4	17	30	25
# Censored[2]	2	2	4	5	3
Survival %[3]	99.2	97.7	91.0	78.9	68.7
Standard Error[3]	0.5	0.9	1.8	2.6	2.9

[1]At beginning of interval
[2]Within interval
[3]At end of interval

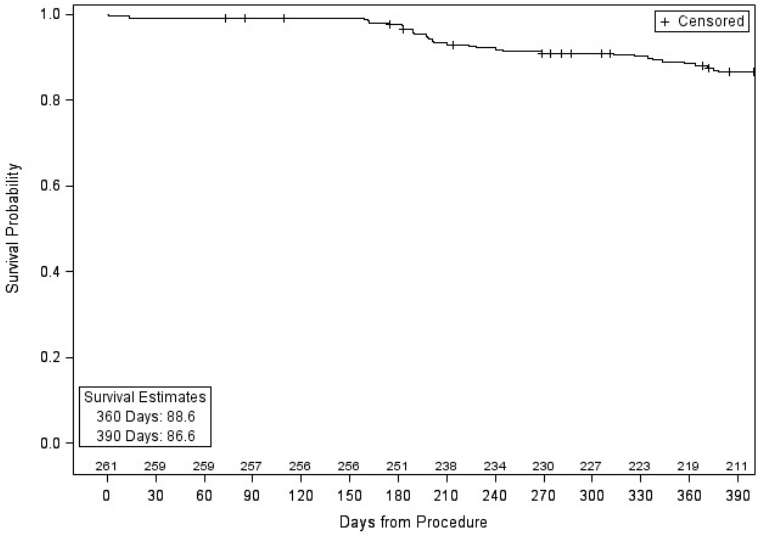


Fig. 5 Kaplan-Meier Freedom from TLR within 12 Months of Procedure

Table 5: Freedom from TLR within 12 Months of Procedure

Timepoint	[0, 90]	[90, 180]	[180, 270]	[270, 360]	[360, 390]
# At Risk[1]	261	257	251	230	219
# Events[2]	2	4	17	6	5
# Censored[2]	2	2	4	5	3
Survival %[3]	99.2	97.7	91.0	88.6	86.6
Standard Error[3]	0.5	0.9	1.8	2.0	2.2

[1]At beginning of interval
[2]Within interval
[3]At end of interval

Secondary endpoints:
Multiple secondary effectiveness endpoints were defined for this study. Tables 6 and 7 summarize the secondary safety and effectiveness endpoints and subjects meeting each endpoint.

Table 6: Secondary Safety Endpoints

Secondary Safety Endpoint	% (n/N)
MAEs through 30 days	0.8% (2/261)
TLR	0.8% (2/261)
Amputation	0.0% (0/261)
Deaths through 30 days	0.0% (0/261)
MAEs through 12 months	16.1% (42/261)
TLR	13.0% (34/261)
Amputation	0.0% (0/261)
Device failures through 12 months	1.3% (3/234)
Failure/Malfunctions	0.4% (1/261)
Stent fracture evidenced by plain film X-ray at 12 months	0.9% (3/324 stents) 1.3% (3/234 subjects)
Device related peri-procedural complications	2.3% (6/261)
Significant distal embolization in target limb	2.3% (6/261)
Thrombosis of target vessel	0.4% (1/261)
Any device related adverse event	19.5% (51/261)

Table 7: Secondary Effectiveness Endpoints

Secondary Effectiveness Endpoint	Mean±SD or % (n/N)
Technical success	100.0% (261/261)
Successful delivery of stent at lesion site	100.0% (261/261)
Stent deployed in lesion with adequate lesion coverage	100.0% (261/261)
Procedural success	93.5% (244/261)
Clinical Success: relief or improvement from baseline symptoms as measured by the Rutherford score for chronic limb ischemia at 30 days as compared to baseline	90.0% (234/260)
Ankle-Brachial Index change from baseline to 30 days post-procedure	0.3 ± 0.2
Ankle-Brachial Index change from 30 days to 12 months post-procedure	-0.1 ± 0.2
Rutherford sustained (without increase of one or more in the score) at 12 months post-procedure from 30 days post-procedure	80.2% (190/237)
Clinically driven target lesion revascularization through 12 months post-procedure	13.0% (34/261)
Patency of target vessel based on systolic velocity ratio ≤ 2.4 and absence of TLR	69.9% (158/226)
Target lesion revascularization through 30 days	0.8% (2/261)
Target lesion revascularization through 12 months	13.0% (34/261)

Rutherford Becker (RB)

The majority of subjects had moderate-severe claudication (Rutherford Becker 2-3) at baseline. At 1 and 12 months post procedure, a majority of subjects were asymptomatic (see Table 8).

Table 8: Rutherford Becker Scale Analysis (Combined Cohort)

	Baseline % (n/N)	**30 days**	**12 Months**
Mean±SD	3.6 ± 0.6	1.6 ± 1.0	1.6 ± 0.9
Rutherford – 0	0.0% (0/261)	62.7% (163/260)	61.6% (146/237)
Rutherford – 1	0.0% (0/261)	19.6% (51/260)	22.4% (53/237)
Rutherford – 2	48.3% (126/261)	11.9% (31/260)	10.5% (25/237)
Rutherford – 3	47.1% (123/261)	4.6% (12/260)	5.5% (13/237)
Rutherford – 4	4.6% (12/261)	0.8% (2/260)	0.0% (0/237)
Rutherford – 5	0.0% (0/261)	0.0% (0/260)	0.0% (0/237)
Rutherford – 6	0.0% (0/261)	0.4% (1/260)	0.0% (0/237)

Ankle-Brachial Index (ABI)

There was an overall improvement in ABI from a mean of 0.7 at baseline to 0.9 at 12 Months (see Table 9).

Table 9: ABI and Change from Baseline in Combined Cohort Through 12 Months

ABI on Target Limb	Baseline	1 Month	6 Months	12 Months
Mean + SD (N)	0.70 ± 0.15 (259)	0.98 ± 0.16 (260)	0.92 ± 0.18 (253)	0.91 ± 0.17 (236)
Median	0.71	0.99	0.94	0.93
Min, Max	0.13, 1.12	0.39, 1.63	0.00, 1.42	0.43, 1.60

Patency

In the combined study cohort (US and Asian subjects), similar short and mid-length lesion effectiveness was observed (67.6% in lesions ≤ 60 mm, 63.3% in lesions 61-100 mm), while patency was reduced in lesions > 100 mm (54.8%). Table 10, 11, and 12 summarize patency by lesion lengths. These tables include the DUS for 23 subjects that were obtained after the 12 months window; these subjects were used in the mITT analysis.

Table 10: 12 Months Efficacy (no TLR and PSVR < 2.0 and ≤ 2.4) by Core Lab Assessed Lesion Length Terciles – Combined Cohort *

	Lesion Length Terciles (Core Lab)		
	Lower (≤ 60) N=83	Mid (61-100) N=104	Upper (> 100) N=74
Pre-Procedure Lesion Length (mm) (core lab assessed)			
N	83	104	74
Mean ± SD	40.7 ± 12.6	80.3 ± 12.2	137.1 ± 26.1
Median	41.6	78.8	133.1
Min, Max	12.2, 60.0	61.2, 100.0	101.0, 227.5
Primary Effectiveness Endpoint (mITT)			
Primary Patency	67.6% (50/74)	63.3% (57/90)	54.8% (34/62)
PSVR < 2.0	71.8% (51/71)	75.9% (63/83)	60.3% (35/58)
No clinically driven TLR	90.4% (75/83)	84.6% (88/104)	86.5% (64/74)
Secondary Effectiveness Endpoint (mITT)			
Secondary Patency	73.0% (54/74)	71.1% (64/90)	64.5% (40/62)
PSVR ≤ 2.4	77.5% (55/71)	84.3% (70/83)	70.7% (41/58)
No clinically driven TLR	90.4% (75/83)	84.6% (88/104)	86.5% (64/74)

* Results based on core lab reported lesion length and includes DUS data collected outside the 12 months visit window

Table 11: 12 Months Efficacy (no TLR and PSVR < 2.0 and ≤ 2.4) By Core Lab Assessed Lesion Length – Combined Cohort*

	Lesion Length by Core Lab Read Angiography	
	≤ 150 N=241	> 150 N=20
Primary Effectiveness Endpoint (mITT)		
Primary Patency	63.4% (135/213)	46.2% (6/13)
PSVR < 2.0	71.9% (143/199)	46.2% (6/13)
No clinically driven TLR	86.3% (208/241)	95.0% (19/20)
Secondary Effectiveness Endpoint (mITT)		
Secondary Patency	70.9% (151/213)	53.8% (7/13)
PSVR ≤ 2.4	79.9% (159/199)	53.8% (7/13)
No clinically driven TLR	86.3% (208/241)	95.0% (19/20)

* Results based on core lab reported lesion length and includes DUS data collected outside the 12 months visit window

Table 12: 12 Months Efficacy (no TLR and PSVR < 2.0 and ≤ 2.4) by Core Lab Assessed Lesion Length – Combined Cohort*

	% (n/N)
Primary Effectiveness Endpoint (mITT)	
Core Lab Lesion Length	
≤ 60	67.6% (50/74)
61-100	63.3% (57/90)
101-150	57.1% (28/49)
> 150	46.2% (6/13)
Secondary Effectiveness Endpoint (mITT)	
Core Lab Lesion Length	
≤ 60	73.0% (54/74)
61-100	71.1% (64/90)
101-150	67.3% (33/49)
> 150	53.8% (7/13)

* Results based on core lab reported lesion length and includes DUS data collected outside the 12 months visit window

Stent Fracture

X-rays for 324 stents (234 subjects) were available for analysis by the angiographic core laboratory to evaluate stent fractures at 12 months post-procedure. The stent fracture rate at 12 months was 0.9% (3/324 stents) and is summarized in Table 13 below. The per subject stent fracture rate was 1.3% (3/234).

Table 13: Summary of Stent Fractures by Stent

Parameter	At 12 Months % (n/N)
Stent fracture	0.9% (3/324)
Fracture type	
I – Single strut fracture only	0.3% (1/324)
II – Multiple single strut fractures that occur at different sites	0.0% (0/324)
III - Multiple strut fractures resulting in complete transection of the stent, without displacement of the stent segment	0.3% (1/324)
IV - Multiple strut fractures resulting in displacement of segments of the stent	0.3% (1/324)[1]
V - Spiral fractures that denotes a spiral dissection of a stent	0.0% (0/324)
Fracture location	
Proximal	0.3% (1/324)
Middle	0.3% (1/324)
Distal	0.3% (1/324)

[1]Caused by physician during non-study peripheral intervention

Adverse Events:

Table 14 provides a summary of the adverse events documented in the OSPREY study. The data are presented as a percentage of subjects experiencing an adverse event.

Table 14: Summary of Adverse Events

Adverse Event by SOC and PT	Overall % (n)	Within 30 Days % (n)	30 Days-6 Months % (n)	6 Months-12 Months % (n)
Any adverse event	85.1% (222)	45.2% (118)	53.3% (139)	55.9% (146)
Blood And Lymphatic System Disorders	6.1% (16)	0.8% (2)	3.1% (8)	3.1% (8)
Cardiac Disorders	16.1% (42)	3.8% (10)	6.5% (17)	9.6% (25)
Congenital, Familial And Genetic Disorders	0.4% (1)	0% (0)	0.4% (1)	0% (0)
Ear And Labyrinth Disorders	0.4% (1)	0.4% (1)	0% (0)	0% (0)
Endocrine Disorders	1.1% (3)	0% (0)	0.4% (1)	0.8% (2)
Eye Disorders	4.2% (11)	0.4% (1)	3.1% (8)	0.8% (2)
Gastrointestinal Disorders	17.2% (45)	4.6% (12)	8.4% (22)	8.0% (21)
General Disorders And Administration Site Conditions	18.4% (48)	8.4% (22)	6.1% (16)	6.9% (18)
Hepatobiliary Disorders	2.7% (7)	0.4% (1)	0.4% (1)	1.9% (5)
Immune System Disorders	2.3% (6)	1.1% (3)	0.4% (1)	0.8% (2)
Infections And Infestations	18.8% (49)	3.8% (10)	10.0% (26)	9.6% (25)
Injury, Poisoning And Procedural Complications	27.2% (71)	6.5% (17)	10.0% (26)	15.3% (40)
Investigations	3.1% (8)	1.9% (5)	0.4% (1)	1.1% (3)
Metabolism And Nutrition Disorders	6.5% (17)	0.8% (2)	2.7% (7)	3.1% (8)
Musculoskeletal And Connective Tissue Disorders	23.4% (61)	8.8% (23)	10.3% (27)	6.5% (17)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	4.6% (12)	0% (0)	2.3% (6)	2.3% (6)
Nervous System Disorders	15.7% (41)	2.3% (6)	6.9% (18)	7.3% (19)
Psychiatric Disorders	3.8% (10)	0.8% (2)	1.9% (5)	1.5% (4)
Renal And Urinary Disorders	4.6% (12)	0.4% (1)	2.3% (6)	2.3% (6)
Reproductive System And Breast Disorders	1.1% (3)	0% (0)	0% (0)	1.1% (3)
Respiratory, Thoracic And Mediastinal Disorders	11.9% (31)	1.9% (5)	3.8% (10)	6.1% (16)
Skin And Subcutaneous Tissue Disorders	10.0% (26)	3.4% (9)	3.8% (10)	3.8% (10)
Surgical And Medical Procedures	0.4% (1)	0% (0)	0.4% (1)	0% (0)
Vascular Disorders	38.3% (100)	18.4% (48)	14.6% (38)	16.9% (44)
MedDRA Perferred Terms shown where number of subjects with event is 5 or more				

Conclusion:

The primary safety endpoint of the OSPREY trial was met. While the pre-specified effectiveness endpoint was not met, the study results are similar to the results of other US marketed stents intended for use in patients with SFA lesions. Overall, the results of the non-clinical and clinical evaluations provide reasonable assurance that Misago is safe and effective. The benefits of Misago outweigh the risks when the device is used as indicated in accordance with the labeling and Instructions for Use (IFU).

MISAGO 1 was a prospective, multicenter, non-randomized study conducted in Europe. The study evaluated a newly developed self-expanding nitinol stent with rapid exchange delivery catheter for the treatment of stenotic or occluded superficial femoral (SF) or popliteal arteries. There were a total of 5 sites which enrolled 55 subjects with the implantation of 81 stents. The primary endpoint was restenosis rate at 6 months assessed by duplex sonography. The technical success rate was 100% while the procedural success rate was 98.2% without death, MI, stroke, or major bleeding. At 6 months follow-up the restenosis rate was 8.5%. Rutherford index at 6 months demonstrated improvement of 73%, without any subjects having symptom deterioration. One case of stent fracture was observed. The results from this first-in-man study indicated acceptable clinical outcomes.

MISAGO 2 was a post-market clinical study to confirm the performance and long term safety of the device for the treatment of occluded or stenotic SFA or popliteal arteries. This multicenter, non-randomized, prospective, observational registry evaluated the absence of clinically driven target lesion revascularization (TLR) at 6 and 12 months. The study enrolled 744 subjects in 76 European and South American sites. At the 12 months follow-up completion, 671 (90.2%) subjects were evaluated. The overall freedom from TLR and freedom from TLR per subject were 96.9% and 97.0% at 6 months, and 89.9% and 91.4% at 1 year, respectively. Total event-free survival rate estimates were 93.2% at 6 months and 84.9% at 1 year. Ischemic symptoms improved since 691 (92.1%) subjects enrolled were symptomatic at baseline and only 136 (21.3%) reported ischemic symptoms at 1 year ($p < 0.001$). Pain-free walking distances significantly increased and mean ABIs in the target limb revealed improvement of ≥ 0.1 or more in 76% of subjects at 12 months ($p < 0.001$). The Rutherford classification improved in 87.5% of subjects or remained stable in 8.0%.

DIRECTIONS FOR USE

Refer to Fig. 1 – 3 and Table 15 for instructions.

1. Preparation prior to stent implantation

1-1 Insert into the blood vessel an introducer sheath of at least 6 Fr., a guiding sheath, or a guiding catheter with an internal diameter of at least 2.16 mm.

1-2 Introduce an angiographic catheter into the blood vessel.

1-3 Image the lesion site by angiography.

1-4 Choose a stent size according to the stent size selection Table below (see Table15).

Table 15: Stent Size Selection Table

Unconstrained stent diameter (mm)	Reference vessel diameter (mm)
6.0	4.0 - 5.0
7.0	5.0 - 6.0
8.0	6.0 - 7.0

1-5 Prepare the device according to standard practice.

1-6 Pre-dilatate the lesion site according to standard practice.

PRECAUTIONS

- Before use, confirm that **all** devices including the stent system function correctly, are **not** damaged, are **not** beyond their expiry date, and are suited for the purpose and procedure.
- Do **not** insert the stent system directly into the vessel without an introducer sheath, guiding sheath, or guiding catheter. (Inserting the stent system directly into the vessel can potentially damage the blood vessel and/or the stent system.)
- Confirm that the guide wire outer diameter does **not** exceed 0.89 mm (0.035 inches). If a larger guide wire has been used, exchange the guide wire.
- Do **not** use a stent smaller than the blood vessel diameter.
- Use guiding sheath or guiding catheter with enough length for each approach such as trans-femoral, trans-brachial, or trans-radial.

2. Preparation of the stent system

2-1 Carefully remove the stent system from its holder.

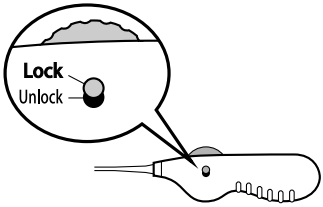
PRECAUTIONS

- Confirm that the stent system is **not** damaged and that the sterility has **not** been compromised.
- Do **not** remove the green plugging tube at this stage. Unplug the plugging tube immediately before the insertion of a guide wire into the distal tip of the delivery catheter (see Fig. 6).

Fig. 6

2-2 Confirm that the thumbwheel on the deployment handle is in the "Lock" position (see Fig. 7).

Fig. 7



PRECAUTIONS

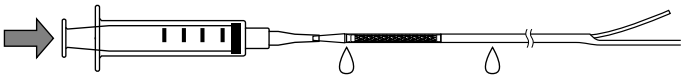
- Stop using the stent system immediately if the thumbwheel is **not** in the "Lock" position at this stage.
- Do **not** depress the thumbwheel until just before stent deployment.

2-3 Fill the enclosed syringe with heparinized physiological saline solution and then connect the syringe to the distal tip (see Fig. 8).

Fig. 8

2-4 Flush with the heparinized physiological saline solution to remove air bubbles (see Fig. 9).

Fig. 9

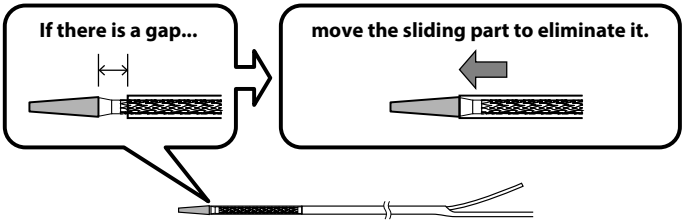


PRECAUTIONS

- Confirm that the air bubbles have been removed by flushing until the heparinized physiological saline solution comes out of the proximal and distal ends of the sheath.
- Repeat step 2-4 if the solution does **not** come out. (Inadequate removal of air bubbles can result in occlusion of the peripheral blood vessels.)

2-5 If you see a gap between the sliding part and the distal tip, move the sliding part to eliminate the gap (See Fig. 10).

Fig. 10



PRECAUTION

- Stop using the stent system immediately if the gap **cannot** be eliminated by moving the sliding part. (This could cause adverse events, such as vessel damage.)

2-6 Wet surface of distal tip and sheath enough with heparinized physiological saline solution to keep them lubricated (See Fig. 11).

Fig. 11

3. Insertion of the stent system

3-1 Maintaining the position of the guide wire in the lesion, remove the dilatation catheter.

3-2 Unplug the plugging tube from the delivery catheter (see Fig. 12).

Fig. 12

3-3 Pass the proximal end of the guide wire through from the distal tip and advance the stent system in line with the guide wire.

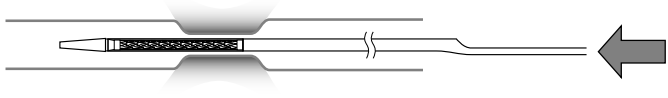
3-4 Maintaining the position of the guide wire in the lesion, insert the stent system into the introducer sheath, guiding sheath, or guiding catheter. For 200 cm usable length, the depth marker on the shaft will help confirm how far the stent system has been advanced.

PRECAUTIONS

- Do **not** insert the stent system without a guide wire support. (This could cause adverse events, such as blood vessel damage.)
- The rapid exchange delivery system will **not** allow guide wire exchanges once the device is inside the patient. (If the guide wire is removed, carefully remove the stent system and re-insert a guide wire and stent system.)
- Loosen the hemostatic valve of the Y-connector attached to the introducer sheath or guiding sheath when inserting the stent system.
- Do **not** advance the stent system by force if you feel any resistance during insertion. (The stent system can catch on and damage the hemostatic valve.)

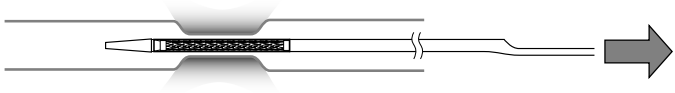
3-5 Insert the stent system into the blood vessel along the fixed guide wire under high-resolution fluoroscopy and advance the stent system through the pre-dilatated lesion (see Fig. 13).

Fig. 13



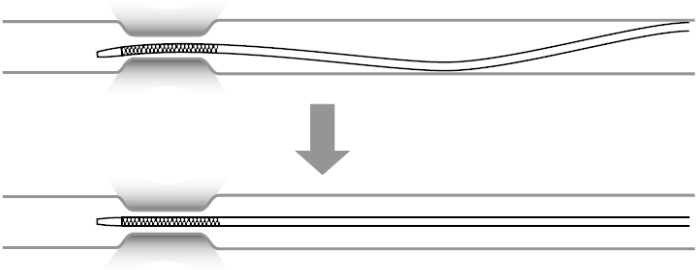
Then, by pulling back the stent system, position the stent within the stenotic lesion while observing the radiopaque markers under fluoroscopy (see Fig. 14).

Fig. 14



At this point, remove the slack in the delivery catheter (see Fig. 15).

Fig. 15

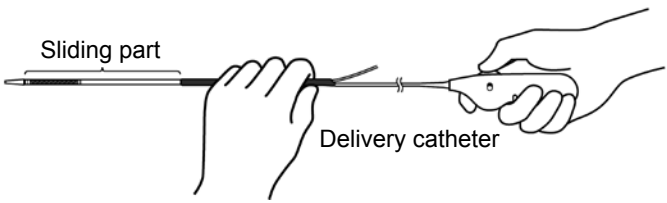


PRECAUTIONS

- Repeat the pre-dilatation step if you feel any resistance (Advancing the stent system by force can potentially damage the blood vessel and/or break or damage the stent system.)
- Do **not** deploy the stent until it is properly positioned. (If the stent is deployed in an incorrect position, it may **not** expand fully.)
- Ensure that the stent is **not** positioned within the introducer sheath, guiding sheath, or guiding catheter. (Deploying the stent within the introducer sheath, guiding sheath, or guiding catheter may deform the stent or damage the delivery catheter.)
- Avoid deploying the stent in positions that could hamper access to major vessel branches. (This could compromise future diagnostic or therapeutic procedures.)
- The stent should **not** come into contact with non-nitinol stents. (Contact between stents made from two different materials can result in potential corrosion of the stents.)

3-6 To maintain the position of the delivery catheter while rotating the thumbwheel, grip the delivery catheter by hand at the operator side (proximal) of the intermediate shaft and do **not** move the delivery catheter at the operator side of the intermediate shaft (see Fig. 16).

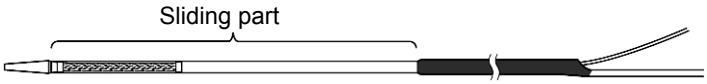
Fig. 16



PRECAUTIONS

- Eliminate any slack in the delivery catheter and fix in position. (The stent can become compressed or elongated during deployment.)
- Do **not** pull the delivery system tight during stent deployment. (The stent can become elongated during deployment.)
- Do **not** hold the sliding part of the delivery catheter (see Fig. 17). (The stent can become compressed during deployment.)

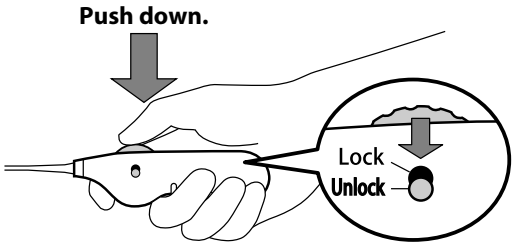
Fig. 17



4. Stent deployment

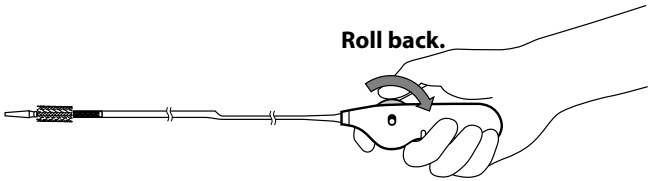
4-1 Grasp the deployment handle firmly and depress the thumbwheel until it clicks (see Fig. 18).

Fig. 18



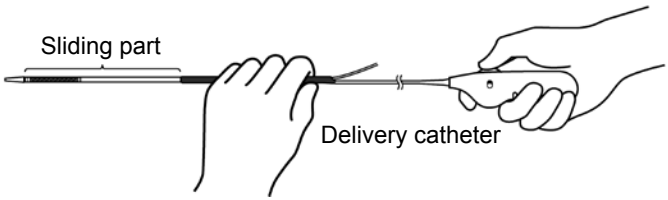
4-2 While observing the stent under high-resolution fluoroscopy, slowly roll back the thumbwheel using the thumb (with successive click sounds). The stent will start to deploy gradually from the distal end (see Fig. 19).

Fig. 19



If the radiopaque markers are observed moving distally, grip with a force commensurate with the force of the forward movement, using the movement of the radiopaque markers as a guide. If the radiopaque markers are observed moving proximally, move the delivery catheter until it is in the appropriate location. Then, grip firmly so that the delivery catheter does **not** move and deploy again by turning the thumbwheel (see Fig. 20).

Fig. 20



PRECAUTION

- When adjusting the position of the stent, always advance the stent system first and then pull it back to position the stent. (The stent can become shortened or elongated during deployment due to flexure of the delivery catheter within the vessel.)

4-3 Continue rolling back the thumbwheel until the stent deployment is completed.

PRECAUTIONS

- Securely fix the delivery catheter so that it does **not** get drawn forward. (The stent can be compressed if the delivery catheter is drawn forward in reaction to resistance on the sliding part (Fig. 3) from vessel occlusion or tortuosity.)
- Ensure that the radiopaque markers for the delivery catheter do **not** move during stent deployment.
- If the sliding part is located at the hemostatic valve or connector, the delivery catheter can slip distally during deployment and the stent may become compressed.
- As a guide, stent deployment commences on rolling back the thumbwheel 5–10 clicks for stents up to 100 mm long and 10–15 clicks for stents at least 120 mm long. Carefully roll back the thumbwheel one click at a time and adjust the position of the stent just prior to deployment if necessary (otherwise the stent can be deployed in the wrong position).
- Ensure that the introducer sheath, guiding sheath, or guiding catheter does **not** move while the stent is deploying. (The stent could become compressed during deployment).
- Deploy the stent completely, even if the delivery catheter bends and corrugates. (Removal of the delivery catheter prior to full deployment of the stent could cause the stent to deploy in an unexpected site.)
- If the stent does **not** start to deploy when the thumbwheel is rolled back, if **no** corrugations can be seen in the delivery catheter, stop rolling the thumbwheel, observe using high-resolution fluoroscopy, and then carefully remove the stent system. (The stent system could become unrecoverable.)
- A partially deployed stent **cannot** be retracted into the sliding part or repositioned. (Retraction or repositioning by force could cause deformation of the stent or damage to the blood vessel and/or delivery catheter.)
- Where multiple stents are deployed in one patient, deploy the stent within the distal lesion first and ensure that there is more than 5 mm but less than 10 mm overlap between the stents by observing the position of the radiopaque markers fluoroscopically.

- Stop rotating the thumbwheel when stent deployment is complete. (Excessive rotation of the thumbwheel after deployment is complete will cause deformation of the inner shaft, which may prevent removal of the delivery catheter due to increased resistance to the guide wire.)
- Do **not** rotate the thumbwheel in a forward direction. (This could damage the stent system.)

4-4 Observe that the deployed stent has expanded sufficiently under high-resolution fluoroscopy.

PRECAUTION

- Do **not** remove the delivery catheter until the stent has expanded sufficiently. (The stent could move from the desired position.)

5. Removal of the delivery catheter

5-1 Confirm under high-resolution fluoroscopy that the stent expands sufficiently so that the distal tip can pass through it.

5-2 Remove the delivery catheter slowly while allowing the guide wire to maintain the position within the lesion site.

PRECAUTION

- If you feel any resistance during withdrawal of the delivery catheter, confirm the cause under high-resolution fluoroscopy and resolve the issue. Remove the delivery catheter, introducer sheath or guiding sheath, and guide wire as one unit. (Removal by force could deform or move the stent, damage the site of deployment, and/or damage or break the delivery catheter.)

5-3 Perform angiography through the introducer sheath, guiding sheath, or guiding catheter to assess the dilated lesion site and to confirm that the stent has expanded to an appropriate diameter compared to that of the reference vessel.

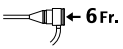
5-4 Take appropriate steps if high-resolution fluoroscopy shows inadequate stent expansion after deployment.

PRECAUTIONS

- Where post-dilatation is needed, use a dilatation catheter with a balloon shorter in length than the stent and an expansion diameter roughly consistent with the reference vessel diameter. After post-dilatation, perform angiography to confirm adequate expansion.
- Do **not** force the dilatation catheter if you feel any resistance during the procedure. (This could deform or move the stent, damage the site of deployment, and/or damage or break the dilatation catheter.)

5-5 Remove the guide wire and perform appropriate hemostatic procedures.

SYMBOLS USED ON LABELING

Unconstrained stent diameter	⌀
Stent length	<L>
Usable length of delivery catheter	<UL>
Reference vessel diameter	
Catalogue number	REF
Contents	
Sterilized using ethylene oxide	STERILE EO
Batch code	LOT
Use by date	
Do **not** reuse	
Do **not** resterilize	
Keep away from sunlight	
Keep dry	
Fragile, handle with care	
Do **not** use if package is damaged	
Stacking limit by 9	
Consult instructions for use	
Recommended introducer sheath	
CAUTION: Federal law restricts this device to sale by or on the order of a physician	Rx ONLY
Non-pyrogenic	
Accessory (Syringe for flushing)	
MR Conditional	

MANUFACTURED BY:

TERUMO CORPORATION

44-1, 2-CHOME, HATAGAYA, SHIBUYA-KU, TOKYO 151-0072, JAPAN

MADE IN JAPAN

TERUMO

Printed in Japan

SX_VXUS_E_50_006