NIR ON™ Ranger™ w/SOX™ PREMOUNTED STENT SYSTEM

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

INSTRUCTIONS FOR USE

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Medinol
Jerusalem, Israel

Boston Scientific
SCIMED

1 DEVICE DESCRIPTION

The NIR ON™ Ranger ™ w/SOX™ Premounted Stent System (NIR ON™ Ranger™ w/SOX™) includes:

- a 316LS surgical grade stainless steel continuous multicellular NIR™ stent premounted on an over-the-wire balloon catheter;
- elastomeric restraining sleeves called "SOX" that cover approximately 1 mm of the distal and proximal ends of the crimped stent;
- two radiopaque markers which aid in the accurate placement of the stent;
- a balloon enabling high pressure inflations that can be used for post-stent dilation.

Table 1. Balloon and Stent Specifications

Stent Length (mm)	System/ Balloon Diameter (mm)	NIR™ Stent Cells	Balloon Length (mm)	Nominal Pressure During Stent Deployment (atm)	Rated Burst Pressure (atm)	Minimum I.D of Guide Catheter (inches)
16	2.5	7	17	7	18	.064
16	3.0	7	17	7	18	.064
16	3.5	7	17	7	16	.064
16	4.0	9	17	7	16	.072
25	2.5	7	26	7	18	.064
25	3.0	7	26	7	18	.064
25	3.5	7	26	7	16	.064
25	4.0	9	26	7	16	.072
32	2.5	7	33	7	18	.064
32	3.0	7	33	7	18	.064
32	3.5	7	33	7	16	.064
32	4.0	9	33	7	16	.072

2 INDICATIONS and USAGE

The NIR™ stent is indicated for improving coronary luminal diameter in the following (see **7.1 Individualization of Treatment**):

- patients with symptomatic ischemic disease due to discrete *de novo* lesions in native coronary arteries (length ≤ 25 mm) with a reference vessel diameter of 3.0 to 4.0 mm;
- treatment of abrupt or threatened closure in patients with failed interventional therapy in lesions with reference diameters in the range of 2.5 to 4.0 mm;
- patients with symptomatic ischemic heart disease due to lesions in saphenous vein bypass grafts with lesion length ≤ 30 mm and reference vessel diameter in the range of 3.0 to 4.0 mm.

Long-term outcome (beyond 6 months) for this permanent implant is unkown at present.

3 CONTRAINDICATIONS

The NIR™ stent is contraindicated for use in:

- Patients in whom antiplatelet and/or anticoagulant therapy is contraindicated
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon.

4 WARNINGS and PRECAUTIONS

(see also **7.1 Individualization of Treatment**)

Warnings

- Judicious selection of patients is necessary since the use of this device carries the associated risk of subacute thrombosis, vascular complications and/or bleeding events.
- Persons allergic to 316LS stainless steel may suffer an allergic reaction to this implant.
- Implantation of the stent should be performed only by physicians who have received appropriate training.
- Stent placement should only be performed at hospitals where emergency coronary artery bypass graft surgery can be readily performed.
- Subsequent restenosis may require repeat dilation of the arterial segment containing the stent. The long-term outcome following repeat dilation of coronary stents is unknown at present.
- When multiple stents are required, stent materials should be of similar composition.

4.1 Stent Handling - Precautions

- **For single use only.** Do not resterilize or reuse. Note product "Use Before" date.
- The NIR ON™ Ranger™ w/SOX™ is designed for use as a unit. The stent is not to be removed from its delivery balloon. The stent is not to be crimped onto another balloon. Removing the stent from its delivery balloon may damage the stent and/or lead to stent embolization.
- Special care must be taken not to handle or in any way disrupt the stent position on the delivery device. In addition, care must be taken not to disrupt the SOX™ which cover the ends of the stent. This is most important during catheter removal from packaging, placement over guidewire, and advancement through hemostasis valve adapter and guiding catheter hub.
- Excessive manipulation, e.g., rolling the mounted stent, may cause dislodgment of the stent from the delivery balloon, or disruption of the SOX™.
- Use only the appropriate balloon inflation media (see section **9. OPERATOR'S INSTRUCTIONS**). Do not use air or any gas medium to inflate the balloon.

4.2 Stent Placement - Precautions

- Do not use the NIR™ stent in the treatment of restenotic lesions as the safety and effectivess have not been established.
- The target lesion should be pre-dilated with a conventional balloon angioplasty catheter prior to stent deployment.
- **Do not prepare or pre-inflate balloon prior to stent deployment** other than as directed. Use balloon purging technique described in the Operator's Instructions.
- Implanting a stent may lead to dissection of the vessel distal and/or proximal to the stented portion, and may cause acute closure of the vessel requiring additional intervention (e.g., CABG, further dilation, placement of additional stents, or other).
- When treating multiple lesions, the distal lesion should be initially stented, followed by stenting of the more proximal lesion(s). Stenting in this order obviates the need to cross the proximal stent in placement of the distal stent and reduces the chances for dislodging the proximal stent.

- Do not expand the stent if it is not properly positioned in the vessel. (See Stent System Removal - Precautions)
- Placement of the stent has the potential to compromise side branch patency.
- Balloon pressures should be monitored during inflation. **Do not exceed rated burst pressure as indicated on product label** (see Table 6). Use of pressures higher than specified on product label may result in a ruptured balloon and potential intimal damage and dissection.
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the vascular site. Complications can include bleeding, hematoma or pseudoaneurysm.

4.3 Stent System Removal - Precautions

If Stent System removal is required prior to deployment, ensure the guiding catheter is co-axially positioned relative to the Stent System and cautiously withdraw the Stent System into the guiding catheter.

Should unusual resistance be encountered when withdrawing the stent towards the guiding catheter, the Stent System, and the guiding catheter should be removed as a single unit. This must be done under direct visualization with fluoroscopy.

When removing the entire Stent System as a single unit:

- **Do not pull the Stent System into the guiding catheter.** Maintain guidewire placement across the lesion and carefully pull back the Stent System until the proximal balloon marker of the Stent System is aligned with the distal tip of the guiding catheter.
- The guiding catheter and the Stent System should be carefully removed from the coronary artery as a single unit.
- The Stent System should be pulled back into the descending aorta toward the arterial sheath. As the distal end of the guiding catheter enters into the arterial sheath, the catheter will straighten allowing safe withdrawal of the Stent System into the guiding catheter and the subsequent removal of the Stent System and the guiding catheter from the arterial sheath.
- Failure to follow these steps, and/or applying excessive force to the Stent System can potentially result in loss or damage to the stent, or Stent System components such as the balloon.

4.4 Post Implant - Precautions

- Care must be exercised when crossing a newly deployed stent with an intravascular ultrasound (IVUS) or a coronary guidewire, or a balloon catheter to avoid disrupting the stent geometry.
- Do not perform Magnetic Resonance Imaging (MRI) scan on patients post-stent implantation until the stent has been completely endothelialized (eight weeks) to minimize the potential for migration. The stent may cause artifacts in MRI scans due to distortion of the magnetic field.

5 ADVERSE EVENTS

5.1 Observed Adverse Events

A total of 1514 patients were enrolled in six multi-center clinical studies as summarized in Table 2.

Table 2. Patient Enrollment in Clinical Studies

All patients in all studies (n =1514)

Study Group	NIR™ Stent	Palmaz-Schatz®	Patient Totals
Feasibility Study	111	-	111
NIRVANA (NIR™ Vascular Advanced North American) Trial			1210
NIRVANA Randomized Trial	418	430	848
NIRVANA Abrupt or Threatened Closure (AC/TC) Registry	207	-	207
NIRVANA Saphenous Vein Graft (SVG) Registry	155	-	155
NIR ON™ Ranger™ w/SOX™ Studies			193
NIR ON™ Native Arteries Registry	162	-	162
NIR ON™ AC/TC Registry	31	-	31
Patient Totals	1084	430	1514

Patients from the NIRVANA Randomized Trial, the Abrupt or Threatened Closure (AC/TC) Registry and the Saphenous Vein Graft (SVG) Registry form the basis of the observed adverse events (n =1210).

Table 3. Adverse Events during the First 6 Months

% [±95% Confidence Interval] (Number), All patients in Randomized Trial, AC/TC Registry, and SVG Registry (n=1210)

	Randomized NIR™ n=418	Palmaz-Schatz® n=430	AC/TC n=207	SVG n=155
ANY Adverse Event	16.2% [12.9%,20.2%] (68)	17.0% [13.6%,20.9%] (73)	30.0% [23.8%,36.7%] (62)	19.4% [13.5%,26.5%] (30)
Early (in-hospital)	7.9% [5.5%,10.9%] (33)	7.9% [5.5%,10.9%] (34)	13.5% [9.2%,19.0%] (28)	5.2% [2.3%,9.9%] (8)
Out-of-hospital	9.1% [6.5%,12.3%] (38)	10.2% [7.5%,13.5%] (44)	16.4% [13.3%,24.3%] (38)	14.2% [9.1%,20.7%] (22)
Non-Q-Wave MI Total	3.6% [2.0%,5.9%] (15)	3.5% [2.0%,5.7%] (15)	5.3% [2.7%,9.3%] (11)	4.5% [1.8%,9.1%] (7)
Early (in-hospital)	3.6% [2.0%,5.9%] (15)	2.8% [1.5%,4.8%] (12)	4.8% [2.3%,8.7%] (10)	2.6% [0.7%,6.5%] (4)
Out-of hospital	0% [0%,0.9%] (0)	0.7% [0.1%,2.0%] (3)	0.5% [0%,2.7%] (1)	1.9% [0.4%,5.6%] (3)
Q-Wave MI Total	0.7% [0.1%,2.1%] (3)	0.7% [0.1%,2.0%] (3)	1.4% [0.3%,4.2%] (3)	0.6% [0%,3.5%] (1)
Early (in-hospital)	0.5% [0.1%,1.7%] (2)	0.7% [0.1%,2.0%] (3)	1.0% [0.1%,3.4%] (2)	0.6% [0%,3.5%] (1)
Out-of hospital	0.2% [0%,1.3%] (1)	0% [0%,0.9%] (0)	0.5% [0%,2.7%] (1)	0% [0%,2.4%] (0)
CABG Total	1.7% [0.7%,3.4%] (7)	2.3% [1.1%,4.2%] (10)	3.9% [1.7%,7.5%] (8)	1.3% [0.2%,4.6%] (2)
Early (in-hospital)	0.2% [0%,1.3%] (1)	0.2% [0%,1.3%] (1)	1.4% [0.3%,4.2%] (3)	0% [0%,2.4%] (0)
Out-of-hospital	1.4% [0.5%,3.1%] (6)	2.1% [1.0%,3.9%] (9)	2.4% [0.8%,5.5%] (5)	1.3% [0.2%,4.6%] (2)
Stent Thrombosis Total	0.5% [0.1%,1.7%] (2)	0.5% [0.1%,1.7%] (2)	1.0% [0.1%,3.4%] (2)	1.3% [0.2%,4.6%] (2)
Early (in-hospital)	0.5% [0.1%,1.7%] (2)	0.2% [0%,1.3%] (1)	0.5% [0%,2.7%] (1)	0.6% [0%,3.5%] (1)
Out-of-hospital	0% [0%,0.9%] (0)	0.2% [0%,1.3%] (1)	0.5% [0%,2.7%] (1)	0.6% [0%,3.5%] (1)
Death Total	0.7% [0.1%,2.1%] (3)	0.7% [0.1%,2.0%] (3)	3.4% [1.4%,6.8%] (7)	5.2% [2.3%,9.9%] (8)
Early (in-hospital)	0% [0%,0.9%] (0)	0.2% [0%,1.3%] (1)	0.5% [0%,2.7%] (1)	0.6% [0%,3.5%] (1)
Out-of hospital	0.7% [0.1%,2.1%] (3)	0.5% [0.1%,1.7%] (2)	2.9% [1.1%,6.2%] (6)	4.5% [1.8%,9.1%] (7)
Bleeding Complications	1.0% [0.2%,2.4%] (4)	1.4% [0.5%,3.0%] (6)	4.3% [2.0%,8.1%] (9)	2.6% [0.7%,6.5%] (4)
Vascular Complications	5.0% [3.1%,7.5%] (21)	4.0% [2.5%,6.3%] (17)	7.2% [4.1%,11.7%] (15)	3.2% [1.1%,7.4%] (5)
Cerebrovascular Accidents	0.2% [0%,1.3%] (1)	0.5% [0.1%,1.7%] (2)	1.0% [0.1%,3.4%] (2)	1.3% [0.2%,4.6%] (2)
Stent Delivery Failures	2.2% [1.0%,4.0%] (9)	3.0% [1.5%,5.1%] (13)	12.6% [8.4%,17.9%] (26)	1.3% [0.2%,4.6%] (2)

Early (in-hospital) refers to events during the hospitalization for the initial stent placement.

In cases where a patient experienced both an in-hospital event and an out-of hospital event, they are counted once in each group. They are counted only once in the event total. Hence, the sum of the in-hospital event rate and the out-of-hospital event rate may not equal the total event rate.

ANY Adverse Event includes death, Q wave MI, non-Q wave MI, emergent CABG, target lesion revascularization, stent thrombosis, bleeding complications, vascular complications, and CVA.

Three (3) patients who received the NIR™ stent died during the NIRVANA Randomized Trial. The 3 deaths occurred between 42 and 118 days post stenting due to sudden cardiac death (n=2), and respiratory failure/cardiomyopathy (n=1).

Seven (7) NIRVANA AC/TC Registry patients died during the clinical study. Of these, 2 deaths were early (within 30 days of stenting) due to sub-acute thrombosis. Five (5) deaths were late and occurred between 50 and 201 days post stenting due to sudden cardiac death (n=1), coronary arteriosclerosis, not related to the stent (n=1), renal failure/sepsis (n=1), head trauma (n=1), and sepsis (n=1).

Eight (8) NIRVANA SVG Registry patients died during the clinical study. Of these, 1 death was early (within 30 days of stenting) due to sub-acute thrombosis. Seven (7) deaths were late and occurred between 95 and 205 days post stenting due to cardiac arrest (n=2), sudden cardiac death (n=2), congestive heart failure (n=1), and cancer (n=2).

Five (5) feasibility patients died during the clinical study. All deaths were late (>30 days post stenting), and occurred due to cardiac arrest (n=3), cancer (n=1), and cerebrovascular accident (n=1).

The NIR ON™ Ranger™ w/SOX™ Studies were conducted to demonstrate the safety of the over-the-wire version of the delivery system (NIR ON™ Ranger™ w/SOX™). The results were compared to the rapid exchange delivery device used in the NIRVANA Trial. Twelve of the 193 patients (6.2%) treated with the NIR™ stent in the NIR ON™ Ranger™ w/SOX™ Studies experienced one or more adverse events (death, Q wave MI, emergent CABG, TLR, stent thrombosis, bleeding complications, vascular complications and CVA) during the first 14 days of follow-up compared to 27 of 418 (6.4%) of the patients in the NIRVANA Randomized Trial, difference -0.2% [-4.4%, 3.9%]. No deaths occurred during the NIR ON™ Ranger™ w/SOX™ Studies (14 days).

5.2 Potential Adverse Events

Adverse events (in alphabetical order) which may be associated with the use of a coronary stent in native coronary arteries (including those listed in Tables 3-5):

- Acute myocardial infarction
- Arrhythmias, including VF and VT
- Death
- Dissection
- Drug reactions to antiplatelet agents/contrast medium
- Emboli, distal (air, tissue or thrombotic emboli)
- Emergent Coronary Artery Bypass Surgery
- Hemorrhage, requiring transfusion
- Hypotension/Hypertension
- Infection and/or pain at the access site
- Ischemia, myocardial
- Perforation
- Pseudoaneurysm, femoral
- Restenosis of stented segment
- Spasm
- Stent embolization
- Stent thrombosis/occlusion
- Stroke/cerebrovascular accident
- Total occlusion of coronary artery

6 CLINICAL STUDIES

A total of 1,514 patients were treated at forty-one North American investigational sites in the four parts of the NIRVANA Trial and two NIR ON™ Ranger w/SOX™ Studies (Table 2).

Primary Endpoints: The primary endpoint for the randomized clinical trial and the SVG Registry was Target Vessel Failure (TVF) at 9 months. TVF was defined as a composite of death, nonfatal myocardial infarction, and clinically driven target vessel revascularization. The primary endpoint for the AC/TC Registry was the incidence of abrupt or sub-abrupt closure rate at 30 days. An independent clinical events committee, masked to treatment assignment, adjudicated all of the major clinical endpoints for the randomized trial. This committee also adjudicated the events for the registries.

Patients Studied: Patients with ischemic coronary artery disease with a *de novo* or restenotic lesion of a native coronary artery ≤ 25 mm in length and a visual reference vessel diameter of 3.0 to 4.0 mm were admitted to the randomized trial. Patients with a maximum of 2 saphenous vein grafts with one or two lesions in each graft were eligible for the SVG Registry if the lesion to be treated had a visual reference vessel diameter 3.0 to 4.0 mm and a length which could be covered by one or two NIR™ stents. Patients who experienced abrupt or threatened abrupt closure during treatment with a non-stent device were eligible for the AC/TC Registry if the lesion to be treated was in a native coronary artery with target lesion ≤ 30 mm in length and reference vessel diameter ≥ 2.5 mm and ≤ 4.0 mm. Patients were eligible if two or more of the following criteria were present: 1) angina or anginal equivalent changes; 2) ischemic electrocardiographic changes; 3) diameter stenosis ≥ 50%; 4) NHLBI Type B or C dissection, with dissection length > 8 mm and ≤ 30 mm; 5) NHLBI Type D, E, or F dissection, with dissection length ≤ 30 mm; or 6) TIMI 0-2 flow due primarily to mechanical obstruction of the treated site.

Methods: The patients underwent balloon angioplasty with an appropriate balloon diameter of 0.5 mm smaller than the reference vessel diameter, if balloon dilation was deemed necessary. Post-stent deployment dilations with a high pressure, non-compliant balloon (balloon to artery ratio of 1:1 or 1.1:1.0) were recommended to assure that the stent was in full contact with the arterial wall to leave a residual stent diameter stenosis of less than 10%.

Clinical follow-up was completed at 2 weeks, 30 days, 6 and 9 months. A subset of patients in the randomized trial as well as in the registries underwent angiographic follow-up at 6 months. Baseline characteristics were similar for the two treatment groups in the randomized trial. All treated patients were included in the intent-to-treat efficacy analysis. Anticoagulation included aspirin 325 mg/day for at least 9 months and ticlopidine 250 mg twice a day for 30 days.

Results: Of the 418 patients receiving the NIR™ stent in the NIRVANA Randomized Trial there were 368 patients with *de novo* lesions and 50 patients with restenotic lesions. The Target Vessel Failure-free rate at 6 months was 88.4% for patients with *de novo* lesions and 87.8% for patients with restenotic lesions with an associated difference of 0.6% and 95% confidence interval of [-9.1,10.3%]. Table 4 shows the results for both groups (restenosis and *de novo* combined). Figure 1 shows the actuarial freedom from Target Vessel Failure.

Table 4. Principal Effectiveness and Safety Results, NIRVANA Randomized Trial

All Patients in the NIRVANA Randomized Trial (n=848)

Efficacy Measures	Randomized NIR™ n=418	PALMAZ-SCHATZ® n=430	Difference [95% C.I.]
Technical Success by QCA	99.8% [99.6%,100%] (406/407)	97.8% [96.0%,99.0%] (409/418)	1.9% [0.4%,3.4%]
Procedure Success by QCA	95.6% [93.1%,97.4%] (389/407)	94.3% [91.6%,96.3%] (394/418)	1.3% [-1.7%,4.3%]
Post Procedure In-Stent % DS	7%±10% (409)	9%±12% (419)	-1.7% [-3.3%,-0.2%]
Range (min,max)	(-39%,39%)	(-30%,100%)	
6 Months Follow-up In-Stent % DS	34%±22% (110)	37%±22% (92)	-2.5% [-8.8%,3.8%]
Range (min,max)	(-31%,100%)	(-35%,100%)	
6 Months Follow-up In-Stent Binary Restenosis Rate (*de novo* Patient Group)	17.2% [10.2%,26.4%] (16/93)	20.5% [12.2%,31.1%] (16/78)	-3.3% [-15.1%,8.5%]
6 Months Follow-up In-Stent Binary Restenosis Rate	20.0% [13.0%,28.7%] (22/110)	21.7% [13.8%,31.6%] (20/92)	-1.7% [-13.0%,9.5%]
TLR-free at 6 Months* (K-M)	94.1% [91.9%,96.4%]	91.2% [88.4%,93.9%]	3.0% [-0.6%,6.6%]
TVF-free at 6 Months* (K-M)	88.4% [85.3%,91.5%]	86.7% [83.4%,90.0%]	1.7% [-2.8%,6.2%]
Safety Measures			
In-Hospital Clinical Events	4.3% [2.6%,6.7%] (18/418)	4.0% [2.3%,6.3%] (17/430)	0.4% [-2.3%,3.0%]
Out-of-Hospital Clinical Events	7.9% [5.5%,10.9%] (33/418)	10.0% [7.3%,13.2%] (43/430)	-2.1% [-5.9%,1.7%]
Bleeding Complications	1.0% [0.3%,2.4%] (4/418)	1.4% [0.5%,3.0%] (6/430)	-0.4% [-1.9%,1.0%]
Vascular Complications	5.0% [3.1%,7.6%] (21/418)	4.0% [2.3%,6.3%] (17/430)	1.1% [-1.7%,3.9%]
Stent Thrombosis	0.5% [0.1%,1.7%] (2/418)	0.5% [0.1%,1.7%] (2/430)	0% [-0.9%,0.9%]
Survival at 30 Days (K-M)	100% [99.1%,100%]	99.8% [99.3%,100%]	0.2% [-0.1%,0.6%]
Survival at 180 Days (K-M)	99.3% [98.4%,100%]	99.3% [98.4%,100%]	0% [-1.1%,1.1%]
MACE rate at 6 Months	11.5% [8.6%,14.9%] (48/418)	13.0% [10.0%,16.6%] (56/430)	-1.5% [-6.0%,2.9%]
Hospitalization Post-Intervention (days)			
Mean±SD (N)	1.4±0.9 (418)	1.5±1.7 (430)	-0.2 (-0.4,0.0)
Range (min,max)	(1,8)	(0,26)	

Technical success: Attainment of <50% residual stenosis (by QCA) and successful delivery and deployment of the assigned stent to the target lesion, without use of a device outside the assigned treatment strategy.

Procedure success: <50% diameter stenosis using the assigned device and no in-hospital major adverse cardiac events (death, MI, emergent CABG, or repeat target lesion revascularization).

QCA: Quantitative Coronary Angiography

% DS: Diameter Stenosis

TLR-free: No target lesion revascularization.

TVF-free: No death, any MI or target vessel revascularization.

In-hospital clinical event: Death, MI, emergent CABG, repeat target lesion revascularization, stent thrombosis, or stroke prior to discharge, as determined by the independent Clinical Events Committee.

Out-of-hospital clinical event: Death, MI, emergent CABG, repeat target lesion revascularization, stent thrombosis, or stroke after discharge, as determined by the independent Clinical Events Committee.

Bleeding complications: Transfusions due to blood loss resulting from the percutaneous revascularization procedure.

Stent Thrombosis: Angiographic thrombus or subacute closure within the stented vessel, or any death not attributed to a non-cardiac cause in the absence of documented angiographic stent patency within the first 30 days.

MACE: Major Adverse Cardiac Event (includes death, MI, emergent CABG and target lesion revascularization).

**Survival estimates by Kaplan-Meier method; Standard Error estimates by Greenwood formula.*

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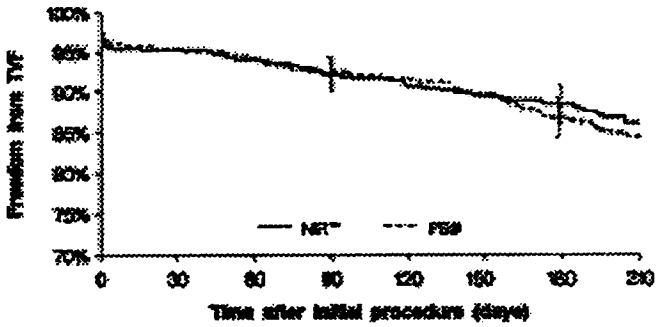
Figure 1. Actuarial Freedom from Target Vessel Failure

All Randomized Patients NIRVANA Randomized Trial (n=848)



Interval ending (days)	0	7	14	30	60	90	120	180	210
NIR™ Stent									
# Entered	418	403	399	399	395	386	378	372	333
# Incomplete	0	0	0	3	4	0	0	30	127
# Lost to Follow-up	0	0	0	0	0	0	0	0	0
# At Risk Entering Interval	418	403	399	396	391	386	378	342	206
# Events	15	4	0	1	5	8	6	9	7
# Events/Month		17	0	2	5	8	6	5	7
% Survived	96.4%	95.5%	95.5%	95.2%	94.0%	92.1%	90.6%	88.4%	86.0%
PS® Stent									
# Entered	430	419	410	407	400	386	378	374	323
# Incomplete	0	3	2	5	9	1	0	32	118
# Lost to Follow-up	0	0	0	0	0	0	0	0	0
# At Risk Entering Interval	430	416	408	402	391	385	378	342	205
# Events	11	6	1	2	5	7	4	19	7
# Events/Month		26	4	4	5	7	4	10	7
% Survived	97.4%	96.0%	95.8%	95.3%	94.1%	92.4%	91.4%	86.7%	84.4%

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Table 5 shows the principal effectiveness and safety results for the two registries. Although statistical comparison is not appropriate, results of the NIR™ arm of the NIRVANA Randomized Trial are included for comparison with these two registries.

Table 5. Principal Effectiveness and Safety Results, NIRVANA Registries

NIRVANA AC/TC Registry and SVG Registry Patients Treated (n=362)

Efficacy Measures	AC/TC n=207	SVG n=155	Randomized NIR™ n=418
Technical Success by QCA	96.8% [93.3%,98.8%] (184/190)	98.6% [95.1%,99.8%] (144/146)	99.8% [98.6%,100%](406/407)
Procedure Success by QCA	90.5% [85.4%,94.3%] (172/190)	96.6% [92.25%,98.9%] (141/146)	95.6% [93.1%,97.4%](389/407)
Post Procedure In-Stent % DS	9%±12% (196)	6%±13% (154)	7%±10% (409)
Range (min,max)	(-41%,47%)	(-23%,100%)	(-39%,39%)
TLR-free at 30 Days* (K-M)	99.1% [97.6%,100%]	98.8% [97.1%,100%]	99.3% [98.5%,100%]
TVF-free at 30 Days* (K-M)	91.8% [88.0%,95.5%]	96.1% [93.1%,99.2%]	95.2% [93.2%,97.3%]
6 Months Follow-up In-Stent % DS	37%±21% (35)	36%±32% (36)	34%±22% (110)
Range (min,max)	(-4%,84%)	(-12%,100%)	(-31%,100%)
6 Months Follow-up In-Stent Binary Restenosis Rate	25.7% [12.5%,43.3%] (9/35)	25.0% [12.1%,42.2%] (9/36)	20.0% [13.0%,28.7%] (22/110)
TLR-free at 6 Months* (K-M)	84.6% [79.6%,89.7%]	92.0% [87.6%,96.3%]	94.1% [91.9%,96.4%]
TVF-free at 6 Months* (K-M)	74.8% [68.7%,80.9%]	83.6% [77.6%,89.6%]	88.4% [85.3%,91.5%]
Safety Measures			
In-Hospital Clinical Events	7.2% [4.1%,11.7%] (15/207)	3.2% [1.1%,7.4%] (5/155)	4.3% [2.6%,6.7%] (18/418)
Out-of-Hospital Clinical Events	17.4% [12.5%,23.3%] (36/207)	13.5% [8.6%,20.0%] (21/155)	7.9% [5.5%,10.9%] (33/418)
Bleeding Complications	4.3% [2.0%,8.1%] (9/207)	2.6% [0.7%,6.5%] (4/155)	1.0% [0.3%,2.4%] (4/418)
Vascular Complications	7.2% [4.1%,11.7%] (15/207)	3.2% [1.1%,7.4%] (5/155)	5.0% [3.1%,7.6%] (21/418)
Stent Thrombosis	1.0% [0.1%,3.4%] (2/207)	1.3% [0.2%,4.6%] (2/155)	0.5% [0.1%,1.7%] (2/418)
Survival at 30 Days (K-M)	98.0% [97.7%,100%]	99.3% [98.1%,100%]	100% [99.1%,100%]
Survival at 180 Days (K-M)	97.0% [94.6%,99.4%]	95.9% [92.7%,99.1%]	99.3% [98.4%,100%]
MACE rate at 6 months	22.7% [17.2%,29.0%] (47/207)	16.1% [10.7%,22.9%] (25/155)	11.5% [8.6%,14.9%] (48/418)
Hospitalization Post-Intervention (days) Mean±SD (N)	2.0±2.2 (207)	1.5±1.4 (155)	1.4±0.9 (418)
Range (min,max)	(1,15)	(1,9)	(1,8)

Technical success: Attainment of <50% residual stenosis (by QCA) and successful delivery and deployment of the assigned stent to the target lesion, without use of a device outside the assigned treatment strategy.

Procedure success: <50% diameter stenosis using the assigned device and no in-hospital major adverse cardiac events (death, MI, emergent CABG, or repeat target lesion revascularization).

QCA: Quantitative Coronary Angiography

% DS: Diameter Stenosis

TLR-free: No target lesion revascularization.

TVF-free: No death, any MI or target vessel revascularization.

In-hospital clinical event: Death, MI, emergent CABG, repeat target lesion revascularization, stent thrombosis, or stroke prior to discharge, as determined by the Independent Clinical Events Committee.

Out-of-hospital clinical event: Death, MI, emergent CABG, repeat target lesion revascularization, stent thrombosis, or stroke after discharge, as determined by the Independent Clinical Events Committee.

Bleeding complications: Transfusions due to blood loss resulting from the percutaneous revascularization procedure.

Stent Thrombosis: Angiographic thrombus or subacute closure within the stented vessel, or any death not attributed to a non-cardiac cause in the absence of documented angiographic stent patency within the first 30 days.

MACE: Major Adverse Cardiac Event (includes death, MI, emergent CABG and target lesion revascularization).

**Survival estimates by Kaplan-Meier method; Standard Error estimates by Greenwood formula.*

The NIR ON™ Ranger™ w/SOX™ Studies were conducted to demonstrate the safety at 14 days of the over-the-wire version of the delivery system (NIR ON™ Ranger™ w/SOX™) as compared to the rapid exchange version used in the NIRVANA Trial. MACE-free rate at 14 days was 100% for the 162 treated with the NIR™ stent in the NIR ON™ Ranger™ w/SOX™ Native Arteries Registry compared to 95.7% for the 418 patients in the NIRVANA Randomized Trial, difference 4.3% [4.28, 4.32%].

7 PATIENT SELECTION and TREATMENT

7.1 Individualization of Treatment

The risks and benefits described above should be carefully considered for each patient before use of the NIR ON™ Ranger™ w/SOX™ Premounted Stent System. Patient selection factors to be assessed should include a judgment regarding risk of prolonged anticoagulation. Stenting is generally avoided in those patients at heightened risk of bleeding (e.g., those patients with recently active gastritis or peptic ulcer disease, see 3 CONTRAINDICATIONS).

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Premorbid conditions that increase the risk of poor initial results or the risks of emergency referral for bypass surgery (diabetes mellitus, renal failure, and severe obesity) should be reviewed. The relation of baseline and procedural variables to Target Vessel Failure (TVF) was examined. The only significant predictor of TVF was post-procedural mean Minimum Lumen Diameter (MLD). TVF was less likely with larger MLD.

Thrombosis following stent implantation is effected by several baseline angiographic and procedural factors. These include vessel diameter less than 3.0 mm, vessel thrombosis, poor distal flow, and/or dissection following stent implantation. In patients that have undergone coronary stenting, the persistence of a thrombus or dissection is considered a marker for subsequent thrombotic occlusion. These patients should be monitored very carefully during the first month after stent implantation because stent thrombosis may occur during this period.

7.2 Specific Patient Populations

The safety and effectiveness of the NIR ON™ Ranger™ w/SOX™ Premounted Stent System has not been established for patients with any of the following characteristics:

- Patients with **unresolved vessel thrombus at the lesion site.**
- Patients with coronary artery **reference vessel diameters < 2.5 mm.**
- Patients with **lesions located** in the unprotected left main coronary artery, ostial lesions, or lesions located at a bifurcation.
- Patients with **diffuse disease** or **poor outflow distal** to the identified lesions.
- Patients with recent **acute myocardial infarction** where there is evidence of thrombus or poor flow.
- Patients with **more than two overlapping stents** due to risk of thrombus.
- Patients for longer than 6 months follow-up.

The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters), or laser angioplasty catheters, to treat in-stent stenosis has not been established.

8 HOW SUPPLIED

STERILE: This device is sterilized with ethylene oxide gas. It is intended for single use only. Non-pyrogenic. Do not use if package is opened or damaged.

CONTENTS:

One (1) NIR ON™ Ranger™ w/SOX™ Premounted Stent System
One (1) envelope containing patient materials and tracking information
One (1) Instructions for Use Manual

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

9 OPERATOR'S INSTRUCTIONS

9.1 *Inspection Prior to Use*

Carefully inspect the sterile package before opening. Do not use after the "Use By" date. If the integrity of the sterile package has been compromised prior to the product "Use By" date (e.g., damage of the package), contact your local SCIMED Representative for return information. Do not use if any defects are noted.

9.2 Materials Required (not included in Stent System package)

Quantity	Material
	Appropriate guiding catheter(s) (see Table 1 - Balloon and Stent Specifications)
1	20 cc syringe
	Normal Heparinized Saline
1	≤0.014 inch x 300 cm length guidewire
1	Rotating hemostatic valve
	Diluted contrast medium 1:1 with normal heparinized saline
1	Inflation Device
1	Torque Device
1	Pre-deployment dilation catheter
Optional	Three-way stopcock

9.3 Preparation

Guidewire Lumen Flush

Step	Action
1	Flush Stent System guidewire lumen with normal heparinized saline.
2	Verify that the stent is positioned between the proximal and distal balloon markers. Check for bends, kinks and other damage. Do not use if any defects are noted.

Balloon Preparation

Step	Action
1	Rinse the stent in sterile saline.
2	Prepare inflation device/syringe with diluted contrast medium.
3	Attach inflation device/syringe to stopcock; attach to inflation port.
4	With tip down, orient Stent System vertically.
5	Open stopcock to Stent System; pull negative for 15 seconds; release to neutral for contrast fill.
6	Close stopcock to Stent System; purge inflation device/syringe of all air.
7	Repeat steps 4 through 6 until all air is expelled. If bubbles persist, do not use device.
8	If a syringe was used, attach a prepared inflation device to stopcock.
9	Open stopcock to Stent System.
10	Leave on neutral.

9.4 *Delivery Procedure*

Step	Action
1	Prepare the vascular access site according to standard PTCA practice.
2	Predilate the lesion/vessel with appropriate diameter balloon having a ratio of 1:1 with the diameter of the vessel.
3	Maintain neutral pressure on inflation device.
4	Backload Stent System onto proximal portion of guidewire while maintaining guidewire position across target lesion.
5	Fully open rotating hemostatic valve to allow for easy passage of the stent and prevent damage to the stent or displacement of the SOX™.
6	Ensure guiding catheter stability before advancing the Stent System into the coronary artery. Carefully advance the Stent System into the hub of the guiding catheter.
7	Note: If the physician encounters resistance to the Stent System prior to exiting the guiding catheter, **do not force passage.** Resistance may indicate a problem and may result in damage to the stent if it is forced. Maintain guidewire placement across the lesion and remove the Stent System as a single unit (see **4.3 Stent System Removal - Precautions**).
8	Advance Stent System over the guidewire to target lesion under direct fluoroscopic visualization. Utilize the proximal and distal radiopaque balloon markers as a reference point. If the position of the stent is not optimal, it should be carefully repositioned or removed (see **4.3 Stent System Removal - Precautions**). Expansion of the stent should not be undertaken if the stent is not properly positioned in the target lesion segment of the vessel.
9	Sufficiently tighten the rotating hemostatic valve. Stent is now ready to be deployed.

9.5 *Deployment Procedure*

Step	Action
1	Inflate the Stent System expanding the stent to a minimum pressure of 7 atm (deployment pressure). Higher pressures may be necessary to expand the stent to optimize stent apposition against the arterial wall. Balloon pressure must not exceed rated burst pressure. (See Table 6)
2	Maintain inflation pressure for 15-30 seconds for full expansion of the stent.
3	Deflate balloon by pulling negative on inflation device until balloon is fully deflated.
4	Confirm stent position and deployment using standard angiographic techniques. For optimal results, the entire stenosed arterial segment should be covered by the stent. Fluoroscopic visualization during stent expansion should be used in order to properly judge the optimum expanded stent diameter as compared to the proximal and distal coronary artery diameter(s). Optimal expansion requires that the stent be in full contact with the artery wall. All efforts should be taken to assure that the stent is not under dilated.
5	If stent sizing/apposition requires optimization, readvance the Stent System balloon, or another balloon catheter of the appropriate size, to the stented area using standard angioplasty techniques.

6	Inflate the balloon to the desired pressure while observing under fluoroscopy. Deflate the balloon. (See Table 6 for NIR ON™ Ranger™ w/SOX™ post deployment compliance.)
7	Reconfirm stent position and angiographic result. Repeat inflations until the desired result is achieved.

9.6 Removal Procedure

Step	Action
1	Ensure balloon is fully deflated.
2	Fully open rotating hemostatic valve
3	While maintaining guidewire position and negative pressure on inflation device, withdraw Stent System. **(see 4.3 Stent System Removal - Precautions)**

9.7 in vitro Information

Table 6. Typical NIR ON™ Ranger™ w/SOX™
Stent and Balloon Compliance Post Stent Deployment

	2.5 mm		3.0 mm		3.5 mm		4.0 mm	
atm	Stent (mm)	Balloon** (mm)	Stent (mm)	Balloon** (mm)	Stent (mm)	Balloon** (mm)	Stent (mm)	Balloon** (mm)
1.0	-	*2.31*	-	*2.77*	-	*3.21*	-	*3.69*
2.0	-	*2.35*	-	*2.81*	-	*3.27*	-	*3.75*
3.0	-	*2.38*	-	*2.86*	-	*3.33*	-	*3.81*
4.0	-	*2.42*	-	*2.91*	-	*3.39*	-	*3.87*
5.0	-	*2.46*	-	*2.95*	-	*3.45*	-	*3.93*
6.0 *Balloon nominal*	-	2.50	-	3.00	-	3.50	-	4.00
7.0 *Stent nominal*	2.50	2.53	3.00	3.05	3.50	3.56	4.00	4.06
8.0	2.55	2.57	3.06	3.09	3.57	3.62	4.08	4.12
9.0	2.59	2.61	3.13	3.14	3.65	3.68	4.17	4.18
10.0	2.64	2.64	3.19	3.18	3.72	3.72	4.25	4.23
11.0	2.69	2.66	3.25	3.20	3.79	3.76	4.33	4.26
12.0	2.73	2.69	3.29	3.23	3.84	3.79	4.38	4.29
13.0	2.76	2.71	3.32	3.25	3.88	3.82	4.42	4.33
14.0	2.79	2.73	3.36	3.27	3.92	3.86	4.46	4.36
15.0	2.82	2.75	3.39	3.30	3.96	3.89	4.51	4.40
16.0	2.85	2.77	3.42	3.32	4.00*	3.93*	4.55*	4.43*
17.0	2.88	2.80	3.45	3.34	-	3.96	-	4.47
18.0	2.91*	2.82*	3.49*	3.37*	-	3.99	-	4.50
19.0	-	2.84	-	3.38	-	4.03	-	4.54
20.0	-	2.86	-	3.42	-	4.06	-	4.57
21.0	-	2.88	-	3.44				
22.0	-	2.91	-	3.46				
23.0	-	2.93	-	3.49				

*Rated Burst Pressure. DO NOT EXCEED.
**Balloon Compliance Post Stent Deployment
Note: Numbers in *Italics* (1 through 5 ATM) are extrapolated values.

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10 PATIENT INFORMATION

In addition to this Instructions for Use, the NIR ON™ Ranger™ w/SOX™ is packaged with additional specific information which include:

- A Patient Implant Card that includes both patient information and stent implant information. All patients will be instructed to keep this card in their possession at all times for procedure/stent identification.
- A Patient Guide which includes information on coronary artery disease, the implant procedure and the NIR™ stent.
- A Device Tracking Form (Device Registration Card and Device Explant Card) which will be completed by the hospital staff and forwarded to SCIMED for the purposes of tracking all patients who have received a NIR™ stent, as required by Federal Regulation.

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