# SCIMED® RADIUS™ STENT WITH DELIVERY SYSTEM
# SUMMARY OF SAFETY AND EFFECTIVENESS DATA

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# SCIMED® RADIUS™ STENT WITH DELIVERY SYSTEM SUMMARY OF SAFETY AND EFFECTIVENESS DATA

## 1 GENERAL INFORMATION

Device Generic Name: ..... Intravascular Stent

Device Trade Name: ..... SCIMED® RADIUS™ Coronary Stent with Delivery System

Applicant's Name and Address:..... SCIMED Life Systems, Inc.
One SciMed Place
Maple Grove, MN 55311

PMA Application Number: ..... P970061

Date of Notice of Approval to the Applicant: .. July 16, 1998

## 2 INDICATIONS FOR USAGE

The SCIMED® RADIUS™ Coronary Stent with Delivery System is indicated for use in patients with symptomatic ischemic heart disease due to discrete *de novo* native coronary artery lesions (length < 30mm) with a reference vessel diameter ranging from 2.75 to 4.25 mm and is intended to improve coronary luminal diameter (see Individualization of Treatment). Long-term outcome (beyond 6 months) for this permanent implant is unknown.

## 3 DEVICE DESCRIPTION

The SCIMED RADIUS™ Coronary Stent with Delivery System **(Figure 1)** includes:

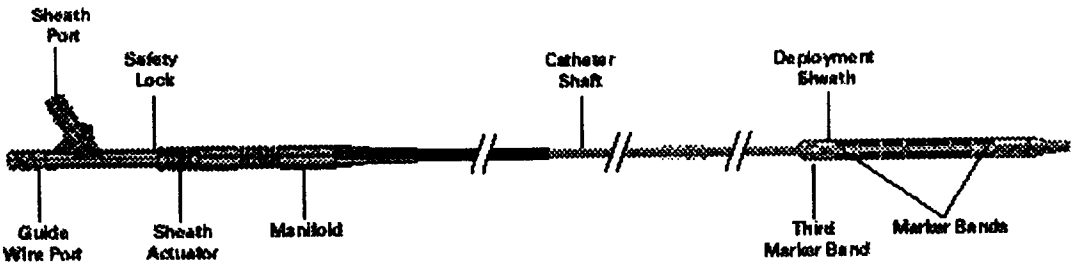
- a self-expanding nitinol multi-segmented stent premounted on an over-the-wire delivery catheter;
- a retractable deployment sheath that completely covers the stent on the delivery catheter;
- a safety lock located on the catheter manifold which is removed prior to stent deployment;
- a sheath actuator located on the catheter manifold which is retracted when stent deployment is desired;
- two radiopaque markers which aid in the accurate placement of the stent and a third radiopaque marker which allows monitoring of sheath retraction.

**Table 1: Stent Specifications**

| STENT ORDER NUMBER | LABELED STENT DIAMETER (mm) | MAXIMUM STENT DIAMETER (mm) | STENT LENGTH AT LABELED DIAMETER (mm) | MINIMUM GUIDE CATHETER I.D. (inches) |
|---|---|---|---|---|
| RAD 14/3.0 | 3.0 | 3.75 | 14 | .066 |
| RAD 14/3.5 | 3.5 | 4.25 | 14 | .066 |
| RAD 14/4.0 | 4.0 | 4.75 | 14 | .066 |
| RAD 20/3.0 | 3.0 | 3.75 | 20 | .066 |
| RAD 20/3.5 | 3.5 | 4.25 | 20 | .066 |
| RAD 20/4.0 | 4.0 | 4.75 | 20 | .066 |

The RADIUS over-the-wire Delivery System has a stent deployment sheath covering the stent which is retracted when stent deployment is desired. The stent is deployed by retracting the sliding sheath actuator located on the catheter manifold; the stent self-expands. A safety lock, located behind the sheath actuator, prevents accidental deployment. Two radiopaque markers are located under the sheath to aid in stent placement. A third marker, located under the proximal end of the sheath allows physicians to monitor sheath retraction.

**Figure 1: RADIUS Stent Delivery System**




# 4 CONTRAINDICATIONS

The SCIMED RADIUS Stent is contraindicated for use in:

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

# 5 WARNINGS AND PRECAUTIONS

*See WARNINGS AND PRECAUTIONS in the final draft labeling (Information for Use).*

# 6 ADVERSE EVENTS

## 6.1 OBSERVED ADVERSE EVENTS:

**Table 2: Summary of Trial Patient Enrollment**

| CLINICAL TRIAL PATIENT ENROLLMENT<br>Patients considered for and met enrollment criteria with signed Informed Consent Form<br>(N=1373) | | | |
|---|---|---|---|
| | RADIUS | Palmaz-Schatz® | Total |
| Feasibility Study | 103 | - | 103 |
| SCORES Roll-in Phase | 173 | - | 173 |
| SCORES Deregistered | 1 | - | 1 |
| SCORES Randomized Trial | 545 | 551 | 1096 |
| *De Novo* subgroup | 497 | 491 | 988 |
| ASSURE subgroup | 36 | 30 | 66 |

### 6.2 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 and 4):

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

## 7 Alternative Practices and Procedures

Alternative treatments of coronary atherosclerotic disease include, diet, medication (e.g. thrombolysis), atherectomy, balloon angioplasty, coronary artery bypass (CABG) surgery or stenting with commercially available stents.

## 8 Marketing History

The SCIMED RADIUS Stent with Delivery System is registered for sale in The Netherlands, but is not currently marketed.

## 9 Summary of Preclinical Studies

### 9.1 Bench Testing

The following *in vitro* tests were performed in accordance with the *FDA Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices, May, 1994.*

## Table 3: Summary of Delivery Catheter Testing

| Test | Samples Tested | Specification | Results |
|---|---|---|---|
| Catheter Profile | (n=30)<br>15 original delivery catheters<br>15 modified delivery catheters | original catheter specification<br>distal tip = 0.024" - 0.034"<br>sheath = 0.057" - 0.063"<br>distal<br>shaft = 0.036" - 0.047"<br>proximal<br>shaft = 0.40" - 0.045"<br>modified catheter specification<br>distal tip = 0.026" - 0.034"<br>sheath = 0.053" - 0.059"<br>distal<br>shaft = 0.043" - 0.049"<br>proximal<br>shaft = 0.42" - 0.052" | distal tip mean±SD (range) inches<br>original 0.28±0.002 (0.024,0.032)<br>modified 0.030±0.0009 (0.029, 0.032)<br><br>sheath mean±SD (range) inches<br>original 0.060±0.001 (0.058, 0.062)<br>modified 0.056±0.0004 (0.056, 0.057)<br><br>distal shaft mean ±SD (range) inches<br>original 0.044±0.002 (0.041, 0.045)<br>modified 0.045±0.0006 (0.044, 0.046)<br><br>proximal shaft mean ±SD (range) inches<br>original 0.042±0.001 (0.041, 0.044)<br>modified 0.044±0.0004 (0.043, 0.045) |
| Distal Tip Bond Tensile | (n=25)<br>10 original delivery catheters<br>15 modified delivery catheters | original catheter specification<br>Distal tip bond tensile ≥2..0 lb<br>modified catheter specification<br>Distal tip bond tensile ≥1.12 lb | Distal tip bond tensile mean±SD (range) lb<br>original 5.22±0.43 (4.45, 5.73)<br>modified 3.77±0.51 (3.03, 5.17) |
| Full Catheter Tensile | (n=30)<br>15 original delivery catheters<br>15 modified delivery catheters | Full catheter tensile ≥2.0 lb | Full catheter tensile mean±SD (range) lb<br>original 3.33±0.33 (2.67, 3.91)<br>modified 3.10±0.35 (2.71, 3.76) |
| Full Catheter Compression | (n=25)<br>15 original delivery catheters<br>10 modified delivery catheters | Catheter must withstand minimum of 2 lb compressive load | original - no visible damage<br>modified - no visible damage |
| Stent Deploy-ment Force | (n=25)<br>15 original delivery catheters<br>10 modified delivery catheters | Deployment force <2 lb | Force mean±SD (range) lb<br>original 0.97±0.22 (0.62, 1.34)<br>modified 0.34±0.06 (0.23, 0.43) |
| Safety Lock Integrity | (n=25)<br>15 original delivery catheters<br>10 modified delivery catheters | Lock shall prevent deployment with minimum of 2 lb applied force | Force applied mean±SD (range) lb<br>original 5.76±1.11 (3.47, 8.05)<br>modified 26.4±2.8 (23.3, 30.8) |
| Proximal Dye Flow | (n=6)<br>5 modified delivery catheter<br>1GR II delivery system | Flow rates shall be comparable to a currently marketed 6F compatible delivery system | Flow mean±SD (range) ml/sec<br>modified 0.52±0.0200 (0.50, 0.54)<br>GR II 0.62±0.0046 (0.62, 0.63) |
| Catheter With-drawal Force | (n=20)<br>10 original delivery catheters<br>10 modified delivery catheters | original catheter specification<br>Withdrawal force <2.0 lb<br>modified catheter specification<br>Withdrawal force <1.12 lb | Force mean±SD (range) lb<br>original 0.65±0.35 (0.29, 1.21)<br>modified 0.46 (0.39, 0.55) |
| Sheath Security | (n=30)<br>15 original delivery catheters<br>15 modified delivery catheters | Security of stent shall not be compromised with ≥0.5 lb applied force to sheath | Force applied = 0.5 lb<br>original - no deployment observed<br>modified - no deployment observed |
| Pull Wire Integrity | (n=25)<br>15 original delivery catheters<br>10 modified catheters | Pull wire shall not shear following application of 1.0 in-lb torque and after 180° rotation | Integrity of wire remained in tact for all original and modified delivery catheters following application of 1.0 in-lb torque and after 180° rotation |

## Table 4: Summary of Finished Device Testing

| Test | Sample Tested | Specification | Results |
|---|---|---|---|
| Metal to Artery Percentage Calculation | calculation only | Metal to artery percentage ≤30% when expanded to labeled diameter | ≤30% metal to artery percentage when expanded to labeled diameter |
| Stent Foreshortening | (n=30)<br>15 14 mm stents (5 of each diameter)<br>15 20 mm stents (5 of each diameter) | Foreshortening ≤5% of stent constrained length when expanded to labeled diameter | 14 mm stent mean±SD (range) mm<br><br>3.0 mm 1.40±0.50 (0.91, 2.02)<br>3.5 mm 2.00±0.61 (1.06, 2.68)<br>4.0 mm 2.47±0.48(2.13, 3.29)<br><br>20 mm stent mean±SD (range) mm<br><br>3.0 mm 1.55±0.23 (1.34, 1.95)<br>3.5 mm 1.49±0.84 (0.80, 2.69)<br>4.0 mm 2.41±0.80 (1.39, 3.50) |
| Stent Expansion Uniformity | (n=15 stents, 5 of each diameter, 27 measurements per stent, 135 total angle measurements) | strut separation 40° ± 15° when expanded to labeled diameter | strut expansion mean±SD (range)° C<br><br>3.0 mm 40±5.12 (30, 52)<br>3.5 mm 40±4.33 (28, 52)<br>4.0 mm 40±3.03 (31, 50) |
| Austenitic final (Af) Transformation Temperature | (n=59)<br>original nitinol material<br>30, 14 mm (10 of each diameter)<br><br>widened trace element material<br>30, 14 mm (10 of each diameter)<br><br>centerless ground material<br>30, 14 mm (10 of each diameter) | Af ≤34° C | Af mean±SD (range) ° C<br><br>original nitinol material<br>all 14 mm 31.6±0.73 (30.7, 33.2)<br><br>widened trace element material<br>all 14 mm 32.5±0.48 (31.5, 33.6)<br><br>centerless ground material<br>all 14 mm 31.3±1.10 (30.0, 33.1) |
| Over-Expansion/Crack Initiation | (n=15, 5 of each diameter) | No strut damage observed at 40X following over-expansion up to 50% above labeled diameter | No damage observed |

## Table 4: Summary of Finished Device Testing, continued

| Test | Sample Tested | Specification | Results |
|---|---|---|---|
| Expansion Force/ Compression Resistance | (n=179)<br>original nitinol material<br>30, 14 mm (10 of each diameter)<br>28, 20 mm (9, 3.0mm/3.5mm)<br>(10, 4.0mm)<br><br>widened trace element material<br>30, 14 mm (10 of each diameter)<br>31, 20 mm (10, 3.0mm/3.5mm)<br>(11, 4.0mm)<br><br>centerless ground material<br>30, 14 mm (10 of each diameter)<br>30, 20 mm (10 of each diameter) | post-deployment maximum force ≤0.0ll lb/ mm at minimum recommended diameter<br><br>post-deployment minimum force ≥0.001 lb/ mm at maximum recommended diameter<br><br>post-deployment minimum compression resistance slope ≥0.020 lb/mm$^2$ | force mean±SD (range) lb/mm<br><br>original nitinol material post-deployment force<br>maximum all 14 mm 0.007±0.00146<br>minimum all 14 mm 0.004±0.00113 (0.002, 0.010)<br>resistance all 14 mm 0.050±0.0073 (0.035, 0.060)<br>maximum all 20 mm 0.007±0.0020<br>minimum all 20 mm 0.004±0.0013 (0.003, 0.009)<br>resistance all 20 mm 0.041±0.010 (0.023, 0.060)<br><br>widened trace element material post-deployment<br>maximum all 14 mm 0.006±0.0005<br>minimum all 14 mm 0.004±0.0003 (0.003, 0.007)<br>resistance all 14 mm 0.049±0.007 (0.038, 0.059)<br>maximum all 20 mm 0.006±0.0007<br>minimum all 20 mm 0.004±0.0006 (0.002, 0.007)<br>resistance all 20 mm 0.052±0.005 (0.042, 0.060)<br><br>centerless ground material post-deployment<br>maximum all 14 mm 0.007±0.0011<br>minimum all 14 mm 0.005±0.0009 (0.004, 0.009)<br>resistance all 14 mm 0.052±0.004 (0.042, 0.060)<br>maximum all 20 mm 0.007±0.0007<br>minimum all 20 mm 0.005±0.0005 (0.003, 0.008)<br>resistance all 20 mm 0.049±0.003 (0.040, 0.053) |

**Table 4: Summary of Finished Device Testing, continued**

| Test | Sample Tested | Specification | Results |
|---|---|---|---|
| Dimensional Verification | (n=15 for strut width and wall thickness, 5 from each of 3 lots, 30 measurements per lot)<br><br>(n=15 centerless ground stents for wall thickness, 5 from each of 3 lots, 40 measurements per lot)<br><br>(n=30 for unconstrained diameter, 10 of each stent diameter) | Segment strut width 0.0060"±0.0025"<br>Connecting strut width 0.007"±0.003"<br>Stent wall thickness 0.005"±0.002"<br>Unconstrained diameter post-deployment: 3.0 mm 3.75±0.20<br>3.5 mm 4.25±0.20<br>4.0 mm 4.75±0.20 | Segment strut mean±SD (range) inches<br><br>Lot 1: 0.00613±0.00034 (0.00570, 0.00684)<br>Lot 2: 0.00697±0.00034 (0.00634, 0.00780)<br>Lot 3: 0.00582±0.0002 (0.00536, 0.00628)<br><br>Connecting strut mean±SD (range)<br><br>Lot 1: 0.00697±0.00034 (0.00634, 0.00780)<br>Lot 2: 0.00680±0.00035 (0.00624, 0.00790)<br>Lot 3: 0.00694±0.00035 (0.00632, 0.00760)<br><br>Wall thickness mean±SD (range)<br><br>Lot 1: 0.00431±0.00014 (0.00400, 0.00454)<br>Lot 2: 0.00432±0.00017 (0.00392, 0.00464)<br>Lot 3: 0.00405±0.00017 (0.00370, 0.00452)<br><br>Centerless ground wall thickness mean±SD (range)<br>Lot 1: 0.00412±0.00015 (0.00390, 0.00450)<br>Lot 2: 0.00468±0.00011 (0.00445, 0.00490)<br>Lot 3: 0.00461±0.00013 (0.00430, 0.00482)<br><br>Unconstrained diameter mean±SD (range) mm<br>3.0mm: 3.74±0.043 (3.65, 3.81)<br>3.5mm: 4.26±0.029 (4.20, 4.30)<br>4.0mm: 4.72±0.031 (4.68, 4.78) |

## Fatigue Testing

Computer aided finite element analysis was performed to predict the stress fatigue life of the RADIUS Stent expanded to the minimum recommended vessel diameter, representing maximum stress conditions for a nitinol self-expanding stent. The analysis indicated that the RADIUS Stent operates safely within the calculated region of endurance stress to yield stress.

Stents were dynamically tested to a minimum of 400,000,000 cycles of pulsatile fatigue in a physiological solution, representing 10 years equivalent real time. During pulsatile testing, stents were distended over a range of 3% to 5% of the deployed diameter. No pitting, cracking,

corrosion, or other damage directly attributable to fatigue testing was observed. Surface cracks observed prior to testing did not exhibit crack growth following testing.

### 9.2 Shelf Life and Package Qualification Studies

Product stability testing of the SCIMED RADIUS Stent with Delivery System was performed. Testing indicated that the stent and delivery catheter perform within product specification and that sterility is maintained for up to one year. Based upon these results, an expiration date of 1 year has been established.

The packaging and packaged product were evaluated to provide assurance that it will withstand the hazards of the distribution environment. These tests included vibration and drop testing. Test results indicated that the package and product are not adversely affected by extreme conditions during shipping.

Due to temperature sensitivity of the nitinol stent material, the device packaging includes a temperature indicator label that will turn black if the packaged device has been exposed to temperatures in excess of 55° C (131° F). Testing was performed to demonstrate that the labels are a reliable indicator of exposure to excessive temperatures.

### 9.3 Biocompatibility Tests

The SCIMED RADIUS Stent is constructed of nitinol, a nickel-titanium alloy. Sufficient information from the literature exists to demonstrate biocompatibility of the material for use in an implantable device [1-3]. The biocompatibility of the stent and delivery catheter have been shown to be acceptable by performance of the following tests conducted in accordance with International Standard ISO-10993 and Good Clinical Laboratory Practice (GLP) for Nonclinical Laboratory Studies, 21 CFR, Part 58:

| | |
|---|---|
| Cytotoxicity | Sensitization |
| Hemolysis | Ames Mutagenicity |
| Acute Systemic Toxicity | 7-Day Muscle Implant |
| Intracutaneous Toxicity | Pyrogenicity (LAL) |

### 9.4 Animal Testing

Animal studies were conducted to evaluate the device design and response to implantation in a nondiseased swine coronary artery model. A total of 49 RADIUS Stents were implanted in 21 animals. Study endpoints were assessed at 72 hours, 28 days, 60 days, 180 days, and 1 year post implantation. Histological evaluation of vascular response and morphometric analysis of tissue reaction to stent implantation were performed on all stented vessel segments at each of the study endpoints. SEM analysis was performed to determine the relative rate and amount of reendothelialization at each time point. SEM analysis was also used to examine the mechanical and corrosion integrity of the stent surface following implantation.

Implantation of the RADIUS Stent did not cause excessive thrombus, clinically significant medial or adventitial damage, inflammation, or clinically significant neointimal formation. Stents were fully reendothelialized at 28 days. Results were determined to be within usual and expected

responses for the animal model and were comparable to historic results of other metallic stents reported in the literature. SEM analysis of explanted stents through 1 year post implantation showed no evidence of mechanical failure or surface corrosion.

An *in vivo* performance evaluation of the delivery catheter was also performed. Overall catheter performance was determined to be satisfactory, the catheter was compatible with accessory devices necessary for stent delivery, and the device was noted as providing a good stent/delivery combination.

## 10. SUMMARY OF CLINICAL STUDIES

As summarized in Table 2, a total of 1372 patients participated in two clinical studies, a non-randomized feasibility study (ESSEX) conducted in Europe and the Stent COmparative REStenosis (SCORES) randomized clinical trial. An IVUS substudy (ASSURE) was conducted as part of the SCORES trial to examine stent behavior at 6 months post-procedure as assessed by IVUS imaging.

### 10.2 ESSEX STUDY

**Purpose:** The primary objective of the ESSEX study was to assess the safety and feasibility of the SCIMED RADIUS Stent with Delivery System (referred to as the RADIUS Stent).

**Design:** The ESSEX study was a prospective, multicenter, non-randomized observational study. ESSEX conducted at 4 sites in Europe: 2 in The Netherlands, 1 in France, and 1 in Belgium.

**Description of Patients:** A total of 103 patients being treated for single elective stent implantation in a *de novo* or restenotic lesion with >50% stenosis, lesion length <14 mm were enrolled. Forty-four percent (44%) of the patients had unstable angina (Braunwald Class I and II); 54% of the patients had stable angina; and 7% had silent ischemia. Seventeen (17) patients required more than one stent, either because the original lesion was not completely covered or because of a proximal or distal dissection.

**Methods:** Computer assisted Quantitative Coronary Angiographic analysis (QCA) at baseline and immediately after the procedure was performed by a central laboratory. Intravascular Ultrasound (IVUS) was used for confirmation of optimal implantation and analyzed on-line by the investigator. Off-line analysis was subsequently carried out at a central core-laboratory. Clinical and angiographic data were analyzed using the intent-to-treat principle.

**Results:** Table 5 shows the salient results of the ESSEX study..

**Table 5: Principal Effectiveness and Safety Results – ESSEX Study**
All patients enrolled in the ESSEX study (N=103)

| | |
|---|---|
| **Efficacy Measures** | |
| Procedure Success by QCA | 100/103 (97%) |
| Diameter Stenosis (%) Post-Procedure | 15 ± 7.0% |
| MACE-free at 1 month | 100/103 (97%) |
| MACE-free at 6 months | 78/103 (76%) |
| In-stent Restenosis (all patients) | 21/100 (21%) |
| **Safety Measures** | |
| MACE at 1 month | 3/103 (2.9%) |
| MACE at 6 months | 25/103 (24%) |
| Major Bleeding complications** | 2/103 (1.9%) |
| Subacute Thrombosis | 0/103 (0.0%) |

*Procedure success = intended therapy successful (< 50% diameter stenosis, post-procedure) without in-hospital clinical events. (Clinical Events(MACE) = Death, MI, CABG, re-PTCA of target lesion)*

*Major bleeding complications = Bleeding complications leading to death, requiring blood transfusion and/or vascular surgery and/or producing a fall in hemoglobin of at least 5g/dl.*

## 10.3 SCORES TRIAL

The Stent COmparative REStenosis (SCORES) Trial, a multicenter, prospective, randomized, controlled clinical trial, compared the SCIMED RADIUS Stent with Delivery System (referred to as RADIUS Stent) to a commercially available stent.

**Purpose:** The objective of the SCORES trial was to demonstrate equivalency in target vessel failure (TVF) rates between the two stent treatments through 6 months post-procedure. Secondary outcome measures included procedural success, target lesion revascularization (TLR), TVR, major adverse cardiac events (MACE) rates, minor complications, and angiographic coronary restenosis rates (>50% diameter stenosis) at 6 month angiographic follow-up. Angiographic comparisons included: minimal lumen diameter (MLD), percent diameter stenosis at 6 months, acute lumen gain, and late lumen loss.

**Design:** A prospective, randomized, clinical trial conducted at 50 US centers compared the RADIUS stent to the PS stent. Randomization was stratified on lesion type (*de novo* or restenotic) and vessel size (≥2.75 mm to <3.0 mm and ≥3.0 mm to ≤4.25 mm in diameter). The randomized trial was preceded by a non-randomized roll-in phase (N-173).

**The primary endpoint** of this trial, was TVF, a composite of death, myocardial infarction (Q- and non-Q-wave MI), coronary artery bypass graft surgery (CABG) of the treated vessel, and repeat intervention of the treated vessel, through 6 months post-procedure. Secondary endpoints were procedure success, MACE through 6 months, TVR, TLR, minor complications through 6 months, and angiographic restenosis at 6 months post-procedure.

**Methods:** Pre-procedure and post-procedure coronary angiograms were analyzed by an independent angiographic core laboratory. An independent Data Safety Monitory Board (DSMB) reviewed MACE event rates and evaluated trends during the trial. An independent Clinical Events Committee adjudicated all MACE, TLR and TVR events.

The anticoagulation regimen administered was aspirin 325 mg/day for at least one year and Ticlopidine™ 250 mg twice daily for at least 30 days. Follow-up intervals were 2, 4 weeks and 6, 9 months. The study randomization was successful as both treatment groups were demographically equivalent. All randomized patients were included in the intent-to-treat efficacy analysis.

**Description of Patients:** Enrollment in the SCORES trial totaled 1270 patients. One hundred seventy three (173) patients were enrolled in the non-randomized roll-in registry and 1097 patients in the randomized trial. One patient was mistakenly randomized into the trial but did not receive treatment and was not counted (not included in Table 1). The resulting analyses are therefore based on 1096 patients (545 RADIUS, 551 PS).

Clinical follow-up to 6 months was reported for 1096 patients including 20 patients who received no stent, but were followed for adverse events. Clinical follow-up to 6 months was obtained on 987/1096 (90%) patients; 504/545 (93%) for the RADIUS treatment group, and 483/551 (88%) for the PS treatment group. Six month angiographic follow-up was obtained on 250/300 (83%) patients; 125/150 (83%) for the RADIUS treatment group, and 125/150 (83%) for the PS treatment group.

Patients were similar between the two groups. Mean ± SD age of the enrolled patients was 62 ± 11 years and 61 ± 11 years for the RADIUS and PS respectively. Most of the pateints, 385/545 (70%), receiving the RADIUS were male and 374/551 (68%) for the PS.

**Results:** Of the 545 patients receiving the RADIUS™ stent in the SCORES trail, 497 patients were treated for *de novo* lesions and 48 patients for restenotic lesions. The target vessel failure-free rate at 6 months was 89% for patients with *de novo* lesions and 64% for patients with restenotic lesions with an associated difference of 24% and 95% confidence interval of [9.0%, 40%]. Likewise, the Out-of-hospital MACE rate was 11% for patients with *de novo* lesions and 35% for patients with restenotic lesions with a difference of -24% [-39%, -11%]. Table 4 shows the results for the 988 patients treated for *de novo* lesions.

## Table 7: Principal Effectiveness and Safety Results for the SCORES Trial

Patients with *de novo* Lesions (N=988)

| EFFECTIVENESS MEASURES | | | |
|---|---|---|---|
| | RADIUS n=497 | PS n=491 | Difference [CI] |
| Technical Success by QCA x/n (%) | 485/494 (98.2) | 450/474 (94.9) | 3.2%[0.9%, 5.5%]* |
| Procedure Success by QCA x/n (%) | 478/494 (96.8) | 442/476 (92.9) | 3.9%[1.1%, 6.7%]** |
| In-Stent % Diameter Stenosis Post-procedure | 12.0±9.7 493 (-29.1, 41.3) | 12.1±9.4 457 (-21.5, 40.0) | -0.1%[-1.1%, 0.9%] |
| In-Stent % Diameter Stenosis at 6 Months Post-procedure | 36.8±19.9 112 (-18.1, 77.9) | 37.0±18.3 111 (2.0, 100.0) | -0.2%[-4.4%, 4.0%] |
| In-Stent Restenosis at 6 Months x/n (%) | 28/112 (25.0) | 21/111 (18.9) | 6.1%[-4.8%, 16.9%] |
| †TLR-free at 6 Months | 93.3%[91.5%, 95.1%] | 92.4%[90.5%, 94.4%] | 0.9%[-2.6%, 4.4%] |
| †TVR-free at 6 Months | 90.6%[88.5%, 92.7%] | 90.0%[87.8%, 92.3%] | 0.6%[-3.4%, 4.6%] |
| †TVF-free at 6 Months[1] | 88.6%[86.4%, 90.9%] | 87.4%[85.0%, 89.8%] | 1.2%[-3.1%, 5.5%] |
| **SAFETY MEASURES** | | | |
| | RADIUS n=497 | PS n=491 | Difference [CI] |
| MACE — In Hospital x/n (%) | 12/497 (2.4) | 12/491 (2.4) | 0.0%[-1.9%, 1.9%] |
| MACE — Out of Hospital x/n (%) | 52/497 (10.5) | 59/491 (12.0) | -1.6%[-5.5%, 2.4%] |
| MACE rate at 6 months x/n (%) | 63/497 (12.7) | 71/491 (14.5) | -1.8%[-6.1%, 2.5%] |
| Stent Thrombosis x/n (%) | 1/497 (0.2) | 2/491 (0.4) | -0.2%[-0.9%, 0.5%] |
| Vascular Complications[2] x/n (%) | 8/497 (1.6) | 4/491 (0.8) | 0.8% [-0.5%, 2.2%] |
| Bleeding Complications[3] x/n (%) | 79/497 (15.9) | 70/491 (14.3) | 1.6%[-2.8%, 6.1%] |
| Stroke/CVA x/n (%) | 4/497 (0.8) | 1/491 (0.2) | 0.6%[-0.3%, 1.5%] |

** Difference statistically significant*

*Technical success: Attainment of the final result of <50% residual stenosis of the target vessel using the assigned treatment device alone (i.e. without the use of other types of stents or new balloon devices).*

*Procedure success: Achievement of the final diameter stenosis of <50% of the target vessel using the assigned treatment device and any adjunctive device without occurrence of a MACE during the hospital stay.*

*QCA: Quantitative Coronary Angiography*

*% Diameter Stenosis (DS): Diameter Stenosis by QCA*

*Instent Restenosis: >50% DS*

*Target Lesion Revascularization (TLR) Free: No repeat PTCA or CABG performed on the coronary lesion originally treated in the trial. (K-M = actuarial freedom from TLR by Kaplan-Meier survival analysis).*

*Target Vessel Revascularization (TVR) Free: No Repeat PTCA or CABG performed on the coronary vessel originally treated in the trial. (K-M = actuarial freedom from TVR by Kaplan-Meier survival analysis).*

*Target Vessel Failure (TVF) Free: No death, Q-wave MI or non-Q-wave, CABG to the target vessel, and/or repeat intervention to the target vessel. (K-M = actuarial freedom from TVF by Kaplan Meier survival analysis).*

*Repeat Intervention: The return of a patient to the catheterization laboratory for re-insertion of a guiding catheter followed by a new angioplasty at the same site.*

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

*In-hospital clinical event: Any MACE occurring prior to hospital discharge, as determined by the Independent Clinical Events Committee.*

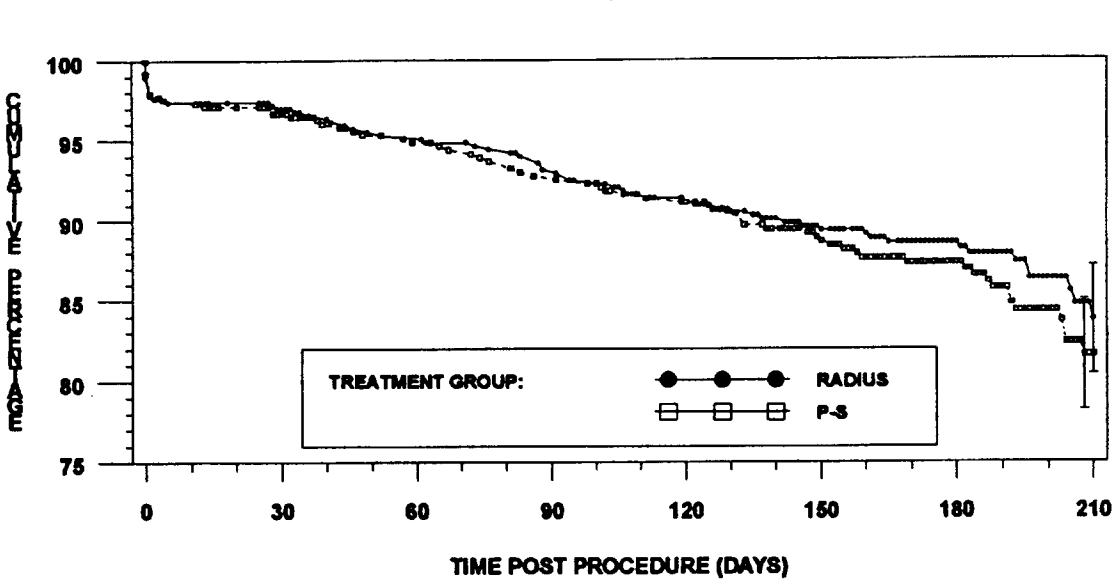
*Out-of-hospital clinical event: Any MACE occurring from hospital discharge up to six months of clinical follow-up, as determined by the Independent Clinical Events committee.*

*Stent Thrombosis: Any cardiac death, subacute closure requiring revascularization of the target site or total closure indicated by QCA within 30 days of the index intervention.*

*Vascular Complications: Any hematoma > 5 cm, arteriovenous fistula, pseudoaneurysm, retroperitoneal bleed, peripheral nerve disorder, and surgical repair.*

*Bleeding Complication: Hematoma, Hemorrhage, Significant access site bleeding, and Groin bleed.*

**Figure 2. Freedom From Any MACE: (Target Vessel Failure: TVF)**
Death, MI (Q-Wave and Non Q-Wave), CABG, Repeat Intervention
Event-Free Survival to 6 Months ± 1.5 SEM, Patients with *de novo* Lesions (N=988)




| | Time After Procedure (days) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | 0 | 7 | 14 | 30 | 60 | 90 | 120 | 150 | 180 | 210 |
| **RADIUS (n=497)** | | | | | | | | | | |
| **Number at Risk** | 497 | 490 | 482 | 479 | 463 | 448 | 435 | 422 | 380 | 257 |
| **Number of Events** | 5 | 13 | 13 | 15 | 23 | 33 | 41 | 50 | 53 | 61 |
| **% Survival** | 99.0 | 97.4 | 97.4 | 97.0 | 95.3 | 93.1 | 91.4 | 89.4 | 88.6 | 83.8 |
| **% SEM** | 0.5 | 0.7 | 0.7 | 0.8 | 1.0 | 1.2 | 1.3 | 1.4 | 1.5 | 2.2 |
| **Palmaz-Schatz (n=491)** | | | | | | | | | | |
| **Number at Risk** | 491 | 474 | 466 | 462 | 436 | 414 | 403 | 387 | 353 | 238 |
| **Number of Events** | 4 | 12 | 14 | 16 | 24 | 33 | 40 | 50 | 55 | 66 |
| **% Survival** | 99.2 | 97.5 | 97.5 | 96.7 | 94.9 | 92.8 | 91.2 | 88.7 | 87.4 | 81.6 |
| **% SEM** | 0.4 | 0.7 | 0.8 | 0.8 | 1.0 | 1.2 | 1.3 | 1.5 | 1.6 | 2.3 |

*Difference not statistically significant by product-limit estimates (Kaplan-Meier) Log Rank or Wilcoxon Chi-Square*

## 10.4 ASSURE SUBSTUDY

**Purpose:** The primary objective of the ASSURE substudy was to compare the deployment geometries between the RADIUS Stent and the Palmaz-Schatz Stent in coronary arteries. The secondary objective was to compare stent and intimal hyperplastic volumes at 6 months.

**Design:** This IVUS study was conducted as a substudy of the SCORES Trial and involved 66 of the randomized SCORES. ASSURE compared the *in vivo* behavior of, and the vascular response to, the RADIUS Stent (N=36) and the PS Stent (N=30) by viewing and comparing ultrasonic images of the target lesion site at baseline, post-procedure, and at 6 month follow-up.

The SCORES protocol allowed the use of IVUS upon the discretion of the investigator to aid in stent deployment. The SCORES protocol was not altered by the ASSURE substudy, except that

investigators participating in the ASSURE substudy were masked to IVUS results. Ultrasonic images were obtained after pre-dilatation (prior to stent placement), following post-dilatation (after angiographic optimization of stent deployment), and at 6-month angiographic follow-up.

**Methods:** Ultrasonic images were obtained after pre-dilatation (prior to stent placement), following post-dilatation (after angiographic optimization of stent deployment), and at 6-month angiographic follow-up.

Case report forms were completed at the site and forwarded to an independent IVUS core laboratory. Recordings of each video case were reviewed at the core lab. Selected video frames representing the cross-sectional ultrasound scans within, distal to and proximal to the lesion were digitized and stored on a computer disk for analysis.

Ultrasonic parameters of acute and 6-month stent diameter, acute and 6-month minimum lumen diameter and neointimal volume at 6 months post-procedure for each patient population were statistically analyzed and compared. Other procedural parameters studied included stent apposition, frequency of stent edge tears, stent symmetry index (stent major axis divided by minor axis after procedural stent opt8imization), and stent conformity index (stent diameter variation as a function of stent length: indicates ability of stent to conform to vessel tapering).

**Table 8: Principal Effectiveness and Safety Results - ASSURE Substudy**
**All patients enrolled in the ASSURE substudy (N=66)**

| Procedural Results | RADIUS (n=36) | PS (n=30) | p-value |
|---|---|---|---|
| Average Reference Vessel Area ($mm^2$) | 8.9 ± 3.22 | 8.3 ± 3.21 | ns |
| Stents per Procedure | 1.1 ± 0.4 | 1.1 ± 0.4 | ns |
| Balloon/Artery Area | 1.17 ± 0.26 | 1.16 ± 0.31 | ns |
| Balloon Size (mm) | 3.5 ± 0.3 | 3.4 ± 0.4 | ns |
| Maximum Balloon Pressure (atm) | 11.90 ± 3.88 | 15.57 ± 2.86 | 0.0004 |
| Minimum Stent Area ($mm^2$) | 6.4 ± 2.01 | 6.8 ± 1.20 | ns |
| Incomplete Stent Apposition (%) | 19.4 | 20.0 | ns |
| Stent Symmetry Index | 0.82 ± 0.09 | 0.82 ± 0.08 | ns |
| Stent Conformity Index | 1.51 ± 0.29 | 1.30 ± 0.14 | <0.01 |
| Edge Tears (%) | 8.3 | 23.3 | ns |
| **Six Month Follow-up Results** | **RADIUS (n=36)** | **PS (n=30)** | **p-value** |
| Stent Volume - Baseline ($mm^3$) | 121.9 ± 36.3 | 144.2 ± 62.8 | ns |
| Stent Volume - 6 month f/u ($mm^3$) | 146.5 ± 47.2 | 136.0 ± 52.2 | ns |
| Intimal Hyperplasia Index | 32.9% | 21.6% | ns |
| Late Lumen Loss ($mm^2$) | 1.76 ± 2.29 | 2.97 ± 2.57 | 0.06 |

**Limitations:** The study has completed follow-up on a limited number of patients (20/66, 30%). The biologic variation between the two arms of the substudy is unknown. Also, due to the need to pass an IVUS catheter through the lesion site in order to obtain measurement data, only cases with sufficient lumens to allow for catheter passage can be analyzed. This creates a study bias toward patients with larger lumens at follow-up.

### 10.5 Gender Bias Analysis

Inclusion criteria, exclusion criteria and study enrollment procedures were designed to avoid gender bias. This fraction of males in the SCORE trial (743/1075 = 69%) is typical of the relative referral rates for coronary intervention.

## 11 Conclusions Drawn from Studies

Random clinical results show that the RADIUS Stent is comparable to a U.S. commercially available coronary stent (control stent) in the treatment of *de novo* native coronary artery lesions.

The preclinical testing information and the results of the clinical trial provide valid scientific evidence and reasonable assurance that the RADIUS Stent with Delivery System is safe and effective when used in accordance with its labeling.

## 12 Panel Recommendations

This PMA was not referred to the Circulatory Systems Devices Panel for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this Panel. This decision was in accordance with the provisions of section 515( c)(2) of the Federal Food, Drug, and Cosmetic Act as amended by the Safe Medical Devices Act of 1990

## 13 FDA Decision

FDA performed an inspection and found the applicant in compliance with the Quality System Regulation (21 CFR Part 820).

FDA issued an approval order on July 16, 1998

## 14 Approval Specifications

**Directions for Use:** See Final Draft Labeling (Information for Use)

**Hazards to Health from Use of the Device**: See INDICATIONS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE EVENTS in the labeling.

**Post-approval Requirements and Restrictions**: See Approval Order

## 15 References


1. Castleman LS, Motzkin SM, Alicandri FP, et al. Biocompatibiliy of Nitinol Alloy as an Implant Material. *Journal of Biomedical Materials Research* 1976; 10:695-731.
2. Cragg AH, De Jong SC, Barnhardt WH, et al. Nitinol Intravascular Stent: Results of Preclinical Evaluation. *Radiology* 1993; 189:775-778.
3. Prince MR, Salzman EW, Schoen, FJ, et al. Local Intravascular Effects of the Nitinol Blood Clot Filter. *Investigative Radiology* 1998; 23:294-300.