



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
1390 Piccard Drive  
Rockville, MD 20850

Ms. April Lavender  
Manager, Regulatory Affairs  
Cook, Inc.  
925 South Curry Pike  
P.O. Box 489  
Bloomington, Indiana 47402

MAY 28 1993

Re: P910030  
Gianturco-Roubin Flex-Stent™ Coronary Stent  
Filed: June 6, 1991  
Amended: August 20 and December 3, 1991; February 20, March 26, April 6  
and 27, June 1 and December 28, 1992; January 6, 1993 and  
April 6, 1993

Dear Ms. Lavender:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Gianturco-Roubin Flex-Stent™ Coronary Stent. This device is indicated for chronic placement in a coronary artery or graft to obtain vessel patency in the treatment of acute or threatened closure associated with an interventional procedure. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

Expiration dating for this device has been established and approved at 24 months. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(8).

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act.

The device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the approved labeling specifies the requirements that apply to the training of physicians who may use the device.

In addition to the postapproval requirements in the enclosure, the postapproval reports shall include the following information:

1. Provide 6-month follow-up information on an initial cohort of 75 patients having undergone stenting of a saphenous vein bypass graft(s) and who are classified as initial successes. The report

93M.0212

AAV1

of the data shall be formatted similar to your PMA. This information is required to establish the long-term effects of the device in saphenous vein bypass grafts.

2. Provide follow-up information on an initial cohort of patients documented as developing a coronary pseudoaneurysm(s) following stent implantation. All such patients should be followed on at least a yearly basis for the life of the patients. This information is required to establish the ultimate fate of arteries in which this complication manifests itself.

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the act.

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to expedite processing.

PMA Document Mail Center (HFZ-401)  
Center for Devices and Radiological Health  
Food and Drug Administration  
1390 Piccard Drive  
Rockville, Maryland 20850

In addition, under Section 522(a) of the act, manufacturers of certain types of devices identified by the act or designated by FDA are required to conduct postmarket surveillance studies. FDA has identified under Section 522(a)(1)(A) the device cleared for marketing by this order as requiring postmarket surveillance.

Within thirty (30) days of first introduction or delivery for introduction of this device into interstate commerce you are required to submit to FDA certification of the date of introduction into interstate commerce, a detailed protocol which describes the postmarket surveillance study, and a detailed profile of the study's principal investigator that clearly establishes the qualifications and experience of the individual to conduct the proposed study. For your information, general guidance on preparing a protocol for a postmarket surveillance study is enclosed.

Page 3 - Ms. April Lavender

Submit five (5) copies to:

Postmarket Studies Document Center  
Room 408 (HFZ-107)  
12720 Twinbrook Parkway  
Rockville, Maryland 20852

Within sixty (60) days of receipt of your protocol, FDA will either approve or disapprove it and notify you of the Agency's action in writing. Do not undertake a postmarket surveillance study without an FDA approved protocol.

Failure to certify accurately the date of initial introduction of your device into interstate commerce, to submit timely an acceptable protocol, or to undertake and complete an FDA approved postmarket surveillance study consistent with the protocol, will cause your product to be misbranded and could lead to the imposition of civil money penalties or other regulatory actions. Any distribution of a misbranded device is a violation of the act and may result in a number of FDA enforcement actions, including (but not limited to) withdrawal of your PMA.

If you have questions concerning postmarket surveillance study requirements, contact the Postmarket Surveillance Studies Branch at (301) 227-8639.

If you have questions concerning this approval order, please contact Tara A. Ryan at (301) 427-1197 or Melpomeni K. Jeffries at (301) 427-1186.

Sincerely yours,



David L. West, Ph.D.  
Deputy Director  
Office of Device Evaluation  
Center for Devices and  
Radiological Health

Enclosure

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Name: Intravascular Stent

Device Trade Name: Gianturco-Roubin Flex-Stent™  
Coronary Stent

Applicant's Name and  
Address: Cook, Incorporated  
925 South Curry Pike  
Bloomington, IN 47402

PMA Number: P910030

Date of Panel Recommendation: May 11, 1992

Date of Approval to the Applicant: MAY 28 1992

II. Disease Description and Patient Population

A. Disease Description

Atherosclerosis is a progressive disease which causes subtotal stenosis or total occlusion of arteries. Patients with coronary atherosclerotic disease may experience chest pain, heart attack (myocardial infarction) or death due to lack of coronary blood flow. Percutaneous transluminal coronary angioplasty (PTCA) is an acceptable method of restoring blood flow and relieving symptoms of coronary atherosclerotic disease. It has the advantages of reduced patient discomfort, lower morbidity, and lower cost compared to coronary artery bypass graft (CABG) surgery.

However, despite the well-documented high rate of technical and long-term clinical success of conventional PTCA, there are instances where the PTCA procedure fails and the artery partially or totally occludes causing an emergency situation. Closure of the artery usually necessitates emergent CABG surgery and may cause myocardial infarction or death. The Gianturco-Roubin Flex-Stent™ Coronary Stent was developed to address this significant medical problem by providing a scaffold to hold open the lumen of the closed artery.

B. Indications for Use

The Gianturco-Roubin Flex-Stent™ Coronary Stent is indicated for chronic placement in a coronary artery or graft to obtain vessel patency in the treatment of acute or threatened closure associated with an interventional procedure.

### C. Contraindications

1. Patients with bleeding diathesis or other disorder, e.g., peptic ulceration or recent cerebrovascular accident, limiting the use of antiplatelet and anticoagulant therapy.
2. Patients with vessels measuring less than 2.0 mm in diameter.
3. Patients with significant vessel tortuosity and/or proximal atherosclerosis in whom adequate guiding catheter support or wire guide access is prohibited.
4. Patients with a large amount of untreated thrombus at the lesion site.

### III. Device Description

The Gianturco-Roubin Flex-Stent™ Coronary Stent is comprised of a stent/balloon catheter, a peel-away sheath introducer and a sidearm fitting. The balloon catheter is used to transport the stent to the desired position in the coronary vasculature and to mechanically distend the stent coil to its luminal diameter inside the coronary vessel. The stent is a continuous length of 316 LVM stainless steel wire that is premounted on the deflated balloon. Two radiopaque marker bands are situated inside the balloon for visualization under fluoroscopy. When the balloon is inflated, the stent expands proportionately with the expansion of the balloon. When the balloon is expanded to the recommended pressure, the luminal diameter of the stent will expand to its specified diameter. The peel-away sheath introducer protects the stent during introduction of the device through the Tuohy-Borst fitting and/or the proximal hub assembly of a coronary guiding catheter. The sidearm fitting is supplied for fluid control during the procedure. Five different size stents are available, ranging from 2.0 mm in diameter to 4.0 mm in diameter.

### IV. Alternate Practices and Procedures

Alternative practices specific to the treatment of acute or threatened closure of a coronary artery are repeat balloon angioplasty (either conventional or with an autoperfusion balloon), medication (e.g., thrombolysis), atherectomy, and emergency coronary bypass graft surgery.

V. Adverse Effects of the Device on Health

The following complications may occur during or following use of the Gianturco-Roubin Flex-Stent™ Coronary Stent:

Groin Hematoma  
Pseudoaneurysm  
Hematuria  
GI Tract Hemorrhage  
Intracranial Hemorrhage  
Angina Pectoris  
Vascular Thrombosis  
Total or partial closure of coronary artery or side branch  
Myocardial Infarction  
Death  
Fever  
Infection and pain at insertion site  
Hypotension  
Cardiac Arrhythmias  
Cardiac Ischemia  
Distal emboli (air, tissue or thrombotic emboli)  
Spasm  
Stroke  
Arterial perforation  
Ventricular fibrillation  
Body rejection or local tissue reaction  
Hemoptysis  
Infection  
Renal insufficiency  
Acute tubular necrosis  
Nausea and vomiting

VI. Marketing History

The device has not been previously marketed in the United States. Permission to export the device to Australia and Belgium has been obtained.

VII. Summary of Nonclinical Studies

A. In-Vitro (Laboratory) Studies

1. Biocompatibility

Gianturco-Roubin Flex-Stent™ Coronary Stents are made from special quality 316L medical grade stainless steel. Sufficient information from the literature was provided to demonstrate that this material has been shown to be a biocompatible implant material. The biocompatibility of the materials in the delivery catheter were shown to be acceptable for short-term

blood contact. The tests performed to establish biocompatibility were:

Irritation Test	Intracutaneous Toxicity
Sensitization Assay	Acute Systemic Toxicity
Cytotoxicity	Hemocompatibility/Hemolysis
Pyrogenicity	Implantation Tests
Mutagenicity	Thromboresistance Study
EtO Residual Analysis	

2. Balloon Burst Strength

Testing consistent with the PTCA Catheter System Testing Guidance Document was performed to determine the balloon catheter's performance properties, capability and reliability. To determine the inflation pressure at which the balloon will burst or a bond will fail, stents were removed from 75 finished balloon catheters and balloons were inflated in 10 p.s.i. increments until failure of the balloon or bond. Results demonstrate that statistically, with a 95% confidence, 99.9% of balloons will not burst at or below the rated burst pressure; therefore, the balloon strength and bond strength are sufficient for use at the rated burst pressures as labeled.

3. Balloon Deflatability Test Data

To determine that the balloon can be completely deflated after delivery of the stent, 5 balloons were inflated and deflated 30 times with a 50% mixture of Renografin-76 in water. Results revealed complete deflation under these test conditions.

4. Balloon Inflation/Deflation Test Data

To determine the time required for inflation and deflation of the balloon, 5 balloons were inflated with a 50% mixture of Renografin-76 in water using a 10 cc syringe. Results show that the time required for balloon inflation or deflation is approximately 5 seconds or less.

5. Balloon Repeat Inflation Test Data

To verify that the balloons can be repeatedly inflated without failure, 30 balloons were inflated 40 times each to pressures greater than or equal to 90 p.s.i. using a mixture of 50% Renografin-76 and 50% water. Results show no balloon failures or changes in the physical characteristics of the balloon.

6. Catheter Body Maximum Flow Rate and Pressure Test

To determine the maximum flow rate and pressure that the catheter body can withstand when contrast is injected through the lumen, Renografin-76 was injected, using a COOK injector,

through 10 catheters. Results demonstrate a 0.5 cc per second flow rate at a pressure of 540 p.s.i.

7. Hand Injection Flow Rate Test

To evaluate the flow rate of contrast agent that can be achieved through the main lumen of the Gianturco-Roubin Flex-Stent™ Coronary Stent balloon catheter by hand injection, four different subjects were instructed to inject 10 cc of Renografin-76 through the main lumen of each catheter as rapidly as possible using a 10 cc syringe. The minimum time required to inject 10 cc of Renografin-76 through the main lumen of a Gianturco-Roubin Flex-Stent™ coronary stent balloon catheter was 78.9 seconds. This corresponds to a maximum injection rate of 0.127 cc/second.

8. Pressure Waveform Test

To determine the natural frequency and the damping coefficient, 9 catheters were subjected to an abrupt pressure change to produce the step response from which the damping coefficient, overshoot, damped resonant frequency, and undamped natural resonant frequency were determined. Results show a damping coefficient of 0.57 and a damped frequency response of 26 Hz, which are sufficient for monitoring blood pressure.

9. Balloon Catheter Radiopacity Test

To determine the radiographic visibility of the balloon position on the balloon catheter, the balloon catheter with marker bands was x-rayed under a water phantom. Results demonstrate adequate visualization of the balloon position by identification of the marker bands.

10. Stent Material Verification

To determine the composition of the stainless steel wire used to construct the stent, the composition was analyzed by the wire manufacturer according to ASTM standard F138-86. Certification demonstrates appropriate chemical composition.

11. Stainless Steel Tensile Strength Test

To determine the tensile strength of the stainless steel and verify that the properties of the wire meet the design specifications for tensile strength, 6 samples of 0.006 inch diameter stainless steel wire were studied. Test results demonstrate an average peak load of 3.27 lbs. ± 0.0236 lbs., which complies with the design specifications.



## 12. Stainless Steel Stent Fatigue Test

To determine the fatigue properties of the stent under long-term implantation, short-term and long-term accelerated stress tests were performed. Flexure of 30 degrees at a rate of 120 cycles per minute for 3 million cycles representing 30 days in vivo demonstrated adequate short-term fatigue characteristics.

To examine long-term fatigue, 8 of the largest and 8 of the smallest diameter stents were flexed 30 degrees at 120 cycles per minute for 107 million cycles to date representing approximately 3 years after which microscopic examination for cracks, breaks, corrosion, and abrasion was performed. Results to date show no evidence of adverse material degradation.

In addition, 5 of the largest and 5 of the smallest diameter stainless steel stents were subjected to an accelerated fatigue test, undergoing approximately 375 million cycles. For a heart rate of 70 beats per minute, this represents the equivalent of 10 years and 70 days of continuous cycling. All 10 stents were removed from the test apparatus and viewed under a microscope at 50X magnification. No signs of corrosion, cracks, fractures or any other anomalies were observed on the surface of any of the stents.

A finite element analysis was conducted to identify the peak stresses in the stent when subjected to a worst case physiological load. Peak residual stresses were estimated based upon material properties and the final geometry of the stent when deployed. Physiologic levels of cyclic stress were superimposed on the residual stresses. The analysis indicates that a sufficient margin of safety exists between operating stresses and material strength and that fatigue failures are unlikely.

## 13. Stent Free Space Calculations

To determine the luminal surface area covered by the stent and the luminal volume reduction due to the stent, free space surface areas and volumes were calculated for each diameter. Results show that 83-91% of the luminal surface remains exposed to blood and 9-17% of the vessel wall is covered by stent material. Results also show that 96-99% of the luminal volume is open to flowing blood and 1-4% of luminal volume is occupied by the stent material. Therefore, adequate free surface area is available for branch vessels and adequate luminal volume is available for blood flow.

## 14. Stent Distensibility

To verify that stents will expand at or below the labeled stent expansion pressure and that the stents are the appropriate size

when inflated at the labeled pressure, the outer stent diameter was measured as a function of pressure. Results show statistically, with a 95% confidence, at least 99.9% of stents can be expected to expand to the proper diameter at the labeled stent expansion pressure.

15. Stent Recoil

To determine the amount of elastic recoil associated with deflation of the balloon after stent expansion, proximal, mid and distal stent outer diameters were measured with and without balloon support. Test results demonstrate the stent exhibits between 0.21 and 0.77 mm of elastic recoil after balloon deflation.

B. In Vivo (Animal) Studies

1. Stent Placement and Patency in Normal Arteries

A study was conducted to determine whether balloon-mounted flexible coil-like stents could be placed safely and precisely within coronary arteries using a percutaneous technique and to examine the immediate and long-term arteriographic patency and the histological response of the arterial wall. Thirty-nine (39) mongrel dogs had the stent placed after PTCA. The results of the in vivo model showed no early thrombotic events were associated with stent placement. Early (3-14 days) histological examination revealed mild thrombus localized to areas of wire entrenchment followed by rapid regrowth of endothelial cells over the trenches and exposed wires. Late (2-12 months) histologic examination revealed that the stented segments had thinning of the media, mild neointimal proliferation over the wires and an otherwise normal intimal surface.

2. Stent Placement and Patency in Atherosclerotic Arteries

A study was conducted to determine the effects of implanting flexible coil-like stents on arterial patency and intimal proliferation after balloon dilatation of atherosclerotic rabbit arteries. Fifteen (15) cholesterol-fed rabbits were studied for 4 weeks. In comparing stented arteries to arteries in the same subject treated by balloon angioplasty alone in the aspirin treated group, the stented vessels showed significantly improved luminal dimensions and limited progression of atherosclerosis.

3. Stent Thrombosis and Anticoagulation Therapy

A study was conducted on an atherosclerotic miniature swine model to analyze thrombosis prevention by 3 regimens: 1) anticoagulation and antiplatelet, 2) antiplatelet alone and

3) control. Twenty-eight (28) animals were studied. Anticoagulation therapy was shown not to affect intimal thickening at 1 month. Results indicated that occlusive thrombosis does not complicate stent implantation in this model, but substantial luminal narrowing, due in part to smooth muscle hyperplasia, can occur.

4. Effect of Magnetic Resonance Imaging (MRI)

To determine the effect of MRI on the stent and stented artery, a 3.0 mm diameter stent was placed in a fresh cadaver coronary artery which was then subjected to maximal MRI imaging energy. Images of the preparation taken immediately and after 20 minutes of MRI were compared to determine if any movement of the stent had occurred. Radiographs were taken before and after MRI in multiple views to exclude stent distortion. The specimen was subsequently examined histologically and compared to a heart that had been stented but not subjected to MRI. No adverse effects were noted. The small mass of the device (15 mg) and the fact that the wires do not make complete circumferential turns appear to prevent any detrimental effects from MRI.

VIII. Summary of the Clinical Investigations

A. Study Objectives

The main objective of this study was to determine the safety and effectiveness of using the Gianturco-Roubin Flex-Stent™ Coronary Stent to obtain vessel patency in the treatment of acute or threatened closure associated with an interventional procedure.

Specific Aims

1. To evaluate the ability to successfully implant the 20 mm long stainless steel Gianturco-Roubin Flex-Stent™ Coronary Stent.
2. To assess the ability of a successfully implanted stent to produce and maintain an open lumen in a segment of a coronary artery that has acutely closed or is in imminent danger of closing.
3. To determine the percent of patients that must subsequently undergo emergent or elective CABG surgery in spite of successful stent implantation.
4. To determine the incidence of myocardial infarction (MI) and the incidence of death after successful stent implantation.
5. To identify and quantitate complications likely associated with the stent implantation procedure.

6. To determine the long-term safety and effectiveness of implanting the Gianturco-Roubin Flex-Stent™ Coronary Stent.

Definitions - General

*Stent* - the Gianturco-Roubin Flex-Stent™ Coronary Stent, a single, non-crossing stainless steel scaffolding device for producing and maintaining an open coronary artery.

*Percent diameter stenosis* - the minimum luminal diameter of the coronary artery divided by its reference diameter (i.e., of a normal segment proximal to the lesion of interest) multiplied by 100.

*Acute Closure* - defined as TIMI 0 or TIMI 1 flow.

*Threatened Closure* - evidenced by deterioration of angiographic, electro-cardiographic, hemodynamic or clinical indicators from baseline values.

- Angiographic indicators may include diameter or area stenosis, reduced flow and vessel wall abnormalities (notably, dissection, intimal tears and irregular filling defects)
- Electrocardiographic indicators may include S-T segment elevation or depression, or arrhythmias
- Hemodynamic indicators may include increased left ventricular end diastolic pressure, increased pulmonary wedge pressure, decreased ejection fraction and decreased blood pressure
- Clinical indicators may include chest pain

Definitions - Acute Effectiveness

*In-Hospital Angiographic Success* - Reduction of stenosis by at least 20% in all lesions in which a stent was successfully implanted.

*In-Hospital Clinical Success After Stenting* - Angiographic success without In-hospital death, MI, or CABG. The incidence of MI, CABG and death were compared with these events in patients suffering periprocedural occlusion in the 1985-86 NHLBI PTCA Registry.

Definitions - Long-term Effectiveness

*Long-term Clinical Effectiveness* - reasonable incidence of CABG surgery, MI and death with respect to these events in patients suffering periprocedural occlusion in the 1985-86 NHLBI PTCA Registry.

*Long-term Angiographic Effectiveness* - retention of patency at 6 months based on mean diameter percent stenosis.

*Quantitative Cineangiographic Analysis* - analysis of pre-PTCA, post-PTCA, pre-stent, post-stent and 6-month follow-up cineangiograms using computer assisted angiographic analysis (CAAS) for accurate and unbiased determination of luminal diameters.

*6-Month Angiographic Restenosis Rate* - A loss of at least 50% of the gain achieved by the angioplasty/stenting procedure.

Definitions - Safety

*Acute Safety* - the analysis of in-hospital complications, device problems and adverse reactions.

*Long-term Safety* - the analysis of after-discharge complications, and long-term adverse reactions.

B. Feasibility Study

Seventeen (17) patients were involved in a Phase I study of an approved IDE to determine if clinical trials of the Gianturco-Roubin Flex-Stent™ Coronary Stent were safe to conduct. Stents were placed in coronary arteries of patients prior to CABG surgery.

The study showed feasibility and indicated that the trial would be safe to begin. Results also indicated the need for anticoagulation therapy after stent placement.

C. Multicenter Study

After IDE approval, 306 patients at 13 investigating centers were enrolled between August 18, 1988 and September 5, 1990. In these patients, 356 stent placements were attempted in 315 procedures. In 292 of 306 (95.4%) patients, 325 stents were placed in a coronary artery. Fourteen (14) patients did not receive stents and were analyzed separately. Failure to place a given stent appropriately was associated with: (1) deployment problems related to interactions of the stent delivery system and the coronary anatomy; (2) suboptimal stent placement; and (3) mechanical deployment problems. However, of these 14 patients, 2 underwent emergent CABG and 1 died; these results were included in the reported incidence of adverse events even though these 3 patients never received stents. Eight patients were successfully stented in each of 2 separate procedures. In 21 of 292 patients, stents were placed in grafts to coronary vessels. These were analyzed in combination with the native vessel stents for comparison to the NHLBI PTCA Registry Study, and separately, since bypass grafts have been reported to succumb to different stenotic mechanisms.

### Inclusion Criteria

1. Conditions associated with arteriographic and hemodynamic evidence of closure, imminent closure or threatened closure (e.g., recurrent rising gradient trends or inability to reduce the final trans-stenotic gradient below 15 mmHg or progressive reduction in lumen diameter over time) following repeated balloon inflations or dissection less than 20 mm in length.
2. Presence of collateral vessels to the vascular distribution of the stented arteries or vein grafts. Contralateral or ipsilateral vessels providing collaterals must not contain a  $\geq 50\%$  diameter stenosis at completion of the PTCA procedure; or, vascular distribution of the stented artery must be small or only moderate in size, that is:
  - a. right coronary or left circumflex arteries in a co-dominant system providing the contralateral vessel does not contain a  $\geq 50\%$  diameter stenosis after the procedure;
  - b. large branches of dominant right coronary or left circumflex arteries;
  - c. large diagonal branches of the left anterior descending artery;
  - d. left anterior descending artery at or beyond its mid portion or after the take off of large branches supplying the septal and diagonal territories.

### Exclusion Criteria

1. Diffuse, 3 vessel coronary artery disease ( $\geq 50\%$  diameter stenosis in 3 of the major coronary arteries and multiple stenoses  $\geq 50\%$  in any 1 of these arteries) in the absence of functional bypass grafts.
2. Moderate or severely impaired left ventricular dysfunction (ejection fraction  $< 35\%$ ).
3. Akinetic wall motion or Q waves in the distribution of the artery to be stented.
4. Diameter of the vessel  $< 2.0$  mm.
5. Distal segments beyond severe bend and branch points precluding stent placement.
6. Bleeding diathesis or other disorder (e.g., peptic ulceration or recent cerebrovascular accident) limiting the use of antiplatelet and anticoagulant therapy.

### Patient Population

Details of the patient demographics, disease status and other risk factors of patients at the time of enrollment are found in Table 1.

The characteristics of the stented patient population are compared to those of patients with similar interventional complications reported in previous studies who did not receive stents (Table 2). Logistical regression analysis and a test for the comparison of proportions were employed to validate the comparison of the treatment group and control (NHLBI) group with respect to the independent variables of sex, age, previous coronary artery bypass grafts, multivessel disease, and intimal tear or dissection.

Details of the vessel characteristics, lesion characteristics and of the stents implanted are presented in Table 3.

Table 1 Patient Population Demographics

	Gianturco-Roubin Flex-Stent™ Clinical Trial 9/20/88 - 9/6/90					
	Acute Closure (n=94)		Threatened Closure (n=198)		Total (n=292)	
	No.	(%)	No.	(%)	No.	(%)
Male	70	74.5	143	72.2	213	72.9
Female	24	25.5	55	27.8	79	27.1
Age ≥65 Years	32	34.0	64	32.3	96	32.9
Mean Age (yrs)	---	(57.8)	---	(59.2)	---	(58.8)
Acute MI	18	19.1	8	4.0	26	8.9
Coronary Bypass Grafts	2	2.1	19	9.6	21	7.2
Multivessel Disease	44	46.8	108	54.6	152	52.1
Intimal Tear or Dissection	69	73.4	159	80.2	228	78.1
Prior CABG	2	2.1	14	7.1	16	5.5
Prior MI	10	10.6	24	12.1	34	11.6
Prior PTCA	51	54.3	138	69.7	189	64.7
Prior Atherectomy	0	0.0	2	1.0	2	0.7
Ejection Fraction						
0-20%	0	0.0	0	0.0	0	0.0
21-30%	4	4.3	2	1.0	6	2.0
31-40%	9	9.6	14	7.1	23	7.9
41-50%	23	24.5	55	27.8	78	26.7
51-60%	26	27.7	44	22.2	70	24.0
60+%	12	12.8	26	13.1	38	13.0
Not Reported	20	21.3	57	28.8	77	26.4



Table 2 Comparison of Demographic Data Between the Patient Population Enrolled in the Gianturco-Roubin Flex-Stent™ Coronary Stent Clinical Trial and Those of Previous Reports of Periprocedural Occlusion after PTCA

	The NHLBI Registry 1985-86 (Detre, 1990)		From Simpfendorfer (1987)	From Ellis (1988)	From Anderson (1987)	From Nigel (1988)	Gianturco-Roubin Flex-Stent™ Clinical Trial 9/20/88 - 9/6/90		
	Successful PTCA (n=1,679) (%)	Periprocedural Occlusion (n=122) y(%)	Acute Closure (n=32) (%)	Acute Closure (n=210) (%)	Acute Closure (n=239) (%)	Acute Closure (n=54) (%)	Acute Closure (n=94) (%)	Threatened Closure (n=198) (%)	Total (n=292) (%)
Male	74.0	66.4	72.0	67.2	69.0	68.5	74.5	72.2	72.9
Female	26.0	33.6	28.0	32.8	31.0	31.5	25.5	27.8	27.1
Age ≥65 Years	26.9	29.9	NR	15.7	NR	NR	34.0	32.3	32.9
Mean Age (yrs)	NR	NR	(59)	NR	(56)	(59)	(57.8)	(59.2)	(58.8)
Acute MI	excluded	excluded	excluded	excluded	excluded	excluded	19.1	4.0	8.9
Coronary Bypass Grafts	3.8	4.4	excluded	excluded	excluded	1.9	2.1	9.6	7.2
Multivessel Disease	51.0	57.4	NR	23.6	27.0	NR	46.8	54.6	52.1
Intimal Tear or Dissection	46.0	78.7	78.0	72.8	NR	79.6	73.4	80.2	78.1
Prior CABG	12.6	12.3	NR	NR	NR	3.7	2.1	7.1	5.5
Prior MI	37.1	32.0	NR	NR	NR	53.7	10.6	12.1	11.6
Prior PTCA	NR	NR	NR	11.4	NR	NR	54.3	69.7	64.7

NR = This information was Not Reported

Table 3 Vessel, Lesion and Stent Characteristics

	ACUTE CLOSURE		THREATENED CLOSURE		TOTALS	
Number of Patients	94		198		292	
Number of Lesions	103		222		325	
Vessel Characteristics:						
	No.	%	No.	%	No.	%
Vessels Stented						
RCA	38	36.9	86	38.7	124	38.2
LAD	40	38.8	70	31.5	110	33.8
LCX	21	20.4	41	18.5	62	19.1
LM (Protected)	2	1.9	4	1.8	6	1.8
Graft to RCA	1	1.0	10	4.5	11	3.4
Graft to LAD	0	0.0	5	2.3	5	1.5
Graft to LCX	1	1.0	6	2.7	7	2.2
Location in Vessel						
Proximal	35	34.0	89	40.1	124	38.2
Middle	51	49.5	81	36.5	132	40.6
Distal	4	3.9	15	6.8	19	5.8
Branches	9	8.7	10	4.5	19	5.8
Graft-Proximal	1	1.0	3	1.4	4	1.2
Graft-Middle	0	0.0	13	5.9	13	4.0
Graft-Distal	1	1.0	6	2.7	7	2.2
LM (Protected)	2	1.9	4	1.8	6	1.8
Not Reported	0	0.0	1	0.5	1	0.3
Vessel Tortuosity						
None	49	47.6	121	54.5	170	52.3
Mild to Moderate	37	35.9	66	29.7	103	31.7
Severe	13	12.6	21	9.5	34	10.5
Not Reported	4	3.9	14	6.3	18	5.5

Table 3 is continued on the next page.

Table 3 Vessel, Lesion and Stent Characteristics (continued)

	ACUTE CLOSURE		THREATENED CLOSURE		TOTALS	
Lesion Characteristics:	No.	%	No.	%	No.	%
Shape						
Eccentric	72	69.9	168	75.7	240	73.8
Concentric	28	27.2	46	20.7	74	22.8
Not Reported	3	2.9	8	3.6	11	3.4
Lesion Length						
0-10 mm	58	56.3	111	50.0	169	52.0
10-20 mm	26	25.2	69	31.1	95	29.2
>20 mm	7	6.8	19	8.6	26	8.0
Not reported	12	11.7	23	10.4	35	10.8
Calcification						
Calcified	16	15.5	43	19.4	59	18.1
Not Calcified	85	82.5	172	77.5	257	79.1
Not Reported	2	1.9	7	3.1	9	2.8
Stent Sizes:						
2.0 mm	4	3.9	7	3.1	11	3.4
2.5 mm	44	42.7	79	35.6	123	37.8
3.0 mm	39	37.9	86	38.7	125	38.5
3.5 mm	14	13.6	33	14.9	47	14.5
4.0 mm	2	1.9	17	7.7	19	5.8

D. Safety and Effectiveness Data

Safety was evaluated by comparing the incidence of major clinical complications seen in this clinical trial with those reported in the 1985-86 NHLBI PTCA Registry. Effectiveness data included acute effectiveness, short-term effectiveness (1 month) and long-term effectiveness (6 months). Data from this study were evaluated using the NHLBI PTCA Registry data on similar patients who failed PTCA procedures as a reference.

Previously published reports indicate that acute closure occurs in 2-11% of all PTCA procedures. From the NHLBI registry of 1,801 patients, 122 patients had acute closure. The acute closure complication was treated with repeat PTCA (49%), with medication (16%), and with bypass surgery (35%). Additionally, 10% of those patients treated with repeat PTCA received bypass surgery before leaving the hospital, making the total in-hospital incidence of bypass surgery in the NHLBI patients with periprocedural occlusion 40.2%. The in-hospital incidence of MI in the NHLBI population was 42.0% and the incidence of in-hospital death was 5.0%. Cumulative values for CABG, MI and death through 6-month follow-up were 46.0%, 42.0% and 7.0%, respectively, for the NHLBI PTCA Registry patients. These results are corroborated in a study by Simpfendorfer (1987). It is to these NHLBI figures that the results of this study are compared.

1. Stent Placement Results

Stent placement was achieved for 325 of 356 stents (91.3%) in 292 of 306 patients (95.4%) during 300 of 315 procedures (95.2%). Of the 292 stented patients, 94 were stented for the indication of acute closure (Acute Closure Group) and 198 were stented for the indication of threatened closure (Threatened Closure Group).

Failure to place a given stent appropriately was associated with (1) deployment problems related to interactions of the stent delivery system and the coronary anatomy; (2) suboptimal stent placement; and (3) mechanical deployment problems (e.g., selection of too small a guiding catheter, or inability to pass the hub of the guiding catheter with the stent delivery catheter).

Twenty-one (21) deployment problems related to interactions of the stent delivery system and the coronary anatomy occurred in 18 patients. Nine of these 18 patients eventually received stents in the same procedure. Inability to reach the lesion (7), inability to cross the lesion (12) and inability to cross a previously implanted stent (2) were reasons reported for these deployment problems.

Suboptimal stent placement occurred in 2 patients. In one patient the balloon did not appear to inflate completely and the stent was moved from the distal to the mid portion of the intended lesion, where it remained safely deployed, as the balloon was withdrawn. In a second patient, the stent came off the balloon prematurely, but was safely deployed proximally to the intended site.

The following is a list of 10 occurrences of mechanical problems with deploying the device that investigators have reported, most of which occurred early in the study. These problems resulted in 4 patients not receiving a stent.

- Unable to pass hub of guiding catheter with stent delivery catheter (5 reports).
- Unable to view guidewire (1 report).
- Unable to track guidewire (1 report).
- Exchange wire undocked (1 report).
- Delivery catheter fit too tightly inside guide catheter (2 reports).

## 2. Acute Clinical Results

Acute clinical success was assessed by evaluating the impact of stenting on (1) the need for in-hospital CABG surgery, 2) the incidence of in-hospital MI, and (3) the in-hospital death rate (Table 4). The results from patients in the acute closure group were compared to those for the matched group of PTCA patients with periprocedural occlusion in the NHLBI Registry. The incidence of CABG surgery was significantly less in the stented group compared to the NHLBI periprocedural occlusion group (7.4% vs 40.2%;  $P < 0.001$ ). The incidence of MI was significantly less in the stented group compared to the NHLBI periprocedural occlusion group (8.5% vs 42.0%;  $P < 0.001$ ).

Table 4 Comparison of the Incidence of In-hospital Events between Patients Stented for Acute Closure in the Gianturco-Roubin Flex-Stent™ Coronary Stent Clinical Trial, Patients Suffering Periprocedural Occlusion after PTCA from the 1985-1986 NHLBI PTCA Registry, and Patients Undergoing Successful PTCA from the 1985-1986 NHLBI PTCA Registry

	Column A	Test of Proportions	Column B	Test of Proportions	Column C
	1985-86 NHLBI Registry (Detre, 1990)		Gianturco-Roubin Flex-Stent™ Clinical Trial 9/20/88 - 9/6/90		1985-86 NHLBI Registry (Detre, 1990)
	Periprocedural Occlusion (n=122) (%)	P Value Column B vs Column A	Acute Closure (n=94) (%)	P Value Column B vs Column C	Successful PTCA (n=1,679) (%)
In-Hospital Events:					
Emergency CABG	32.0	<0.001	3.2	0.336	1.4
Elective CABG	8.2	0.382	4.3	0.184	1.8
Total CABG	40.2	<0.001	7.4	0.059	3.2
Death	5.0	0.452	2.1	0.620	1.0
Q Wave MI	NR	...	4.3	...	NR
Non-Q Wave MI	NR	...	4.3	...	NR
Total MI	42.0	<0.001	8.5	0.009	3.0

NR = This information not reported.

The total MIs reported in the present study include acute MI's known to have occurred prior to the PTCA procedure, MIs due to prolonged balloon inflation, MIs due to the acute closure complication that occurred during the initial PTCA procedure, and MI's occurring after the stenting procedure. In contrast, patients with acute MI were excluded from the NHLBI patient group. Therefore, the effect of including patients suffering acute MI immediately prior to the PTCA/stenting procedure in our study population was analyzed.

Table 5 presents the incidence of CABG surgery, MI and death in the stented patient population with and without the acute MI patients included. The rates of CABG, MI and Death are not significantly different when the emergent MI patients are excluded but are, for the most part, slightly lower. The 1.3% death rate is not significantly different because of the small sample size.

Table 5 The Incidence of CABG Surgery, MI and Death Based on 1) the Entire Group of Patients Stented for Acute Closure and 2) Based on this Same Group of Patients, but Excluding those Patients with Emergent MI Prior to the PTCA Procedure

	Indication: Acute Closure		
	All Patients (n=94)	Patients with Emergent MI Excluded (n=76)	P Values
In-Hospital Events After Stent Placement:			
Emergency CABG	3 (3.2%)	3 (3.9%)	0.863
Elective CABG	4 (4.3%)	3 (3.9%)	0.797
Total CABG	7 (7.4%)	6 (7.9%)	0.866
Death	2 (2.1%)	1 (1.3%)	0.847
Q Wave MI	4 (4.3%)	3 (3.9%)	0.797
Non-Q Wave MI	4 (4.3%)	2 (2.6%)	0.858
Total MI	8 (8.5%)	5 (6.6%)	0.862
Cumulative Events <sup>†</sup> at 6 Months:			
Total CABG	15 (16.0%)	12 (15.8%)	0.861
Death	3 (3.2%)	1 (1.3%)	0.761
MI	9 (9.6%)	6 (7.9%)	0.907

<sup>†</sup> Includes In-hospital events

The results of patients stented for threatened closure were compared to those for patients stented for acute closure. Table 6 presents this comparison showing no significant differences.

Table 6 Comparison of the Incidence of In-hospital and After-discharge Events Between Patients Enrolled in the Gianturco-Roubin Flex-Stent™ Coronary Stent Clinical Trial for the Indication of Acute Closure and for the Indication of Threatened Closure after Failed PTCA

	Acute Closure (n=94) (%)	Threatened Closure (n=198) (%)	P Value
<b>In-hospital Events:</b>			
Emergency CABG	3.2	3.0	0.787
Elective CABG	4.3	2.5	0.671
Total CABG	7.4	5.6	0.736
Death	2.1	1.5	0.909
Q Wave MI	4.3	2.5	0.639
Non-Q Wave MI	4.3	1.5	0.293
Total MI	8.5	4.0	0.191
<b>Cumulative† Events at 6 Months:</b>			
Total CABG	16.0	16.7	0.986
Death	3.2	4.5	0.835
MI	9.6	5.6	0.311

† Includes In-hospital events

### 3. Acute Angiographic Results

For the 292 patients with successful placement, the combined effect of the PTCA dilatation with its complication, and the stent placement resulted in a reduction of average stenosis from 86.6% before PTCA to 13.8% ( $P < 0.05$ ) after stenting (Table 7). The clinical scenario after the complication and prior to stenting was complex. In certain circumstances, vessels were totally occluded and temporarily reopened with repeat balloon dilatation. Other vessel segments had dissection flaps which are difficult to assess angiographically. Therefore, stenosis measurements taken immediately prior to stenting are approximate. With that considered, average stenosis after PTCA and before stenting was 64.0% compared to 13.8% after stenting (Table 7).



**Table 7 Immediate Angiographic Results**

	Pre-PTCA	Post-PTCA	Pre-Stent	Post-Stent
Diameter Stenosis (%)	86.6 ±10.8	58.1 ±25.9	64.0 ±24.2	13.8 ±10.8
Range (%)	57-100	0-100	10-100	0-61

*In-Hospital Angiographic Success After Stenting:* Reduction of the stenosis by at least 20% was accomplished in 290 of 292 (99.3%) patients in whom a stent was implanted.

*In-Hospital Clinical Success After Stenting:* Angiographic success without in-hospital death, MI, or CABG surgery was achieved in 253 of 290 (87.2%) successfully stented patients.

*Dimensional Stability of Stents in vivo:* In a published report by Raizner (1991), the dimensional stability of the Gianturco-Roubin Flex-Stent™ Coronary Stent was assessed by quantitative coronary angiography. Recoil of the 3.0 mm stent was analyzed using a CAAS system to measure the mean diameter of the entire stent lumen immediately after deployment, at 30 minutes after deployment, and at 1-4 days (mean 1.8 days) post placement in 10 patients. Table 8 presents the results of Raizner's analysis. Raizner concluded that the Gianturco-Roubin Flex-Stent™ coronary stent achieves the anticipated dimension of the normal segment of the artery and remains dimensionally stable after implantation. No long-term decreases in stent diameter have been reported.

**Table 8 Mean Stent Diameter and Ratio of Stent to Normal Arterial Diameter (S:A) after Implantation of 3.0 mm Stents**

Time After Stenting	Stent Diameter (mm) (n=10)	S:A Ratio
Immediately	2.91 ±0.29	0.96
30 Minutes	2.87 ±0.32	0.96
1.8 Days	3.00 ±0.42	0.98

#### 4. Long-Term Clinical Results

To evaluate the long-term impact of stenting, the need for CABG surgery, the incidence of MI and the incidence of death were examined during the first 6 months after stenting. The cumulative incidence of in-hospital and after-discharge events for the stented patients in the acute closure group were compared with the matched group of NHLBI patients with periprocedural occlusion (see Table 9). The incidence of CABG surgery was significantly less in stented patients in this study compared to unstented patients in the NHLBI PTCA Registry (16.0% vs 46.0%;  $P < 0.001$ ). The incidence of MI was also less in the stented group (9.6 vs 42.0%;  $P < 0.001$ ).

Table 9 Comparison of the Incidence of Cumulative Events between Patients Stented for Acute Closure in the Gianturco-Roubin Flex-Stent™ Coronary Stent Clinical Trial, Patients Suffering Periprocedural Occlusion after PTCA from the 1985-1986 NHLBI PTCA Registry, and Patients Undergoing Successful PTCA from the 1985-1986 NHLBI PTCA Registry

	Column A	Test of Proportions	Column B	Test of Proportions	Column C
	1985-86 NHLBI Registry (Detre, 1990)		Gianturco-Roubin Flex-Stent™ Clinical Trial 9/20/88 - 9/6/90		1985-86 NHLBI Registry (Detre, 1990)
	Periprocedural Occlusion (n=122) (%)	<u>P Value</u> Column B vs Column A	Acute Closure (n=94) (%)	<u>P Value</u> Column B vs Column C	Successful PTCA (n=1,679) (%)
Cumulative Events <sup>†</sup> at 6 Months:					
Total CABG	46.0	<0.001	16.0	<0.001	6.0
Death	7.0	0.355	3.2	0.672	2.0
MI	42.0	<0.001	9.6	0.002	3.0

† Includes In-hospital events

5. Long-Term Angiographic Results

Of the 292 patients receiving stents, 5 were withdrawn from the study by the physician for unrelated health problems, 39 patients received CABG surgery without a reported stenosis value, 1 patient was lost to follow-up, and 11 died before follow-up, leaving 236 patients available for angiographic follow-up. Of these 236, 19 patients refused follow-up recatheterization and data have not been reported on 3, yielding a follow-up compliance rate of 214/236 (90.7%). Mean time to follow-up was  $180.4 \pm 59.6$  days.

Although the intent of stenting in this study was not to prevent the expected restenosis following PTCA, the restenosis rate was evaluated. The angiographic index of restenosis used was a loss of at least 50% of the gain achieved by the angioplasty/stenting procedure.

A decrease in the percent diameter stenosis from the pre-PTCA stenosis was sustained at follow-up. The average percent diameter stenosis was 86.6% before the PTCA procedure and 44.4% at 6-month follow-up. The average percent diameter stenosis prior to stenting was 64.0% compared with 44.4% at follow-up. The average change in percent diameter stenosis from post-stent to follow-up was -30.3%. There was no difference in post-stent and follow-up percent diameter stenosis between the acute closure group of patients and the threatened closure group of patients.

The percent diameter stenosis at follow-up was examined for a relationship with the stented artery (RCA, LAD, LCX), location of the stent within the artery (proximal, mid, distal), and nominal expanded stent diameter (2.0, 2.5, 3.0, 3.5, 4.0 mm). The percent diameter stenosis at follow-up was not found to be significantly different between vessels, between locations within the vessels, or between stents of different diameters, except for a slight, but significant difference ( $P=0.046$ ) between 3.0 and 4.0 mm diameter stents.

6. Multiple stents

Twenty-two (22) patients received multiple stents. No difference in percent diameter stenosis was observed at follow-up when compared with patients receiving single stents. Three patients with multiple stents (13.6%) underwent CABG surgery compared with 16.4% for the total stented patient population. One patient (4.5%) suffered an MI compared with 6.8% for the total stented population. No patient receiving multiple stents died.

7. Stented grafts

Twenty-one (21) patients had stents placed in grafts to coronary arteries. No difference in percent diameter stenosis was observed at follow-up when compared with patients receiving stents to native

arteries. Three patients with stents in grafts (14.3%) underwent CABG surgery. No patients suffered MI. Two patients died before follow-up.

8. Quantitative Angiographic Analysis

Quantitative computer-assisted angiographic analysis (CAAS) was performed by the core laboratory on 50 complete sets of cineangiograms randomly selected from patients without a subsequent complication or intervention precluding angiographic follow-up at 6 months. In this subset, the mean minimum diameter before PTCA was  $0.96 \pm 0.47$  mm compared with  $2.73 \pm 0.55$  mm after stenting, which represents an average increase of 1.8 mm. The increase in mean minimum diameter from before PTCA ( $0.96 \pm 0.47$  mm) to follow-up ( $1.92 \pm 0.82$  mm) was 0.96 mm. In terms of percent diameter stenosis, results showed 73.9% pre-PTCA, 25.5% post-stent and 46.8% at follow-up. There was no difference between the acute closure group of patients and the threatened closure group of patients. A summary of the percent diameter stenosis results in the overall stented population and in the core group is presented in Table 10.

Table 10 Means and Standard Deviations for Percent Diameter Stenosis and Absolute Minimum Luminal Diameter at the Stent Site for all Patients with Angiographic Follow-up and for a Subset of Patients with Cineangiographic Analysis done by the Core Laboratory

	Pre-PTCA	Post-Stent	Follow-Up
All patients with angiographic follow-up (n=209)			
Percent Diameter Stenosis	86.6 $\pm$ 10.8	13.8 $\pm$ 10.8	44.4 $\pm$ 30.4
Core Laboratory analyzed patients (n=50)			
Percent Diameter Stenosis	73.9 $\pm$ 10.5	25.2 $\pm$ 11.4	46.8 $\pm$ 19.3
Minimum Luminal Diameter (mm)	0.96 $\pm$ 0.47	2.73 $\pm$ 0.55	1.92 $\pm$ 0.82

9. Summary of Safety Data

In-Hospital and 6-Month Cumulative

The incidence of death, MI and CABG surgery for the combined groups of acute and threatened closure patients from this study (n=292) is shown in Table 11. These results are compared to both patients undergoing successful PTCA and PTCA patients with periprocedural occlusion reported in the NHLBI PTCA Registry. The incidence of emergency CABG in stented patients (3.1%) was significantly less than the incidence in NHLBI patients with periprocedural occlusion (32.0%). The incidence of emergency CABG in stented patients (3.1%) is not statistically different from that of NHLBI patients undergoing successful PTCA (1.4%). The same is true for elective CABG. The total incidence of CABG in stented patients (6.2%) was statistically greater than in successful NHLBI PTCA patients (3.2%), but significantly less than in NHLBI periprocedural occlusion patients (40.2%).

In the present study, reasons reported for performing emergency CABG surgery included stenosis of another non-stented vessel, perforation due to prior laser angioplasty, additional PTCA-caused dissection proximal to the stent site, additional dissection longer than 20 mm, and thrombotic reocclusion of the stented vessel. Reasons given for elective CABG surgery included dissection of the RCA ostium due to a guiding catheter, occlusion of the vessel proximal or distal to the stent site, occlusion at the stent site, thrombosis and chest pain, and at the family's or family physician's discretion unrelated to stent patency. In no case did the stent collapse.

Table 11 Comparison of the Incidence of In-hospital and After-discharge Events between All Successfully Stented Patients in the Gianturco-Roubin Flex-Stent™ Coronary Stent Clinical Trial, Patients Suffering Periprocedural Occlusion after PTCA from the 1985-1986 NHLBI PTCA Registry, and Patients Undergoing Successful PTCA from the 1985-1986 NHLBI PTCA Registry

	Column A	Test of Proportions	Column B	Test of Proportions	Column C
	1985-86 NHLBI Registry (Detre, 1990)		Gianturco-Roubin Flex-Stent™ Clinical Trial 9/20/88 - 9/6/90		1985-86 NHLBI Registry (Detre, 1990)
	Periprocedural Occlusion (n=122) (%)	P Value Column B vs Column A	All Successfully Stented Patients (n=292) (%)	P Value Column B vs Column C	Successful PTCA (n=1,679) (%)
<b>In-Hospital Events:</b>					
Emergency CABG	32.0	<0.001	3.1	0.064	1.4
Elective CABG	8.2	0.045	3.1	0.216	1.8
Total CABG	40.2	<0.001	6.2	0.018	3.2
Death	5.0	0.118	1.7	0.451	1.0
Q Wave MI	NR	...	3.1	...	NR
Non-Q Wave MI	NR	...	2.4	...	NR
Total MI	42.0	<0.001	5.5	0.045	3.0
<b>Cumulative Events† at 6 Months:</b>					
Total CABG	46.0	<0.001	16.4	<0.001	6.0
Death	7.0	0.322	4.1	0.046	2.0
MI	42.0	<0.001	6.8	0.002	3.0

† Includes In-hospital events

NR = This information not reported

The incidence of total MI was less for stented patients (5.5%) than for PTCA patients with periprocedural occlusion (42.0%), but slightly higher (P=0.045) than for successful PTCA patients (3.0%). There was no significant difference in in-hospital death rates between stented patients and NHLBI patients with periprocedural occlusion (1.7% versus 5.0%, respectively). Nor was there a significant difference in the death rate between stented patients and NHLBI patients undergoing successful PTCA (1.7% versus 1.0%, respectively).

The cumulative (in-hospital plus after-discharge) incidence of CABG surgery, MI and death for the combined groups of acute closure and threatened closure patients were examined as part of the analysis of long-term safety. The cumulative need for CABG surgery in stented patients (16.4%) was less than in periprocedural occlusion patients in the NHLBI study (46.0%), but greater than in successful PTCA patients (6.0%).

The incidence of myocardial infarction in stented patients (6.8%) was less than in the NHLBI periprocedural occlusion patients (42.0%), but higher than in successful PTCA patients (3.0%).

The cumulative death rate in stented patients (4.1%) was not different than for the NHLBI periprocedural occlusion patients (7.0%). The cumulative death rate in stented patients when all patient deaths in this study (including salvage cases; n=4) are included (4.1%), was slightly higher (P=0.045) than for successful PTCA patients (2.0%).

The incidence of in-hospital death in the control periprocedural occlusion group was 2.4 times greater than in the stented group (5.0% vs 2.1%); however, because of the relatively small number of patients who died in each group (control = 6 of 122 vs stented = 2 of 94), this difference did not reach statistical significance. The same was true of the cumulative incidence of death at follow-up, which was 2.2 times greater in the control periprocedural occlusion group compared to the stented group (7.0% vs 3.2%; or control = 9 of 122 vs stented = 3 of 94). While there may be statistical methods showing that the death rate of the stented group is less than that of the control group, the conservative statistical analysis we used did not show significance at the sample size studied.

#### Other Safety Issues

Suspected thrombosis of the stented arterial segment has been reported in 27 (9.2%) patients. In 19 of these patients, the segment was successfully reopened with repeat PTCA and/or thrombolytic therapy. In 8 patients, the stented segment was not reopened; 5 of these patients went on to CABG surgery and 3 were managed medically. Thrombosis may be initiated by intimal wall injury due to balloon inflations prior to stenting resulting in

release of thrombogenic factors that cannot be resolved by stenting. Anticoagulation therapy is necessary to control thrombosis in this setting.

Because of the need for rigorous anticoagulation therapy, blood loss (the majority of which is associated with the arterial puncture site) must be carefully monitored. By paying special attention to the anticoagulation regimen, the incidence of bleeding complications requiring transfusion has decreased during the clinical trial. An investigators' meeting was held 03/19/90 in which anticoagulation therapy was discussed and the regimen refined. The incidence of significant bleeds in patients stented before 03/19/90 was 24.6%, while the incidence from 03/19/90 to 09/5/90 was only 14.4%.

Also, there have been reports of 21 (7.2%) pseudoaneurysms involving the catheter insertion site in the groin. Hematuria has been reported in 6 (2.1%) patients. Hemoptysis was reported in 2 (0.7%) patients. These complications are associated with the anticoagulation therapy utilized.

Other events possibly associated with the stenting procedure included:

- spasm of the coronary artery after stenting was reported in 3 (1.0%) patients; it resolved spontaneously and rapidly in all 3;
- hypotension requiring an intra-aortic balloon pump was reported in 3 (1.0%) patients;
- ventricular fibrillation was reported in 3 (1.0%) patients; all of whom were successfully defibrillated;
- side branch closure was reported in only 2 (0.7%) patients;
- ventricular tachycardia which spontaneously resolved was reported in 1 (0.3%) patient;
- one case (0.3%) of pulmonary edema during the PTCA/stent procedure was reported;
- fever was reported in 7 (2.4%) patients.



Other reported adverse events included:

- pneumonia - 3 (1.0%) patients;
- urinary tract infection - 2 (0.7%) patients;
- renal insufficiency - 2 (0.7%) patients;
- acute tubular necrosis - 2 (0.7%) patients; and
- extended nausea and vomiting 1 (0.3%) patient.

Device Failures and Replacements

No device failures (e.g., fracture, migration, or vessel wall perforation) have occurred in this study.

10. Summary of the Clinical Results

Table 12 presents an overall summary of the clinical results of this study.

Table 12 Summary of Clinical Results

	ACUTE CLOSURE	THREATENED CLOSURE	TOTALS
Number of Patients Stented	94	198	292
Number of Lesions Stented	103	222	325
Success Rates:			
In-hospital Angiographic Success	93 (98.9%)	197 (99.5%)	290 (99.3%)
In-hospital Clinical Success	77 (82.8%)	176 (89.3%)	253 (87.2%)
Complication Rates (Cumulative to 6 Month Follow-up):			
CABG Only	12 (12.8%)	26 (13.1%)	38 (13.0%)
MI Only	7 (7.4%)	8 (4.0%)	15 (5.1%)
Death Only	2 (2.1%)	8 (4.0%)	10 (3.4%)
CABG & MI Only	2 (2.1%)	3 (1.5%)	5 (1.7%)
CABG & Death Only	1 (1.1%)	1 (0.5%)	2 (0.7%)
MI & Death Only	0 (0.0%)	0 (0.0%)	0 (0.0%)
CABG & MI & Death	0 (0.0%)	0 (0.0%)	0 (0.0%)
Restenosis Rate:			
>50% Loss of Initial Gain Achieved by Stenting	37.1%	36.7%	36.8%
Percent Diameter Stenosis:			
Pre-PTCA	89.5 ±10.8	85.2 ±10.6	86.6 ±10.8
Post-STENT	14.4 ±11.9	13.5 ±10.2	13.8 ±10.8
At 6 Month Follow-Up	45.3 ±27.4	43.9 ±31.9	44.4 ±30.4

IX. Conclusions From the Nonclinical and Clinical Studies

The nonclinical studies indicate that the Gianturco-Roubin Flex-Stent™ Coronary Stent has the appropriate physical and performance characteristics for its intended use, as stated in the labeling

The biocompatibility tests and supporting data demonstrate that the materials used in the delivery system are biocompatible for short-term blood contact and the stent itself is acceptable for long-term implantation.

The multicenter clinical study showed that the Gianturco-Roubin Flex-Stent™ Coronary Stent reduces the need for CABG surgery, reduces the incidence of MI, and provides an improved long-term angiographic appearance of the stented coronary artery in patients with acute closure. The nonclinical and clinical studies demonstrate with reasonable assurance that the Gianturco-Roubin Flex-Stent™ Coronary Stent is safe and effective for chronic placement in a coronary artery to obtain vessel patency in the treatment of acute or threatened closure associated with an interventional complication, when used according to the Labeling and Instructions for Use.

X. Panel Recommendations

On May 11, 1992, the Circulatory System Devices Panel, recommended that the premarket approval application for the Gianturco-Roubin Flex-Stent™ Coronary Stent be approved subject to CDRH's approval of an amendment which the manufacturer must submit including the following information:

1. The following modifications in the Instructions for Use:
  - a. The adverse effects of systemic stent embolus and coronary pseudoaneurysm should be added to the section labeled "Potential Adverse Effects."
  - b. The prothrombin time requirements prior to stenting should be removed.
  - c. Under the section entitled "Removal of Unexpanded Stent," guide wire removal should not be included as a part of stent/balloon catheter removal.
  - d. A statement should be added which specifies that patients require 3 days of bed rest following the stent procedure.
  - e. A definition for threatened closure should be added.
  - f. A statement is needed which notes that the effects of magnetic resonance imaging on the stent have not, as yet, been fully documented.
2. Concurrence with the following requirements for postapproval studies:
  - a. Postapproval reports which shall include, in addition to the requirements in the enclosure, follow-up information on an initial cohort of patients having undergone stenting of a

bypass graft(s) and classified as initial successes. Seventy-five patients classified as clinical success should be followed for 6 months, and the data in the report shall be formatted similar to your PMA. This information is required to establish the long-term effects of the device on vein grafts.

- b. Postapproval reports which shall include, in addition to the requirements in the enclosure, follow-up information on an initial cohort of patients documented as developing a coronary pseudoaneurysm(s) following stent implantation. All such patients should be followed on at least a yearly basis for the life of the patients. This information is required to establish the ultimate fate of arteries in which this complication manifests itself.

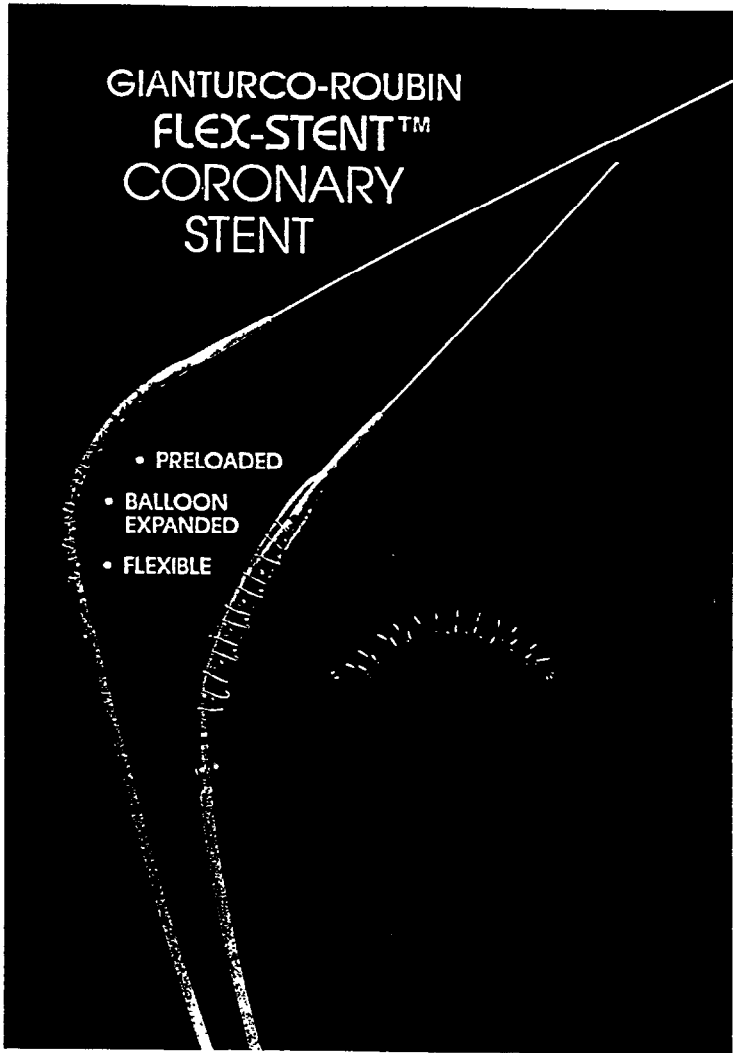
#### **XI. FDA Decision**

FDA concurred with the recommendations of the Circulatory System Devices Panel and issued an approvable letter on October 8, 1992. On December 28, 1992 and January 6, 1993, Cook, Inc., submitted amendments to the application making the changes recommended by the Panel and providing fatigue resistance data as requested by FDA. Between September 8 and 10, 1992, A Good Manufacturing Practices (GMP) inspection was performed and revealed that the company was in compliance with the GMP regulation (21 CFR, Part 820). FDA found the information contained in these amendments to be adequate and issued an approval letter to Cook, Inc.

#### **XII. Approval Specification**

Continued approval of the device is contingent upon the submission of postapproval reports to the Food and Drug Administration as described in the approval letter (Attachment A). A copy of the draft final Instruction for Use is attached (Attachment B).

**IMPORTANT INFORMATION: PLEASE READ PRIOR TO USE.**



**Technical Information  
Suggested Instruction For Placement**



A Division of  
COOK INCORPORATED

**COOK®**  
**CARDIOLOGY**

## CONTENTS

<b>INTENDED USE .....</b>	<b>1</b>
<b>CONTRAINDICATIONS FOR USE .....</b>	<b>1</b>
<b>POTENTIAL ADVERSE EFFECTS .....</b>	<b>1, 2</b>
<b>WARNINGS .....</b>	<b>2</b>
<b>PRECAUTIONS .....</b>	<b>2, 3</b>
<b>SUGGESTED PRE- AND POST-STENT PLACEMENT DRUG PROTOCOL</b>	
<b>PRE-STENT PLACEMENT .....</b>	<b>3</b>
<b>POST-STENT PLACEMENT .....</b>	<b>3</b>
<b>PRIOR TO SHEATH REMOVAL .....</b>	<b>3</b>
<b>POST-SHEATH REMOVAL .....</b>	<b>3, 4</b>
<b>PATIENT-DISCHARGE MEDICATION REGIME .....</b>	<b>4</b>
<b>SUGGESTED INSTRUCTIONS FOR PLACEMENT</b>	
<b>GENERAL USE INFORMATION .....</b>	<b>4</b>
<b>LESION/VESSEL PREPARATION .....</b>	<b>4, 5</b>
<b>WIRE GUIDE USE AND SELECTION .....</b>	<b>5</b>
<b>GUIDING CATHETER SELECTION .....</b>	<b>5, 6</b>
<b>SELECTION OF STENT SIZE .....</b>	<b>6</b>
<b>STENT/BALLOON EXPANSION PRESSURE GUIDELINES .....</b>	<b>6</b>
<b>PREPARATION OF BALLOON CATHETER .....</b>	<b>7, 8, 9</b>
<b>DEPLOYMENT OF STENT .....</b>	<b>10</b>
<b>Stent Positioning .....</b>	<b>10</b>
<b>Balloon Expansion .....</b>	<b>10, 11</b>
<b>Balloon Deflation and Removal .....</b>	<b>11</b>
<b>MULTIPLE STENT PLACEMENT RECOMMENDATIONS .....</b>	<b>11</b>
<b>REMOVAL OF UNEXPANDED STENT .....</b>	<b>11, 12</b>
<b>FURTHER DILATATION OF STENTED SEGMENTS .....</b>	<b>12</b>
<b>PRODUCT WARRANTY .....</b>	<b>12</b>
<b>REFERENCES .....</b>	<b>13, 14</b>

# GIANTURCO-ROUBIN FLEX-STENT™ CORONARY STENT

## INTENDED USE

The Gianturco-Roubin Flex-Stent™ Coronary Stent is indicated for chronic placement in a coronary artery or graft to obtain vessel patency in the treatment of acute or threatened closure associated with an interventional procedure. The balloon expandable stent is supplied preloaded on an appropriate balloon catheter. It is supplied sterile in peel-open packages and is intended for one-time use.

## DEFINITIONS OF ACUTE CLOSURE AND THREATENED CLOSURE

### Acute Closure

Acute closure is defined as TIMI 0 or TIMI 1 flow.

### Threatened Closure

Threatened closure is evidenced by deterioration of angiographic, electrocardiographic, hemodynamic or clinical indicators from baseline values.

- Angiographic indicators may include diameter or area stenosis, reduced flow and vessel wall abnormalities (notably, dissection, intimal tears and irregular filling defects)
- Electrocardiographic indicators may include S-T segment elevation or depression, or arrhythmias
- Hemodynamic indicators may include increased left ventricular end diastolic pressure, increased pulmonary wedge pressure, decreased ejection fraction and decreased blood pressure
- Clinical indicators may include chest pain

## CONTRAINDICATIONS FOR USE

1. Patients with bleeding diathesis or other disorder, e.g. peptic ulceration or recent cerebrovascular accident, limiting the use of antiplatelet and anticoagulant therapy.
2. Patients with vessels measuring less than 2.0 mm in diameter.
3. Patients with significant vessel tortuosity and/or proximal atherosclerosis in whom adequate guiding catheter support or wire guide access is prohibited.
4. Patients with a large amount of untreated thrombus at the lesion site.

## POTENTIAL ADVERSE EFFECTS

Adverse effects associated with the use of the Gianturco-Roubin Flex-Stent™ Coronary Stent are similar to those experienced with standard PTCA and include the adverse effects of progressive disease, drug therapy, use of the delivery system and long-term implantation of the stent.

### Primary Adverse Effects

Groin Hematoma  
Pseudoaneurysm  
Hematuria  
Hemorrhage (Intracranial and GI)  
Angina Pectoris  
Vascular Thrombosis  
Total or partial closure of coronary artery  
or side branch  
Myocardial Infarction  
Death

### Possible Adverse Effects

Fever  
Infection and pain at insertion site  
Hypotension  
Cardiac Arrhythmias  
Cardiac Ischemia  
Distal emboli (air, tissue or thrombotic emboli)  
Spasm  
Stroke  
Arterial Perforation  
Ventricular Fibrillation  
Body rejection or local tissue reaction  
Hemoptysis  
Systemic Stent Embolization  
Coronary Pseudoaneurysm

Other events reported during the clinical trial include pneumonia, urinary tract infection, renal insufficiency, acute tubular lesions, nausea and vomiting. Adverse effects may require surgery, redilatation or drug therapy.

#### **WARNINGS**

1. If a stent is implanted to open an acutely closed, unprotected left main coronary artery, subsequent coronary artery bypass graft surgery should be considered as a definitive treatment due to the large amount of myocardium likely at risk.
2. Administration of appropriate anticoagulant and coronary artery vasodilator therapy is critical to successful stent implantation and follow-up to minimize the risk of thrombus or bleeding complications. Guidelines for a suggested pre- and post-stent medication therapy protocol are provided in the Instructions for Use.
3. Stenosis of a sidebranch may result from a dissection or intimal flap complication caused by the initial intervention for which the stent is indicated. Deployment of a stent under these circumstances may, or may not, resolve the sidebranch occlusion. Upon stent placement, the dissection involving the sidebranch may adversely affect sidebranch flow which may necessitate further intervention. The fate of branch vessels which are crossed by the stent is unknown at present.
4. The long-term outcome following repeat dilatation of endothelialized stents is unknown at present.

#### **PRECAUTIONS**

1. Use of the Intracoronary Stent requires advanced coronary angioplasty technical skills. The following instructions will give technical guidance but do not obviate formal training in the use of the device.
2. **Do not remove stent from catheter; the stent cannot be removed and placed on another balloon catheter for deployment.**
3. Special care must be taken not to handle or in any way disrupt the delicate wrap of the coils on the balloon. This is most important during catheter removal from packaging, placement over wire guide and advancement through Tuohy-Borst adapter and guiding catheter hub.
4. Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon.
5. Balloon pressures should be monitored during inflation. **Do not exceed balloon rated burst pressure as indicated on product label.** Use of higher pressure range than specified on product label may result in a ruptured balloon with possible intimal damage.
6. Expansion of the stent should not be undertaken if the stent is not appropriately positioned in the vessel. If the position of the stent is not optimal, it should not be expanded. (See Removal of Unexpanded Stent instructions.)
7. **Do not attempt to pull an unexpanded stent back through the guiding catheter, dislodgement of the stent may result.**
8. Prior to stent expansion, utilize high resolution fluoroscopy to verify stent coils have not been damaged during positioning.
9. Significant amounts of air in the balloon may cause uneven expansion of stent coils and difficulty in deployment of the stent.
10. **Do not pre-inflate balloon prior to stent deployment.** Use balloon purging technique described in the Instructions for Use.
11. The use of mechanical atherectomy devices (e.g., directional atherectomy catheters, Rotablaters™, or LASER atherectomy devices) is not recommended in the stented region.



12. The stent may cause artifacts in MRI scans due to distortion of the magnetic field. A MRI scan should not be requested until the site of stent implant has had a chance to heal in order to minimize the risk of migration of the stent under a strong magnetic field. The full interaction between the Flex-Stent™ and MRI scanning is unknown at this time.
13. Persons with allergic reactions to 316L stainless steel may suffer an allergic response to the implant.

#### **SUGGESTED PRE- AND POST-STENT PLACEMENT DRUG PROTOCOL**

**NOTE:** This drug protocol is provided as a guideline and was developed by primary investigative sites for the Gianturco-Roubin Flex-Stent™ Coronary Stent. Administration of anticoagulants will vary with patient conditions and medical histories.

**CAUTION:** Critical attention to pre- and post-stenting anticoagulation is required for successful use of the device.

#### **Pre-Stent Placement**

- Soluble aspirin
- Dipyridamole
- Calcium channel blocker
- Dextran 40 10% at 50-75 cc/hour until sheaths are removed and patient is back on heparin and PTT is within therapeutic range at 45-80 seconds
- Heparin during procedure to maintain ACT > 300 seconds
- Nitroglycerin by intracoronary injection
- Thrombolytic agent may be administered by slow intracoronary injection if there is evidence of untreated thrombus

#### **Post-Stent Placement**

- Additional nitroglycerin may be given by intracoronary injection
- Thrombolytic agent may be administered by slow intracoronary injection if there is evidence of residual thrombus

#### **Prior to Sheath Removal**

- Draw ACT every 30 minutes until level  $\leq 150$
- Remove femoral sheath when ACT is  $\leq 150$  (approx. 3-4 hours post-stenting)
- Continue Dextran 40 10% infusion at 50-75 cc/hr until sheaths are removed and PTT meets the criteria specified below (i.e., 45-80 seconds)

#### **Post-Sheath Removal**

- Maintain groin pressure for a minimum of 60 minutes
- Draw ACT at one hour post-sheath removal and administer heparin drip at 1000 units/hour (with additional boluses if necessary) to adjust ACT to approximately 200 seconds and/or one hour post-sheath removal, administer the following heparin dosage:
  - If PTT  $\geq 80$  seconds, start heparin drip at 1000 units/hour
  - If  $65 \leq \text{PTT} \leq 79$  seconds, give heparin bolus of 1000 units then begin heparin drip at 1000 units/hour
  - If PTT  $\leq 64$  seconds, give heparin bolus of 2000 units then begin heparin drip at 1000 units/hour
- Document groin checks every 30 minutes for 4 times after heparin drip is started
- Check PTT 2 hours after starting heparin drip

- Adjust the heparin treatment according to the following PTT scale:
  - If  $40 \leq \text{PTT} \leq 45$  seconds, increase drip rate by 200 units/hour
  - If  $35 \leq \text{PTT} \leq 39$  seconds, increase drip rate by 200 units/hour and give 1000 units heparin IV bolus
  - If  $\text{PTT} \leq 34$  seconds, increase drip rate by 200 units/hour and give 2000 units heparin IV bolus
- Continue to check PTT every 6 hours until heparin drip is discontinued. PTT should be maintained between 45-80 seconds
- Begin the following drug regime as soon as patient can tolerate:
  - Soluble aspirin
  - Dipyridamole
  - Calcium channel blocker
  - Anticoagulant therapy—As needed to achieve PT of 18-20 seconds or 1.5X control for PT reagents with ISI equal to 2.7 (INR equals 3.0-4.0)
- Wean patient from heparin after 3-4 days when PT indicates adequate anticoagulation with anticoagulant therapy (18-20 seconds). **Note:** To minimize groin bleeding complications, the patient should remain on complete bed rest for 24 hours after sheath removal. During the next 24-48 hours, bed rest should be maintained with gradual increase in activities (e.g. bathroom privileges). Approximately 72 hours after sheath removal, consideration may be given to resumption of normal activities.

#### **Patient-Discharge Medication Regime**

- Soluble aspirin
- Dipyridamole
- Calcium channel blocker
- Anticoagulant therapy—As needed to achieve PT of 18-20 seconds or 1.5X control for PT reagents with ISI equal to 2.7 (INR equals 3.0-4.0)

## **SUGGESTED INSTRUCTIONS FOR PLACEMENT OF THE GIANTURCO-ROUBIN FLEX-STENT™ CORONARY STENT**

**CAUTION: Use of the Gianturco-Roubin Flex-Stent™ Coronary Stent requires advanced coronary angioplasty technical skills. Mandatory attendance at an accredited stent training symposium is required before use of this device. A cardiac surgery team should be on standby while stent implantation is being performed.**

**Prior to use of this device, review the enclosed videotape and the instructions for use information in this booklet. If you have not had an in-service with a tabletop stent/balloon demonstration model, please contact your local COOK Cardiology representative to arrange a convenient time. The following instructions provide technical guidance, but do not obviate the need for formal training with this device.**

#### **GENERAL USE INFORMATION**

Standard techniques for placement of a femoral sheath, guiding catheter and wire guide should be employed during use of the Gianturco-Roubin Flex-Stent™ Coronary Stent device.

#### **LESION/VESSEL PREPARATION**

The lesion and vessel must be adequately predilated before use of the stent.

In general, dilatation with a balloon diameter with a ratio of 1:1 with the diameter of the

vessel is required. For example, since the stent size should be chosen to match the diameter of the vessel, predilate with a 2.5 mm balloon when using a 2.5 mm stent.

Predilatations of the vessel must take into account proximal atherosclerotic plaque which may inhibit advancement of the stent and in addition atherosclerotic plaque beyond the lesion which may prevent advancement of the device across the primary lesion. In preparing the vessel, optimal coronary vasodilation and anticoagulant and antiplatelet therapy is essential.

**NOTE:** A coronary artery segment containing an endothelialized stent may be redilated using standard angioplasty techniques. The long-term outcome following repeat dilatation of endothelialized stents is unknown at present.

**WIRE GUIDE USE AND SELECTION**

Successful use of the stent usually requires support of an .018 inch or .016 inch wire guide. A standard .018 inch wire with a soft, flexible tip is recommended to improve tracking and catheter support. Prior to starting the case, if stenting is anticipated, an .018 inch wire guide compatible balloon system is preferred.

If the case is started with a .014 inch wire system for predilatation, the following procedure may be followed if stenting is indicated.

1. Convert the .014 inch wire guide to an exchange length.
2. Remove the .014 inch compatible balloon.
3. Place an .018 inch compatible balloon into the vessel and across the lesion.
4. While maintaining the position of the balloon catheter in the vessel, exchange the .014 inch wire guide for the .018 inch wire.
5. Position the flexible tip of the wire guide until it is well seated distally beyond the site selected for stent placement. **NOTE:** Having the "firm" segment of the coronary wire guide shaft in the proximal part of the vessel will assist successful stent placement.
6. Convert the .018 inch wire guide to exchange length and remove balloon catheter.

**GUIDING CATHETER SELECTION**

Correct guiding catheter selection and technique is necessary for use of the stent.

Assure that inside lumen of the guiding catheter is of sufficient size to allow unobstructed passage of the stent/balloon catheter. COOK INCORPORATED Guiding Catheters (Order Number Example: **GC8[9]-NT-100-P-NS-JL4**) are fabricated to assure proper inside diameter dimensions for stent usage.

**IMPORTANT: MINIMUM INSIDE DIAMETER REQUIREMENTS FOR THE GUIDING CATHETER ARE SHOWN IN TABLE 1.**

**TABLE 1**

STENT/BALLOON CATHETER REORDER NUMBER	BALLOON INFLATED DIAMETER (mm)	EXPANDED STENT DIAMETER (mm)	STENT LENGTH (mm)	MINIMUM I.D. REQUIREMENTS FOR GUIDING CATHETER
GRBS-2.0-20	2.5 mm	2.0 mm	20 mm	.077 inch
GRBS-2.5-20	3.0 mm	2.5 mm	20 mm	.077 inch
GRBS-3.0-20	3.5 mm	3.0 mm	20 mm	.077 inch
GRBS-3.5-20	4.0 mm	3.5 mm	20 mm	.089 inch
GRBS-4.0-20	4.5 mm	4.0 mm	20 mm	.089 inch

Standard coronary catheter curves must be selected to provide adequate guide catheter "back-up support" to achieve successful stent placement.

**NOTE:** Standard Judkins catheter curves have proven to be most useful, but other catheter shapes may be employed. Left Amplatz, Arani, Multipurpose, Left Coronary Bypass catheter shapes may be needed depending upon the anatomy of the aortic root, coronary ostium and proximal vessel segment.

In general, all large lumen 8 French guiding catheters will be suitable for placement of 2.0 mm, 2.5 mm and 3.0 mm stents. Large lumen 9 French guiding catheters will be necessary for placement of 3.5 mm and 4.0 mm stents. If use of a 3.5 mm or 4.0 mm stent is anticipated, the procedure should be started with a 9 French guiding catheter.

If additional guiding catheter support is required prior to stenting, catheter exchanges can be successfully made over a well positioned .018 inch coronary wire guide.

**NOTE:** It is recommended that the guiding catheter used in conjunction with stent placement have a highly visible, radiopaque distal tip.

#### **SELECTION OF STENT SIZE**

Careful stent sizing is important to successful stenting. In general, the stent size should be chosen to match the diameter of the vessel. If in doubt, slight undersizing is preferable to oversizing.

Actual balloon inflation diameter must be taken into consideration when using the stent in diffusely diseased vessels. (See Balloon Inflated Diameter dimensions on page 5.)

**NOTE:** The inflated balloon diameter measures .5 mm larger than the labeled luminal diameter of the stent to allow for stent recoil (approximately .5 mm) upon expansion.

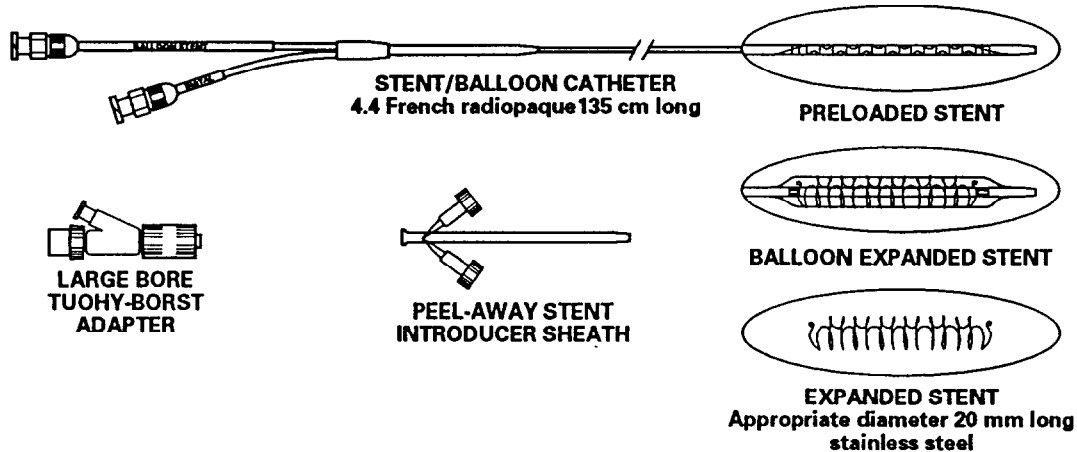
**CAUTION:** Due to the compliant nature of the stent/balloon catheter material, prolonged pressurization in excess of the maximum recommended balloon pressure as specified on product label will result in over-distension of the stent and balloon.

**CAUTION:** Oversizing of the stent and use of higher than recommended inflation pressures may cause distal dissection. It is recommended that the stent size chosen closely approximates the diameter of the vessel and that recommended stent inflation pressures be used for stent deployment.

#### **STENT/BALLOON EXPANSION PRESSURE GUIDELINES**

<b>STENT/BALLOON CATHETER REORDER NUMBER</b>	<b>RECOMMENDED STENT EXPANSION PRESSURE (ATM)</b>	<b>RECOMMENDED BALLOON RATED BURST PRESSURE (ATM)</b>
<b>GRBS-2.0-20</b>	7	8
<b>GRBS-2.5-20</b>	5	8
<b>GRBS-3.0-20</b>	6	7
<b>GRBS-3.5-20</b>	4	6
<b>GRBS-4.0-20</b>	3	5

## GIANTURCO-ROUBIN FLEX-STENT™ CORONARY STENT COMPONENTS



### PREPARATION OF BALLOON CATHETER

1. Remove the stent/balloon catheter from the package and inspect the stent coil wrap to assure it has not been damaged.
2. Flush balloon catheter distal lumen with heparinized saline in routine manner.
3. Prepare balloon lumen with standard contrast-saline mixture as follows:

**WARNING: Do not attempt pre-inflation technique to purge balloon lumen.  
Do not use air or any gaseous medium to inflate the balloon.**

- a. Using a 20 cc syringe containing 5 cc of contrast-saline mixture, apply **negative** pressure for 20-30 seconds.
- b. Release pressure allowing negative pressure to draw mixture into balloon lumen.
- c. Detach syringe, leaving a meniscus of mixture on the hub of the balloon lumen.
- d. Prepare inflation device in standard manner and purge to remove all air from syringe and tubing.
- e. Attach inflation device to balloon lumen directly, ensuring no air bubbles remain at connection.
- f. Pull **negative** pressure on inflation device.

**CAUTION: Significant amounts of air in the balloon may cause uneven expansion of stent coils and difficulty in deployment of the stent.**

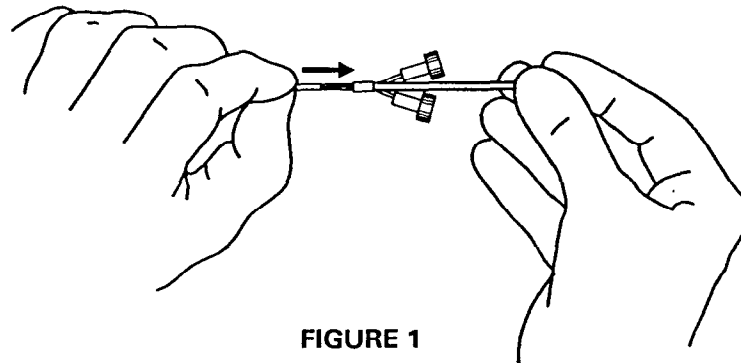


FIGURE 1

4. Moisten the stent with heparinized saline. **CAUTION: Do not use gauze sponges as fibers may disrupt stent.** Carefully pass the stent/balloon section of the catheter into the cuffed end of the peel-away stent introducer sheath. The stent should be protected by the peel-away sheath (Figure 1).

**CAUTION: If resistance is encountered, do not force passage. Resistance may indicate damage to stent.**

5. Attach a standard Tuohy-Borst "Y" adapter to the lumen extension marked "DISTAL" of stent/balloon catheter and flush in standard fashion to purge air.
6. Remove existing Tuohy-Borst adapter from guiding catheter leaving wire guide in position.
7. Advance large bore Tuohy-Borst adapter (supplied in set) over wire guide. Do not attach it to the guiding catheter hub.

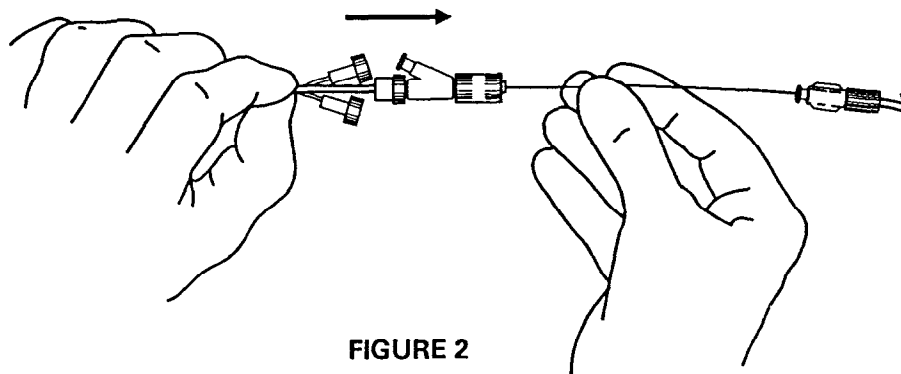


FIGURE 2

8. Maintaining peel-away stent introducer position, advance stent/balloon catheter over wire guide and into the fully opened, large bore Tuohy-Borst adapter supplied in set (Figure 2).

**CAUTION: If resistance is encountered, do not force passage. Resistance may indicate damage to stent.**

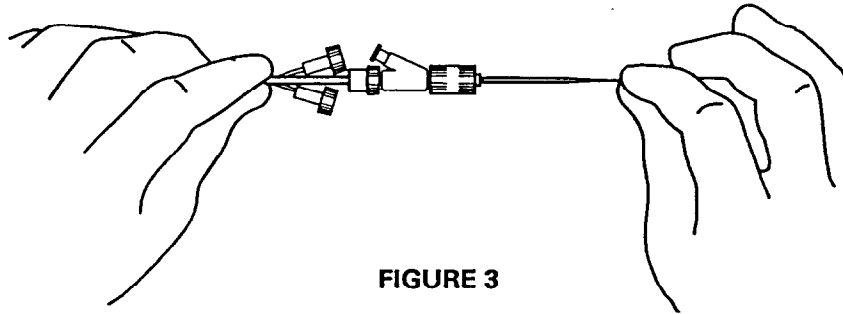


FIGURE 3

9. Continue advancement of stent/balloon catheter completely through Tuohy-Borst "Y" adapter (Figure 3).
10. Reinspect the stent coil wrap to assure it is not damaged.
11. Carefully advance the stent/balloon catheter over the wire guide and into the hub of the guiding catheter.

**CAUTION: If resistance is encountered, do not force passage. Resistance may indicate damage to stent.**

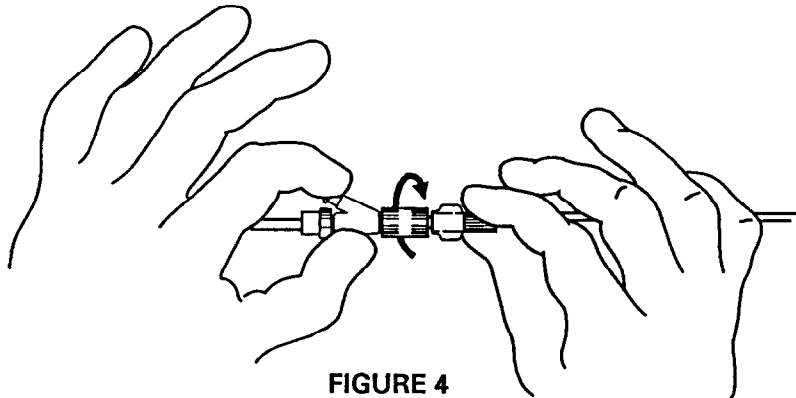


FIGURE 4

12. Luer lock large bore Tuohy-Borst side-arm fitting to hub of the guiding catheter (Figure 4).
13. Peel away stent introducer sheath.
14. The stent/balloon catheter can now be advanced through the guiding catheter.

**CAUTION: If resistance is encountered, do not force passage. Resistance may indicate damage to stent.**

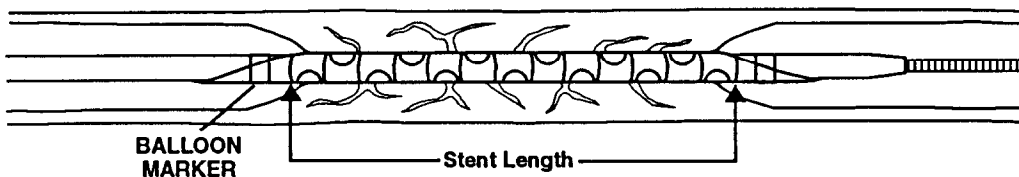
## DEPLOYMENT OF STENT

### Stent Positioning

1. Ensure guiding catheter stability before advancing the balloon into the coronary artery.

**CAUTION:** If initial guiding catheter position is lost, avoid pulling or pushing guiding catheter over the stent. If this is done, the distal end of the guiding catheter may damage the stent coils.

**CAUTION:** If stent/balloon catheter does not readily advance, do not force. Stent coil may accordion over balloon. If stent will not advance in spite of good guiding catheter support, consider dilating proximal obstructing plaque and/or using a smaller stent. Refer to instructions for Removal of Unexpanded Stent.



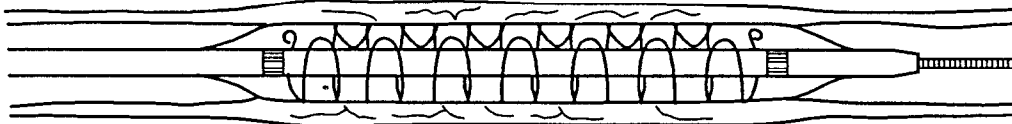
2. Position the stent across the lesion, using the proximal marker on the balloon as a reference point. The stent begins 1-2 mm distal to this marker. Optimal placement requires the proximal end of the stent to be deployed a few mm proximal to the beginning of the arterial segment to be stented. The stent does not shorten as it is expanded.

**WARNING:** Expansion of the stent should not be undertaken if the stent is not properly positioned in the stenotic segment of the vessel. If the position of the stent is not optimal, it should be repositioned or removed. (See Removal of Unexpanded Stent instructions.)

### Balloon Expansion

Prior to stent expansion, utilize high resolution fluoroscopy to verify stent coils have not been damaged during positioning.

1. To expand the stent, inflate the balloon to the stent expansion pressure indicated on product label.



2. Increase inflation pressure to firmly embed stent coils into vessel intima. A 30-60 second inflation at higher pressure is recommended for full expansion. **Do not exceed rated burst pressure of balloon as indicated on product label.**

**CAUTION:** In smaller or diffusely diseased vessels, the use of high balloon inflation pressures may over expand the vessel distal to the stent and could result in vessel dissection.



Actual balloon inflation diameter must be taken into consideration when using the stent in diffusely diseased vessels. (See Balloon Inflated Diameter dimensions on page 5.)

**NOTE:** The inflated balloon diameter measures .5 mm larger than the labeled luminal diameter of the stent to allow for stent recoil (approximately .5 mm) upon expansion.

**CAUTION:** Due to the compliant nature of the stent/balloon catheter material, prolonged pressurization in excess of the maximum recommended balloon pressure as specified on product label will result in over-distension of the stent and balloon.

**CAUTION:** Oversizing of the stent and use of higher than recommended inflation pressures may cause distal dissection. It is recommended that the stent size chosen closely approximates the diameter of the vessel and that recommended stent inflation pressures be used for stent deployment.

### **Balloon Deflation and Removal**

1. Using a 20 cc syringe, deflate the balloon. Allow adequate time for full balloon deflation.

**NOTE:** Negative pressure created by a 20 cc syringe provides better negative pressure than standard inflation devices.

2. **Very slowly** advance the balloon approximately 1 mm to help disengage the wings of the balloon from the stent. Avoid pushing the proximal "shoulder" of the balloon onto the coil itself.
3. **Very slowly** withdraw the balloon from the stent, maintaining negative suction, allowing movement of myocardium to gently dislodge balloon from stent. Maintain position of guiding catheter to prevent it from being drawn into vessel.

**NOTE:** Observation of the patient and angiographic evaluation of the stent site should be performed periodically within the first 30 minutes after stent placement. If stent placement is associated with the onset of thrombus or suspected thrombus in the region of the stented segment, intracoronary infusions of a thrombolytic agent is recommended.

### **MULTIPLE STENT PLACEMENT RECOMMENDATIONS**

If more than one stent placement is required for a patient, the following recommendations should be considered:

1. In relationship to the lesion site, the most distal area of narrowing should be stented first, followed by more proximal locations. **Positioning a coronary stent distal to a stent already in place can be difficult. Reintroduction of the balloon stent through the coronary stent may displace it.**
2. Coronary stents placed in tandem should touch one another or slightly overlap.

### **REMOVAL OF UNEXPANDED STENT**

If there are doubts about the integrity of the stent coil wrap, do not attempt to expand the stent. The stent/balloon catheter should be withdrawn until resistance is felt against the distal tip of the guiding catheter. The guiding catheter and stent/balloon catheter should then all be removed as one unit through the introducer sheath.

**CAUTION: Do not attempt to pull an unexpanded stent back through the guiding catheter, dislodgement of the stent may occur.**

**FURTHER DILATATION OF STENTED SEGMENTS**

If the initial angiographic result is suboptimal, the stent may be further expanded using a low profile, non-compliant balloon catheter. The stented segment should be recrossed carefully with a very flexible wire guide to avoid dislodging the fine stent coils.

**PRODUCT WARRANTY**

We warrant that at the time of manufacture, this product was prepared and tested in accordance with Good Manufacturing Practices specified by the United States Food and Drug Administration and was true to label. Because of biological differences in individuals, no product is 100% effective under all circumstances. In addition, because we have no control of the condition under which the product is used, diagnosis of the patient, the method of use or administration, and handling of the product after it leaves our possession, we do not warrant either a good effect or against an ill effect following the product's use. The foregoing warranty is exclusive and in lieu of all other warranties either written, oral, or implied (including any warranties of merchantability or fitness for purpose). No representative of the company may change any of the foregoing and the buyer accepts the product subject to all terms hereof.

## REFERENCES

Drug Protocol and Technical Information developed and provided by:

G.S. Roubin, M.D., Ph.D., Interventional Cardiology and Catheterization Laboratories, University of Alabama at Birmingham, Birmingham, Alabama.

C. A. Pinkerton, M.D., Cardiac Catheterization Laboratories, St. Vincent Hospital and Health Care Center, Indianapolis, Indiana.

1. C. Dotter: "Transluminally Placed Coil-Spring Endarterial Tube Grafts, Long Term Patency in Canine Popliteal Artery," *Investigative Radiology*, 4 (1969), 329-332.
2. D. Maas, L. Kropf, L. Egloff, D. Demierre, M. Turina, A. Senning: "Transluminal Implantation of Intravascular 'Double-helix' Spiral Prostheses: Technical and Biological Considerations," *ESAO Proceedings*, 9 (1982), 252-257.
3. A. Cragg, G. Hund, J. Rysavy, F. Castaneda, W. Castaneda-Zuniga, K. Amplatz: "Non-surgical Placement of Arterial Endoprostheses: A New Technique Using Nitinol Wire," *Radiology*, 147 (1983), 261-263.
4. C. Dotter, R. Buschmann, M. McKinney, J. Rösch: "Transluminal Expandable Nitinol Coil Stent Grafting: Preliminary Report," *Radiology*, 147 (1983), 259-260.
5. D. Maas: "Transluminal Implantation of Expandable Vascular Endoprostheses: A New Concept," *Circulation*, 70 (1984), 245.
6. D. Maas, C. Zollikofer, F. Hargiader, A. Senning: "Radiological Follow-up of Transluminally Inserted Vascular Endoprostheses: An Experimental Study Using Expanding Spirals," *Radiology*, 152 (1984), 659-663.
7. J. Palmaz, R. Sibbitt, S. Reuter, F. Garcia, F. Tio: "Expandable Intrahepatic Portocaval Shunt Stents: Early Experience in the Dog," *American Journal of Radiology*, 145 (1985), 821-825.
8. J. Palmaz, R. Sibbitt, S. Reuter, F. Tio, W. Rice: "Expandable Intraluminal Graft: A Preliminary Study," *Radiology*, 156 (1985), 73-77.
9. K. Wright, S. Wallace, C. Charnsangavej, C. Carrasco, C. Gianturco: "Percutaneous Endovascular Stents: An Experimental Evaluation," *Radiology*, 156 (1985), 69-72.
10. G. Roubin, C. Gianturco, J. Brown, K. Robinson, S. King: "Intracoronary Stenting of Canine Coronary Arteries After Percutaneous Coronary Angioplasty (PTCA)," *Circulation*, 74 (1986), 458.
11. J. Palmaz, S. Windeler, F. Garcia, F. Tio, R. Sibbitt, S. Reuter: "Atherosclerotic Rabbit Aortas: Expandable Intraluminal Grafting," *Radiology*, 160 (1986), 723-726.
12. G. Duprat, K. Wright, C. Charnsangavej, S. Wallace, C. Gianturco: "Flexible Balloon-expanded Stent for Small Vessels," *Radiology*, 162 (1987), 276-278.
13. U. Sigwart, J. Puel, V. Mirkovitch, F. Joffre, L. Kappenberger: "Intravascular Stents to Prevent Occlusion and Restenosis After Transluminal Angioplasty," *The New England Journal Of Medicine*, 316 (1987), 701-706.
14. R. Schatz, J. Palmaz, F. Tio, F. Garcia, O. Garcia, S. Reuter: "Balloon-expandable Intracoronary Stents in the Adult Dog," *Circulation*, 76 (1987), 450-457.
15. R. Schatz, J. Palmaz: "Intravascular Stents for Angioplasty," *Cardiology*, (1987), 27-31.
16. P. Serruys, Y. Juilliere, M. Bertrand, J. Puel, A. Rickards, U. Sigwart: "Additional Improvement of Stenosis Geometry in Human Coronary Arteries by Stenting After Balloon Dilatation," *American Journal of Cardiology*, 61 (1988), 71G-76G.
17. U. Sigwart, P. Urban, S. Golf, U. Kaufmann, C. Imbert, A. Fischer, L. Kappenberger: "Emergency Stenting for Acute Occlusion After Coronary Balloon Angioplasty," *Circulation*, 78 (1988), 1121-1127.

18. M. Goldsmith: "Artery-expanding Stents Widen Hopes for Patients with Atherosclerosis," *JAMA*, 259 (1988), 327.
19. K. Robinson, G. Roubin, R. Siegel, A. Black, R. Apkarian, S. King: "Intra-arterial Stenting in the Atherosclerotic Rabbit," *Circulation*, 78 (1988), 646-653.
20. C. Mullins, M. O'Laughlin, G. Vick, D. Mayer, T. Myers, D. Kearney, R. Schatz, J. Palmaz: "Implantation of Balloon Expandable Intravascular Stents by Catheterization in Pulmonary Arteries and Systemic Veins," *Circulation*, 77 (1988), 188.
21. S. King: "Percutaneous Transluminal Coronary Angioplasty: The Second Decade," *American Journal of Cardiology*, 62 (1988), 2K-6K.
22. R. Schatz: "A View of Vascular Stents," *Circulation*, 79 (1989), 445-457.
23. S. King: "Vascular Stents and Atherosclerosis," *Circulation*, 79 (1989), 460-462.
24. G. Rodgers, A. Raizner, D. Cromeens, K. Wright, C. Stevens, G. Roubin, S. Minor: "Coronary Spasm Induced by Stent Implantation." Abstract, *Journal American College of Cardiology*, 13 (1989), 194A.
25. A. Matsumoto, G. Teitelbaum, K. Barth, M. Carvlin, M. Savin, E. Strecker: "Tantalum Vascular Stents: In Vivo Evaluation with MR Imaging," *Radiology*, 170 (1989), 753-755.
26. B. Waller: "'Crackers, Breakers, Stretchers, Drillers, Scrapers, Shavers, Burners, Welders and Melters': The Future Treatment of Atherosclerotic Coronary Artery Disease? A Clinical-Morphologic Assessment," *Journal American College of Cardiology*, 13 (1989), 969-987.
27. S. Ellis, E. Topol: "Intracoronary Stents: Will They Fulfill Their Promise as an Adjunct to Angioplasty?," *Journal American College of Cardiology*, 13 (1989), 1425-1430.
28. M. Liu, G. Roubin, S. King: "Restenosis After Coronary Angioplasty," *Circulation*, 79 (1989), 1374-1387.
29. S. Ellis, R. Shaw, S. King, R. Myler, E. Topol: "Restenosis After Excellent Angiographic Angioplasty Result for Chronic Total Coronary Artery Occlusion: Implications for Newer Percutaneous Revascularization Devices," *Journal American College of Cardiology*, 64 (1989), 667-668.
30. D. Dichek, R. Neville, J. Zwiebel, S. Freeman, M. Leon, W. Anderson: "Seeding of Intravascular Stents with Genetically Engineered Endothelial Cells," *Circulation*, 80 (1989), 1347-1353.
31. K. Garrat, M. Heras, D. Holmes, G. Roubin, J. Chesebro: "Platelet Deposition and Thrombosis in Arterial Stents: Reduction with Hirudin Compared with Heparin Plus Antiplatelet Therapy." Abstract, *AHA*, November, 1989.
32. G. Rodgers, S. Minor, K. Robinson, D. Cromeens, S. Woolbert, L. Stephens, J. Guyton, K. Wright, G. Roubin, A. Raizner: "Adjuvant Therapy for Intracoronary Stents: Investigations in Atherosclerotic Swine," *Circulation*, 82 (1990), 560-569.
33. K. N. Garratt, D. R. Holmes, G. S. Roubin: "Early Outcome After Placement of a Metallic Intracoronary Stent: Initial Mayo Clinic Experience," *Mayo Clinic Proceedings*, 66 (1991), 268-275.

COOK CARDIOLOGY  
 A DIVISION OF COOK INCORPORATED  
 P. O. Box 489  
 Bloomington, IN 47402 U.S.A.  
 Phone: 812 339-2235  
 Toll Free: 800 457-4500  
 Toll Free FAX: 800 554-8335

WILLIAM A. COOK AUSTRALIA PTY. LTD.  
 A COOK GROUP COMPANY  
 Brisbane Technology Park  
 12 Electronics Street  
 Eight Mile Plains  
 Brisbane, QLD 4113 AUSTRALIA  
 Phone: 07 841-1188