P990008

Summary of Safety and Effectiveness Data

COOK® MBC PTCA Balloon Dilatation Catheter

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Summary of Safety and Effectiveness Data

COOK® MBC PTCA Balloon Dilatation Catheter
COOK® INCORPORATED

I. General Information

Generic Name of the Device:	Percutaneous transluminal coronary angioplasty catheter
Device Trade Name:	COOK® MBC PTCA Balloon Dilatation Catheter
PMA Number:	P990008
Name/Address of Applicant:	COOK® INCORPORATED 925 South Curry Pike P.O. Box 489 Bloomington, IN 47402

II. Indications for Use

The COOK® MBC PTCA balloon dilatation catheter is indicated for balloon dilatation of hemodynamically significant coronary artery or bypass graft stenosis in patients evidencing coronary ischemia for the purpose of improving myocardial perfusion.

III. Contraindications

- Unprotected left main coronary artery.
- Coronary artery spasm in the absence of a significant stenosis thought to be of hemodynamic significance.

IV. Warnings and Precautions

A. Warnings

- This device is intended for one time use only. Do NOT resterilize and/or reuse it.
- Prior to angioplasty, the catheter should be examined to verify functionality and ensure that its size and shape are suitable for the specific procedure for which it is to be used.
- The inflated diameter of the balloon should approximate the diameter of the coronary artery just proximal and distal to the stenosis. The danger of coronary dissection increases as the balloon to artery ratio increases past 1-to-1.
- The catheter system should be used only by physicians thoroughly trained in the performance of percutaneous transluminal coronary angioplasty.

- When the catheter is in the body, it should be manipulated while under high-quality fluoroscopic observation. Do not advance or retract the catheter unless the balloon is fully deflated under vacuum. If strong resistance is met during manipulation, discontinue the procedure and determine the cause of the resistance before proceeding.
- Balloon pressure should not exceed the rated burst pressure. Use of a pressure monitoring device is recommended to prevent over-pressurization.
- PTCA should only be performed at hospitals where emergency coronary artery bypass graft surgery can be immediately performed in the event of a potentially injurious or life-threatening complication. A cardiac surgery team must be on alert when a PTCA procedure is being performed.
- Use only the appropriate balloon inflation medium. Never use air or any gaseous medium to inflate the balloon.
- Use the catheter prior to the "**Use Before**" date specified on the package.

B. Precautions

- Before insertion of the dilatation catheter, administer appropriate anticoagulant, antiplatelet, and coronary vasodilator therapy.
- Caution should be taken not to over tighten a Tuohy-Borst type hemostatic adapter around the dilatation catheter shaft as lumen constriction may occur, affecting inflation/deflation of the balloon.

V. Device Description

The COOK® MBC PTCA balloon dilatation catheter is a percutaneous transluminal coronary angioplasty (PTCA) balloon catheter. This device is provided sterile and is intended for one-time use. This device is used in conjunction with conventional PTCA equipment, including, but not limited to, a vascular access set, arterial sheath, guiding catheter, guide wire and indeflator device.

The COOK® MBC PTCA balloon catheter is a double lumen catheter with a balloon near the distal tip. The catheter features a minimally compliant balloon constructed from high density polyethylene material. The balloon is designed to expand to a specified diameter and length at a specific pressure as labeled. The balloon catheter is provided in an overall length of 135 cm.

The catheter is compatible with 0.014-inch standard PTCA guide wires. Two radiopaque marker bands located at the proximal and distal ends of the balloon segment facilitate fluoroscopic visualization of the balloon during use.

VI. Alternative Practices and Procedures

Alternative treatments for coronary artery disease are medical therapy, coronary atherectomy, coronary laser, coronary stent, coronary endarterectomy, coronary artery bypass graft surgery, and other commercially available PTCA catheters.

VII. Marketing History

The COOK® MBC PTCA balloon dilatation catheter has not been commercially available.

VIII. Adverse Effects of the Device on Health

Possible adverse effects associated with percutaneous transluminal coronary angioplasty include, but are not limited to:

- coronary artery dissection, perforation, rupture or other injury
- conduction disturbance
- acute myocardial infarction
- unstable angina
- arteriovenous fistula
- coronary artery spasm
- total occlusion of the coronary artery or bypass graft
- hemorrhage or hematoma
- embolism
- infection
- restenosis of the dilated artery
- hypo/hypertension
- death

IX. Summary of Non-clinical Studies

A. Summary of the Nonclinical Laboratory Studies (*In-vitro*)

Balloon Minimum Burst Strength Test

Fifteen (15) balloon catheters of each size were tested to determine the rated burst

pressure.

The burst pressure data were analyzed using factors for one-sided tolerance to determine with 95% confidence that 99.9% of these balloons would not burst at or below the calculated rated burst pressure. The results are presented in Table 1. All balloon catheters had rated burst pressures of $\geq$ 12 atm. To provide an additional margin of safety, all balloons are labeled with a recommended pressure of 11 atm.

Table 1. Mean Burst, Rated Burst and Maximum Recommended Pressures

Balloon Catheter Size (mm)	Mean Burst Pressure (atm)	Rated Burst Pressure (atm)	Recommended Pressure (atm)
MBC-2.5-15	16.8	14	11
MBC-2.5-20	16.2	12	11
MBC-2.5-30	16.2	14	11
MBC-2.5-45	15.7	12	11
MBC-3.0-15	15.9	13	11
MBC-3.0-20	15.3	12	11
MBC-3.0-30	15.4	13	11
MBC-3.0-45	15.7	13	11
MBC-3.5-15	16.4	13	11
MBC-3.5-20	15.9	12	11
MBC-3.5-30	15.6	12	11
MBC-3.5-45	16.0	13	11
MBC-4.0-15	15.3	12	11
MBC-4.0-20	15.0	12	11
MBC-4.0-30	14.9	12	11
MBC-4.0-45	14.8	12	11

Balloon Distensibility Test

Fifteen (15) balloon catheters of each size were tested to determine how the balloon diameter varies with increasing balloon inflation pressure.

Table 2 presents the pressure at which nominal diameter is achieved, the rated burst pressure, the diameter at the rated burst pressure, and the ratio of the diameter at rated burst pressure to the nominal diameter.

Table 2. Pressures Required for Nominal Diameter and Diameter at Rated Burst Pressure

Balloon Catheter Size (mm)	Mean Pressure for Nominal Diameter (atm)	Rated Burst Pressure (atm)	Diameter at Rated Burst Pressure (mm)	Ratio of Diameter at Rated Burst Pressure to Nominal Diameter
2.5X15	6.5	14	2.84	1.14
2.5X20	5.8	12	2.79	1.11
2.5X30	6.4	14	2.83	1.13
2.5X45	6.4	12	2.77	1.11
3.0X15	6.6	13	3.33	1.11
3.0X20	6.8	12	3.29	1.10
3.0X30	6.9	13	3.34	1.11
3.0X45	7.5	13	3.31	1.10
3.5X15	6.4	13	3.90	1.11
3.5X20	7.1	12	3.83	1.09
3.5X30	7.4	12	3.82	1.09
3.5X45	7.5	13	3.87	1.11
4.0X15	7.1	12	4.36	1.09
4.0X20	7.5	12	4.35	1.09
4.0X30	7.5	12	4.35	1.09
4.0X45	7.6	12	4.33	1.08

Table 3 presents balloon compliance (diameter versus inflation pressure) for all sizes of the COOK® MBC PTCA balloon dilatation catheter.

Table 3. Balloon Compliance (Diameter vs Pressure) for the COOK® MBC PTCA Catheters

Balloon Diameter (mm):		2.5				3.0				3.5				4.0			
Balloon Length (mm):		15	20	30	45	15	20	30	45	15	20	30	45	15	20	30	45
Inflation Pressure (atm)	2	2.31	2.34	2.32	2.31	2.76	2.74	2.74	2.67	3.22	3.18	3.12	3.15	3.61	3.55	3.52	3.46
	3	2.35	2.37	2.36	2.34	2.81	2.79	2.79	2.75	3.27	3.22	3.21	3.21	3.68	3.63	3.62	3.64
	4	2.39	2.42	2.39	2.38	2.85	2.83	2.83	2.79	3.33	3.27	3.27	3.27	3.75	3.70	3.70	3.70
	5	2.43	2.45	2.43	2.43	2.90	2.89	2.88	2.85	3.39	3.34	3.33	3.32	3.82	3.77	3.77	3.78
	6	2.46	2.50	2.47	2.48	2.96	2.94	2.94	2.90	3.46	3.41	3.40	3.39	3.91	3.86	3.86	3.86
	*7	2.51	2.55	2.52	2.53	3.02	3.01	3.00	2.97	3.53	3.48	3.47	3.46	3.99	3.95	3.95	3.95
	8	2.57	2.60	2.58	2.58	3.08	3.08	3.07	3.03	3.60	3.56	3.55	3.54	4.07	4.05	4.04	4.04
	9	2.62	2.66	2.63	2.63	3.14	3.14	3.13	3.10	3.67	3.63	3.62	3.61	4.15	4.13	4.13	4.12
	10	2.67	2.70	2.67	2.68	3.19	3.19	3.19	3.16	3.73	3.70	3.69	3.68	4.22	4.20	4.21	4.19
	**11	2.71	2.74	2.71	2.72	3.24	3.24	3.24	3.21	3.79	3.76	3.75	3.75	4.29	4.27	4.27	4.26
	12	2.75	2.78	2.75	2.76	3.29	3.29	3.29	3.26	3.84	3.82	3.82	3.81	4.36	4.34	4.34	4.33
	13	2.79	2.82	2.79	2.80	3.34	3.34	3.34	3.31	3.89	3.88	3.87	3.87	4.42	4.40	4.40	4.39
	14	2.82	2.86	2.82	2.84	3.38	3.38	3.39	3.36	3.95	3.94	3.93	3.93	4.47	4.47	4.46	4.46
	15	2.86	2.89	2.86	2.87	3.42	3.42	3.43	3.40	4.00	3.99	3.98	3.98				

* Applying 7 atm inflation pressure will produce near nominal diameter for all balloons.

** 11 atm is the labeled rated burst pressure.

Note: Values of balloon diameter printed were measured up to 25% above the rated burst pressure (shaded area) for the specified balloon.

Balloon Inflation/Deflation Time Test

Two (2) catheters of each size were tested to show that the inflation and deflation times for these catheters are within clinically acceptable limits.

All the balloons inflated in no more than four (4) seconds and deflated in less than fourteen (14) seconds. Inflation times for all 16 balloon sizes were similar, averaging 3.1 ± 0.4 seconds. Deflation times were more closely related to balloon size, with larger diameter, longer balloons deflating more slowly than smaller balloons.

These inflation/deflation times are similar to those of devices currently on the market and are adequate for the intended use.

Balloon Fatigue Test

Thirty (30) catheters of each size were tested to determine with 95% confidence that at least 90% of the balloons will sustain 40 repeated inflations to the maximum recommended pressure (11 atm).

All test samples successfully passed this fatigue test. The COOK® MBC PTCA balloon catheter should have adequate fatigue resistance when used according to the Instructions for Use.

Bond Strength Test

Twenty (20) catheters of various sizes were tested to determine the strength of bonds in the catheter.

Two bond sites were tested for this report. Test loads exceeded the strength of the 3 Fr bulk material before either bond site failed. Therefore, the strength of the bond sites is considered adequate for the intended use.

Catheter Diameter and Balloon Profile

All PTCA catheters of the current design have a shaft that is 3.5 Fr OD (0.044 ± 0.0015 inch) at its proximal end and 3.0 Fr OD (0.04 ± 0.0015 inch) along its distal most 25 cm. Catheters of each size were tested to determine the largest outside diameter along the distal half of the working length of the balloon and catheter tip when the catheter is in its deflated state. Table 4 presents the results of this test.

Table 4. Deflated Balloon Profile

Balloon Catheter (mm)	Largest Outer Diameter (in)
2.5X15	0.044
2.5X20	0.043
2.5X30	0.042
2.5X45	0.044
3.0X15	0.047
3.0X20	0.047
3.0X30	0.047
3.0X45	0.048
3.5X15	0.057
3.5X20	0.057
3.5X30	0.056
3.5X45	0.058
4.0X15	0.059
4.0X20	0.061
4.0X30	0.058
4.0X45	0.060

Over-the-Arch Torque Strength Test

Ten (10) catheters of various sizes were tested to determine the torque strength of the catheter when its distal tip is not free to rotate. With the distal tip prevented from rotating, a high number of catheter rotations (in excess of 70) is needed to cause the catheter to fail. It is unlikely the catheter would be subjected to this number of rotations in clinical use.

Over-the-Arch Torque Response Test

Five (5) catheters of different sizes were tested to evaluate the torque response characteristics of the catheter by analyzing the degree of distal tip rotation for a given proximal end rotation.

Ten complete rotations of the proximal end of the catheter produced no rotation of the distal end. The balloon catheter did not transmit enough torque to cause the distal end to rotate when torque was applied to the proximal end.

B. Animal Testing (*In-vivo*)

Animal testing was not required on this device.

C. Biocompatibility Testing

Appropriate compliance with the criteria specified for material and biocompatibility toxicity testing was undertaken in accordance with the recommendations of the PTCA Catheter System Testing Guidance Document and Tripartite Biocompatibility Guidance for Medical Devices prepared by the Toxicology Sub-Group of the Tripartite Subcommittee on Medical Devices in September of 1986. The tests performed to establish biocompatibility were conducted by an independent laboratory (NamSA®, Northwood, OH) and included:

1. Delayed Contact Sensitization (Guinea Pig Maximization Method)
2. Irritation (U.S.P. Intracutaneous Toxicity Study in the Rabbit)
3. Cytotoxicity (U.S.P. MEM Elution Test)
4. Systemic Toxicity (U.S.P. Mouse Systemic Toxicity Test)
5. Hemolysis (Extraction Method)
6. Implantation (7 Day Rabbit Muscle Implant Test)
7. Mutagenicity (Ames Salmonella Mutagenicity Assay with Saline and DMSO Extracts)

The results of these tests provided no evidence to suggest that the device is not biocompatible.

D. Sterilization, Packaging and Shelf-Life Testing

COOK® Incorporated sterilizes devices using a sterilization cycle that has been validated to a 10^{-6} sterility assurance level. This process is routinely monitored, calibrated and operated in adherence with the *Guidance for Industrial Ethylene Oxide Sterilization of Medical Devices: Association for the Advancement of Medical Instruction.* COOK® Incorporated has tested to determine the resistance data (D-value) for the product in the package. The design and raw materials of the balloon catheter as well as its proposed packaging raise no new questions regarding sterility of the device when subjected to the validated sterilization cycles. The COOK® MBC PTCA balloon catheter is packaged in a peel-pouch system that is currently used for previously approved, commercially available devices. The shelf life studies reveal that the package configuration and materials provides an acceptable bacterial barrier and that two years is an appropriate sterility expiration period.

X. Summary of the Clinical Investigation

This study was intended to collect data regarding procedural success and the incidence of major adverse cardiac events in patients treated for myocardial ischemia with the COOK® MBC PTCA Balloon Catheter. This study was designed as a multicenter, prospective registry in which 150 patients eligible for elective coronary angioplasty who met the inclusion/exclusion criteria were enrolled from 6 investigative sites. Recognizing there are numerous PTCA balloon catheters available for performing conventional angioplasty, none is considered the "gold standard." Therefore, no contemporary control group was justifiable for performing a randomized, controlled study.

A. Structured Abstract

Title: A Multicenter Registry Evaluating the COOK® MBC PTCA Balloon Catheter for Dilating the Stenotic Portion of a Coronary Artery or Bypass Graft for the Purpose of Improving Myocardial Perfusion

Investigators: Six (6) U.S. sites participated. In addition to the 5 principal investigators, 23 other physicians served as operators using the MBC PTCA Balloon Catheter during this study.

Purpose: To evaluate procedural success and the incidence of major adverse cardiac events including death, Q-wave MI, CABG or repeat PTCA within 30 days of the procedure in which the COOK® MBC PTCA Balloon Dilatation Catheter was used.

Design: A multicenter, prospective registry study to collect: 1) qualitative and quantitative angiographic data recorded by both the investigators during the procedure and by post-procedure independent core lab analysis; and 2) data to assess the incidence of clinically significant ischemic events including death, Q-wave MI, CABG, and repeat PTCA of the culprit vessel.

Demographics: One hundred fifty (150) patients were enrolled in the MBC Balloon Catheter Clinical Study. Mean age = 62 ± 11 years, 65% were male, 33% were diabetic, 29% were obese, 64% were hypertensive, 67% had high cholesterol, 12% had prior PTCA to the culprit lesion, 16% had prior CABG, 42% had prior MI, 63% had multiple vessel disease, and a mean LVEF=50%. The culprit vessels were LAD (43%), LCX

(17%), RCA (34%), RAMUS (2%), and the SVG (4%). Key lesion characteristics included lesion class of B_2 and C (41%), moderate or severe tortuosity (28%), diffuse disease (24%), calcification (6%), and branch point (11%). Mean lesion length was 9.97±4.97 mm.

Method: Demographics, clinical and procedural angiographic data were collected from 150 patients consecutively enrolled. QCA was performed by the Cardiovascular Angiography Analysis Lab at The Methodist Hospital Center in Houston, Texas.

Conclusions: Of the 150 patients enrolled in the COOK® MBC PTCA Balloon Catheter registry, 13 patients were not treated with the MBC balloon catheter and 137 underwent dilatation with the MBC balloon catheter. Twenty-two (22) patients were treated with the MBC balloon catheter only. In 115 patients, the MBC balloon was used to predilate the vessel prior to placing a stent. The 30-day combined incidence of death, Q-wave MI and target lesion revascularization was 0.9% [95% CI = 0.0, 3.7] for all patients enrolled in the clinical study (N=150). These results indicate that the COOK® MBC PTCA Balloon Catheter can be successfully used as a definitive therapy when appropriate, or to predilate a vessel prior to elective stent placement. The low incidence of adverse events suggests that no new safety issues are raised by this device.

B. Subject Selection and Exclusion Criteria

Patients were entered into the study if they met all of the following inclusion criteria and none of the exclusion criteria.

Inclusion Criteria:

Patients must meet all the following inclusion criteria:

1. Patient must be eligible to undergo elective PTCA of a *de novo* or restenosed lesion(s) in a native coronary artery or graft.
2. Normal reference vessel diameter (RVD) must be 2.5 mm to 4.0 mm.
3. All lesions requiring intervention must be considered to be treatable with the COOK® MBC PTCA balloon catheter as the first and only interventional device.
4. Patient or legal guardian must have signed the informed consent document.

Exclusion Criteria:

Patients must be excluded if any of the following conditions are true:

1. Patient will not agree to be available for follow-up.
2. Intolerance to contrast agent or aspirin.
3. Severely impaired left ventricular function (LVEF < 35%).
4. Presentation in cardiogenic shock.
5. Candidate is not acceptable for coronary artery bypass surgery.
6. Acute myocardial infarction or an MI within past 3 days.
7. Previous diagnosis of coronary artery spasm.
8. Totally obstructed coronary arteries.
9. Left main coronary artery disease.
10. Diffuse disease.
11. Calcified stenosis.
12. Prior intervention has been performed during this procedure with any other approved or investigative device (e.g., rotational atherectomy, directional atherectomy, another PTCA balloon, etc.).

C. Study Population

One hundred fifty (150) patients were enrolled in the COOK® MBC PTCA Balloon Catheter Clinical Study. Table 5 presents baseline patient demographics and clinical characteristics for the 150 patients enrolled in the clinical study.

Table 5. Baseline Demographics and Clinical Characteristics (N=150)

		n	%	95% CI
Number of Males		97	64.7	56.4, 72.2
Smoking Status				
Current Smoker		30	20.0	14.1, 27.5
Quit Smoking		61	40.7	32.8, 49.0
Never Smoked		52	34.7	27.2, 42.9
Not Reported		7	4.7	2.1, 9.8
Diabetes		50	33.3	26.0, 41.6
Obesity		43	28.7	21.7, 36.7
Hypertension		96	64.0	55.7, 71.6
Hypercholesterolemia		101	67.3	59.1, 74.6
Previous PTCA to Lesion Site		18	12.0	7.5, 18.6
Previous CABG		24	16.0	10.7, 23.1
Previous MI		63	42.0	34.1, 50.3
Multi-Vessel Disease		95	63.3	55.0, 70.9
Pre Procedure Angina Class	0	9	6.0	3.0, 11.4
	1	18	12.0	7.5, 18.6
	2	27	18.0	12.4, 25.3
	3	45	30.0	22.9, 38.1
	4	28	18.7	13.0, 26.0
	Not Reported	23	15.3	10.2, 22.3
Target Lesion Vessel	LAD	64	42.7	34.7, 51.0
	LCX	26	17.3	11.8, 24.6
	RCA	51	34.0	26.6, 42.2
	RAMUS	3	2.0	0.4, 5.7
	SVG	6	4.0	1.6, 8.9
Age (years)				
	Mean±SD	62±11		
	Range	30-82		
	N	150		
Ejection Fraction (%)				
	Mean±SD	49.7±10.22		
	Range	10-74		
	N	133		

95%CI=95% upper and lower confidence intervals

Table 6 presents baseline angiographic characteristics of the culprit lesion site prior to the PTCA procedure. Data from the Case Report Forms (CRF) and the angiographic core lab analysis are presented for comparison.

Table 6. Baseline Angiographic Characteristics of the Culprit Lesion Prior to the Initial PTCA Procedure

	Data from CRF (N=150)			Core Lab Analysis (N=149)		
Average Reference Vessel Diameter (mm)						
Mean ±SD	3.08±0.51			3.09±0.52		
Range	1.65 - 4.38			1.97 - 4.27		
N	137			148		
Minimum Lumen Diameter (mm)						
Mean ±SD	0.75±0.52			0.71±0.39		
Range	0.03 - 2.90			0.18 - 1.99		
N	137			148		
Lesion Length (mm)						
Mean ±SD	14.6±6.2			9.97±4.97		
Range	5.0 - 40.0			3.59 - 36.64		
N	110			148		
	n	%	95% CI	n	%	95% CI
Lesion Classification						
A	14	9.3	5.4, 15.5	24	16.1	10.8, 23.2
B_1	64	42.7	34.7, 51.0	64	43.0	35.0, 51.3
B_2	54	36.0	28.5, 44.3	54	36.2	28.7, 44.6
C	16	10.7	6.4, 17.0	7	4.7	2.1, 9.8
Not Reported	2	1.3	0.2, 4.7	0	0.0	0.0, 2.5
Proximal Tortuosity						
None	45	30.0	22.9, 38.1	32	21.5	15.4, 29.1
Mild	75	50.0	41.8, 58.2	76	51.0	42.7, 59.2
Moderate	23	15.3	10.2, 22.3	36	24.2	17.7, 32.0
Severe	3	2.0	0.4, 5.7	5	3.4	1.2, 8.1
Not Reported	4	2.7	0.7, 6.7	0	0.0	0.0, 2.5
Diffuse Disease	28	18.7	13.0, 26.0	36	24.2	17.7, 32.0
Any Calcification	26	17.3	11.8, 24.6	9	6.0	3.0, 11.5
Angulation > 45°	12	8.0	4.4, 13.9	5	3.4	1.2, 8.1
Eccentric	124	82.7	75.5, 88.2	88	59.1	50.7, 67.0
Branch Point	22	14.7	9.6, 21.6	17	11.4	7.0, 17.9
Ostial Location	6	4.0	1.6, 8.9	6	4.0	1.7, 8.9
Other Stenoses >50% in Target Vessel	21	14.0	9.1, 20.8	18	12.1	7.5, 18.7

95% CI=95% upper and lower confidence intervals

D. Study Period

Patients were enrolled from January 14, 1998 through October 5, 1998.

E. Safety and Effectiveness Data

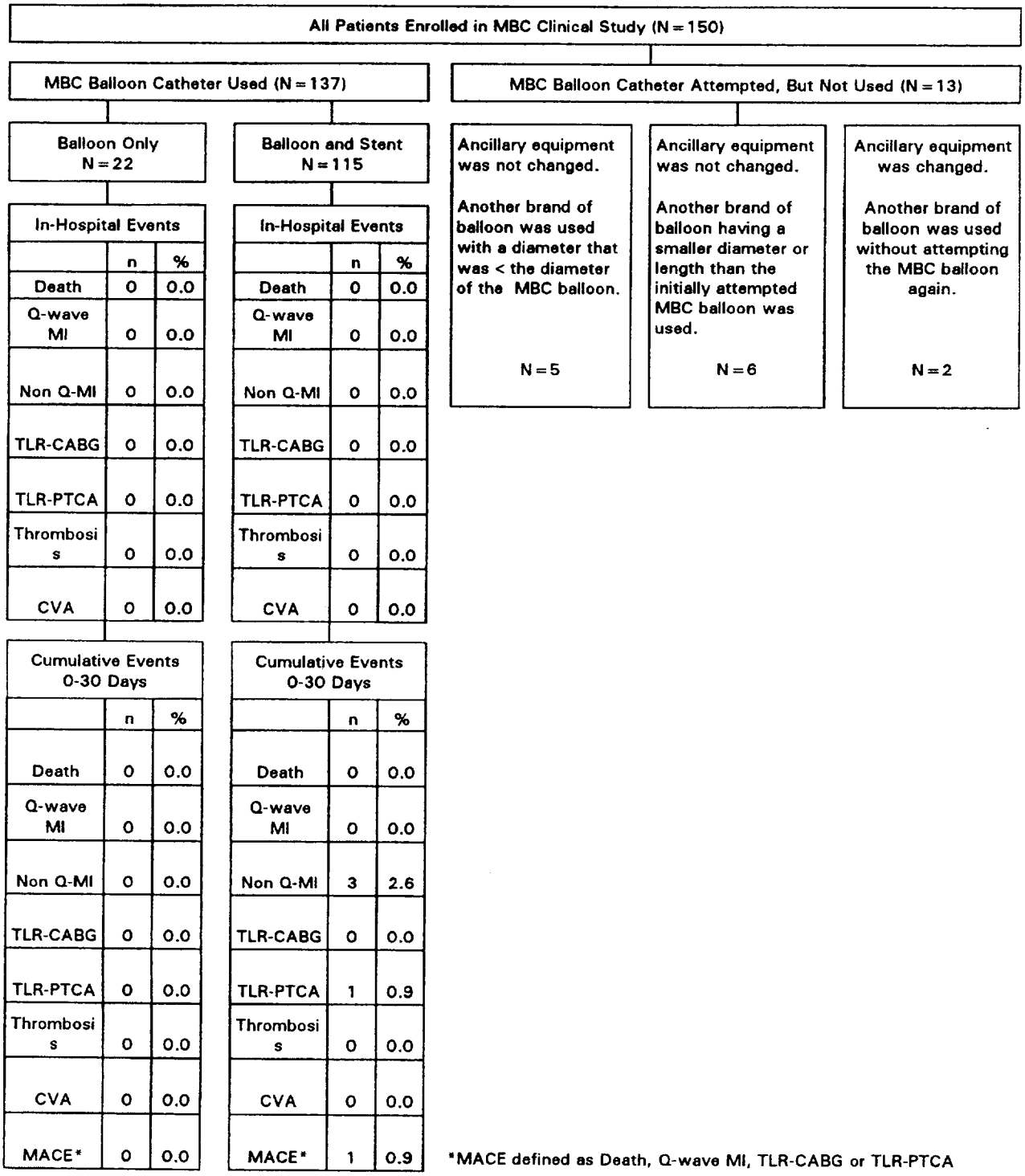
The results of this study must be interpreted keeping in mind current practice in interventional cardiology. In particular, angioplasty balloons alone are rarely used as definitive therapy. The vast majority of patients treated for coronary artery disease by interventional cardiologists now receive stents on an elective basis. That is, the use of a stent is planned in advance and is rarely determined by the outcome of the balloon dilatation procedure. Thus, the "success" of the balloon dilatation procedure can no longer be defined in isolation in traditional terms (i.e., <50% residual diameter stenosis with at least a 20% reduction). The balloon is frequently used simply to adequately open the lesion so that a stent can be placed. Thus, a "successful" angioplasty procedure may now rightly be considered one in which either a balloon alone produces a residual diameter stenosis <50%, or a balloon provides initial dilatation permitting a stent to be placed thereby producing a residual diameter stenosis <50%, with no major adverse cardiac events in-hospital.

The results of this study are presented with these considerations in mind. The outcome following use of the COOK® MBC PTCA balloon catheter are presented both for those patients in whom the balloon was used alone and those patients who received stents following dilatation with the MBC balloon. The procedural outcome was assessed based upon the entire procedure whether the MBC balloon was used alone or to predilate the vessel to permit stent placement.

Figure 1 presents the flow diagram for patients enrolled in this study. Twenty-two (22) patients were treated with the MBC balloon catheter alone. In 115 patients, the MBC balloon was used to predilate the vessel prior to placing a stent. In 13 patients, the MBC balloon was not used. However, these 13 cases fall into 3 categories, not all of which should be considered a failure of the balloon. In 5 cases, another brand of balloon of at least equal size to the original MBC balloon was used successfully without changing the ancillary equipment. These 5 cases (3.3%) can be considered technical failures of the MBC balloon to perform successfully. In 6 cases, a balloon of another brand was used

that was smaller in either diameter or length than the MBC balloon originally attempted. In these 6 cases, a smaller MBC balloon was either not available or attempted before changing to another brand. These cases should not be considered technical failures of the balloon since the optimum size MBC balloon was not attempted before changing to a different device. In 2 cases, ancillary equipment was changed and another brand balloon was used without using an MBC balloon with the new ancillary equipment. These 2 cases should not be considered technical failures of the balloon since changing the ancillary equipment may have altered the environment such that an MBC balloon would have been successful had it been attempted.

Figure 1. Patient Flow Diagram



In-Hospital Events

	Balloon Only N = 22		Balloon and Stent N = 115	
	n	%	n	%
Death	0	0.0	0	0.0
Q-wave MI	0	0.0	0	0.0
Non Q-MI	0	0.0	0	0.0
TLR-CABG	0	0.0	0	0.0
TLR-PTCA	0	0.0	0	0.0
Thrombosis	0	0.0	0	0.0
CVA	0	0.0	0	0.0

Cumulative Events 0-30 Days

	Balloon Only N = 22		Balloon and Stent N = 115	
	n	%	n	%
Death	0	0.0	0	0.0
Q-wave MI	0	0.0	0	0.0
Non Q-MI	0	0.0	3	2.6
TLR-CABG	0	0.0	0	0.0
TLR-PTCA	0	0.0	1	0.9
Thrombosis	0	0.0	0	0.0
CVA	0	0.0	0	0.0
MACE*	0	0.0	1	0.9

*MACE defined as Death, Q-wave MI, TLR-CABG or TLR-PTCA

Table 7 presents qualitative and quantitative angiographic characteristics of the culprit lesion site after the PTCA procedure with the COOK® MBC balloon catheter. The data are analyzed separately for those patients in whom only the MBC balloon was used and those patients who were subsequently stented after using the MBC balloon. (Note: Data are from the Case Report Forms.)

Table 7. Status of the Culprit Lesion after Using the MBC Balloon

	MBC Balloon Only (N=22)			MBC Balloon+Stent (Prior to Stenting) (N=115)			All Patients Treated with MBC Balloon (N=137)		
	n	%	95% CI	n	%	95% CI	n	%	95% CI
Dissection									
Yes	4	18.2	5.2, 40.3	33	28.7	20.8, 38.0	37	27.0	19.95, 35.38
Dissection Type									
No Dissection	18	81.8	59.7, 94.8	82	71.3	62.0, 79.2	100	73.0	64.62, 80.05
Linear	3	13.6	2.9, 34.9	27	23.5	16.3, 32.5	30	21.9	15.48, 29.93
Spiral	0	0.0	0.0, 15.4	2	1.7	0.2, 6.1	2	1.5	0.18, 5.17
Not Reported	1	4.5	0.1, 22.8	4	3.5	1.0, 8.7	5	3.6	1.35, 8.74
Dissection Grade									
No Dissection	18	81.8	59.7, 94.8	82	71.3	62.0, 79.2	100	73.0	64.62, 80.05
A	2	9.1	1.1, 29.2	13	11.3	6.4, 18.9	15	10.9	6.47, 17.71
B	1	4.5	0.1, 22.8	14	12.2	7.1, 19.9	15	10.9	6.47, 17.71
C	0	0.0	0.0, 15.4	4	3.5	1.0, 8.7	4	2.9	0.80, 7.31
D	0	0.0	0.0, 15.4	2	1.7	0.2, 6.1	2	1.5	0.18, 5.17
E	0	0.0	0.0, 15.4	0	0.0	0.0, 3.2	0	0.0	0.00, 2.66
F	0	0.0	0.0, 15.4	0	0.0	0.0, 3.2	0	0.0	0.00, 2.66
Not Reported	1	4.5	0.1, 22.8	0	0.0	0.0, 3.2	1	0.7	0.02, 4.00
Dissection Length (mm)									
Mean±SD	8.0 ± 2.8			10.4 ± 8.2			10.3 ± 7.9		
Range	6.0 - 10.0			2.0 - 35.0			2.0 - 35.0		
N	2			26			28		
Intimal Flap	2	9.1	1.1, 29.2	15	13.0	7.7, 20.9	17	12.4	7.61, 19.39
Thrombus Present	0	0.0	0.0, 15.4	4	3.5	1.0, 8.7	4	2.9	0.80, 7.31
Spasm	0	0.0	0.0, 15.4	7	6.1	2.7, 12.6	7	5.1	2.26, 10.64
ST Segment Changes	1	4.5	0.1, 22.8	10	8.7	4.5, 15.8	11	8.0	4.28, 14.25
Side Branch Closure	0	0.0	0.0, 15.4	0	0.0	0.0,3.2	0	0.0	0.00, 2.66
Angina	2	9.1	1.1, 29.2	11	9.6	5.1, 16.8	13	9.5	5.35, 15.99
TIMI Flow									
0	0	0.0	0.0, 15.4	0	0.0	0.0, 3.2	0	0.0	0.00, 2.66
1	0	0.0	0.0, 15.4	0	0.0	0.0, 3.2	0	0.0	0.00, 2.66
2	0	0.0	0.0, 15.4	3	2.6	0.5, 7.4	3	2.2	0.45, 6.27
3	22	100.0	84.6, 100.0	110	95.7	89.7, 98.4	132	96.4	91.26, 98.65
Not Reported	0	0.0	0.0, 15.4	2	1.7	0.2, 6.1	2	1.5	0.18, 5.17

95% CI=95% upper and lower confidence intervals

Table 8 presents quantitative angiographic characteristics of the culprit lesion site prior to (Baseline) and after the PTCA procedure (Post-PTCA). The data are analyzed separately for those patients in whom only the MBC balloon was used, those patients who were subsequently stented after using the MBC balloon, those patients not treated with the MBC balloon and all patients enrolled in the study. (Note: All data are from the angiographic core lab analysis.)

Table 8. Angiographic Core Lab QCA Analysis of the Culprit Lesion

	MBC Balloon Only (N=22)	MBC Balloon+Stent (Prior to Stenting) (N=115)	Patients Not Treated with the MBC Balloon (N=13)	All Patients (N=150)
Baseline				
Average Reference Vessel Diameter (mm)				
Mean±SD	2.67±0.46	3.22±0.48	2.59±0.32	3.08±0.52
Range	2.08 - 3.80	1.97 - 4.27	1.97 - 3.12	1.97 - 4.27
N	21	114	13	148
Minimum Lumen Diameter (mm)				
Mean±SD				
Range	0.56±0.74	0.75±0.39	0.49±0.34	0.70±0.39
N	0.26 - 1.91	0.18 - 1.99	0.26 - 1.58	0.18 - 1.99
	21	114	13	148
Percent Diameter Stenosis (%)				
Mean±SD				
Range	79.8±11.8	76.8±10.3	81.7±10.3	77.7±10.6
N	49.7 - 89.7	51.6 - 94.1	49.4 - 89.7	49.4 – 94.1
	21	114	13	148
Post-PTCA				
Average Reference Vessel Diameter (mm)				
Mean±SD	2.61±0.45	3.18±0.47	2.46±0.27	3.04±0.53
Range	1.92 - 3.76	1.96 - 4.22	2.05 - 2.91	1.92 – 4.22
N	21	113	12	146
Minimum Lumen Diameter (mm)				
Mean±SD	1.89±0.49	1.99±0.56	1.62±0.37	1.94±0.54
Range	1.18 - 3.11	0.33 - 3.58	1.15 - 2.27	0.33 – 3.58
N	21	113	12	146
Percent Diameter Stenosis (%)				
Mean±SD	27.9±9.53	37.4±14.2	34.5±11.0	35.8±13.7
Range	3.29 - 43.8	1.68 - 88.6	20.7 - 47.7	1.7 – 88.6
N	21	113	12	146

Figures 2 and 3 present the cumulative frequency distribution curves for MLD and %DS, respectively, with separate curves for patients who were treated with the MBC balloon only, with the MBC balloon followed by stenting, and for patients in whom the MBC balloon was not used.

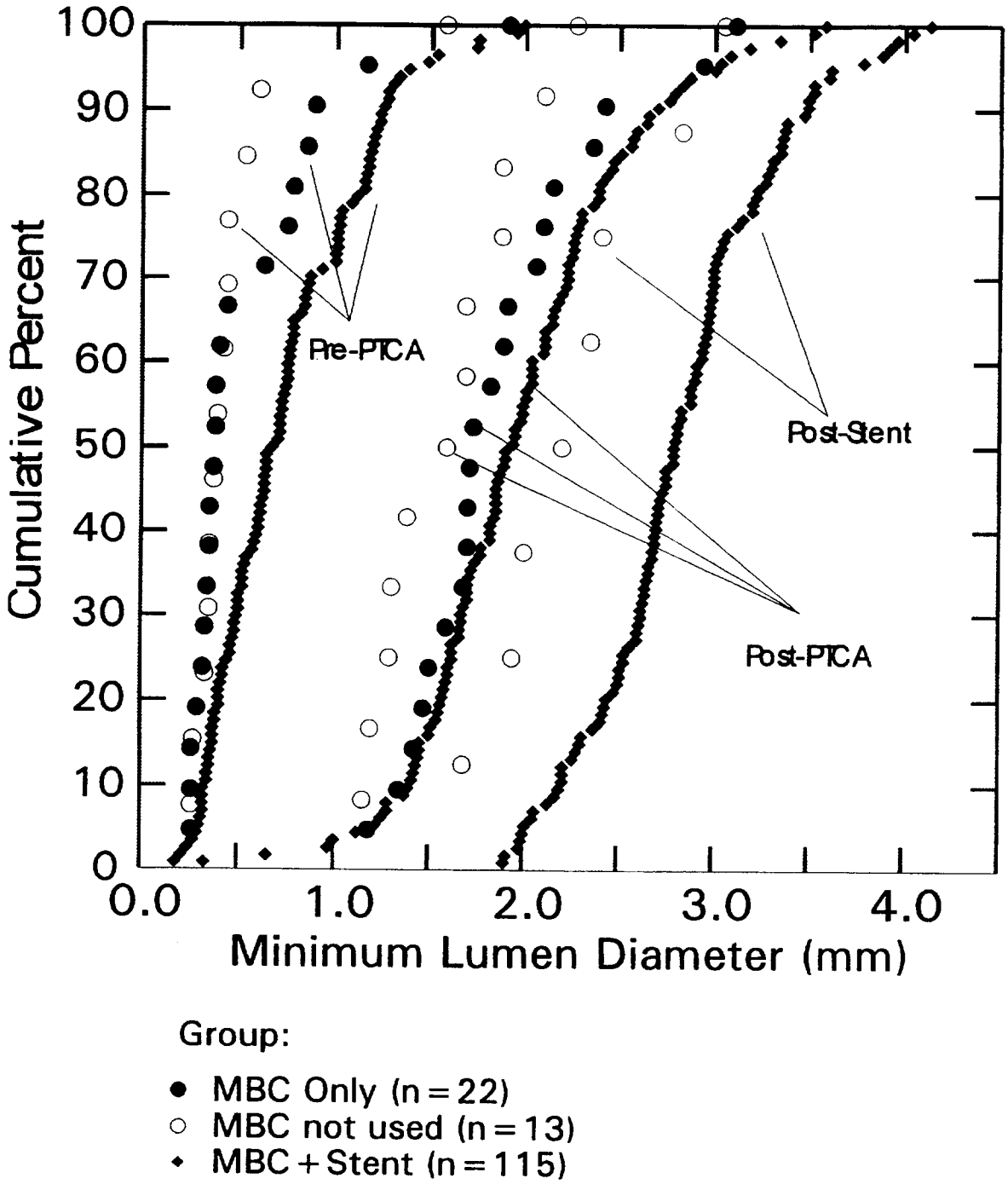
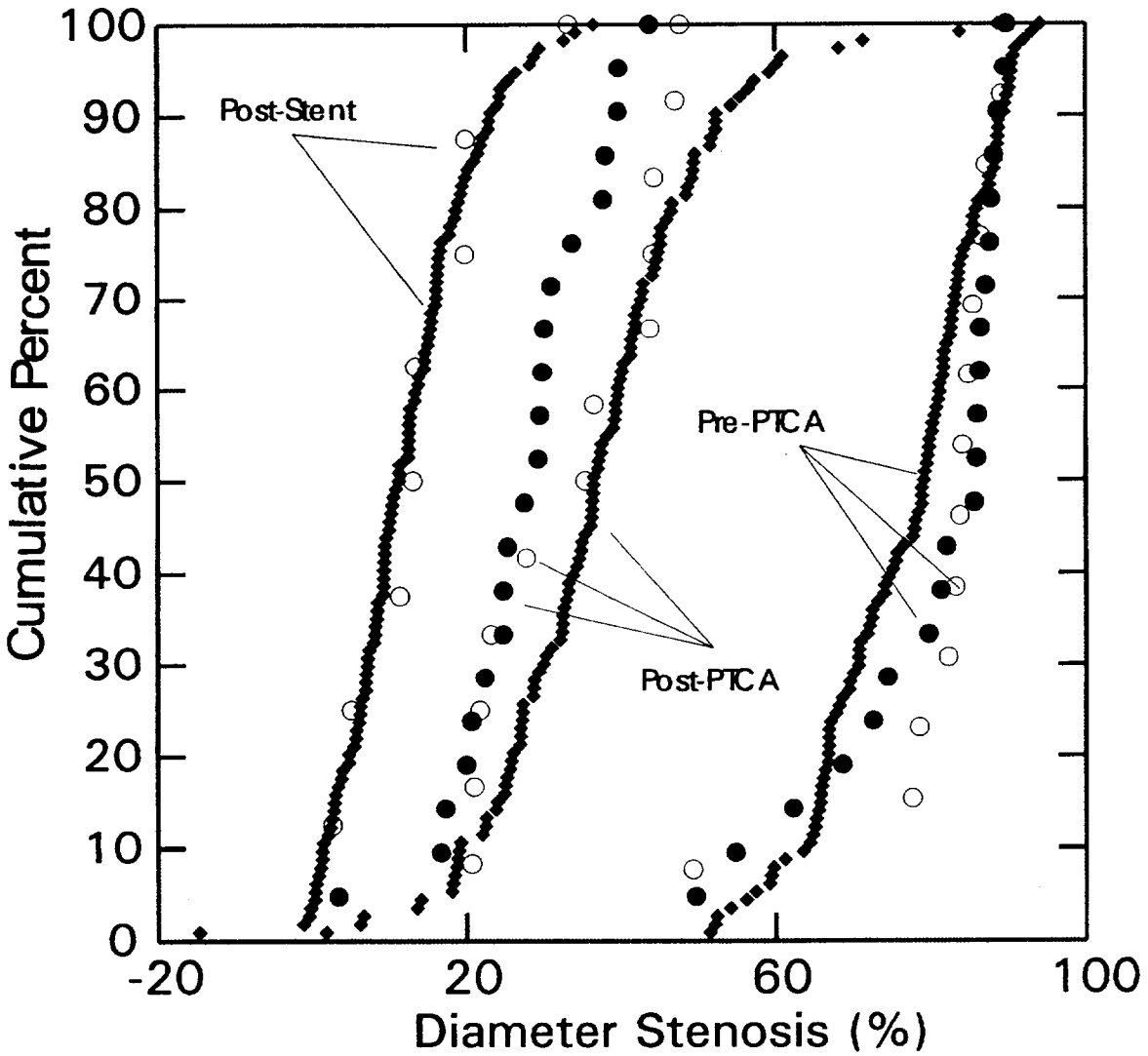


Figure 2. Cumulative percent of patients versus Minimum Lumen Diameter in patients receiving the MBC PTCA Balloon only, the MBC balloon followed by discretionary stenting, and in patients in whom the MBC balloon was not used.



Group:

- ● MBC Only (n = 22)
- o MBC not used (n = 13)
- ◆ MBC + Stent (n = 115)

Figure 3. Cumulative percent of patients versus Percent Diameter Stenosis in patients receiving the MBC PTCA Balloon only, the MBC balloon followed by discretionary stenting, and in patients in whom the MBC balloon was not used.

F. Principal Effectiveness and Safety Results

The clinical outcome for the patients enrolled is summarized in Tables 9 and 10. This section provides additional information with respect to adverse events that occurred subsequent to the PTCA procedure.

Table 9. Principal Effectiveness and Safety Results

All Patients Enrolled in the MBC Study (N = 150)						
	0-Discharge			0-30 Days		
	n	%	95% CI	n	%	95% CI
Clinical Efficacy Measures:						
Death	0	0.0	0.0, 2.4	0	0.0	0.0, 2.4
Q-MI*	0	0.0	0.0, 2.5	0	0.0	0.0, 2.5
Non-Q Wave MI*	2	1.3	0.2, 4.8	3	2.0	0.4, 5.8
CABG	0	0.0	0.0, 2.4	0	0.0	0.0, 2.4
PTCA	0	0.0	0.0, 2.4	1	0.9	0.0, 3.7
Death/Q-MI/CABG/PTCA*	0	0.0	0.0, 2.5	1	0.9	0.0, 3.7
Death/Any MI/CABG/PTCA*	2	1.3	0.2, 4.8	3	2.0	0.4, 5.8
Safety Measures:						
Thrombosis*	0	0.0	0.0, 2.5	0	0.0	0.0, 2.5
CVA*	0	0.0	0.0, 2.5	0	0.0	0.0, 2.5
Vascular Event Requiring Surgery*	1	0.7	0.0, 3.7	1	0.7	0.0, 3.7
Bleeds or Vascular Complications*	0	0.0	0.0, 2.5	1	0.7	0.0, 3.7
Patients treated with the MBC Balloon Only (N = 22)						
	0-Discharge			0-30 Days		
	n	%	95% CI	n	%	95% CI
Clinical Efficacy Measures:						
Death	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4
Q-MI	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4
Non-Q Wave MI	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4
CABG	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4
PTCA	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4
Death/Q-MI/CABG/PTCA	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4
Death/Any MI/CABG/PTCA	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4
Safety Measures:						
Thrombosis	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4
CVA	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4
Vascular Event Requiring Surgery	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4
Bleeds or Vascular Complications	0	0.0	0.0, 15.4	0	0.0	0.0, 15.4

95% CI=95% upper and lower confidence intervals

*The percentage and 95% CI were based upon N=12 and N=149 because data were not available for one patient.

Other Reported Events

For the patients enrolled in the MBC study (N=149), the following additional events within 30 days of the procedure, were reported: 3 PTCA procedures to other lesions, 12 incidences of chest pain, 1 incidence of ventricular tachycardia, 5 episodes of bradycardia, 3 episodes of hypotension, 4 hematomas, 1 groin bleed and 2 transfusions.

G. Gender Bias Analysis

The patient population enrolled in this study was 64.7% (97/150) male. Patients were either treated with the MBC Balloon only (n = 22; 9 female, 13 male), predilated with the MBC Balloon followed by stent placement (n = 115; 37 female, 78 male), or not treated with the MBC Balloon (n = 22; 7 female, 6 male). This distribution of outcomes is not significantly different (p = 0.253 by Pearson Chi-square).

With regard to clinical outcomes, there was only one (0.7%) MACE event within 30 days of the procedure in the entire 150 patient population. This event is described in detail in Appendix III of the PMA amendment submitted on July 19, 1999. This event did occur in a female patient. Thus, the distribution of MACE events was 0.0% in males and 1.9% in females. This distribution is not significantly different (p = 0.353 by Fisher's exact test).

In summary, acute procedure success rates for all patients and for patients with eligible lesions did not differ significantly by patient gender nor did MACE rates.

XI. Conclusions Drawn From Studies

The results of the laboratory studies demonstrate that there are no biocompatibility issues and that the COOK® MBC PTCA Balloon Dilatation Catheter has the appropriate physical and performance characteristics for its intended use. The COOK® MBC PTCA Balloon Dilatation Catheter was evaluated *in vivo* and successfully demonstrate that the catheter system would function safely and effectively in actual use in the coronary anatomy.

The results of the clinical study indicate that the COOK® MBC PTCA Balloon Dilatation Catheter is safe and effective for the treatment of patients with coronary artery disease. Therefore, it is reasonable to conclude that the benefits of use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the directions for use.

XII. Panel Recommendation

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by the panel.

XIII. FDA Decision

FDA issued a PMA approval letter to Cook, Inc., on SEP 2 7 1999 FDA also performed an inspection of the manufacturing facilities and found the applicant in compliance with the Quality System Regulation (21 CFR Part 820).

XIV. Approval Specifications

Direction for use: See Final Draft Labeling (Information for Use).

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings and Precautions, and Adverse Events in the Final Draft Labeling. Information for Use

Post-approval Requirements and Restrictions: See Approval Order.