SUMMARY OF SAFETY AND EFFECTIVENESS

1. GENERAL INFORMATION

Classification (Generic) Name: Percutaneous Transluminal Coronary Angioplasty Catheter

Device Trade Name: Cutting Balloon™

Applicant's Name and Address: Interventional Technologies, Inc.
3574 Ruffin Road
San Diego, CA 92123

PMA Number: P950020

Date of Panel Recommendation: Refer to Section 12

Date of Notice of Approval to Applicant: APR 18 2000

2. INDICATIONS FOR USE

The Cutting Balloon is indicated for dilatation of stenoses in coronary arteries for the purpose of improving myocardial perfusion in those circumstances where a high pressure balloon resistant lesion is encountered. In addition, the target lesion should possess the following characteristics: discrete (≤15 mm in length) or tubular (10 to 20 mm in length) with a reference vessel diameter ranging from 2.0 mm to 4.0 mm; readily accessible to the device; light to moderate tortuosity of proximal vessel segment, non-angulated lesion segment (<45°), smooth angiographic contour; and absence of angiographically-visible thrombus and/or calcification.

3. DEVICE DESCRIPTION

The Cutting Balloon consists of a non-compliant balloon with 3 or 4 atherotomes™ (microsurgical blades) mounted longitudinally on its outer surface. When the Cutting Balloon is inflated, the atherotomes score the plaque, creating initiation sites for crack propagation. This process, referred to as atherotomy®, allows dilatation of the target lesion with less force.

The Cutting Balloon catheter shaft consists of two lumens. The outer lumen is used to inflate and deflate the balloon. The inner lumen permits the passage of a PTCA guidewire to aid placement of the Cutting Balloon. At the proximal end of the catheter is a Y-connector with standard luer fittings.

4 CONTRAINDICATIONS

The Cutting Balloon is contraindicated for use in:

Coronary artery spasm in the absence of a significant stenosis.

5. WARNINGS AND PRECAUTIONS

See Warnings and Precautions in the final labeling (Instructions for Use).

6. ADVERSE EVENTS

6.1 Observed Adverse Events

The Adverse Events reported in this section were those observed in two clinical investigations: the Resistant Lesion Registry (RLR), which demonstrated the ability of the Cutting Balloon to dilate lesions in a series of patients whose lesions could not be dilated with conventional balloon angioplasty; and the Global Randomized Trial (GRT), a multi-centered, randomized trial designed to compare the Cutting Balloon with conventional angioplasty. Twenty-nine patients were entered into the RLR and a total of 1245 patients were randomized in the GRT; 622 to the Cutting Balloon arm and 623 to the PTCA arm. Seven patients (5 in the Cutting Balloon arm and 2 in the PTCA arm) were deregistered after randomization but before receiving the assigned treatment. Therefore, there were 1238 valuable patients in the GRT.

In the RLR, dissection was the only in-lab complication recorded. Dissections occurred 14 times: six times prior to Cutting Balloon treatment; two times after Cutting Balloon treatment; and six times as part of the post-Cutting Balloon adjunctive treatment.

One patient death from a cardiac arrest and acute pulmonary edema occurred in the RLR 24-48 hours post-procedure. This patient was treated for a mid-RCA lesion with a series of four inflations with a PTCA balloon catheter, followed by a single inflation with the Cutting Balloon. A dissection was noted following use of the Cutting Balloon. Adjunctive treatment included two inflations with a second PTCA balloon catheter followed by placement of a stent.

The major adverse events occurring in the GRT are listed below (Table 1).

Table 1. Global Randomized Trial (GRT) Major adverse events occurring within 270 days (1238 patients)

Adverse Event	*Cutting Balloon**	*Conventional Balloon**	*Difference [95% CI†]*
MACE‡	13.6% (84/617)	15.1% (94/621)	-1.5% [-5.4%, 2.4%]
Death	1.3% (8/617)	0.3% (2/621)	1.0% [0.0%, 2.0%]
MI	4.7% (29/617)	2.4% (18/621)	1.8% [-0.3%, 3.9%]
Q Wave MI	1.5% (9/617)	1.1% (7/621)	0.3% [-0.9%, 1.6%]
Non-Q Wave MI	3.2% (20/617)	1.3% (11/621)	1.5% [-0.3%, 3.2%]
Emergent CABG	1.0% (6/617)	1.0% (6/621)	0% [-2.3%, 1.7%]
TLR§	11.7% (72/617)	14.8% (92/621)	-3.1% [-6.9%, 0.6%]
CABG (per pt.)	1.5% (9/617)	2.1% (13/621)	-0.6% [-2.1%, 0.8%]
PTCA (per pt.)	10.5% (65/617)	12.7% (79/621)	-2.2% [-5.8%, 1.4%]
Subacute Closure	1.3% (8/617)	1.6% (10/621)	-0.3% [-1.5%, 3.0%]
Bleeding Complications	0.3% (2/617)	0.0% (0/621)	0.3% [-1.9%, 0.7%]
Vascular Complications¶	0.3% (2/617)	0.2% (1/621)	0.1% [-1.9%, 1.0%]
Clinical Perforations	0.8% (5/617)	0.0% (0/621)	0.8% [-0.4%, 2.3%]

* - Numbers are % (counts/sample size).

† - Difference = $S_{CB} - S_{PTCA}$ $SE_{Diff} = \text{sqrt}[(SE_{CB}^2 + SE_{PTCA}^2]$ $CI = Diff \pm 1.96 * SE_{Diff}$

‡ - Major Adverse Cardiac Events (MACE): Death, Q Wave MI, emergent CABG, target lesion CABG or TL-PTCA.

§ - Target lesion revascularization (TLR) at 9 months: any "clinically-driven" PTCA (TL-PTCA) or bypass surgery (TL-CABG) performed on the target lesion after documentation of recurrent angina and/or evidence of myocardial ischemia by stress testing.

¶ - Vascular complications: Any vascular complication requiring surgical repair.

There were eight deaths among the patients randomized to the Cutting Balloon arm. Two deaths occurring during the procedure involved perforations. In the first case, the perforation was associated with contrast extravasation and a Grade F dissection which was treated with balloon angioplasty and one stent. QCA reported TIMI 3 flow with a 35% residual stenosis and persistent contrast extravasation at the end of the procedure. Tamponade developed and the patient died during surgery. An intramyocardial hematoma was identified. In the second case, the coronary artery ruptured at the Cutting Balloon site and the patient developed ventricular fibrillation. The patient was resuscitated and

treated emergently for tamponade, but expired following CABG. In both of these cases, the Cutting Balloon was oversized. The balloon:artery ratio, as determined by QCA, was 1.25:1 and 1.8:1, respectively.

A perforation also occurred in the death of another patient who was randomized to the Cutting Balloon arm, but treated with a PTCA balloon because of a failure to cross the lesion with the Cutting Balloon. This patient died 105 days post-procedure due to complications of a CABG performed at that time.

One patient died within an hour of the procedure from a presumed re-occlusion.

A fifth patient died at 130 days post-procedure from a reported heart attack. Two deaths occurred following exacerbation of a pre-existing chronic obstructive pulmonary disease and respiratory failure (20 days), and emergency surgery for an abdominal aortic aneurysm (50 days). The remaining death was reported as the result of respiratory failure caused by chronic obstructive pulmonary disease.

Perforation was observed in five cases, all in the Cutting Balloon arm. As described above, in two of these cases the patient died acutely. Perforations were treated with PTCA, a stent or both.

6.2 Potential Adverse Events

Potential adverse events include, but are not limited to, the following:

Death
Acute myocardial infarction
Total occlusion of the coronary artery or bypass graft
Coronary vessel dissection, perforation, rupture, or injury
Aneurysm
Restenosis of the dilated vessel
Unstable angina
Embolism
Arrhythmias, including ventricular fibrillation
Hypo/hypertension
Coronary artery spasm
Hemorrhage or hematoma
Arteriovenous fistula
Drug reactions, allergic reactions to contrast medium
Infection.

6.3 Observed Device Malfunctions

There were no cutting Balloon malfunctions in the RLR.

A total of 15 Cutting Balloon malfunctions were recorded in the GRT. Two devices failed to inflate. Thirteen cases of balloon leak or rupture were reported: 9 with the first inflation and 4 with the second inflation.

7. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative treatments for patients with high pressure balloon resistant lesions are conventional balloon angioplasty, stents, atherectomy devices or medical therapy.

8. MARKETING HISTORY

The Cutting Balloon carries the CE Mark and is available for commercial distribution in Japan, Canada, Australia and New Zealand, Austria, Belgium, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Italy, the Netherlands, Norway, Portugal, Russia, Spain, Sweden, Switzerland, Turkey and the United Kingdom. The Cutting Balloon has never been withdrawn from any market for reasons related to the safety and effectiveness of the device.

9. SUMMARY OF PRECLINICAL STUDIES

9.1 Biocompatibility Testing

The Cutting Balloon was tested for biocompatibility in accordance with ISO 10993-1 using Good Laboratory Practices (GLP).. The following tests were conducted: USP systemic toxicity, intracutaneous reactivity, cytotoxicity, Guniea Pig sensitization, hemolysis, and C3a complement activation. The results of all biocompatibility testing were acceptable.

9.2 Bench Testing

Comprehensive bench testing of the physical properties of sterilized devices was conducted as recommended in the "FDA Guidance for the Submission of Research and Marketing Applications for Interventional Cardiology Devices: PTCA Catheters, Atherectomy Catheters, Lasers, Intravascular Stents."

Balloon minimum burst strength.-- A total of 20 Cutting Balloons of various diameters and lengths were tested for burst strength. Statistical analysis shows that, with 95% confidence, at least 99.9% of the balloons have a burst strength above the labeled recommended rated burst pressure (RBP) of 10 atmospheres (Table 2).

Table 2. Balloon Minimum Burst Strength

$\bar{x} \pm s$*	$\bar{x} - Ks$ †	$\bar{x} - Ks > RBP?$†
19.5 ± 1.2 atm	14.2 atm	Yes.

* Mean burst pressure ±standard deviation, based on a sample of 20.

† Statistical tolerance limit test for RBP of 10 atm.

Balloon Compliance (distensibility).-- A total of 90 Cutting Balloons (five devices of each diameter and length) were tested for compliance and distensibility. Over the pressure range of 2-8 atmospheres, the diameters for all balloon sizes were consistent with the labeled diameter (Figures 1 and 2). Testing was repeated with 10 balloons (5 each of 2.25×10 mm and 4.00×10 mm) with similar results.

Balloon Inflation/Deflation Performance.-- A total of 36 Cutting Balloons (two devices of each diameter and length) were tested. Average times required to fully inflate and deflate the Cutting Balloon with radiopaque contrast media were found to be suitable for human use. Inflation times ranged from 0.5 to 2.1 seconds; deflation times ranged from 3.2 to 16.5 seconds.

Crossing Profile.-- To determine the crossing profile of the Cutting Balloon, 5 samples of each balloon diameter were measured. The crossing profile of the Cutting Balloon averaged 0.041 inches for the 2.0 mm to 3.25 balloons, 0.044 inches for the 3.5 mm to 3.75 mm balloons and 0.046 inches for the 4.0 mm balloon.

Balloon Fatigue (Repeated Balloon Inflation).-- A total of 30 Cutting Balloons of various diameters and lengths were tested. All Cutting Balloons passed the test of 40 consecutive inflation/deflation cycles to 10 atmospheres without failure.

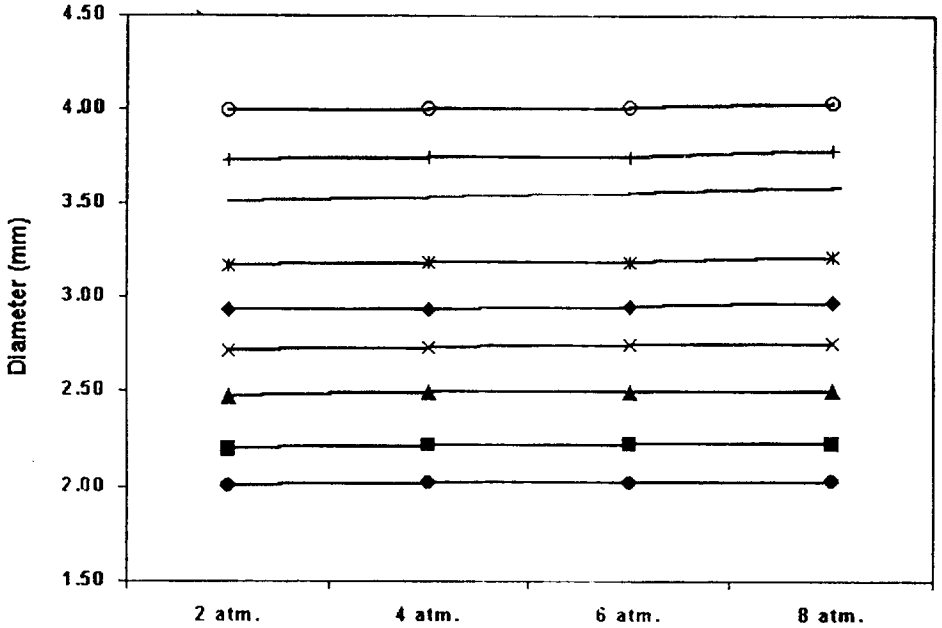

Figure 1. Balloon compliance (distensibility), 10 mm models with nominal inflated diameters of 2.00 to 4.00 mm, in 0.25 mm increments.

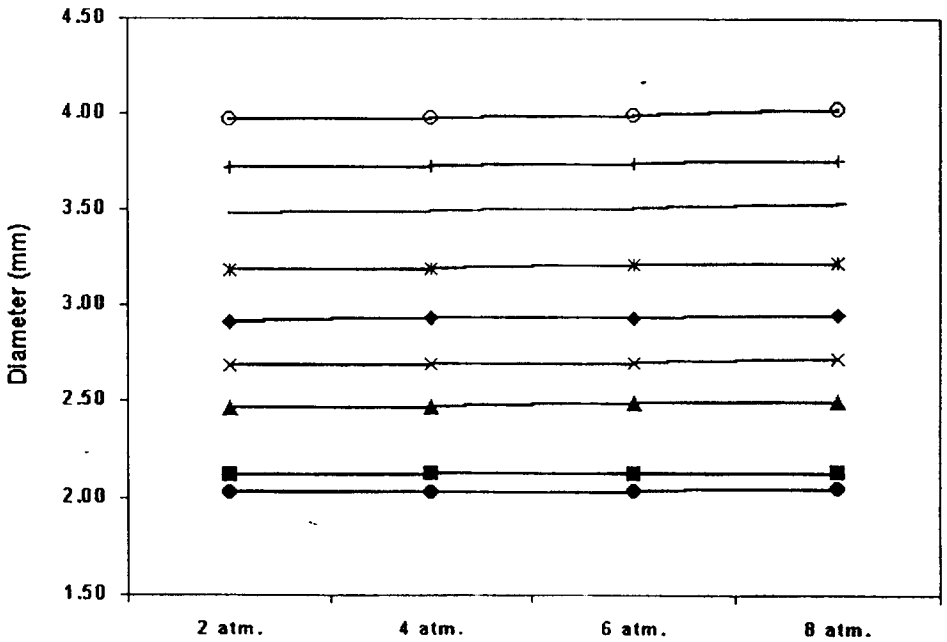

Figure 2. Balloon compliance (distensibility), 15 mm models with nominal inflated diameters of 2.00 to 4.00 mm, in 0.25 mm increments.

Bond Strength.-- A minimum of 15 Cutting Balloons of various diameter and length were tested to demonstrate the strength of the bonded joints. The results of all tensile testing determined that the bond strength was acceptable (Table 3). The blades were also pull-tested (Table 4). The force at failure and the failure mode were recorded. In the majority of cases (84% of the 10 mm test samples, 91% of the 15 mm test samples) the failure involved blade fracture at the clamping point. In these cases, the bond strength exceeded the structural strength of the blade. In the remaining cases, the pad separated from the balloon surface. The forces involved in this testing exceed the forces observed during clinical use.

Table 3. Bond Strength

Bond tested	$\bar{x} \pm sd^*$ ***(n)***
Balloon-to-catheter	2.70 ± 0.23 lb (15)
Catheter transition joint	3.14 ± 0.38 lb (15)
"Y" Body to Catheter	8.45 ± 0.59 lb (15)
"Y" body to luer	28.86 ± 2.38 lb (15)
Marker to Guidewire Tubing	1.03 ± 0.09 lb (20)
Wireport to Guidewire tubing	1.04 ± 0.09 lb (20)

* Mean force at failure ± standard deviation, sample size in parentheses.

Table 4. Blade Pull Strength

Nom. Infl. Diameter	$\bar{x} \pm sd$* *10 mm*	$\bar{x} \pm sd$* *15 mm*
2.00 mm	0.58 ± 0.08 lb	0.82 ± 0.18 lb
2.25 mm	0.70 ± 0.14 lb	0.76 ± 0.15 lb
2.50 mm	0.72 ± 0.17 lb	0.65 ± 0.19 lb
2.75 mm	0.47 ± 0.04 lb	0.75 ± 0.09 lb
3.00 mm	0.57 ± 0.16 lb	0.70 ± 0.16 lb
3.25 mm	0.45 ± 0.09 lb	0.72 ± 0.13 lb
3.50 mm	0.62 ± 0.09 lb	0.68 ± 0.18 lb
3.75 mm	0.55 ± 0.08 lb	0.68 ± 0.06 lb
4.00 mm	0.70 ± 0.18 lb	0.66 ± 0.15 lb

* Mean force at failure ± standard deviation, in lbs, based on a sample of 5.

9.3 Sterility and Shelf-life Qualification Studies

Sterilility Testing.-- The Cutting Balloon is sterilized via e-beam radiation. The product was validated for dosimetric release based on the Sterilization of Healthcare Products-- Requirements for Validation and Routine Control, Radiation Sterilization, ANSI/AAMI/ISO 11137-1994, Method 1.

Pyrogen Testing.-- Pyrogen testing, based on a USP-based *Limulus* amoebocyte lysate (LAL) pyrogen test procedure, occurs on a lot-by-lot basis prior to product release.

Shelf-life Testing.-- The Cutting Balloon has a shelf-life of 18 months, based on the comparison of sterilized devices (n = 20) to accelerated-aged (18 months, n = 20) and real time aged (19 months, n = 20) devices. The testing sequence subjected each device in each of the three groups to: microscopic examination for damage; verification of the continuity of the lumen; various measurements of dimensional conformance; burst testing; and pull testing of multiple bonds. All three groups met all acceptance criteria, demonstrating that device functionality is unaffected after 19 months of real-time aging.

9.4 Animal Testing

The Cutting Balloon was evaluated in the non-diseased arteries of pigs. The Cutting Balloon maintained its physical and structural integrity and could be inflated and deflated in succession with no measurable decrease in the device's performance. Cine angiography was conducted before, during and after the use of the Cutting Balloon and there was no evidence or indication of vessel damage or perforations at the site of balloon inflation. The Cutting Balloon could be maneuvered to each site of interest under fluoroscopic guidance, including marginal branches. The Cutting Balloon demonstrated no evidence of guide catheter backout caused by over-stiffness of the catheter shaft or excessive resistance to catheter movement within the guide catheter. No significant thrombosis was observed upon removal of the Cutting Balloon catheters.

9.5 Cadaver Study

The Cutting Balloon was tested in the atherosclerotic coronary arteries of eight human cadaver hearts. There was no evidence of blade breakage, detachment or other malfunction.

10. SUMMARY OF CLINICAL STUDIES

10.1 Resistant Lesion Registry (RLR)

The Resistant Lesion Registry (RLR) contains registry data on 30 lesions in 29 patients. All patients were enrolled at a single site between November 1996 and November 1999.

Study Endpoints: The primary endpoint was acute lesion success defined as a reduction in lumen narrowing of at least 20%. The secondary endpoint was procedural success. Procedural success was defined as lesion success, a final residual stenosis of ≤ 50% after all devices are used and no major adverse events (MACE, defined as death, CABG, or non-fatal MI).

Study Population: The RLR patients were selected for treatment on the basis of failed conventional angioplasty, defined as failure to reduce the lumen diameter narrowing by >20% and a final residual stenosis by ≥50% with PTCA balloon inflation pressures > 10 atmospheres. The demographics, risk factors and prior history of these patients are shown in Table 5.

Table 5. Demographics, Risk Factors and Prior Procedures, Resistant Lesion Registry (RLR).

Demographics:	% Male	69% (20/29)
	Age	65 ± 8.4
	Angina Class (CCS)	2.8 ± 0.8
Risk Factors:	Diabetes	14% (4/28)
	Smoking	39% (11/28)
	High Blood Pressure	29% (8/28)
	Hyperlipidemia	48% (13/27)
Prior Procedures:	Myocardial Infarction	33% (9/27)
	CABG	22% (6/27)
	PTCA	22% (6/27)

Methods: Patient data were obtained prospectively on 6 patients under a formal clinical protocol and retrospectively on 23 patients. For both prospective and retrospective patient groups, conventional balloon angioplasty was used as the initial treatment in all but two cases. In these two cases the Cutting Balloon was used as the first treatment for dilatation of an unprotected left main, a vessel known to be resistant to PTCA dilatation. Physician discretion was used to further decrease the residual stenosis with additional adjunctive devices following treatment with the Cutting Balloon.

Results: Of the 29 patients entered into the RLR, balloon resistant lesions were treated in 26 native vessels and 4 saphenous vein grafts (SVGs). Patients were treated with a sequence of devices including the Cutting Balloon. The Cutting Balloon was usually used as the second (14 cases) or third (10 cases) device in each treatment sequence. In three cases, the Cutting Balloon failed to cross the lesion on the initial attempt. Successful crossing was achieved with the second attempt (2 cases) following an additional crossing with a PTCA balloon. In the third case there were no further attempts to cross the lesion.

In most cases, the Cutting Balloon was inflated once (78%, 25/32); while the number of inflations with the PTCA catheter, prior to the Cutting Balloon, varied from 1 (31%, 14/45), 2 (36%, 16/45), 3 (18%, 8/45), to ≥4 (16%, 7/45) inflations. Inflation pressures ranged from 8-16 atmospheres for the Cutting Balloon and 4-25 atmospheres for the PTCA catheters. The average inflation pressure for the Cutting Balloon was significantly less than the average pressure used for the PTCA catheters [9.3±1.8 atmospheres (n=32) versus 15.4±3.6 atmospheres (n = 45), $p < 0.0001$].

The principal safety and efficacy results of the RLR are shown in Table 6. The primary and secondary endpoints, used for the prospectively enrolled patients, were also applied to the patients enrolled retrospectively.

Table 6. Prinicpal Effectiveness and Safety Results Resistant Lesion Registry (n=29 patients, 30 lesions)

Effectiveness Measures:		*Cutting Balloon, %, (freq.), [95% CI]*
Acute Lesion Success		78% (18/23) [56%, 93%]
Procedural Success		74% (17/23) [52%, 90%]
% Diameter Stenosis - Initial		73% (30) [70%, 77%]
	Post-PTCA	51% (17) [44%, 59%]
	Post-Cutting Balloon	36% (22) [28%, 45%]
	Final	16% (30) [8%, 23%]
Safety Measures:		
MACE		3% (1/30) [1%, 10%]
Dissection, Prior to Cutting Balloon		20% (6/30) [8%, 39%]
Dissection, Cutting Balloon + Adjunctive Use		27% (8/30) [12%, 47%]

There were 20 (69%) males and 9 (31%) females treated with the Cutting Balloon in the RLR study. This gender distribution is similar to that of patients undergoing percutaneous balloon angioplasty procedures, as described in the medical literature. Although a higher percentage of females than males achieved acute lesion success [89% (8/9) versus 50% (10/20)] and procedural success [78% (7/9) versus 50% (10/20)], the small sample size does not allow a valid statistical comparison between these two subgroups. The only MACE event in the RLR study occurred in a female patient.

10.2 Global Randomized Trial (GRT)

The Global Randomized Trial (GRT) was a multi-centered, randomized trial designed to compare the Cutting Balloon with conventional angioplasty. Patient enrollment in the GRT occurred between June 1994, and November 1996, at 31 centers in the US, Canada, France, Belgium and the Netherlands. Of the 1245 patients enrolled, 622 were assigned to the Cutting Balloon arm and 623 to the PTCA arm. Seven patients (5 in the Cutting Balloon and 2 in the PTCA arm) were deregistered after randomization but before receiving the assigned treatment. Deregistration occurred for the following reasons: resolution of the stenosis between the prior angiogram and the index procedure (3 cases), the presence of calcification requiring atherectomy (1 case), and

failing to meet the inclusion criteria (3 cases).

Study Endpoints: The primary endpoint was angiographic restenosis at 6 months. Secondary endpoints included TLR and MACE at 9 months. A clinical events committee blinded to treatment assignment adjudicated all major clinical events.

Study Population: Patients, between the ages of 25 and 75 years, with atherosclerotic coronary artery disease were eligible for enrollment in the GRT if they were suitable candidates for coronary artery bypass graft surgery and the target lesions were *de novo* Type A or B lesions in native arteries without total obstructions or visible thrombus, and were accessible to the Cutting Balloon.

Methods: Patients were prospectively randomized to treatment with either the Cutting Balloon or PTCA. Access to the target lesion was gained through the femoral artery approach. The reference vessel diameter (located just proximal to the target lesion) was measured by quantitative angiography.

Selection of the Cutting Balloon with the appropriately sized balloon diameter was based on the reference vessel diameter. If necessary, tandem dilatations were allowed for lesion lengths ≤ 20 mm. Oversizing of the balloon was not recommended in the PTCA arm.

The protocol allowed for a single inflation of the Cutting Balloon up to 8 atmospheres for a maximum of 90 seconds. Subsequent dilatation(s) with a PTCA balloon were allowed only if the residual stenosis was > 40%. In the PTCA arm, the inflation times and pressures were left to the discretion of the investigator. Serial inflations with a single balloon, or subsequent inflations with increased diameter PTCA balloons were allowed to achieve a ≥20% reduction in stenosis and a ≤50% residual stenosis. Multiple violations of the procedural protocol were reported in the Cutting Balloon arm [33% (212/617) of the Cutting Balloon subjects were not treated per protocol].

Clinical follow-up was performed at 6 weeks, 6 months and 9 months. Baseline quantitative coronary angiography (QCA) was performed pre-procedure, following device use, and after the final treatment in all patients. Follow-up quantitative coronary angiography at 6 months was required in all patients. Anticoagulation included aspirin 325 mg/day throughout the study.

Results: The acute and 6 month angiographic and clinical results demonstrated that the Cutting Balloon was similar to PTCA with respect to Procedure Success (defined as achievement of <50% residual diameter stenosis and freedom from in-hospital major adverse cardiac events [MACE, defined as death, Q wave MI, emergent coronary artery bypass surgery, or repeat target lesion revascularization]), 30-Day incidence of MACE, and Angiographic

Restenosis (defined as >50% minimum lumen diameter stenosis at follow-up angiography). The principal safety and efficacy results are shown in Table 7.

Table 7. Principal Effectiveness and Safety Results (Intent-to-Treat) All Randomized Lesions Treated (1238 Patients, 1385 Lesions)

Efficacy Measures (per lesion)	Cutting Balloon (N=689)	PTCA (N=696)	Relative Risk [95% C.I.]	Difference [95% C.I.]
Lesion Success	95.5% (642/672)	96.5% (668/692)	0.99 [0.97,1.01]	-1.0% [-3.1%,1.1%]
Device Success	77.7% (473/609)	77.8% (460/617)	1.00 [0.94,1.06]	-0.1% [-4.8%,4.5%]
Procedure Success	92.9% (566/609)	94.7% (584/617)	0.98 [0.95,1.01]	1.0% [-1.1%,3.1%]
MLD after Device (mm) Range (min,max)	2.05±0.52 (672) (0.00, 4.14)	2.13±0.53 (692) (0.00, 4.07)	N/A	-0.08 [-0.14,-0.03]
%DS after Device Range (min, max)	29%±14% (672) (-13%, 100%)	27%±13% (692) (-12%, 100%)	N/A	1.6% [0.1%,3.0%]
MLD after 6 months (mm) Range (min,max)	1.63±0.62 (551) (0.00, 3.44)	1.65±0.61 (559) (0.00, 3.40)	N/A	-0.02 [-0.10,0.05]
%DS after 6 months Range (min, max)	42%±19 (551) (-11%, 100%)	42%±19% (559) (-4%, 100%)	N/A	0.1% [-2%,2%]
Restenosis Rate at 6 months	31.4% (173/551)	30.4% (170/559)	1.03 [0.87,1.23]	1.0% [-4.5%,6.4%]
TLR-free at 9 months*	89.3%	86.1%	1.04 [1.00,1.08]	3.2% [-0.3%,6.7%]
TVR-free at 9 months†	88.5%	84.6%	1.05 [1.00,1.09]	3.9% [0.3%,7.5%]
TVF-free at 9 months‡	86.9%	84.8%	1.03 [0.98,1.07]	2.2% [-1.7%,6.1%]

Safety Measures and Other Clinical Events (per patient)	(N=617)	(N=621)	Relative Risk [95% C.I.]	Difference [95% C.I.]
MACE ≤ 30 days	3.7% (23/617)	2.7% (17/621)	1.36 [0.74,2.52]	1.0% [-1.0%,3.0%]
MACE> 30 days	10.0% (62/617)	12.9% (80/621)	0.78 [0.57,1.06]	-2.8% [-6.4%,0.7%]
Perforations	0.8% (5/617)	0% (0/621)	N/A	0.8% [-0.4% 2.3%]
Vascular Complications	0.3% (2/617)	0.2% (1/621)	2.01 [0.19,21.11]	0.2% [-0.4%,0.7%]

Numbers are % (counts/sample size) or Mean ± 1 SD. CI = Confidence interval.

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

Relative Risk = S_{CB}/S_{PTCA} SE_{RR}= sqrt[$(SE_{CB}/S_{CB})^2$ +$(SE_{PTCA}/S_{PTCA})^2$] CI=RR*exp(1.96*SE_{RR})

Difference = S_{CB} . S_{PTCA} SE_{Diff}= sqrt[$(SE_{CB}^2$ + SE_{PTCA}] CI=Diff±1.96*SE_{Diff}

Lesion success: Lesion success was defined as the achievement of a final residual dimater stenosis of <50% (by QCA core laboratory) using any percutaneous method.

Device success: Achievement of a final residual diameter stenosis of <50% (by QCA core laboratory) in the absence of unplanned coronary stenting, randomized treatment failure or crossover.

Procedure success: Achievement of a final residual diameter stenosis of <50% (by QCA core laboratory) in the absence of : In-Hospital MACE or target lesion revascularization within 7 days after the index procedure.

* - TLR-free: Survival free from target lesion revascularization at 9 months estimated using Kaplan-Meier methods.

† - TVR-free: Survival free from target vessel revascularization at 9 months estimated using Kaplan-Meier methods.

‡ - TVF-free: Survival free from target vessel failure (death, Q wave myocardial infaction, or target vessel revascularization) at 9 months estimated using Kaplan-Meier methods.

Major Adverse Cardiac Events (MACE): Death, Q wave MI, emergent CABG, target lesion CABG or TL-PTCA.

Primary endpoint: Death, Q wave MI, emergent CABG, target lesion revascularization, or subacute closure within 30 days of the index procedure.

Vascular complications: Any vascular complication requiring surgical repair.

11. CONCLUSIONS DRAWN FROM THE STUDIES

The results of the preclinical testing and the Resistant Lesion Registry, along with the safety information obtained in the Global Randomized Trial, provide valid scientific evidence and reasonable assurance that the Cutting Balloon™ is safe and effective when used in a manner consistent with the product labeling.

12. PANEL RECOMMENDATIONS

A Circulatory System Device Panel meeting was held on March 4, 1996, to discuss approval of the device for the treatment of Type A and B coronary artery lesions. At that time only the acute results from a subset of patients in the GRT were available for review. The Panel recommended not approvable based on the need for completion of the GRT and suggested that the Cutting Balloon might benefit the population of patients with balloon resistant lesions.

Based on a review of the March 4, 1996, Panel proceedings, and the clinical data provided in the PMA, it was determined that a second Panel meeting was not necessary for review of this device.

13. FDA DECISION

The applicant's manufacturing facility was inspected and was found to be in compliance with the Good Manufacturing Practices (GMP) regulation (21 CFR, Part 820).

The FDA issued an approval order on APR 18 2000.

14. APPROVAL SPECIFICATIONS

Directions for Use: See labeling.

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

Post-approval Requirements and Restrictions: See Approval Order.