Cordis

a Johnson-Johnson company

ENDOVASCULAR

CAUTION: *Federal (USA) law restricts this device to sale by or on the order of a physician.*

Instructions for Use
PALMAZ® Balloon Expandable Stent for the Renal Arteries

STERILE. The PALMAZ® Balloon Expandable Stent and crimping tube are sterilized with gamma radiation. Nonpyrogenic. The stent is radiopaque. For single use only. Do not autoclave.

IMPORTANT: The crimping tube packaged with the PALMAZ Stent is not compatible with the POWERFLEX® Plus PTA Catheter.

NON-STERILE. The crimping tool and introducer tube, *provided separately,* are supplied NON-STERILE and must be sterilized prior to use. The crimping tool and introducer tube should be sterilized by autoclaving in accordance with hospital procedures.

DEVICE NAME

The device brand name is the PALMAZ® Balloon Expandable Stent.

1.0 DEVICE DESCRIPTION

The PALAMZ® Balloon-Expandable Stent is a 316L stainless steel, slotted tube which is expanded with the use of the recommended delivery systems (refer to Table 1).

The delivery system, the POWERFLEX® PLUS PTA Catheter, consists of a dual lumen shaft design with a distal inflatable balloon. Two radiopaque marker bands indicate the dilating section of the balloon.

Available Stent Lengths (mm):	10, 15 and 20.
Expanded Stent Diameters (mm):	4, 5, 6, 7 and 8 (determined by the diameter of the fully inflated delivery catheter).
Stent Material:	Electropolished stainless steel (316L), cut from seamless tubing.
Stent Geometry:	14 circumferential rows of slots. Slotted tube pattern.
Nominal Stent Foreshortening:	1.5 mm or less for the 10 mm length stent. 2.3 mm or less for the 15 mm length stent. 3.1 mm or less for the 20 mm length stent.

Delivery System Usable Length: 40 cm, 65 cm, 80 cm, 110 cm and 135 cm (Not all recommended balloon catheter sizes are sold in all catheter lengths.)

Recommended Delivery Balloon: The PALMAZ® Balloon-Expandable Stent is sold unmounted for use with the Cordis POWERFLEX® PLUS PTA Catheter. A plastic crimping tube is also provided with the stent. **IMPORTANT: When using the POWERFLEX® PLUS balloon catheter, use the crimping tube that is packaged with the balloon, NOT the Stent. The crimping tube supplied with the Stent is NOT compatible with the POWERFLEX® PLUS balloon catheter.**

Nominal Balloon Inflation Pressure: 10 atm (1013 kPa)

Recommended Cordis Catheter Sheath Introducer: 6F (2.0 mm) with 4 – 6 mm POWERFLEX® PLUS
7F (2.3 mm) with 7 & 8 mm POWERFLEX® PLUS

Table 1

Stent Description		Stent Lengths		POWERFLEX® PLUS	Recommended Cordis Catheter Sheath Introducer (CSI) and Guiding Catheter	
Product Code	Nominal Dia (mm)	Unexpanded (mm)	Expanded (mm)	Catalog Number[1]	CSI Size French	Guiding Catheter Size French
P104R	4	10.0	9.9	412-4010	6F	8F
	5	10.0	9.7	412-5010	6F	8F
	6	10.0	9.4	412-6010	6F	8F
	7	10.0	9.0	412.7010	7F	9F
	8	10.0	8.5	412-8010	7F	9F
P154R	4	15.0	14.8	412-4015	6F	8F
	5	15.0	14.5	412-5015	6F	8F
	6	15.0	14.0	412-6015	6F	8F
	7	15.0	13.4	412-7015	7F	9F
	8	15.0	12.6	412-8015	7F	9F
P204R	4	20.0	19.7	412-4020	6F	8F
	5	20.0	19.3	412-5020	6F	8F
	6	20.0	18.7	412-6020	6F	8F
	7	20.0	17.8	412-7020	7F	9F
	8	20.0	16.8	412-8020	7F	9F

Use Cordis Crimping Tool CRT20 and Introducer Tube INTR4 for all product codes and lengths.

French size conversions: 6F (2.0mm), 7F (2.3mm), 8F (2.7mm), 9F (3.0mm)
[1]Catheter suffices for the POWERFLEX PLUS refers to the usable catheter length. Any of the following catheter length suffixes may be used: T (40cm), V (65cm), S (80cm), L (110cm) and X (135cm). NOTE: Not all balloon sizes are sold in all catheter lengths.

2.0 INDICATION FOR USE

The PALMAZ® Balloon-Expandable Stent is indicated for use in patients with atherosclerotic disease of the renal arteries following suboptimal percutaneous renal angioplasty (PTRA) of a de novo or restenotic lesion ($\leq$ 22 mm in length) located within 10 mm of the aortorenal artery border and with a reference vessel diameter of $\geq$ 4 mm and $\leq$ 8 mm. Suboptimal PTRA results are defined by one or more of the following unfavorable results.

1) $\geq$50% residual stenosis by visual estimate
2) $\geq$20mmHg peak translesional pressure gradient
3) $\geq$10mmHg mean translesional pressure gradient
4) Grade D dissection (a spiral shaped filling defect within the lumen of the vessel) or any dissection with significant compromise in lumen flow

3.0 CONTRAINDICATIONS

The PALMAZ Balloon-Expandable Stent is contraindicated for use in patients who have a lesion that cannot be crossed with a wire and/or balloon catheter.

4.0 WARNINGS

1. The stent and delivery balloon should be used only by physicians trained in interventional techniques such as percutaneous transluminal angioplasty (PTA) and placement of intravascular stents.
2. Persons with bleeding diathesis or uncontrollable hypercoagulability are not suitable candidates for stent implantation.
3. Persons with lesions in arteries to transplanted or bypassed kidneys are not suitable candidates for stent implantation.
4. The long-term outcome following repeat dilatation of endothelialized stents is unknown at present.
5. Persons with allergic reactions to stainless steel or its components (for example, nickel) may suffer an allergic response to this implant.
6. Caution should be taken with patients with poor renal function who, in the physician's opinion, may be at risk for a contrast medium reaction. Note: Patients with serum creatinine $\geq$ 3.0 mg/dl were excluded from the ASPIRE2 clinical study. (See Section 7, Clinical Study Information.)
7. The stent may cause a thrombus, distal embolization, or may migrate from the site of implant down the arterial lumen. Appropriate sizing of the vessel is required to reduce the possibility of stent migration. In the event of thrombosis of the expanded stent, thrombolysis and PTRA should be attempted.
8. Before insertion of the primary dilatation catheter, the appropriate antiplatelet and anticoagulant therapy should be administered. Aspirin may be used as potential antiplatelet therapy. Antiplatelet therapy should be maintained for at least 24 hours prior to the procedure and for at least three months post-procedure.

9. In patients requiring the use of antacids and/or H2 antagonists before or immediately after stent placement, oral absorption of antiplatelet agents (e.g., aspirin) may be adversely affected.

5.0 PRECAUTIONS

Stent Handling Precautions

1. The PALMAZ Balloon-Expandable Stent and Crimping Tube are supplied STERILE. The Stent and Crimping Tube are intended for single use only. Do not resterilize and/or reuse the device.
2. Store in a cool, dry, dark place.
3. Use the PALMAZ Balloon-Expandable Stent prior to the "Use By" date printed on the package.

Stent Placement Precautions

4. When using the POWERFLEX PLUS balloon catheter, use the crimping tube that is packaged with the balloon, NOT with the stent. The crimping tube supplied with the stent is NOT compatible with the POWERFLEX PLUS balloon catheter.
5. Maximum balloon inflation pressure must not exceed the recommended inflation pressure specified on the catheter label.
6. Use of an inflation device with a manometer is recommended during this procedure so as to minimize the risk of over-inflation. Over-stretching of the artery may result in rupture and life threatening bleeding
7. The inflation diameter of the balloon used during stent delivery should approximate the diameter of the dilated lesion and intended arterial implant site.
8. When catheters are in the body, they should be manipulated only under fluoroscopy using radiographic equipment that provides high quality imaging.
9. Circumferential tear of the carrier balloon distal to the stent and prior to complete expansion of the stent may cause the balloon to become tethered to the stent, requiring surgical removal. In case of rupture of the recommended balloon catheter, it can be withdrawn and a new balloon catheter exchanged over a guidewire to complete expansion of the stent.
10. To avoid the possibility of dissimilar metal corrosion, do not implant stents of different metals in tandem where overlap or contact is possible, with an exception: stents made of 316L stainless steel are compatible with stents made of nickel titanium alloy.

Post-Stent Placement Precautions

11. As with any type of vascular implant, infection secondary to contamination of the stent may lead to thrombosis, pseudoaneurysm or rupture into a neighboring organ or the retroperitoneum.
12. In the event of complications, such as infections, pseudoaneurysm or fistulization, surgical removal of the stent may be required. Standard surgical procedure is appropriate
13. The stent may cause artifacts with MRI scans due to distortion of the magnetic field. The artifacts caused by the 316L stainless steel stent should not be greater than that caused by surgical metal clips. An MRI scan should not be used until the stent implantation site has had a chance to heal (estimated to be 8 weeks), in order to minimize the risk of migration of the stent under a strong magnetic field.

6.0 ADVERSE EVENTS

6.1 Observed Adverse Events

A total of 51 patients with proximal renal artery disease were evaluated in the ASPIRE (Analysis of Stents versus PTA In Renal Arteries) clinical feasibility study. There were no major in-hospital complications reported during the study. There were eight major adverse events in 51 patients out to 720 days, which included four deaths and four cases of target lesion revascularization.

Note: The remaining adverse event information and the information in the subsequent section (Clinical Studies) is based upon the ASPIRE2 Pivotal study.

A total of 208 patients were evaluated as part of the multi-center, prospective, non-randomized study to evaluate the safety and effectiveness of the PALMAZ Balloon-Expandable Stent in patients with atherosclerotic proximal renal artery stenosis that was suboptimally treated with percutaneous transluminal renal angioplasty (PTRA).

As shown in Table 2, there were twenty major device or procedure-related adverse events reported in 208 patients out to 270 days. One patient experienced a significant embolic event postoperatively and died at 80 days of cardiac arrest due to renal failure.

There were eleven deaths (5.2%) that were non-device and procedure related. Five of the deaths were cardiac-related and six were non-cardiac. Two patients died due to myocardial infarction, one patient at 145 days and the other at 253 days. Three patients died due to cardiac arrest: one patient at 90 days, one patient at 127 days and one patient at 243 days. One patient died at 48 days subsequent to an embolic event from the aorta and superior mesenteric artery. One patient died at 81 days following aortic valve replacement surgery. One patient died at 87 days subsequent to viral pneumonia with acute inflammatory pneumonitis and respiratory distress. One patient died at 140 days subsequent to hyperkalemia due to renal failure and severe cardiomyopathy. One patient experienced a device or procedure related significant embolic event at day 7. This patient subsequently died at day 164 due to sepsis. One patient died at day 208 due to a cerebral vascular accident.

Table 2. Device or Procedure Related Observed Adverse Events to 270 Days for the PALMAZ Balloon-Expandable Stent ASPIRE 2 Clinical Study

Parameter	Percent (N=208 Patients)	95% CI
In-hospital Event		
Major Adverse Event (Death, QMI, TLR, Embolic)	3 (1.4%)	[0.3%, 4.2%]

Death (device or procedure-related)	0 (0.0%)	[0.0%, 1.8%]
Q-wave MI	0 (0.0%)	[0.0%, 1.8%]
Target lesion revascularization	0 (0.0%)	[0.0%, 1.8%]
Significant embolic event[(1)]	3 (1.4%)	[0.3%, 4.2%]
Stent Thrombosis	1 (0.5%)	[0.0%, 2.7%]
CVA	0 (0.0%)	[0.0%, 1.8%]
Major bleeding	2 (1.0%)	[0.1%, 3.4%]
Major Vascular	5 (2.4%)	[0.8%, 5.5%]
Out-of-hospital Event		
Major Adverse Event (Death, QMI, TLR, Emboli)	17 (8.2%)	[4.8%, 12.8%]
Death (device or procedure related)	1 (0.5%)	[0.0%, 2.7%]
Q-wave MI	0 (0.0%)	[0.0%, 1.8%]
Target lesion revascularization	10 (4.8%)	[2.3%, 8.7%]
Significant embolic event[(1)]	8 (3.8%)	[1.7%, 7.4%]
Stent Thrombosis	1 (0.5%)	[0.0%, 2.7%]
CVA	0 (0.0%)	[0.0%, 1.8%]
Major bleeding	1 (0.5%)	[0.0%, 2.7%]
Major Vascular	5 (2.4%)	[0.8%, 5.5%]
Combined (In-and-Out-of-hospital)		
Major Adverse Event (Death, QMI, TLR, Emboli)	20 (9.6%)	[6.0%, 14.5%]
Death	1 (0.5%)	[0.0%, 2.7%]
Q-wave MI	0 (0.0%)	[0.0%, 1.8%]
Target lesion revascularization	10 (4.8%)	[2.3%, 9.3%]
Significant embolic event[(1)]	11 (5.3%)	[2.7%, 9.3%]
Stent Thrombosis	2 (1.0%)	[0.1%, 3.4%]
CVA	0 (0.0%)	[0.0%, 1.8%]
Major bleeding	3 (1.4%)	[0.3%, 4.2%]
Major Vascular	10 (4.8%)	[2.3%, 8.7%]

Note: (1) Significant embolic event (SEE) is defined as causing end-organ damage, (e.g., unanticipated kidney/bowel infarct, lower extremity ulceration or gangrene) or loss of kidney function. Five patients were categorized as SEE due to a true embolic event. Three patients were categorized as SEE due to contrast reaction, secondary to acute tubular necrosis (ATN).

6.2 POTENTIAL ADVERSE EVENTS

Adverse events (in alphabetical order) that may be associated with implantation of a stent in renal arteries (in addition to those listed in Table 2) include:

- Allergic reaction to stainless steel or its components
- Aneurysm
- Death
- Dissection
- Embolization of plaque or cholesterol
- Failure to deliver the stent to the intended site
- Fistulization
- Hematoma requiring treatment
- Hemorrhage
- Infection/fever
- Myocardial ischemia/infarction
- Nephrectomy/renal transplantation
- Peripheral neuropathy
- Persistent abdominal pain
- Persistent vessel spasm
- Pseudoaneurysm
- Reaction to contrast media
- Renal failure/dialysis
- Restenosis of vessel (greater than 50% obstruction)
- Rupture or perforation of vessel
- Stent migration or embolization
- Stroke
- Thrombosis/vessel occlusion

6.3 Stent Delivery Failures

Stent treatment of 252 lesions was attempted in the ASPIRE2 Pivotal Study. There were five stent delivery failures. The circumstances of the delivery failures are as follows: stent was deployed distal to the intended location with a second stent successfully delivered (n=3); unable to deploy stent, stent was retrieved and a subsequent stent successfully delivered (n=1); unable to deploy stent, stent was retrieved (n=1).

7.0 CLINICAL STUDY INFORMATION

A feasibility study (ASPIRE) was conducted to evaluate the safety and deliverability of the PALMAZ Balloon-Expandable Stent design in treating proximal renal artery stenosis. A total of 51 patients (N = 63 lesions), at seven investigation centers in the United States, with de novo or restenotic renal artery lesions located in vessels that had a $\geq$ 70% stenosis, reference vessel diameter of 4 to 7 mm were treated with the PALMAZ Balloon-Expandable Stent. The mean pre-procedure percent diameter stenosis (N = 60 lesions) of 61.3 $\pm$ 14.4, 95% CI of [57.6, 65.1] decreased to 4.6 $\pm$ 8.9, 95% CI of [2.3, 6.9] post-procedure. At one-year follow-up, the percent diameter stenosis (N = 24 lesions) was 26.9 $\pm$ 23.8, 95% CI of [16.8, 36.9]. There were no in-

hospital major adverse events (i.e., death, renal infarct of treated kidney, renal bypass of treated kidney, or revascularization of target lesion). Four deaths and four reports of target lesion revascularization occurred during the two-year follow-up period. The rate of other complications including renal failure, bleeding complications, and vascular complications was 23.5%.

The ASPIRE feasibility study was followed by a multi-center, prospective, non-randomized study (ASPIRE2). The purpose of the ASPIRE2 study was to evaluate the effectiveness and safety of the PALMAZ Balloon-Expandable Stent in patients with atherosclerotic proximal renal artery stenosis that was suboptimally treated with PTRA, as compared to a pre-specified performance criteria of a 40% nine-month restenosis rate. The study population consisted of 208 patients enrolled at 23 investigational centers in the United States. A total of 252 lesions were treated with one stent placed in 231 lesions and 2 stents placed in 21 lesions. Forty-three patients were treated for bilateral renal artery disease. The ASPIRE2 study is summarized below.

Study Endpoints: The primary endpoint was the restenosis rate at 9-months, determined by duplex ultrasound. Secondary endpoints included:

- Acute procedural success defined as <30% residual stenosis immediately after stent deployment as determined by the Core Laboratory (if no quantitative angiographic analysis was available, visual estimates were used) and ≤ 5 mm Hg residual translesion.
- Worsening renal function defined by a rise in serum creatinine at 30 days, 6 months, 9 months and 24 months:
  - If baseline level is ≤ 2.0 mg/dl, a ≥ 50% increase in serum creatinine.
  - If baseline level is > 2.0 mg/dl, a 1 mg % increase in serum creatinine.
- Blood pressure measurement change / antihypertensive medication at 30 days, 6 months, 9 months and 24 months: cured, improved, no improvement or censored.
- Absence of major adverse events at 30 days, 3 months, 6 months, 9 months and 24 months:
  - Incidence of device or procedure-related death, procedure related Q-wave myocardial infarction, target lesion revascularization (TLR) or significant embolic events (defined as end-organ damage, e.g., unanticipated kidney/bowel infarct, ulcerated or gangrenous foot).

An independent clinical events committee adjudicated all of the major adverse events (MAEs) and other events. Endpoints were analyzed on an intent-to-treat basis

Patients Studied: Eligible patients had either de novo or restenotic renal artery lesions with a ≥ 70% stenosis, a reference vessel diameter of 4 to 8 mm located within 10 mm of the aorta and suboptimally treated with PTRA. Patients with a total occlusion of the renal artery or having advanced renal disease as evidenced by serum creatinine of ≥ 3.0 mg/dl or kidney length of < 8 cm were excluded from the study. Baseline characteristics for the patients in the ASPIRE2 study are presented in Table 3.

Table 3. Baseline Characteristics
(N = 208 patients, 252 lesions)

Characteristic	
Age (yrs), mean ± SD (N)	69.6 ± 9.9 (208)
Number of men	36.5% (76/208)
History of smoking	67.8% (141/208)
History of coronary artery disease	38.5% (80/208)
History of diabetes mellitus	26.0% (54/208)
Atherosclerotic peripheral vascular disease (other than renal artery stenosis)	44.2% (92/208)
Reference vessel diameter (mm), mean ± SD (N)	4.83 ± 1.09 (244)
Minimum lumen diameter (mm), mean ± SD (N)	1.84 ± 0.75 (244)
Lesion length (mm), mean ± SD (N)	6.54 ± 3.23 (242)
Percent diameter stenosis, mean ± SD (N)	61.5 ± 13.8 (244)

Methods: Patients eligible for the study underwent a PTRA on a single renal artery and had an angiographically documented suboptimal result defined by the presence of unfavorable lesion morphology consisting of one or more of the following: an inadequate angiographic result as defined by a ≥50% lumen diameter narrowing; a 20 mm Hg peak translesion pressure gradient; a 10 mm Hg or greater mean translesional pressure gradient; and Grade D dissection or any dissection with significant compromise in lumen flow. Patients were to be treated with no more than two stents per renal artery. Baseline clinical and angiographic data were collected on standardized case report forms by clinical coordinators at the clinical sites. Clinical follow-up visits were conducted at 30 days, 6 months and 9 months post-procedure. Baseline quantitative angiography was performed pre-procedure, post-PTRA, and post-procedure in all patients. Duplex Ultrasound was utilized to make an initial determination of restenosis at the 9-month follow-up. If restenosis was observed by Duplex Ultrasound, a confirmatory angiogram was performed to document the amount of restenosis present. Computer assisted quantitative angiographic analysis (QA) and Duplex Ultrasound were performed at central laboratories.

ASPIRE2 Study Results: In suitable patients, stent placement in renal arteries following failed angioplasty resulted in improved acute angiographic outcomes and a nine month restenosis rate of 17.4%, 95% CI of [11.9%, 21.9%]. Clinical follow-up was available on 93.3% (194/208) and angiographic and/or duplex ultrasound follow-up was available on 73.6% (153/208) of patients at 9 months (270 ±30 days). The major adverse event rate (defined as device or procedure related death, Q-wave myocardial infarction, target lesion revascularization, or significant embolic event) at 270 days was 9.6%, 95% CI of [6.0%, 14.5%]. Freedom from target lesion revascularization at 270 days was 95.5% with 95% CI of [93.0%, 98.0%]. The principal effectiveness and safety results are presented in Table 4. The freedom from major adverse events Kaplan-Meier curve is presented in Figure 1.

The ASPIRE2 study included 43 patients who had a contralateral renal artery lesion treated with the PALMAZ Stent. The patients with bilateral stenosis had the most significant lesion treated with PTRA first. If the results were suboptimal, the lesion was treated with a stent and the patient was enrolled into the study. Treatment of the contralateral lesion involved PTRA and stent placement, or primary stenting of the lesion. Stent placement in the patients who had both renal arteries treated resulted in a nine month restenosis rate of 16.8%, 95% CI of [7.8%, 26.0%] with a 270-day major adverse event rate of 14.0% with 95% CI of [6.3%, 25.7%]. Freedom from target lesion revascularization at 270 days for the patients treated bilaterally was 97.5% with 95% CI of [94.2%, 100.0%]. The lesion-based endpoint values for patients with bilateral lesions may not be independent, and therefore may be correlated. The effectiveness measures presented herein from the ASPIRE2 study were not based upon the analysis of correlated lesion data, but rather the analysis of independent lesion data. Statistical comparisons between the unilateral and bilateral stented patients revealed no consistent pattern of difference in response to stenting between the two groups.

A twenty-four month follow-up visit was conducted to obtain blood pressure measurements, hematology evaluations and the recording of adverse events. The twenty-four month clinical safety and effectiveness data obtained on the 208 patients enrolled in the ASPIRE2 Study is presented in Table 4. There were a total of 41 major adverse events reported for the 208 patients and consisted of the following: one device or procedure related death, 30 target lesion revascularizations and 10 significant embolic events. Freedom from target lesion revascularization at 720-days was 85.9% with 95% CI of [81.4%, 90.4%]. The mean serum creatinine level at twenty-four months (N = 153 patients) was 1.46 mg/dl ± 0.81 mg/dl, 95% CI of [1.33, 1.58]. The mean systolic and diastolic blood pressure at twenty-four months (N = 158 patients) was 149.4 mm Hg ± 25.3 mm Hg, 95% CI of [145.3, 153.2] and 76.9 mm Hg ± 11.9 mm Hg, 95% CI of [75.0, 78.7], respectively . The mean number of antihypertensive medications reported taken by the patients at twenty-four months (N = 182 patients) was 2.30 ± 1.26, 95% CI of [2.1, 2.5].

TABLE 4. PRINCIPAL EFFECTIVENESS AND SAFETY RESULTS

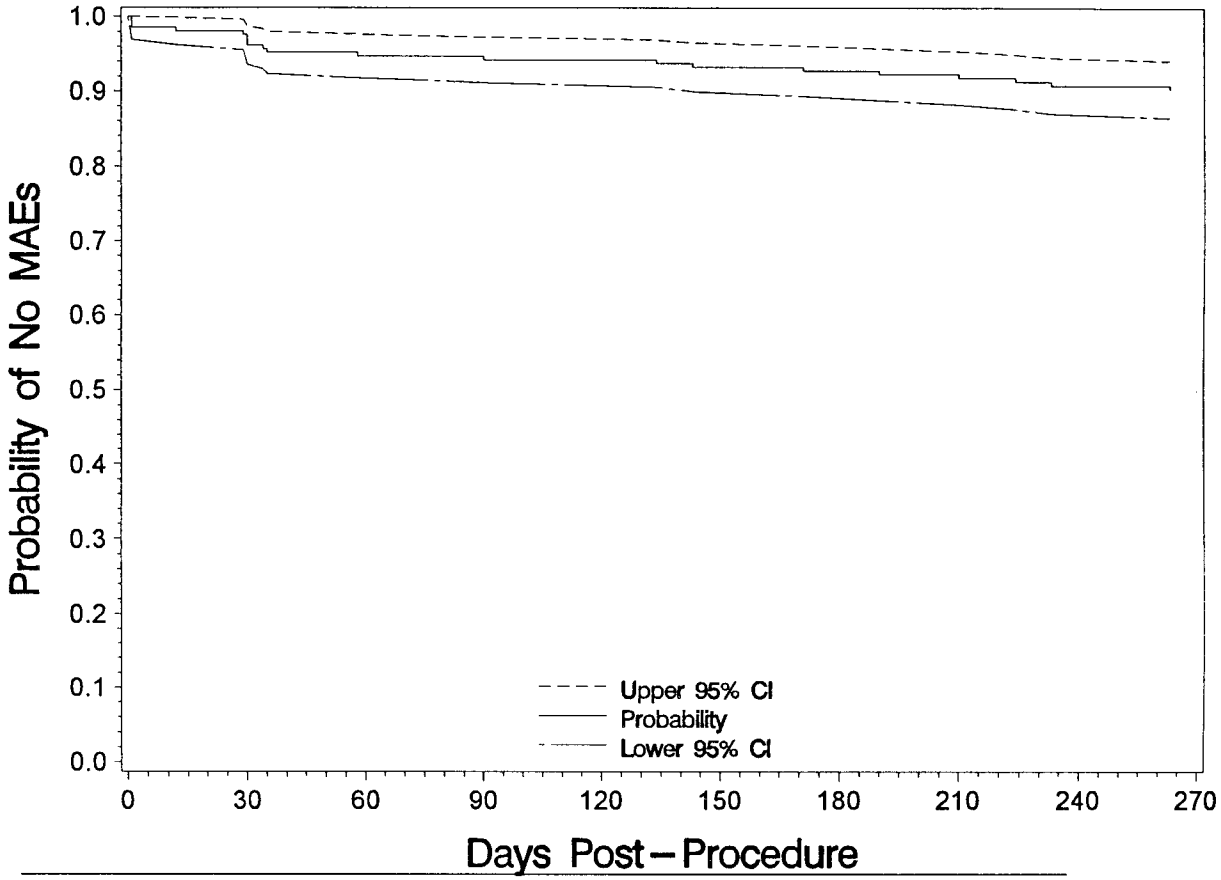
Effectiveness Measures	All Patients (N = 208) All Lesions (N = 252)	95% C.I.
Acute Procedure Success	80.2% (182/227)	[74.4%, 85.2%]
Post-Procedure in-lesion % DS	10.26 ± 11.1 (244)	(8.86, 11.67)
Range (min, max)	(-35.3, 61.31)	
Post-Procedure in-stent % DS	-2.17 ± 17.5 (243)	(-4.39, 0.05)
Range (min, max)	(-86.8, 54.24)	
Post-Procedure in-lesion MLD	4.31 ± 0.98 (244)	(4.19, 4.43)
Range (min, max)	(1.62, 6.89)	
Post-Procedure in-stent MLD	4.87 ± 1.07 (243)	(4.74, 5.01)
Range (min, max)	(1.89, 8.50)	
9 Month Restenosis Rate (Lesion based)	17.4% (32/184)	[11.9%, 21.9%]
TLR-free at 270 Days (Lesion Based, K-M)	96.7%	[94.5%, 98.9%]
Primary Patency (QA/Duplex Ultrasound)	81.0% (149/184)	[74.6%, 86.4%]
Primary Patency (Clinical)	96.8% (244/252)	[93.8%, 98.6%]
Secondary Patency (QA/Duplex Ultrasound)	82.6% (152/184)	[76.3%, 87.8%]
Secondary Patency (Clinical)	99.2% (250/252)	[97.2%, 99.9%]
Average Systolic Blood Pressure (mmHg)		
Baseline	167.6 ± 25.2 (208)	[164.2, 171.0]
9 Months*	149.1 ± 24.0 (178)	[145.6, 152.6]
24 Months*	149.3 ± 25.3 (158)	[145.3, 153.2]
Average Diastolic Blood Pressure (mmHg)		
Baseline	81.5 ± 13.1 (208)	[79.8, 83.3]
9 Months*	77.3 ± 12.1 (178)	[75.5, 79.0]
24 Months*	76.9 ± 11.9 (158)	[75.0, 78.7]
Average Number of Antihypertensive Medications		
Baseline	2.8 ± 0.9 (208)	[2.7, 3.0]
9 Months*	2.4 ± 1.2 (196)	[2.2, 2.6]
24 Months*	2.3 ± 1.3 (182)	[2.1, 2.5]
Safety Measures		
In-hospital Major Adverse Events	1.4% (3/208)	[0.3%, 4.2%]
Out-of-hospital Major Adverse Events to 9 Months	8.2% (17/208)	[4.8%, 12.8%]
In-hospital and Out-of-hospital MAEs to 9 Months	9.6% (20/208)	[6.0%, 14.5%]
MAE-free at 270 days (K-M)	90.3%	[88.2%, 94.4%]
In-hospital and Out-of-hospital MAEs to 24 Months	19.7% (41/208)	[14.5%, 25.8%]
Stent Thrombosis (9 Months)	1.0% (2/208)	[0.1%, 3.4%]
CVA (9 Months)	0.0% (0/208)	[0.0%, 1.8%]
Major Bleeding (9 Months)	1.4% (3/208)	[0.3%, 4.2%]
Major Vascular (9 Months)	4.8% (10/208)	[2.3%, 8.7%]
Average Serum Creatinine Level (mg/dl)		
Baseline	1.36 ± 0.52 (207)	[1.29, 1.43]
9 Months	1.40 ± 0.61 (173)	[1.30, 1.49]
24 Months	1.46± 0.81 (153)	[1.33, 1.58]

Numbers are % (count/available field sample size) Mean ± Standard Deviation or Range (Min,Max).
CI – Confidence Interval
*P-value of <.001 for the test for difference of means between each time point and baseline, based on paired t-test.
Acute Procedure Success - Acute procedure success was defined as angiographic success of < 30% residual stenosis as determined by the Core Laboratory (if no QA, visual estimates were used), and ≤ 5 mmHg mean residual gradient.

Restenosis - ≥ 50% diameter stenosis by QA at 9 month follow-up or if QA not available then renal to aortic ratio within the stent of 3.5 or greater or an absolute peak systolic velocity within the stent greater than 200 cm/sec via duplex ultrasound.
TLR-free at 270 Days - No target lesion revascularization within 270 Days using Kaplan-Meier estimates.
Primary Patency (Angiographic or Duplex Ultrasound) - < 50% diameter stenosis by QA at 9 month follow-up or if QA not available then a renal to aortic ratio within the stent of less than 3.5 and an absolute peak systolic velocity within the stent less than 200 cm/sec via duplex ultrasound performed 9 months post-study procedure without any reintervention.
Secondary Patency (Angiographic or Duplex Ultrasound) - < 50% diameter stenosis by QA at 9 month follow-up or if QA not available then a renal to aortic ratio within the stent of less than 3.5 and an absolute peak systolic velocity within the stent less than 200 cm/sec via duplex ultrasound performed 9 months post-study procedure with or without repeat percutaneous reintervention.
Primary Patency (Clinical) – No target lesion revascularization through last follow-up.
Secondary Patency (Clinical) - No repeated target lesion revascularization through last follow-up.
Major Adverse Event (MAE)** - The following procedure or device related events were considered to be major adverse events:
-death
-Q-wave myocardial infarction
-target lesion revascularization
-loss of kidney function or significant embolic events
** - Major Adverse Events were adjudicated by the Clinical Events Committee
Stent Thrombosis - After successful stent deployment, angiographic thrombus within the stented vessel during the first 30 days following stent deployment.
CVA - Acute neurological deficits recorded by the clinical sites.
Major Bleeding - Transfusion of blood products due to blood loss resulting from the percutaneous revascularization procedure, or blood loss resulting in change in anticoagulation regimen.
Major Vascular - Occurrence of hematoma, false aneurysm, AV fistula, retroperitoneal bleed, peripheral ischemia/nerve injury, procedure related transfusion, or vascular surgical repair.

Figure 1. Freedom from Major Adverse Events (To 270 Days):

All Patients (N=208)



	Days Post-Procedure				
	0	Discharge	30	180	270
# Entered	208	208	204	195	182
# Censored	0	0	3	5	180
# At risk	208	208	204	192	177
# Events	0	4	8	6	2
# Events/Month		10	2.7	0.8	0.2
% Survived	100	98.1	94.2	91.3	90.3
SE		1	1.6	2	2.1

8.0 INDIVIDUALIZATION OF TREATMENT

The risks and benefits should be considered for each patient before use of the PALMAZ Balloon-Expandable Stent. Patients must be acceptable candidates for balloon angioplasty with stent deployment. Patients selected for treatment should include those having a failed PTRA result defined as meeting one or more of the following criteria:

- ≥ 50% residual stenosis (visual estimate)
- ≥ 20 mm Hg peak translesional pressure gradient
- ≥ 10mm Hg mean translesional pressure gradient
- Grade D dissection (a spiral shaped filling defect within the lumen of the vessel) or any dissection with significant compromise in lumen flow

Lesions to be treated may be in unilateral or bilateral renal arteries, de novo or previously treated (by PTRA, not with stents). Accessory arteries may be treated if ≥ 4 mm in diameter.

8.1 Use in Special Populations

The safety and effectiveness of the PALMAZ Balloon-Expandable Stent has not yet been established in the following patient populations:

- Patients with more than one lesion in a renal artery.
- Patients with renal arteries < 4 mm or > 8 mm in normal diameter by visual estimate.
- Patients with a total occlusion of the renal artery.
- Patients with lesions requiring more than two stents.
- Patients with lesions due to any causes of renal artery stenosis, other than atherosclerosis.
- Patients with advanced renal disease as evidenced by serum creatinine greater than or equal to 3.0mg/dl or kidney length < 8 cm.
- Patients with a recent Q-way myocardial infarction.
- Patients with an abdominal aortic aneurysm > 4.0 cm in diameter.
- Patients with confirmed pregnancy.
- Patients with a total occlusion of the renal artery.
- Patients with a stenosis of the common femoral artery.

9.0 HOW SUPPLIED

The PALMAZ Balloon-Expandable Stent and plastic crimping tube are supplied sterile. The stent is supplied in three nominal lengths: 10 mm, 15 mm, and 20 mm and is designed to be expanded from 4 to 8 mm in diameter. The PALMAZ Balloon-Expandable Stent is provided unmounted and is recommended for use with commercially available Cordis POWERFLEX Plus balloon catheter (see Table 1).

IMPORTANT: When using the POWERFLEX PLUS balloon catheter, use the crimping tube that is packaged with the balloon, NOT the Stent. The crimping tube supplied with the Stent is NOT compatible with the POWERFLEX PLUS balloon catheter.

The stent is mounted on the balloon catheters utilizing Cordis (CRT20) crimping tool (provided separately). The Cordis (INTR4) introducer tube (provided separately) may be used for passage of the balloon/stent assembly through the catheter sheath introducer gasket. The crimping tool and introducer are provided non-sterile and must be sterilized by autoclaving in accordance with hospital procedures.

10.0. OPERATOR'S MANUAL

10.1 Pre-Procedure

a. The patient may be started on enteric coated or non-enteric coated aspirin 81-500 mg per day beginning one or two days prior to the procedure if deemed appropriate to the physician.

b. The percutaneous placement of the stent in the renal artery should be done in an angiography procedure room. Angiography should be performed to map out the extent of the lesion. If thrombus is present or suspected, thrombolysis should precede stent deployment using standard acceptable practice. Access vessels must be sufficiently patent, or sufficiently recanalized, to proceed with further intervention. Patient preparation and sterile precautions should be the same as for any angioplasty procedure.

10.2 Select Stent Size

a. Measure the length of the target lesion to determine the length of stent required. Size the stent length to extend slightly proximal and distal to the lesion, taking foreshortening in to account (refer to Table 1 for stent length when fully expanded).

b. The appropriate stent length should be selected based on covering the entire obstructed segment with a single stent. Should more than one stent be required, place the stent most distal from the puncture site first, followed by placement of the proximal stent in tandem.

c. Measure the diameter of the lesion to determine the appropriate size delivery system for stent expansion.

10.3 Stent Preparation

a. Open the carton to reveal the pouch containing the stent and crimping tube. Do not use if the inner tray is open or damaged.

b. Inspect the stent package for damage to the sterile barrier. Remove the stent and crimping tube from the package and rinse in sterile heparanized saline.

c. **IMPORTANT: When using the POWERFLEX PLUS balloon catheter, use the crimping tube that is packaged with the balloon, NOT the Stent. The crimping tube supplied with the Stent is NOT compatible with the POWERFLEX PLUS balloon catheter.**

10.4 Preparation of Stent Delivery Catheter

a. Select a stent delivery balloon, which is of a size that approximates the true diameter of the renal artery.

b. See Instructions for Use provided with the recommended balloon catheter. **Note: Preinflation of the balloon catheter is NOT recommended prior to mounting the stent on the balloon.**

10.5 Preparation of Stent Delivery System

a. Remove the balloon protector and visually inspect the balloon to ensure that it is properly folded to its lowest profile.

b. Attach a stopcock to the catheter's inflation port.

c. Open the stopcock and induce negative pressure.

d. Hold the proximal end of the catheter above the distal end. Hold the balloon vertically with the balloon tip pointing down.

e. Close the stopcock.

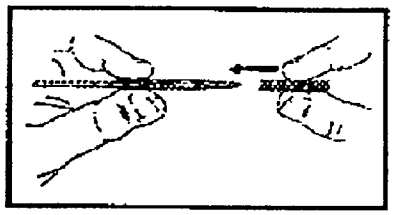
f. Ensure that the air contained in the balloon and inflation lumen is removed. Repeat steps c through e.

g. Place the balloon catheter through a guide catheter that is long enough to reach the lesion, with the balloon extending completely outside the guide catheter.

h. Visually inspect the balloon to assure that it is properly folded to its lowest profile in preparation for the stent application to the balloon.

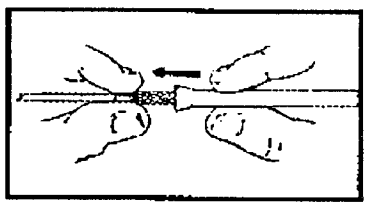
i. Mount the stent on the balloon utilizing the appropriate hand-operated reusable mechanical crimping tool, provided separately (see steps below). The mechanical crimping tool is provided NON-STERILE and must be sterilized prior to use. Plastic crimping tubes and metal introducer tubes are not interchangeable. **(See III below regarding crimping tubes.)**

I. Slide the stent over the distal end of the balloon, maintaining the balloon fold, until the radiopaque markers are equidistant from the ends of the stent.

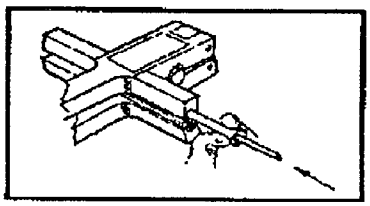


II. Gently pre-crimp the stent on the balloon manually (with fingers). This will enable the crimping tube to more easily slide over the stent once loaded on the catheter.

III. **IMPORTANT: When using the POWERFLEX PLUS balloon catheter, use the crimping tube that is packaged with the balloon, NOT the Stent. The crimping tube supplied with the Stent is NOT compatible with the POWERFLEX PLUS balloon catheter.** Place the plastic crimping tube over the stent. Insert the stent/tube assembly into the crimping tool until the edges of the stent are aligned within the jaws of the crimping tool. The stent is now in a position to be crimped onto the balloon.



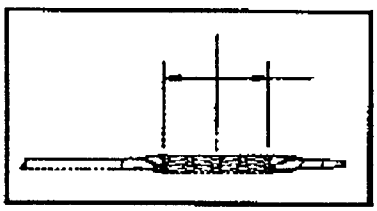
IV. Close the crimping tool until it comes to a fixed stop. The fixed stop prevents excessive crimping and subsequent damage to the stent or balloon. The tool delivers a radial compressive force to the stent.



V. Rotate stent and balloon approximately 90° and repeat step IV.

VI. After crimping, withdraw the balloon, stent and tube assembly from the crimping tool. Remove the tube from the stent and discard it.

VII. Visually inspect the balloon/stent assembly to assure proper placement of the stent between the radiopaque markers of the balloon. Do not reposition stent or manually re-crimp. Carefully pull the stent/balloon assembly back into the guide catheter so that the stent is completely within, and the tip of the balloon extends slightly past, the edge of the guide catheter.



h. Open the stopcock allowing the inflation lumen and the balloon lumen to fill with diluted contrast medium. **NOTE**: Never use air or any gaseous medium to inflate the balloon. The delivery system is not designed for use with power injection systems.

10.6 Insertion of Cordis Sheath Introducer (CSI) and Guidewire

a. Access should be obtained in the standard fashion through the femoral approach. The brachial route may be used in cases where the anatomy dictates this would be a more favorable approach. Gain access at the appropriate site utilizing the recommended CSI (see Table 1). A CSI of the appropriate size and length should be used.

CAUTION: Always use a CSI for the implant procedure to protect the puncture site and avoid dislodging the stent from the balloon.

b. Place the stent/balloon catheter assembly and guiding catheter through the CSI to the aortic bifurcation, using the guidewire as a leader to avoid penetration of the vessel and stent dislodgment.

c. Insert a .035" (.89mm) guidewire of the appropriate length across the lesion to be stented through the CSI. **NOTE**: If the physician determines that predilation is necessary, standard PTA techniques may be used. Maintain lesion access with the .035" (.89mm) guidewire.

d. Insert a sterile stainless steel introducer tube (supplied NON-STERILE) through the hemostatic valve of the introducer assembly (CSI). This tube facilitates insertion of the stent/balloon assembly through the introducer and prevents the hemostatic valve from potentially stripping the stent from the balloon during insertion.

10.7 Stent Deployment Procedure – NOTE: When ready to proceed with stent deployment, 3000 to 5000 units of heparin (depending on patient size) may be given intravenously or intra-arterially.

a. The stent/balloon assembly within the guiding catheter is advanced over the guidewire and through the CSI. Carefully cross the lesion site with the stent.

b. Verify correct stent positioning using multiple oblique views as necessary. After correctly positioning the stent within the renal artery, retract the guiding catheter to completely expose the stent/balloon and expand the stent by inflating the POWERFLEX PLUS balloon catheter to the nominal inflation pressure. Appropriate expansion of the balloon/stent should be determined fluoroscopically. Do not exceed the labeled rated burst pressure (RBP). See Table 5 for the nominal pressure and the labeled RBP.

Ideal positioning of the stent is within the renal artery ostium entirely covering the lesion with no more than 1-2mm of stent extending into the aorta.

10.8 Delivery System Withdrawal

a. After deploying the stent, deflate the balloon by pulling a vacuum, allowing adequate time for the balloon to fully deflate prior to removal.

b. Carefully rotate the balloon counterclockwise to ensure separation of the balloon from the stent.

c. While maintaining negative pressure on the balloon, slowly withdraw the balloon from the stent. Observe removal of the balloon under fluoroscopy to ensure that the balloon disengages from the stent.

d. Remove the deflated balloon, keeping the guidewire in place in the renal artery. A post-stent angiogram should be obtained. After a satisfactory post stent angiogram is obtained, remove the guiding catheter and then the guidewire.

e. Remove the CSI.

f. Discard the delivery system and guidewire.

g. The diameter of the stent may be increased post-placement by repeat balloon dilatation with the same and/or larger diameter balloons. The labeled maximum diameter of the stent should not be exceeded.

h. If the stent does not entirely cover the lesion, a second stent may be placed, with 1-3mm of the overlap between the two stents. Efforts should be made to achieve an optimal result with a minimal residual stenosis and to eliminate the peak-to-peak pressure gradient.

10.9 Post Stent Placement

Compress the puncture site to achieve hemostasis.
NOTE: Physician experience and discretion will determine the appropriate post-procedure drug regimen for each patient.

10.10 In Vitro Information

The data below are based on *in vitro* testing of the PALMAZ Stent on the POWERFLEX PLUS delivery systems. Actual diameters *in vitro* are within 10% of the specified diameter at both nominal and rated burst pressure (RBP). The balloon and stent compliance data should be used to determine what pressure will be needed to achieve the intended stent diameter.

FIGURE 2 - Compliance Chart
Stent Diameter as a Function of Pressure

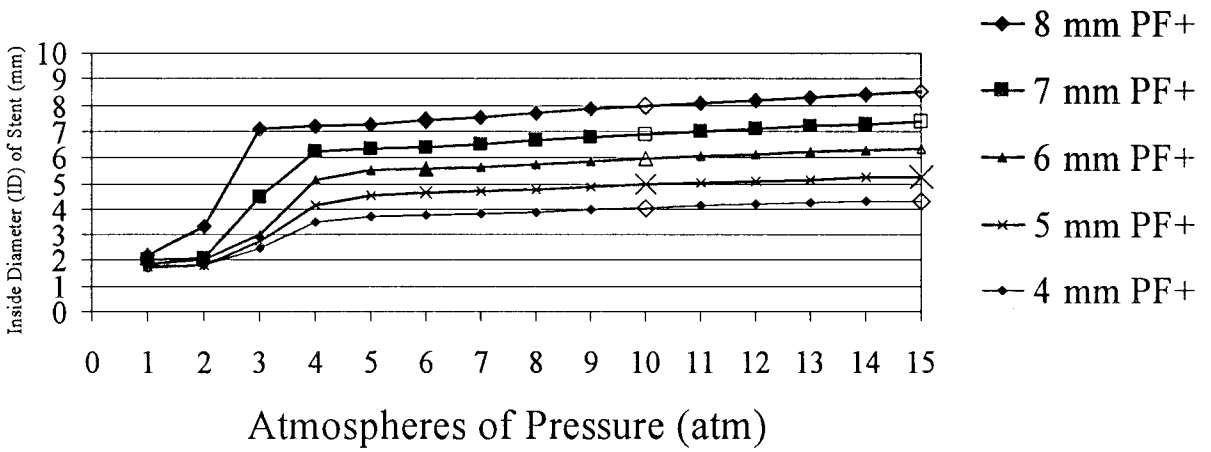


FIGURE 2 NOTES:

- The open markers represent the Nominal and the Rated Burst Pressure (RBP) specifications for the POWERFLEX PLUS (PF+) balloon. Do not exceed the RBP of 15 atmospheres of pressure.
- Each line represents the average stent diameter combining the data from the P104R, P154R and P204R stents.

Table 5 – Compliance Table for the PALMAZ Stent on the POWERFLEX PLUS Balloon Catheter (PF+)

	Expanded Inside Diameter (mm) of the Stent				
Inflation Pressure	4 mm PF+	5 mm PF+	6 mm PF+	7 mm PF+	8 mm PF+
1 atm	1.71	1.76	1.84	2.00	2.20
2 atm	1.82	1.80	2.03	2.06	3.32
3 atm	2.45	2.72	3.01	4.50	7.08
4 atm	3.51	4.14	5.13	6.25	7.19
5 atm	3.70	4.56	5.49	6.33	7.27
6 atm	3.75	4.62	5.59	6.41	7.41
7 atm	3.82	4.68	5.65	6.52	7.54
8 atm	3.90	4.77	5.75	6.65	7.69
9 atm	3.98	4.86	5.86	6.78	7.84
10 atm (Nominal)	**4.06**	**4.95**	**5.96**	**6.90**	**7.99**

11 atm	4.13	5.02	6.05	7.01	8.10
12 atm	4.19	5.09	6.13	7.11	8.21
13 atm	4.25	5.15	6.20	7.20	8.31
14 atm	4.30	5.22	6.28	7.28	8.42
15 atm (RBP)	**4.34**	**5.27**	**6.34**	**7.36**	**8.51**

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