

Summary of Safety and Effectiveness

The AneuRx Stent Graft System

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Summary of Safety and Effectiveness Data

The AneuRx Stent Graft System

1. General Information

Device Generic Name: Endovascular Stent Graft and Delivery Catheter

Device Trade Name: AneuRx Stent Graft System

Applicant's Name and Address: Medtronic AVE, Inc.
2330 Circadian Way
Santa Rosa, CA 95407

PMA Application Number: P990020

Date of Panel Recommendation:..... June 23, 1999

Date of Notice of Approval to the Applicant: ... September 28, 1999

2. Indications and Usage

The AneuRx Stent Graft System is indicated for the endovascular treatment of infrarenal abdominal aortic or aorto-iliac aneurysms having:

- *Adequate iliac/femoral access;*
- *Infrarenal non-aneurysmal neck length of at least 1 cm at the proximal and distal ends of the aneurysm and a vessel diameter 10-20 percent smaller than the labeled device diameter;*
- *Morphology suitable for endovascular repair;*
- *One of the following:*
 - A diameter > 5 cm;*
 - A diameter of 4-5 cm and has increased in size by 0.5 cm in the last 6 months; or*
 - Twice the diameter of the normal infrarenal aorta.*

3. Contraindications

There are no known contraindications currently associated with this device.

4. Warnings and Precautions

See WARNINGS AND PRECAUTIONS in the labeling (Instructions for Use)

5. Device Description

The AneuRx Stent Graft System consists of the AneuRx Stent Graft (bifurcated design) and Delivery Catheter, the AneuRx Iliac Stent Graft and Delivery Catheter and the AneuRx Deployment Handle. Two additional system components, the AneuRx Iliac Extender Cuff and Delivery Catheter and the AneuRx Aortic Extender Cuff and Delivery Catheter, may be used to modify the length and/or diameter of the implanted AneuRx Stent Graft.

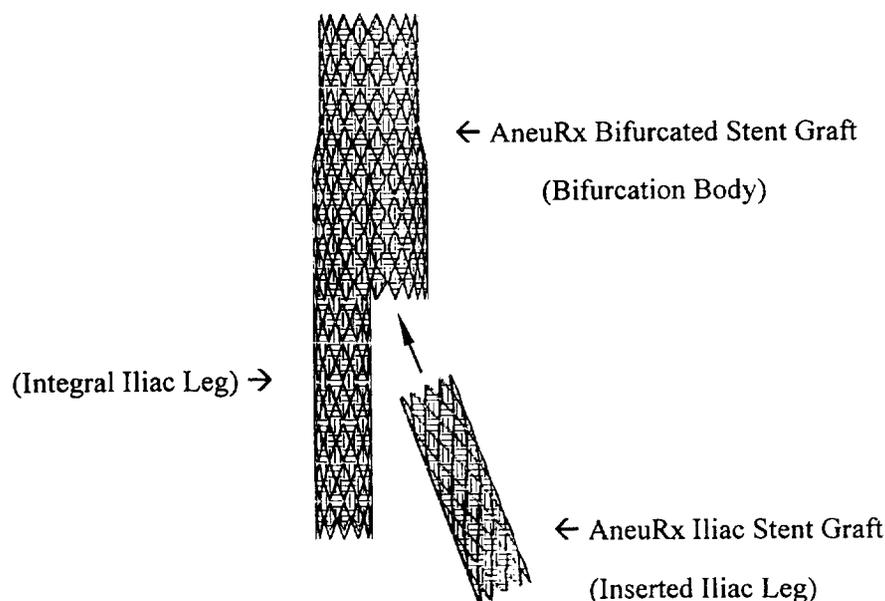


Figure 1: AneuRx Bifurcated and Iliac Stent Grafts

The bifurcated device is tube-shaped at the top and bifurcated at the bottom. When placed within the aneurysm, the device reinforces the wall of the diseased artery and directs blood flow into the iliac arteries. As shown in Figure 1, the Bifurcated Stent Graft consists of the Bifurcation Body and the Integral Iliac Leg. The Iliac Stent Graft (Inserted Iliac Leg) is a separate component which is positioned following placement of the Bifurcated Stent Graft shown in Figure 2. Radiopaque markers are located at the ends of each device to aid in proper positioning within the aneurysm.

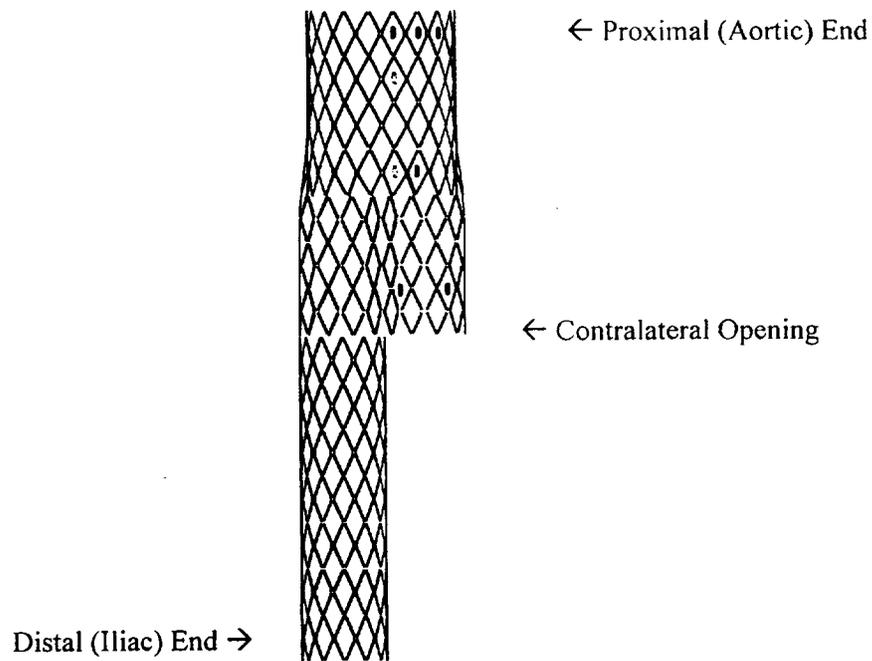


Figure 2: AneuRx Bifurcated Stent Graft

The additional system components, the Iliac Extender Cuff and Delivery Catheter and the Aortic Extender Cuff and Delivery Catheter, are designed to be positioned (overlapping) inside of the implanted Stent Graft in the iliac or aortic sections. Placement of these additional devices modifies the implanted Stent Graft by increasing the length and/or diameter of the Stent Graft at either end. This modular design allows the physician to customize the length and/or diameter of the Stent Graft to fit various anatomies and aneurysm morphologies. Both modular components are manufactured from the same polyester graft material, Nitinol stent rings and polyester thread used to manufacture the AneuRx Bifurcated Stent Graft. All Stent Grafts are available in a range of sizes.



Figure 3: AneuRx Iliac Stent Graft

The AneuRx Stent Graft is constructed from self-expanding Nickel-Titanium (Nitinol, NiTi) alloy stent rings and woven polyester graft tubes. Each stent ring consists of a series of diamond-shaped segments connected side-to-side in the circumferential direction to form a ring (see Figure 4). The diamond-shaped segments are cut, using a laser, from a single piece of Nitinol tubing. No joints or welds are necessary to form a stent ring.

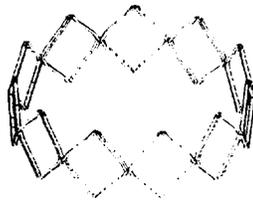


Figure 4: A Single Stent Ring (not to scale)

The stent rings are individually sewn using braided polyester thread, along the entire length of the graft, end to end in a circumferential direction (not overlapping) to form a fully supported structure on the exterior of the graft. This configuration is designed to provide column strength (resistance to deflection in the axial direction), and hoop strength (resistance to deflection in the circumferential direction), while providing the flexibility necessary to conform to the individual patient's anatomy. The Nitinol stents allow the graft to be self-anchoring, adhering to the internal surface of the vessel wall by friction fit.

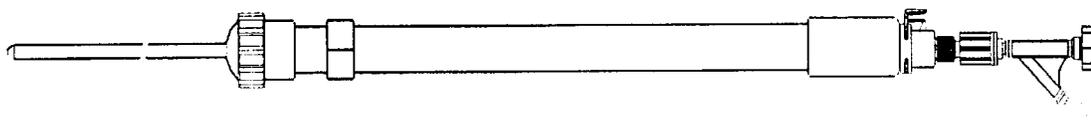


Figure 5: AneuRx Stent Graft Delivery Catheter

Each individual Stent Graft component is preloaded inside an AneuRx Delivery Catheter shown in Figure 5. The Delivery Catheter, supplied sterile for single use only, allows endovascular placement of the AneuRx Bifurcated Stent Graft, Iliac Stent Graft (same as Inserted Iliac Leg) and Iliac and Aortic Extender Cuff Stent Grafts via the arterial vasculature (e.g., femoral or iliac arteries). Using fluoroscopic guidance, the Delivery Catheter is properly positioned within the patient's vasculature. The Stent Graft is then deployed from the Delivery Catheter using the AneuRx Deployment Handle shown in

Figure 6. The Deployment Handle is a reusable device that may be attached to both the 16 French and 21 French Delivery Catheters to assist in deployment. The Deployment Handle is supplied non-sterile and must be steam sterilized prior to each use.

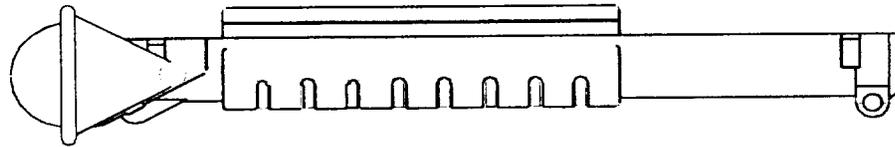


Figure 6: AneuRx Stent Graft System Deployment Handle

The AneuRx Stent Grafts are available in the following sizes:

Bifurcated Stent Graft

Model Number	Diameter (Proximal/Distal)	Lengths
YRBR2012	20 mm x 12 mm	13.5 cm/16.5 cm
YRBR2213	22 mm x 13 mm	13.5 cm/16.5 cm
YRBR2414	24 mm x 14 mm	13.5 cm/16.5 cm
YRBR2615	26 mm x 15 mm	13.5 cm/16.5 cm
YRBR2816	28 mm x 16 mm	13.5 cm/16.5 cm

Iliac Stent Grafts

Model Number	Diameter	Lengths
YRIR12	12 mm	8.5 cm/11.5 cm
YRIR13	13 mm	8.5 cm/11.5 cm
YRIR14	14 mm	8.5 cm/11.5 cm
YRIR15	15 mm	8.5 cm/11.5 cm
YRIR16	16 mm	8.5 cm/11.5 cm

Extender Cuff Stent Grafts

Model Number	Diameter	Lengths
YREC12	12 mm	5.5 cm
YREC13	13 mm	5.5 cm
YREC14	14 mm	5.5 cm
YREC15	15 mm	5.5 cm
YREC16	16 mm	5.5 cm
YREC20	20 mm	3.75 cm
YREC22	22 mm	3.75 cm
YREC24	24 mm	3.75 cm
YREC26	26 mm	3.75 cm
YREC28	28 mm	3.75 cm

Deployment Handle

Model Number
YR5100

6. Alternative Practices or Procedures

The generally accepted standard of care for the treatment of AAA's involves dissecting the aneurysm and placing a synthetic graft inside the diseased tissue. Surgical repair of AAA's is indicated when the risk of rupture is believed to exceed the risks of open surgery. Due to the high risk of rupture for AAA's greater than 5 cm in diameter, and the mortality associated with rupture, surgical repair of such aneurysms is the standard of care.

7. Marketing History

The AneuRx Stent Graft System is available in many countries throughout the world including Europe, Asia, and Australia. The AneuRx Stent Graft System has not been withdrawn from marketing in any country for any reason related to safety or effectiveness.

¹Zarins, C.K., Harris, E.J. (1997) "Operative Repair for Aortic Aneurysms: The Gold Standard." *Journal of Endovascular Surgery*, 4: 232-241.

8. Adverse Events

Adverse Event	Early ≤30 Days Stent Graft		Early ≤30 Days Control		Late >30 Days Stent Graft		Late >30 Days Control	
	%	(n/N)	%	(n/N)	%	(n/N)	%	(n/N)
Deaths	2%	(7/416)	0%	(0/66)	5%	(4/16) ⁷	9%	(6/66)
Other Adverse Events								
AAA Rupture	0.2%	(1/416)	0%	(0/66)	0.2%	(1/416)	0%	(0/66)
Bleeding ¹	4%	(18/416)	3%	(2/66)	0.2%	(1/416)	0%	(0/66)
Cardiac Failure/Infarction	2%	(7/416)	6%	(4/66)	0.7%	(3/416)	0%	(0/66)
Edema ²	1%	(5/416)	0%	(0/66)	<1%	(2/416)	0%	(0/66)
Wound Healing Complications ³	4%	(17/416)	5%	(3/66)	1%	(4/416)	0%	(0/66)
Impotence	0%	(0/416)	0%	(0/66)	0.2%	(1/416)	0%	(0/66)
Pulmonary Complications ⁴	2%	(7/416) ⁸	8%	(5/66) ⁸	<1%	(2/416) ⁹	5%	(3/66) ⁹
Renal Failure ⁵	4%	(15/416)	0%	(0/66)	1%	(3/416)	0%	(0/66)
Gastrointestinal Complications ⁶	3%	(4/416) ¹⁰	14%	(9/66) ¹⁰	1%	(5/416)	0%	(0/66)
Vascular Occlusion (includes thrombosis and thromboembolism)								
Arterial	2%	(8/416)	2%	(1/66)	0.5%	(2/416)	0%	(0/66)
Venous	0%	(0/416)	0%	(0/66)	0.5%	(2/416)	0%	(0/66)

¹ Includes: hematuria, brachial and femoral hematomas, elevated PT/INR, groin hemorrhage, retroperitoneal bleed, urethral bleeding

² Includes: scrotal and foreskin edema, lower extremity swelling

³ Includes: delayed wound healing, lymphatic leak, seroma

⁴ Includes: bilateral pleural effusions, shortness of breath, respiratory failure/arrest, atelectasis, pneumonia

⁵ Includes: renal insufficiency/failure, dialysis, elevated creatinine

⁶ Includes: angiodysplasia of stomach, bowel ischemia, ileus, constipation, nausea/vomiting, ulcers, rectal bleeding, cholecystitis, diarrhea, bowel obstruction, GI bleed, small bowel mesentery bleed, sigmoid colon necrosis

⁷ Four (1%, 4/416) late deaths (>30 days post-procedure) occurred that were classified as device related. One (≤1%, 1/416) death had an unknown cause at the time of the data analysis. One death was undetermined but possibly occurred by cerebral embolism. One death was due to renal failure and pulmonary complications. One death was due to neurological complications.

⁸ p = 0.015

⁹ p = 0.02

¹⁰ p = 0.002

9. Summary of Preclinical Studies

9.1 Laboratory Studies

The following *in vitro* tests were performed in accordance with consensus documents. Since no single standard or guidance document has yet been developed for stent grafts, two documents were “merged” and have become the basis for tests presented in this summary.

The two documents are:

- Association for the Advancement of Cardiovascular Instrumentation, Cardiovascular Implants – Vascular Prostheses (ANSI/AAMI VP20-1994)
- Interventional Cardiology Devices Branch, Division of Cardiovascular, Respiratory and Neurological Devices, Office of Device Evaluation, Guidance for the Submission of Research and Marketing Application for Interventional Cardiology Devices, May 1994

Table 1: Summary of Finished Device Testing

Test	Samples Tested	Specification	Results
<p>Stent Graft Expansion Integrity - To show that the Stent Graft maintains its integrity upon deployment from a compressed state.</p>	<ul style="list-style-type: none"> • (10) 20x12mm (16.5cm length) Bifurcated Stent Grafts • (10) 28x16mm (16.5cm length) Bifurcated Stent Grafts • (10) 16mm (11.5cm length) Iliac Stent Grafts • (10) 12mm (11.5cm length) Iliac Stent Grafts 	<p>Following compression, sterilization and deployment into 37°C water, the Stent Graft shall have:</p> <p>The sum total of broken stitches per Stent Ring cannot include the top stitch (crown or junction), central (node) and lower stitch patterns(junction or crown) with:</p> <p><i>Bifur, long</i> - No more than 7 broken sutures total; <i>Bifur, short</i> - No more than 6 broken sutures total, <i>Iliac, long</i> - No more than 4 broken sutures total, <i>Iliac, short</i> - No more than 3 broken sutures total, <i>Cuff</i> - No more than 2 broken sutures total</p> <p>Example: a single Stent Ring cannot have a top broken junction stitch, a bottom broken junction stitch and a broken central (node) stitch but may have any combination (a single broken junction and node or two broken junctions, top and bottom) provided the total number does not exceed the limit for the device.</p> <p>No holes with area >0.2mm².</p> <p>Graft runs with a maximum dimension <1.5mm are acceptable, but the quantity is limited to not more than 5 per cm of Stent Graft length.</p>	<p>All devices met the acceptance criteria and passed the test.</p>

Test	Samples Tested	Specification	Results
Stent Graft Internal Pressure vs. External Diameter - To determine the static external diameter of the Stent Graft (as a function of internal pressure) by measuring the change in diameter directly under static internal pressure loading.	<ul style="list-style-type: none"> • (10) 20x12mm (16.5cm length) Bifurcated Stent Grafts • (10) 28x16mm (16.5cm length) Bifurcated Stent Grafts • (10) 16mm (11.5cm length) Iliac Stent Grafts • (10) 12mm (11.5cm length) Iliac Stent Grafts 	The Stent Graft diameter must not change more than 10% in response to an internal pressure of 100mm Hg.	The greatest percent diameter change noted during this test was 7%. All Stent Grafts met the acceptance criteria, indicating that the AneuRx Stent Graft diameter does not change more than 10% in diameter in response to human physiologic pressures.
Stent Graft Dimensional Verification - To verify the Stent Graft expands to its labeled diameter.	<ul style="list-style-type: none"> • (10) 20x12mm (16.5cm length) Bifurcated Stent Grafts • (10) 28x16mm (16.5cm length) Bifurcated Stent Grafts • (10) 16mm (11.5cm length) Iliac Stent Grafts • (10) 12mm (11.5cm length) Iliac Stent Grafts 	Iliac and Bifurcated Stent Grafts shall expand to full diameter following compression, loading, sterilization, and deployment in 37°C water. The tolerance for the 12-16mm sizes is ±1.0mm. The tolerance for the 20-28mm sizes is +1.5/-1.0mm.	All Stent Grafts met the acceptance criteria.
Stent Graft Dynamic Compliance - To determine the dynamic compliance of the AneuRx Stent Graft by measuring the change in external diameter in response to a pressure pulse.	<ul style="list-style-type: none"> • (10) 20x12mm (16.5cm length) Bifurcated Stent Grafts • (10) 28x16mm (16.5cm length) Bifurcated Stent Grafts • (10) 16mm (11.5cm length) Iliac Stent Grafts • (10) 12mm (11.5cm length) Iliac Stent Grafts 	The stent graft shall have a minimum dynamic compliance of 0.1 % per 100mmHg.	All Stent Grafts had a mean compliance of 0.2% to 3.1% at 100mm Hg. All Stent Grafts met the acceptance criteria.
Stent Graft Joint Strength - To determine the force necessary to pull one stent graft or modular component from another following implantation.	<ul style="list-style-type: none"> • (10) 20x12mm (16.5cm length) Bifurcated Stent Grafts • (10) 28x16mm (16.5cm length) Bifurcated Stent Grafts • (10) 16mm (11.5cm length) Iliac Stent Grafts • (10) 12mm (11.5cm length) Iliac Stent Grafts 	Stent Graft joint strength must be in excess of 40 grams of force at 1cm overlap.	All Stent Grafts met the acceptance criteria of a minimum joint strength greater than 40 grams at 1cm overlap.
Stent Graft Kink Radius - To determine the radius of curvature to which the Stent Graft can conform before a kink initiates.	<ul style="list-style-type: none"> • (10) 20x12mm (16.5cm length) Bifurcated Stent Grafts • (10) 28x16mm (16.5cm length) Bifurcated Stent Grafts • (10) 16mm (11.5cm length) Iliac Stent Grafts • (10) 12mm (11.5cm length) Iliac Stent Grafts 	The minimum kink radius/diameter for 20x12mm Bifurcated Stent Grafts and 12mm Iliac Stent Grafts must be less than or equal to 6.0cm. The minimum kink radius/diameter for 28x16mm Bifurcated Stent Grafts and 16mm Iliac Stent Grafts must be less than or equal to 8.0cm.	All Stent Grafts met the acceptance criteria.

Test	Samples Tested	Specification	Results																		
Stent Graft Column Strength - To quantify the longitudinal strength of the Stent Grafts.	<ul style="list-style-type: none"> (14) 28mm (5.5cm length) Iliac Stent Grafts (10) 12mm (5.5cm length) Iliac Stent Grafts 	The Stent Grafts shall have a minimum longitudinal compression strength of 40 grams at 5mm deflection.	The mean column strength for the 28mm Stent Grafts was 1294±754 grams (range 341-3123 grams). The mean column strength for the 12mm Stent Grafts was 341±93 grams (range 173-518 grams). All Stent Grafts met the acceptance criteria.																		
Delivery Catheter Deployment Force - To determine the force exerted on the Delivery Catheter during deployment of the AneuRx Stent Graft.	<ul style="list-style-type: none"> (12) 16 French Delivery Catheters (16mm Iliac) (10) 21 French Delivery Catheters (28x16 Bifurcated) 	The 21 French Delivery Catheter deployment force must not exceed 40 lbs. The 16 French Delivery Catheter deployment force must not exceed 30 lbs.	Mean deployment force for the 21 French catheters was 11.5 ±0.9 lbs. (range 10.4-12.8 lbs) and the mean deployment force for the 16 French catheters was 7.3± 1.0 lbs. (range 6.0-8.8 lbs). All catheters met the acceptance criteria under simulated clinical conditions.																		
Delivery Catheter Flexibility - To demonstrate that the Delivery Catheter is flexible enough to be used in tortuous vessels without kinking.	<ul style="list-style-type: none"> (15) 16 French Catheters (20) 21 French Catheters 	Catheter shall be kink resistant in a 1.0-inch bend radius.	No kinking of the catheters was observed. All catheters met the acceptance criteria.																		
Delivery Catheter Tensile Tests - To ensure critical bonds on the Delivery Catheter are adequate in strength and will not fail under normal conditions.	Bond Nosecone to Peek Guidewire Lumen Graft Cover to Slider Outer Pebax Tubing to CPC Connector Hypotube to End Seal Runners to Inner/Outer Pebax Tubing *Stainless Steel Nosecone, **Hytrek Nosecone	<table border="1"> <thead> <tr> <th></th> <th>16 French Catheter</th> <th>21 French Catheter</th> </tr> </thead> <tbody> <tr> <td>Nosecone to Peek Guidewire Lumen Graft Cover to Slider</td> <td>15*, 30**</td> <td>12*</td> </tr> <tr> <td>Outer Pebax Tubing to CPC Connector</td> <td>12</td> <td>10</td> </tr> <tr> <td>Hypotube to End Seal</td> <td>15</td> <td>12</td> </tr> <tr> <td>Runners to Inner/Outer Pebax Tubing</td> <td>12</td> <td>10</td> </tr> <tr> <td></td> <td>12</td> <td>10</td> </tr> </tbody> </table>		16 French Catheter	21 French Catheter	Nosecone to Peek Guidewire Lumen Graft Cover to Slider	15*, 30**	12*	Outer Pebax Tubing to CPC Connector	12	10	Hypotube to End Seal	15	12	Runners to Inner/Outer Pebax Tubing	12	10		12	10	All bonds must have a tensile strength of 5 pounds or greater. The Graft cover to slider bond must have a tensile strength of 30 pounds or greater for the 16 French catheters and 40 pounds or greater for the 21 French catheters.
	16 French Catheter	21 French Catheter																			
Nosecone to Peek Guidewire Lumen Graft Cover to Slider	15*, 30**	12*																			
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Runners to Inner/Outer Pebax Tubing	12	10																			
	12	10																			

Test	Samples Tested	Specification	Results
<p>Stent Graft Fatigue - To determine the fatigue characteristics of the final Stent Graft product by subjecting the devices to 10 million cycles of simulated implant conditions. Ten million cycles represents three months of pressure waves created by the human heart assuming an average heart rate of 72 beats per minute. The influence of overlapping Stent Grafts on fatigue performance was also examined.</p>	<ul style="list-style-type: none"> • (10) 12mm (5.5cm length) Extender Cuff Stent Grafts • (10) 28mm (5.5cm length) Extender Cuff Stent Grafts 	<p>The Stent Graft shall be able to withstand 10 million cycles in a 5-7% compliant tube (10% undersized) pulsed with a minimum 40mm Hg pressure in 37° C saline with no more than 2 additional broken sutures (based on pre-test inspection) and no broken stents.</p>	<p>The 28mm Extender Cuff Stent Grafts had no broken sutures or stents. The test apparatus containing the 12mm Extender Cuff Stent Grafts experienced an equipment failure 124 hours into testing. A motor speed controller failed, resulting in several of the stent grafts being forced to the end of the tubing by the increased pressure wave. All samples were removed from testing at that time and visually examined. Four of the 10 samples had multiple broken stents and sutures. The four samples with extensive damage were removed from testing and the test was resumed. The remaining six 12mm Extender Cuff Stent Grafts completed the test and met all acceptance criteria.</p>
<p>Delivery Handle Re-use Testing - To investigate the effect of multiple cleaning and sterilization cycles on the Delivery Handle in order to support the maximum number of recommended re-use sterilization cycles.</p>	<ul style="list-style-type: none"> • (6) Delivery Handles 	<p>The Delivery Handle must pass 20 steam sterilization cycles and function satisfactorily after each one.</p>	<p>All Delivery Handles were functional after 20 steam sterilization cycles. Some separation of a glue joint on the main body of one handle was noticed after 17 cycles; however the handle still functioned through 3 more (20 total) sterilization cycles. All Delivery Handles met the acceptance criteria.</p>

Test	Samples Tested	Specification	Results
Stent Graft Water Permeability - To determine the rate of water leakage per unit area through the Stent Graft under a pressure of 120mm Hg.	<ul style="list-style-type: none"> • (10) 12mm (5.5cm length) Extender Cuff Stent Grafts • (13) 28mm (3.75cm length) Extender Cuff Stent Grafts 	The Stent Graft must have a water permeability/leakage rate less than 700 ml/min/cm ² .	The 12mm Extender Cuff Stent Grafts had a mean water permeability of 521 ml/min/cm ² and the 28 mm Extender Cuff Stent Grafts had a mean water permeability of 547 ml/min/cm ² . All Stent Grafts met the acceptance criteria.
Delivery Catheter Crossing Profile - To ensure the outside diameter of the AneuRx Stent Graft Delivery Catheter is as labeled.	<ul style="list-style-type: none"> • (10) 16 French Catheters (16mm Iliac) • (10) 21 French Catheters (28x16mm Bifurcated) 	The 21 French graft cover must have a maximum outside diameter of 0.277 inches. The 16 French graft cover must have a maximum outside diameter of 0.213 inches.	All ring gauges passed over the Delivery Catheters successfully. All catheters met the acceptance criteria and have a crossing profile within specifications.
Delivery Catheter Wire Pass - To ensure all delivery catheters can accept a 0.038 inch guidewire with ease.	<ul style="list-style-type: none"> • (10) 16 French Catheters (16mm Iliac) • (10) 21 French Catheters (28x16mm Bifurcated) 	All Delivery Catheters must not exceed a maximum frictional force of 100 grams to pull a stiff 0.038 inch guidewire through its guidewire lumen.	The guidewire passed successfully through all Delivery Catheters. All Delivery Catheters met the acceptance criteria.
Delivery Catheter Hemostasis - To demonstrate the Delivery Catheter will maintain hemostasis during normal clinical use.	<ul style="list-style-type: none"> • (10) 16 French Catheters (16mm Iliac) • (10) 21 French Catheters (28x16mm Bifurcated) 	The Delivery Catheter must not leak more than 2cc/min.	No leakage or drop in pressure was noted on any Delivery Catheter. All Delivery Catheters met the acceptance criteria. The AneuRx Delivery Catheter provides adequate hemostasis.

Test	Samples Tested	Specification	Results
<p>Shelf-Life Study - To ensure the Stent Grafts, after having been compressed, loaded, packaged, sterilized, and stored on the shelf for one year, will still deploy and meet design specifications.</p>	<p>The following samples were tested for functionality:</p> <ul style="list-style-type: none"> • (1) 28mm (3.75cm length) Extender Cuff Stent Graft • (2) 26mm (3.75cm length) Extender Cuff Stent Grafts • (1) 24mm (3.75cm length) Extender Cuff Stent Graft • (2) 22mm (3.75cm length) Extender Cuff Stent Grafts • (1) 20mm (3.75cm length) Extender Cuff Stent Graft <p>The following samples were tested for sterility:</p> <ul style="list-style-type: none"> • (1) 15mm (8.5cm length) Iliac Stent Graft / Delivery Catheter • (1) 12mm (5.5cm length) Extender Cuff Stent Graft / Delivery Catheter • (2) 13mm (5.5cm length) Extender Cuff Stent Graft / Delivery Catheters • (1) 20mm (3.75cm length) Extender Cuff Stent Graft / Delivery Catheter • (1) 22mm (3.75cm length) Extender Cuff Stent Graft / Delivery Catheter • (1) 24mm (3.75cm length) Extender Cuff Stent Graft, Negative Control • (1) 26mm (3.75cm length) Extender Cuff Stent Graft, Positive Control 	<p>The AneuRx Stent Graft must have a shelf life of at least one year and perform as intended.</p>	<p>The AneuRx Stent Graft will maintain sterility and will function after an extended shelf life.</p>
<p>Packaging Performance Testing – To ensure the AneuRx Stent Graft System packaging materials prevent damage to the AneuRx Stent Graft System and maintain sterile barrier properties during shipping to the end user.</p>	<ul style="list-style-type: none"> • Five stent graft systems in a five-pack shipping carton • Ten stent graft systems in a ten-pack shipping carton 	<p>Following completion of all shipping tests, (vehicle stacking, vibration and drop testing) packaging materials must remain intact; labels must remain intact and legible. The pouch material / seals must be undamaged upon visual inspection and confirmed by dye migration testing.</p>	<p>The AneuRx Stent Graft System packaging materials remained intact and all seals and pouch material was undamaged. Sterile barrier integrity was confirmed by dye migration testing.</p>

Test	Samples Tested	Specification	Results
<p>Characterization of Stent Performance at Low Temperature - To characterize performance of the Nitinol stents at temperatures below 37 °C in the event an implanted patients core body temperature was to be lowered for a subsequent procedure (e.g., open heart surgery).</p>	<ul style="list-style-type: none"> • (5) 28mm Stent Rings • (5) 20mm Stent Rings • (5) 16mm Stent Rings • (5) 12mm Stent Rings 	<p>The radial force at 26 °C must be greater than zero and at least 3 times larger than the sensitivity threshold of the load cell (0.002 lb.).</p>	<p>The radial force delivered by the stents at temperatures below 37 °C, stays significantly above zero in a wide temperature range down to 15 °C. The available radial force at 26 °C for all stents was measured to be more than 50% of that at 37 °C, therefore the stent would still be applying an outward pressure at 26 °C to keep the stent graft from migrating in the event the body temperature of an implanted patient were to be lowered.</p>

9.2 Animal Studies

AneuRx has conducted three *in-vivo* animal trials to evaluate the performance of the AneuRx Stent Graft System. The *in-vivo* tests were performed using straight Stent Grafts and bifurcated Stent Grafts. The *in-vivo* studies were conducted to evaluate and document the performance of the Stent Graft devices and the delivery system. The clinical performance attributes evaluated include:

- The ability of the delivery system to effectively navigate vasculature to deliver the Stent Graft to the proper anatomical location prior to deployment,
- The ability of the delivery catheter to adequately and accurately deploy the Stent Graft into the vasculature,
- The ability of the Stent Graft to exclude the aneurysm,
- Performance of the Stent Graft in high-flow areas,
- Adequacy of the friction fit method in attaching the Stent Graft to the aortic wall, and
- Feasibility and utility of the modular design.

Each of these studies evaluated a different aspect of clinical performance of the AneuRx Stent Graft System. Implantation in the thoracic aorta of sheep demonstrated the performance of the device in a high-flow area, allowing documentation of the lack of migration of the device after implantation, and the ability to deploy one Stent Graft device within another modular unit. Implantation in an *in situ* aortic aneurysm in sheep documented the lack of migration, aneurysm exclusion and outflow patency characteristics. Implantation in *in situ* aortic aneurysms in dogs demonstrated lack of migration, aneurysm exclusion, modularity and flow characteristics for the bifurcated units, and the ability to maneuver the bifurcated delivery system through narrow and tortuous vasculature. By conducting these studies in three different models, substantiation of each of these parameters was often obtainable in more than one model.

Methods: Straight CVC Endovascular Prostheses were deployed in a total of 36 sheep and 18 dogs. The device was deployed in the thoracic aorta of 18 sheep, and at the site of a surgically fabricated *in situ* infrarenal aortic aneurysm in another 18 sheep. CVC Bifurcated Endovascular Prostheses were deployed within surgically fabricated *in situ* infrarenal aortic aneurysms in 18 dogs. The implanted animals have been sacrificed as summarized below.

Sacrifice Schedule of Animals Implanted with CVC Endovascular Prostheses

Sacrifice Timepoint	AAA Ovine Straight EP (n=18 implanted)	Thoracic Ovine Straight EP (n=18 implanted)	AAA Canine Bifurcated EP (n=18 implanted)	Total
One Week	3	3	4	10
One Month	3	3	3	9
Three Months	3	3	4	10
Six Months	6	7	6	19
One Year	3	2	1	6

In these three animal models, each of which tests multiple and different aspects of potential clinical performance, the AneuRx Stent Graft was successfully advanced to the desired location and implanted. When desired, the AneuRx Stent Graft was deployed accurately within another Stent Graft device. In 34 of the 36 animals studied, devices excluded the aneurysm as desired. The Stent Graft generally remained patent, except for some of the iliac legs inserted into the old bifurcated design in the canine model. Clinical complications were rare, and with one exception, were transient and caused no obvious long-term adverse effects.

Additionally, the implanted Stent Grafts were well-tolerated by the native vessels indicating an acceptable level of biocompatibility for the AneuRx Stent Graft device.

9.3 Biocompatibility Studies

AneuRx has conducted biocompatibility testing to establish the safety and biocompatibility of all patient-contacting materials used to manufacture the Medtronic AneuRx Stent Graft and Delivery Catheter. All biocompatibility testing was conducted in compliance with Good Laboratory Practice (GLP) regulations by contract laboratories specializing in the conduct of safety evaluation testing. Tests initiated prior to July 1, 1995 were conducted in accordance with the Tripartite Biocompatibility Guidance for Medical Devices. Tests initiated on or after July 1, 1995, were conducted in accordance with ISO 10993-1 - Biological Evaluation of Medical Devices. Biocompatibility testing was performed on the following patient-contacting materials:

- Polyester Graft Material with Tantalum Markers - Raw Materials
- Nickel Titanium Stent - Raw Material
- Stent Graft Devices - Finished Product
- Stent Graft Delivery System - Finished Product

The Polyester Graft Material with Tantalum Markers (raw materials), the Nickel Titanium Stent (raw material) and the Stent Graft Devices (finished product) successfully passed each individual test. These results indicate that the test articles are biocompatible and safe for use in manufacturing of a permanent implant device designed to come into direct contact with blood.

The Stent Graft Delivery System successfully passed each individual test, indicating that the Stent Graft Delivery Catheter - Finished Product is biocompatible and safe for use as an externally communicating device, having limited contact with circulating blood.

Overall, results of biocompatibility testing performed confirm that the Medtronic AneuRx Stent Graft and Delivery Catheter are considered to be safe at the cellular, systemic, local and immunological levels.

Below are tabulated biocompatibility summaries.

Table 1

Test Material: Polyester Graft Material with Tantalum Markers (Raw Materials)

Test	Purpose	Results & Conclusions
USP Muscle Implantation Test with Histopathology in the Rabbit (90 days) Lot number M950058	To evaluate the potential for local irritation or a toxic response to material implanted in direct contact with living muscle tissue.	Results: Macroscopic: non-reactive Microscopic: Moderately irritating* Conclusion: Passed

*Histopathology revealed that the test material was moderately irritating when compared to the control material. However, the irritation seen was considered to be a result of the physical structural characteristics of the embedded material and not due to any inherent toxic quality of the test material.

Table 2

Test Material: Nickel Titanium Stent (Raw Material)

Test	Purpose	Results & Conclusions
USP Muscle Implantation Test with Histopathology in the Rabbit (90 days) Lot number M950057	To evaluate the potential for local irritation or a toxic response to material implanted in direct contact with living muscle tissue.	Results: Macroscopic: non-reactive Microscopic: Moderately irritating* Conclusion: Passed

*Histopathology revealed slight irritation in the test compared to the control groups. Inflammatory reaction and fibrosis around the test implant was extremely minimal.

Table 3

Test Material: Stent Graft Devices (Finished Product)

Test	Purpose	Results & Conclusions
USP Systemic Injection Test Lot number M950062	To determine whether leachables extracted from the test article would cause systemic toxicity following injection into mice.	Results: No mortality or toxicity observed Conclusion: Passed
USP Intracutaneous Test Lot number M950062	To determine whether leachables extracted from the test article would cause significant irritation or toxicity when injected intracutaneously.	Results: The difference between the mean scores for each of the sample extracts and corresponding blanks was 1.0 or less. Conclusion: Passed
Guinea Pig Maximization Test Lot number M950062	To determine to what extent a test material has the potential for acting as a contact sensitizer in guinea pigs.	Results: SCI* and CSO* extractions: None of the test group or negative control animals exhibited scores higher than "1". Conclusion: Passed
Cytotoxicity – Elution Test Lot numbers M950063, M950101, M950102, F050056	To determine the <i>in-vitro</i> biological reactivity of mammalian cell cultures to specific extracts prepared from the test samples in physiological media.	Results: None of the cell cultures treated with the sample extract scored a reactivity grade greater than "1" (mild reactivity) Conclusion: Passed

Test	Purpose	Results & Conclusions
Hemolysis – Direct Contact Lot number M950063	To determine if the composition of the sample has the ability to cause hemolysis <i>in- vitro</i> .	Results: Average hemolysis was 1.9% Conclusion: Passed
Thrombogenicity Lot number M950062	To quantitate the thrombogenic potential of the test samples	Results: No statistically significant difference between the clot time of the sample and the polypropylene negative control. Conclusion: Passed
Salmonella Typhimurium Reverse Mutation Assay (Ames Test) Lot number M950062	To determine whether a 0.9% saline extract of the test article would cause mutagenic changes in histidine – dependent strains of Salmonella Typhimurium.	Results: The extract tested against the five strains did not meet the criteria for a potential mutagen Conclusion: Passed

* 0.9% Sodium Chloride for Injection

** Cottonseed Oil

35

Table 4

Test Material: Stent Graft Delivery System (Finished Product)

Test	Purpose	Results & Conclusions
USP Systemic Injection Test Lot number M950083	To determine whether leachables extracted from the test article would cause systemic toxicity following injection into mice.	Results: No mortality or toxicity observed. Conclusion: Passed
USP Intracutaneous Test Lot number M950083	To determine whether leachables extracted from the test article would cause systemic irritation or toxicity when injected intracutaneously.	Results: The difference between the mean scores for each of the sample extracts and corresponding blanks was 1.0 or less. Conclusion: Passed
Guinea Pig Maximization Test Lot number M950083	To determine to what extent a test material has the potential for acting as a contact sensitizer in guinea pigs.	Results: SCI* extractions: None of the test groups or negative control animals exhibited scores higher than "1". Conclusion: Passed
Cytotoxicity – Elution Test Lot number M950083	To determine the in-vitro biological reactivity of mammalian cell cultures to specific extracts prepared from the test samples in physiological media.	Results: None of the cell cultures treated with the sample extract scored a reactivity grade greater than "0" (none). Conclusion: Passed

Test	Purpose	Results & Conclusions
Hemolysis – Direct Contact Lot number M950083	To determine if the composition of the sample has the ability to cause hemolysis <i>in-vitro</i> .	Results: Average hemolysis was <1%. Conclusion: Passed
Thrombogenicity Lot number M950097	To quantitate the thrombogenic potential of the test samples.	Results: No statistically significant difference between the clot time of the sample and the polypropylene negative control. Conclusion: Passed

* 0.9% Sodium Chloride for Injection

9.4 Additional Studies

Magnetic Resonance Imaging (MRI) Safety Testing- to ensure there will be no adverse effects to the patient in the event a patient requires a MRI procedure after the Stent Graft has been implanted.

Samples Tested – (1) 28x16mm (16.5cm length) Bifurcated Stent Graft, corresponding 16mm contralateral iliac leg and 28mm (3.75cm length) diameter Extender Cuff Stent Graft. This Stent Graft represents the largest diameter, longest length and greatest mass of metal with an Aortic Extension Cuff added for additional length and mass.

Specification – A patient with an implanted AneuRx Stent Graft must be able to undergo subsequent MRI procedures without adverse effects to the patient from the Stent Graft (e.g., migration, RF heating).

Results – The Medtronic AneuRx Stent Graft has been determined to be MRI Safe. When presented in a patient undergoing an MRI procedure, the Medtronic AneuRx Stent Graft will not present additional risk to the patient, but may affect the image quality depending on the pulse sequence that is used and the imaging area of interest evaluated using MRI.

Safety information for the use of magnetic resonance imaging (MRI) procedures (i.e., imaging, angiography, functional imaging and spectroscopy) pertains to the

use of a shielded MRI systems with static magnetic fields of 1.5T or less, spatial gradient of 450 gauss/cm or less, gradient magnetic fields of 10 Tesla/second or less, and a maximum whole body averaged specific absorption rate (SAR) of 1.4 W/kg for 30 minutes of imaging. The effects of performing MRI procedures using MR systems and conditions above these levels have not been determined.

10. Summary of Clinical Studies

10.1 Objectives

To document the safety and effectiveness of the AneuRx System in the treatment of infrarenal aortic or aorto-iliac AAAs by:

- Demonstrating the effectiveness of the Stent Graft through successful deployment and aneurysm exclusion both acutely and long term.
- Comparing the relative safety and clinical utility of the endovascular treatment of AAA to open surgical repair.

To show that endovascular stent graft repair of abdominal aortic aneurysms using the Medtronic AneuRx Stent Graft System is a safe and effective alternative to conventional open surgical repair of abdominal aortic aneurysms.

10.2 Study Design

The clinical evaluation for the AneuRx Stent Graft System was a prospective, non-randomized, multicenter clinical study designed to compare endovascular repair to conventional open surgical repair in terms of safety, procedural parameters and hospital activities. The study was initiated in April 1996.

Safety comparisons were made by evaluating morbidity and mortality of the surgical and stent graft subjects. Procedural parameters and hospital activities were compared by evaluating factors such as procedural blood loss, duration of procedure and anesthesia times, length of hospital stay, length of time in the intensive care unit, time to resumption of normal diet, etc. Due to the very different nature of the surgical and endovascular approaches, the aneurysm exclusion rate will not be compared, but is presented with descriptive statistics along with other unique endpoints of the endovascular approach such as stent graft migration, and stent graft patency.

Thirteen clinical sites were involved in the study. Each of the sites was required to first enroll five control subjects in the Surgical Control Group prior to initiating enrollment of subjects for endovascular stent graft treatment (Stent Graft Treatment Group).

Follow-up

Surgical Control Group subjects and Stent Graft Treatment Group subjects were followed at the same post-operative intervals. Follow-up evaluations were scheduled for pre-discharge, 1 month, 6 month, and 1 year post procedure. A later protocol amendment added 2, 3, 4 and 5 year post-procedure follow-up evaluations for Stent Graft Treatment Group Subjects. At each of these intervals the subject's health is evaluated, endpoints are recorded and quality of life questionnaires are completed.

The only difference in the follow-up regimen between the two groups is the additional imaging procedures necessary to evaluate the effectiveness of the device by measuring endpoints such as migration, aneurysm exclusion and patency (see below for a complete description of each endpoint).

Primary Outcome Measures

Delivery Success

Vessel access was achieved and the physician was able to insert the delivery catheter and deliver it to the treatment site. If the aneurysm cannot be accessed with the delivery catheter, it is considered a delivery failure. This endpoint is measured only during the procedure.

Deployment Success

The stent graft(s) was advanced through the vasculature to the desired location and fully deployed within 0.5 cm of the intended location. Deployment success is verified during the procedure with fluoroscopy.

Morbidity and Mortality

At each follow-up evaluation and each hospital stay, all complications suffered by both the stent graft treatment group and the surgical control group were collected. Complications will be categorized and reported according to severity. A comparison between the surgical control group and the stent graft treatment group will be made to evaluate the relative safety of the endovascular procedure

Stent Graft Migration

Post implantation movement of the stent graft relative to the native aorta is considered migration. Migration can be measured by CT, angiography, ultrasound, or pathological analysis and is evaluated at discharge and at all follow-up visits.

Aneurysm Exclusion

An endoleak is defined as evidence of blood flow around or through the stent graft into the aneurysm. All endoleaks are considered an exclusion failure; however, some endoleaks may be tolerated and followed to determine clinical impact. Aneurysm exclusion is measured by CT examination at discharge and at the 6-month, 1, 2, 3, 4, and 5-year follow-up visits, and by color duplex ultrasound or CT at the 1-month follow-up visit.

Stent Graft Patency

Blood flow through the treated vessel and stent graft must be obtained. Core Lab interpretation of non-patency was any occlusion, whether complete or partial. Hospital interpretation of non-patency was complete occlusion of any part of the device requiring interventional treatment.

Stent Graft Occlusion (Non-Patency)

Stent graft occlusion is defined as a complete blockage of the initial implanted lumen diameter of any prosthesis as evidenced by CT, angiography, ultrasound or pathological analysis, and is considered a patency failure.

Device Integrity

The device must remain intact with no visible defects as measured by CT examination or color duplex ultrasound at all follow-up examinations. This applies to the integrity of the device as it relates to the stent (all struts intact, no kinks or breaks) as well as to the graft material (no tears or holes).

Additional primary endpoints have been added as a result of recent discussions with FDA. They are as follows:

Aneurysm Rupture

Rupture of the abdominal aortic aneurysm during attempted endovascular repair or subsequent to successful stent graft delivery and deployment, due to any possible cause at any point in time.

Expansion of the AAA by >0.5 cm

Increase of the maximum AAA diameter by more than 0.5 cm from pre-discharge imaging (or baseline imaging if no pre-discharge imaging is available) to any time during the follow-up interval or between any two consecutive follow-up intervals as determined by core lab interpretation of the CT scan imaging.

Conversion to surgical repair

Conversion to open surgical repair of the AAA due to unsuccessful delivery or deployment of the stent graft, due to complications or other clinical situations which precluded successful endovascular treatment, or at any time following initial successful endovascular treatment for any reason.

Additional procedure required

Number of patients in which more than one procedure was required to successfully treat the patient (i.e. an additional stent graft procedure for placement of extension cuffs to treat endoleak or migration, or treatment for graft non-patency). These patients may be evaluated for secondary success.

Secondary Outcome Measures

Duration of Surgical Procedure

The time from which the first incision is made to the time the last suture is completed.

Time Spent in the ICU

Number of days spent in the intensive care unit following the procedure.

Days of Hospitalization

Number of days spent in the hospital post-procedure.

Amount of Blood Loss

Blood lost during the procedure that could not be returned to the patient by autotransfusion.

Number of Patients Requiring Transfusion of Stored Blood

The percentage of patients that required any blood transfusion with stored blood or blood-products.

Time to Extubation

41

Expressed as days until patient is extubated post-procedure.

Time to Unassisted Ambulation

Number of days until patient is able to ambulate from bed on his/her own.

Time to Resumption of Normal Diet

Number of days until patient is prescribed a regular diet (e.g. solid food)

Quality of Life Assessments

Both groups answered a Quality of Life questionnaire pre and post procedure as well as at all follow-up evaluations. These assessments were designed to help determine the impact on the patient (both physically and mentally) of surgical treatment compared to endovascular treatment.

10.3 Description of Patients and Gender Bias

Subjects

At the time of this analysis a total of 416 subjects were enrolled into the Phase II study. Subjects were enrolled into two groups, the Surgical Control Group and the Stent Graft Treatment Group. A total of 66 subjects were enrolled in the Surgical Control Group.

Surgical Control Group

Sixty-six subjects were enrolled in the Surgical Control Group of the Phase II study. The Phase II protocol called for five control patients to have surgical repair of their abdominal aortic aneurysms at each clinical site prior to initiating enrollment of patients in the Phase II Stent Graft Treatment Group. One site enrolled an additional Surgical Control Group subject bringing the total number of Surgical Control Group patients to 66, instead of 65.

Stent Graft Treatment Group

There were 13 investigational sites involved in enrollment of patients in the Phase II Stent Graft Treatment Group. As of December 7, 1998, 416 patients were enrolled in the Phase II Stent Graft Treatment Group. Patients enrolled in the study were implanted with a Bifurcated Stent Graft and Iliac Stent Graft (inserted iliac leg). See Device Description for a detailed description of the device.

Gender Bias

There were a total of 416 subjects enrolled in the Stent Graft Treatment Group of the study, 89% were male and 11% were female. In comparison, there were 66 subjects enrolled in the Surgical Control Group, 85% were male and 15% were female. The results of the clinical study indicate that women treated with this device may have a higher incidence of mortality compared to their male counterparts.

A review of the literature reveals that the gender of patients undergoing conventional abdominal aortic aneurysm repair are 82% male and 18% female.^{2,3,4,5,6,7,8,9}

² Pleumeekers H, Hoes AW, van der Hoes E, Van Urk H, Grobbee DE, (1994) "Epidemiology of abdominal aortic aneurysms." European Journal of Vascular Surgery 8, 119-128

³ Clark ET, Gewertz BL, Hisham SB, Zarins CK. Current results of elective aortic reconstruction for aneurysmal and occlusive disease. J Cardiovasc Surg 31:438-41, 1990.

10.4 Results

Enrollment by Center

Institution	Principal Investigator	Location	Surgical Patients	Stent Graft Patients
Harbor - UCLA	Rodney White, MD	Torrance, CA	5	66
Baptist East Hospital	Edward Kinney, MD	Louisville, KY	5	31
Stanford Univ. Medical Ctr	Christopher Zarins, MD	Stanford, CA	5	46
Northside Cardiology	Donald Schwarten, MD	Indianapolis, IN	5	49
Northwestern Univ. Medical School	Jon Matsumura, MD	Chicago, IL	5	10
Cleveland Clinic Foundation	Timothy Sullivan, MD	Cleveland, OH	5	41
Ochsner Clinic	Samuel Money, MD	New Orleans, LA	6	26
Sanger Clinic	Robert Bersin, MD	Charlotte, NC	5	28
Springfield Memorial Hospital	Kim Hodgson, MD	Springfield, IL	5	52
Washington Hospital Center	John Laird, MD	Washington, DC	5	18
Arizona Heart Institute	Edward Diethrich, MD	Phoenix, AZ	5	30
West Columbia Hospital	William Moore, MD	West Columbia, SC	5	9
Pittsburgh Vascular Center	Mark Wholey, MD	Pittsburgh, PA	5	10
		Total	66	416

⁴ Chen JC, Hildebrand HD, Salvian Aj, Hsiang YN, Taylor DC. (1997) "Progress in abdominal aortic aneurysm surgery: four decades of experience at a teaching center." *Cardiovascular Surgery*, Vol.5 No.2; 150-156.

⁵ Melton JL, Bickerstaff LK, Hollier LH, et al. (1984) "Changing incidence of abdominal aortic aneurysms: a population-based study." *American Journal of Epidemiology*, Vol.120 No.3; 379-386

⁶ Crawford ES, Salwa AS, Babb JW, et al. (1981) "Infrarenal abdominal aortic aneurysm: factors influencing survival after operation performed over a 25-year period." *Annals of Surgery*, June 1981, 699-709.

⁷ Johnston KW, Scobie TK. (1988) "Multicenter prospective study of nonruptured abdominal aortic aneurysms I. Population and operative management." *J Vasc Surg* 7:69-81

⁸ AbuRahma AF, Robinson PA, Boland JP, et al. Elective resection of 332 abdominal aortic aneurysms in a southern West Virginia community during a recent five-year period. *Surgery* 109:244-51, 1991.

⁹ Sullivan CA, Rohrer MJ, Cutler BS. Clinical management of the symptomatic but unruptured abdominal aortic aneurysm. *J Vasc Surg* 11:799-803, 1990.

Demographics

(66 Surgical Control Group Subjects, 416 Stent Graft Treatment Group Subjects, unless otherwise noted)

Demographic	Stent Graft (N = 416) ¹	Control (N = 66)
Age (years)	73 (45-93)	69 (49-85)
Alcoholism	3%	5%
Angina pectoris	18%	23%
Cancer	26%	26%
Cerebrovascular disease	14%	12%
Chronic obstructive pulmonary disease ²	24%	36%
Chronic renal failure	2%	6%
Diabetes	12%	9%
Family history of aneurysm disease	10% (n=415)	14%
Gender		
Female	11%	15%
Male	89%	85%
History of CVA (n=49)	11%	8%
Hypertension	64%	56%
Immunodeficiency	0%	2%
Myocardial infarction prior to last 6 months	33%	24%
Myocardial infarction within previous 6 months	4%	3%
Obesity	18%	18%
Peripheral vascular disease	20% (n=415)	24%
Previous surgery in affected area ³	26%	14%
Prior coronary intervention procedure	45% (n=415)	53%
Radiation of the affected area	3%	2%
Symptomatic cardiac arrhythmia ⁴	12%	3%
Symptomatic congestive heart failure	8%	3%
Systemic infection - current	0%	0%
Thromboembolic events	4% (n=413)	6%
Tobacco use	86% (n=414)	82%

1 Unless otherwise noted, N = 416

2 p = 0.037

3 p = 0.027

4 p = 0.029

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Aneurysm Diameter Distribution

Diameter Range	Stent Graft				Control			
	Neck N=346		Aneurysm N=390		Neck N=47		Aneurysm N=53	
	n	%	n	%	n	%	n	%
<20	16	4.6	0	0	2	4.3	0	0
20 – 29 mm	325	93.9	0	0	41	87.2	0	0
30 – 39 mm	5	1.5	6	1.5	3	6.4	1	1.9
40 – 49 mm	0	0	68	17.4	0	0	8	15.1
50 – 59 mm	0	0	199	51.0	1	2.1	25	47.2
60 – 69 mm	0	0	80	20.5	0	0	9	17.0
70 – 79 mm	0	0	25	6.4	0	0	4	7.6
80 – 89 mm	0	0	9	2.3	0	0	4	7.6
≥90 mm	0	0	3	0.8	0	0	2	3.8

Aneurysm Length Distribution

Length Range	Stent Graft				Control			
	Neck N=360		Aneurysm N=333		Neck N=46		Aneurysm N=44	
	n	%	n	%	n	%	n	%
<20	100	27.8	3	0.9	14	30.4	0	0
20 – 29 mm	126	35.0	1	0.3	24	52.2	0	0
30 – 39 mm	71	19.7	5	1.5	4	8.7	2	4.6
40 – 49 mm	40	11.1	8	2.4	2	4.4	1	2.3
50 – 59 mm	10	2.8	19	5.7	1	2.2	4	9.1
60 – 69 mm	10	2.8	41	12.3	0	0	8	18.2
70 – 79 mm	2	0.6	58	17.4	1	2.2	7	15.9
80 – 89 mm	1	0.3	70	21.0	0	0	0	0
≥90 mm	0	0	128	38.4	0	0	22	50.0

ASA Grades

(66 Surgical Control Group Subjects, 416 Stent Graft Treatment Group Subjects)

ASA Grade	Surgical Control Group	Stent Graft Treatment Group	Difference [95% CI]
1	0%	1.0%	-1.0%[-2.8%, 0.9%]
2	7.6%	9.6%	-2.0%[-9.1%, 5.0%]
3	68.2%	64.4%	3.8%[-8.5%,16.0%]
4	24.2%	25.0%	-0.4%[-11.6%,10.9%]

AAA Classification

(64 Surgical Control Group Subjects, 416 Stent Graft Treatment Group Subjects)

AAA Classification	Surgical Control Group	Stent Graft Treatment Group	Difference [95% CI]
A	14.1%	19.5%	-5.5% [-14.8%, 3.9%]
B	34.4%	56.3%	-21.9% [-34.4%, -9.3%]
C	34.4%	13.0%	21.4% [9.3%, 33.4%]
D	9.4%	7.0%	2.4% [-5.2%, 9.9%]
E	7.8%	4.3%	3.5% [-3.4%, 10.3%]

Type of Anesthesia Used

(66 Surgical Control Group Subjects, 415 Stent Graft Treatment Group Subjects)

Anesthesia Type	Surgical Control Group	Stent Graft Treatment Group	Difference [95% CI]
General	100%	67%	33% [28%, 38%]
Epidural	0	22%	-22% [-27%, -17%]
Local	0	11%	-11% [-15%, -7%]

Adverse Events

See Section 8 above.

Principal Safety Results (N=416)

The time intervals capture the events between the follow up time periods. Denominators that are < 416 reflect patients that were successfully treated with the Stent Graft, measures that are determined by cine, and the actual readable images sent to the corelab by the investigational sites. The denominators are determinable measures based on the image quality.

Five of 415 (1.2%) patients underwent open surgical repair due to iliac access difficulty or due to the unsuccessful delivery, deployment or positioning of at least one of the stent graft components. One patient (0.2%) refused placement of an Extender Cuff for treatment of endoleak and instead opted for open surgical repair. Two patients (0.5%) were converted to open surgical repair following rupture of the AAA.

Patients with technical success underwent an additional procedure(s): 19 patients for Extender Cuff placement due to endoleak, with or without migration, and 8 for non-patent endovascular grafts.

Safety Measures and other Clinical Events	Pre-discharge to six months	Pre-discharge to one year
Aneurysm Rupture	1/405 (0.2%)	1/405 (0.2%)
Conversion to Surgical Repair	7/415 (1.7%)	8/415(1.9%)
Additional Procedure Required	16/405 (3.9%)	27/405 (6.7%)

Principal Effectiveness Results

416 patients were enrolled in the study. Denominators that are < 416 reflect a subset of the patients implanted with a Stent Graft and with readable images sent to the corelab by the investigational sites.

Principal Effectiveness Results

Efficacy Measures	Pre-discharge N=416 ²	Pre-discharge N=189	6 months N=189	1 year N=189
Delivery Success/ Deployment Success	405/415 (97.6%)	————	————	————
Stent Graft Migration	Baseline	Baseline	3/173 (1.7%) 16 patients did not have a KUB or CT corelab evaluation.	3/187 (1.6%) 1 patient did not have a readable KUB or CT. 1 patient refused return visit.
Aneurysm non- Exclusion (evidence of endoleak)	165/354 (46.6%)	74/169 (43.8%) 20 patients did not have a CT corelab evaluation.	38/162 (24.0%) 27 patients did not have a CT corelab evaluation.	30/172 (17.4%) 17 patients did not have a CT corelab evaluation.
Stent Graft Patency	352/352 (100%)	167/168 (99.4%) 20 patients did not have a CT corelab evaluation. 1 patient did not have a readable CT.	156/162 (96.3%) 27 patients did not have a CT corelab evaluation.	166/171 (97.1%) 18 patients did not have a CT corelab evaluation. 1 patient did not have a readable CT.
Device Integrity ¹				
1. Stent graft fractures	1. 0/383 (0%)	1. 0/137 (0%) 51 patients did not have a KUB corelab evaluation. 1 patient did not have a readable KUB.	1. 0/113 (0%) 76 patients did not have a KUB evaluation.	1. 0/133 (0%) Read by KUB only. 56 patients did not have a KUB evaluation.
2. Kinking and/or twisting	2. 14/351 (3.9%)	2. 11/186 (5.9%) 3 patients did not have a KUB or CT corelab evaluation.	2. 3/174 (1.7%) 15 patients did not have a CT or KUB evaluation.	2. 5/188 (2.6%) 1 patient refused return visit.
Morbidity and Mortality	<i>Contained in Section 5. ADVERSE EVENTS</i>			

¹No patient with a device kink or twist had nonpatency, migration, or required additional procedures for correction.

Secondary Outcome: Surgical Control vs. Stent Graft

Endpoint	Surgical Control Mean (range)	Stent Graft Mean (range)	Difference [95% CI]
Duration of Anesthesia (min) ¹	293 (125-623) N=65	255 (110-814) N=415	38 [14, 62]
Duration of Procedure (min) ²	210 (90-498) N=65	174 (71-680) N=415	36 [16, 56]
Blood Loss (cc) ²	1617 (200-8000) N=65	544 (0-3500) N=410	1073 [886,1261]
Patients Requiring Blood Transfusion (%) ²	55 N=65	24 N=410	31 [18, 44]
Days to Endotracheal Extubation ²	1.3 N=60	0.2 N=374	1.1 [0.6, 1.5]
Days to Unassisted Ambulation ²	3.6 N=65	1.4 N=392	2.2 [1.8, 2.5]
Days to Resumption of Normal Diet ²	4.9 N=60	1.3 N=389	3.6 [3.2, 3.9]
Days in ICU ²	3.5 (0-72) N=66	0.9 (0-83) N=396	2.5 [1.1, 3.9]
Hospital Length of Stay (LOS, days) ²	9.3 (3-72) N=50	3.4 (0.8-84) N=406	5.9 [4.3, 7.6]

1 p < 0.002

2 p < 0.001

Successful Delivery and Deployment

(Stent Graft Treatment Group, n=415)

Prosthesis Type	Devices Attempted	Successful Delivery	95% Confidence Interval	Successful Deployment	95% Confidence Interval
Bifurcated Device	416	98.1%	[96.8%, 99.4%]	97.8%	[96.4%, 99.2%]
Contralateral Limb	465	99.8%	[98.6%, 100%]	99.6%	[98.3%, 99.9%]
Extension Cuff	237	98.7%	[96%, 99.7%]	98.7%	[96.0%, 99.7%]

Additional Procedures: Type of Cuff Place for Each Type of Endoleak

Leak Location*	Number of Patients	Therapy / Number of Patients
Proximal	7	Proximal Cuff / 7
Junction	5	Iliac Leg Cuff / 5
Collateral Vessel	2	Proximal Cuff / 1 Distal Cuff / 1
Distal	5	Distal Cuff / 5
Indeterminate	1	Proximal and Distal Cuff / 1

*One patient had both a proximal and distal leak

Additional Procedures: Non-Patent Stent Graft Therapies

Number of Patients with Non-Patent Stent Graft	Therapy
3	Femoral-Femoral Bypass
2	Thrombectomy
1	Embolectomy
1	Axillary-Popliteal Bypass
1	Angioplasty with Stent Placement

Aneurysm Expansion by Follow-up Period¹

Type	Pre-discharge N=416	Pre-discharge N=158	6 months N=158	1 year N=158
Expansion of the AAA by >5mm	Baseline evaluation	Baseline evaluation	4/147 ² (2.7%)	6/158 (3.8%)

¹ 416 patients were enrolled in the study. Denominators that are < 416 reflect the number of patients implanted with a Stent Graft and the actual readable images sent to the corelab by the investigational sites. The denominators are determinable measures based on the image quality. One patient suffered an MI after enrollment and prior to implantation.

² Patients required to have both pre-discharge and 6 month data for determination. 11 patients did not have both values.

Aneurysm Growth in the Presence of Endoleaks at 12 months (N = 172)

Location	Enlarged ¹	Unchanged	Decreased ²	Unknown ³
Proximal Attachment Site	0	1	0	0
Distal Attachment Site	0	2	0	0
Junctional (modular)	0	2	0	1
Collateral	1	15	0	0
Unknown	1	6	0	1
Total	2	26	0	2

¹ Defined as size change of >5 mm.

² Defined as size change of <5 mm.

³ No data or no conclusion regarding aneurysm size changes.

Elective Conversions, by Primary Cause of Failure

Cause	During procedure	Before 30 days	1 month	6 months	1 year
AAA Rupture	0	0	0	0	0
Leak: Collateral Vessels Filling Aneurysm	0	0	1	0	0
Unsuccessful vessel access or device malposition	0	0	0	0	0
Total	0	0	1	0	0

Emergent Conversions, by Primary Cause of Failure

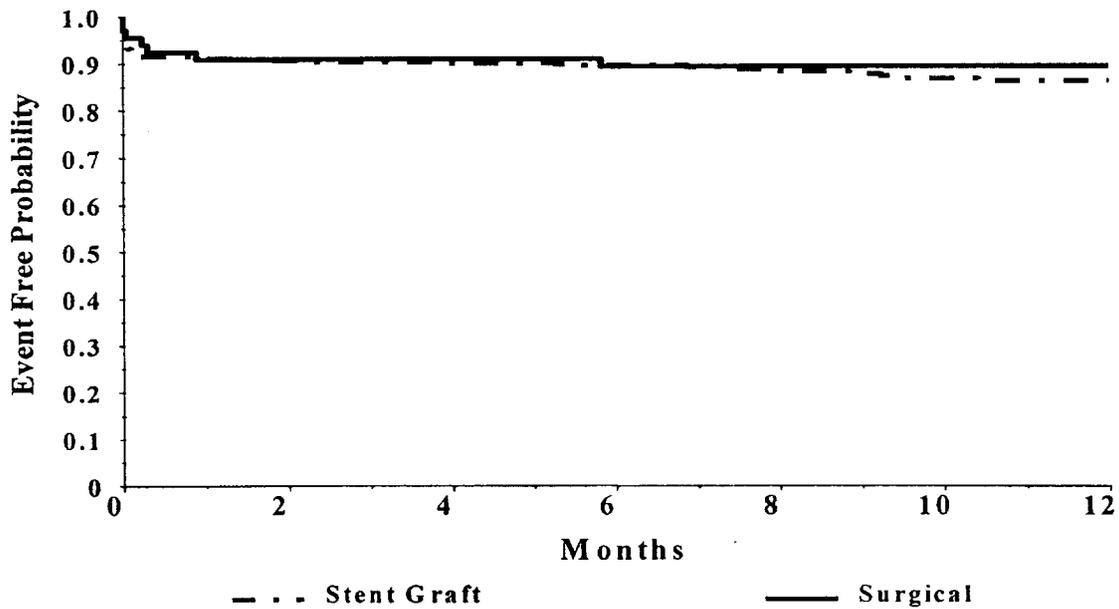
Cause	During procedure	Before 30 days	1 month	6 months	1 year
AAA Rupture	0	1	0	0	1
Leak: Collateral Vessels Filling Aneurysm	0	0	0	0	0
Unsuccessful vessel access or device malposition	4	1	0	0	0
Total	4	2	0	0	1

Freedom from Cardiac Events

(66 Surgical Control Group Subjects, 415 Stent Graft Treatment Group Subjects)

Interval	Treatment	1 Month	6 Month	12 Month
Stent Graft				
# Patients	415	402	353	274
# Censored	2	25	72	267
# Patients with Cardiac Events	11	24	7	7
Kaplan-Meier Estimated Probability of Freedom from Cardiac Events	97%	92%	90%	86%
Surgical				
# Patients	66	64	58	53
# Censored	0	2	4	53
# Patients with Cardiac Events	2	4	1	0
Kaplan-Meier Estimated Probability of Freedom from Cardiac Events	97%	91%	89%	89%

Freedom From Cardiac Events (Kaplan Meier estimates)



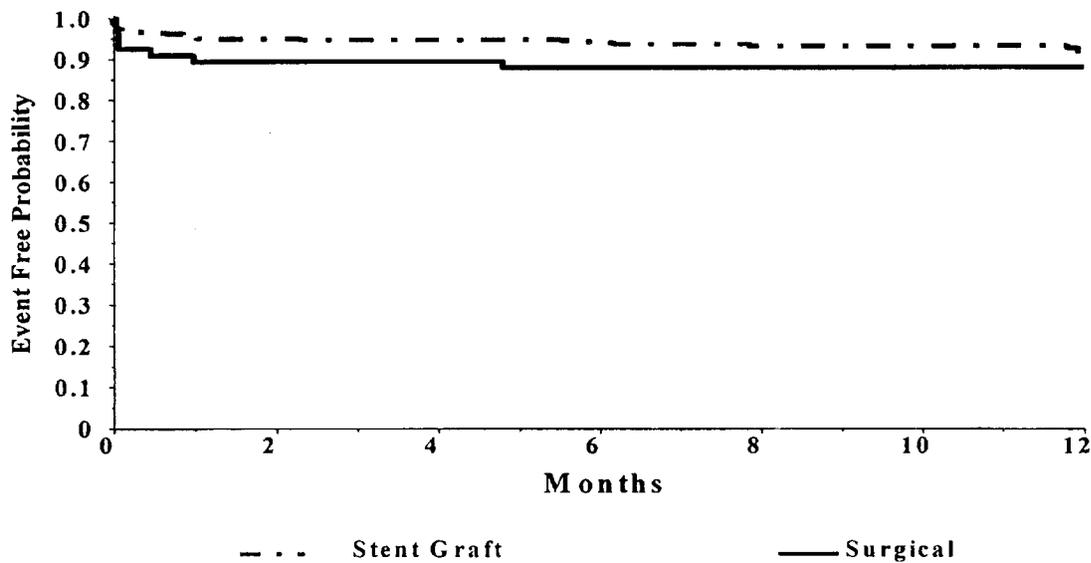
p= 0.588 (log-rank test)

Freedom from Neurological Events

(66 Surgical Control Group Subjects, 415 Stent Graft Treatment Group Subjects)

Interval	Treatment	1 Month	6 Month	12 Month
Stent Graft				
# Patients	415	408	371	293
# Censored	1	24	72	289
# Patients with Neurological Events	6	13	6	4
Kaplan-Meier Estimated Probability of Freedom from Neurological Events	99%	95%	94%	92%
Surgical				
# Patients	66	66	57	54
# Censored	0	0	2	54
# Patients with Neurological Events	0	7	1	0
Kaplan-Meier Estimated Probability of Freedom from Neurological Events	100%	89%	88%	88%

Freedom From Neurological Events (Kaplan-Meier estimates)



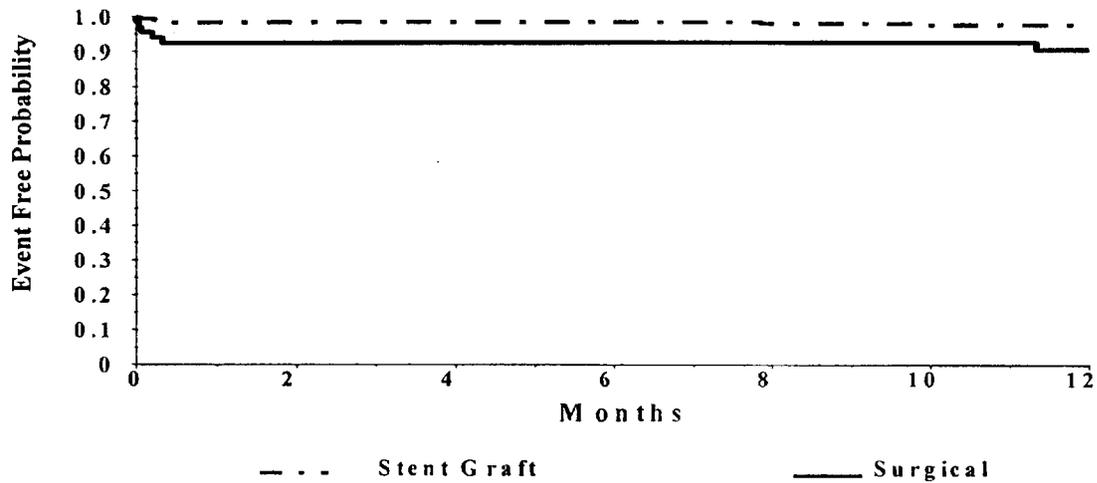
p= 0.202 (log-rank test)

Freedom from Pulmonary Events

(66 Surgical Control Group Subjects, 415 Stent Graft Treatment Group Subjects)

Interval	Treatment	1 Month	6 Month	12 Month
Stent Graft				
# Patients	415	412	381	302
# Censored	2	25	79	300
# Patients with Pulmonary Events	1	6	0	2
Kaplan-Meier Estimated Probability of Freedom from Pulmonary Events	100%	98%	98%	97%
Surgical				
# Patients	66	65	59	55
# Censored	0	2	4	54
# Patients with Pulmonary Events	1	4	0	1
Kaplan-Meier Estimated Probability of Freedom from Pulmonary Events	99%	92%	92%	90%

Freedom From Pulmonary Events (Kaplan-Meier estimates)



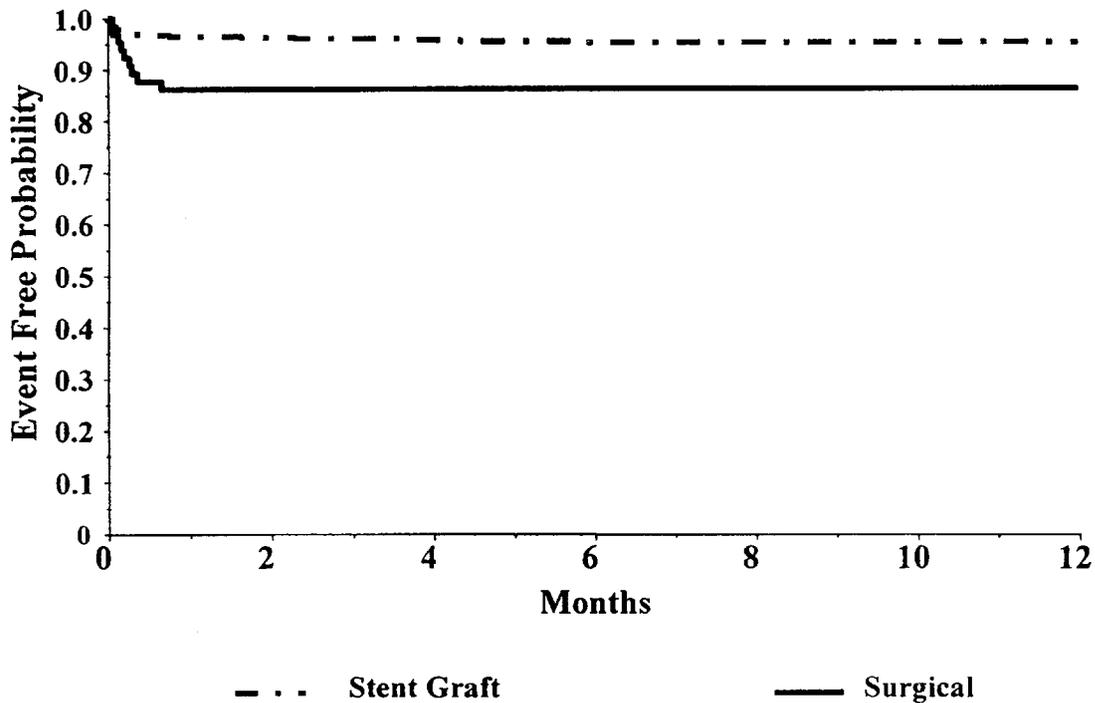
p= 0.006 (log-rank test)

Freedom from Gastrointestinal Events

(66 Surgical Control Group Subjects, 415 Stent Graft Treatment Group Subjects)

Interval	Treatment	1 Month	6 Month	12 Month
Stent Graft				
# Patients	415	413	378	297
# Censored	1	22	76	297
# Patients with Gastrointestinal Events	1	13	5	0
Kaplan-Meier Estimated Probability of Freedom from Gastrointestinal Events	100%	97%	95%	95%
Surgical				
# Patients	66	66	55	52
# Censored	0	2	3	52
# Patients with Gastrointestinal Events	0	9	0	0
Kaplan-Meier Estimated Probability of Freedom from Gastrointestinal Events	100%	86%	86%	86%

Freedom From Gastrointestinal Events (Kaplan-Meier estimates)



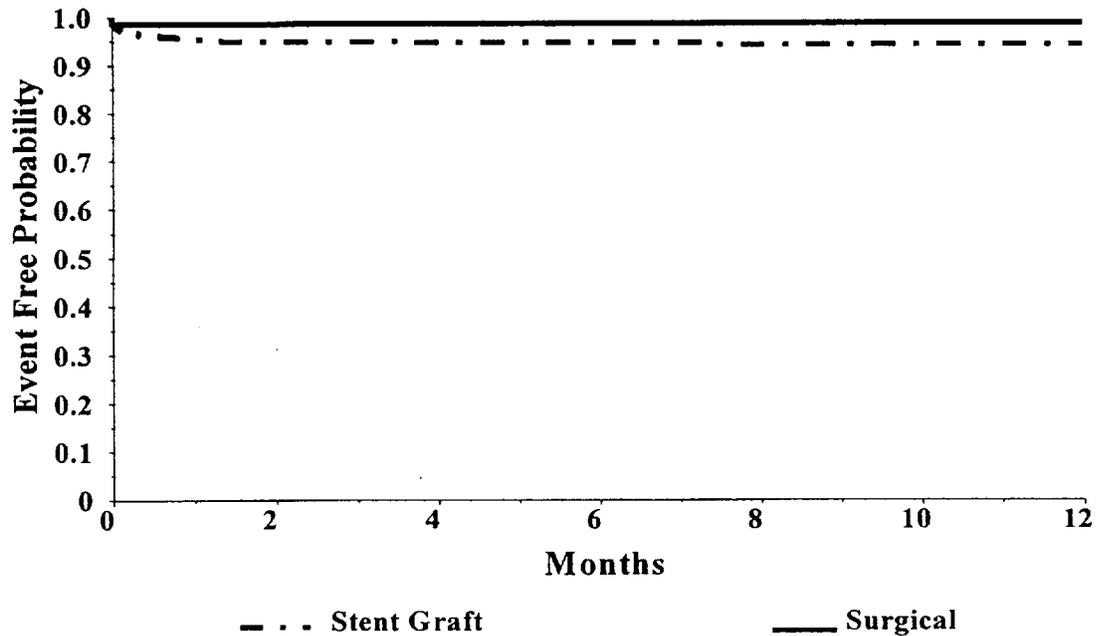
p= 0.004 (log-rank test)

Freedom from Thromboembolic Events

(66 Surgical Control Group Subjects, 415 Stent Graft Treatment Group Subjects)

Interval	Treatment	1 Month	6 Month	12 Month
Stent Graft				
# Patients	415	408	371	292
# Censored	1	25	75	291
# Patients with Thromboembolic Events	6	12	4	1
Kaplan-Meier Estimated Probability of Freedom from Thromboembolic Events	99%	96%	95%	94%
Surgical				
# Patients	66	65	63	59
# Censored	0	2	4	59
# Patients with Thromboembolic Events	1	0	0	0
Kaplan-Meier Estimated Probability of Freedom from Thromboembolic Events	99%	99%	99%	99%

Freedom From Thrombotic/Embolic Events (Kaplan-Meier estimates)



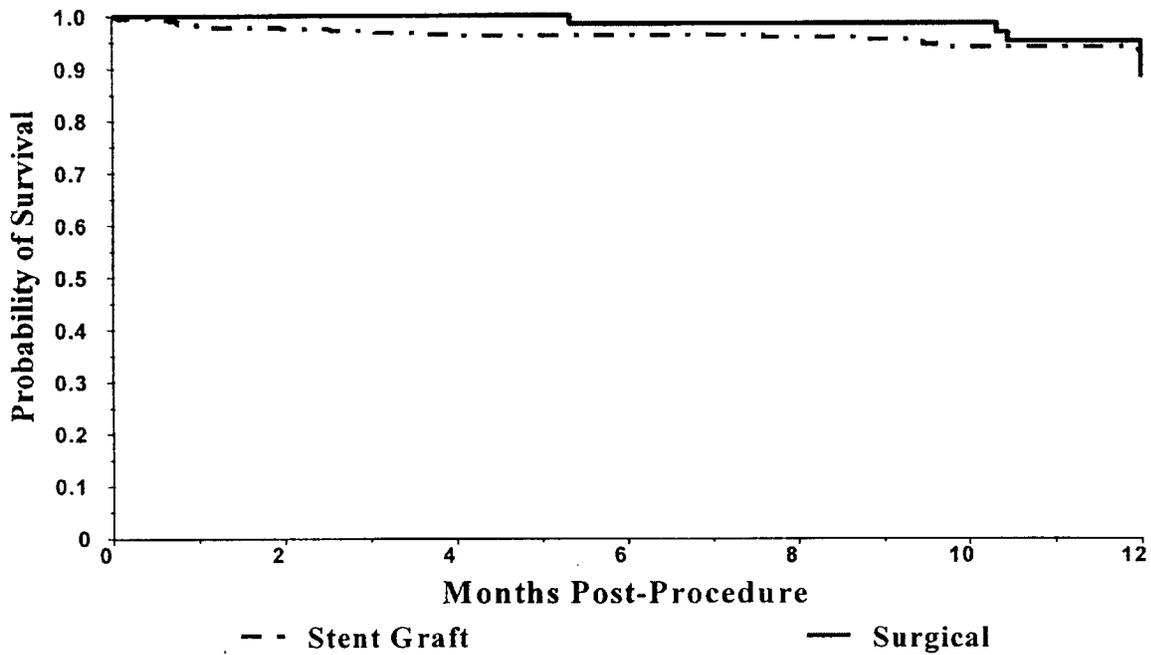
p= 0.153 (log-rank test)

Survival

(66 Surgical Control Group Subjects, 415 Stent Graft Treatment Group Subjects)

Interval	Treatment	1 Month	6 Month	12 Month
Stent Graft				
# Patients	415	415	391	307
# Censored	0	17	76	296
# Patients Dead	0	7	8	11
Kaplan-Meier Estimated Probability of Survival	100%	98%	96%	91%
Surgical				
# Patients	66	66	65	61
# Censored	0	1	3	56
# Patients Dead	0	0	1	5
Kaplan-Meier Estimated Probability of Survival	100%	100%	98%	89%

Kaplan-Meier Survival Curve



p= 0.900 (log-rank test)

Quality of Life Survey Results

Quality of Life (QOL) surveys were completed by patients as a clinical utility endpoint only and were not a study endpoint.

QOL data were available for 427 patients total (398 were from the Stent Graft Treatment Group and 29 were from the Surgical Control Group). 50% of the patients in each group completed QOL surveys at baseline, discharge, and one month. Overall, the QOL survey demonstrated good psychometric properties, and Cronbach's alpha was greater than 0.70 for all scales. At discharge and one month, Stent Graft patients had more favorable scores than the Surgery group for all QOL scales. By the sixth month, differences in QOL scale scores between groups were resolved. In regard to patient satisfaction, 60% of patients in the Stent Graft group evaluated their treatment at discharge as "excellent" compared to 35% in the Surgery group.

The results support the hypotheses that patients undergoing the less invasive AneuRx Stent Graft procedure experience faster return to normal functioning and are more satisfied with their treatment than the group undergoing open surgical repair. The study findings, however, must be considered cautiously in light of the small sample of surgery patients.

10.5 Device Failures and Replacements

The tables below summarize all complaints received from the investigational centers, for all cases reported in this summary including high risk cases. Also included is the corrective action taken to address each issue. Complaints have been categorized by whether they involved the Stent Graft, the Delivery Catheter, or the Deployment Handle.

Complaint Description	#	Corrective Action
<i>Delivery Catheter</i>		
Quick Disconnect Detached from Catheter and Inner Assembly	5	Devices examined. Manufacturing change improved bond joint strength.
Difficulty Deploying	7	Devices examined. Surgical procedures reviewed. Customers contacted. Customers retrained that the reusable handle life is limited to 20 uses.
Safety Clip Missing	2	Inspection procedure reviewed. Operators retrained.
Slider Pull Out	2	Devices examined. Manufacturing change improved the molded slider.
Non-Deployment	4	Devices examined. Surgical procedures reviewed. Customers contacted. Engineering testing performed. Design change made to improve the slider mechanism. Action request opened to resolve the quick disconnect mechanism inadvertently unlocking.
<i>Stent Graft</i>		
Radiopaque markers were mismounted	2	Operators and inspectors retrained. Verification step added to manufacturing procedure. Action request opened to investigate marker design system in process of design review.
Stent Graft was Loaded Incorrectly	1	Action request opened to evaluate marker placement.
<i>Deployment Handle</i>		
Inoperable Crank	1	Device examined. Inspection procedures for handle revised. Clinical staff retrained.
Knob Melted During Sterilization	2	Devices examined. Customers reminded of re-sterilization procedures.

In all cases where failure of the device resulted in a damage or a destroyed device an alternate device was available to complete the procedure.

11. Conclusions Drawn from the Studies

The clinical benefits associated with this system are a lower rate of severe, treatment-related complications as compared to open surgery, significantly fewer days in the ICU and in the hospital, and less blood loss and blood replacement. The risks associated with the device include perigraft flow and endoleaks, an increase in aneurysm size, and aneurysm rupture.

12. Panel Recommendation

The Circulatory Devices Panel met on June 23, 1999 to discuss the Medtronic AneuRx Stent Graft System for abdominal aortic and aorto-iliac aneurysms. The Panel recommended approval with the following conditions:

1. The sponsor should perform a post-approval study to assess the long-term effects of the device over a 5 year period.
2. Additional information should be collected on women in order to further assess/evaluate the differences (e.g. mortality) found between men and women entered into the study. The data currently collected will be sufficient to support labeling that identifies these differences.
3. The sponsor should develop an in-depth Physician Training Plan.

13. FDA Decision

CDRH concurs with the recommendation made by the Circulatory Devices Panel for the AneuRx Stent Graft System indicated in the treatment of abdominal aortic and aorto-iliac aneurysms (AAA), i.e., approval with conditions as noted above. This PMA was reviewed under the modular PMA process, and was granted expedited review status due to the unique, less-invasive technology proposed for the repair of abdominal aortic aneurysms. FDA has also required tracking (21 CFR 821) for endovascular grafting systems due to the limited experience with these devices, the lack of long-term data, and the potential for catastrophic failure leading to a significant adverse clinical outcome.

14. Approval Specifications

Directions for Use: See Labeling.

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

Post-Approval Requirements and Restrictions: See Approval Order.