Results of endoluminal grafting in an experimental aortic aneurysm model

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We studied the impact of an endoluminally placed stented aortic graft on the geometry of a surgically created abdominal aortic dilation (AAD) in nonatherosclerotic mongrel dogs. Patulous iliac vein patch infrarenal aortoplasty produced a fusiform AAD, doubling the aorta diameter. Lumbar and mesenteric aortic tributaries were preserved and no mural thrombus formed. AADs created in 23 dogs were endoluminally excluded through transfemoral placement of a thin-wall Dacron graft 4 ± 2 months later. Balloon-expandable stents were used to anchor each end of the graft to the aorta. The graft was crimped radially in its body and longitudinally at its ends to provide longitudinal and radial expandability in these respective zones. Serial color duplex, angiography, and direct caliper measurements were made. Before graft placement, a $19\% \pm 11\%$ diameter growth was observed. At graft placement, flow arrest immediately occurred in the space between the graft and the AAD intima in all cases. Although microscopic recanalization of the thrombus in this space was seen at sacrifice 6 and 12 months later, no macroscopic duplex flow was imaged. A $10\% \pm 11\%$ reduction in AAD diameter was measured at 6 months ($p < 0.001$), with no further reduction at 12 months. Graft dimensions remained stable. No anastomotic leaks developed. AAD growth stopped during the first year after effective endoluminal exclusion in normotensive dogs despite patent side branches (<1.5 mm internal diameter) and no mural thrombus at the time of graft placement. Whether microscopic recanalization of the thrombus that forms outside the graft has an impact after 1 year remains to be seen. (J Vasc Surg 1996;23:819-31.)

This experiment was initiated after the pioneering report by Parodi et al.[1] of successful endoluminal grafting of abdominal aortic aneurysms (AAAs) with stented grafts in patients. In their original animal experiments, a portion of the infrarenal aorta was replaced with a large Dacron fusiform graft to mimic an aneurysm.[2] Mural thrombus formed by the time of stented graft placement. The Dacron aneurysm analog had no side branches. The question arose that if lumbar or mesenteric circulation persisted, could an

atherosclerotic aneurysm still enlarge even if axial lumenal blood flow is diverted by the graft? This concern originated from clinical experiences with nonresective therapy of AAAs[3-8] and has been reported after endoluminal bypass.

Another feasibility issue was encountered regarding deployment. Each graft needed to be tailor-made for each patient on the basis of intricate preoperative measurements. Since AAAs are three-dimensional tortuous structures, these measurements were vulnerable to error. Limited flexibility to correct for milimeter variances in diameter and length was one problem that could not be addressed by the noncrimped, thin, knitted Dacron grafts used. Additionally, graft delivery needed to be refined to limit twisting and kinking of the graft during deployment.

As endoluminal graft applications expand outside the AAA arena to trauma and occlusive disease, these issues are being addressed by refinements in devices, imaging, and technique.[9-15]

This experiment is the first in a series designed to simultaneously look at biologic and technologic issues in this evolving field. As a first step we addressed what,

if any, importance exists to the side branches that eminate from an endoluminally excluded artery. Intuitively, we expected that the space between the graft in an endoluminally excluded AAA and the lumenal surface should thrombose. After all axial flow is diverted, the lower-pressure retrograde lumbar mesenteric flow should have nowhere to go. Flow should cease and thrombosis of the entire space should follow, especially in the presence of the AAA mural thrombus and of the foreign body of the graft. AAA growth should then cease. However, if there are large enough branches and a significant pressure gradient, flow may be maintained into and out of this space. Perhaps recanalization of this thrombus may occur. A pathway from the inferior mesenteric artery to a lumbar artery, for example, may develop. Is this significant enough to encourage further AAA growth?

Before embarking on the development of an atherosclerotic hypertensive model analogous to human beings, we chose to address this issue in a normal artery in a normotensive animal. The setting is somewhat analogous to stented-graft therapy of a traumatic aneurysm in the young patient in which the treated artery would have numerous tributaries. Basic questions such as does the space thrombose? How fast does it thrombose? Can it recanalize? Can the vessel continue to enlarge? were addressed.

With the guidance of Dr. Parodi, Johnson & Johnson Interventional Systems Inc. (JJIS) (Warren, N.J.) developed a thin, woven Dacron graft that addresses many of the deployment concerns we listed. It was manufactured to accommodate variances in aortic length and diameter and to resist kinking and twisting as it leaves its introducer sheath. The crimping that builds in the required memory to accomplish this is described. This technical advance is implemented in this experiment. We evaluated the stability of the stented anastomoses, the resistance of the graft to dilation, incorporation of the stented graft, the concern over extravasation of foreign body, and the deployment issues previously referred to.

MATERIAL AND METHODS

Twenty-seven young heartworm-free mongrel hounds (25 to 30 kg) were evaluated in the AAALAC-approved Biologic Research Laboratory at the University of Illinois. All animals were treated according to the standards set forth in the Guide for the Care and use of Laboratory Animals.[16] After a 2-week conditioning period, each dog underwent surgical creation of an abdominal aortic dilation (AAD) by vein patch aortoplasty.

Within 6 months (4 ± 2 months), transfemoral placement of a stented aortic graft was performed in 23 dogs. Dogs were killed 6 months later (n = 13) and 1 year later (n = 7). Three remain alive for long-term evaluation. Two killed at 1 year had double-stented grafts placed (one inside the other). These two were treated to evaluate a method to correct improper deployment scenarios.

Four control dogs underwent a 2-week conditioning period followed by AAD creation. They were not treated with a stented aortic graft and were killed at 6 months.

Anesthesia. Each dog treated with a stented graft was anesthetized in a similar fashion four times during the study: at AAD creation, at stented graft placement, at Duplex follow-up 1 month later, and at sacrifice. Each dog was sedated with acepromazine (0.05 mg/kg IV) and atropine (0.5 mg/kg IV), endotracheally intubated, and placed on a Harvard respirator. Thiopental (3 to 5 mg/kg IV) and halothane (to effect) provided effective anesthesia. Buprenex (0.05 mg/kg IM as needed) was used after surgery for comfort. Pentobarbital euthanasia solution (100 mg/kg IV) was used to kill them.

Creation of AAD. The abdomen was shaved, prepped with betadine, and draped sterily. Kefzol (0.5 gm IV) was given at the beginning and at the end of the procedure. The aorta was exposed through a midline laparotomy. The left common iliac vein and the infrarenal aorta were mobilized. Heparin (100 U/kg IV) was given. The 10-mm diameter thin-walled iliac vein was harvested and opened longitudinally to create a patulous vein patch. No adverse sequelae of this vein harvest, such as limb swelling, occurred. Vascular control of the infrarenal aorta was obtained, preserving all aortic tributaries. A longitudinal 4-cm by 2-mm anterior ellipse of aorta was excised in lieu of performing a linear aortotomy to facilitate the aortoplasty procedure. The aortoplasty was completed by sewing the nearly transparent iliac vein patch to the aortotomy with continuous 7.0 Prolene. The procedure lasted 140 ± 27 minutes. All subjects were ambulatory and tolerated food by morning. Estimated blood loss was 0.1 ± 0.1 liters. Lactated Ringer's IV solution 1.1 ± 0.3 liters was given.

Stent graft placement. After induction of general endotracheal anesthesia, both groins were shaved, prepped with betadine, and draped sterily. Kefzol (0.5 gm IV) was given at the beginning and at the end of the procedure. A radiopaque ruler was positioned posteriorly parallel and to the left of the spine. The left femoral artery was exposed. A 30-cm long 14F introducer sheath (Meditech, Boston Scientific,

Waltham, Mass.) containing a hemostatic valve was introduced into the femoral artery by the Seldinger technique. The sheath was advanced to below the lowest renal artery, identified by contrast aortography with 50% angiovist under C-arm fluoroscopy. By using road mapping and the posterior ruler, precise localization of the proximal and distal necks of the AAD and its orientation in the aorta were obtained. The imaged field was fixed to avoid parallax errors. JJIS supplied the dimensions of the stented graft.

A 14F metal cylinder guide (JJIS) 15 cm long was used to temporarily render the hemostatic valve of the 14F introducer sheath incompetent, permitting the passage of the stented graft mounted on the balloon angioplasty catheter into the introducer sheath and up into the proximal infrarenal aorta. The sheath was then withdrawn to the iliac level, and the balloon was inflated to create the proximal anastomosis by expanding the proximal stent anchored to the graft into the aortic wall. The stent was overexpanded 20% compared with the aorta diameter. The expanded stent measured 1.2 ± 0.2 cm in diameter and 3.2 ± 0.3 cm in length. The location of the proximal anastomosis was calculated from the length of the graft, the length of the aorta, and the location of the AAD. The entire AAD had to be excluded without impinging on the renal or iliac orifices. Next, the balloon was withdrawn into the body of the graft and reinflated with dilute contrast to expand it to its maximum diameter.

A second, shorter stent was to be used to effect the distal "anastomosis." Mounted on a second balloon angioplasty catheter (Meditech 10 mm × 6 cm balloon), a catheter exchange was performed over a 0.035-inch guide wire. The radiopague markers at the distal aspect of the graft guided the deployment. The expanded distal stent measured 1 ± 0.9 cm in diameter and 1.5 ± 0.1 cm in length. The catheter and wire were removed, and the femoral arteriotomy was closed with 7.0 Prolene. The procedure lasted 92 ± 33 minutes. Estimated blood loss was 0.1 ± 0.2 liters.

Two of the dogs killed at 1 year were treated with two stented grafts. In both, the proximal stent was incorrectly deployed to satisfactorily position the graft across the entire AAD; in one case it was placed too high, in the other too low. In both, a second stented graft was then coaxially easily positioned inside the first stented graft.

Description of graft. The JJIS stented graft is illustrated in Fig. 1. It consists of a Palmaz stent attached to one end of a woven Dacron graft. The stent is balloon-expandable and is made of 316L

stainless steel. The diameter of the proximal and the distal stented anastomosis is directly determined by the size of the balloon deploying the stent. The graft is constructed from type 56 textured Dacron yarn in a plain weave with a wall thickness of 0.115 mm. The graft is dumbbell shaped with longitudinal crimps in the end zones and circumferential crimps in the center zone. The end zones measure 15 mm in length and the center zone measures 30 mm in length, with a diameter of 10 mm. Two radiopaque markers were sutured externally to each end of the graft to assist in placement. The radial expandability at the ends and the longitudinal expandability in the body were built into the graft by the crimping technique.

The graft was delivered to us sewn to a balloon-expandable stent and mounted on a 12-mm by 6-cm balloon angioplasty catheter (Meditech). It was delivered from the manufacturer aligned in a metal cylindrical guide. The graft was furled into a cylindrical guide (described in the previous section) in the manner described by Parodi.[17]

Pathologic examination. Grafts were harvested from the dogs at 6 months and at 1 year postoperatively. Following general endotracheal anesthesia, abdominal duplex scan and fluoroscopic arteriography were performed. The abdomen was opened and the aorta dissected out from the scar tissue. In situ measurements were made and the animal was then euthanized. The aorta was submitted for histologic examination after iced 10% formalin fixation.

Geometric measurements. Measurements are illustrated in Fig. 2. Four techniques were used. AAD diameters were measured at the largest cross section, independent of measurement technique.

In situ caliper measurements were made at AAD creation and just before sacrifice. External caliper measurements were made of AAD, aorta, and iliac diameters and AAD and aortic lengths. The major limitation of caliper in situ data was caused by scar tissue at sacrifice.

Color duplex (Accuson 128 XP) measurements were obtained immediately before and after stented graft placement, 1 month later, and just before sacrifice. Internal and external diameters, areas, perimeters, and lengths were obtained. A limitation of serial duplex scan data included positioning of the cursor consistently from one measurement session to the next. Cursor positioning was further complicated by the wall thickness and the presence of scar tissue. Timing with pulsation was also a variable. For the sake of conciseness, the percent changes in duplex diameters with time were tabulated as averages obtained from measurements made in the sagittal,
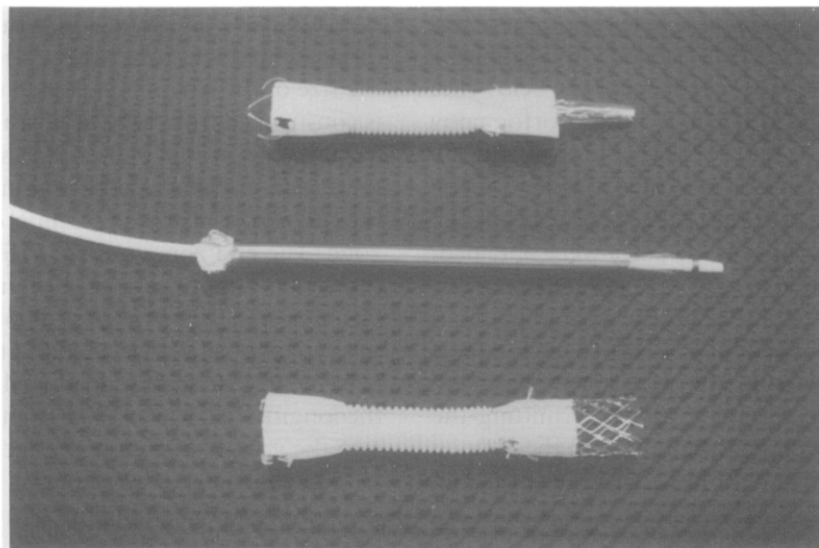
Fig. 1. Woven thin-walled Dacron graft prototype. Ends are crimped perpendicular to body to allow radial expandability, accommodating aortas of different diameters. Crimping in body permits longitudinal extendability to accommodate aortas of different lengths. Proximal stent came attached to graft. Both were premounted on balloon angioplasty catheter. *Middle* picture shows low profile of stented graft assembly after folding it into metal introducer. *Top and bottom* pictures show Palmaz stent before and after inflation.

transverse anteroposterior, and transverse left-right planes.

Fluoroscopic angiography was obtained immediately before and after stented graft placement and at sacrifice and recorded on videotape. Angiovist 50% was used as the contrast agent, injected intra-arterially. On playback of the videotape, the radiopaque ruler allowed measurement of internal diameters and lengths of the AAD, graft, stents, aorta, and iliacs. One limitation of this measurement relates to the positioning of the ruler relative to the aorta. Because the dogs were placed in a concave holding device, we were able to position the ruler is as close a plane as possible with the aorta in relation to the axis of the fluoroscope. Since much of our data are represented as a ratio between measurements obtained between two time points utilizing the same technique, errors inherent in the measurements are partially compensated for. Other theoretical limitations of our fluoroscopic data included parallax and videotape resolution. To reduce these errors, measurements were taken as close to the center of the image and/or to the radiopaque ruler as possible.

A limited number of cut film angiograms were done, and measurements were derived from the film with calipers in comparison to the radiopaque marker.

Graft porosity, burst strength, and tensile testing. Testing was performed by an independent laboratory (Bipore, Inc.; Northvale, N.J.) follow-

ing the Association for the Advancement of Medical Instrumentation protocol.[18] Burst strength (psi) was measured by placing the graft over a latex bladder distended in increments by a pressure source. Tensile strength was measured in an Instron Model 1011 Universal Testing Instrument. Porosity $(ml/min/cm^2)$ was measured as the volume of saline collected per unit time across a measured surface area.

Data analysis. Data are expressed as a percent change of a dimension with time and reported as mean and SD. The number of subjects varies per calculation on the basis of the data that were available. Paired t test and the Newman-Keuls multiple comparisons test were used to evaluate the significance of the dimensional differences measured between the nontreated AAD and the treated AAD at 1, 6, and 12 months. Comparative evaluations were also made immediately after stent graft placement to data 1, 6, and 12 months later.

The percent change of a dimension $(\Delta \mathscr{D}^*)$ between two time points is calculated as: 100^* $[(\mathscr{D}_2/\mathscr{D}_1) - 1]$, where $(\mathscr{D}_2/\mathscr{D}_1)$ is the ratio of the value of the dimension $\mathscr{D}$ at two time points, the earlier observation being the denominator. Negative percentages represent an interval decrease in that dimension.

The $\Delta \mathscr{D}^*$ are then averaged across all subjects in the treatment interval to represent the percent change
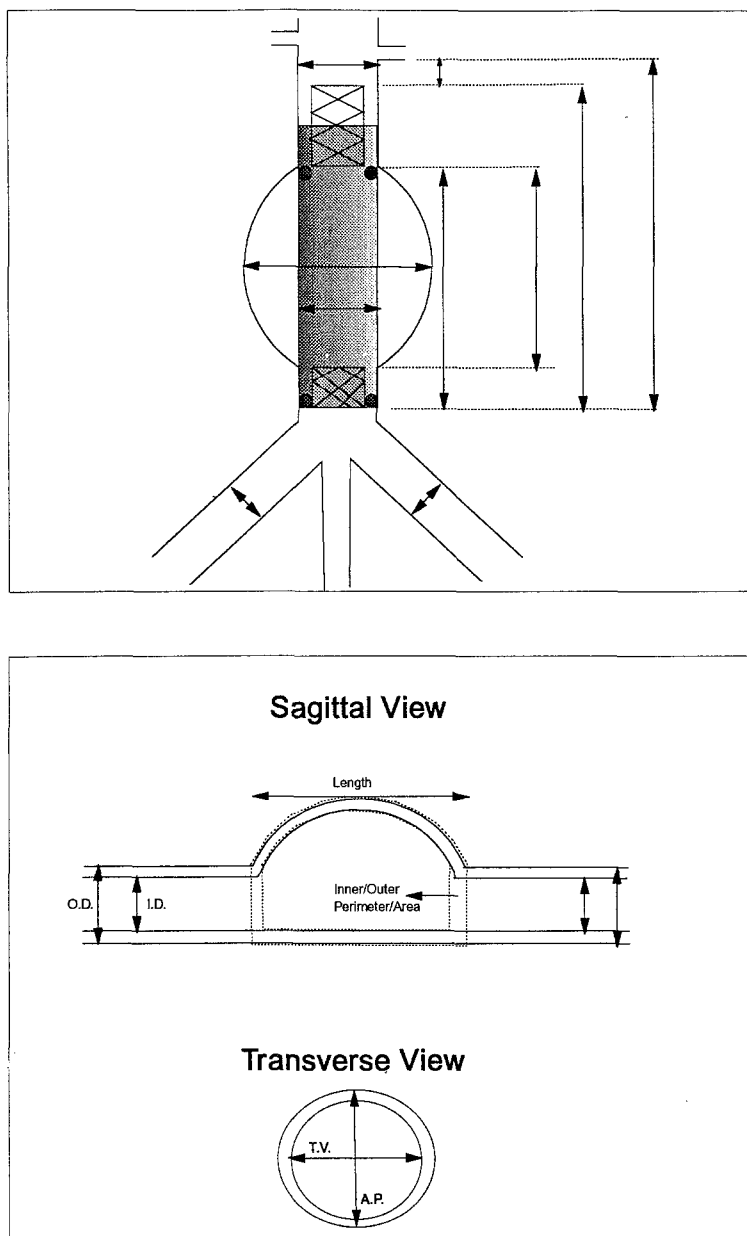
Fig. 2. Measurements obtained.

in a dimension for all animals studied in the interval $\Delta \mathscr{D}^*_1$.

Lastly, for the purposes of summarizing the data with all four measurement modalities, aggregate dimensional changes were calculated for each interval. First, the $\Delta \mathscr{D}^*$ obtained from data from each measurement modality of the same dimension were averaged together to calculate a composite percent change of that dimension, $\Delta \mathscr{D}^*$. Next, the aggregate percent change in a dimension for an interval ($\Delta \mathscr{D}^*_1$) was calculated in a manner similar to $\Delta \mathscr{D}^*_1$ but by using the $\Delta \mathscr{D}^*$ values in lieu of the $\Delta \mathscr{D}^*$ values. $\Delta \mathscr{D}^*_1$

represents an estimate of growth or shrinkage of a dimension in a given interval after stent graft placement for all animals in that interval.

RESULTS

Baseline dimensions before stented graft placement are tabulated in Table I. Four pairs of lumbar vessels, the inferior mesenteric artery, and several smaller tributaries originate from the infrarenal aorta. All were preserved. All measured <1.5 mm ID. The patch itself encompassed 2.7 ± 1 branches. The graft overlayed the orifices of 4 ± 2 branches. The dogs

Table I. Baseline measurements of infrarenal aorta and AAD

| | Lengths (cm) | | | | Diameters (cm) | | | |
| | Infrarenal | | | | Normal aorta | | AAD | |
	Aorta	Patch	Renal to patch	Patch to trifurcation	Outer	Inner	Outer	Inner
In situ caliper		3.4 ± 2 (27)	4.4 ± 1 (27)	3 ± 7 (27)	1 ± 0.1 (27)		1.8 ± 0.2 (27)	
Duplex		3.3 ± 2.2 (23)			1 ± 0.1 (23)	0.9 ± 0.9 (23)	2 ± 0.2 (23)	1.9 ± 0.3 (23)
Fluoroscopic angiogram	11.4 ± 1.1 (16)	3.1 ± 0.3 (22)				1.1 ± 0.1 (21)		2.1 ± 0.3 (22)
Cut film angiogram	11.2 ± 1.3 (7)	3.2 ± 0.5 (7)				1 ± 0.1 (9)		2.3 ± 0.3 (7)

gained 0.5 ± 3 kg between creation of AAD and stented graft placement. They gained 1.4 ± 2 kg between graft placement and death.

The rate of growth of the untreated AAD was variable and is plotted in Fig. 3. Each mark on the graph represents an individual animal.

Proximal aorta dimensional changes are summarized in Table II. The values in the control column represent the percent diameter change between creation of the AAD and placement of the stented graft. The values in the 1-, 6-, and 12-month columns represent the percent diameter change between the placement of the stented graft and the follow-up study at 1, 6, and 12 months, respectively.

Immediate thrombosis of the space between the stented graft outer surface and the AAD inner surface followed deployment in every animal. This was seen on the Duplex image immediately after the graft was placed. Thrombosis occurred despite residual heparin. Two weeks after stent graft placement, this thrombus appeared grossly identical to that found in a pseudoaneurysm cavity seen clinically (data from pilot experiments not included in this study). On sacrifice at 6 months and at 1 year, this thrombus appeared grossly to be of mixed consistency: partly firm and partly soft, such as one would see laminating an aortic aneurysm clinically. However, histologically, microscopic areas of thrombus recanalization identified as endothelial-lined spaces containing red cells were seen at 6 months and at 1 year.

AAD duplex and in situ caliper percent changes are summarized in Table III. Interval comparisons are made as in Table II. The *p* values represent comparison between AAD growth before stent graft placement to AAD growth 1, 6, and 12 months after stent graft placement. The stented anastomoses never leaked. For this reason, the dimensions of the AAD were not discernible by angiography after stented

graft exclusion. Extravasation of the stent graft outside the aortic wall was never seen.

In Table IV, aggregate AAD dimensional changes (by all measuring modalities) were averaged to give a composite percent change of each AAD dimension. Included are the baseline fluoroscopic and cut film angiogram data before stented graft placement. AAD growth did not occur after stented graft placement. Rather, a small but significant decrease in AAD size was seen 6 months after stented graft placement, with no further significant decrease seen at 1 year.

Table V tabulates geometric data concerning the graft. At sacrifice, the grafts were thoroughly incorporated in fibromuscular tissue ingrowth (Fig. 4). Caliper measurements were performed on four grafts extricated from the aorta (two at 1 year and two at 6 months), showing virtually no difference in outer diameter compared with the preimplant manufacturer's data. At sacrifice, graft thickness measured 1.9 ± 0.4 mm (n = 18) by duplex, which is greater than the preimplant thickness (1.1 mm). This figure was attributable to the ingrowth of tissue (pseudointima formation). This finding was also observed in the angiographic data (diminished luminal diameter).

There was an angiographic −1 ± 4 (n = 15) percent change in graft length (not significant) between deployment of the proximal and distal stents. At 6 months, a 1 ± 14 (n = 12) percent change in graft length was measured between the stents (not significant). At 1 year a 4 ± 18 (n = 5) percent change in graft length was observed (not significant). The length of the infrarenal aorta was also relatively constant: 11 ± 1 cm (n = 16) to 12 ± 2 cm (n = 19) from stented graft placement to sacrifice.

The diameters of the right and left iliac arteries were not significantly different at 6 months and 1 year despite the trauma to the intima on the left side during the tight passage of the introducer sheath at
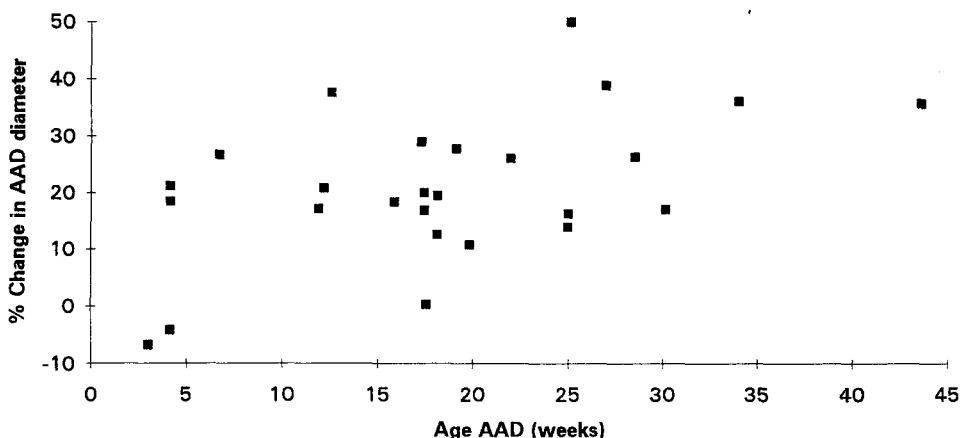
Fig. 3. Graph illustrating percent change in AAD diameter for each animal between creation of AAD and intervention. Rate of AAD diameter growth in model is not linear. We attribute this partly to maturation of scar tissue forming over time around surgically created AAD.

Table II. Geometric data of proximal aorta

Percent change in diameter by:	From AAD creation to before stented graft	From placement of stented graft to:		
		1 Month	6 Months	12 Months
Duplex	0 ± 8 (23)	4.6 ± 10 (16)	-2.7 ± 10 (12)	-1.5 ± 10 (4)
In situ caliper			-8 ± 27 (12)	4 ± 26 (7)
Cut film angiogram			9 ± 12 (9)	
Fluoroscopic angiogram			-7 ± 10 (11)	-8 ± 17 (5)

graft placement. No iliac or femoral vessels occluded or developed severe stenoses. Mild intimal hyperplasia was seen on the left histologically. The iliac diameter measured 6 ± 1 mm in outer diameter. Minimal changes (within measurement error) were observed in iliac diameters at 6 months and at 1 year when compared with their diameters at stented graft placement.

Graft burst strength was measured in three grafts before implantation (285 psi, 280 psi, and 265 psi, respectively) and in three grafts 6 months after implantation (275 psi, 280 psi, and 290 psi, respectively). Graft tensile strength was measured in four grafts before implantation (74.71 lbs, 73.42 lbs, 67.95 lbs, and 62.72 lbs, respectively) and in four grafts 6 months after implantation (64.72 lbs, 78.35 lbs, 57.07 lbs, and 89.92 lbs, respectively). Porosity was measured in four grafts before implantation (200 ml/min/cm², 190 ml/min/cm², 180 ml/min/cm², and 160 ml/min/cm², respectively) and 6 months after implantation (30 ml/min/cm², 180 ml/min/cm², 140 ml/min/cm², and 0 ml/min/cm², respectively). No significant difference was observed in burst strength and tensile strength before and 6 months after implantation. A significant decrease in

porosity was observed and was attributed to tissue ingrowth. The variability in porosity likely relates to how thoroughly the graft was excised from this tissue ingrowth.

To evaluate slippage of the proximal stent, its distance from the renal orifice to the stent was measured by angiography. Within the limitations of our measurements, this distance was not significantly different from graft placement to sacrifice: 4 ± 10 (N = 12) percent change at 6 months and a -5 ± 5 (N = 3) percent change at 12 months. In a separate pilot experiment, a thin pseudointima was seen to be already completely covering the struts of the proximal stent in two dogs sacrificed at 2 weeks, providing a secure anchor. At 6 months and 1 year, a collagen-rich but elastin-poor neointima was seen incorporating the entire stent and graft.

Mild curvature of the graft was seen by angiogram at sacrifice in 40% of cases (8 of 20). This curvature was seen in three of the subjects at the time of the original deployment. This finding was imaged at 1 month by duplex scan in each instance. Little progression was seen at later evaluations. When the mild curvature of the graft was observed, it was within the AAD, where the graft had room to gently deform

Table III. Abdominal aortic dilation duplex and in situ caliper dimensions

Percent change in:	From AAD creation to before stented graft	From placement of stented graft to:		
		1 Month	6 Months	12 Months
Duplex				
Diameter	21 ± 12 (26)	8.3 ± 16 (21)*	−3.3 ± 13 (13)*	0 ± 17 (6)*
Length	5 ± 7 (26)	−7.3 ± 19 (8)*	−18 ± 12 (13)*	−14 ± 11 (6)*
In situ caliper				
Diameter	29 ± 4 (4)		−0.1 ± 16 (13)*	9.3 ± 18 (7)*
Length	11 ± 8 (4)		−18 ± 9 (13)*	−21 ± 8 (7)*

*$p < 0.001$.

Table IV. Abdominal aortic dilation composite data

Percent change in:	From AAD creation to before stented graft	From placement of stented graft to:		
		1 Month	6 Months	12 Months
Diameter	19 ± 11 (n = 26)	0 ± 12 (n = 18)*	−10 ± 11 (n = 13)*	−5 ± 15 (n = 7)*
Length	6 ± 7 (n = 25)	0 ± 6 (n = 5)	−17 ± 12 (n = 13)*	−14 ± 9 (n = 7)*

*$p < 0.001$.

into the early soft thrombus. Mature organized thrombus seemed to act more like a cast resisting further deformation. The curvature seemed to represent redundancy in the length of the graft. Slippage of the proximal stent was not observed that could account for this finding. Either the grafts were not fully deployed to length before distal stent placement, or some relaxation of the radially crimped portion of the Dacron graft occurred in the days after deployment. Of note, however, is that the crimps never became effaced. At death, each crimp seemed to be well preserved. In fact, each was solidly encased in scar tissue. Graft patency was not affected by this curvature. At death, the grafts were uniformly well supported by the mature thrombus that formed between the graft and the AAD intima.

Although kinking was avoided in this experiment, a 40% stenosis was seen just distal to the proximal stent immediately after deployment of one graft. This 40% stenosis seemed by intraluminal ultrasound (CVIS Corporation; Sunnyvale, Calif.) to be caused by an axial misalignment (twist). Twisting was seen in a pilot experiment before this series: on death, one of the external metal markers had been caught in the orifice of an aortic tributary and prevented the graft from unfurling properly. At the death of the animal with the 40% stenosis, there was evidence suggesting that this was another instance of the same complication. The problem with entrapment of the external metal marker has since been solved by a gold stripe being applied to the length of the graft. Otherwise, no significant axial misalignment was observed in the remaining subjects. The crimps in the body of the graft seemed to resist any propensity of the graft to kink or twist during deployment in this nearly linear model.

No leaking developed around the proximal and distal stents. On external inspection of the adventitial surface of the aorta at autopsy, the stent struts above the graft were visible deep in the vessel wall. The diameter of the proximal and distal stents and of the aorta in which they were incorporated did not change 6 months or 1 year after placement.

DISCUSSION

Endovascular treatment of abdominal aortic aneurysms a priori may not necessarily exclude the possibility of persistent aneurysmal enlargement from persistent perfusion through lumbar and mesenteric vessels into the space between the endovascular graft and the inner surface of the aortic aneurysm. This may lead to further aneurysm growth and rupture. Aneurysm models used in previous studies did not fully address this concern because the excluded aneurysms, usually prosthetic, lacked branches.

This study helps to begin to address this question in a model in which all side branches are left patent, no mural thrombus forms before treatment, and normal intima exists. Despite this nonthrombogenic environment, we have demonstrated that flow arrests in the space between the graft and the AAD wall immediately after stented graft placement despite residual heparin anticoagulation. Additionally, despite retrograde filling of lumbar and mesenteric tributaries up
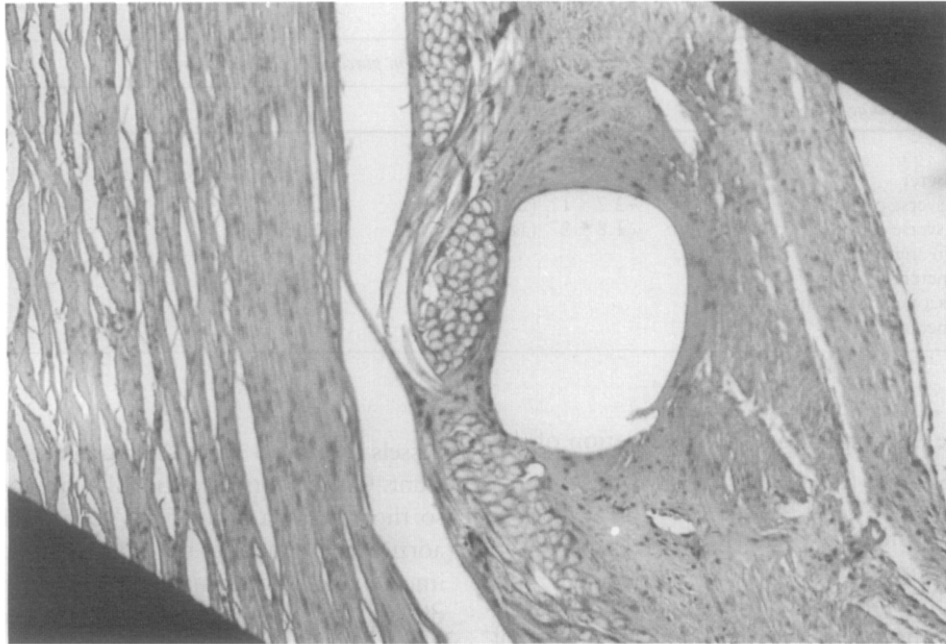
Fig. 4. Illustration of graft incorporation. Steel strut of stent was gently removed *(open circle)*. Note how graft is totally incorporated by ingrowth of tissue.

to but not into the AAD, and microscopic evidence of thrombus recanalization, no further enlargement of the AAD occurred over a 1-year follow-up period.

A limitation of this model is the influence that the scar tissue that forms at the site of AAD creation has on the growth of the AAD it encases. During the period of observation, which ranged from 3 to 45 weeks before stent graft placement, no ruptures occurred and the AADs grew an average of 19% ± 11% before graft placement. This growth was nonlinear, as illustrated in Fig. 3.

Three issues in this study prevent extrapolation of this data to atherosclerotic larger vessel disease in hypertensive elderly patients. First, these dogs were normotensive, with mean blood pressure less than 70 mm Hg. Second, the internal diameters of their aortic side branches were typically less than 1.5 mm. Hypertensive patients with larger branches may be able to sustain flow in the space. Third, because of the smooth nature of the nonatherosclerotic AAD necks in our model and the longitudinally crimped design of the ends of our graft, excellent apposition of the graft to the aortic lumenal surface was achievable in each of our subjects. There is only one other report of a longitudinally crimped graft in the literature.[19] As discussed below, whether this may be uniformly achievable in atherosclerotic aneurysm necks was not tested in this study.

Extrapolation of our data to stented graft therapy

of traumatic arterial injury, saccular aneurysms, pseudoaneurysms, and atherosclerotic vessels may be possible as long as the anastomoses become well incorporated, hypertension is controlled, and side branches are small. However, extrapolation to stented graft therapy of arteriovenous fistulae, or of traumatic injury in which extravasation from a multibranched artery occurs into a cavity (e.g., thorax) should not be drawn from our model. In both instances, a low resistance pathway exists by which flow outside the graft can be potentially maintained. Stented graft therapy may, however, facilitate subsequent definitive operative therapy of these problems.

Further data analysis demonstrates the benefit of the memory imparted to the grafts by crimping. These grafts deployed without kinks and significant twists. This deployment contrasts with our earlier pilot dog experiments in which noncrimped grafts were used and twisting was seen. This twisting and kinking was also reported by others[2] in experiments using noncrimped, knitted Dacron grafts in dogs. Crimping of the graft is effective in permitting a uniform, reproducible unfurling of the thin Dacron graft used. Although extrapolation to the tortuous human arterial anatomy cannot be made from our neatly linear aortic model, there is no doubt that the crimping technique vastly improves the unfurling of the graft. The mild curvature we reported in our results may be from the "relaxing" of the crimped

Table V. Evaluation of mid-graft dimensions in aorta

| | From placement of stented graft to: | | |
Percent change in:	1 Month	6 Months	12 Months
Duplex			
Diameter	1.8 ± 12 (23)	−3.2 ± 15 (13)	1 ± 17 (6)
Transverse perimeter	−2.7 ± 11 (20)	−0.3 ± 17 (13)	2.5 ± 14 (5)
Transverse area	1.8 ± 27 (18)	−11 ± 16 (13)	15 ± 19 (4)
Cut film angiogram			
Diameter		−5.5 ± 14 (9)	
Fluoroscope angiogram			
Diameter		−11 ± 12 (11)	−8 ± 8 (5)

graft into the AAD space before solidification of the encasing thrombus.

The anastomoses did not leak during follow-up. The radial expandability built into the ends of the graft by the longitudinal crimps allowed sufficient freedom to fully expand the underlying stent to secure the graft into the wall. The diameter of the proximal and distal stents and the underlying aorta did not change with time. Stents were overexpanded >20% into the proximal infrarenal aorta and did not slip. On autopsy, the stents were firmly embedded in a thick neointima. Microscopically, the stents and graft did not penetrate the internal elastic lamina but were embedded in a collagen-rich neointima. The thin, woven Dacron graft did not significantly enlarge and was prevented from doing so by the thick organizing thrombus around it. Graft burst strength and tensile strength did not change. The favorable decrease in porosity was attributed to tissue ingrowth. Double-stented grafts in two dogs were effective in treating deployment complications; no difference in outcome was observed.

Incorporation of the stented graft was universal in this young, healthy dog model. Extrapolation to an atherosclerotic aortic aneurysm is limited by the issue of incorporation. The fibrous cap on the atherosclerotic aortic surface and the irregularities from calcification are obstacles to uniform stent apposition to the aortic surface. This apposition is necessary for incorporation. Balloon-expandable stents offer a better chance of surface apposition compared with self-expandable stents. Still, the aortic surface may be so significantly diseased that healthy incorporation may not be achieveable. Leaks at the proximal aortic anastomosis have been reported clinically. They have been attributed to poor incorporation and to further aortic degeneration, causing aortic enlargement at the stented anastomoses. From our data, these two issues may be directly linked: enlargement should be preventable by the steel struts if they were fully incorporated, like scaffolding. Our experience in normal

vessels shows no aortic enlargement underlying the stent. On the contrary, the fully incorporated stent is so thoroughly a part of the aortic wall that further aortic enlargement at the stented anastomosis seems improbable. Unfortunately, full incorporation may be difficult to achieve in an atherosclerotic calcified aorta.

The technology of stented graft placement is evolving.[20-38] Basic questions have risen regarding the feasibility of this technology. The data reported herein confirm that a properly deployed stented graft is effective in treating a dilated artery containing no mural thrombus despite patent side branches measuring <1.5 cm in diameter in a normotensive animal up to 1 year of follow-up.

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DISCUSSION

Dr. Fred N. Littooy (Maywood, Ill.). The primary question to be answered by those investigating the endovascular repair of abdominal aortic aneurysms is the fate of the aneurysm wall. That is, will the properly excluded abdominal aortic aneurysm wall remain intact or rupture with time? Also, what are the difficulties in properly exclud-

ing the abdominal aortic aneurysm wall, and how can these difficulties be overcome? Past clinical experiences with aortic exclusion with extra anatomic or in-line bypass have provided some useful information about this. Extraanatomic bypass without aortic ligation has resulted in late rupture rates of 15% to 20%. Conversely, with aortic ligation and in-line bypass in well over 300 cases reported from Albany, no expansion, rupture, or leakage occurred. Eleven patients had persistent flow in the aneurysm sac by Doppler exam; six of these eventually thrombosed, and no increase in diameter occurred in any of those 11 patients. Endovascular repair of abdominal aortic aneurysm presents several potential problems in the short- and long-term treatment results. Incomplete sealing of the anastomosis could allow formation of extraluminal channels or persistent patency of side branches such as lumbar, inferior mesenteric, or middle sacral arteries that could possibly cause expansion of the wall outside the graft. Can intravascular stents provide long-term attachment of a prosthetic graft to an atherosclerotic wall that is known to dilate with aging of the patient? What happens to the excluded aortic wall and to the thrombus within it and around the graft? There has been some evidence of a proliferative response at graft-stent arterial interfaces, and this raises the question of stenosis at the anastomosis over the long term. Within the aneurysm, radial stretching of the graft could also cause continued dilatation of the aortic wall. Parodi, who has the greatest experience to date with endovascular repair of abdominal aortic aneurysms, has noted only one dilatation of a treated aorta. This was attributed to improper placement of the distal stent into the thrombus instead of the aortic wall. Animal models to date have had many limitations in the study of the efficacy of endovascular repair of abdominal aortic aneurysm. The authors are to be congratulated; their model overcomes many of these limitations. They preserved the aortic wall and patent side branches and avoided prosthetic material. They nicely demonstrated that with the proper placement of the endovascular graft, the excluded aortic wall did not dilate or rupture despite patent side branches—even in animals monitored up to 1 year. Their animal model did not address the inability to mimic the features of the diseased aortic wall that is encountered in patients and how that may affect the anchoring of the stent into the aortic wall to prevent migration when coupled with the dilation that occurs with age. Do the authors have any suggestions as to how to study this in animals? Also, did you see any evidence of a proliferative healing response at the graft-stent aortic interface that might lead to stenosis in the long term? Recently, Criado et al. have developed an animal model that leads to rupture within 6 days if left untreated, which would provide evidence of the efficacy of this type of experimental treatment. Did you see rupture in any of your long-term animals who had no stent placed? I think the gauntlet is down that animal and human

experiences to date have shown no evidence that the properly excluded aneurysm wall will rupture. But do these stents provide secure long-term attachment to the aortic wall, and will the long-term complication rate be ≤3% that is seen in present-day abdominal aortic aneurysm repair?

Dr. Darwin Eton. The ability for the proximal stent to be incorporated in the wall is critical to the success of stented graft therapy. Unlike in our healthy vascular model, incorporation may not be uniformly achievable in the fibrotic calcific neck that we see in atherosclerotic patients.

The neointima that covers the stent and the graft did not create a hemodynamically significant stenosis at one year follow-up. Little progression in its thickness was imaged between six months and one year.

Rupture did not occur in our model. The scar forming after AAD creation encasing the dilation may have provided some resistance to aortic expansion over the one year follow-up.

Endoluminal replacement of the aorta is feasible within the limitations described in the paper. Whether the long-term complication rate will be as low as standard therapy cannot be concluded from this paper.

A satisfactory atherosclerotic model with which to evaluate this technology is lacking. Plenty of data is now available clinically, the ultimate model setting. Concerns exist as to the "anchor" and "seal" properties of the proximal stented atherosclerotic aortic anastemosis. These concerns are based on the variability in the incorporation of the proximal stent into atherosclerotic intimal tissue. Stents, however, do offer another opportunity. We have elected to separate the "seal" property of a stented anastomosis from the "anchor" property. This would make clinical investigation a little safer, and the data obtained easier to digest. This is accomplished by placing stents at the distal end of grafts and using them to secure the distal anastomosis. We have preliminary data in a dog model, whereby we balloon-expanded stents so as to secure the distal aorta into the end of an aortic tube graft or, conversely, to secure the tube graft into the distal aorta. These stents act primarily as "seals". These anastomoses take a couple of minutes to perform. The technology has the potential of being able to facilitate and accelerate aortoiliac surgery. Other benefits include less of a need for dissection in the pelvis, and we hypothesize a diminished potential for pseudoaneurysm formation with time, since the native vessel and the graft overlap for at least a centimeter and are not simply aligned in end-to-end fashion.

At this time, the technology for total endoluminal vascular surgery is in its infancy. I am introducing the concept of endoluminally assisted operative aortic surgery so that benefits from this technology may be reaped by a larger number of patients in the immediate future. My belief is that advances in surgery and anesthesia in the past decade

have led to uniform improved outcomes from aortic surgery. Using an anterior extra-peritoneal approach, we have limited the ileus and discomfort postoperatively enough that the mean discharge time in our last forty patients is five days. Similar data is being achieved with the traditional retro-peritoneal approach. We will be hard-pressed to improve on these outcomes. However, we expect that the stent technology available today combined with these operative approaches will be synergistic in that they will facilitate one another. Duration of surgery, blood and fluid replacement, and operative dissection may potentially be reduced. Although discharge mean may not change, the standard deviation of that mean may become narrower.