CLINICAL RESEARCH STUDIES

Explant analysis of AneuRx stent grafts: Relationship between structural findings and clinical outcome

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Objective: **We reviewed the structural findings of explanted AneuRx stent grafts used to treat abdominal aortic aneurysms, and relate the findings to clinical outcome measures.**

Methods: **We reviewed data for all bifurcated AneuRx stent grafts explanted at surgery or autopsy and returned to the manufacturer from the US clinical trial and worldwide experience of more than 33,000 implants from 1996 to 2003. Devices implanted for more than 1 month with structural analysis are included in this article. Explant results were analyzed in relation to cause of explantation and pre-explant evidence of endoleak, enlargement, or device migration.**

Results: **One hundred twenty explanted stent grafts, including 37 from the US clinical trial, were analyzed. Mean implant duration was 22 ± 13 months (range, 1-61 months). Structural abnormalities included stent fatigue fractures, fabric abrasion holes, and suture breaks. The mean number of nitinol stent strut fractures per explanted device was 3 ± 4, which represents less than 0.2% of the total number of stent struts in each device. The mean number of fabric holes per explanted device was 2 ± 3, with a median hole size of 0.5 mm^2. Suture breaks were seen in most explanted devices, but composed less than 1.5% of the total number of sutures per device. "For cause" explants (n = 104) had a 10-month longer implant duration ($P = .007$) compared with "incidental" explants (n = 16). "For cause" explants had more fractures (3 ± 5; $P = .005$) and fabric holes (2 ± 3; $P = .008$) per device compared with "incidental" explants, but these differences were not significant ($P = .3$) when adjusted for duration of device implantation. Among clinical trial explants the number of fabric holes in grafts in patients with endoleak (2 ± 3 per device) was no different from those without endoleak (3 ± 4 per device; P = NS). The number of fatigue fractures or fabric holes was no different in grafts in clinical trial patients with pre-explant aneurysm enlargement compared with those without enlargement. Pre-explant stent-graft migration was associated with a greater number of stent strut fractures (5 ± 7 per device; $P = .04$) and fabric holes (3 ± 3 per bifurcation; $P = .03$) compared with explants without migration. Serial imaging studies revealed inadequate proximal, distal, or junctional device fixation as the probable cause of rupture or need for conversion to open surgery in 86% of "for cause" explants. Structural device abnormalities were usually remote from fixation sites, and no causal relationship between device findings and clinical outcome could be established.**

Conclusions: **Nitinol stent fatigue fractures, fabric holes, and suture breaks found in explanted AneuRx stent grafts do not appear to be related to clinical outcome measures. Longer term studies are needed to confirm these observations. (J Vasc Surg 2004;40:1-11.)**

Endovascular repair has gained wide acceptance in the treatment of abdominal aortic aneurysm, with favorable results with a variety of devices.[1-6] However, adverse events, including aneurysm rupture, migration, endoleak, and aneurysm enlargement, are cause for concern.[7-11] Adverse clinical events may result from device structural failure, including hook fractures, stent corrosion, stent fractures, and fabric tears.[12-17] However, the relationship between structural characteristics of implanted endovascular devices, clinical performance, and long-term outcome of endovascular aneurysm repair is poorly understood.[18] Most reports of device mechanical failure have been largely based on radiographic findings,[19] and few explanted devices have been subjected to detailed morphologic and structural analysis.[20] The purpose of this investigation was to evaluate the structural characteristics of explanted AneuRx stent grafts and to relate the findings to clinical outcome measures.

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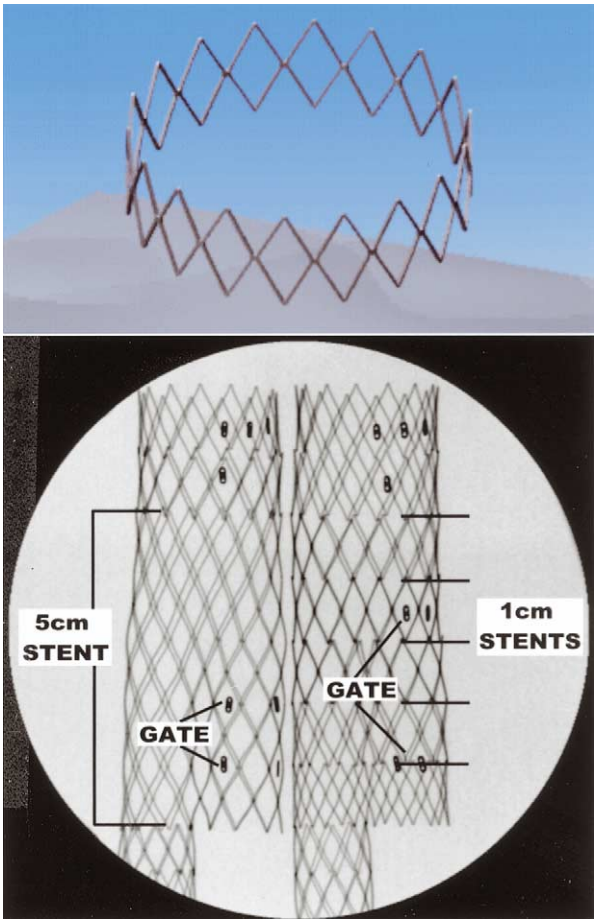

Fig 1. Nitinol exoskeleton is composed of individual 1-cm long stent rings *(top)* joined end-to-end and attached to the graft fabric with sutures. Each stent diamond has four struts. The early prototype "stiff" bifurcation module *(bottom left)* had a single 5-cm long bifurcation stent. The flexible segmented design *(bottom right)* was used in most clinical trial patients, and is the design used in the commercially marketed stent graft.

MATERIAL AND METHODS

AneuRx stent-graft structure. The AneuRx stent graft is composed of an exoskeleton of nitinol stent rings sutured to a polyester fabric graft. The bifurcation module contains seven aortic rings and 14 to 17 iliac rings, depending on the length of the stent graft. There are 728 to 1020 (mean, 907 ± 82) nitinol diamond strut elements in each bifurcation module. The initial bifurcation design contained a single 5-cm long bifurcated stent segment, which resulted in a stiff bifurcation. This was used in the early clinical experience and in the first 174 patients in the clinical trial. The current segmented bifurcation design, used in 1019 patients in the clinical trial, includes 1-cm long stent rings throughout the stent graft, which results in a flexible bifurcation (Fig 1). The woven polyester fabric material used in current AneuRx devices was introduced in December 1997 during the clinical trial. This reduced porosity material (RPM) fabric was used in 936 patients in the clinical trial; in the initial 257 clinical trial patients a less densely woven polyester fabric (preRPM fabric) was used (Fig 2). Stent rings are joined to each other and to the fabric with 5-0 polyester sutures. There are 1619 to 2079 suture attachments in each bifurcation module.

Method. All bifurcated AneuRx stent-graft devices implanted from June 1996 to July 2003, and subsequently explanted and returned to the manufacturer (Medtronic Vascular) were reviewed (N = 161). Devices returned after unsuccessful implantation or those in place for less than 30 days were excluded from this analysis (n = 28), as were 13 explanted devices with no structural analysis because of histologic sectioning. One hundred twenty explanted devices from the worldwide experience, including 37 explanted in the US clinical trial, are included in this report.

Explant analysis included gross inspection and photography of the "as received" specimen, x-ray imaging, tissue digestion and cleaning of the stent graft, magnified optical imaging, and ultrastructural analysis of the stent graft. Scanning electron microscopy of each stent fracture surface was used to differentiate acute overload fractures (induced by mechanical trauma during the explant procedure) from fatigue fractures (present in vivo before explantation). Overload fractures were characterized by micro-ovoid coalescence surface anatomy, whereas fatigue fractures showed radial lines that originated at the fracture origin and fanned out parallel to the direction of crack growth[21] (Fig 2). Graft defects included fabric weave separation, fabric abrasion holes, and explantation-induced cuts. The contour of each fabric defect was traced, and cross-sectional area was calculated with Scion Image Software, version 4.0.2. Fabric holes were defined as defects larger than 0.2 mm^2 in cross-section, the manufacturing specification for the graft fabric and the approximate cross-sectional area of a 25-gauge needle. Suture abnormalities included fraying and broken sutures.

The primary and secondary reasons for surgical conversion and stent-graft explantation were determined from the explanting surgeon's operative report and clinical summary. The cause of death, and the status of the aneurysm and stent graft were determined from the autopsy report. All explants retrieved at surgical conversion, as well as those retrieved at autopsy where the cause of death was aneurysm rupture or stent-graft complication, were grouped as "for cause" explants. Explants retrieved at autopsy where the cause of death was unrelated to the aneurysm or stent graft were considered "incidental" explants. Clinical records, and preoperative and post-implantation imaging studies were reviewed by two experienced surgeons, independent of explant findings, to determine the reason for clinical events leading to "for cause" explantation. For the 37 clinical trial explants, pre-explant imaging evidence of endoleak, aneurysm enlargement, or stent-graft migration, as determined by the core laboratory (phase II patients) or clinical center (phase III patients), were related to quantitative explant analysis findings.

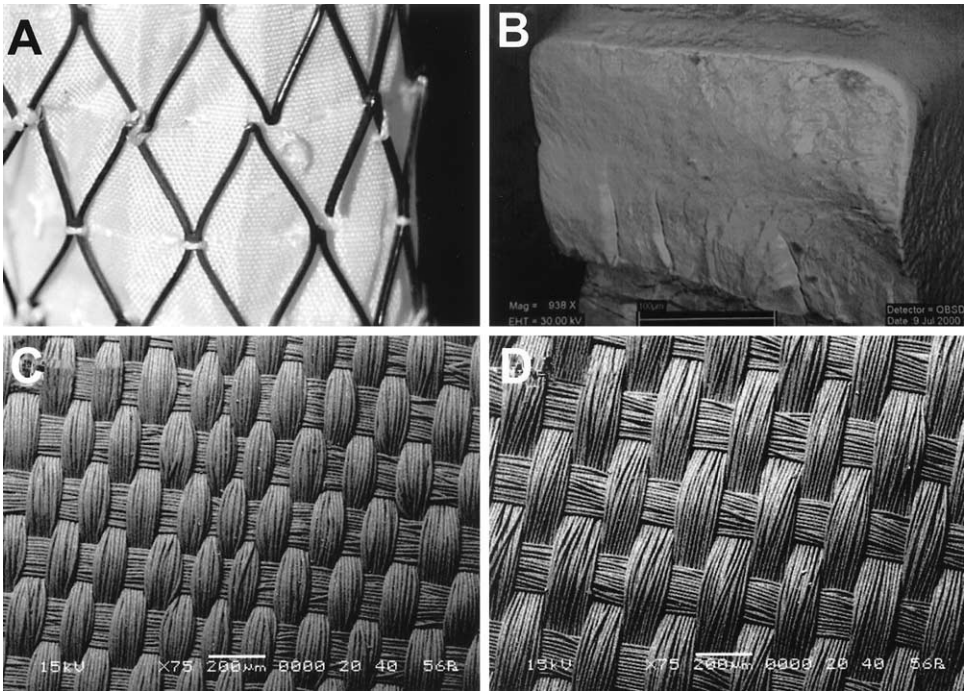

Fig 2. A, Explanted device demonstrates a broken suture between aortic stent rings 3 and 4, and a stent strut fracture in stent ring 4. **B,** Scanning electron microscopy image confirms that this stent strut fracture is a fatigue fracture, by the fault lines visible on the fracture surface. **C,** Reduced porosity material (RPM) fabric used in most patients in the clinical trial and in the commercially marketed stent graft. **D,** PreRPM fabric used in the initial devices had a less dense fabric weave.

Statistical analysis. Results were expressed as mean ± SD for continuous data, and as percentage for categorical data. Differences among groups were determined with the Wilcoxon rank sum test for continuous data, and the χ^2 or Fisher exact test for binary comparisons. Analysis of covariance was performed to adjust for factors that were unbalanced between the groups and could potentially affect the outcomes. Differences at $P < .05$ were considered statistically significant.

RESULTS

Explant patient population. The explant patient cohort (N = 120) was similar to the population of patients treated in the US clinical trial.[1] Mean age in the explant patient group at the time of device implantation (72 ± 7 years) was not different from age in the clinical trial patient group (73 ± 8 years). There was no difference in gender distribution between the explant (88% men, 12% women) and clinical trial groups (89% men, 11% women). Mean duration of device implantation before explantation was 22 ± 13 months (range, 1-61 months). The distribution of stiff versus flexible bifurcation module stent design in the worldwide explant group (5% vs 95%) was significantly different from the distribution among clinical trial patients (14% vs 86%; $P = .004$). The distribution of preRPM versus RPM fabric in the worldwide explant group was 11% versus 89%, significantly different from the distribution in clinical trial patients (21% vs 79%; $P = .008$).

Reasons for explantation. The primary and secondary reasons for device explantation, as determined by the explanting physician, are shown in Table I. Aneurysm enlargement with or without endoleak was the most common reason for surgical conversion, followed by aneurysm rupture and stent-graft migration. Three autopsy explants (two in the clinical trial group) were from patients who died of aneurysm rupture, and are included among the "for cause" rupture explants. There were 104 "for cause" explants and 16 "incidental" autopsy explants.

Nitinol stent fatigue fractures. One or more mitinol stent fatigue fractures were observed in 66% of explanted devices, and no fractures in 34% of devices. The mean number of strut fractures per explanted device was 3 ± 4 (range, 0-29). Stent strut fractures represented less than 0.2% of the total number of stent struts in each device. The total number of fatigue fractures per explanted device is shown in Fig 3. Only six explants (5%) had 10 or more strut fractures. The maximum number of strut fatigue fractures in a bifurcation module was 13. The maximum number of fractures in any module was 29, and were found in an aortic extender cuff that was severely angulated and distorted.

The distribution of stent fractures among modular device components is shown in Table II. Most fatigue fractures were found in the bifurcation module, with 2 ± 3 fractures per bifurcation. Bifurcation fractures were associated with severe neck angulation, and were usually located in aortic stent rings 3 (70% of fractures) and 4 (12% of

Table I. Reason for graft explanation

	Worldwide (N = 120)	*Clinical trial (N = 37)*
	104	31
"For cause" explanation		
Rupture*	17	7
Symptomatic AAA	3	0
Component separation or migration	3	0
Aneurysm enlargement	3	3
Endoleak or inadequate seal	4	1
Unknown	4	3
Symptomatic AAA (nonruptured)	4	0
Migration	1	
Aneurysm enlargement	1	
Endoleak	1	
Infection	1	
Component separation	4	5
Migration	14	2
Aneurysm enlargement	39	15
Endoleak	31	12
Type I	6	4
Type II	14	2
Type III	6	3
Unknown source	5	3
No endoleak	8	3
Endoleak without enlargement	11	0
Type I	9	
Type II	1	
Type III	1	
Aortoenteric fistula	4	2
Infection	4	0
Limb occlusion	7	0
"Incidental" autopsy explantation	16	6

AAA, Abdominal aortic aneurysm.
*Three grafts in worldwide group and two in clinical trial group were explanted at autopsy.

fractures), where the circular aortic stent contour transitions to a bi-oval configuration. Iliac limb fractures were less common, and were localized in areas of severe iliac angulation. Fatigue fractures were rarely seen in the seal zones of the device to the aortic neck or iliac arteries or in the modular iliac junction.

Fabric holes and weave separation. Fabric weave separation was observed in explants with the early preRPM fabric, and was most prominent in areas of suture pull and fabric stretch in severe angulations and bends. Weave separation resulted in spaces between fabric fibers of less than 0.2 mm^2. Fabric abrasion and fabric holes were related to wear of the fabric against the apex of metallic stent diamonds in areas of severe angulation and suture breaks. Fabric holes were rarely seen in relation to stent strut fractures.

One or more fabric holes larger than 0.2 mm^2 were observed in 45% of explanted devices, and no fabric holes were found in 55% of devices. The mean number of holes per explanted device was 2 ± 3 (range, 0-17). Mean fabric hole size was 0.7 ± 0.7 mm^2, with a median hole size of 0.5 mm^2 (approximately the size of a 21-gauge needle). The total number of fabric holes per explanted device is shown in Fig 4. Only four explanted devices (3%) had 10 or more holes. The distribution of fabric holes per device module is shown in Table II. Fabric holes were most often found in the bifurcation module, with 1 ± 2 holes per bifurcation. There were no significant differences in the number of stent fractures or fabric holes between preRPM fabric explants and RPM fabric explants.

Suture integrity. Broken and abraded sutures were found in almost all explanted devices, most commonly in areas of severe angulation. Suture breakage was most often seen at junction stitches between stent rings (Fig 2), and breakage enabled partial stent ring separation or overlap. The median number of broken sutures per explanted device studied was 22, which was less than 1.5% of the total number of sutures in each device.

Duration of implant. The number of fatigue fractures and fabric holes as a function of implantation time is shown in Fig 5. The number of explants at each time point is indicated in the figure. The device with the largest numbers of fatigue fractures (29 fractures on one extender cuff) had been implanted for 30 months.

"For cause" versus "incidental" explantation. A comparison of "for cause" explantation and "incidental" explantation is shown in Table III. Patients in the worldwide "for cause" explantation group were 6 years younger than patients in the "incidental" explantation group ($P = .003$), and their devices had been implanted 10 months longer ($P = .007$). Preoperative patient risk factor analysis in the 37 clinical trial explants revealed a higher rate of symptomatic cardiac arrhythmia ($P = .02$) in the "incidental" explant group, consistent with documented cardiac cause of death in 70% of this group. Explant analysis revealed a significantly greater number of stent fatigue fractures and fabric holes in "for cause" explants compared with "incidental" explants ($P = .005$ and $P = .008$, respectively; Wilcoxon rank sum test). However, when analysis of covariance was used to adjust for differences in duration of implantation, the differences in fatigue fractures and fabric holes between the two groups were not significant ($P = .3$ for both).

Endoleak. Among clinical trial patients endoleak was documented on the final imaging study before explantation in 26 patients, and was absent in 11 patients. Endoleak rate was higher with "for cause" explants (81%) compared with "incidental" explants (17%; $P = .005$). There was no significant difference in endoleak rate between explants with fabric holes (76%) compared with those with no fabric holes (63%). Similarly, there was no significant difference in endoleak rate between explants with stent fractures (78%) compared with those with no stent fractures (57%). There was no significant difference in the number of fabric holes or stent strut fractures between explants from patients with endoleak compared with those without endoleak (Table IV).

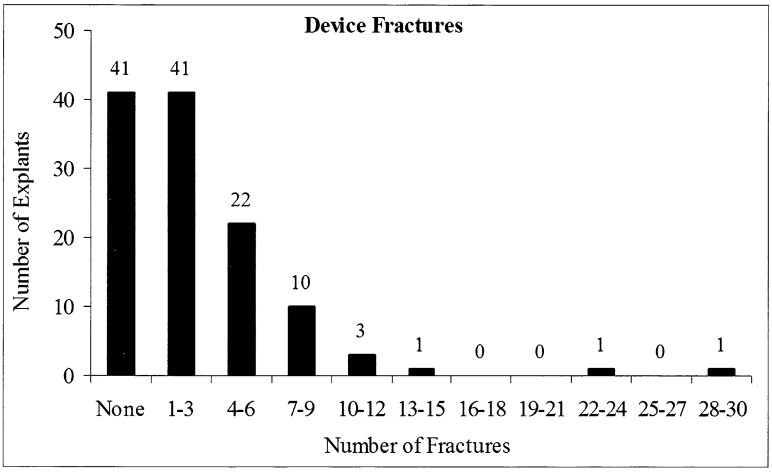

Fig 3. Number of stent strut fatigue fractures per explanted device.

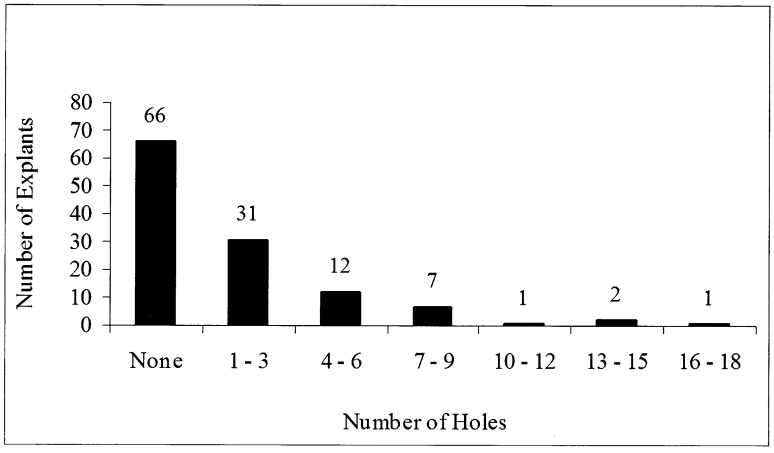

Fig 4. Number of fabric holes (>0.2 mm^2) per explanted device.

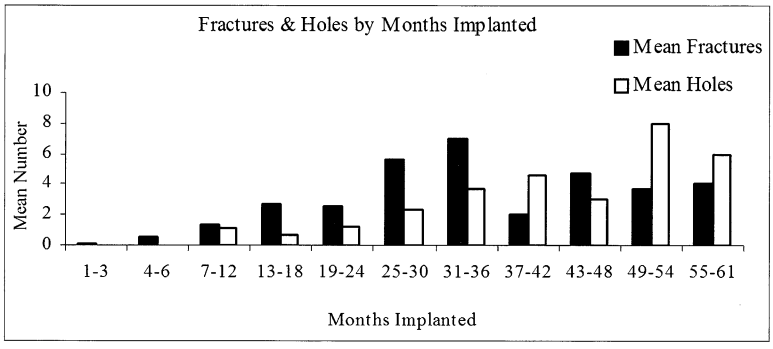

Fig 5. Fractures and holes as a function of number of months the device was implanted. Number of explants at each time point is indicated on the x-axis.

Aneurysm enlargement. Among patients in the clinical trial group, aneurysm enlargement (diameter increase >5 mm compared with baseline computed tomography scan) before explantation was documented in 15 patients; 22 aneurysms exhibited no enlargement. There was no significant difference in enlargement rate between explants

Table II. Stent fatigue fractures and fabric holes by device module

	Bifurcation		*Iliac limb*		*Extender cuff*	
	n	*%*	*n*	*%*	*n*	*%*
Worldwide explanations (N = 120)						
One or more fatigue fractures	76	43	8	7	8	7
No. of fractures (mean ± SD)	2.4 ± 3.0	1.0 ± 2.0	0.1 ± 0.3		0.5 ± 2.9	
One or more fabric holes			22	18	14	12
No. of holes (mean ± SD)			0.5 ± 1.3		0.4 ± 1.7	
Clinical trial explantations (N = 37)						
One or more fatigue fractures	21	57	2	5	4	11
No. of fractures (mean ± SD)	1.7 ± 2.0		0.1 ± 0.4		0.9 ± 4.8	
One or more fabric holes	16	43	6	16	2	5
No. of holes (mean ± SD)	1.6 ± 2.6		0.5 ± 1.2		0.2 ± 0.9	

Table III. "For cause" versus "incidental" explant analysis

	Worldwide explants (N = 120)			*Clinical trial explants (N = 37)*		
	For cause (n = 104)	*No cause (n = 16)*	P	*For cause (n = 31)*	*No cause (n = 6)*	P
Age at implant (y)	71 ± 6.9	77 ± 7.0	.003	71 ± 7.9	74 ± 7.5	NS
Gender (%male:female)	88:12	80:20	NS	87:13	67:33	NS
Pre-RPM:RPM fabric (%)	12:88	6:94	NS	23:77	17:83	NS
Implant duration (mo)	24 ± 13	14 ± 12	.007	31 ± 9	24 ± 10	NS
Any device fracture						
n	74/104	5/16	.002	21/31	2/6	NS
%	71	31		68	33	
Stent fractures per device	3.3 ± 4.5	1.1 ± 2.5	.005*	3.2 ± 5.3	0.5 ± 0.8	NS (.06)*
Any device hole						
n	51/104	3/16	.02	20/31	1/6	NS
%	49	19		65	17	(.07)
Fabric holes per device	2.2 ± 3.4	0.2 ± 0.4	.008*	2.6 ± 3.6	0.2 ± 0.4	.03*

*Based on Wilcoxon rank sum test. When analysis of variance is used to control for duration of implant, $P = .3$.

with fabric holes (38%) compared with explants without holes (44%). Similarly, there was no significant difference in aneurysm enlargement between explants with fatigue fractures (39%) compared with those with no fractures (43%). There was no significant difference in the number of fabric holes or strut fractures between explants from patients with or without aneurysm enlargement (Table V).

Device migration. In the clinical trial group, pre-explant imaging studies documented stent-graft migration in 14 patients; 23 patients had no stent-graft migration. Explants with stent fractures in any device module were more likely to have migrated (52%) than were explants with no fractures (14%; $P = .02$). The number of stent fractures was higher in explants from patients with stent-graft migration than in explants with no migration ($P = .04$; Table VI). The number of fabric holes was higher in bifurcation modules from patients with stent-graft migration ($P = .03$); however, there was no significant difference in the total number of fabric holes per device ($P = .08$; Table VI).

Clinical case review. Retrospective review of clinical records and sequential imaging studies revealed evidence of short or absent device fixation length, either proximally at the aortic neck, distally to the iliac artery, or at a modular junction site in 86% of "for cause" explant cases. This review suggested that inadequate device fixation was a major cause of clinical events leading to rupture or surgical explantation in each case. A case example, demonstrating inadequate fixation of the modular iliac limb as the cause of aneurysm rupture is shown in Fig 6. No structural abnormalities were found in the left iliac limb, whereas focal fatigue fractures and fabric holes were found in the bifurcation module. Most structural abnormalities found in explanted devices were remote from stent-graft fixation sites, and no causal relationship between device structural findings and clinical outcome could be established.

DISCUSSION

Despite a 7-year clinical experience, little information is available on the structural characteristics of implanted AneuRx devices, because clinical results are good[1,6] and relatively few devices have been retrieved for analysis. The sample of 120 explanted stent grafts in this study is a small

Table IV. Endoleak analysis (clinical trial patients)*

	Endoleak (n = 26)	*No endoleak (n = 11)*	P
Fabric holes per bifurcation module	1.4 ± 2.4	1.9 ± 3.1	NS
Fabric holes per device	2.1 ± 3.2	2.5 ± 3.9	NS
Stent fractures per bifurcation module	1.9 ± 2.0	1.3 ± 1.9	NS
Stent fractures per device	3.3 ± 5.7	1.3 ± 1.9	NS

Values represent mean ± SD.
*Patients with endoleak present on last imaging study prior to explantation compared with patients without endoleak.

Table V. Enlargement analysis (clinical trial patients)*

	Enlargement (n = 15)	*No enlargement (n = 22)*	P
Fabric holes per bifurcation module	1.3 ± 2.2	1.8 ± 2.9	NS
Fabric holes per device	1.6 ± 2.8	2.6 ± 3.7	NS
Stent fractures per bifurcation module	1.4 ± 1.8	1.9 ± 2.1	NS
Stent fractures per device	3.8 ± 7.3	2.0 ± 2.1	NS

Values represent mean ± SD.
*Patients with aneurysm enlargement (>5 mm) documented on serial imaging studies before explanation compared with patients with no enlargement.

Table VI. Migration analysis (clinical trial patients)*

	Migration (n = 14)	*No migration (n = 23)*	P
Stent fractures per bifurcation module	2.5 ± 2.0	1.2 ± 1.8	.04
Stent fractures per device	4.6 ± 7.3	1.6 ± 2.2	.04
Fabric holes per bifurcation module	2.5 ± 3.2	1.0 ± 2.0	.03
Fabric holes per device	3.6 ± 4.6	1.4 ± 2.1	.08

Values represent mean ± SD.
*Patients with evidence of device migration on serial imaging studies before explantation compared with patients without migration.

fraction of the 33,000 AneuRx devices implanted worldwide. Nonetheless, it is the largest reported systematic structural analysis of explanted aortic devices. Although there were some early changes in stent design (stiff to flexible) and fabric weave (preRPM to RPM), the AneuRx device has remained the same over the past 7 years. Thus these explant results largely reflect the currently marketed device. However, the sample of explants is sharply skewed toward the minority of patients with serious adverse events, inasmuch as 87% of worldwide explants were retrieved at surgical explantation or after aneurysm rupture. Among the 1193 clinical trial patients, those with aneurysm rupture or surgical conversion represented less than 4% of patients,[6] but accounted for 84% of the explants in this study. Device recovery rate in clinical trial patients who underwent surgical conversion is 80%, but device recovery is only 4% in patients who died of non-aneurysm-related causes. Thus it is unclear how representative these explant findings are for the entire population of implanted devices.

Structural analysis revealed the presence of one or more focal abnormalities in most explanted AneuRx devices, including stent fatigue fractures, fabric holes, or suture disruption. The structural abnormalities observed were few, 2 or 3 stent fractures and fabric holes per device, particularly when considered in light of the total number of structural elements in each device. Thus, for example, the number of stent strut fractures found represented less than 0.2% of the total number of stent struts in a bifurcated device. Nonetheless, a relatively small number of stent fractures in critical areas of the stent graft may potentially have an adverse effect on the structural strength of the device. Similarly, even small fabric holes may potentially result in type III endoleaks, pressure transmission into the aneurysm sac, aneurysm enlargement, and possible aneurysm rupture.

To assess the clinical significance of the observed stent and fabric abnormalities we reviewed the subset of 37 clinical trial explants, because these patients, as part of the clinical trial, had well-documented clinical follow-up with serial imaging studies before explantation. We found no difference in the number of fabric holes or fatigue fractures in the explanted devices from patients with endoleaks compared with those without endoleaks before explantation. Similarly, no relationship could be established between pre-explantation aneurysm enlargement and fabric holes or fatigue fractures noted in explanted devices. These observations suggest that the structural findings did not account for adverse aneurysm-related events such as endoleak and enlargement, although the current sample size may not be large enough to rule out this possibility. On the other hand,

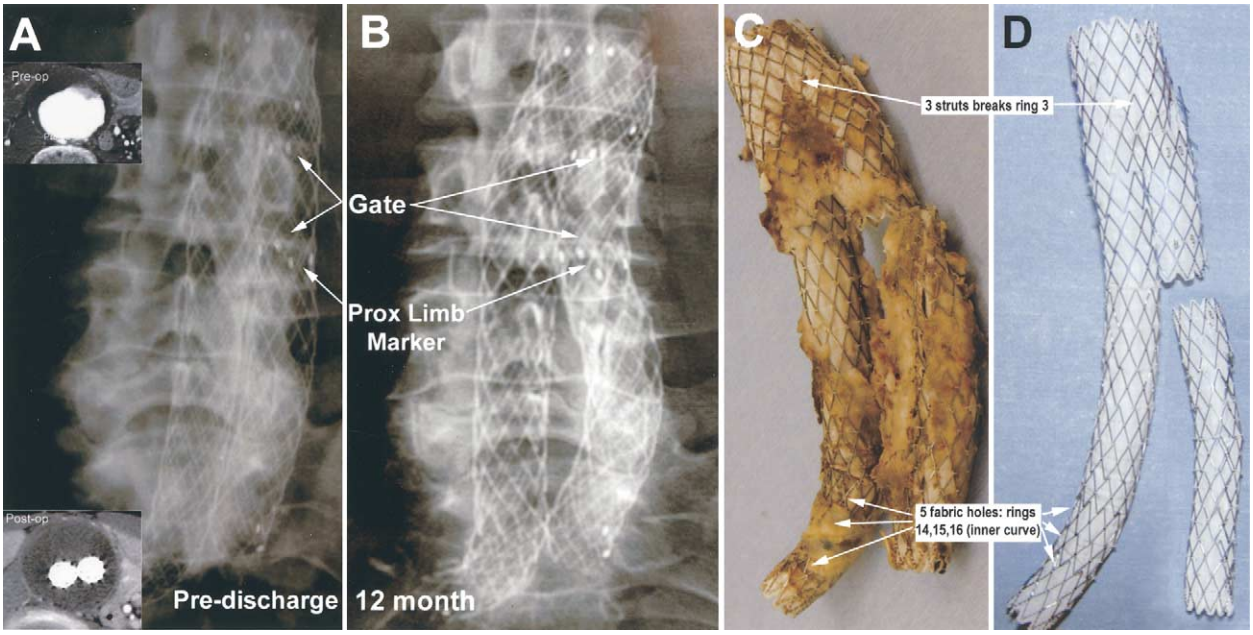

Fig 6. Explant case example. **A,** A 24 × 14 × 16.5-cm-long bifurcation module was implanted through the right femoral artery to treat a 5.5-cm abdominal aortic aneurysm. A 14 × 8.5-cm-long left iliac limb was used and positioned below the bifurcation junction gate (see markers). The left iliac limb was too short, and barely reached the left iliac artery. The aneurysm was successfully excluded from the circulation, with no evidence of endoleak (see inserts). However, insecure fixation both proximally and distally of the left iliac limb was apparent on the x-ray film. **B,** Bowing of the left iliac limb and slight angulation of the bifurcation module was apparent on x-ray film at 12 months. There continued to be no endoleak, and no change in aneurysm size. **C,** Aneurysm ruptured at 21 months as a result of separation of the iliac limb from the bifurcation module. The AneuRx stent graft was explanted during successful surgical conversion. **D,** Explant analysis revealed fatigue fractures in ring 3 of the bifurcation module *(top arrows)*, and fabric holes in the angulated right iliac limb at rings 14 to 16, remote from the aneurysm sac *(bottom arrows)*. There were no abnormalities in the left iliac limb.

stent-graft migration noted on pre-explantation imaging studies was associated with a small increase in both fatigue fractures and fabric holes found in explanted devices. It was not possible to determine with any degree of certainty whether these structural findings developed before or after the stent graft migrated.

Stent fractures found in this study were most commonly located in the bifurcation module, with most fractures found in aortic rings 3 and 4. At this location the round aortic stent ring configuration changes to a bi-oval contour to accommodate the two iliac limbs. Stent struts in this region are exposed to higher residual strain, and most stent strut fractures in this region were individual and uninvolved with the fixation seal zone (Fig 2). In one instance, five strut fractures were found in aortic stent ring 3. This was the largest number of fractures found in a single stent ring, and was associated with multiple suture breaks. This patient had severe aortic neck angulation and eccentric compression of the bifurcation module from an angulated proximal aortic extender cuff. The bifurcation module separated from the aortic extender cuff after 2 years, and the patient underwent successful open surgical repair.[22] It is believed that the angulation stress and motion between the proximal extender cuff and bifurcation module led to separation of the extender cuff.[22] The second most common site of fatigue fractures was the distal portion of iliac limbs in areas of severe angulation and tortuousity. These fractures were often outside of the aneurysm sac (Fig 6).

Fabric holes were usually related to fabric abrasion against the apex of a stent diamond in areas of severe angulation. These focal stent–diamond tip perforations were small and were often located in iliac limbs, remote from the aneurysm sac. Median hole size was 0.5 mm^2, approximately the size of a 21-gauge needle. Fabric holes observed in explanted devices were likely to have been plugged with thrombus or tissue in vivo, and thus it is not surprising that there was no significant relationship between endoleak and fabric holes. It is possible that such sealed holes may account for pressure in the aneurysm sac without evidence of endoleak (endotension) and thus lead to aneurysm enlargement. However, we found no relation between fabric holes and aneurysm enlargement. Aneurysm enlargement after endovascular repair in AneuRx clinical trial patients, although associated with the presence of an endoleak, is not associated with increased risk for aneurysm rupture.[23] Removal of tissue and thrombus material from the stent-graft surface after opening the aneurysm sac during surgical conversion may induce pinpoint bleeding

through openings in the fabric.[24] Explant analysis of devices from patients with clinically reported "microleaks"[24,25] revealed that they had received preRPM fabric devices, which had weave separation but no evidence of fabric holes. No microleaks have been reported in patients who have received the AneuRx device made with RPM material. Intrinsic polyester fabric failure has been noted in aortic grafts used in open surgery,[26,27] thus stimulating continuing improvement in fabric design. It is likely that advanced fabric designs will reduce the risk for abrasion-induced holes in the future.

A comparison of explants removed "for cause" with those recovered at "incidental" autopsy revealed a significantly greater number of fatigue fractures and fabric holes in "for cause" explants. However, there was also a significant difference in average implant duration between the groups, 24 months for "for cause" explants versus only 14 months for "incidental" explants. Since stent fatigue fractures and fabric abrasion holes are time-dependent, analysis of covariance was used to adjust for the difference in duration of implantation. The differences in the number of fatigue fractures and fabric holes between groups were not significant when adjusted for the differences in implant duration. Only 16 "incidental" autopsy explants were available for analysis, compared with 104 "for cause" explants. While it is possible that increasing the number of explants in the "incidental" group, particularly those with longer implant time, would reveal significant differences between the groups, this is not certain. Furthermore, it is likely that the disparity between the groups will continue, given the marked difference in device recovery rate between surgical explants and "incidental" explants at autopsy.

Perhaps the most meaningful clinical observations came from the review of x-ray films and serial computed tomography scans in patients with "for cause" explants. Image analysis revealed evidence of short stent-graft fixation length proximally, distally, or at the iliac junction in 86% of "for cause" explants. Inadequate stent-graft fixation can be present despite complete aneurysm exclusion with no endoleak for prolonged periods, as demonstrated by the case shown in Fig 6. These observations are consistent with previous reports that poor stent-graft fixation is the primary predisposing factor for aneurysm rupture after endovascular repair with the AneuRx stent graft.[10] Short proximal fixation length is also a primary predictor of migration of AneuRx stent grafts.[28] Short proximal fixation may be the result of low initial deployment of the device or severe angulation of the aortic neck. Most stent, fabric, and suture defects were remote from fixation and seal zones, and thus did not appear to be related to the cause of explantation. Most structural abnormalities in explants that migrated were localized in areas of increased angulation stress, which suggests they developed or were accentuated as a result of stent-graft migration. However, longer follow-up and analysis of a larger number of explants will be needed to better determine the relationship between structural findings and migration.

SUMMARY

Stent fatigue fractures, fabric holes, and suture breaks were found in most explanted AneuRx stent grafts. These structural findings were not significantly related to pre-explant aneurysm enlargement or endoleak; however, longer studies with larger sample sizes are needed to confirm these results. Pre-explant device migration was associated with a greater number of explant stent fractures and fabric holes. Although "for cause" explants had a greater number of structural abnormalities than did "incidental" explants, these differences may be explained by differences in duration of device implantation. Most devices explanted "for cause" had evidence of insecure proximal, distal, or junctional fixation, which could account for the adverse clinical event. Thus a clear relationship to explant structural findings could not be established. Longer studies are needed to fully determine the significance of these explant findings.

APPENDIX

The Medtronic Explant Program has provided important information that has been used to enhance the AneuRx stent-graft system. Improvements approved by the US Food and Drug Administration in January 2004 include use of a more densely woven graft material, high-density graft material, which enhances the robustness of the graft fabric.

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DISCUSSION*

Dr Timothy A. M. Chuter (San Francisco, Calif). I would like to thank the committee for the opportunity to review this interesting paper. Those of you who cannot wait to see this information in print should read Appendix Two of the recently published 6-year report that described 115 AneuRx explants. The findings were essentially the same. Indeed, most of the patients were the same. Of the 48 patients in the current study, 45 were included in the previous report.

As Dr Zarins said, all three forms of stent-graft failure occurred at relatively low rates when the prevalence was expressed as a proportion of the total number of components, but that's not the point. A broken chain is still broken even if 99% of the links remain intact. It is not as though there was much redundancy built into the design of the AneuRx stent graft. Each component performed an important and unduplicated function. The important issue here is whether the strut breakages, suture breakages, and holes in the graft caused migration, endoleak, endotension, or aneurysm dilatation or rupture. So, did broken struts cause stent-graft migration or disruption? The answer is probably no. Most fractures occurred in the midsection of the stent graft, not at the ends, where stent failure would lead to failed attachment. What about suture breaks? Did they seriously disrupt the shape of the stent graft or allow the graft fabric to flap against the apex of the stent? The answer is yes in some cases. The mean number of breaks was 25 to 30 per stent graft. Most occurred at points of angulation, and some were associated with abrasion holes. And last, but not least, the holes. It appears weave separation rarely caused holes in the new, more tightly woven RPM fabric, but abrasion remained a persistent problem. The mean number of abrasion holes in this study was 2.2 per patient. They occurred at acute graft angulations and suture breaks. In the 115 explant series the mean area of these abrasion holes was 0.7 mm. Assuming the holes were roughly circular, the mean diameter would be 0.95 mm, which would certainly be large enough to transmit pressure, if not flow, to the aneurysm. Apparently the presence or absence of holes did not correlate with the rate of endoleak, but, as Dr Zarins has told us, many times endoleaks are of no significance when one is talking about AneuRx cases. I have four questions for Dr Zarins.

Number one, what was the mean diameter of the abrasion holes in this study? Number two, how many patients exhibited transgraft leakage at conversion? I have seen two quite striking cases. There must be others, and perhaps they should be included in the report. Might a prevalence of graft holes be responsible for the relatively low rate of aneurysm shrinkage seen after endovascular repair with the AneuRx stent graft compared, for example, with the Talent device? And finally, since stent graft angulation caused suture breakage and abrasion holes, would Dr Zarins suggest further narrowing the selection criteria for the AneuRx device?

Dr Christopher K. Zarins. Indeed the structural integrity is key for long-term device performance.

With regard to the questions, the mean area was 0.7 mm^2, but the holes are small, as you saw them, in relationship to the size of the stent. So they are small holes, approximately the size of a 21-gauge needle.

In terms of the transgraft flow, there were in fact four cases that were related to the so-called microleak phenomenon. In this phenomenon, in the operating room the surgeon will remove mural thrombus from the surface of the graft, perhaps manipulate the graft a little bit, and can produce holes with bleeding through the graft fabric. You can actually do this with any open surgical technique. If you have a polyester fabric sewn in place, you put a needle in it, and that spreads the weave of the fabric, and then you have bleeding through the needle hole, and of course you hold it

*The text of this discussion reflects what was said at the Western Vascular Society meeting. As a result of peer review, there have since been extensive changes to the manuscript, most notably the addition of 120 patients to address the concern about type II statistical error and an entirely new analysis of the data. The article is based on 48 patients plus these 120 new patients.

for a couple of seconds, and that bleeding seals. This I think is actually what happens in these fabric weave separations, or so-called microleaks. The cases that have been published on this phenomenon all had the preRPM fabric, so I think that weave separation is perhaps not really an issue with the current device.

With regard to the shrinkage rate, shrinkage or lack of shrinkage and enlargement in these devices is primarily related to type II endoleaks, which do persist in these devices, and the presence or absence of a type II endoleak is related to size changes. I do not believe they are related to these fabric abrasion holes, although I can't rule out that possibility.

In terms of patient selection and angulation, I think there is no evidence to suggest that we should change our selection criteria. In fact, these devices perform quite well in angulated areas, although in angulations it is subject to stresses, stent fractures, abrasion holes, and suture breaks, as we have discussed, but this does not seem to be related to clinical outcome or clinical performance in these areas.

Dr James Edwards (Portland, Ore). Was there any correlation between the number of fractures or suture breaks and the length of time the devices had been in place? I would expect an increased failure rate or increased number of structural defects with increased implant time.

Dr Zarins. There was not a statistically significant relationship between implant duration time and the number of fatigue fractures among clinical trial patients. That does not mean there could not be, because the average implant time was 30 months, and the number of devices harvested was quite small compared with the total population of devices. So I can't rule out the possibility that there is a time-related relationship, but there was not in this cohort of patients.

Dr Lloyd M. Taylor, Jr (Portland, Ore). Do you have any information that we can use for comparison purposes on the anticipated number of defects in the fabric of standard open implanted polyester grafts? We have a lot of information from your study, which is very valuable. But the question is, in routine aneurysm repair are there defects in the fabric as well in explanted specimens? Do you know anything about that?

Dr Zarins. Well, there is a very large body of data on graft fabric defects in open surgical repair. There are many iterations and evolution of graft fabrics of various types of design and weave strength. You may recall the old Wesolowski graft, which was an ultra-lightweight fabric that ultimately broke down. The fabric degenerated and caused aneurysmal dilatation of the graft fabric. So I think the graft fabric is a very important issue, both open surgical and endograft designs, and it is, in fact, what really holds everything together. The fabric itself is a very, very critical component in both open and endografts. On the basis of the findings from this explant program, I believe the manufacturer is planning on increasing, yet again, the strength and durability of the fabric that is used in this particular device.

Dr Sam Ahn (Los Angeles, Calif). I still have a hard time accepting your conclusion that there is no causal relationship between the structural defects and the clinical outcome. I just wonder if that lack of conclusion of that relationship could be due to a type II statistical error, since this is a relatively small series. You are looking at a very select group of patients, those that underwent graft explantation. There may be a lot of other structural defects in other patients that aren't causing problems and we just haven't discovered them yet. I was wondering if you could comment on the possibility that this could be a sampling error or a type II statistical error. Also, a second point is that, as I have listened to a lot of talks, including yours, about device failures, every time they present some example of a failure it seems like, in retrospect, if we had not "pushed the envelope" in that particular patient that failure might not have happened. I wonder if the message from your paper is that we should not "push the envelope" so much, and maybe we shouldn't treat so many patients with really adverse anatomic factors.

Dr Zarins. I cannot exclude the possibility of a statistical error since we had only 48 devices from 1193 patients. Error can also be made on the basis of generalization from anecdotal cases. For example, a study of 25 explanted devices, or 25 failures, found angulation of the neck, leading some to say, "Ah, that means we should not do angulated cases." Well, the error there is that you never looked at the successes. In our own experience we have a lot more successes with angulations than we have failures, long-term successes that work very, very well. So you can't necessarily conclude that, because you have a couple of failures, everyone who has that feature, like an angulation, is going to fail. It's not actually true (see footnote on previous page).

Dr William Quinones (Los Angeles, Calif). It is precisely because of that that I raise one question, and that is, are you looking at the patients who are still "successes" to see if there is any evidence of any of these types of failures with perhaps an increased or more intense follow-up program and imaging? That's my first question.

In relationship to the first question, the reason I think that is important is because it will answer the question. If you know that there are specific defects in a patient that are still in place and nothing happens, then it supports your conclusion, but if we start seeing some of these defects prior to a failure of the implant, then I think you may need to modify your conclusion.

My second question is, have you shared this information with the FDA, and if you have, what has been their recommendation in terms of follow-up for the patients who still have the implant?

Dr Zarins. Yes, this has been shared with the FDA, and the outcome of that recommendation of the FDA is, in fact, what you suggested in the first part of your question, that is, closer follow-up of anyone who has been identified to have anything that has been suggested as being an adverse issue, for example, the stiff device. We know that the risk for rupture with a stiff device is higher than with the segmented flexible device. However, that was a very early issue related to the stiffness, pulling out in areas of angulation. The response was to follow these patients at 3-month or 6-month intervals instead of yearly intervals. In fact, nothing has happened to these patients. It was an early issue. So a regulatory response to demand follow-up or early imaging may or may not be that productive. Our own practice is to follow up patients on the basis of clinical parameters and clinical outcome measures, and in fact the clinical outcome measures are quite good. I think the ultimate answers will come out in the long-term follow-up, because the follow-up is going to be forever in this cohort of patients, and we hope we will collect as large a number of explants, either autopsy or surgical explant, and be able to further answer some of these questions.