THE NEW GOLD STANDARD?

EVAR data achieves the 5-year milestone
This supplement to Endovascular Today examines endovascular aneurysm repair (EVAR) as it achieves the milestone of 5-year follow-up data. AneuRx studies that began in three phases from 1996 to 1999 have now produced data spanning 5 to 8 years. These data now allow us to consider the question: Is EVAR the new gold standard?

To answer that question, Endovascular Today, supported by a grant from Medtronic Vascular, has assembled 4 excellent authors: Drs. Craig Kent and Christopher Zarins evaluate the long-term data and attempt to determine how EVAR compares to surgical repair. Dr. Robert Lookstein examines those technologies that hold promise for further improving EVAR results and patient follow-up. Dr. Rod White discusses the necessity of explantation evaluation for assessing the long-term effectiveness of EVAR. We hope you enjoy reading this supplement and that these articles contribute to the ongoing discussion of whether EVAR is—or will become—our new gold standard for aneurysm repair.

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Endovascular aortic aneurysm repair (EVAR) arrived into the spotlight in 1999 when the FDA approved two devices for clinical use. Since FDA approval, there has been burgeoning interest in this procedure. Data from state and national databases indicate that up to 50% of all elective abdominal aortic aneurysms (AAAs) are now being treated with EVAR. This enthusiastic growth, however, has been the focus of intense scrutiny. Proponents of EVAR note significant benefits over open repair with regard to short-term outcomes, whereas those who challenge EVAR raise issues of costs and long-term effectiveness. Clinical investigators continue to closely examine maturing data from prospective trials. Hospital administrators eager to both manage expenses but stay on the cutting edge of medical technology are closely monitoring reimbursement and the cost of endovascular devices. An additional driver of immeasurable importance is the desire of the general public for less-invasive interventions. In this article, each of these issues will be addressed with the goal of assessing the current role of endovascular therapy in the treatment of AAA.

**EARLY OUTCOMES**

Early results of EVAR have been encouraging, with a number of recent studies demonstrating reductions in perioperative mortality, rate of complication, and length of stay in patients treated with endovascular techniques. Moreover, these excellent results appear to have led to rapid diffusion of this technique. In a recent analysis of the New York State discharge database (SPARCS), we found that the introduction of EVAR appeared to coincide with an approximately 20% increase in the overall rate of intervention for aneurysmal disease. In the year 2001, less than 40% of all aneurysms were repaired with endovascular techniques, whereas in 2002, EVAR was used in more than half of aneurysm repairs. Additionally, the number of institutions in New York State performing EVAR nearly tripled from 2000 to 2002.

The difference in mortality between these two approaches was striking. In 2001, the chance of death with open surgery was 3.6% compared to 1.1% for EVAR. In 2002, there was a similar disparity in mortality (4.2% for open repair and 0.8% with EVAR). The rate of complications was also diminished with EVAR. In 2002, there were fewer cardiac complications (8% vs 3%), less frequent pulmonary dysfunction (9% vs 1%), and fewer transfusions (12% vs 3%) in patients treated with EVAR. These outcomes were achieved despite EVAR being used in a generally more ill population. Hypertension, diabetes, coronary artery disease, and hyperlipidemia were more frequent in patients treated with EVAR than those who underwent open surgery. As might be predicted, length of stay was dramatically reduced in the EVAR cohort. Similar findings were derived from a recent review of the National Inpatient Sample, a database that allows analysis of national trends. Again, despite the fact that a greater proportion of elderly patients were treated with EVAR, mortality was 1.3% for EVAR versus 3.8% with open repair.

**Figure 1.** A paradigm depicting that the AAA-related mortality for both interventions would become equivalent 10 years after the initial procedure.
MID- AND LONG-TERM RESULTS

Despite encouraging early outcomes, many patients treated with EVAR will require reintervention. The need for ongoing monitoring of patients treated with EVAR is clear. The most widely employed method of graft monitoring is computerized axial tomography, although ultrasound is used at some centers. New data are emerging regarding the use of intrasac pressure as a method of monitoring patients after EVAR. Studies in animals, as well as early human clinical trials suggest that pressure devices attached to the graft at the time of implantation may eventually replace, or at least reduce, the need for CT monitoring. If this technology comes to fruition, the expense and inconvenience of monitoring will diminish.

Reintervention is required in a substantial number of patients who have been treated with EVAR. The most common reasons for secondary intervention have been aneurysm rupture, enlargement with or without endoleak, graft limb occlusion, and/or stent migration. The overall frequency of reintervention has varied substantially and there are a number of explanations for this variability. First and foremost, during the past 10 years, multiple devices have been introduced and evaluated, including several that have been withdrawn from use. Most large series of EVAR blend the long-term results of multiple grafts, despite the increasing realization that durability is device specific. Also, the indications for reintervention vary significantly from institution to institution and continue to evolve. For example, at some institutions, type II endoleaks are aggressively treated, whereas at other institutions, treatment is reserved for patients who experience aneurysm enlargement.

The reported frequency of reintervention ranges from 8% to 35% at 1 year and 20% to 35% at 3 years. Several issues are important when considering long-term outcomes. First is the severity and complexity of reinterventions. Of all reinterventions, the vast majority (approximately 70%-90%) will be performed using endovascular techniques. In these patients, the risk and inconvenience is small. Some patients do require multiple procedures (10%-15%), and with multiple reinterventions patient disability and risk is increased. One to six percent of patients undergoing EVAR will, at some point, require open surgical conversion; the mortality is greater in these patients than if an open repair had been the primary treatment. Nevertheless, the majority of these procedures are solitary, require only local anesthesia, and are well tolerated by patients.

What will the future bring? On the optimistic side, one might predict that as graft designs improve and, with a better understanding of which patients require reintervention, the frequency will diminish. Alternatively, as our experience with endovascular repair expands and the number of patients with long-term implants increases, the magnitude of the problem might expand. The final common outcome that should be measured when interventions for AAAs are compared is aneurysm-related mortality. For both EVAR and open repair, this includes death at the time of the initial treatment, as well as subsequent mortality related to rupture and or reintervention.

There has been recent concern that the annual rate of aneurysm-related death (following the initial intervention) is greater with EVAR than after open repair. While this is likely to be true, there are several caveats to consider. First, because the mortality associated with EVAR in the perioperative period is 2% to 3% less than that of open repair, even if the late mortality for EVAR is higher it will take some time for the overall mortality of EVAR to “catch up” to open repair. Second, the rate of reinterventions and complications after open repair has, in general, not been as closely scrutinized. Possibly with closer follow-up we will find that the late mortality for open repair is higher than is currently thought. Last, it is also important to realize that the average life expectancy for patients treated for aneurysm disease is 8 years. If the late mortality associated with EVAR is 0.4% per year versus 0.2% per year for open repair (numbers derived from a December 14, 2003, FDA notification), this would equate to a cumulative excess mortality associated with EVAR over 8 years of 1.6% versus 0.8% for open repair. This 0.8% difference is substantially less than the 2% to 3% “savings” in mortality afforded by EVAR at the time of initial operation. Under this circumstance, the overall mortality for both interventions would become equivalent (ie, the lines would cross) 10 years after the initial procedure (longer...
than the average life expectancy of these patients). This hypothetical paradigm is outlined in Figure 1.

COST

New technology is costly and endovascular repair is no exception. At the time of introduction of EVAR, it was postulated that the increased cost of the device would be outweighed by the savings from the decreased hospital stay. The majority of economic analyses, however, have shown that at least for the initial hospitalization, the cost of EVAR exceeds that of traditional surgery. This is not a problem unique to EVAR. The cost of drug-eluting stents, left ventricular assist devices, as well as a multitude of other new pharmaceuticals and devices, is placing increasing economic pressure on our health care system. That said, our society at least to this point, has not restricted access to new technology.

“The majority of economic analyses, however, have shown that at least for the initial hospitalization, the cost of EVAR exceeds that of traditional surgery.”

We seem willing to pay for therapies that are less invasive and allow longer life. We, and others, have performed cost-effective analyses comparing EVAR to traditional surgery. There appear to be three important variables in these analyses. The first factor, as previously mentioned, is the cost of the initial intervention. A second variable is the cost associated with monitoring patients and for reinterventions. The magnitude of these costs is still unclear but they are not inconsequential. A third variable not often considered is the economic savings associated with a reduction in the rate of perioperative complications with EVAR. If a patient has a stroke, a myocardial infarction, or develops renal failure after an open surgical repair but not after EVAR, the savings for EVAR can be substantial. Complications are costly. For example, the cost for a patient who has a major stroke can be as high as $160,000 over a 5-year period. Data from state and national datasets clearly demonstrate a lower rate of complications associated with EVAR.

Ultimately, the impact of all three factors needs to be considered when the cost-effectiveness of the two techniques is compared. Nevertheless, new technology, including EVAR, is undeniably expensive. At least at this point in time, insurers and hospitals appear to have accepted its economic impact.

PATIENT PREFERENCE

One of the driving forces for the development of endovascular interventions is the desire of patients for less-invasive therapy. In the context of AAA repair, it has been suggested that an endoluminal approach results in less postoperative pain and weakness, as well as gastrointestinal and sexual dysfunction. The result is an overall improvement in patient’s quality of life (QOL). Most interventionalists who have participated in both open and endovascular procedures would agree that, at least for the first 30 days after intervention, the difference in patient disability can be quite significant. Of course, there are exceptions; the endovascular procedure gone awry or an open aneurysm repair in a 60-year-old patient who is discharged on the third postoperative day. A number of investigators have studied patient QOL after both open and endovascular repair. In a subpopulation of patients from a Dutch randomized trial, QOL was assessed using a patient questionnaire administered at various time points after the procedure. Patients undergoing EVAR experienced a higher QOL in the early postoperative period. Identical findings have been reported by several additional authors. By 6 months, however, QOL appears to reach equivalence for open repair and EVAR. Thus, this initial benefit to patients persists for a defined period of time. Less clear is whether there may be a reversal in QOL in patients beyond 6 months. Reasons for this might include the need for lifelong monitoring with CT or the need in some patients for reintervention. Larger studies with longer follow-up will be necessary to define the impact of late events on patient acceptance of endovascular techniques.

With regard to medical treatments, patients are assuming an increasingly dominant role in decisions about their care. Factors that contribute to patient’s decisions are complex; these decisions are not always based upon statistics or a rational weighing of risks and benefits. Many patients, particularly those in their later years, are much more interested in what will happen during the next 6 months of their life versus the next 6 years. If they choose endovascular repair, they will experience a potentially less stressful operation that is associated with a significantly lower mortality and morbidity. Admittedly, beyond 6 months, endovascular repair results in the inconvenience of long-term monitoring and the stress, morbidity, and mortality associated with reinterventions and/or late aneurysm rupture. From a scientific standpoint, the cumulative risk from the latter could potentially outweigh the former. However, a large number of patients, even when fully informed of these
relative risks, will choose an approach that leads to less immediate risk and discomfort. What is our obligation as interventionalists? First and foremost, to conduct prospective, well-designed scientific studies of the various available alternatives. Data are most important and remain a very powerful factor in influencing patient behavior. Second, it is necessary, to the best of our ability, to be certain that our patients are educated and well informed about the various options. Fortunately, many of the physicians experienced in traditional open aneurysm repair also perform endovascular interventions. Thus, patients can be made fully aware of the advantages and disadvantages of both techniques, without the introduction of bias. The ultimate decision, however, is that of the patient and we are finding with increasing frequency that less-invasive procedures are what patients want.

**IS EVAR THE GOLD STANDARD?**

So, is EVAR the gold standard for the treatment of AAAs? The answer is no. There currently is not a gold standard, nor with the availability of two excellent techniques, should there be. In many patients, EVAR will be the preferred approach; however, there are still a number of patients who will achieve greatest benefit from traditional open surgery. Is EVAR here to stay? The answer is most certainly yes. Fourteen years of experience have demonstrated that EVAR is far from a failed experiment. Both regionally and nationally, EVAR is currently used with the same or a greater frequency than standard open repair. Initial outcomes are encouraging. This technology can be widely applied. Long-term outcomes remain to be defined. Nevertheless, our patients want this technology despite our admonitions and despite the unavailability of randomized long-term data. That said, we should encourage and participate in ongoing comparative evaluations of open versus endovascular repair. Moreover, we should participate in clinical and scientific research that can lead to improved devices, patient selection, and a better understanding of the natural history of EVAR-associated complications. With many such studies currently underway, it seems likely that short- and long-term outcomes associated with EVAR will continue to improve. Ultimately, our approach for patients with aneurysms should be no different than our global approach to patient care. Individualize each patient. Choose the technique that satisfies the patient’s physical and emotional needs, as well as provides an effective and durable outcome.

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From 1996 to 1999, a total of 1,193 patients with infrarenal abdominal aortic aneurysms were treated with the AneuRx (Medtronic, Santa Rosa, CA) stent graft during the course of a multicenter clinical trial. This patient experience is unique because it represents the largest multicenter experience with a single endovascular device and provides the longest comprehensive follow-up of a closely monitored patient cohort. Long-term primary outcome measures reveal 97% freedom from rupture, 97% freedom from aneurysm-related death, 91% freedom from surgical conversion and 62% probability of survival at 5 years by Kaplan-Meier analysis. Secondary outcome measures include stent graft patency in 91%, endoleak in 15%, aneurysm enlargement in 15%, and stent graft migration in 6% of patients at 5 years. The patients treated in this trial represent the very first clinical experience with endovascular repair at most of the 19 clinical sites and thus provide important lessons learned during the evolution of a new endovascular strategy to treating aneurysms. These lessons include the importance of patient selection, proper imaging and precise stent graft positioning, and the importance of fixation in avoiding adverse outcomes, such as migration and rupture. This knowledge is now applied to current clinical practice.

The AneuRx stent graft system has evolved to a fourth-generation device since completion of the clinical trial with improvements in stent design, fabric material and delivery system. These improvements to these product iterations should ensure continued long-term success.

The cumulative clinical trial data and commercial experience involving more than 40,000 implants show that the AneuRx stent graft is a safe and effective therapy option for patients with AAA disease (Figure 1). This experience provides a unique opportunity to reflect on what has been learned about the device as well as about the durability of endovascular repair.

THE CLINICAL TRIAL, PATIENT SELECTION, AND DEVICE CHANGES

The AneuRx Clinical Trial

The AneuRx clinical trial was conducted in three phases at 19 US investigational centers from 1996 to 1999. The Phase I study consisted of 40 patients treated...
from 1996 to 1997. The Phase II study included 424 patients treated with the AneuRx stent graft and 66 control patients treated with open surgical repair from 1997 to 1998. The Phase III study included 639 patients treated from 1998 to 1999 (Table 1). Patient selection criteria included an abdominal aortic aneurysm with an infrarenal neck length of at least 10 mm and a neck diameter between 18 and 26 mm, with a maximum distal iliac diameter of 15 mm. Since completion of the trial, patient selection criteria have been modified to include a recommended 15-mm aortic seal zone, a 25-mm iliac seal zone, and an aortic neck angulation of <45º. A cohort of 90 patients who did not meet the inclusion criteria of the trial were treated with the AneuRx stent graft in a high-risk study arm and these patients are also included in the data analysis. During the course of the clinical trial, the AneuRx device evolved from a first-generation device that had a stiff bifurcation stent design and a looser fabric weave (257 patients) to a second-generation device that had a flexible bifurcation stent design and a denser fabric weave (936 patients). Since completion of the clinical trial, a third-generation device, incorporating an improved delivery system with a tapered nosecone and reduced friction to reduce device “pull-down” during retraction of the delivery system, was introduced in 2002. A fourth-generation device with a high-density fabric designed to reduce porosity and to increase abrasion resistance will be introduced in summer 2004 (Figure 2). The first-generation devices, as well as the early learning curve experienced by investigators, must be considered when evaluating the results of this clinical trial.

RESULTS
Primary Outcome Measures
The primary outcome measures are related to the primary objectives of aneurysm repair, namely prevention of rupture and prevention of death from rupture or
from efforts to treat the aneurysm (AAA death). AAA death includes death from any cause within 30 days of primary or secondary treatments and any death related to the aneurysm or endovascular device. Conversion to open surgical repair and all-cause mortality are included as primary outcome measures. A summary of early and late results as well as Kaplan-Meier estimates are shown in Table 2.

The Kaplan-Meier estimates of the primary endpoints at 5 years, freedom from aneurysm rupture, including intraoperative, and early and late ruptures was 97%. Similarly, freedom from aneurysm-related death at 5 years was 97%. There were 286 patients at risk at the 4- to 5-year time interval and the Kaplan-Meier curves are flat, which suggests no increasing late risk of rupture or aneurysm-related death.

Freedom from surgical conversion by Kaplan-Meier analysis at 5 years was 91%. A total of 45 patients (3.8%) underwent surgical conversion at >30 days. Operative mortality rate for patients undergoing late surgical conversion is 13%. Patient survival at 5 years was 62%, with the majority of deaths due to nonaneurysm-related causes.

Secondary Outcome Measures
Endoleak was present in 13% of patients at 4 years, and 15% of patients at 5 years, and is ongoing throughout the course of the trial. Aneurysm enlargement >5 mm was present in 14% of patients at 4 years and 15% of patients at 5 years. Stent graft migration was noted in 9% of patients at 4 years and 6% at 5 years. Primary stent graft patency was 96% at 4 years and 91% at 5 years.

These outcome measures have been studied extensively and are the subject of ongoing investigation. Much has been learned since completion of the clinical trial and lessons learned have been incorporated into training courses and applied to current clinical practice. It is expected that the knowledge gained and improve-

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<tr>
<th>Table 1. US AneuRx Clinical Trial</th>
<th>Patient entry 1996 - 1999</th>
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<tbody>
<tr>
<td>Phase 1</td>
<td>40 patients</td>
</tr>
<tr>
<td>Phase 2</td>
<td>424 stent graft vs 66 open surgery</td>
</tr>
<tr>
<td>Phase 3</td>
<td>639 patients</td>
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<tr>
<td>Phase 2/3</td>
<td>90 high risk / compassionate use</td>
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<tr>
<td>Total</td>
<td>1,193 patients</td>
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| Table 2. Primary Outcome Measures |

<table>
<thead>
<tr>
<th>AneuRx US Clinical Trial (n = 1,193)</th>
<th>Intraoperative</th>
<th>≤30 days</th>
<th>&gt;30 days</th>
<th>Total</th>
<th>Kaplan-Meier freedom from event at 5 years</th>
</tr>
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<tbody>
<tr>
<td>Aneurysm Rupture</td>
<td>2/1,193</td>
<td>3/1,193</td>
<td>15/1,193</td>
<td>20/1,193</td>
<td>97.2%</td>
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<tr>
<td></td>
<td>0.2 %</td>
<td>0.3 %</td>
<td>13 %</td>
<td>1.7 %</td>
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<tr>
<td>Aneurysm-Related Death</td>
<td>0</td>
<td>22/1,193</td>
<td>10/1,193</td>
<td>32/1,193</td>
<td>96.8%</td>
</tr>
<tr>
<td></td>
<td>18 %</td>
<td>8 %</td>
<td>2.7 %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conversion to Surgical Repair</td>
<td>11/1,193</td>
<td>4/1,193</td>
<td>45/1,193</td>
<td>60/1,193</td>
<td>91.1%</td>
</tr>
<tr>
<td></td>
<td>0.9 %</td>
<td>0.3 %</td>
<td>38 %</td>
<td>5.0 %</td>
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<tr>
<td>Death (all causes)</td>
<td>0</td>
<td>22/1,193</td>
<td>283/1,193</td>
<td>305/1,193</td>
<td>61.5%</td>
</tr>
<tr>
<td></td>
<td>18 %</td>
<td>324 %</td>
<td>26 %</td>
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ments in practice will result in improved short- and long-term outcomes.

LESSONS LEARNED

Rupture
The first aneurysm rupture after AneuRx repair was reported in 2000 and failure analysis of ruptures in 2000 revealed that stent graft fixation, rather than the presence or absence of an endoleak, was the primary predictor of risk of rupture. It was noted that patients with the first-generation stiff device were at higher risk of sustaining aneurysm rupture than those treated with the second-generation flexible device. Furthermore, the important influence of neck angulation and length of proximal and distal fixation zones was appreciated from failure analysis after completion of the trial, leading to changes in the instructions for use to include a proximal fixation length of 15 mm (rather than the 10 mm used during the trial), a distal fixation zone of 25 mm (not specified during the trial), and neck angulation of <45° (not specified during the trial).

Endoleak
The primary treatment endpoint during the clinical trial was success in device deployment and elimination of flow in the aneurysm sac (endoleak). Approximately 15% of patients have evidence of ongoing endoleak (usually type II) in long-term analysis, but no differences have been noted in the endpoints of aneurysm rupture, surgical conversion, stent graft migration, or patient survival between patients with and those without endoleak. Endoleak is closely related to an increased likelihood of aneurysm enlargement after endovascular repair, but the significance of such enlargement in terms of risk of aneurysm rupture is still undefined. Continuing close follow-up of such patients is warranted (Table 3). Thus far, there have been no aneurysm ruptures among patients in the AneuRx clinical trial with type II endoleaks, associated with or without aneurysm enlargement.

Enlargement
Decrease in aneurysm size is often considered to be primary evidence of success of endovascular aneurysm repair. Aneurysm size changes and remodeling after endovascular repair may cause loss of fixation and seal, particularly if there is short overlap of modular devices and short fixation zones. The first-generation stiff AneuRx device was particularly prone to this mechanism of failure due to lack of flexibility of the bifurcation module. In an analysis of aneurysm enlargement in the AneuRx clinical trial, 4-year Kaplan-Meier analysis revealed no increase in risk of rupture or decrease in patient survival among 46 patients who experienced enlargement of 5 mm or more after endovascular repair. Predictors of enlargement included patient age, aneurysm size, and the presence of an endoleak. Less than half of patients with evidence of aneurysm enlargement have thus far required treatment and rupture and adverse events were not related to the presence of enlargement. Treatment, when needed, can usually be performed by endovascular means. Eight patients have undergone elective surgical conversion for aneurysm enlargement with two deaths.

Migration
A detailed analysis of migration among clinical trial patients has been carried out in an effort to understand the causes and prevention of migration using the AneuRx device. Migration at any time (>5 mm) after device implantation was noted in 94 of 1,119 patients (8.4%) who had more than one postprocedure image study to evaluate migration. Among these 94 patients, there was one rupture that was successfully treated with open repair. Treatment was required in 29 patients with seven surgical conversions (including the one for rupture) and 22 patients treated with stent graft extenders. No treatment has been required thus far in 69% of

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**Table 3. Key Lessons Learned**

<table>
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<th>Preoperative:</th>
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<tr>
<td>• Accurate CT measurement: adventitia to adventitia</td>
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<tr>
<td>• Proper patient selection</td>
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<tr>
<td>• Proper stent graft oversizing</td>
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<table>
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<tr>
<th>Intraoperative:</th>
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<tr>
<td>• Use proper C-arm gantry to correct for angulation</td>
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<tr>
<td>• Placement at the renal arteries for maximal proximal fixation</td>
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<tr>
<td>• Extend to hypogastric arteries for maximal distal fixation</td>
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<tr>
<td>• Generous overlap of modular components</td>
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<tr>
<th>Postoperative:</th>
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<tbody>
<tr>
<td>• Compliance to follow-up regimen</td>
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<td>• Inadequate fixation requires intervention</td>
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patients. Univariate and multivariate analysis based on Core Lab (University of Virginia) analysis of CT scans for evidence of migration revealed that the significant predictors of migration were length of follow-up ($P<.006$), clinical implant site ($P<.001$), and length of proximal stent graft fixation ($P<.005$). Remarkably, there was variability in migration rate from 0% to 30% among clinical sites, suggesting that factors other than the device itself may be of primary importance in preventing migration. Further analysis revealed that the length of fixation of the proximal end of the stent graft to the aortic neck was a primary predictor of migration. This is consistent with the lessons learned from the rupture analysis, which showed the importance of stent graft fixation. Furthermore, experimental studies to evaluate the importance of iliac fixation reveal a three-fold increase in resistance to in vivo displacement with increased iliac fixation length. This supports the implantation technique of extending to the level of the hypogastric artery in patients to take advantage of the longitudinal columnar support provided by the AneuRx device. These lessons on the causes of migration tell us that it is predictable and preventable. What has been learned after completion of the clinical trial has led to a different concept of successful device deployment based on fixation length. The difference in our concept of successful placement now compared to the clinical trial is shown in (Figure 3).

**DEVICE IMPROVEMENTS**

The AneuRx device has evolved over the past 8 years and is now in its fourth generation. The first (stiff bifurcation and pre-RPM fabric) and second-generation devices (flexible bifurcation design and reduced porosity fabric) were used during the clinical trial from 1996-1999. The third generation of the device introduced in 2002 (the Xpedient delivery system) features a tapered nosecone and provides the option of sheathless access. In addition, a lubricious coating was added to the inside of the graft cover, greatly reducing the likelihood of the device to displace and migrate during retraction of the runners and nosecone. Recently, the fourth generation of the device (March 2004) incorporated a high-density fabric to reduce porosity and enhance durability.

**CONCLUSION**

Kaplan-Meier analysis of 1,193 patients treated with the AneuRx stent graft at 5 years revealed a low aneurysm rupture rate and a low risk of aneurysm-related death, suggesting long-term durability in the effectiveness of the procedure. These clinical results provide evidence that the AneuRx stent graft continues to be a safe and effective treatment option for appropriately selected patients with infrarenal abdominal aneurysms.

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The last decade has seen tremendous growth in the use of endografts for the treatment of aortic aneurysms. With the introduction of second- and third-generation devices, more patients are being considered for endovascular repair. This growth has led to great interest in identifying the most effective method to follow endograft patients to ensure their safety and promote the advancement of this technology. Recent advances for the follow-up of these patients include Web-based surveillance software that will organize the patient file and automate the follow-up schedule, advanced MRI that will allow the physician to characterize the state of the excluded sac, specifically in regard to endoleak and endotension, and remote aneurysm sac pressure sensors that may make CT scan surveillance obsolete.

SURVEILLANCE SOFTWARE

As endovascular stent grafts become more prevalent, there will be an increasing number of patients requiring detailed follow-up, leading to extensive databases monitoring the aneurysm diameter, volume, presence of endoleak, and status of the proximal and distal landing zones. In an attempt to simplify these databases, industry has developed software to facilitate the follow-up of these patients in an organized, easy-to-use format. One such software package is Stent Graft Tracker by Medtronic, Inc. (Santa Rosa, CA) (Figure 1).

Stent Graft Tracker is a Web-based application that allows physicians to manage patient follow-up and track the main aneurysm endpoint progress. Physicians will log in to the system with a unique username and password and will access a database of the patients they have created in the system. With every new follow-up visit, the physician can record the most relevant data such as aneurysm sac diameter, aneurysm sac volume, presence of endoleaks, and prosthesis migration. Physicians will also be able to upload images linked to every measurement and record notes regarding the case. Finally, the program sends physicians monthly e-mail reminders of patient follow-up due. Stent Graft Tracker will simplify the follow-up of endograft patients and organize the data in a physician’s office. The product is expected to be available in the summer of 2004.

ADVANCED MR IMAGING

A criticism of CT angiography for follow-up of endograft patients has been the inability of CT to accurately characterize the type of endoleak with a high degree of specificity. Similarly, CT cannot characterize the aneurysm sac for the presence or absence of endotension. Recent technological advances have allowed MRI sequences to be developed that have the ability to give physicians a wealth of information about the state of the excluded aneurysm sac after endovascular aneurysm repair (EVAR). These breakthroughs may answer these important clinical questions.

Figure 1. Stent Graft Tracker is a surveillance software that will allow physicians to have a Web-based organized database specifically for their endograft patients. The software will simplify the monitoring of aneurysm size, endoleaks, and office visits.
The most interesting breakthroughs have been in time-resolved or “cine” MRA techniques. This real-time imaging for MRA allows one to visualize the transit of contrast down the aorta and into all the aortic branches (Figure 2). This “virtual MR flush aortogram” can be used to visualize the direction of flow into an endoleak cavity. This technique has already been used clinically with excellent initial results. Time-resolved MRA technique has been compared with conventional angiography in 12 patients with documented endoleaks on postoperative CT scans. There was 100% correlation between the M RAs and the conventional arteriograms in characterizing the type of endoleak.2

Another advancement in MRI technology has been the use of different pulse sequences to characterize the state of the thrombus in the aneurysm sac. This has been studied with standard sequences, such as T1 and T2.3 Recently, “white blood” pulse sequences such as FIESTA and TRUSP have been reviewed (Figure 3). These sequences give bright signal for flowing blood and dark signal for soft tissue and organized thrombus. A recent review of this sequence demonstrated excellent sensitivity for detecting endoleak without the administration of intravenous contrast. The sequence was also able to characterize several cases of endotension in which there was no enhancement within the sac, but there was blood and serum filling a growing aneurysm sac.4 These cases were confirmed by direct puncture of the aneurysm revealing a serum-filled sac or sac hygroma.

One limitation of MRI techniques in the follow-up of endograft patients is the somewhat limited applicability for only those patients with nitinol-based endografts. Stainless steel-based endografts and embolization coils are not MRI compatible and generate a tremendous amount of metallic artifact. As a result, many centers are using more nitinol-based endografts. Similarly, all embolization procedures are being performed with platinum embolization coils.

REMOTE PRESSURE-SENSING TECHNOLOGY

There has been great interest in the ability to remotely record the pressure inside the excluded aneurysm sac.5 Interest in remotely monitoring internal sac pressure is predicated on the belief that the successfully treated aneurysm sac will be depressurized as compared to systemic pressure. In contrast, an aneurysm that continues to be pressured may be at continued risk for expansion and possible rupture.

Two remote pressure-sensing technologies have been...
developed and used clinically. The first human implantation of a remote sensor was the Remon Impressure (Remon Medical Technologies, Caesarea, Israel) pressure sensor (Figure 4) in June 2003 at Mount Sinai Medical Center in New York City. The Impressure device measures pressure using ultrasound energy to activate a piezoelectric capacitor that measures the ambient pressure and transmits the reading back to the ultrasound transducer. To date, 17 patients have been enrolled in the initial clinical site. The pressure sensor has demonstrated excellent correlation between direct catheter measurements in the operating room and has shown excellent mid-term results with the majority of patients currently at 6-month follow-up.6

The second device to reach clinical use is the CardioMEMS (Atlanta, GA) remote pressure sensor. This device utilizes radiofrequency energy to charge a capacitor implant that measures the ambient pressure and transmits the measurement to the receiver outside the patient. This device was initially implanted in five patients in Brazil in April 2004. The initial results for this device have also been encouraging.

The goal of this technology is the ability to remotely monitor the status of the excluded aneurysm sac that will obviate the need for routine CT scans.

**SUMMARY**
The future of endograft surveillance is changing at a rapid rate. As more patients with aortic aneurysms are treated with the endovascular technique, there will be a growing population of patients in postoperative surveil-

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**Figure 3.** MRI diagnosis of endotension. CT scan in a patient 4 years after EVAR of a thoracic aneurysm with a 3-cm sac enlargement. Both contrast-enhanced CT angiography and MR angiography show no evidence of endoleak (A, B). White blood MRI pulse sequence shows bright signal in the sac, which is similar to the aortic lumen (C). Direct puncture of the sac confirmed the diagnosis of sac hygroma (D).

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lance for the rest of their lives. The extensive databases that endovascular specialists will need to maintain will undoubtedly prove to be overwhelming. Automated patient surveillance software will add organization and uniformity to the manner in which endograft patients are followed. Currently, CT scans are most frequently used to monitor endograft patients, which expose the patients to ionizing radiation and nephrotoxic contrast agents. Even state-of-the-art CT technology leaves several questions unanswered with respect to the aneurysm sac after EVAR. The most important question is whether there is an endoleak and, if so, what type? MRA has been shown in previous studies to be more sensitive than CT angiography for the detection of endoleaks, especially type II leaks. With the recent introduction of time-resolved techniques, MRA may now be able to answer these questions with a degree of certainty not previously available.

Another frequent question that CT cannot answer is why certain aneurysms shrink postoperatively and others remain a stable size or even enlarge in the absence of endoleak. Recent advancements in the understanding of the MRI characteristics of the excluded aneurysm sac may offer information that can answer these questions much more effectively than CT scans.

Remote pressure sensors will soon be found to be reliable in the long term. This will make routine scheduled imaging obsolete. Once an aneurysm has depressurized, it will be followed with noninvasive pressure measurements for the rest of the patient’s life. If there are changes in the pressure status of the sac, the patient will be referred for imaging, likely an MRA, to see if the patient has an endoleak and, if so, what type of leak. The patient will then be treated accordingly.

Currently, the most important piece of data for the postoperative patient is the aneurysm diameter and the presence or absence of endoleak. Very soon, these concerns will be replaced by the aneurysm pressure and the composition of the excluded aneurysm sac.

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Figure 4. The Remon Impressure remote pressure transducer (A). The device measures 9 mm X 3 mm X 1.5 mm. The device transmits a pressure waveform to an ultrasound transducer that displays the measurement on a monitor (B).
Throughout the nearly 50-year history of the evolution of thoracoabdominal aortic vascular implants, significant data regarding factors that promote durability of devices in this dynamic and critical environment has been extensively studied. Successful performance of cardiovascular implantation in this location requires firm tissue fixation to ensure long-term stability.

Historically, the initial use of fabrics and homograft prostheses for aortic replacements quickly demonstrated that long-term durability was dependent on permanent fixture to relatively normal, viable, adjacent vascular tissue to preserve the integrity of anastomotic sites. If implantation occurred in nonviable or degenerating vascular tissues, the anastomoses had a high frequency of pseudoaneurysms and were complicated by hemorrhagic events when the anastomoses were disrupted.

Extensive analysis of thoracoabdominal vascular devices demonstrates that human vascular tissues poorly incorporate conventional vascular prostheses fabricated from porous Dacron and Teflon materials, even though in vivo animal studies used to evaluate these materials before clinical use frequently show extensive tissue incorporation. This limited ingrowth of clinical implants in the thoracoabdominal aorta also differs from histologic analyses of devices in peripheral arteries in subcutaneous locations, in which more extensive incorporation may occur. In any location, limited fixation of the vascular graft at anastomotic sites can potenti ate pseudoaneurysm formation when viable arterial wall is not securely attached to the device.

The explantation data from human cardiovascular devices provides a reference point for the evaluation of evolving endoluminal prostheses. Although it can be argued that the intravascular location of endovascular prostheses offers a different environment for incorporation of these devices, there is substantial evidence that secure fixation remains essential for long-term stability. During the early evolution of endovascular device development, circumferential stent deployment provided secure means for incorporation of devices in early animal and clinical experiments, whereas other alternatives that did not provide firm fixation of the fabric to the arterial wall were unsuccessful. At the present time, the clinical experiment that is being conducted using endovascular devices is to examine and determine the means to enhance vascular prosthesis fixation to the arterial wall using various methods, including the widely accepted concept of metal stent apposition to adjacent viable tissue.

The underlying characteristic of aneurysmal arteries is continued elongation and dilation of the vessel wall in segments of the artery that are not replaced or covered by conventional vascular prosthesis or endoluminal devices, respectively. At some point, oversizing of endovascular devices to maintain a firm fixation seal can potentially be defeated by continued arterial enlargement if secure tissue fixation is not present to maintain the integrity of the anastomotic site.

To study and identify the parameters critical to the long-term performance and future enhancement of endovascular prostheses, focused efforts to retrieve and perform explant analysis of human devices is essential. Although noninvasive vascular imaging has progressed rapidly, a clinical correlation from explant analysis to the observed images will dramatically enhance our ability to perform imaging surveillance and make appropriate determinations regarding clinical indications for secondary interventions and to provide information essential for future device development.

RETRIEVAL AND ANALYSIS

A challenging area in investigational cardiovascular surgery has been the systematic retrieval and analysis of cardiovascular devices, with limited methodologies and reports being generated to optimize this effort. Many manufacturers perform explant analyses of their devices, but infrequently disclose the findings. Explants are rarely retrieved...
from patients who have died because the retrieval process requires patient consent and family cooperation in a grieving environment. For this reason, most explant data focus on failed procedures in which devices are retrieved as part of a secondary intervention. Although this information can be useful to identify the cause of failures, the scope of information is often not representative of findings that may occur in the majority of patients with successful implants.

Evaluation of explants from failed devices or emergency conversions is important to address failure modes, but explants retrieved from these procedures frequently have artifacts related to harvesting methods. Most importantly, explants from conversions do not address the factors that promote long-term stability (ie, the most critical factor in the majority of patients).

The focus of this article is to review our experience in organizing an explant retrieval program and to outline the methods that have been utilized to acquire devices after long-term implantation. Several important observations have resulted from this effort. The analyses provide data for enhancing interpretation of current surveillance examinations and help determine appropriate patient selection and follow-up criteria based on the clinical explant information. In the current environment, in which several commercial devices have been implanted for significant intervals in patients, it is our opinion that an appropriate informed consent for a patient should include information regarding the mechanisms of fixation and long-term durability for these devices, and that manufacturers should focus an effort to provide this type of data to clinicians and patients as it becomes available.

Explant analyses are frequently very difficult to conduct, particularly because retrieval of devices from patients who die and who undergo autopsies is dramatically decreasing. In light of these challenges, a specific effort to enhance explant analysis and direct data accumulation has been supported by the Lifeline Registry of the Society For Vascular Surgery, and the information provided in this report is part of a prototype analysis that has occurred in our institution during this evolution. This analysis involves several critical stages, from informing the patient regarding the investigational nature of longitudinal analysis over the interval of implant function, to compliance with regulatory requirements and HIPAA guidelines during data acquisition, storage, and analysis in an expedient manner.

**PATIENT CONSENT AND REGULATORY COMPLIANCE**

The acquisition, analysis, and storage of patient data entails several essential components if the intent is to maintain patient confidentiality, and yet be able to publish clinical and scientific data regarding outcomes. These components are covered during clinical and investigational trials prior to approval of devices using a conventional mechanism in which the patient signs a consent approved by Institutional Review Board (IRB), with analysis of data provided to federal agencies (eg, FDA) by the manufacturers. We have extended this prototype to all patients who undergo implantation of endovascular prostheses and incorporate principles that have been addressed as part of the development of the Lifeline Registry of the Society For Vascular Surgery to enable not only acquisition, storage, and analysis of data from investigational studies, but also to perform similar investigations on data from patients after release of devices for general practice.

To enable expedient and appropriate data acquisition, we obtain consent from all patients (including those being entered into investigational studies and those receiving commercially approved devices) at the time of endovascular prosthesis implantation using a consent form approved by the IRB of our institution. The consent form informs the patient that data will be acquired longitudinally and stored in national registries and local databases for analysis related to long-term function of the device. The patients also are asked to sign consent for explantation of the prosthesis, if appropriate circumstances arise after the death of the patient, along with HIPAA consents to enable storage, retrieval, and reporting of data using mechanisms that preserve patient confidentiality.

The surveillance consent from the IRB asks for permission to follow the patient for the remainder of their life, and the HIPAA consent forms are for 10 years. Such consent enables...
us to appropriately inform patients with endografts that they require long-term surveillance, and it provides permission to obtain and store this data in a HIPAA-compatible fashion over the duration of the patient’s life. It also creates an opportunity to inform the patient regarding the importance of serial follow-up, describes the methods that will be used, including the image and data analysis, and begins the process of making the patient aware of the long-term implications and importance of participating in the longitudinal data analysis.

We find that patients are interested in, and compliant with, this process and are particularly interested in the images that provide a serial record of device performance and potential need for additional interventions. At follow-up visits, images are reviewed with patients if they desire. We believe that the level of compliance with surveillance is enhanced by this mechanism, as is our ability to obtain explants when patients die because the patient and their family have become committed to enhancing the quality of care in this area through an understanding of the importance of the explant data. Information regarding the function and options for participation in the Lifeline Registry are available from several sources, including the registry Web site www.lifelineregistry.com or by contacting the administrative offices at New England Research Institute.1

RETRIEVAL DIFFICULTIES

Explant retrieval has become particularly difficult because the number of routine autopsies performed in hospitals has dramatically decreased, and because patients with implanted devices are infrequently available for explant. Because we have educated patients regarding the importance of this process, we have been notified by several patients who are in a terminal condition, or by families after the death of a patient, that the patient requested that the explant be provided for analysis. We are frequently able to arrange device retrieval on the basis of the consents that have been obtained without requiring a full postmortem examination. The devices are obtained by initially performing en bloc dissection of the infrarenal abdominal aorta from above the visceral vessels to the external iliac arteries, including all surrounding soft tissue and adherent structures.

Care is taken not to deform or disturb the device, with particular care taken to retrieve the prosthesis and preserve the specimen in formalin as soon as possible after the patient has died. After fixation with formalin, the luminal surface of the device can be inspected with an endoscope to observe surface characteristics of the prosthesis, but only if one is careful during explantation to not deform the specimen and create artifacts that would compromise further analysis. The prosthesis is then submitted for pathological examination after embedding the entire specimen in acrylic to enable sectioning of the device, including the stent and fabric materials, while preserving the histologic nature of the surrounding tissues. Levels at which the device will be sectioned can be chosen based on x-rays of the specimen. This also provides information regarding structural integrity for the prosthesis (Figure 1). Histologic sections can then be analyzed and compared to the sequential imaging obtained prior to treatment by means of a detailed analysis of device integrity, tissue apposition, and evidence of tissue fixation. The following explant analysis provides an example of the information that can be obtained.

EXAMPLE PATIENT EXPLANT

A 68-year-old man underwent implantation of a 28-mm diameter X 13-cm length AneuRx (Medtronic, Inc., Santa Rosa, CA) bifurcated device on January 8, 1998. The aneurysm was 5 cm in diameter and had increased in size by 1 cm diameter during the previous 6 months to 2.5 times the normal aortic diameter. The device deployment was uneventful and, during the first several months, the patient was found to have an inferior mesenteric artery lumbar leak that eventually thrombosed. The diameter of the aneurysm progressively decreased until death, with a CT at 9 months prior to death at 4.25 years and 3 months after deployment. At that time, the aneurysm had nearly regressed and the patient had long proximal and distal fixation length. Approximately 5 years after device deployment, the patient became aware that he had terminal cancer and contacted us regarding retrieval of the

![Figure 2. Composite illustration demonstrating colorized rotational images prepared using MMS (Medical Metrix Systems, West Lebanon, NH) Preview Software of the 4.25-year surveillance contrast CT images of the nearly regressed AAA (center) compared to the 5-year centerline CT slices (left) and the histologic sections (right) from levels 2 through 6, as shown on Figure 1.](image-url)
device. Retrieval was successfully accomplished after his death at 5 years and 2 weeks after initial device deployment.

Inspection of the prosthesis demonstrated that there was firm fixation of the proximal aortic neck and iliac limbs, which were encased in a diffuse fibrous reaction in the aortic tissues. Comparison of the centerline CT measurements acquired at 4.25 years to the 5-year histology demonstrated that there was a clear correlation between the CT image and the histologic appearance at the fixation sites (Figure 2).

Additional comparisons were made between intravascular ultrasound (IVUS) examinations made just prior to deployment of the device in January 1998 to the eventual histology and incorporation of the prosthesis. It was apparent from examining the IVUS images that moderate soft plaque over approximately 50% of the diameter with a calcified lesion in the arterial wall did not prevent firm fibrous encapsulation of the outer nitinol stent structure in the AneuRx device when appropriately sized to the media of the arterial wall (Figure 3).

**DISCUSSION**

The importance of device retrieval after endovascular prosthesis deployment is demonstrated by this example case and should be available for all devices that are commercially available so that the mechanism of long-term incorporation is available to treating physicians, and it should be part of the patient informed consent. Obviously, for new prototype devices, this information is not available, but aggressive explant protocols and attempts at retrieval should become available over time to enable accumulation of a data base on all devices.

The method of histologic examination described in this manuscript precludes information that is gained by harvesting devices and digesting tissue from the prosthesis to examine the structural integrity of the fabric and stent. Extensive evaluation of devices using this methodology has been addressed in a separate manuscript and has led to serial modifications in the fabric and stent configuration of the AneuRx device to enhance long-term durability.

**CONCLUSION**

The specimen described in this article demonstrates the utility of the external stent structure of the AneuRx device and supports this method of fixation when the device is appropriately sized and apposed to viable arterial tissues in the proximal neck and distal fixation locations of adequate length and diameter. This fixation occurs even in light of atherosclerotic disease in the aortic segment, as demonstrated, and is an important indication of the types of information that can be acquired regarding vessel characterization prior to implantation as a predictor of healing and long-term stability. The ability to compare CT images to histologic appearance translates to accurate surveillance, and interpretation of the images and will provide enhanced surveillance recommendations once adequate data are accumulated.

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