

# Endovascular TODAY

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## Xcelerate Your Options



Global Leaders Discuss  
Medtronic's Market-  
Leading Portfolio of  
Endovascular Aortic  
Stent Grafts.



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# The Talent™ Abdominal Stent Graft

A look at the Talent Abdominal Stent Graft, the Xcelerant® Hydro Delivery System, and the VITALITY Trial.

BY MICHAEL WILDERMAN, MD; PATRICK J. GERAGHTY, MD; AND LUIS A. SANCHEZ, MD

During the last 15 years, endovascular repair of abdominal aortic aneurysms (EVAR) has become widely accepted as a means of treating aneurysms located in the infrarenal portion of the aorta. In addition, as more endovascular grafts with broader applications become commercially available, the number of EVARs performed worldwide continues to increase. Juan Parodi, MD, and colleagues reported the first endoluminal repair of abdominal aortic aneurysms (AAA) in 1991.<sup>1</sup> Since that time, numerous devices have undergone clinical trials, and some have been approved for general use.<sup>2-15</sup> EVAR has been shown to reduce perioperative morbidity, mortality, length of hospital stay, and postprocedure disability. Two randomized trials, the EVAR-1 and DREAM trials, demonstrated a significantly lower mortality rate for EVAR when compared to open repair but a higher need for reinterventions (mostly endovascular) in their patient cohort.<sup>4,14</sup> EVAR is ideally suited for older patients and those with medical or surgical contraindications for open surgical

“The Talent Abdominal Stent Graft has been in the world market for more than 12 years and has undergone minor but critical improvements before its recent approval in the US.”

repair, especially those who have had previous aortic interventions, but it has been increasingly used for all anatomically suitable patients based on the published 5-year results of currently approved devices that have reported excellent rates of freedom from aneurysm rupture (97.2–99.8%), conversion to open repair (91–98.4%), and aneurysm-related deaths (96.8–100%).<sup>16</sup>

## TALENT STENT GRAFT

The Talent Abdominal Stent Graft (Medtronic Vascular, Santa Rosa, CA) (Figure 1) is an advanced second-generation modular system for treatment of AAA based on the original Talent Abdominal Stent Graft design. The Talent Abdominal Stent Graft has been in the world market for more than 12 years and has undergone minor but critical improvements before its recent approval in the US. The device's polyester and nitinol construction was an excellent choice and has not been associated with major material fatigue or transgraft endoleaks since its creation. Its suprarenal wire frame was designed to allow tissue incorporation onto the suprarenal aortic wall and to provide long-term migration resistance and graft stability. The Talent Abdominal Stent Graft has undergone minor improvements associated with electropolishing of the nitinol skeletal support and changing of the connecting bar in the ipsilateral leg from its lateral position to a medial position to avoid material fatigue of this component. The stent graft system received market approval by the FDA in April 2008, based on the results of the most recent Talent trial (eLPS



Figure 1. The Talent Abdominal Stent Graft.



**Figure 2. The CoilTrac Delivery System.**

trial). At 5 years, follow-up from the pivotal trial demonstrated that the freedom from aneurysm-related mortality was 96.5%, the freedom from aneurysm rupture was 98.2%, the freedom from secondary procedures was 94.8%, and the freedom from open conversion was 99.1%.<sup>17,18</sup> These results are comparable to all other approved devices and were obtained in a more challenging population of patients. In the eLPS trial, patients with proximal necks  $\geq 5$  mm in length and moderate neck angulation (up to 60°) were included. The Talent Abdominal Stent Graft has been approved to treat patients whose aortic necks are shorter than for all other approved devices (10 mm required), very angulated (up to 60°), and large (up to 32 mm in diameter with 36-mm devices). In addition, nonclinical testing has demonstrated that the Talent Abdominal Stent Graft is MRI compatible. It can be scanned safely in both 1.5 T and 3.0 T MR systems (from Talent instructions for use).

The device entered the market in the US during the summer of 2008, with its broad range of sizes and the CoilTrac Delivery System (Figure 2), an earlier model used to treat AAA. This delivery system was very suitable to load the Talent device, but it lacked trackability, and it also required a moderate amount of force to deploy the

endovascular graft due to significant friction within the delivery system. The newer delivery system, known as the Xcelarent Hydro Delivery System (Figures 3 and 4), has major advantages over the CoilTrac Delivery System. The hydrophilic coating aids in its trackability within blood vessels and will diminish the risk of access vessel damage associated with nonhydrophilic large introducer systems. The Xcelarent Hydro Delivery System was shown in bench testing to generate 68 times less friction than the previous delivery system, which did not have a hydrophilic coating. In addition, it features a uniquely integrated sheath that is tapered at both ends. This dual-taper sheath is designed to facilitate insertion and retraction of the entire delivery catheter by minimizing the time that the surface area of the sheath is in contact with the arterial wall. This integrated sheath also lends itself to a lower-profile design to further aid in advancing the device through small and/or tortuous vessels. Another advantage of the delivery system is the dual-action style that enables precise slow deployment during critical portions of the procedure and more rapid deployment afterward. Overall, the Xcelarent Hydro Delivery System will further improve the accurate deliverability of the Talent Abdominal Stent Graft in all types of arterial anatomical situations.



**Figure 3. The Xcelarent Hydro Delivery System.**



**Figure 4. The entire Xcelarent Hydro Delivery System includes the hydrophilic coating and a tapered tip.**



The Talent Abdominal Stent Graft with the Xcelerant Hydro Delivery System is being introduced in the US endovascular market. The first case treated with this system in September 2008 was an 81-year-old man who presented with abdominal pain and a history of a small AAA. A CT scan revealed a 5.6-cm infrarenal AAA. The anatomy of his AAA, as determined by three-dimensional reconstructions, included a fairly short (12 mm) 32-mm-diameter neck, and he was considered a good candidate for treatment with the Talent Abdominal Stent Graft. The patient was treated with a 36-mm device with an excellent result. The device readily advanced through the tortuous iliac anatomy and was easy to deploy, with minimal force necessary for accurate graft deployment. The patient had an uncomplicated hospital course and was discharged home on postoperative day 1.

## VITALITY TRIAL

As a condition of approval of the Talent Abdominal Stent Graft, the FDA requested a postapproval study to evaluate the device under market conditions. The VITALITY trial has been organized for this purpose. Dr. Luis Sanchez of the Washington School of Medicine is the national principal investigator of this study. The primary endpoint for this trial is freedom from aneurysm-related mortality at 5 years (1,826 days). Aneurysm-related mortality is defined as death from rupture of the AAA or from any procedure intended to treat the AAA. If a death occurs within 30 days of any procedure intended to treat the AAA, it is presumed to be aneurysm-related.

In addition, the trial will evaluate some other metrics, such as technical success and major adverse events within 30 days of the initial or subsequent procedures, including all-cause mortality, bowel ischemia, myocardial infarction, paraplegia, procedural blood loss >1,000 mL, renal failure, respiratory failure, or stroke. In addition, the study will look at 12-month and subsequent yearly events, such as all-cause mortality, aneurysm-related mortality, aneurysm rupture, aneurysm growth rate, conversions to open repair, stent graft migration (defined as >10 mm compared to first postprocedure CT scan), stent graft patency, and stent graft integrity. The study incorporates the test group of patients (166) from the initial trial, plus 94 new patients that will be prospectively enrolled. The goal is to follow all of the patients for a minimum of 5 years. We expect to start the VITALITY trial in the last quarter of 2008.

## CONCLUSIONS

Although more research needs to be done, and more data need to be collected, the Medtronic Talent Abdominal Stent Graft using the Xcelerant Hydro Delivery System is a

very attractive, promising, and broadly applicable endovascular graft to treat a variety of anatomic situations in patients with AAA. ■

*Michael Wilderman, MD, is Vascular Surgery Fellow, Section of Vascular Surgery, Department of Surgery, Washington University School of Medicine, St. Louis, Missouri. He has disclosed that he holds no financial interest in any product or manufacturer mentioned herein. Dr. Wilderman may be reached at wildermanm@wudosis.wustl.edu.*

*Patrick J. Geraghty, MD, is Associate Professor of Surgery and Radiology, Section of Vascular Surgery, Department of Surgery, Washington University School of Medicine, St. Louis, Missouri. He has disclosed that he is a paid consultant to Stereotaxis, Inc. Dr. Geraghty may be reached at geraghtyp@wudosis.wustl.edu*

*Luis A. Sanchez, MD, is Professor of Surgery and Radiology, Section of Vascular Surgery, Department of Surgery, Washington University School of Medicine, St. Louis, Missouri. He has disclosed that he is a paid consultant to Medtronic. Dr. Sanchez may be reached at sanchezl@wudosis.wustl.edu.*

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# Talent™ Thoracic Stent Graft With Xcelerant® Delivery System

A review of the recently approved device, the delivery system, and THRIVE study design.

BY KARTHIK KASIRAJAN, MD

**A**lthough the Talent Thoracic Stent Graft (Medtronic Vascular, Santa Rosa, CA) has been sold outside of the US since 1998, the cases described in this article are some of the first few combining the Talent Thoracic Stent Graft with the Xcelerant Delivery System (Figure 1). The Talent Thoracic Stent Graft was, until recently, available with the CoilTrac Delivery System in the VALOR trial and since the product's FDA approval in June 2008. The Xcelerant Delivery System has been used in the VALOR II thoracic trial, which is studying the Valiant® Thoracic Stent Graft in the treatment of descending thoracic aneurysms.

The Talent Thoracic Stent Graft is currently being converted exclusively to the Xcelerant Delivery System since this enhanced delivery system was approved this summer. The Xcelerant Delivery System (Figure 1) is more easily trackable in patients with tight angles, and the shorter nose cone of the Xcelerant Delivery System is easier to navigate around the aortic arch than that of the CoilTrac Delivery System. The Xcelerant Delivery System helps provide a highly controlled and precise proximal deployment to accurately place the device at the intended target zone. In the author's experience, the ability to deploy the device gradually helps to fine-tune the location of the proximal graft deployment, thereby achieving a circumferential approximation to the inner curvature of the aorta and



Figure 1. The Talent Thoracic Stent Graft on the Xcelerant Delivery System.

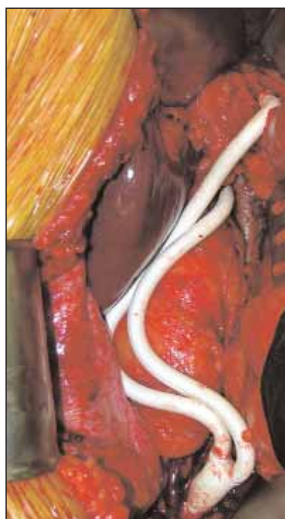


Figure 2. Right iliac to superior mesenteric artery and celiac artery bypass.



Figure 3. The Talent Thoracic and Abdominal Stent Grafts prior to deployment of the contralateral limb.



Figure 4. Completion angiogram on the patient with the Talent Thoracic and Abdominal Stent Grafts with visceral debranching.



**Figure 5.** Aneurysmal degeneration of the false lumen in a patient with a previous type A dissection repair.

avoiding any inadvertent proximal or distal migration during deployment.

The first case was a 54-year-old man who had a dumbbell-shaped, 6.7-cm, type IV thoracoabdominal aneurysm, with a transplanted kidney in the left iliac fossa. The patient had a history of Marfan's syndrome with previous brachial and subclavian and axillary artery aneurysm repairs. He was deemed to be at high risk for open surgery due to the connective tissue disorder, renal failure, and chronic obstructive pulmonary disease. Hence, we decided to perform a staged visceral

debranching procedure. In the first stage, a bypass was performed from the right iliac artery to the celiac/superior mesenteric artery (Figure 2). After a 1-week recovery period, one Talent Thoracic Stent Graft (34- X 34- X 112-mm) was deployed as a proximal main device, and a 38- X 34- X 112-mm device was used as a distal extension. These were then used as a proximal landing zone for a standard Talent bifurcated Abdominal Stent Graft (Figure 3).

The completion angiogram demonstrated excellent flow to both the celiac and superior mesenteric arteries with no evidence of an endoleak (Figure 4). The patient recovered well with no paraplegia and was discharged a week after the endografting procedure.

In the second case, a 72-year-old male, who previously had a type A dissection and an open surgery to replace part of his ascending aorta and arch (elephant trunk), was treated for a proximal descending thoracic aneurysm (Figure 5). The complicating factor was the acute angle between the arch and the descending thoracic aorta (Figure 6).

The case plan was to deploy three devices. The first proximal main was a TF3434112X. Two 38- X 34- X 112-mm Talent Thoracic Stent Grafts were then deployed to extend the length of coverage distally. Despite the steep proximal angle, the Xcelerant Delivery System was easy to track (Figure 7), and the deployment was controlled and precise, allowing the graft to be deployed accurately, just to the left of the subclavian artery. The final angiogram (Figure 8) showed no endoleak, and the patient was discharged the next day.

### THRIVE: DESCENDING THORACIC AORTIC ANEURYSM ENDOVASCULAR REPAIR POSTAPPROVAL STUDY

THRIVE is the Talent Thoracic Stent Graft postmarket, nonrandomized, multicenter study to evaluate the long-term clinical performance of the stent graft for treatment

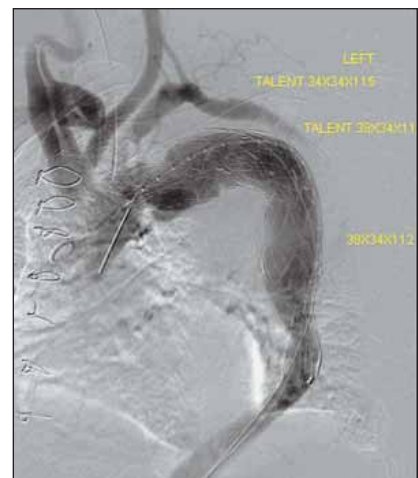
(Continued on page 31)



**Figure 6.** Diagnostic angiogram demonstrates the acute angle between the arch and the descending thoracic aorta.



**Figure 7.** The Talent Thoracic Stent Graft on the Xcelerant Delivery System demonstrating the short nose cone allowing for more proximal trackability and additionally demonstrating the flexibility of the entire stent system across difficult angulations.



**Figure 8.** A completion angiogram demonstrates accurate graft deployment with exclusion of the aneurysm.



# US Experience With the Talent™ Abdominal Stent Graft

Results of the Talent Abdominal US trial show that the eLPS Talent expands the indication of EVAR to approximately 20% more patients.

**BY IRENE C. TURNBULL, MD; RAJESH MALIK, MD; SHARIF H. ELLOZY, MD;  
ALEXANDER SALLOUM, MD; AGELIKI G. VOYOUKA, MD; VICTORIA J. TEODORESCU, MD;  
MICHAEL L. MARIN, MD; AND PETER L. FARIES, MD**

Since the introduction of endovascular repair for the treatment of abdominal aortic aneurysms (AAAs) by Parodi et al,<sup>1</sup> there has been a rapid worldwide expansion of the technique, along with various modifications to the stent grafts that are employed. These modifications range from the original surgeon-made devices to the currently commercially fabricated devices, and there have been at least 16 different devices involved in endovascular AAA repair (EVAR).<sup>2</sup> As the stent graft industry has evolved, the indications for EVAR have also changed, resulting in widening indications of its use.<sup>3</sup> However, anatomical constraints still continue to be a main factor that excludes a large number of patients as candidates for EVAR.<sup>4</sup>

The appropriate selection of cases and devices to be used has an impact on successful aneurysm exclusion and perioperative and postoperative complications. The inclusion of patients with challenging aneurysm morphology increases the risk of failure of the repair.<sup>5</sup> The devices have characteristics that satisfy different aspects of the anatomic and physiologic conditions of the AAA, which vary among patients, and therefore, the choice of stent graft must be evaluated individually.<sup>3,5</sup>

The most recent version of the Talent Abdominal Stent Graft (Medtronic Vascular, Santa Rosa, CA), the enhanced Low-Profile System (eLPS), received approval from the FDA for its commercial distribution in April 2008. There is extensive experience with its use, with more than 73,000 devices distributed worldwide, including the eLPS version of the Talent Abdominal Stent Graft using different types of delivery systems. The device features a bare-metal frame in the proximal aortic fixation portion of the stent graft, which provides for suprarenal fixation. It has been

used in short and angulated proximal aortic necks.<sup>6,7</sup>

This article describes the clinical outcomes using the Talent Abdominal Stent Graft in the US pivotal trial and the impact of this experience on the indication of EVAR for patients with challenging aortic neck morphology.

## TALENT ABDOMINAL STENT GRAFT: LONG-TERM CLINICAL OUTCOMES

The data that support the safety and efficacy of the Talent Abdominal Stent Graft were obtained from different trials. The various study groups that contributed to these data include the pivotal trial, physician-sponsored Investigational Device Exemption (IDE) studies on the stent graft and the delivery system, IDE studies inclusive of previous iterations of the stent graft, expanded access cases (emergency or compassionate use), and additional clinical information, as well as clinical and commercial experience outside the US.

The Talent Abdominal Stent Graft pivotal trial utilizing the eLPS version resulted in a prospective clinical dataset obtained from 13 sites across the US. A total of 166 subjects were enrolled in the test group (eLPS group) from February 25, 2002, through April 14, 2003. Outcomes from 243 subjects who underwent open surgical AAA repair at facilities across the US were included in the control group; these data were obtained from the Society for Vascular Surgery Endovascular AAA Surgical Controls Project. An independent core lab and Clinical Events Committee evaluated and adjudicated major adverse events for the eLPS group. Outcomes between the eLPS and control groups were compared at 30-day and 12-month follow-up.

The patients underwent CT angiography for analysis of the baseline aneurysm characteristics, which were then



TABLE 1. BASELINE ANEURYSM MORPHOLOGY: eLPS GROUP

Characteristic	Site Reported				Core Lab Reported			
	N	Min	Max	Mean±SD	N	Min	Max	Mean±SD
Maximum aneurysm diameter (mm)	166	43	87	57.1±8.4	156	38	88	55±9.2
Proximal neck diameter (mm)	165	16	32	25.6±3.3	156	16	32	25.3±3.5
Right iliac diameter (mm)	164	6	16	9.3±1.5	155	6	14	9.2±1.5
Left iliac diameter (mm)	164	6	14	9.3±1.4	155	6	15	9.3±1.5
Proximal neck length (mm)	166	3	85	23.9±12.8	154	3	75	22.9±12.4
Aortic neck angle (°)	157	0	60	18.7±15.4	127	0	72	30.5±15.8

reviewed both at the site where each patient was treated and at a core lab facility. The aortic diameter was recorded for patients in both groups. The mean maximum aneurysm diameter was 57.1±8.49 for the eLPS group and 56.9±11.59 for the control group, the difference being not significant ( $P=.826$ ). Additional morphological characteristics were analyzed for the eLPS group, which included proximal neck diameter, proximal neck length, aortic neck angle, and bilateral iliac artery diameter. The anatomical configuration measurements were comparable between the site and core lab reports, except for the aortic angle, in which a greater angulation of the aortic neck was reported at the core lab (Table 1). The composite anatomic factor severity score proposed by the Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery grades the factors that affect outcomes in a scale ranging from 0 to 3 (from absent to severe).<sup>8</sup> Of the individuals included in the eLPS group, the morphological features of the aneurysm included cases that were scored as moderate and severe based on the categorization of the initial morphological state:

- Aortic neck length >10 mm and <15 mm was scored as moderate (present in 35 of 154 evaluated patients [22.7%]).
- Aortic neck length <10 mm was scored as severe (present in 17 of 154 evaluated patients [11%]).

Preliminary reports on the perioperative clinical outcomes demonstrated significant superior results in the eLPS group when compared to the surgical control group, as described in the Medtronic Talent Abdominal Stent Graft instructions for use (IFU). The rate of freedom from major adverse events group was significantly superior when compared to the surgical control group (89.2% vs 44%). At 1-year follow-up, the patients from the eLPS group continued to show superior freedom from major

adverse events (80.4% vs 41.7%). Additional clinical outcome measures at 1-year follow-up were comparable between the two groups, with a slight superiority of the eLPS group. The freedom from aneurysm-related mortality rate at 1 year was 97.9%; there were no aneurysm ruptures or conversions to open repair in the first 12 months after the procedure.

Further analysis of the technical and clinical outcomes was performed for the eLPS group during the first 12 months after the initial procedure. The clinical outcomes were excellent, with rates that surpass 90% for successful aneurysm repair at 12 months, freedom from type I or type III endoleak, and freedom from secondary endovascular procedures. Almost all subjects remained free from events of migration. These observations extended to the 5-year reports of those patients who have completed the interval, maintaining excellent rates of freedom from aneurysm rupture, freedom from secondary endovascular procedure, and freedom from surgical conversion.

## DISCUSSION

The Talent Abdominal Stent Graft is a modular stent graft preloaded in a delivery system. It has four components that consist of a bifurcated body, a contralateral iliac limb, an iliac extension cuff, and an aortic extension cuff. In addition, the converter and occluder configurations allow for its use as either a bifurcated or an aorto-uni-iliac device. The stent graft is composed of a Dacron fabric and a nitinol frame, with a 15-mm bare-metal portion in the proximal end that allows for suprarenal fixation. Extensive bench testing led to the development of its most recent version, the eLPS, as an improvement to earlier iterations. The eLPS has a new metal surface finish and a connecting bar along the medial side of the ipsilateral iliac limb.<sup>9</sup>

TABLE 2. MOST COMMON FACTORS FOR EXCLUSION FROM EVAR

Author (Year)	No. of Patients	Eligible for EVAR	Overall Unfavorable Neck Anatomy	Proximal Neck Morphology Factors			
				Length <15 mm	Angulation >60°	Diameter >28 mm	Presence of Thrombus
Carpenter (2001) <sup>14</sup>	307	66%	-	54%	14%	40%	10%
Arko (2004) <sup>13</sup>	220	55%	74%	44%	-	25%*	7%
Moise (2006) <sup>4</sup>	547	63%	-	48%	10%	32%	5%
Cotroneo (2006) <sup>3</sup>	130	39.30%	51.9%	24.1%	-	6.3%†	7.6%

\*Neck diameter >26 mm.

†Neck diameter >30 mm.

The concept of suprarenal fixation has been described as a feature that expands the indication of EVAR.<sup>10</sup> This characteristic allows successful stent graft deployment in patients with shorter and angulated necks. Previous reports on the Talent Abdominal Stent Graft have outlined the particular benefit of its use when treating patients with unfavorable proximal neck anatomy,<sup>9,11</sup> and this is exemplified by the published results of the Talent LPS pivotal trial (which is the earlier version of the eLPS) in which 38.6% of patients had a neck length of 15 mm or less, and 19% had a proximal aneurysm neck of 10 mm or shorter. In the assessment of outcomes, the incidence of endoleaks at 12 months was not significantly different when comparing patients with short necks (<15 mm) to those with longer necks (4% vs 13%;  $P=.2$ ). Also, the rates of diameter sac changes and migration were no different between these two groups.<sup>9</sup>

The number of patients who are considered eligible to undergo EVAR varies from 80% to as low as 25% to 30%, in some reports.<sup>3</sup> Morphological characteristics that are a main reason for denial of endograft repair include aortic neck diameter, neck length, angulation, presence of thrombus, and neck configuration.<sup>12,13</sup> The morphology of the proximal aortic neck has an impact on the effectiveness of the repair in attaining exclusion and long-term durability of the repair.<sup>3,5,12</sup>

Adverse proximal neck morphology is the most common cause for exclusion from EVAR and the most challenging factor. Cotroneo et al reported that unfavorable anatomy of the proximal neck was the main factor for ineligibility for EVAR in 51.9% of patients; when each characteristic of the neck morphology was analyzed, an infrarenal neck length <15 mm was the most common exclusion factor (present in 24.1% of patients), followed by neck diameter >30 mm (present in 6.3% of patients).<sup>3</sup> Similarly, other studies have also reported a neck length <15 mm as the cause of exclusion from EVAR in 24.1% to 54% of patients (Table 2).<sup>4,13,14</sup>

The conditions that must be met to enable the use of the eLPS Talent Abdominal Stent Graft for EVAR include iliac/femoral access vessel morphology that is compatible with vascular access techniques, devices, and/or accessories; a proximal aortic neck length of  $\geq 10$  mm; a proximal aortic neck angulation of <60°; a distal iliac artery fixation length of 15 mm; an aortic neck diameter of 18 to 32 mm; iliac artery diameters of 8 to 22 mm; and vessel morphology suitable for endovascular repair.

When comparing the parameters of aneurysm morphology, the eLPS Talent Abdominal Stent Graft expands the indication of use of EVAR when dealing with shorter necks, larger aortic neck diameter, and larger iliac artery diameter. All other FDA-approved devices require a neck length >15 mm, the largest acceptable aortic neck diameter of <32 mm, and a maximum iliac artery diameter of <22 mm, according to their IFU.<sup>15</sup> A direct correlation of the percentage of patients with short neck length and the increase in number of patients eligible for EVAR with the use of the Talent eLPS is not possible because the anatomic suitability for EVAR is not dependent upon only one restraining characteristic, and the presence of other exclusion factors can preclude its use. It is estimated that approximately 20% of patients considered ineligible for endovascular repair will be benefited by the use of the Talent eLPS.

When one or more anatomic constraint criteria are not completely fulfilled with either device, the possibility of a graft-related complication increases. Abruzzese et al compared outcomes of EVAR when performed outside of at least one device-specific IFU in 222 of 565 (39.3%) stent grafts. The stent grafts employed were AneuRx (Medtronic Vascular), Excluder (Gore & Associates, Flagstaff, AZ), and Zenith (Cook Medical, Bloomington, IN). Events in which stent graft placement was performed outside of the IFU occurred more frequently in cases with larger maximum sac diameter, shorter neck length, larger neck diameter,

greater neck angulation, and greater sac angulation. With regard to the clinical outcomes, patients who had procedures performed outside of the IFU had lower rates of freedom from aneurysm-related mortality and from graft-related adverse events at 1 and 5 years after the initial procedure.<sup>15</sup> Cautionary notes have been published regarding the extended use of endovascular repair when facing limiting anatomic constraints, considering a more conservative approach.<sup>2,5,15,16</sup> Thus, the choice to expand the indication of EVAR remains a measure that must be considered individually. Inclusion of subjects that have challenging aneurysm anatomy requires careful attention to the potential risk for associated stent graft and procedure complications and also requires dedicated follow-up.

## CONCLUSION

Aortic neck length, diameter, and angulation are not the only limiting factors when planning an endovascular repair, but they have been described as the most prevalent factors for contraindication for EVAR. The results of the Talent Abdominal US trial have shown that the eLPS Talent is an excellent choice of stent graft in these cases, expanding the indication of EVAR to an estimated 20% of patients who otherwise could not undergo endovascular repair. In these patients, the satisfactory rates of successful aneurysm repair, as reflected by the excellent clinical outcomes, were maintained. The inclusion of patients with challenging anatomy places them at higher risk for adverse outcomes, therefore careful attention to potential procedure-related associated complications, as well as dedicated long-term follow-up, are required. ■

*Irene C. Turnbull, MD, is from the Department of Surgery, Mount Sinai School of Medicine in New York, New York. She has disclosed that she holds no financial interest in any product or manufacturer mentioned herein. Dr. Turnbull may be reached at (212) 241-5386; irene.turnbull@mssm.edu.*

*Rajesh Malik, MD, is a vascular surgery fellow, Department of Surgery, Mount Sinai School of Medicine in New York, New York. He has disclosed that he holds no financial interest in any product or manufacturer mentioned herein. Dr. Malik may be reached at (212) 241-5386; rajesh.malik@mssm.edu.*

*Sharif H. Ellozy, MD, is Assistant Professor, Division of Vascular Surgery, Department of Surgery, Mount Sinai School of Medicine in New York, New York. He has disclosed that he receives honoraria for speaker fees from Medtronic. Dr. Ellozy may be reached at (212) 241-5315; sharif.ellozy@mssm.edu.*

*Alexander Salloum, MD, is a vascular surgery fellow, Department of Surgery, Mount Sinai School of Medicine in*

*New York, New York. He has disclosed that he holds no financial interest in any product or manufacturer mentioned herein. Dr. Salloum may be reached at (212) 241-5386; alexander.salloum@mssm.edu.*

*Ageliki G. Vouyouka, MD, is Assistant Professor, Division of Vascular Surgery, Department of Surgery, Mount Sinai School of Medicine in New York, New York. She has disclosed that she holds no financial interest in any product or manufacturer mentioned herein. Dr. Vouyouka may be reached at (212) 241-5315; ageliki.vouyouka@mountsinai.org.*

*Victoria J. Teodorescu, MD, is Associate Professor, Division of Vascular Surgery, Department of Surgery in Mount Sinai School of Medicine, New York, New York. She has disclosed that she holds no financial interest in any product or manufacturer mentioned herein. Dr. Teodorescu may be reached at (212) 241-5315; victoria.teodorescu@mssm.edu.*

*Michael L. Marin, MD, is Professor and Chair, Department of Surgery, Mount Sinai School of Medicine, New York, New York. He has disclosed that he is a paid consultant to Medtronic. Dr. Marin may be reached at (212) 241-5392; michael.marin@mountsinai.org.*

*Peter L. Faries, MD, is Professor and Chief, Division of Vascular Surgery, Department of Surgery, Mount Sinai School of Medicine, New York, New York. He has disclosed that he is a paid consultant to Medtronic. Dr. Faries may be reached at (212) 241-5386; peterfaries@mountsinai.org.*

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# Review of VALOR at 1 Year

The 30-day and 12-month results of endovascular treatment using the Talent™ Thoracic Stent Graft System for patients with thoracic aortic aneurysms.

BY RONALD M. FAIRMAN, MD

*Excerpted and adapted from the September 2008 Journal of Vascular Surgery article by Fairman RM et al.<sup>1</sup>*

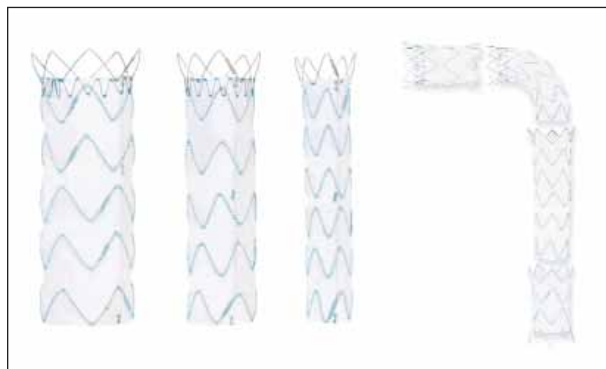
**T**he Talent Thoracic Stent Graft (Medtronic Vascular, Santa Rosa, CA) is a minimally invasive endovascular device that offers an alternative treatment for patients with thoracic aortic aneurysm. This report summarizes the pivotal 30-day and 12-month results of the Medtronic Vascular Talent Thoracic Stent Graft System for the Treatment of Thoracic Aortic Aneurysms (VALOR) trial. These endovascular results are compared with retrospective open surgical data on 189 patients from three centers of excellence: the Cleveland Clinic Foundation (Cleveland, OH), Massachusetts General Hospital (Boston, MA), and the Hospital of the University of Pennsylvania (Philadelphia, PA). The VALOR trial was a prospective, nonrandomized, multicenter clinical study conducted in the US to evaluate the safety and efficacy of the Talent Thoracic Stent Graft with the CoilTrac Delivery System in the treatment of thoracic aortic diseases. Enrollment occurred from December 2003 to June 2005 at 38 institutions across the country.

## PATIENT SELECTION

The pivotal test group population consisted of 195 patients who were considered candidates for open surgical repair and were low to moderate risk (0, 1, and 2) per the modified Society for Vascular Surgery criteria. The patient's aneurysm had to be  $\geq 5$  cm or  $\geq 2$  times the diameter of the nonaneurysmal aorta. The aneurysm had to be at least 20 mm distal to the left common carotid and 20 mm proximal to the celiac artery, have a proximal and distal nonaneurysmal aortic neck diameter of between 18 and 42 mm, and proximal and distal nonaneurysmal aortic neck lengths of at least 20 mm. A notable exclusion criterion was previous surgical or endovascular treatment of an infrarenal aortic aneurysm.

## DEVICE DESCRIPTION AND DEPLOYMENT

The implanted endoprosthetic portion of the Talent Thoracic Stent Graft is composed of a polyester graft fabric sewn to a self-expanding nickel-titanium (chemically polished nitinol) wire frame (Figure 1). Stent graft oversizing of 2 to 4 mm relative to the native aortic diameter (measured as adventitia to adventitia) was recommended to provide



**Figure 1. Talent Thoracic Stent Graft devices.** (Reprinted with permission from Fairman RM et al. J Vasc Surg. 2008.<sup>1</sup>)

the necessary outward radial force, maintaining stent graft apposition against the aortic wall. The overall design concept is modular, such that additional main sections, as well as proximal and distal extensions, are introduced separately and mated in vivo as needed to complete the exclusion of the thoracic aortic aneurysm.

The loaded delivery system is inserted in the femoral or iliac artery, tracks through the vasculature, and delivers the stent graft at the target site. Deployment of the proximal stent graft occurs as the outer sheath is withdrawn, initially exposing the proximal bare spring and the first covered stent spring. A minimum overlap of 30 mm was required for multiple stent grafts.

## RESULTS

Vessel access and deployment of the study device at the intended site was successful in 194 (99.5%) of the 195 patients enrolled in the VALOR trial. One patient did not receive a study device because of access failure. Iliac conduits were required for arterial access in 21.1% of the patients. A mean number of  $2.7 \pm 1.3$  stent graft devices were implanted per patient. Approximately 25% of the patients had proximal main Talent Thoracic Stent Graft components implanted with diameters  $< 26$  mm (three patients, 1.9%) or  $> 40$  mm (49 patients, 23.2%). The highest implantation zone of the bare-spring segment of the most proximally implanted device was zone 1 in 6.7% of patients, zone 2 in 26.8%, zone 3 in 35.6%, and zone 4 in 30.9%.

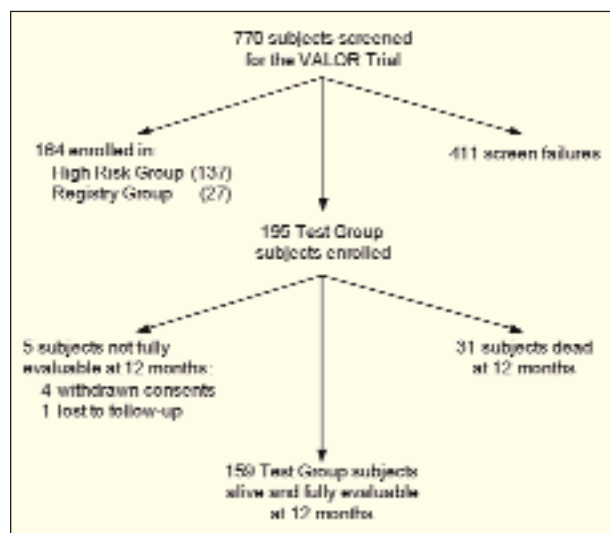


Figure 2. Freedom from all-cause mortality follow-up. (Reprinted with permission from Fairman RM et al. J Vasc Surg. 2008.<sup>1</sup>)

The decision to revascularize the left subclavian artery was left to the implanting physician and was performed before the initial stent graft procedure in 10 of 194 patients (5.2%).<sup>2</sup> The VALOR test group showed superiority compared to open surgery in regards to subjects requiring blood transfusion, procedural blood loss, and length of procedure, as well as intensive care unit and overall hospital stay ( $P<.001$ ).

### Mortality

Four of the 195 VALOR patients (2.1%) died  $\leq 30$  days after implantation. Causes of death for these patients included atheroembolic multisystem failure, stroke, periprocedural cardiac arrest, and complications from a myocardial infarction and perforated ulcer. The VALOR test group experienced a significantly lower rate of early mortality compared to the open surgical group (2.1% vs 7.9%,  $P<.01$ ) (Table 1). All-cause mortality at 12 months is presented in Table 2 (16.1% vs 20.6%,  $P=.29$ ). Freedom from all-cause mortality is presented for both groups in Figure 2. Predictors of all-cause mortality at 12 months in the VALOR patients included prior stroke, with an odds ratio of 3.72 ( $P=.008$ ), and aneurysm length, with an odds ratio of 1.008 ( $P=.017$ ) for each additional millimeter.

### Aneurysm-Related Mortality

Six of the 192 patients (3.1%) in the VALOR test group died of an aneurysm-related cause through 12 months of follow-up. Four patients died  $\leq 30$  days of the procedure. Two additional late deaths were adjudicated as aneurysm-related. In the open surgery group, 22 of 189 patients

TABLE 1. ALL-CAUSE MORTALITY AT 30 DAYS

Group	30-Day Mortality, % (m/n)*
VALOR test group	2.1 (4/195)
Open surgery	7.9 (15/189)

\* $P<.01$   
(Reprinted with permission from Fairman RM et al. J Vasc Surg. 2008.<sup>1</sup>)

TABLE 2. ALL-CAUSE MORTALITY AT 12 MONTHS

Group	12-Month Mortality, % (m/n)*
VALOR test group	16.1 (31/192)
Open surgery	20.6 (39/189)

\* $P=.29$   
(Reprinted with permission from Fairman RM et al. J Vasc Surg. 2008.<sup>1</sup>)

TABLE 3. ENDOLEAKS AT 1 AND 12 MONTHS (CORE LAB)

Endoleaks	At 1 Month, % (m) (n=174)	At 12 Months, % (m) (n=123)
Endoleaks of any size	25.9% (45)	12.2% (15)
Type I	4% (7)	4.9% (6)
Type II	15.5% (27)	4.9% (6)
Type III	1.7% (3)	0% (0)
Type IV	0% (0)	0% (0)
Indeterminate	4.6% (8)	2.4% (3)

(Reprinted with permission from Fairman RM et al. J Vasc Surg. 2008.<sup>1</sup>)

(11.6%) died of aneurysm-related causes, and this difference was statistically significant at  $P<.002$ .

### Conversion to Surgery

One patient (0.5%) was converted to open surgical repair approximately 9 months after implantation for complications related to an apparent infection in the stented segment of the aorta. This patient was alive and fully evaluable at the 12-month postimplantation follow-up.

### Major Adverse Events

One or more major adverse events (MAEs) occurred in 41% (80 of 195) of the VALOR patients  $\leq 30$  days after implantation compared with 84.4% (151 of 179) in the open surgery group ( $P<.001$ ). Most of the individual MAE categories in the endovascular group were lower, but vascular complications were higher in the VALOR patients, at 21% (41 of 195), compared with open surgery patients at 12.3% (22 of 179).

### Cerebrovascular Accidents

Seven VALOR patients (3.6%) had a periprocedural stroke. Three patients had resolution of stroke-related disability at 12 months, death, or last follow-up. Logistic regres-

sion analysis was performed on occurrence of stroke  $\leq 30$  days after the implantation procedure. Patients who had a history of abdominal aortic aneurysms had an odds ratio of 7.1 for the occurrence of stroke ( $P=.031$ ), and implantation in zone 1 or zone 2 had an odds ratio of 15.2 for the occurrence of stroke ( $P=.018$ ).

### SPINAL ISCHEMIA

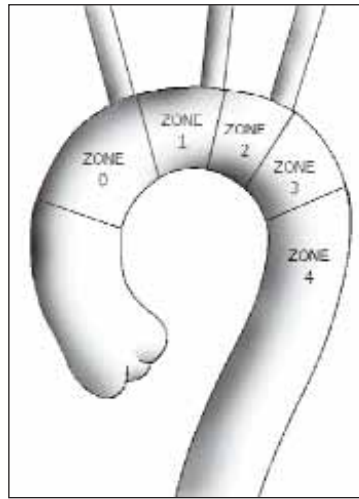
Postoperative paraplegia occurred  $\leq 30$  days in three of 195 VALOR patients (1.5%) and in a fourth patient at 32 days after implantation. All patients had placement of a lumbar drain at the time neurologic deficits were identified. None of these patients experienced recovery at the 1-year follow-up or by the time of death, and none of the patients with paraplegia had a previously treated abdominal aortic aneurysm. Onset of paraparesis occurred  $\leq 30$  days in 14 VALOR patients (7.2%). The proportion of patients with unresolved paraparesis within 12 months of last known follow-up fell to 3.1% (6 of 192).

Logistic regression analysis was performed on the incidence of paraplegia or paraparesis within  $\leq 30$  days after the implantation procedure. The only covariate that was found to be a significant predictor was the use of a conduit for access, with an odds ratio of 4.13 ( $P=.02$ ).

### Stent Graft Effectiveness

The core laboratory identified seven patients with a type I endoleak by the 30-day follow-up visit, as noted in Table 3. Most endoleaks were type II. Sixteen patients had 17 additional endovascular procedures, of which two procedures (1%) occurred in the 30-day period before discharge, and 15 procedures (8.1%) occurred at 31 to 365 days. Fourteen procedures were performed to resolve an endoleak. One patient had a procedure to resolve migration and to cover a pseudoaneurysm. One patient was treated for an aneurysmal expansion, and one patient was treated for a second aneurysm.

The core laboratory noted four stent graft migrations at  $\leq 12$  months. Two migrations involved the proximal end of the graft moving distally, and two involved the distal end of the graft moving proximally. Only one patient required an additional intervention related to the migration. Aneurysm sac diameter was stable or shrinking in 91.4% of patients. In 11 patients (8.5%), the increase in maximal aneurysm diameter was  $>5$  mm during this interval, and seven of these patients had endoleaks during



**Figure 3. Zones of implantation.** (Reprinted with permission from Fairman RM et al. *J Vasc Surg*. 2008.<sup>1</sup>)

follow-up. No study patient had loss of stent graft patency or instances of compression or collapse of the endograft  $\leq 12$  months.

### DISCUSSION

The Talent Thoracic Stent Graft was first implanted in Australia in January 1996 and received CE Mark approval in April 1998. The original device has undergone two iterative changes leading up to this pivotal clinical trial, including a delivery system change and chemical polishing of the nitinol stent. Most importantly, the device has not been withdrawn from the commercial market for any reasons related to safety or effectiveness.

The Talent Thoracic Stent Graft offers a wider range of diameter options than

is currently available in the commercial US market. Of the patients implanted with diameters  $<26$  or  $>40$  mm, 25% would not have been eligible for endovascular repair using commercially available devices owing to diameter-sizing constraints.

In 33.5% of patients, the bare-spring segment of the most proximally implanted device was in zones 1 or 2 of the aortic arch. The uncovered proximal stent allows for crossing of the great vessels and proximal fixation in the arch without occluding blood flow. There were no instances of asymmetric opening or asymmetric deployment of the proximal bare spring in this pivotal VALOR trial. In addition, there were no instances of erosion or perforation of the aortic wall by the uncovered proximal nitinol stent. Despite concerns about embolic stroke during endovascular maneuvers in the arch, the incidence of perioperative stroke in this series was remarkably low at 3.6%, and nearly half of these patients had resolution of stroke-related disability at 12 months, death, or last follow-up.

Although the delivery systems were mostly 24 and 25 F in size, successful vessel access and deployment occurred in 99.5% of cases, with iliac artery conduits used in 21%. A subset analysis failed to reveal any correlation between French size, conduit use, or vascular complications at 30 days. The use of conduits in this study is comparable to that reported in other contemporary series,<sup>3,4</sup> and experience has dictated that vascular access complications are frequent and may result in death. The need for conduits should be anticipated before arterial injury, particularly in elderly women with small, calcified, stenotic external iliac arteries. Because the longest Talent covered device available for this pivotal trial was 116 mm,  $2.7 \pm 1.3$  devices



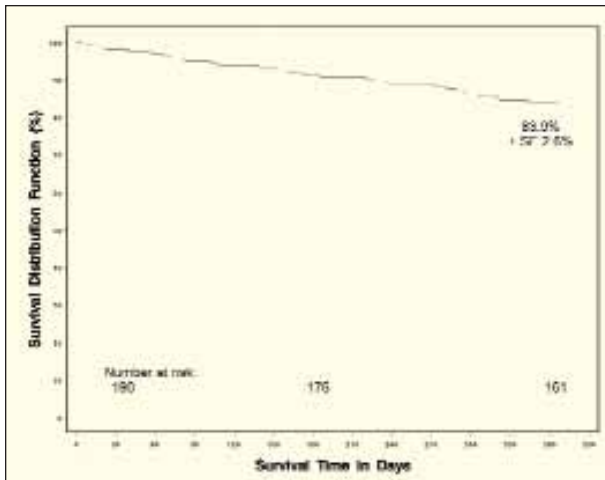


Figure 4. Kaplan-Meier plot of freedom from all-cause mortality. (Reprinted with permission from Fairman RM et al. J Vasc Surg. 2008.<sup>1</sup>)

were placed per patient (range, 1–7 devices). Longer covered endografts would have resulted in fewer devices placed per patient. Despite this, the incidence of serious vascular complications in the VALOR pivotal trial compares favorably with the Gore TAG phase II multicenter trial (Gore & Associates, Flagstaff, AZ) in which longer endografts were introduced and deployed through an indwelling 22- or 24-F sheath.

The 30-day paraplegia rate was low, and paraparesis was moderately high in the acute phase. Despite the 30-day paraparesis rate, this event carried a reasonably favorable prognosis, as demonstrated by the unresolved paraparesis rate of 3.1% at 12 months or last known follow-up. Strategies potentially mitigating paraplegia, such as spinal drains, were used at the discretion of the investigator when the perceived risk was significant. An interesting observation is that covariate analysis revealed conduit use was predictive of paraplegia or paraparesis. This is consistent with published reports defining retroperitoneal hemorrhage/hematoma, perioperative hypotension, and injury to the external iliac artery as contributing factors for spinal cord ischemia.<sup>5</sup> Future studies will need to identify effective perioperative spinal cord monitoring techniques and interventions, as well as postoperative treatment algorithms.

Although a mean number of  $2.7 \pm 1.3$  stent graft components were implanted per patient, no junctional or type III endoleaks were detected at the 12-month follow-up. Continued follow-up of these patients will be necessary to document the long-term efficacy of the device; however, several single-center series using the Talent Thoracic Stent Graft have demonstrated durability.<sup>6-8</sup>

The VALOR trial results support the use of the Talent Thoracic Stent Graft as a safe and effective alternative to

open surgical repair in patients with descending thoracic aortic aneurysms. These elderly patients, despite their significant comorbidities, had low mortality at 30 days and 12 months, as well as low aneurysm-related mortality at 12 months, supporting a high rate of successful aneurysm treatment. Specifically, the device showed statistically superior performance with respect to acute procedural outcomes, 30-day MAEs, perioperative mortality, and 12-month aneurysm-related mortality compared with open surgery. These data are particularly meaningful given that the open surgery data were derived from high-volume centers with a reputation for surgical excellence and where the best surgical outcomes would be anticipated.

A review of the recent medical literature allows for comparison between the Talent Thoracic Stent Graft experience vs the Gore TAG device based on Kaplan-Meier estimates (Figure 4).<sup>9,10</sup> Similar rates in 30-day and 12-month all-cause mortality and 12-month aneurysm-related mortality rates have been reported. When serious MAE rates are compared through 12 months by organ system, the VALOR test group and the subjects with a Gore TAG device have essentially the same profile of MAE rates. These comparisons demonstrate that despite fundamental differences in stent graft design, the Talent Thoracic Stent Graft as used in the VALOR test group performed in a substantially similar manner to the Gore TAG device when implanted in a similar group of study subjects.

The Talent Thoracic Stent Graft with Xcelarent® Delivery System was approved by the FDA in midsummer 2008 and is now available in the US. ■

*Ronald M. Fairman, MD, is Chief, Division of Vascular Surgery, at University of Pennsylvania Medical Center in Philadelphia, Pennsylvania. He is the principal investigator of the VALOR trial, and he has disclosed that he receives grant/research funding from Medtronic. Dr. Fairman may be reached at (215) 614-0243; ron.fairman@uphs.upenn.edu.*

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# EVAR Utilizing the AneuRx AAAdvantage<sup>®</sup> and Talent<sup>™</sup> Abdominal Stent Grafts With the Xcelerant<sup>®</sup> Hydro Delivery System

Clinical results, technical maneuvers, and considerations when encountering difficult anatomical situations, and how to avoid long-term complications in the treatment of infrarenal abdominal aortic aneurysms.

BY FRANK R. ARKO, MD

It has been more than a decade since Juan Parodi first described endovascular aortic aneurysm repair (EVAR).<sup>1</sup> This therapy has since gained widespread acceptance by vascular surgeons as a safe and effective alternative to open repair for high-risk patients with abdominal aortic aneurysms (AAAs). Large randomized trials have demonstrated that EVAR is associated with fewer blood transfusions, lower perioperative morbidity and mortality, shorter intensive care unit/hospital stay, and quicker recovery when compared to open surgery.<sup>2,3</sup>

Favorable clinical results combined with increased patient demand for minimally invasive procedure have resulted in an increased application of EVAR, and this treatment modality is now being extended to younger, healthier patients. Although the volume of AAA repair has remained relatively constant, the percentage of patients treated with endovascular interventions has substantially increased. Nowygrod et al recently reported that almost 50% of AAA repairs were performed via the endovascular route,<sup>4</sup> and the volume of abdominal aneurysms treated by endovascular repair is expected to continue to rise. Further, as EVAR is replacing traditional open repair, improvements in overall patient outcomes have been demonstrated with an overall decrease in length of hospital stay, decreased need for rehabilitation after hospital discharge, and overall improved mortality rates in patients diagnosed with AAAs.<sup>5</sup>

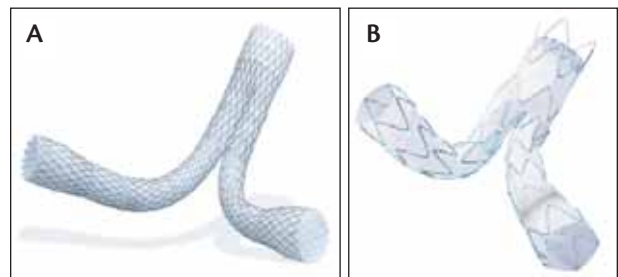


Figure 1. The AneuRx (A) and Talent (B) Abdominal Stent Grafts.

Although it seems that EVAR is becoming a desirable option for many patients, it is essential to realize that the feasibility of the procedure may be limited at times by patient anatomy and technical difficulties. Specific anatomical difficulties can be imposed by challenging access, short tortuous and calcified aortic and iliac landing zones, and the presence of coincident complex iliac aneurysms. Renal failure has also presented a concern for patients being considered for treatment with EVAR because the contrast loads required for the procedure, as well as for continued postoperative surveillance, may place the patient at risk.

However, increased experience with EVAR has revealed that surgical technique can overcome many of the aforementioned difficulties imposed on interventionists when

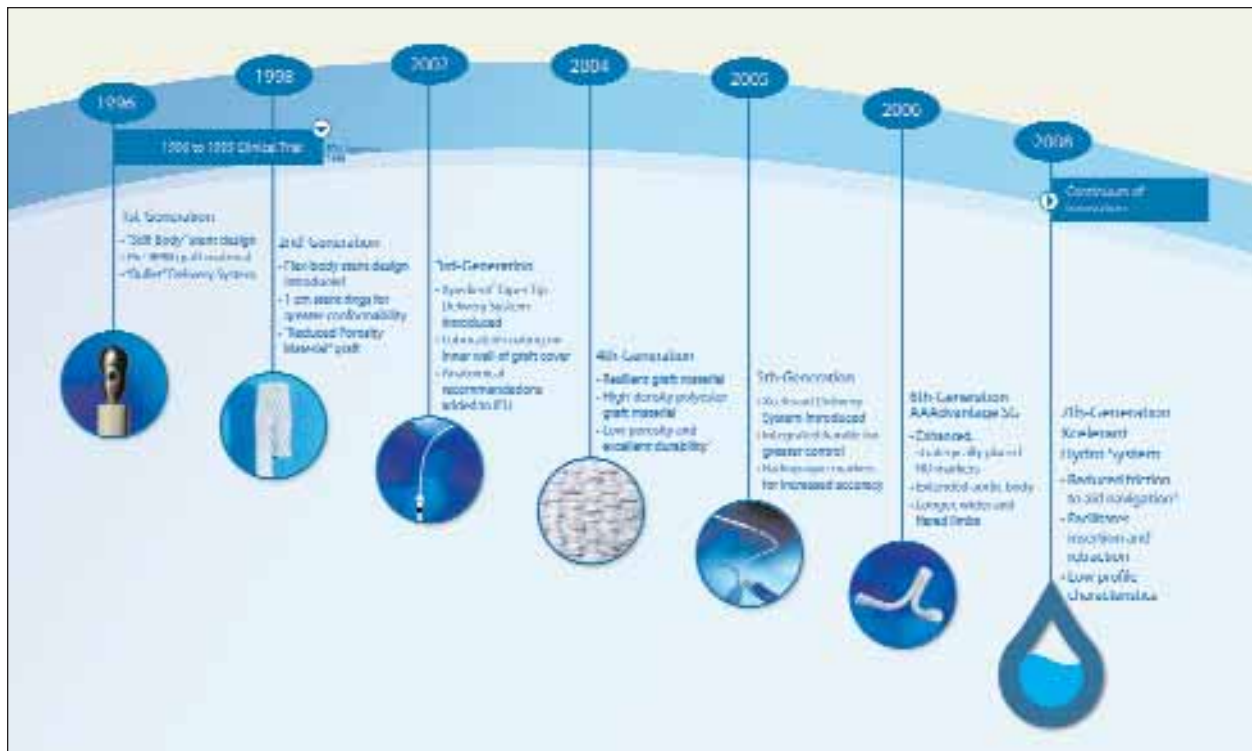


Figure 2. Evolution of the AneuRx Abdominal Stent Graft since the first implantation in 1996.

attempting to apply EVAR to patients with challenging anatomy and patients complicated by renal failure. These techniques not only improve our patient outcomes by increasing the safety of this operation but also increase the volume of patients that may be treated with endovascular repair by allowing us to perform EVAR in patients with anatomy once considered a contraindication to EVAR. Certain maneuvers may also increase the ease of performing traditional EVAR because advanced percutaneous procedures may significantly lower operative time and patient recovery.<sup>6,7</sup>

The purpose of this article is to discuss two commercially available devices—the AneuRx AAAAdvantage and Talent Abdominal Stent Grafts with the Xcelerant Hydro Delivery System (Medtronic Vascular, Santa Rosa, CA)—and their use in the repair of infrarenal AAAs.

### ANEURX STENT GRAFT

The AneuRx Abdominal Stent Graft was one of the first endografts approved in the US. It is a modular endograft system that utilizes an exoskeleton of 1-cm self-expanding elements. The self-expanding, thin-wall polyester graft material, supported by diamond-shaped elements, supplies high radial force for reliable, secure sealing without barbs, hooks, or balloons (Figure 1).

To date, the AneuRx Abdominal Stent Graft has under-

gone eight modifications since the original clinical trial (Figure 2). The first-generation device consisted of a stiff-body design with a prerduced porosity graft material and a bullet delivery system. In 1998, the stent graft was made more flexible by changing the body of the stent graft from a single 5-cm nitinol stent to make the body a series of 1-cm diamond-shaped rings, adding more flexibility to the graft. Furthermore, the graft material was changed to a reduced porosity material.

In 2002, the delivery system was changed to the Xpedient Delivery System with a tapered nose cone, allowing the device to be placed without a sheath. In 2004, the graft material was again changed to the Resilient graft material, which is associated with the greatest amount of sac shrinkage as compared to other contemporary graft materials.<sup>8</sup> In 2005, the Xcelerant Delivery System was added, allowing for easier deployment of the stent graft. In 2006, the AneuRx AAAAdvantage Stent Graft was offered, which added an extended aortic body of 4 cm; contoured stent rings; longer, larger, and flared iliac limbs to decrease the number of components required for repair; and enhanced radiopaque markers. Finally, in 2008, a hydrophilic coating was added to the delivery system. Currently, the AneuRx AAAAdvantage Stent Graft is available to treat up to 26-mm aortic neck diameters that are 15 mm in length with <45° of angulation.



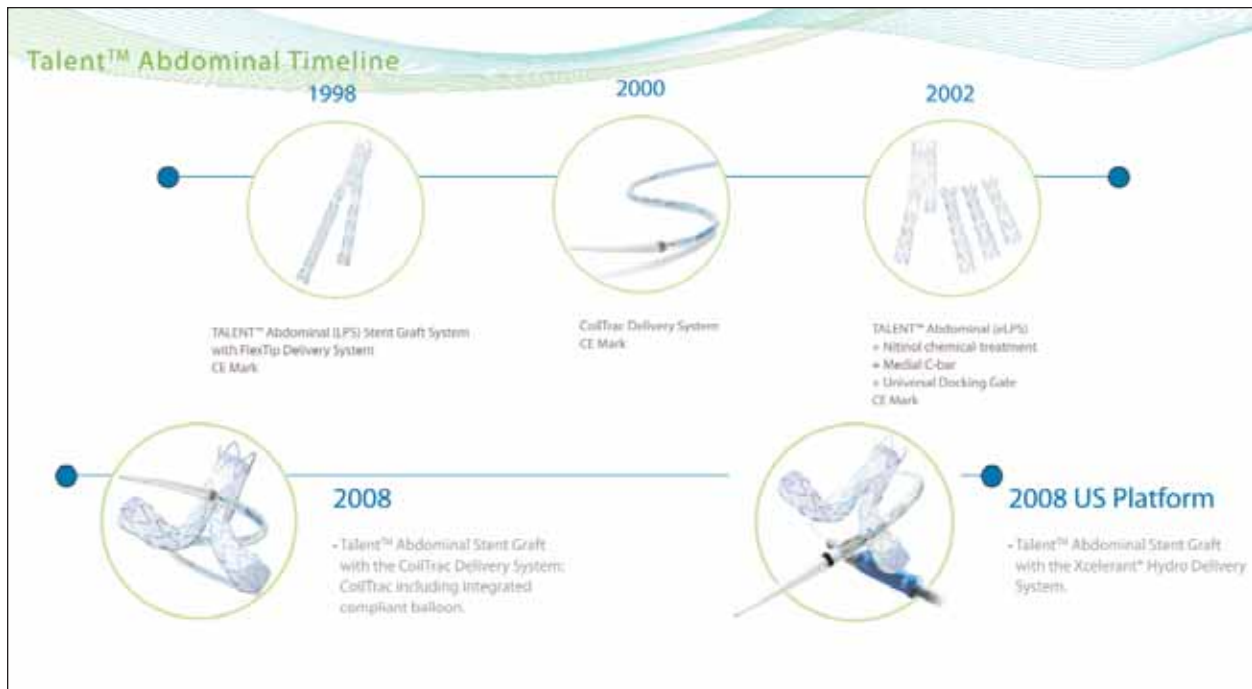


Figure 3. Evolution of the Talent Abdominal Stent Graft.

### TALENT ABDOMINAL STENT GRAFT

The Talent Abdominal Stent Graft is a modular endograft system that utilizes a self-expanding skeleton of serpentine nitinol stent springs inlaid in a woven polyester fabric (Figure 1). The stents are discontinuous and are spaced along a full-length nitinol spine. The latter wire provides columnar strength to a graft that is otherwise flexible enough to accommodate aortoiliac angulations. The spine also prevents twisting and longitudinal infolding of the stent graft during deployment. A suprarenal, 16-mm-long bare spring extends above the fabric to support additional proximal fixation. This feature was designed to treat shorter infrarenal necks.

The Talent Abdominal Stent Graft has also undergone several changes since 1998. In 2000, the FlexTip Delivery System was changed to the CoilTrac Delivery System with an integrated Reliant balloon. In 2002, the nitinol became chemically treated, and the connecting bar was placed medially. Furthermore, there was an added universal docking system for the contralateral gate (Figure 3), which is available on the Xcelerant Delivery System with hydrophilic coating. The Xcelerant Delivery System is 37% easier to advance and has an 85% reduction in drag force during deployment compared to the CoilTrac Delivery System. The Talent Abdominal Stent Graft allows treatment of up to 32-mm neck diameters with a neck length of 10 mm with <60° of angulation.

### CLINICAL TRIAL UPDATE

#### AneuRx Abdominal Stent Graft

A total of 1,193 patients were treated with the first- and second-generation AneuRx Abdominal Stent Grafts at 19 US investigational centers from 1996 to 1999. These patients were enrolled in three study phases. Phase 1, consisting of 40 patients, enrolled patients from June 1996 to April 1997. Phase 2 began in April 1997 and ended in September 1998, with 424 patients enrolled and treated and one patient enrolled and not treated. Phase 3 enrolled 639 patients beginning in August 1998 and ending on September 30, 1999. Ninety additional patients not meeting the trial's inclusion criteria were enrolled in a high-risk arm of the trial. A total of 174 patients received the first-generation "stiff" stent in the aortic body of the device. The remaining 1,019 patients received the multisegmented "flexible" 3-cm aortic body with the reduced-porosity material, which is no longer available because the aortic body has now been increased to 4 cm, and the graft fabric density has been increased by another 67%. Table 1 includes the results of the study.

#### Talent Abdominal Stent Graft Data

Criado et al published the US pivotal trial on the Talent Abdominal Stent Graft in 2003. Two hundred forty patients who received the Talent stent graft were compared to 126 surgical control patients. In 45.3% of patients, the neck was 26 mm or larger; in 38.6%, the neck was 15 mm or less; and in 19%, the neck was 10 mm or shorter. Deployment success

was achieved in 237 of 240 patients (98.7%). The overall mortality rate during implantation of the Talent Abdominal Stent Graft was 0.8%. Freedom from endoleak at 12 months was 90%. Unfavorable neck anatomy did not influence the endoleak rate. Stent graft migration was defined as 5 mm or greater displacement. Only three patients of 240 (1.2%) had any migration. Rates of migration were no different between patients with short (<15 mm) or wide (>26 mm) proximal necks compared to those with long (>15 mm) or narrow (<26 mm) proximal necks, and there were no aneurysm ruptures.<sup>9</sup> The premarket approval clinical data evaluated 166 patients at 13 centers and compared these data to the Society for Vascular Surgery surgical control group. Freedom from aneurysm-related mortality within 1 year was 97.9%. Freedom from all-cause mortality within 1 year was 93.5%, with only one stent graft migration >10 mm (0.8%, [1/127]). The stent graft patency rate was 100%, and freedom from secondary procedures was 96.5% at 1 year, with no surgical conversions or aneurysm ruptures at 1 year.

### ACCESS-RELATED ISSUES DURING EVAR

EVAR requires adequate vessel size in order to place the device to exclude the aneurysm. For each of the currently available devices, the external iliac and common iliac arteries need a minimum diameter of 7 mm for the main device. Certain conditions will make access more difficult, but certain technical maneuvers can overcome these conditions. Small external iliac arteries, vessel tortuosity, and heavily calcified vessels with aortoiliac occlusive disease make EVAR more difficult.

### Femoral Artery Exposure

Standard femoral artery access is achieved via a transverse or longitudinal incision. We have found that the use of small transverse incisions just below the inguinal ligament is beneficial during EVAR. With this exposure, dissection just below



Figure 4. Placement of the 10-F Prostar device within the common femoral artery before stent graft placement utilizing the Preclose technique for percutaneous EVAR, which can be utilized with all endografts.

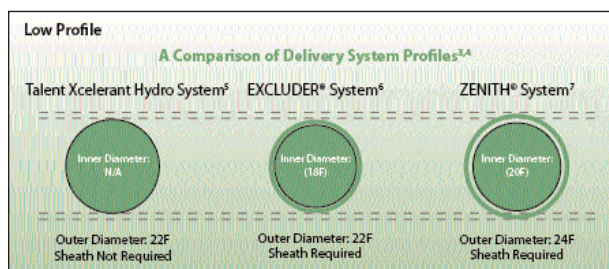
the inguinal ligament gains access to the common femoral artery typically in a relatively soft area of the artery. Furthermore, the femoral bifurcation is avoided, making control of the femoral artery easier, avoiding dissection of the profunda and superficial femoral arteries. When using this approach even in patients with heavily calcified vessels, we have usually found the femoral artery to have a soft anterior spot just distal to the inguinal ligament that can be used to puncture the artery. If the vessel is still heavily calcified, the inguinal ligament can be divided to allow access to the very distal external iliac artery, if necessary. Once the femoral artery is dissected out, proximal and distal control of the vessel is obtained with vessel loops. Wire access is then obtained in the standard Seldinger fashion.

There is growing experience with a truly percutaneous

TABLE 1. RUPTURE, CONVERSION, AND DEATH IN US ANEURX CLINICAL TRIAL

	No. of Patients					Follow-Up (%)				
	Intraoperative	<30 d	>30 d	Total		1 y	2 y	3 y	4 y	5 y
Aneurysm rupture	2/1,193 (0.17)	3/1,193 (0.25)	21/1,193	26/1,193	Freedom from rupture	99.5	98.7	98.4	97.4	96.8
Surgical conversion	11/1,193 (0.92)	4/1,193 (0.34)	52/1,193	67/1,193	Freedom from conversion	98.5	97	95.3	93.4	92.2
ARD	0	23/1,193 (1.93)	15/1,193	38/1,193	Freedom from ARD	98	97.6	97.2	96.8	96
Death	0	23/1,193 (1.93)	379/1,193	402/1,193	Probability of survival	91.5	82.7	77	68.6	60.1

ARD indicates aneurysm-related death.



**Figure 5. Comparison of delivery devices and sheaths from various commercially available endografts. Not shown is the AneuRx Xcelerant Hydro Delivery System, which is 21 F.**

technique using the 10-F Perclose device (Abbott Vascular, Santa Clara, CA) or using two 6-F Proglide devices (Abbott Vascular). With this technique, sutures are placed before the insertion of the sheath or device and then are used to close the femoral arteriotomy. This is often referred to as the *Preclose technique*. Using ultrasound guidance to confirm access to the common femoral artery, the artery is accessed, and a 7-F sheath is placed. A femoral arteriography is performed to confirm the sheath is within the common femoral artery. Either a single 10-F Prostar or two 6-F Proglides can be used. The 7-F sheath is removed, and the Prostar is advanced over the wire with the sutures deployed within the vessel (Figure 4). Once the device is deployed, wire access is regained through the rapid-exchange port. The device is removed, and either an 11- or 16-F sheath can be placed for hemostasis. After the procedure, the sutures are used to close the femoral artery. This technique can be used with any of the currently available devices, including the AneuRx AAAAdvantage and Talent Abdominal Stent Grafts with the Xcelerant Delivery System. When first learning this technique, it is best to avoid small, calcified vessels, as well as extremely tortuous vessels.

### Iliac Access

Once wire access is obtained, before placing any large sheath or device, it is best to have a stiffer wire in place for the sheath or device to track. Stiff wires that are available to straighten out the vessels include the Amplatz Super Stiff (Cook Medical, Bloomington, IN), the Meier Wire (Boston Scientific Corporation, Natick, MA), or the Lunderquist (Cook Medical). The AneuRx AAAAdvantage Stent Graft has a 21-F delivery system, and the Talent Abdominal Stent Graft has a 22-F delivery system with a hydrophilic coating and does not require a delivery sheath. The addition of the coating has resulted in a 67% reduction in the friction forces to place the graft within small or tortuous vessels. Currently, the Excluder (Gore & Associates, Flagstaff, AZ) can be placed within an 18-F sheath. It should be remembered that this is the inner diameter of the sheath and corresponds to

nearly a 21-F outer diameter of the sheath, making the two virtually equivalent (Figure 5). The contralateral limb for 16-mm diameters and smaller requires a 16-F delivery system; flared limbs for >16-mm diameters require a 19-F delivery system with AneuRx AAAAdvantage Stent Graft and an 18-F delivery system with Talent Abdominal Stent Graft without the need for a sheath.

In vessels with extreme tortuosity, even advancing a stiff wire through a catheter can be difficult in this situation with the stiff wire not advancing and the catheter coming back. This can sometimes be overcome with the use of a “buddy wire.” When the stiff wire will pass initially through a catheter, a stiff Glidewire (Terumo Interventional Systems, Somerset, NJ) can be passed through the catheter, which will usually track easily. Leaving the stiff Glidewire within the catheter, a second wire—typically a Glidewire—can be placed within the sheath and into the descending thoracic aorta. A catheter is then advanced over the Glidewire. With the stiff Glidewire and catheter already in place, a stiffer wire, such as an Amplatz or Lunderquist wire, can be advanced through the second catheter to straighten out the external iliac artery for placement of the device. Even in these extremely tortuous vessels, both the AneuRx AAAAdvantage and Talent Abdominal Stent Grafts on the Xcelerant Delivery System track very well to the intended location.

Although the Talent Abdominal Stent Graft does allow for treating more adverse neck anatomy, it does require a slightly larger delivery sheath. The Talent Abdominal Stent Graft is delivered through a 22-F delivery system for up to 28-mm devices, and a 24-F delivery system is required for 30- to 36-mm devices. Currently, the only other FDA-approved device to treat a >28-mm neck is the Zenith (Cook Medical). However, its 28-, 30-, and 32-mm devices require a 20-F sheath to deliver the device (inner diameter); the 36-mm device requires a 22-F sheath (inner diameter). Therefore, all larger devices require delivery using the outer diameter of their sheaths of nearly 24 F (Figure 5).

Other adjunctive maneuvers besides using a stiff wire for device placement in small or tortuous vessels include the use of placing mineral oil on the outer sheath to decrease the amount of friction on the sheath. However, the advent of the hydrophilic coating on the Xcelerant Delivery System has made this maneuver obsolete. Gradually increasing the size of small vessels by passing dilators can also be beneficial. Furthermore, external abdominal pressure in the location of the external iliac artery can also be helpful in advancing the device within the aneurysm in small tortuous vessels.

In some patients without adequate external iliac arteries or severely diseased external iliac arteries, the use of a conduit can be used to obtain adequate access for placement of the endograft (Figure 6). To do this, an oblique incision is made just superior to the inguinal ligament. Facial layers are



divided, and exposure of the iliac bifurcation is achieved. The common, internal, and external iliac arteries are controlled. A longitudinal arteriotomy is made, and an end-to-side anastomosis is performed with a polypropylene suture. A 10-mm Dacron graft allows for passage of all devices. With the distal graft clamp, the conduit can then be accessed in the standard fashion for placement of the device. This can be extremely beneficial in preventing damage and/or rupture to the external iliac artery, especially in women or during thoracic EVAR.

### PROXIMAL AORTIC NECK ISSUES

It has been previously shown that placing the stent graft as close to the renal arteries as possible at the original implantation significantly decreases the risk of migration. There are certainly some conditions that are going to increase the risk of migration or proximal type I endoleaks. These risks include a short angled neck as well as a reverse funnel neck. Currently, all devices are approved for use with a proximal neck length of 15 mm except the Talent Abdominal Stent Graft, which is approved for use with a 10-mm neck. The technique and precision of device implantation, along with patient selection, are significant factors in predisposing patients to subsequent adverse events in the future—especially migration. Migration has been reported with all devices with an incidence between 2.3% and 9.5% in clinical trials with a follow-up of 1 to 4 years.<sup>10-15</sup> When evaluating device-specific outcomes, Ouriel et al found no significant differences in the risk of migration among various devices. In that report, the risk of migration ranged from 0% with the Talent and Ancure to 8.2% with the Zenith.<sup>13</sup> In a more recent study from the Massachusetts General Hospital, Abbruzzese et al evaluated 177 Cook Zenith (31%), 111 Gore Excluder (20%), and 277 Medtronic AneuRx (49%) stent grafts. In the study, 39.3% of grafts were placed outside of at least one instructions for use parameter. Mean follow-up was 30±21 months and was significantly shorter ( $P<.001$ ) for the Cook Zenith (20 months) compared to the Gore Excluder (35 months) and Medtronic AneuRx (31 months), respectively. Overall actuarial 5-year freedom from aneurysm-related death, reintervention, and graft-related event rates were similar among these three devices. The investigators concluded that EVAR performed with the three commercially available devices provided similar clinically relevant outcomes.<sup>12</sup>

In the US AneuRx clinical trial, the risk of migration at 5 years was 6.4%. The definition of migration in this US clinical trial was any movement of the stent graft. When comparing this definition to other clinical trials, the Gore Excluder defined migration as >10 mm of movement; the Cook Zenith definition of migration was 5 mm. At 2 years, the risk of migration with the Cook Zenith in the US clinical trial

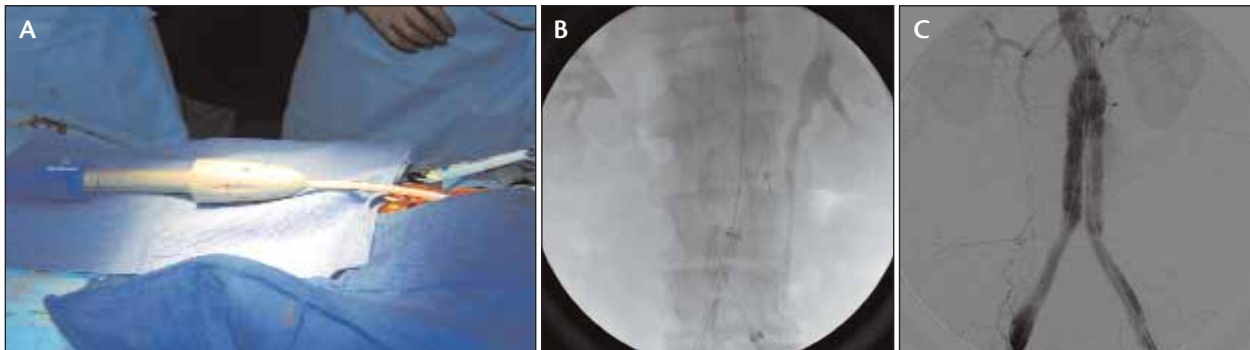


**Figure 6.** In heavily diseased external iliac arteries, the use of a conduit although rare can be helpful in advancing the delivery system. A small transverse incision just above the inguinal ligament is made, and a 10-mm Dacron graft is sewn to the iliac bifurcation. This allows easy access to the abdominal aorta during EVAR and the thoracic aorta during thoracic EVAR.

was 4.8% and 4.3% in the standard and high-risk groups, respectively. Furthermore, one must remember that the US clinical trial used more liberal criteria for patient selection and had the influence of the physicians' early learning curve, as well as very early generation delivery systems. The inclusion criteria in the US AneuRx clinical trial required only a 10-mm neck, whereas the other stent grafts utilized a 15-mm neck, and the Talent Abdominal Stent Graft utilized a 5-mm neck.

In order to maximize and improve the proximal fixation, there are some maneuvers that can be used. The first of these is magnification views and appropriate angulation of the fluoroscopy unit. Typically, adjustment of the image intensifier in the caudal direction will open up the infrarenal neck and give it its true length. Typically, the infrarenal aortic neck begins to angle anteriorly following the course of the lumbar spine. Adjusting the image intensifier 10° to 20° is usually sufficient to open up the proximal neck.

Even when placing the device as close to the renal arteries as possible during initial deployment, there is continued risk of migration, especially if there is a short neck; significant disease of the aortic neck, including thrombus and calcification; neck angulation, and adverse neck contour, such as a reverse funnel neck.<sup>12-17</sup> However, it is important to remember that the stent graft relies on three points of fixation, including the proximal aortic neck and the right and left common iliac arteries. In vivo animal analysis has shown that by maximizing the distal iliac fixation, the amount of force required to displace the stent graft is significantly



**Figure 7.** The Talent Abdominal Stent Graft being deployed on the Xcelerant Delivery System (A). Controlled deployment allows accurate placement just at the level of the lowest renal artery (B). Final angiogram demonstrates maximum proximal and distal fixation without evidence of endoleak (C).

increased by 67%. This has been demonstrated with both infrarenal and suprarenal devices with no significant improvement when hooks are present. The importance has also been shown clinically again with infrarenal and suprarenal devices.<sup>18-22</sup> Figure 7 shows the Xcelerant Delivery System with slow, controlled deployment of the Talent stent graft just below the level of the renal arteries. The final panel shows the stent graft just below the level of the renal arteries and extending all the way to the iliac bifurcation.

Since the first use of the AneuRx Abdominal Stent Graft in 1996, several design improvements have been made, including two major delivery system and graft material upgrades. Furthermore, there is an extended aortic body to improve proximal fixation and seal. Postsurveillance Registry and Lifeline Registry data evaluating the AneuRx Abdominal Stent Graft are similar to the US AneuRx clinical trial cohorts, with no statistically significant differences in freedom from death, rupture, or surgical conversions between the registries and the phase 2 cohort. Furthermore, there has been only one migration reported of 334 patients in the postmarket registries, representing a low rate of migration of the AneuRx Abdominal Stent Graft (0.3%) at the 2- to 3-year interval.

Although the AneuRx AAAAdvantage Stent Graft is limited by a proximal neck of <26 mm and a length of 15 mm, the Talent Abdominal Stent Graft is indicated for a neck diameter of up to 32 mm and a neck length of 10 mm in diameter. This device was recently approved by the FDA and has more than 45,000 implants worldwide. In an article by Brown et al comparing the Cook Zenith and the Medtronic Talent Abdominal Stent Graft within the EVAR trials in the United Kingdom, no statistically significant differences were found in regard to secondary interventions, aneurysm-related death, or all-cause mortality.<sup>23</sup> Many physicians may assume that the use of barbs on the Zenith endograft would be associated with a significantly lower risk of migra-

tion. To date, however, there has been no report demonstrating an improvement of the Zenith over the Talent Abdominal Stent Graft in this regard. Badger et al have demonstrated further that there is no clinically significant difference between the Cook and Talent Abdominal Stent Grafts in midterm outcome or migration between the two devices.<sup>24</sup> Furthermore, Murphy et al demonstrated that there was no significant difference in the in vivo pull force to cause displacement of these two stent grafts both with suprarenal fixation.<sup>20</sup>

### COMPLEX ILIAC ARTERY ANEURYSMS

In patients with aortoiliac aneurysms, there are three options available to the implanting physician. For ectatic iliac vessels, the use of flared limbs has simplified the repair of aneurysms with large common iliac arteries. Flared limbs as large as 24 mm allow vessels up to 20 to 22 mm to be safely treated without the use of coil embolization of the internal iliac artery and thus maintaining flow to the internal iliac artery. This is available with both the AneuRx AAAAdvantage and Talent Abdominal Stent Grafts. However, when using these flared limbs, it is still important to try to achieve between 20 to 25 mm of seal to prevent a retrograde type I endoleak. With aneurysmal common iliac arteries, it is usually safe to perform coil embolization of the internal iliac artery and bring the stent graft into the external iliac artery. The advantages of these two stent grafts are that both are made of nitinol and are similar to other self-expanding stent grafts with excellent radial force. Furthermore, the Talent Abdominal Stent Graft is available in 8-mm sizes for extension into the iliac arteries without requiring much oversizing.

### PATIENTS WITH RENAL INSUFFICIENCY

In patients with renal insufficiency, it is important to limit the amount of contrast used during the implantation of the

stent graft. First, the use of iso-osmolar contrast agents such as Visipaque (GE Healthcare Technologies, Waukesha, WI) should be used in patients with chronic renal insufficiency. This can be used as well in a 50:50 dilution with normal saline to further reduce the nephrotoxic effects of the contrast agent. It is often assumed that the use of gadolinium should be used in patients with chronic renal insufficiency. However, it is sometimes difficult to see, especially in obese patients. Furthermore, on review of the literature, gadolinium is often found to be of no benefit in reducing the risk of renal toxicity; the US FDA has notified healthcare professionals regarding the potential risk for nephrogenic systemic fibrosis/nephrogenic fibrosing dermopathy in patients with renal failure exposed to high doses of gadolinium-containing contrast agents.<sup>25,26</sup> If administration of iodinated contrast medium is deemed necessary in patients at high risk, then volume expansion should be offered, and the lowest possible dose of nonionic iso-osmolar contrast medium should be used. Prophylactic administration of fenoldopam or acetylcysteine has not offered consistent protection. Intravenous acetylcysteine could be considered, and we routinely use it in our patients. Recently, sodium bicarbonate infusion has been shown to reduce the risk of contrast-induced nephrotoxicity.

The other technique that can be used to limit the amount of contrast used during EVAR is the use of intravascular ultrasound (IVUS). IVUS can be used to localize the renal arteries with the device being placed to this level (Figure 4). It can give real-time aortic neck diameter, as well as left and right common iliac artery diameter. Using pull-back measurements, lengths can also be obtained including aortic neck length and renal-to-iliac bifurcation length. After deployment of the stent graft, it can then be used to assess adequate apposition of the stent graft to the aorta as well as iliac arteries and assess the precision of deployment of the graft to the renal arteries proximally and iliac artery bifurcation distally. The use of IVUS can routinely limit the amount of contrast used to under 50 mL, and in many cases, the use of contrast can be completely avoided.

If IVUS is unavailable, another technique that can be used to localize the renal arteries for placement of the proximal device is to place a catheter within the lowest renal artery. With the catheter in place, it can be seen under fluoroscopy, and small doses of contrast can be injected to further localize the lowest renal artery.

## CONCLUSION

Since the first report of EVAR by Dr. Parodi, there have been significant advances in aneurysm repair using endovascular approaches. With more experience, each implanting physician can improve his technique for device implantation. EVAR continues to play an ever-increasing role in the

management of aneurysms throughout the entire body. Improving technologies will continue to allow for endovascular treatment in patients with increasingly difficult anatomical features. ■

*Frank R. Arko, MD, is Associate Professor of Surgery, and Chief of Endovascular Surgery at the University of Texas Southwestern Medical Center in Dallas, Texas. He has disclosed that he receives speaking honoraria and research support from Medtronic. Dr. Arko may be reached at (214) 645-0533; frank.arko@utsouthwestern.edu.*

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# Design Considerations Behind the Medtronic Dissection Trial

This Investigational Device Exemption trial will explore the Valiant® Thoracic Stent Graft in treatment of acute, complicated type B aortic dissections.

BY W. ANTHONY LEE, MD

**A**ortic dissection is a relatively rare entity, with an incidence of 2.9 cases per 100,000 per year.<sup>1</sup> Although most acute dissections may be satisfactorily managed medically, urgent intervention is indicated in those that are complicated by malperfusion or rupture. Treatment options have included (1) direct aortic replacement, with mortality rates ranging from 20% to 50% and complications of paraplegia, stroke, acute renal failure; (2) extra-anatomic revascularization (eg, femoral-femoral bypass) for lower extremity ischemia; and (3) percutaneous fenestrations for visceral malperfusion.<sup>2</sup>

Since the advent of thoracic aortic stent grafts, endovascular treatment of complicated aortic dissections has been used as a potentially minimally invasive alternative to conventional aortic surgery. The goals of therapy involve restoration of true lumen flow with closure of the primary tear and restoration of visceral/lower extremity perfusion. Although some of the earliest published reports on the treatment of this condition date back to 1994,<sup>3</sup> most of the experience in the US started in 2005 with the first commercial availability

of a thoracic endograft. It is important to note that currently, there is no FDA-approved device for this indication. To address this, Medtronic Vascular will be initiating a sponsored Investigational Device Exemption (IDE) multicenter clinical trial investigating the safety and efficacy of the Valiant Thoracic Stent Graft in the treatment of acute, complicated type B aortic dissections.

## ACUTE COMPLICATED TYPE B AORTIC DISSECTION

A (Stanford) type B aortic dissection is defined by the location of the primary tear and extent of the dissection distal to the left subclavian artery. This condition is equivalent to a type III dissection in the DeBakey classification system. Dissections are typically further classified according to the acuity of their presentations. An *acute* dissection is defined as symptoms of <2-week duration, and *chronic* dissection as those being >2 weeks. Clinicians have frequently used terms such as *subacute* to describe those that are between 2 weeks to 3 months, but this has not been standardized.

The immediate clinical course of acute dissections can



Figure 1. Adjunctive branch-vessel stenting for malperfusion.



be complicated by frank rupture of the false lumen or visceral, renal, or lower extremity malperfusion secondary to static and/or dynamic obstruction.<sup>4</sup> Other less moribund conditions that may be considered as *complicated* have included persistent pain and hypertension that are refractory to maximal medical therapy.

“... how much to oversize remains controversial given the underlying abnormality of the undissected segment.”

Technically, endovascular repair of aortic dissections differ substantively in a number of respects from repair of degenerative aneurysms. First, the proper sizing of the endograft can be difficult. The only anatomic reference is the undissected segment between the left common carotid and subclavian arteries. Even if the true reference diameter were known, how much to oversize remains controversial given the underlying abnormality of the undissected segment; prevailing opinion has favored minimal 5% to 10% oversizing instead of the usual 10% to 20%. Regardless, the endograft is invariably larger than the re-expanded true lumen, and device infolding can become an issue.

Second, due to the proximity of the primary tear to the left subclavian artery, the proximal landing zone frequently must extend to the left common carotid artery. Proper management of the left subclavian artery must be considered to prevent risk of vertebrobasilar, myocardial, spinal cord, and left arm ischemia.<sup>5</sup>

Third, how much of the thoracic aorta should be covered is an unsettled matter. Although initially it was felt that coverage of the primary tear alone was sufficient, observations that favor more extended coverage include the fact that there are often multiple re-entry tears throughout the distal thoracic aorta that may serve as persistent inflow to the false lumen, and the false lumen appears to thrombose only to the level of the endograft and the distal dissected segment, remaining patent with risk of late aneurysmal dilation. This approach, however, must be tempered by the increased risk of spinal cord ischemia from the extended coverage and cost of additional devices.

Lastly, in cases of malperfusion, adjunctive branch-vessel stenting may be required (Figure 1). Use of a self-expanding versus balloon-expandable and covered versus uncovered stents must be individualized to the patient and the vessel being treated. Furthermore, how

aggressively the interventionist should attempt to exclude the false lumen by using covered stents depends on the location, size, and number of such sites, which should be weighed against the added risk and complexity of the overall procedure. At this time, the benefit of such an approach in the natural history of acute dissections is unknown.

## MEDTRONIC VALIANT THORACIC STENT GRAFT

The Medtronic Valiant Thoracic Stent Graft is a second-generation device that has a number of noteworthy design improvements over its predecessor, the Talent Thoracic Stent Graft (Figure 2). It is constructed of nitinol Z-stent exoskeleton and polyester fabric. The proximal component has an 8-crown bare-stent segment that can be placed over the origins of the arch vessels and facilitates conformation to the curvature of the arch. This is important because a large majority of the repairs must extend to the left common carotid artery as previously mentioned. Other changes include availability of 15- and 20-cm length devices and elimination of the longitudinal connecting bar, obviating the need to orient the device.

The deployment forces that made the original Talent Thoracic Stent Graft difficult to unsheathe, especially in the proximal thoracic aorta and in tortuous anatomies, have been overcome by the Xcelerant Delivery System. This should be familiar to most operators who have used other Medtronic stent grafts, with a rotating torque-transfer handle that enables a slow, controlled delivery of the proximal segments of the endograft for accurate positioning and rapid deployment of the remaining segment.

## WHY AN ACUTE DISSECTION TRIAL?

There are two main reasons for performing an acute dissection trial in the US. The first is clinical equipoise. Despite the scattered practice of endovascular treatment of aortic dissections under physician-sponsored IDE or off-label use of commercially available devices, the evidence behind its safety and efficacy lacks establishment. Individual case series are small, retrospective, and, most importantly, composed of uncontrolled and heterogeneous study cohorts and methodologies. The disparate results are, therefore, difficult to interpret and compare from one study to another. Even formalized registries, such as the IRAD (International Registry of Aortic Dissections), suffer from the voluntary nature of such distributed databases and its consequent reporting bias and data that are not subject to independent audit.

Although there may be a number of theoretical benefits to endovascular treatment of aortic dissections, these are extrapolated from clinical trials using devices intended for treatment of degenerative aneurysms, and whether the same minimally invasive benefits can be transferable to dissections is unknown. This is especially true in the subset of uncomplicated type B dissections, whose current standard of care is medical management and even to complicated type B dissections, for which direct aortic replacement, extra-anatomic bypass, and/or percutaneous fenestrations have been the mainstay of therapy with acceptable outcomes.<sup>6</sup>

The second important reason for conducting a clinical trial is to obtain an on-label indication. Although the practice of off-label use of aortic stent grafts and other medical devices has de facto become standard of care, this is being increasingly scrutinized by the federal government, and future reimbursement for procedures may become restricted to indication-specific usage of medical devices. Although a myriad of objections may be raised for such an onerous policy toward application of potentially life-saving therapy, there is evidence to suggest that off-label use of medical devices, in general, are associated with poorer outcomes and have uncovered certain failure modes that were not encountered during the clinical trials.<sup>7</sup> When complications occur, this may have important medicolegal ramifications both to the manufacturer for tacit promotion and the operator for the use of these medical devices regardless of the informed consent process.

## CURRENT STATUS OF PROSPECTIVE EVIDENCE

To date, the only level 1 evidence that is available regarding endovascular management of aortic dissections is the INSTEAD (Investigation of Stent Grafts in Patients with Type B Aortic Dissection) trial led by Christoph Nienaber, MD, from the University of Rostock in Germany. The study design was a prospective, multicenter, randomized, controlled clinical trial involving 136 patients—70 in the endovascular group and 66 in the medical treatment group—at 11 European centers.

The primary objective of the INSTEAD trial was to evaluate the clinical performance, safety, and effectiveness of the Talent Thoracic Stent Graft versus conventional antihypertensive treatment in subacute/chronic (>2–52 weeks) type B aortic dissections. The primary endpoint was all-cause mortality at 12 months, and the secondary outcomes included false lumen thrombosis, cardiovascular morbidity, aortic expansion, quality-of-life measures, hospital stay, endograft safety and per-

formance, and crossover rate analyzed on an intention-to-treat basis.

The study concluded that for uncomplicated, chronic type B dissections, a primary strategy of antihypertensive medical therapy is recommended, with secondary endograft treatment reserved for failures of medical management. This was based on a higher (not statistically different) rate of all-cause mortality in the stent graft arm, 10% (7/70), versus medical treatment, 3% (2/66), at 12 months. However, there was a significantly higher rate of false lumen thrombosis in the stent graft arm (97% vs 53%), and seven patients (11%) crossed over to endovascular repair for malperfusion, progression/expansion, and rupture. Interestingly, the patients in the medical arm of this trial did much better than prior studies, which showed 1-year mortality rates of 10% to 28%,<sup>8</sup> while the stent graft arm was comparable with published data.<sup>9</sup>

More recently, another study commenced in Europe to examine the role of endovascular treatment of aortic dissections. The VIRTUE (Valiant Thoracic Stent Graft Evaluation for the Treatment of Descending Thoracic Aortic Dissections) study is a Medtronic-sponsored, prospective, single-arm clinical registry designed to evaluate the Valiant Thoracic Stent Graft for the treatment of acute and chronic type B aortic dissections. The study plans to recruit 100 patients from 18 European centers. The primary endpoint is procedure-, device-, or disease-related mortality at 12 months. Patients will undergo serial imaging for 36 months after the procedure, with the results evaluated by a core lab, which should provide important data regarding late morphologic changes after endograft treatment.

## CHALLENGES TO DESIGN OF A DISSECTION TRIAL

Nearly every manufacturer of a thoracic endograft is currently in the process of designing a clinical trial to investigate the safety and efficacy of stent grafts in aortic dissections. One should keep in mind that the design of sponsored clinical trials is principally focused on meeting the study endpoints in the most efficient and expeditious manner in order to obtain approval or on-label indication of a medical device. Although valid clinical questions are often answered in a scientific and transparent manner, the fiscal and temporal constraints of conducting a large study do not always allow investigation of subject matters that may be perceived as most clinically interesting or relevant.

Specifically, with regard to endovascular therapy of aortic dissections, two issues must be considered. First,



Figure 2. The Valiant Thoracic Stent Graft.

what is the ideal cohort that should be studied? Even for the subset of type B aortic dissections, there are complicated, uncomplicated, acute, and chronic categories that are vastly different in terms of their presentations, goals of therapy, and outcomes. Second, in a study examining a radically different type of treatment using a complicated medical device such as a thoracic endograft, the optimal control group remains uncertain. The test group necessarily has two confounding but inseparable variables—the endovascular therapy itself and the actual device used in the therapy. Given that certain outcomes after endovascular aortic therapy are device related,<sup>7</sup> it would be desirable to, independently of each other, determine the safety and efficacy of the therapy itself, as well as how safely and effectively a device treats aortic dissections.

The conventional choice of a control group in most of the early endograft IDE trials has been a contemporaneous cohort of surgical repairs. In the setting of complicated dissections, the relative infrequency of these conditions would make timely enrollment of such a cohort unrealistic. Moreover, surgery for these conditions has been largely, by default, regionalized to select tertiary-care centers; most of the experiences span an extended period of time, and the outcomes are susceptible to institutional variations in technique and perioperative management. Finally, sample-size calculations and endpoint determinations depend on known benchmarks and other objective performance criteria, all of which are virtually nonexistent for this disease and its therapy. Therefore, at the present time, the best option may be pooled data from physician-sponsored

IDE studies and/or literature surveys of peer-reviewed publications.

### MEDTRONIC DISSECTION TRIAL

The Medtronic Dissection Trial is a manufacturer-sponsored IDE clinical trial investigating the safety and efficacy of the Valiant Thoracic Stent Graft in the treatment of acute, complicated type B aortic dissections. Although the final study design has not been completed, the initial phase of the study will gather the necessary data to serve as the control arm in the trial and establish the objective performance criteria. Select centers of excellence in surgical and endovascular aortic therapy will participate in a retrospective review of patients surgically treated for rupture and/or malperfusion as a complication of their acute type B dissection over a 5-year period. Outcomes will include mortality, morbidity, and other relevant clinical measures at 30 days and 1 year. These data will be validated by an independent clinical research organization for accuracy and uniformity. The design of the test (stent graft) arm and primary and secondary endpoints will follow the complete acquisition of these control data. ■

*W. Anthony Lee, MD, is Associate Professor of Surgery, Division of Vascular Surgery and Endovascular Therapy, University of Florida, Gainesville, Florida. He is the national principal investigator of the Medtronic Dissection Trial, and he has disclosed that he is a paid consultant to Medtronic. Dr. Lee may be reached at (352) 273-5484; anthony.lee@surgery.ufl.edu.*

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# Performance of Thoracic Stent Grafts

An experimental study to evaluate the performance of stent grafts in the aortic arch as a function of neck angulation and oversizing.

BY LUDOVIC CANAUD, MD; AND PIERRE ALRIC, MD, PhD

**T**reatment of thoracic aortic diseases is a challenging entity. Conventional thoracic aortic surgery is primarily used in relatively healthy patients, and even from expert high-volume centers, the 30-day mortality rate for the descending thoracic aorta remains high, ranging from 4% to 9%.<sup>1,2</sup> In 1994, Dake et al<sup>3</sup> reported the first successful endovascular repair of thoracic aortic disease. Currently, endovascular endograft placement represents a valid option with low risk for a wide range of acute and chronic thoracic aortic pathologies.

However, endovascular therapy brings its own challenges, and specific complications have been reported, such as endoleaks, migration, and collapse (Figure 1). Anatomic factors (length, angulation of the necks, and morphology of the aortic wall) are the important predictors of success and the most important exclusion criteria. Successful thoracic endovascular repair requires adequate graft fixation to avoid migration, endoleak, and collapse. Other factors, such as the ability of the device to conform to the many anatomic variations of aneurysms may also affect the result. Currently, conformability in the arch anatomy, especially in the inner curvature, is not easily achieved using most of the current endografts. Successful endovascular treatment requires strict patient selection and a good knowledge of the performance of commercially available endografts. Also, we believe that the choice of the endograft for the particular patient's anatomy can prevent many potential complications.

In the present experimental study using human cadaveric aortas, we sought to compare the proximal anchorage of the four stent grafts currently available in Europe in this aortic zone as a function of neck angulation and graft oversizing. To our knowledge, no previous study has examined the relationship between proximal landing zone angulation and proximal anchorage of the thoracic endograft.

## METHODS

Experiments were performed using 15 human thoracic cadaveric aortas. Four commercial endografts were evalu-

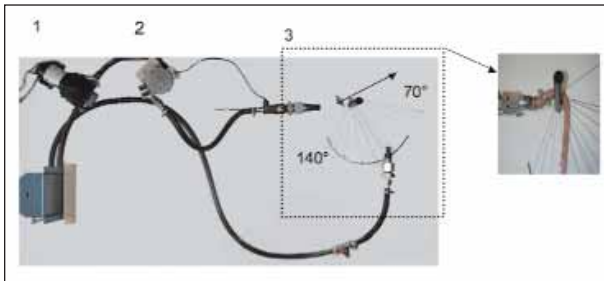


**Figure 1. Stent graft collapse after endovascular repair of a traumatic aortic disruption.**

ated: TAG (Gore & Associates, Flagstaff, AZ); Zenith TX2 (Cook Medical, Bloomington, IN); Valiant® (Medtronic Vascular, Santa Rosa, CA) and Relay (Bolton Medical, Sunrise, FL). A bench test model (Figure 2) with pulsatile flow was devised to assess endograft anchorage as a function of proximal landing zone angles from 70° to 140° (length of the proximal landing zone, 2 cm) and oversizing (4.8% to 36.8%). This model consisted of a high-pressure pump in a closed system, controlled by an electromagnetic sluice gate associated with a pressure regulator to modulate the flow. The intraluminal lip length was measured as a function of proximal landing zone angulation during static and dynamic tests; endograft collapse was also investigated. A 10-mm, 0° optic (Richard Wolf, Vernon Hills, IL) was introduced into the aorta through the aortic wall during dynamic tests and through the aortic lumen during static tests. The gap was measured thanks to the 10-mm optic. The flow character and velocity in the aorta were measured using a Sirecust 620 (Siemens Medical Solutions USA, Inc., Malvern, PA) at the entry and exit points of the endograft.

The endografts were also tested as a function of neck angle and oversizing in extreme anatomical conditions subjected to a high-pressure fluid flow model.





**Figure 2.** Custom-built bench test model of pulsatile fluid flow simulated an aortic arc. Angulations were variable according to the position of the distal connector in the rail. 1=high-pressure pump; 2=pressure regulator; 3=electromagnetic sluice gate. (Reprinted with permission from Canaud L, et al. Proximal fixation of thoracic stent-grafts as a function of oversizing and increasing aortic arch angulation in human cadaveric aortas. *J Endovasc Ther.* 2008;15:326-334.)

## RESULTS

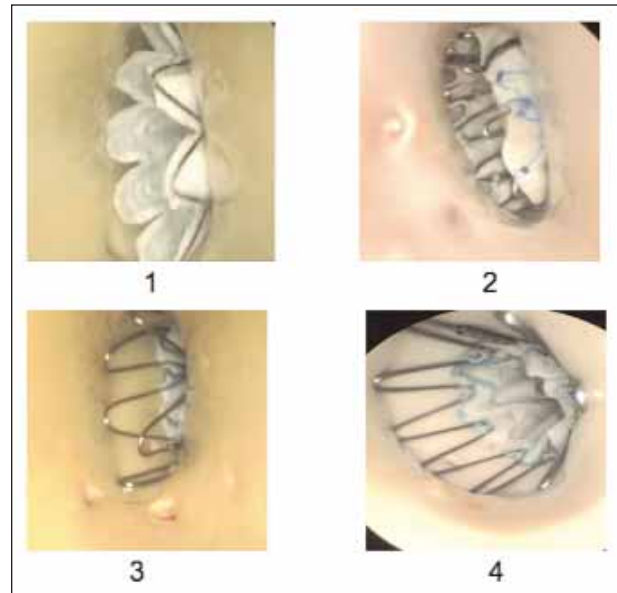
With the Zenith TX2 endograft, a lack of apposition between the proximal endograft and inferior aortic wall appeared from a neck angle of 70° upward. This lack of apposition was also observed for the Relay and TAG devices, from a neck angle of 80° and 90°, respectively and was greater with the Relay device than with the TAG device. The most effective anchorage in an angulated proximal landing zone was observed with the Valiant Thoracic Stent Graft; the prosthesis and bare spring were always in contact with the wall. No migrations or collapses were observed during static and dynamic tests, but the lack of apposition of the Zenith TX2 device caused a hemodynamically significant stenosis with a pressure decrease from 300/150 to 250/120 mm Hg at an angulation of 140°.

The TAG and Relay endografts showed poor apposition but only at the proximal landing zone (open bare-stent segment for the Relay endograft and scalloped flares for the TAG endograft). In contrast to the TX2 graft, the TAG and Relay devices did not cause hemodynamically significant stenosis due to lesser apposition of the endograft “body” to the aortic wall. When one of the devices was not well apposed to the aortic wall, we observed that the intraluminal lip length increased with increased oversizing due to wrinkling of the prosthesis (Table 1 and Figure 3).

## DISCUSSION

### Fundamentals of the Relationship Between Proximal Anchorage of Endografts and Complications After TEVAR

In cases of severely angulated proximal aortic necks, endografts are unable to conform to the inner curvature of the arch. Because of the stiffness of the stent graft, increased angulation of the proximal landing zone decreases the length of the graft in contact with the aortic wall.



**Figure 3.** Proximal anchorage of the different stent grafts at 140° angulation: TAG (1), Zenith TX (2), Relay (3), Valiant (4). (Reprinted with permission from Canaud L, et al. Proximal fixation of thoracic stent-grafts as a function of oversizing and increasing aortic arch angulation in human cadaveric aortas. *J Endovasc Ther.* 2008;15:326-334.)

Endografts protrude into the lumen of the aortic arch. The intraluminal lip appears to be a revealing sign of an ineffective proximal anchorage of thoracic endograft (Figure 4).

**Endograft collapse.** According to Muhs et al,<sup>4</sup> this lack of device wall apposition of the leading edge of the endograft is a factor leading to endograft collapse.

**Type I endoleak.** It seems extremely likely that this lack of device wall apposition is a major risk factor for endoleak. Due to poor wall apposition, the blood will leak around the proximal end of the endograft, and a type I endoleak will develop.

**Endograft migration.** Distal migration of the endograft can be the cause of late failure. The proximal endograft that is not in apposition to the aortic wall could be pushed away from the inner curve of the isthmus by the blood flow. This effect is magnified by the wrinkles due to oversizing.

### Experimental Model

Preclinical testing has a limited ability to predict clinical failures, in part due to limitations inherent with replicating in vivo conditions. Preclinical testing rarely incorporates proximal landing zone angulation, and the values for forces (pressure, flow) have not been standardized. Abel et al<sup>5</sup> suggested that the evaluation of parameters such as proximal landing zone angle and oversizing was essential during pre-

**TABLE 1. LOSS OF DEVICE-WALL APPPOSITION OF THREE STENT GRAFTS MEASURED AT VARIOUS ANGULATION AND CATEGORIES\***

Endograft	70°	80°	90°	100°	110°	120°	130°	140°	Oversizing (%)
Relay	0	0.5	0.5	1	2	3	3.5	4	<10
TAG	0	0	0.5	0.5	1	2	3	3.5	
Zenith	1	2	2	2.75	3	3	4	4	
Relay	1.1	2	2.2	2.9	3	3.4	4.7	4.8	10–20
TAG	0	0	1.5	2	2.5	3	3.5	4	
Zenith	1.2	1.9	2.7	3	3.2	3.6	4.1	4.2	
Relay	2	2.4	3	3.6	4.2	4.5	5	5.2	20–30
TAG	0.7	1.4	1.9	2.4	2.9	3.6	4.6	4.8	
Zenith	2.2	2.6	3.4	3.8	4	4.6	5.2	5.4	
Relay	3	3.4	3.9	4.5	5.2	5.9	6.3	7	>30
TAG	1.7	2	3	3.7	4	5	5.7	6	
Zenith	3.4	3.9	4.3	5.1	5.5	6.2	6.5	7.5	

\*Mean values of the loss of device wall apposition (mm) for the Relay and TAG stent grafts and of the loss of device wall apposition of the Zenith stent graft body for each degree of angulation tested and for relative increases of diameter oversizing. The Valiant Thoracic Stent Graft showed no loss of aortic wall apposition.

(Reprinted with permission from Canaud L, et al. Proximal fixation of thoracic stent-grafts as a function of oversizing and increasing aortic arch angulation in human cadaveric aortas. J Endovasc Ther. 2008;15:326-334.)

clinical testing of thoracic endografts. These investigators recommended the use of worst-case simulation conditions to allow the assessment of device performance under extreme anatomic conditions.

We tried to reproduce as closely as possible the conditions of the living human being. We used postmortem aortas that had similar histological characteristics as an aorta obtained from a living person. High pressure was used to create a dynamic testing model at the physiological loads and boundary conditions that the endograft is likely to experience under its intended use. The large degree of aortic arch angulation was tested in order to reproduce isthmus angulation associated with aortic arch classifications (type I, II, or III).<sup>6</sup>

Weaknesses of our model, which suggest further research, include the duration of the experiment and the fact that the grafts were within nonaneurysmal aortas. In our study, we were unable to demonstrate an association between severe neck angulation and migration or collapse, possibly because the duration of the experiment was too short.

### Design of Thoracic Endografts

The major difference in design between the Zenith TX2 endograft and the other grafts is the absence of open bare-stent segments or scalloped flares. A decrease in the length of the graft apposed to the aortic wall due to increased angulation may impair the function of the hooks and barbs in mitigating migration.

The difference in performance between the Valiant and



Figure 4. CT scan and angiography demonstrating a poor apposition of the stent graft along the inner curve of the aortic arch, with the stent graft protruding into the lumen of the aorta. (Reprinted with permission from Canaud L, et al. Proximal fixation of thoracic stent-grafts as a function of oversizing and increasing aortic arch angulation in human cadaveric aortas. J Endovasc Ther. 2008;15:326-334.)

Relay Stent Grafts may be explained by a greater radial force (confirmed by macroscopic intima injuries), the number of peaked springs (Valiant, 8; Relay, 6), and the high amplitude joint between the spring and the peaked spring causing angulation of the peaked spring up to an angle of 80°. Comparison of the TAG and Valiant Thoracic Stent Grafts showed that the different design features resulting in superior or proximal fixation include the radial force of the Valiant Thoracic Stent Graft, the shorter length of the scalloped flares than the peaked spring of the Valiant Thoracic Stent Graft, and the high amplitude joint between the spring and the peaked spring.

In this specific situation (eg, proximal landing zone angulation), the major implications of endograft design to provide secure proximal anchorage seem to be the radial force and the presence of a proximal open stent segment. Also, the design of the proximal open stent segment plays a role in the effectiveness of the proximal anchorage of thoracic endografts. Our research indicates that the increase of the stent graft oversizing when the stent graft is not well apposed increases this lack of device wall apposition.

## CONCLUSION

The most effective anchorage in an angulated aortic neck was observed with the Valiant Thoracic Stent Graft, followed by the TAG and Relay devices, respectively. A lack of apposition of the prosthesis body of the Zenith device was observed, resulting in a hemodynamically significant stenosis at a neck angulation of 140°. ■

*Ludovic Canaud, MD, is from the Department of Vascular and Thoracic Surgery, Hospital Arnaud de Villeneuve, CHU Montpellier, France. He has disclosed that he holds no financial interest in any product or manufacturer mentioned herein. The study in J EVT upon which this article is based was an independent study not funded by Medtronic. Dr. Canaud may be reached at ludoviccanaud@hotmail.com.*

*Pierre Alric, MD, PhD, is from the Department of Vascular and Thoracic Surgery, Hospital Arnaud de Villeneuve, CHU Montpellier, France. He has disclosed that he holds no financial interest in any product or manufacturer mentioned herein. Dr. Alric may be reached at p-alric@chu-montpellier.fr.*

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*(Dr. Kasirajan, Continued from page 7)*

of descending thoracic aneurysms of degenerative etiology in subjects who are candidates for endovascular repair. A minimum of 15 sites will be included in the study and will begin enrolling patients in early 2009. The THRIVE study examines some of the clinical endpoints of the VALOR trial and will include long-term follow-up on all 195 patients in the VALOR trial, as well as 256 new patients implanted with the Talent Thoracic Stent Graft with Xcelarent Delivery System since its commercial approval. Dr. Karthik Kasirajan, at Emory University in Atlanta, Georgia, is the national principal investigator of the study. The goal of THRIVE is to evaluate the long-term safety and effectiveness of the Talent Thoracic Stent Graft up through 5 years.

The primary endpoint of the study is freedom from aneurysm-related mortality at 5 years. Additionally, the following secondary endpoints will be collected:

- Technical success
- Procedure- or device-related adverse events
- Major adverse events
- Technical observations (ie, endoleak, migration)
- Secondary procedures
- Conversion to surgery

Some of the specific endpoints that will be in an annual clinical update include rates of aneurysm rupture, secondary endovascular procedures, conversion to surgical repair, aneurysm-related mortality, major adverse events, endoleak, aneurysm enlargement, prosthesis migration, patency, misaligned deployment, aortic perforation, and retrograde dissection.

The follow-up visits are being requested at 1 month, 6 months (conditional), 12 months, and annually for the remainder of the study. Follow-up will include a contrast-enhanced CT scan, chest x-ray, and physical examination.

The THRIVE study will also look at the clinical outcomes of female patients and non-Caucasian patients enrolled and subset these in the annual reports. Finally, the study will evaluate the effectiveness of the Medtronic physician training program by tracking the 30-day outcomes of novice implanters who have not previously implanted the Talent thoracic stent graft. The study will compare the 30-day outcomes of these implanters' first five cases and the outcomes of their subsequent five cases for a total of 10 implants. ■

*Karthik Kasirajan, MD, is Assistant Professor of Surgery, Vascular Surgery and Endovascular Therapy, The Emory Clinic, Atlanta, Georgia. He has disclosed that he holds no financial interest in any product or manufacturer mentioned herein. Dr. Kasirajan may be reached at (404) 778-3470; karthik.kasirajan@emoryhealthcare.org.*

