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INNOVATING FOR CLINICAL PERFORMANCE

Valiant® Mona LSA Stent Graft

Selected by the FDA for an early feasibility pilot program

Innovating for Clinical Performance

From Benchtop to Bedside With the Valiant Mona LSA Thoracic Stent Graft

How physicians, engineers, and regulatory agencies can work together to best serve patients with new technologies.

BY FRANK R. ARKO, III, MD

Left subclavian artery (LSA) coverage during thoracic endovascular aortic repair (TEVAR) is often necessary due to anatomic factors and is performed in up to 40% of TEVAR procedures.[1] Society for Vascular Surgery practice guidelines recommend that preoperative revascularization should be performed in patients who need elective TEVAR in which proximal seal necessitates coverage of the LSA. Furthermore, routine preoperative LSA revascularization is strongly recommended in selected patients who have anatomy that compromises perfusion to critical organs. However, in patients who need urgent TEVAR in which LSA coverage is necessary, revascularization should be individualized and addressed expectantly.[2]

Data to date are inconclusive as to the appropriate management of the LSA during TEVAR. LSA coverage is associated with an increased risk of arm ischemia, vertebrobasilar ischemia, and possibly spinal cord ischemia and anterior circulation stroke; left subclavian revascularization should be performed before coverage.[3,4] However, others have found that the use of selective revascularization is safe and does not appear to increase the risk of neurologic events.[5,6]

The Valiant® Mona LSA Stent Graft (Medtronic, Inc., Minneapolis, MN), the clinical configuration of the new Thoracic Branch Stent Graft[a] program, was developed to solve these clinical challenges and extend the benefits of endovascular repair without surgery to more patients with thoracic aortic aneurysms.

The intention was to design a technology leveraging the proven clinical effectiveness of the FDA-approved Medtronic Valiant Thoracic Stent Graft in the management of thoracic aortic disease while maintaining flow to the LSA without the need for surgical bypass.

The Valiant Thoracic Stent Graft consists of a monofilament polyester fabric graft with nitinol springs. It is indicated for the treatment of isolated lesions (excluding dissections) of the descending thoracic aorta. The stent graft system incorporates an eight-peak proximal stent design that distributes radial force evenly across the aortic wall. There is no connecting bar between stents, which makes the graft highly conformable. Advantages of the delivery system include tip capture for enhanced control and precise deployment, as well as a hydrophilic coating that facilitates delivery through difficult access vessels.

Multiple publications have addressed the use of the Valiant Stent Graft in the treatment of thoracic aortic pathology, including the TRAVIATA registry, the VIRTUE registry, the Valiant® Captivia® registry, and the pivotal

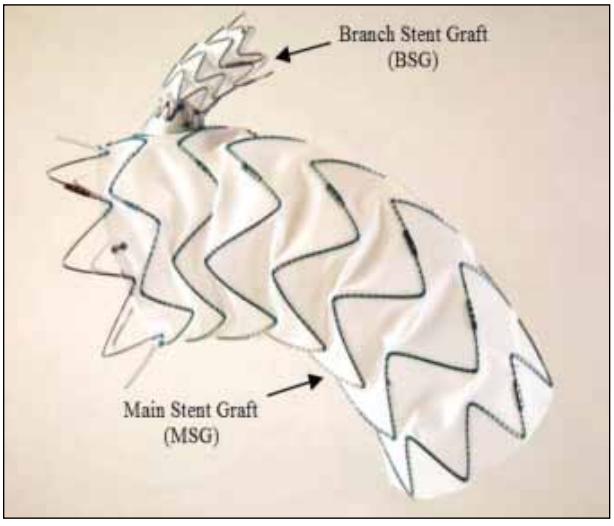

Figure 1. The Valiant Mona LSA Stent Graft is used exclusively for clinical investigation. Not approved commercially anywhere.

[a]Technology under development, not approved commercially anywhere.

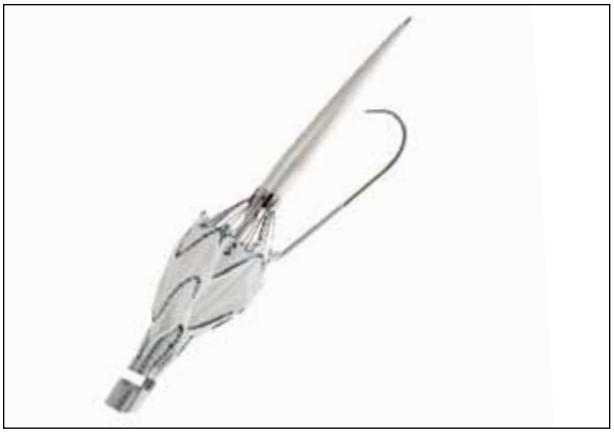

Figure 2. The Valiant Mona LSA Stent Graft with dual-wire system with precannulated branch graft.

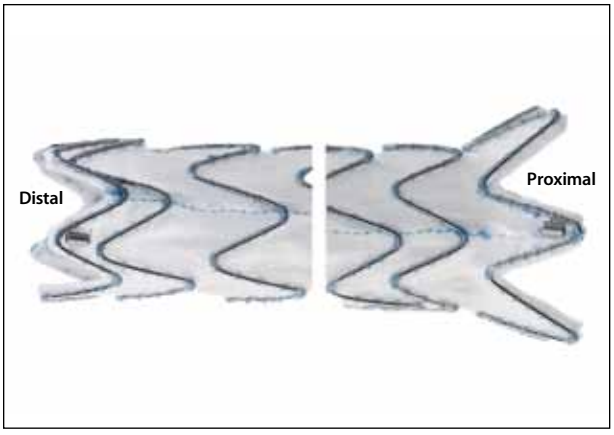

Figure 3. Branched graft for the Mona LSA Stent Graft. Available sizes include 10-, 12-, and 14-mm grafts, all of which are 4 cm in length.

results of the VALOR II trial.[7-11] The VALOR II trial reported 30-day, 12-month, and 3-year results of the Valiant Stent Graft in patients with thoracic aortic aneurysms. This was a prospective, nonrandomized, pivotal trial at 24 sites in the United States that enrolled a total of 160 patients. Technical success was achieved in 96.3% of patients being treated. Perioperative mortality was 3.1%, with 0.6% paraplegia, 1.9% paraparesis, and 2.5% stroke rates. Aneurysm-related mortality at 1 year was 4%, with no ruptures or conversions to open surgery. The 3-year outcomes presented at the TCT conference in 2012[11] showed an aneurysm-related death rate from 1 to 3 years of 0.9%, with no conversion and only two ruptures. These results demonstrate that the Valiant Stent Graft is safe and effective in the treatment of descending thoracic aortic aneurysms.[10]

The development of the Valiant Mona LSA Stent Graft leveraged this clinical performance and combined the physician/engineer teams, thus maximizing the understanding of anatomy and physiology with complex engineering principles to limit the potential risks of extending a device into the aortic arch. The key to success was to develop a stent graft and branch graft that would accommodate the aortic anatomy rather than forcing the aorta to accommodate to the stent graft.

THE VALIANT MONA LSA STENT GRAFT

The Valiant Mona LSA Stent Graft is a modified Valiant Captivia device (Medtronic, Inc., Minneapolis, MN) with a single-branch stent graft designed to perfuse the LSA. It is an off-the-shelf device that utilizes the Valiant Captivia tip-capture mechanism for accurate deployment. The main body of the graft has the same eight-peak, self-expanding FreeFlo proximal design (Figure 1). The modification to the device is the addition of a flexible cuff with a radiopaque coil at the base.

The stent graft delivery system is a modified Valiant Captivia system. It has a dual-wire lumen, with the main lumen over the entire device and a second lumen that precannulates the flexible cuff. This allows for loading the branch graft on the back table with a hydrophilic wire that is ≥ 260 cm in length (Figure 2). The proximal nose cone has four grooves that allow for passage of the wire out of the branch while the outer sheath constrains the main device; these grooves allow resheathing of the device over the second wire.

The left subclavian branch stent graft itself is composed of a nitinol helical wireform and a polyester graft material with a proximal flare to provide a seal between components. The branch graft itself comes in three sizes of 10, 12, and 14 mm in diameter, with an overall length of 40 mm. It is delivered from a femoral approach through a 15-F hydrophilic delivery system (Figure 3).

STENT GRAFT DEPLOYMENT AND DELIVERY

Indications for the device require a minimum of 10 mm of distance between the left carotid artery and the LSA. Based on preoperative CT angiography with 3D reconstructions, appropriate angles for deployment of the stent graft can be utilized to identify the anatomy, orient the device, and limit any manipulations of the device in the arch. A pigtail catheter is placed up the contralateral groin through a 5-F sheath. Placement of a stiff wire up over the arch through the ipsilateral femoral artery is performed. A 260-cm hydrophilic wire is advanced through the second lumen port, cannulating the cuff. Left brachial access is achieved with ultrasound guidance, and a 55-cm, 7-F sheath is advanced to the LSA

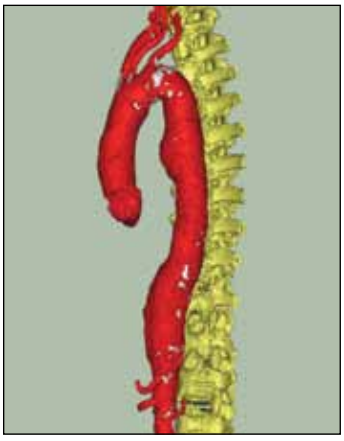

Figure 4. Preoperative CTA of first in-human implant. The distance between the left common and left subclavian arteries is 10 to 11 mm. The thoracic aorta is 61 mm with a dumbbell shape. The patient underwent TEVAR from the LSA to the celiac artery. She was discharged to home in 5 days without complications.

origin. An 18- X 30-mm EnSnare (Merit Medical Systems, South Jordan, UT) is placed just within the aortic arch from the left subclavian orifice along the greater curve. The main device is then advanced over the stiff wire to just proximal from the left subclavian orifice. Care is taken to keep the orientation of the cuff toward the greater curvature.

With the main device in the descending aorta just proximal to the LSA, the second wire is advanced and snared along the greater curvature. At this point, wire wrap needs to be evaluated and prevented. The second lumen wire is then snared and brought out of the 7-F sheath in the brachial artery. Utilizing the preoperative angles, there should be clear separation of the two-wire system as the device is advanced to the LSA. Aortography utilizing preoperative imaging is then performed to allow for any minor adjustment and alignment of the cuff with the orifice of the LSA. Any major realignment of the graft should be performed in the descending aorta to minimize torque on the device and the risk of embolization and stroke in the arch.

The main stent graft is then deployed slowly and advanced forward while constrained, bringing the main body of the graft to the level of the left carotid artery while there is gentle pulling of the second wire from the brachial sheath to engage the cuff in the orifice of the LSA. The main graft is fully deployed with release of the tip-capture mechanism. It is important to remember that the cuff has been designed so that it does not need to extend into the orifice of the LSA. Furthermore, the design of the cuff allows for alignment to be off by up to 30º without affecting the branch graft patency. The delivery system is resheathed after recapture of the tip and then removed from the patient. The proximal stent graft may be molded with a Reliant® balloon (Medtronic, Inc., Minneapolis, MN). The LSA branch graft is advanced over the second wire and deployed through the branch cuff, allowing the proximal flared portion of the branch graft to seal against the branch cuff. Retrograde arteriography through the brachial sheath is performed to identify the orifice of the left vertebral artery. Deployment of the branch graft should maintain patency of this artery. Standard ballooning may be performed between the components of the graft, and completion aortography is used to assess the patency of the arch vessels and the left subclavian branch graft. Assessment for endoleaks is also performed at this time.

The Valiant Mona LSA Stent Graft is manufactured in a 150-cm length. Thus, in thoracic aneurysms that require more than one component, a distal Valiant® device may be implanted as well.

FIRST IN-HUMAN EXPERIENCE

The Valiant Mona LSA Stent Graft was selected by the US Food and Drug Administration (FDA) for participation in the FDA's innovation pathway. This new program allows for early clinical investigation within the United States. The Guidance on Early Feasibility studies limits enrollment to fewer than 10 patients for devices in early development for a specific indication. The innovation pathway allows for proof of principle and initial clinical safety. It is a key principle of the program that an early feasibility study is appropriate when nonclinical testing

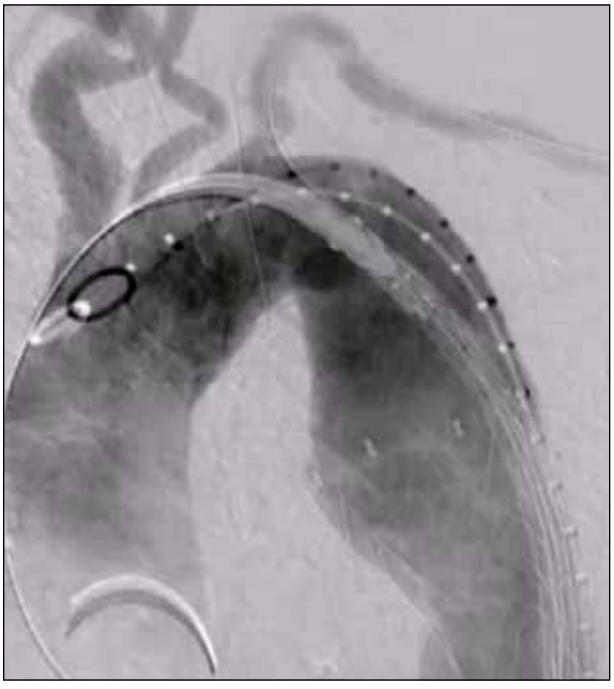

Figure 5. Intraoperative arteriogram with the distal component implanted first, with the Mona LSA Stent Graft being advanced up into the arch after the second wire has been snared from the left brachial approach.

Figure 6. The branch graft has been deployed into the LSA. The proximal portion of the main graft has perfect alignment up to the left carotid artery. The branch graft is widely patent, and the aneurysm is completely excluded.

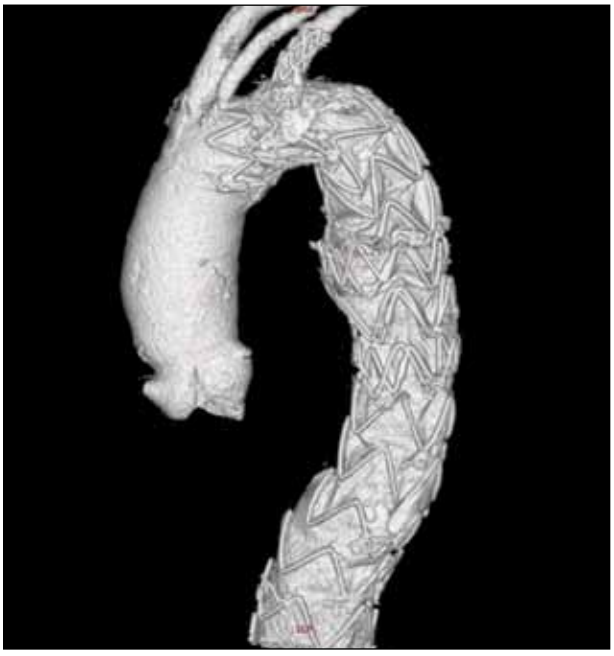

Figure 7. Thirty-day follow-up CTA with complete exclusion of the aneurysm. All three supra-aortic branches are patent, including the branch graft in the left subclavian artery.

is not adequate to advance development, and clinical experience is necessary. However, this early feasibility study must be justified by an appropriate risk-benefit analysis with adequate human subject protection. FDA approval of the early feasibility study IDE application may be based on less nonclinical data than expected for a traditional feasibility or pivotal trial.

The first in-human Valiant Mona LSA Stent Grafts were implanted as part of this program in seven patients at two sites, including the Carolinas Medical Center in Charlotte, North Carolina, and the Cleveland Clinic in Cleveland, Ohio. The first human implant was performed at Sanger Heart and Vascular Institute at the Carolinas Medical Center on April 11, 2013. The patient was an 81-year-old woman with a 6.1-cm thoracic aneurysm that required LSA coverage. The proximal seal zone was 42 mm in diameter, with the distance between the left common carotid artery and the LSA being 11 mm. The LSA origin was 8.5 mm in diameter. Coverage was to the celiac artery, as it was a dumbbell-shaped aneurysm (Figure 4). The planned treatment was performed through a left iliac conduit. The patient was treated with the distal component (46–46-mm distal extension) with a 46-mm Valiant Mona LSA in the arch. The branch graft implanted was a 10-mm branch stent graft (Figures 5 and 6). The patient did well without any complications and was discharged home 5 days after the procedure. Follow-up CTA at 30 days (Figure 7) demonstrated excellent proximal and distal seal without any evidence of an endoleak. Aneurysm diameter remained unchanged.

DISCUSSION

Conventional repair of aortic arch pathology is associated with significant mortality and stroke rates of 6% to 20% and 2% to 18%, respectively.[12,13] Aneurysms involving the aortic arch have been treated with open surgical techniques that require cardiopulmonary bypass with hypothermic circulatory arrest. The use of endovascular stent grafts has clearly allowed for the application of interventions in the descending aorta as well as the visceral aorta.

Given the current results of open surgical repair, these techniques have been extended for use in the aortic arch. Techniques have included the use of in situ fenestrations utilizing different tools, branch grafts, and chimney grafts placed parallel to the thoracic graft, with varying results in small numbers of patients. Utilization of a hybrid approach will typically be performed in stages, with the first surgical stage typically being a carotid-carotid bypass and/or a carotid-subclavian revascularization. This is followed by thoracic stent graft repair with placement of the graft to the innominate or left carotid artery, respectively.

Chimney grafts parallel to the main thoracic graft, typically in the carotid or subclavian arteries, have been used in the aortic arch with varying results. Concerns regarding this technique include its unknown and untested durability and the continued risk of type I endoleaks between components through the curvature of the arch.[14] The use of in situ techniques to create fenestrations within the graft after deployment across the supra-aortic vessels has been reported. As first reported by Murphy et al, good results have been shown with the use of a laser for in situ techniques.[15,16] As is seen in other series evaluating endovascular repair of aortic arch pathology, the number of patients treated is small, with limited follow-up.

There have also been case reports describing favorable outcomes with the use of homemade branch grafts.[17,18] Any method that requires treatment of the arch should be performed with careful preoperative planning (comprising preoperative imaging, ease of device use, durability, and the absence of access issues), expert endovascular skills, and appropriate imaging equipment, as these are imperative for a successful result.

The goal of the Medtronic early feasibility study of the Valiant Mona LSA Stent Graft was to validate the procedure in humans and to assess safety and performance acutely and at 30 days, with continued follow-up to 5 years. Specific imaging data were collected to further augment current understandings within the thoracic arch. Results of acute performance will be presented at the 2013 VEITH Symposium.

If successful, the Valiant Mona LSA system could potentially obviate the need for LSA bypass, extend the benefits of endovascular repair without surgery to more patients with thoracic aortic aneurysms, and quell the controversy that is related to whether the LSA needs to be, should be, or can be covered. ■

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Branch Technology: Innovation in the Development Process

Increasing AAA and TAA patient applicability while ensuring quality from design to market.

BY PETER LARSON, MS, BS; EMILIE SIMMONS, MS; AND PAIGE BOTA, BS, PHD

The Thoracic Branch and Abdominal Branch Stent Grafts[a] are currently under development and are built on the Valiant® Thoracic and Endurant® Abdominal technologies (Medtronic, Inc., Minneapolis, MN). The Valiant Mona LSA Stent Graft, the clinical configuration of the Thoracic Branch Stent Graft, is currently under study in an FDA-approved feasibility study, and the Abdominal Branch Stent Graft is in development. These innovations are expected to expand applicability with an off-the-shelf device for patients whose aortic landing zone is insufficient for traditional endovascular aneurysm repair (EVAR)/thoracic endovascular aneurysm repair (TEVAR).

THE NEED FOR INNOVATIVE EVALUATION METHODS

The expectations with respect to quality, durability, and performance of branched stent grafts are unchanged from traditional (nonbranched) devices. As a result, these devices were designed and developed using industry standards similar to those for the development of traditional nonbranched devices. However, current industry standard requirements are not designed to specifically test the nuances of branched grafts, therefore requiring the development of new evaluation methods.[1]

A key aspect in developing these new evaluation methods was to fully understand the anatomical and physiological requirements of the intended patient population. Studies were carried out to understand the use requirements in animals and humans, which allowed engineering teams to develop the appropriate performance evaluation methods (including simulated use, durability, computational, and performance methods) tailored to the targeted patient population. This article focuses on two types of evaluation methods that were used to design these innovations—simulated-use evaluation and durability testing.

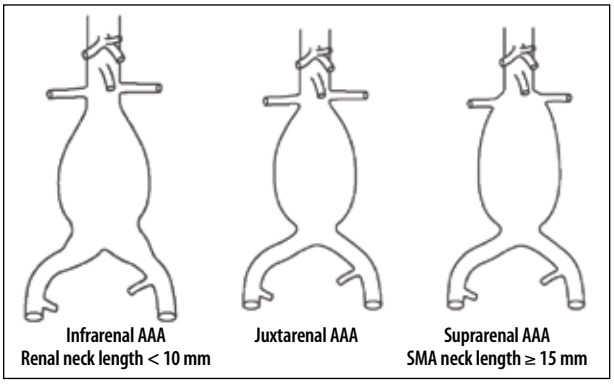

Figure 1. Anatomical scope for the Abdominal Branch Stent Graft system.

BRANCH TECHNOLOGY OVERVIEW

As described in detail in the previous article by Dr. Arko, the clinical configuration of the Thoracic Branch Stent Graft, Valiant Mona LSA Stent Graft system, is currently being evaluated in an early feasibility clinical trial. The Valiant Mona LSA Stent Graft is a modular system composed of two self-expanding stent grafts that are designed to perfuse the left subclavian artery (LSA) when the device is implanted in Zone 2 of the aorta for the exclusion of a thoracic aortic aneurysm (TAA). The main stent graft is built off of the commercially available Valiant Stent Graft but has been modified to incorporate a flexible cuff to accommodate a branch stent graft that extends into the LSA.

The Abdominal Branch Stent Graft system is designed to treat patients with short-neck infrarenal (< 10 mm), juxtarenal, and suprarenal aneurysms (Figure 1), which are estimated to comprise 20% to 30% of the total AAA population (data on file). These patients are currently being treated with the use of several methods, including custom devices, with off-label solutions, such as chimney configurations that have unproven durability;[2] or with open surgery.

[a]Technology under development, not approved commercially anywhere

The Abdominal Branch Stent Graft system is intended to treat these patients with a durable, off-the-shelf solution. The Abdominal Branch device is composed of a bifurcated aortic stent graft with a scallop for the superior mesenteric artery, two self-expanding, ePTFE-covered renal branch stent grafts, and Endurant® II limbs.

The bifurcated stent graft leverages features from the commercially available Endurant II Stent Graft. The graft material, suprarenal stent, iliac stents, and several of the markers are identical to those used in the Endurant II Stent Graft. The seal stent and body stents are unique to this device and are designed to maximize patient applicability while maintaining patency of the branch vessels. The renal branch cuffs were added to the bifurcated stent graft to allow mating with the renal branch stent graft. The renal branch stent graft was designed to be highly flexible in order to accommodate significant vessel tortuosity and motion.

SIMULATED-USE EVALUATIONS TO REFINE DEVICE DESIGN AND PROCEDURE

Thoracic Branch: Perfusing the LSA

The Valiant Mona LSA Stent Graft delivery system is built on the Captivia® delivery system platform (Medtronic, Inc., Minneapolis, MN), which incorporates tip capture to allow for controlled deployment, allowing the device to be placed accurately within the intended seal zone. Building off of this platform, the design team was faced with the challenge of how to provide rotational alignment of the system to ensure alignment of the cuff with the LSA. To optimize the procedure and hone the rotational alignment technique, the team utilized in vitro simulated-use testing and in vivo preclinical models to obtain physician and engineering feedback.

The goal of in vitro simulated-use testing was to evaluate the performance of the endovascular system in a clinically relevant environment that simulated the intended-use conditions, such as pressure, flow, and vessel compliance. To develop the test models, several geometric anatomical parameters were identified to aid in the quantification of aspects of the diseased anatomy. These parameters included tortuosity of the vessel, angulation at the landing zones, and the LSA take-off angle. To obtain these parameters, CT scans from several clinical studies and databases, including Valiant clinical trials, were analyzed and reconstructed. In total, the anatomic geometries of more than 600 patients were analyzed and quantified. Using these parameters, several clinically relevant simulated-use silicone models of the thoracic aorta and iliac arteries were created with varying degrees of tortuosity (Figure 2).

With anatomically relevant simulated-use models, the engineering team was able to partner with physicians to evaluate the use and performance of the device, as well as implement device and procedural refinements as needed to ensure deployment accuracy of the cuff and enhance ease of use. In addition to the simulated-use bench model testing, preclinical studies were performed with physicians, providing insights into the procedure and device not possible through simulated-use bench model testing alone. The preclinical models were able to evaluate the dynamic aortic motion, the translation of two-dimensional angiographic images to three-dimensional rotational alignment of the cuff, and the hemostasis management of a two-wire system. Both simulated-use and preclinical models advanced our understanding and appreciation for the methods and visual cues necessary for successful device deployment.

Figure 2. Example of Valiant Mona LSA simulated-use silicone model to evaluate the performance in a clinically relevant environment that simulates intended use conditions such as pressure, flow, and vessel compliance.

Abdominal Branch: Perfusing the Renal and SMA

Developing an off-the-shelf device is significantly more challenging in branch endovascular therapy than traditional EVAR. Physician input revealed the complexity of the procedures currently used to implant branched AAA stent grafts. This complexity is associated with long and unpredictable procedure durations, high fluoroscopy exposure, and the use of a large number of ancillary devices.[3,4] Based on this knowledge, the Abdominal Branch Stent Graft team first focused on developing a logical and repeatable procedure and then on designing delivery systems to facilitate that procedure. Clinically relevant simulated-use models were constructed by analyzing and quantifying real patient anatomies. Initial prototype devices were designed from predicate device components, allowing physicians to perform deployments and provide immediate procedural feedback. The feedback acquired from these initial deployments expedited our refinement of procedural and device concepts and led to significant improvements of the simulated-use model. Simulated-use evaluation by physicians continues to be a key driver for device refinements. The simulated-use model has evolved to a state-of-the-art setup, which utilizes fluoroscopic imaging, physiologic pressure and pulsatile flow, contrast injection, and challenging anatomic features.

TRANSLATING ANATOMIC MOTION INTO FATIGUE TESTING FOR ENSURED DURABILITY

Thoracic Branch: Ensuring Durability in the Relative Motions Between the LSA and the Aorta

In addition to accurately reaching the landing zone, perfusing the LSA, and excluding the aneurysm, the Valiant Mona LSA Stent Graft was designed to ensure robust durability and performance throughout the life of the patient. To define the use conditions, and because the published literature on thoracic aortic and LSA dynamics were limited, our research and development team leveraged the data sets of the more than 600 patient anatomies discussed previously in the simulated-use section. An initial design iteration of the stent graft system was evaluated as part of a chronic porcine model to assess acute performance and deliverability of the device, as well as chronic patency of the branch device. However, upon completion of the study, stent strut fractures were identified within the branch device, indicating that the extent of relative motion between the aorta and LSA exceed the capabilities of the device and that a new branch stent graft design would be required. As a result of these findings, a thorough evaluation and quantification of human aortic and LSA motion was conducted.

The magnitude of cardiac and respiratory motions of the LSA and the aorta was initially quantified from several multiphase CTAs and two-dimensional angiographic cines in porcine models and later analyzed for human subjects (Figure 3; Table 1). When comparing the porcine cardiac preoperative data to the combined porcine cardiac and respiratory data, the data demonstrated the majority of relative motion between the LSA and aorta was cardiac induced and located in the anterior/posterior plane. When comparing the cardiac preoperative data to the cardiac postoperative data, the relative motions are decreased in the stented patients. When comparing the porcine and human preoperative cardiac motions, the motion from the porcine model was greater. In addition, preliminary

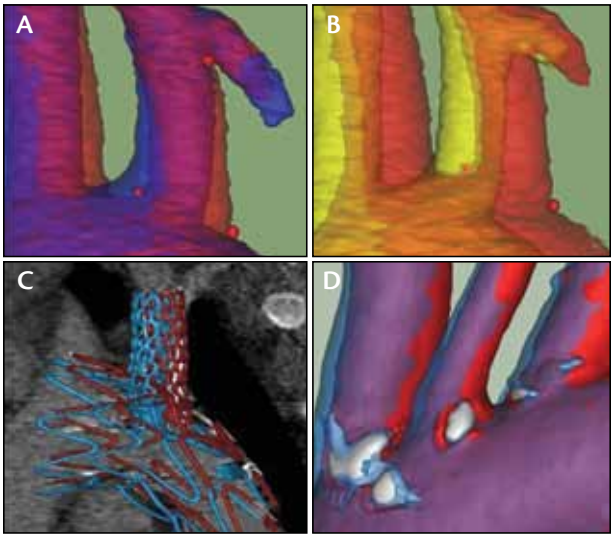

Figure 3. Valiant Mona LSA use conditions using multiphase CTA for porcine cardiac preoperative data throughout systole (purple) and diastole (orange) (A), porcine cardiac and respiratory preoperative data throughout systole inhale (yellow) and diastole exhale (red) (B), porcine cardiac postoperative data throughout systole (blue) and diastole (red) (C), and human cardiac preoperative data throughout systole (purple) and diastole (red) (D).

two-dimensional angiographic cine data of stented aneurysmal human aortas were captured from an approximate 30° left anterior oblique view angle and then analyzed to quantify respiratory and cardiac motions. From these human studies, the relative motion between the thoracic aorta and the LSA was minimal: 0.7 mm in the anterior/posterior plane and 0.7 mm in the caudocranial plane.

As these use conditions became better understood and defined, so did the benchtop fatigue tests and designs. These updated and new fatigue tests were able to identify and challenge the critical design features,

TABLE 1. CONTRIBUTIONS OF RELATIVE CARDIAC AND RESPIRATORY MOTIONS BETWEEN THE LSA AND THE AORTA

Maximum Relative Displacement Between the LSA and the Aorta Using Multiphase 4D CTAs (dimensions in mm)

Direction of Maximum Relative Displacement	Porcine			Human
	Cardiac Preoperative (n = 8)	Cardiac and Respiratory Preoperative (n = 5)	Cardiac Postoperative (n = 14)	Cardiac Preoperative (n = 7)
Left-Right	± 0.6	± 1.0	± 0.2	± 0.8
Anterior/Posterior	± 2.4	± 2.9	± 1.4	± 1.6
Caudocranial	± 0.7	± 0.7	± 1.0	± 1.0

Abbreviations: 4D, four-dimensional.

such as the cuff and branch graft flexibility, to ensure durability. The stent graft evolved into its current state through design loops as motion data were gathered and the system was challenged through more refined tests. In the end, it was evident a more flexible system was required. As a result, the stent graft transitioned from a stiff junction (both cuff and branch graft) into a flexible system able to dissipate the relative motions between the LSA and the aorta. This development culminated in the durability results found in both the preclinical model and benchtop fatigue tests.

Abdominal Branch: Ensuring Durability in the Relative Motions Between the Renals and the Aorta

The Abdominal Branch program is the first program at Medtronic to develop a stent graft that branches the renal arteries and the abdominal aorta. The Abdominal Branch program has leveraged best practices from the Thoracic Branch program. Specifically, the team partnered with Prof. Christopher Cheng at Stanford University to obtain data on renal tortuosity and motion. In a unique study published in the *Journal of Vascular and Interventional Radiology,* 16 AAA patients underwent three-dimensional gradient-echo MRA imaging before treatment.[5] The MRA data were used to reconstruct each patient's anatomy at inspiration and expiration (Figure 4). These reconstructions were utilized to extract values for maximum angulation, change in angulation, and radius of curvature both at the ostia and at the mid-renal arteries. These variables were adopted as boundary conditions in new fatigue tests to challenge the device in its anticipated clinical environment. Evaluations to date indicate the Abdominal Branch Stent Graft shows promise for a durable, off-the-shelf solution needed to treat these challenging patient anatomies.

ADVANCING TECHNOLOGY

With complex patient anatomies, a deeper understanding of the use conditions is required to develop a durable branched stent graft system. With increased emphasis on collecting and analyzing the use conditions of the in vivo environment, the Valiant Mona LSA Stent Graft and Abdominal Branch Stent Graft systems have been designed with ease of use and durability in mind. Through the implementation of innovative techniques to better understand the anatomy of the target populations, new bench tests were developed to advance the methods of endovascular device design. The encouraging results of these developments are evident in the two branch device programs. The Valiant® Mona LSA has been successfully implanted in seven patients in the United States as part of the Early Feasibility IDE, and the Abdominal Branch system is progressing toward its final design before clinical use. ■

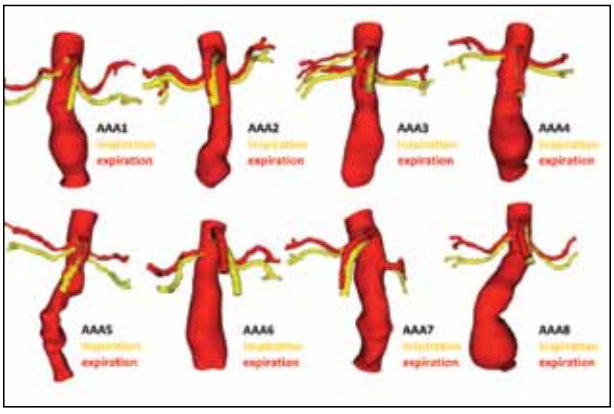

Figure 4. Abdominal Branch use conditions: renal artery and superior mesenteric artery motion at inspiration and expiration.

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Why Evidence Matters in Innovation

The importance of clinical evidence in today's medical practice.

BY KENNETH OURIEL, MD, MBA

It is axiomatic that health care costs are escalating at an unsustainable rate that, until recently, exceeded that of the economy as a whole.[1] The growth is, in large part, a result of inpatient procedure-based hospital care. Appropriately, focus has been centered on those interventions with undefined or marginal long-term clinical benefit. Third-party payors are placing increasing scrutiny on these procedures. Objective evidence of clinical benefit and cost-effectiveness is becoming a prerequisite to payment for many interventions.

In their 2006 book *Redefining Health Care: Creating Value-Based Competition on Results*, Michael E. Porter and Elizabeth Olmstead Teisberg advanced the concept of value-driven health care.[2] Simplistically, value was defined as the ratio of quality to cost. In a pure market-driven model, consumers (patients) would be able to accurately assess quality. Costs (price) would be well-defined a priori and also borne directly by the consumer.

VALUE-DRIVEN HEALTH CARE?

Current health care paradigms in the United States and elsewhere are far from value-driven. Patients and even health care providers are often unable to accurately judge quality. There exist few readily accessible and objective quality indices.[3] What few outcome measures do exist are highly dependent on the severity of illness and thus of marginal utility when applied to a specific patient or a unique clinical scenario. Price, a driver of non–health care decisions, has not been a major factor in health care. A patient's choice of treatment is usually made at a time when the ultimate cost of care cannot be accurately estimated by his or her providers because the complexity of the treatment is often impossible to predict prospectively. Of possibly greater importance is the isolation of the consumer from the economic burden of treatment. Absent a high-deductible insurance plan, economic issues play a marginal role in a patient's decision-making process.[4]

A patient's choice of treatment is usually made at a time when the ultimate cost of care cannot be accurately estimated by his or her providers because the complexity of the treatment is often impossible to predict prospectively.

Pricing issues are neither the subject of this article nor likely to be soluble in the foreseeable future. By contrast, the objectification of quality is not only attainable but is rapidly becoming a prerequisite for payors and patients alike. Quality must be assessed in the context of at least three criteria to ensure comparability among different physicians, hospitals, and patients.

First, outcome measures must be standardized—that is, evaluated and reported in a consistent manner. As one example, comparing the risk of major adverse events after endovascular and open surgical aneurysm repair is only meaningful when similar definitions and time frames are used for both treatment groups. Second, outcome measures must be considered in the context of the baseline illness severity of the patients. For example, the risk of perioperative death in a New York Heart Association functional class III patient about to undergo aneurysm repair should not be estimated from a study of healthier patients. Last, outcome measures should be easily accessible to and understandable by physicians and the lay public. Only then are such data useful for guiding treatment decisions.

MEDTRONIC INITIATIVES FOR LONG-TERM EVIDENCE

The quest for evidence begins with the acquisition of useful clinical data from clinical trials performed before regulatory approval of a product. The design and execution of well-designed trials are based upon the reporting of standard, relevant outcome measures and specification of the baseline characteristics of the population being studied. Ideally, the sample size should be large enough to allow robust multivariable analyses that can identify individual predictors of outcomes. After product approval, postmarket studies should be performed to confirm the findings of the premarket trials in a real-world setting. These studies should be rigorously monitored and adjudicated in order to guarantee and maintain the quality and consistency of the collected data. Finally, clinicians should be cognizant of their own results, benchmarking against registries such as the Society for Vascular Surgery Quality Initiative.[5] Such societal registries offer a means for collecting enough baseline patient characteristics to allow severity-based outcome assessments.

The Medtronic Endurant® program (Medtronic, Inc., Minneapolis, MN) is a good example of an initiative designed to provide the outcome evidence necessary for the acceptance of a new innovation. The initial Endurant® clinical trials were designed with well-defined, standard definitions for outcome measures.[6] The study populations were well-characterized with respect to baseline comorbidities and anatomic measures, with a total of 274 patients studied in the European and United States premarket approval trials.

After regulatory approval in Europe and the United States, the Endurant device was evaluated in a large global prospective study, the ENGAGE registry.[7] ENGAGE was designed to assess long-term clinical outcomes within the context of contemporary, real-world use of Endurant in 1,263 patients. Such large sample sizes allow for subgroup analyses highly relevant to the risks that an individual patient might expect after aneurysm repair with the Endurant device.

The midterm results from the US IDE trial were presented in 2013, with an absence of aneurysm-related mortality, postimplantation rupture, migration, or open surgical conversion in 107 patients followed to 3 years.[8] Contemporaneous with this report, over 100,000 Endurant® II Stent Grafts have been implanted by now, approximately 5 years after the initial introduction of the device in Europe. The Endurant paradigm is being repeated by Medtronic's IN.PACT® program of drug-eluting balloons for lower extremity occlusive disease.[9] Outcomes of drug-eluting balloon therapy were evaluated with well-designed and monitored clinical trials followed by large registries similar in size to ENGAGE, enrolling a globally diverse, real-world series of patients.

The design and execution of well-designed trials are based upon the reporting of standard, relevant outcome measures and specification of the baseline characteristics of the population being studied.

Medtronic's Endurant and IN.PACT programs serve as models for the evidence-based approach to any new medical device. In combination with continued data acquisition through participation in clinically rigorous registries along with the eventual incorporation of economic data, the ultimate "value" of these innovative devices will be defined in a manner consistent with that espoused by Porter and Teisberg. This is precisely the level of evidence that will be required if novel technologies are to be introduced into the armamentarium of the practicing clinician at this juncture, when intense scrutiny of quality and cost is becoming the norm. The bar for evidence-based medicine has been raised, and companies such as Medtronic are leading the way. ■

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Empowering EVAR Clinical Performance

Endurant II Stent Graft Durable Outcomes in the ENGAGE Real-World Registry

BY PIETER P.H.L. BROOS, MD; PHILIPPE W.M. CUYPERS, MD, PHD; JOEP A.W. TEIJINK, MD, PHD; AND MARC R.H.M. VAN SAMBEEK, MD, PHD

During the last 20 years, endovascular repair of abdominal aortic aneurysms (AAAs) has evolved and is now generally accepted as a preferred option to conventional open surgical repair. A recently published meta-analysis of 25,078 patients undergoing endovascular aneurysm repair (EVAR) and 27,142 patients undergoing open surgical repair for AAAs showed significant reduction in 30-day mortality in the EVAR arm, but no difference was seen after 2 years.[1] A significantly higher proportion of reintervention procedures after EVAR was also noted.

Medtronic, Inc. (Minneapolis, MN) designed the market-leading Endurant® Stent Graft system to address the limitations of previous stent graft designs. A small-amplitude M-shaped proximal stent was designed to improve sealing at the proximal neck while potentially allowing for greater sizing flexibility. Radial strength was also improved while allowing a lower-profile delivery system. Active suprarenal fixation was added to prevent endograft migration. The Endurant Stent Graft system received CE Mark approval in July 2008 and US Food and Drug Administration approval in December 2010. Subsequently, the Endurant® II Stent Graft received FDA and CE Mark approval, with additional enhancements such as a lower-profile delivery system with extended hydrophilic coating, additional limb lengths, and enhanced radiopacity of the contralateral gate.

After a safety assessment trial in Europe,[2] the Endurant Stent Graft Natural Selection Global Postmarket Registry (ENGAGE) was undertaken to quantify the performance of Endurant within the context of contemporary, real-world use. ENGAGE is a multicenter, nonrandomized, single-arm prospective registry.

Procedural details and the early results from the ENGAGE registry have previously been published, showing high rates of clinical and technical success.[3] These results were very promising for the use of the Endurant Stent Graft system in a real-world study population, but longer follow-up was needed to assess the endograft's durability and effectiveness. Herein, we present the 1- and 2-year results of the ongoing ENGAGE registry.

ENGAGE REGISTRY STUDY DESIGN

Unprecedented in size, scope, and geographic representation, the ENGAGE Registry represents the combined experience of 79 high-volume sites in 30 countries across six continents. Enrollment started in March 2009 and was completed in April 2011; ENGAGE recruited 1,263 patients who were primarily implanted with the Endurant device. The eligibility criteria for ENGAGE were minimal in order to reflect real-world clinical practice.[4] To avoid selection bias, participating sites were requested to enroll patients consecutively. Ruptured AAAs were not considered for enrollment into ENGAGE. Data collected on each patient were recorded on a web-based electronic case report form to ensure reliable data collection, data management, secure authentication, and traceability; 100% of the data were reviewed, and more than 40% of patients' source documentation was monitored randomly.

RESULTS

Baseline

At the time of writing this article, 1-year data on all 1,263 patients and 2-year data on a cohort of 500 patients (39.6%) have been presented. The baseline char-

TABLE 1. PATIENT DEMOGRAPHICS AND RISK FACTORS

Variable		N = 1,263
Age (years), mean ± SD (range)	73.1 ± 8.1	(43–93)
Male sex	89.5%	(1130/1,263)
ASA classification		
Class I	6.1%	(77/1,262)
Class II	41.8%	(527/1,262)
Class III	41.5%	(524/1,262)
Class IV	10.6%	(134/1,262)
Symptoms		
Asymptomatic AAA	83.9%	(1,059/1,262)
Symptomatic AAA	16.1%	(203/1,262)
Mean AAA diameter (mm)	60.3 ± 11.7	(30–119)
Treated outside IFU	17.9%	(226/1,263)
Risk factors		
Tobacco use	49.3%	(607/1,232)
Hypertension	75.4%	(940/1,246)
Hyperlipidemia	60.5%	(719/1,189)
Diabetes	19%	(236/1,245)
Cardiac disease	53.5%	(675/1,262)
Cancer	20.5%	(254/1,242)
Family history of aneurysms	6.7%	(84/1,262)

acteristics are shown in Table 1. Patient demographics and risk factors were typical for abdominal aneurysms, comprising 90% men who were a mean age of 73.1 ± 8.1 years. Most of the patients were American Society of Anesthesiologists (ASA) class II or III, with a variety of cardiovascular risk factors and comorbidities. ENGAGE reflects a challenging, real-world population:

- 18% of patients were beyond the IFU;
- 16% of patients with symptomatic AAAs;
- 10.6% of patients were ASA risk class IV;
- 10.5% of patients were women.

No ruptured aneurysms were included. The mean AAA diameter was 60.3 ± 11.7 mm. Two hundred twenty-six endografts (17.9%) were implanted outside the IFU criteria. Stokmans et al described the procedural data and evaluation in a previous publication.[3]

Technical Outcomes and Secondary Procedures

The technical outcomes are presented in Table 2. Type I and III endoleaks were present at 1- and 2-year follow-up in 0.6% and 1.1% of patients, respectively. Migration of the main body was not reported. AAA shrinkage (> 5 mm) at 1 year continued from 41.1% to 56.1% at 2-year follow-up. Kaplan-Meier estimates a freedom from secondary endovascular procedures of 94.1% at 1 year and 93% at 2 years (Figure 1). The majority of secondary procedures were performed for iliac limb occlusion or stenosis.

Patient Outcomes

The patient outcomes are shown in Table 3. The conversion rates were reported in 0.6% of patients at 1 year and 0.8% of patients at 2 years. One or more major adverse events at 1- and 2-year follow-up were reported in 11.3% and 17.4% of patients, respectively. Myocardial infarction and renal failure were the most prevalent major adverse events after 2 years. In total, there were only three patients who had an abdominal aneurysm rupture within 2-year follow-up.

Mortality

The Kaplan-Meier estimate for 1-year overall survival was 91.7% and 86.4% for 2 years (Figure 2). The 2-year estimate for aneurysm-related survival was 98.1%. To date, only three cases of device-related mortality were reported.

DISCUSSION

The endovascular approach for the treatment of AAAs is a dynamic, ever-changing endeavor. For years, we were challenged to decrease complications and reinterventions while safely treating more complex anatomy, especially for cases unfit for open repair. With broader IFU criteria, the Endurant Stent Graft makes EVAR suitable for more AAA patients.

The ENGAGE registry was undertaken to quantify the performance of the Endurant Stent Graft system within the context of contemporary, real-world use. Eligibility for treatment with Endurant was left to the discretion of the investigator; ENGAGE represents a high-quality database of 1,263 AAA patients with high external validity. To guarantee and maintain the quality and completeness of data, site monitoring is routinely performed to ensure consistency and quality in the collected data. Protocol endpoints important in demonstrating the clinical performance of Endurant at 1 month and beyond are 100% monitored. The rigor behind the data collection in ENGAGE is unprecedented for a real-world postmarket study.

The necessity for secondary interventions at 2 years was 7%, which was remarkably lower compared to the 12% reported in the DREAM (Dutch Randomised Endovascular Aneurysm Management) trial and the 13.7% reported in the OVER (Open Versus Endovascular Repair) trial.[5] The difference in secondary intervention rates could be influenced by the more conservative approach to type

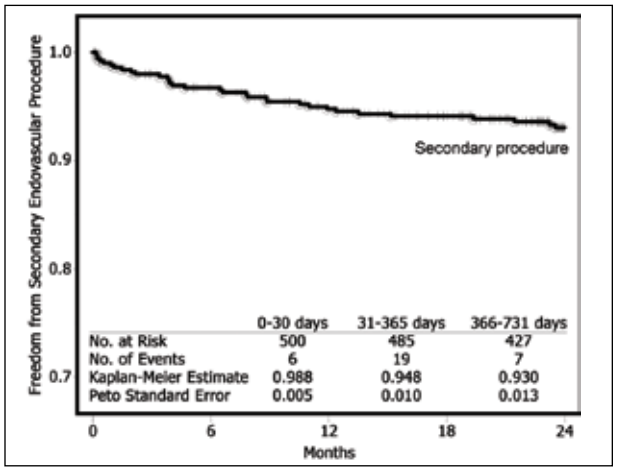

Figure 1. Kaplan-Meier estimates for secondary endovascular procedures.

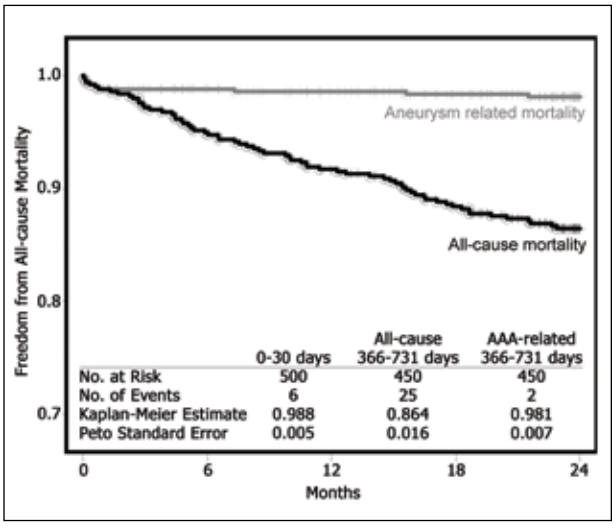

Figure 2. Kaplan-Meier estimates for all-cause mortality and AAA-related mortality.

II endoleaks in current practice. However, with 17.9% of patients treated outside the IFU, it should be taken into consideration that the eligibility criteria for ENGAGE were less strict than for DREAM and OVER.[6,7]

The majority of secondary interventions in ENGAGE were performed for iliac limb occlusion or stenosis. It is noted that a recently published independent analysis of the use of Endurant in 496 patients across three Dutch centers revealed that the incidence of limb occlusion after implantation of Endurant was 4% at 1.7 years (median follow-up), with most events occurring ≤ 2 months after implantation. In that analysis, "technical justification" (eg, extreme oversizing, positioning the graft at the kink of the iliac vessel, etc.) was the primary reason for occlusion in 60% of patients.[8]

Stent graft migration after EVAR is a serious complication and often results in emergency treatment. EUROSTAR (European Collaborators on Stent Graft Techniques for Abdominal Aortic Aneurysm Repair Registry) reported on several patients with endograft migration (4.3 cases per 100 patient years).[9] With the more contemporary stent graft, ENGAGE reports no endograft migration for Endurant, which is related to the improved fixation of the endograft to the aortic wall. Aneurysm rupture after EVAR is very rare, with a prevalence of 0.2% at 2 years in the 500-patient cohort.

At 1 and 2 years, freedom from AAA-related mortality in ENGAGE remained consistent at 98.6% and 98.1%, respectively. Compared with the landmark EVAR-1 and DREAM trials, the overall mortality rates in ENGAGE at 1 and 2 years were comparable. This is remarkable considering that ENGAGE did not exclude ASA class IV patients (10.6%) with a worse prognosis.

CONCLUSION

ENGAGE represents the largest contemporary EVAR registry with a single manufacturer's endograft. This study has raised the bar in terms of evidence-based medicine as it relates to EVAR. These data clearly set Endurant apart from other stent grafts in terms of both magnitude and quality of evidence. Not all registries are created equal in terms of breadth and quality. Because ENGAGE patients are enrolled consecutively and because all of the data from

TABLE 2. TECHNICAL PERFORMANCE AFTER 1- AND 2-YEAR FOLLOW-UP

Variable	1 Year (N = 1,263)		2 Years (N = 500)	
Type I/III endoleak	0.6%	(6/1,072)	1.1%	(4/375)
Migration main body	0%	(0/1,242)	0%	(0/490)
Significant decrease (> 5 mm) aneurysm sac	41.1%	(385/936)	56.1%	(185/330)
Significant increase (> 5 mm) aneurysm sac	3.4%	(32/936)	3.9%	(13/330)
Stent graft occlusion	3.5%	(44/1,242)	2.7%	(13/490)
Stent graft kinking	2%	(25/1,242)	2%	(10/490)

TABLE 3. PATIENT OUTCOMES AT 1- AND 2-YEAR FOLLOW-UP				
Variable	1 Year (N = 1,263)		2 Years (N = 500)	
One or more major adverse events	11.3%	(141/1,246)	17.4%	(84/483)
All-cause mortality	7.5%	(93/1,246)	13.7%	(66/483)
Bowel ischemia	0.2%	(3/1,246)	0.6%	(3/483)
Myocardial infarction	2%	(25/1,246)	2.7%	(13/483)
Paraplegia	0%	(0/1,246)	0%	(0/483)
Renal failure	1.1%	(14/1,246)	1.4%	(7/483)
Respiratory failure	0.1%	(1/1,246)	0.2%	(1/483)
Stroke	0.5%	(6/1,246)	0.6%	(3/483)
Secondary endovascular procedure (any type)	5.6%	(71/1,263)	6.4%	(32/500)
Conversion to surgery	0.6%	(7/1,263)	0.8%	(4/500)
Aneurysm rupture	0.2%	(2/1,263)	0.2%	(1/500)

ENGAGE are reviewed and verified by the investigators, medical practitioners can have confidence knowing that the ENGAGE results reflect the collective global experience with Endurant.

The 2-year results continue to demonstrate the durability, safety, and effectiveness of the Endurant Stent Graft. Despite numerous cases of challenging anatomy, rates of type I endoleak and migration are very low. Longer-term data are needed, but in this most recent analysis, the Endurant Stent Graft system demonstrates early markers for EVAR success. ENGAGE will continue follow-up for a total of 5 years. Two-year data of all 1,263 patients and 3-year data of the first 500 treated patients will be presented at the VEITH Symposium in November 2013. ■

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Empowering EVAR Clinical Performance

Consistent Durable Outcomes At 3-Year Follow-Up Across Endurant Trials*

BY SHARIF H. ELLOZY, MD

Endovascular aneurysm repair (EVAR) has gradually become the gold standard for the treatment of infrarenal abdominal aortic aneurysms (AAAs) since the FDA approved the first devices in September 1999. Multiple generations of devices have been developed, but the characteristics of the ideal stent graft are consistent. Namely, the device has to be durable, comformable to variant anatomy, and safe to deliver. It needs to be deployed in a precise and reliable fashion. With these characteristics in mind, Medtronic, Inc. (Minneapolis, MN) developed the Endurant® Stent Graft, using a novel multidisciplinary approach that incorporated feedback from > 150 physicians, clinical imaging, computational modeling, and in vitro bench testing.[1]

The Endurant® II Stent Graft, the second-generation Endurant Stent Graft, is composed of woven polyester and electropolished nitinol stents. The suprarenal component is a laser cut nitinol stent with anchoring pins, enhancing proximal fixation. The M-shaped proximal stent allows for conformability and seal in irregular and short necks. The limbs are designed for flexibility and conformability in tortuous anatomy. The delivery system is low profile and hydrophilic, allowing it to track through challenging access vessels. Ultimately, however, the most important characteristic to consider in evaluating a device is the durability of the repair—migration resistance, low endoleak rate, aneurysm sac stability or shrinkage, and low secondary intervention rate. In addition to the 2-year follow-up data available through the ENGAGE study, 3-year follow-up results are now available from the US IDE evaluation of Endurant.

US IDE CONTROLLED TRIAL

The US regulatory trial of the Endurant Stent Graft system was a prospective, two-arm, multicenter trial. The bifurcated arm enrolled 150 patients at 26 sites in the United States and the aortouniiliac (AUI) arm enrolled 44 patients at 15 sites. The sites were a combination of academic and private hospitals, and practitioners from multiple specialties participated. Of note, the study was designed for a minimal neck length of

TABLE 1. 1-YEAR OUTCOMES ACROSS TRIALS

	EU Trial (N = 80)[3]	US IDE (N = 150)[2]	ENGAGE Registry (N = 1,263)[4]
Type I endoleak	0%	0%	0.4%
Whole body migration	0%	0%	0%
Conversion to surgery	0%	0%	0.6%
Aneurysm-related mortality	95% freedom from all-cause mortality[a]	0%	1.5%
Secondary endovascular procedure	3.8%	95.3% freedom from secondary endovascular procedure	5.6%

[a]0% postoperative rupture at 1 year.

*Trials and registry evaluated the Endurant® stent graft system.

TABLE 2. 3-YEAR OUTCOMES FROM US IDE TRIAL			
US IDE Trial	**(N = 150) 1-Year Results[2]**	**(N = 138) 2-Year Results[5]**	**(N = 124) 3-Year Results[6]**
Type I endoleak	0%	0%	0.9%[a]
Whole body migration	0%	0%	0%
Aneurysm sac diameter: decrease or stable	99.2%	96.9%	95.4%
Aneurysm-related mortality	0%	0%	0%
Conversion to surgery	0%	0%	0%
Freedom from secondary endovascular procedure	95.3%[b]	93.9%	91.5%

[a]One subject experienced a new type I endoleak at the 3-year time frame that led to an aneurysm expansion. The subject refused intervention and voluntarily entered hospice and died on day 1,212 due to an aneurysm rupture.
[b]Value is calculated from 31–365 days

10 mm, which was the shortest neck length of any US trial up to that point. Fifteen patients (10%) had a neck length between 10 and 14 mm. Other anatomic criteria included an infrarenal neck angulation of 60° or less and an iliac sealing zone of at least 15 mm. This article will discuss the midterm results from the Endurant® US IDE bifurcated arm.

Consistent Results at 1-, 2- and 3-Year Follow-Up

Acute procedural outcomes were very good. Implantation was completed successfully in 149 patients (99.3%). The single failure was due to an inability to cannulate the contralateral gate after implantation of the main bifurcated body. There were no deaths at 30 days, and major adverse events were seen in only six patients (4%). Outcomes at 1-year follow-up, initially published in the *Journal of Vascular Surgery*, were very promising. Six patients died during the first year of causes unrelated to their aneurysm. No patients were lost to follow-up. There were no type I endoleaks, no instances of migration, no ruptures, and no sac enlargements. Sac shrinkage was observed in 64 of 136 patients (47%) at 1 year.[2]

These results are comparable to the 1-year outcomes reported in the Endurant EU trial[3] and the ENGAGE Registry,[4] a global registry of Endurant® cases (Table 1).

The US IDE results at 2 years (Table 2) continued to demonstrate the durability of repair.[5] There were no late type I endoleaks and no instances of migration. The sac size had decreased in 60.3% of patients, remained stable in 36.6% of patients, and increased in only 3.1% of patients. Through 2-year follow-up, 93.9% of patients were free from secondary procedures.

From the most recent 3-year follow-up for the US IDE trial,[6] the Endurant Stent Graft continues to deliver sustained clinical performance across key endpoints. From the 3-year data, the type I endoleak rate was 0.9% (n = 1/107) with no instances of migration, post-implant rupture, or conversion to open repair. As well, aneurysm sac diameter had decreased in 62.7% of patients, remained stable in 32.7% of patients, and increased in only 4.5% of patients. Through the most recent 3-year follow-up, 91.5% of patients were free from secondary procedures.

Ultimately, the durability of the Endurant II Stent Graft is further emphasized with the consistency of outcomes between the rigorous US IDE trial and the ENGAGE global registry. In particular, a good measurement of durability is the AAA sac diameter decrease, which is similar in both trials at 2 years (Figure 1): in the ENGAGE registry, a sac size reduction was reported in 56.1% of patients, stable sacs in 40.0% of patients, and an increase in sac size in only 3.9% of patients at 2-year follow-up.

CONCLUSION

Despite its use in patients with challenging anatomy, the Endurant Stent Graft has proven to be safe and efficacious. Durable aneurysm exclusion has been achieved in the controlled setting of the US IDE and Endurant

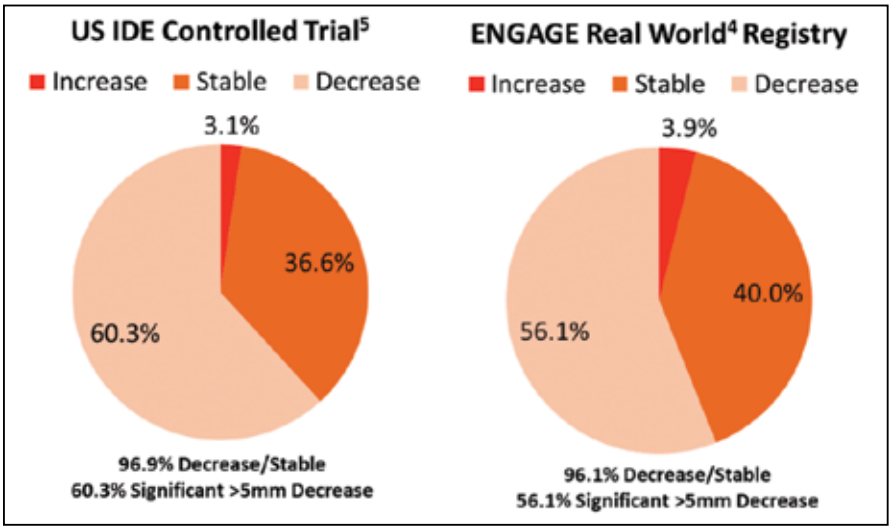

Figure 1. AAA sac diameter change through 2 years.

EU clinical trials, as well as in a real-world registry such as ENGAGE. Finally, these results continue to be consistent at 3-year follow-up, which brings further confidence in the Endurant II Stent Graft's midterm performance, treating over 100,000 patients on a worldwide basis.[7] ■

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Addressing Challenging AAA Anatomies With Confidence

Hence J.M. Verhagen, MD, PhD, discusses how the Endurant II Stent Graft has performed well in challenging anatomy, enabling physicians to successfully treat a broader range of AAA patients.

What are the biggest anatomical challenges that limit the practice of endovascular aneurysm repair (EVAR)?

Anatomical features that limit the practice of EVAR are traditionally a proximal aortic length < 15 mm, diameter > 26 mm, neck angulation > 60°, reverse taper, or thrombus burden. These characteristics comprise a "hostile neck." In particular, the anatomic characteristic that most limits the application of EVAR is an infrarenal neck < 15 mm. Short necks do not always allow for adequate seal of the device to healthy aorta, and of course, angulation makes delivery and placement more difficult than in standard anatomy (ie, > 15-mm anatomy).

How does this affect abdominal aortic aneurysm (AAA) patient selection and long-term outcomes?

For standard EVAR, patients with necks 15 mm or greater have many options. Once you start treating patients with shorter necks, on-label treatment options are limited.

Short necks do not necessarily mean unfavorable angulation, and unfavorable angulation doesn't necessarily mean a short neck, so careful patient selection must always be considered. You must take each patient's unique anatomy into account when making a decision about AAA treatment and what type of endograft to use. Even in the short- and midterm, infrarenal neck length < 15 mm has been associated with an increased risk of complications such as endoleak or device migration. With the increased availability of devices such as Endurant® II Stent Graft (Medtronic, Inc., Minneapolis, MN), however, we are seeing improved clinical outcomes for this subgroup of patients (ie, short necks).

What are some characteristics of Endurant II that enable the treatment of short necks?

The Endurant II Stent Graft was thoughtfully designed, with special consideration given to short-neck anatomy. It offers precise, millimeter-by-millimeter deployment, which is extremely useful when you only have a small amount of healthy vessel for landing. The device uses suprarenal fixation and anchor pins to enable secure active graft fixation even when placement is limited by a short neck. Correspondingly, we see that in clinical studies, Endurant II has 0% migration out to 3 years.

The enhanced tip-capture mechanism in Endurant® II allows for adjustment proximally or distally, even after deployment of up to three stent rings, so again, you are able to adjust the device even when the aortic neck is > 10 mm. As a result, the delivery and deployment success rates for Endurant II are > 99%.

Could you summarize the data you presented at Charing Cross and SVS this year that analyzed Endurant performance?

The ENGAGE registry evaluated the global, real-world use of the Endurant II Stent Graft, consecutively enrolling more than 1,200 patients at 79 sites across six continents, with planned follow-up out to 5 years. The goal of ENGAGE is to gather real-world data on patients treated with the Endurant II Stent Graft, and thus, inclusion criteria were less strict than other registries. Because this trial enrolled such a large number of patients, we are able to analyze a cohort of patients with short necks. We found that Endurant II performs just as well in short necks in particular (10- to 15-mm anatomy) as it does in standard necks (15- to 20-mm anatomy). There was extensive monitoring and analysis of the data in ENGAGE—100% data managing review, independent data monitoring, and an independent clinical event committee—meaning that these are high-quality registry data.

When we looked at the current subanalysis of neck

length, we found the following: 123 patients had neck lengths of 10 to 15 mm, 227 were 15 to 20 mm, and 873 patients had neck lengths > 20 mm. We now have follow-up data at 30 days, 1 year, and 2 years, and we are seeing that there is no difference in performance related to neck length. Specifically, at the time of the initial implant procedure, there were no type I endoleaks in patients with 10- to 15-mm neck lengths compared to the 15- to 20-mm and > 20-mm neck groups, respectively. At 1 year, this difference remained insignificant, and we also observed a 0% rate of migration across all three groups. At 2 years, this was also sustained. The rates of secondary procedures to correct a type I or III endoleak were also quite low (0%, 1.3%, and 1.9% for the short, standard, and > 20-mm neck length groups, respectively).

Current analysis supports the use of Endurant II in necks that are at least 10 mm, which is consistent with its labeled indication. We can say with confidence that Endurant II performs equally well in standard EVAR neck lengths. Of course, the need for longer-term data remains, but overall, these results at 2 years are very encouraging.

What strategies do you employ for overcoming the associated risks of treating necks shorter than < 10 mm?

One has to bear in mind that treating that sort of anatomy is outside the instructions for use for standard EVAR. It is important to realize that there's probably a good reason for that. In a very recent presentation from our group during ESVS 2013, we analyzed ENGAGE data for risk factors for proximal neck complications after EVAR with the Endurant Stent Graft. It showed that EVAR for AAAs with a neck length of 10 to 15 mm was associated with very few neck-related adverse events (type IA endoleak, conversion, unintentional renal artery coverage, deployment complications, or migration), resulting in the same results as can be expected when AAAs with longer necks are treated. It also showed that a neck length of < 10 mm increases the risk for intra- or postoperative neck-related adverse events by approximately ninefold. This highly significant finding should be taken into account when an endovascular option is considered for treating a < 10-mm-neck aneurysm. Personally, I'd select a fenestrated option in those cases. Of course, using a chimney technique has been advocated for this anatomy as well, but I still consider that concept a far less desirable method.

What are some of the specific challenges of treatment in women, particularly in relation to anatomy?

The aortoiliac anatomy of women makes them a challenging population to treat via EVAR. Complications are somewhat more common in women versus men, often due to the increased age at the time of diagnosis and treatment and greater atherosclerotic risk factors present in women compared to men. We see more tortuous and occluded anatomy in older populations, which is especially true in women, and women generally have smaller vessels to begin with. These anatomic factors further impede the device delivery process, and shorter and more angulated aortic necks make acquiring an adequate landing zone and achieving a good seal more difficult. Thus, understanding the performance of a stent graft in this type of anatomy is a good indicator for its overall performance in challenging anatomy.

What other features of Endurant II enable successful treatment specifically in women?

Endurant II's low profile and hydrophilic coating allow for easier access, which is key in overcoming the challenging aortoiliac anatomy common in women who, as previously mentioned, typically have smaller and more tortuous iliacs. The Endurant II delivery system is kink-resistant as well, which helps when you are navigating difficult anatomy.

The sheer size of the ENGAGE registry allowed for close scrutiny of results in female anatomy. What is the significance of this, and what were the results?

Women have been shown to have worse outcomes after EVAR, including higher mortality, a higher rate of access complications, and a greater risk of endoleaks. However, results for Endurant II are promising. Based on what we see in ENGAGE, Endurant II has narrowed the outcome gap between sexes, despite the presence of more challenging aortoiliac anatomies and comorbidities in women.

Endurant II achieved equivalent outcomes regardless of sex. Early outcomes in the ENGAGE registry were similar in women and in men, with similar rates of technical success, similar freedom from type I and III endoleak, and no difference in presence of type I endoleak.

At 30 days, there was no statistically significant difference found between men and women in the rate of the occurrence of limb occlusion, type I endoleak, or the need for a secondary endovascular procedure. In addition, at 1 year, there was no difference between men and women in freedom from major adverse events or survival. Knowing this, we can again remain confident in the overall performance of the Endurant II Stent Graft. ■

Hence J.M. Verhagen, MD, PhD, is Professor and Chief of the Department of Vascular Surgery, Erasmus University Medical Centre in Rotterdam, The Netherlands. He has disclosed that he is a consultant to Medtronic, Inc. and Gore & Associates. Dr. Verhagen may be reached at +31 107031810; h.verhagen@erasmusmc.nl.

Indications

The Endurant® II bifurcated stent graft is indicated for the endovascular treatment of infrarenal abdominal aortic or aorto-iliac aneurysms. The Endurant II aorto-uni-iliac (AUI) stent graft is indicated for the endovascular treatment of infrarenal abdominal aortic or aortoiliac aneurysms in patients whose anatomy does not allow the use of a bifurcated stent graft. The Endurant II stent graft system is indicated for use in patients with the following characteristics:

- Adequate iliac/femoral access that is compatible with vascular access techniques, devices and/or accessories
- Proximal neck length of ≥10 mm
- Infrarenal neck angulation of ≤60°
- Aortic neck diameters with a range of 19 to 32 mm
- Distal fixation length(s) of ≥15 mm
- Iliac diameters with a range of 8 to 25 mm
- Morphology suitable for aneurysm repair

Contraindications

The Endurant II Stent Graft System is contraindicated in:

- Patients who have a condition that threatens to infect the graft.
- Patients with known sensitivities or allergies to the device materials.

Warnings and Precautions

- The long-term safety and effectiveness of the Endurant II Stent Graft System has not been established. All patients should be advised that endovascular treatment requires lifelong, regular follow-up to assess the health and the performance of the implanted endovascular stent graft. Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or changes in the structure or position of the endovascular graft) should receive enhanced follow-up. Specific follow-up guidelines are described in the Instructions for Use.
- Patients experiencing reduced blood flow through the graft limb, aneurysm expansion, and persistent endoleaks may be required to undergo secondary interventions or surgical procedures.
- The Endurant II Stent Graft System is not recommended in patients unable to undergo or who will not be compliant with the necessary preoperative and postoperative imaging and implantation studies as described in the Instructions for Use.
- Renal complications may occur: 1) From an excess use of contrast agents. 2) As a result of emboli or a misplaced stent graft. The radiopaque marker along the edge of the stent graft should be aligned immediately below the lower-most renal arterial origin.
- Studies indicate that the danger of micro-embolization increases with increased duration of the procedure.
- The safety and effectiveness of the Endurant II Stent Graft System has not been evaluated in some patient populations. Please refer to the product Instructions for Use for details.

MRI Safety and Compatibility: Non-clinical testing has demonstrated that the Endurant II Stent Graft is MR Conditional. It can be scanned safely in both 1.5T & 3.0T MR systems under certain conditions as described in the product Instructions for Use. For additional information regarding MRI please refer to the product Instructions for Use.

Adverse Events

Potential adverse events include (arranged in alphabetical order): amputation; anesthetic complications and subsequent attendant problems (e.g. aspiration), aneurysm enlargement; aneurysm rupture and death; aortic damage, including perforation, dissection, bleeding, rupture and death; arterial or venous thrombosis and/or pseudoaneurysm; arteriovenous fistula; bleeding, hematoma or coagulopathy; bowel complications (e.g., ileus, transient ischemia, infarction, necrosis); cardiac complications and subsequent attendant problems (e.g. arrhythmia, myocardial infarction, congestive heart failure, hypotension, hypertension); claudication (e.g., buttock, lower limb); death; edema; embolization (micro and macro) with transient or permanent ischemia or infarction; endoleak; fever and localized inflammation; genitourinary complications and subsequent attendant problems (e.g., ischemia, erosion, femoral-femoral artery thrombosis, fistula, incontinence, hematuria, infection); hepatic failure; impotence; infection of the aneurysm, device access site, including abscess formation, transient fever and pain; lymphatic complications and subsequent attendant problems (e.g., lymph fistula); neurologic local or systemic complications and subsequent attendant problems (e.g., confusion, stroke, transient ischemic attack, paraplegia, paraparesis, paralysis); occlusion of device or native vessel; pulmonary complications and subsequent attendant problems; renal complications and subsequent attendant problems (e.g., artery occlusion, contrast toxicity, insufficiency, failure); stent graft: improper component placement; incomplete component deployment; component migration; suture break; occlusion; infection; stent fracture; graft twisting and/or kinking; insertion and removal difficulties; graft material wear; dilatation; erosion; puncture and perigraft flow; surgical conversion to open repair; vascular access site complications, including infection, pain, hematoma, pseudoaneurysm, arteriovenous fistula, dissection; vascular spasm or vascular trauma (e.g., iliofemoral vessel dissection, bleeding, rupture, death); vessel damage; wound complications and subsequent attendant problems (eg, dehiscence, infection, hematoma, seroma, cellulitis)
Please reference product Instructions for Use for more information regarding indications, warnings, precautions, contraindications and adverse events.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

Indications

The Valiant® Thoracic Stent Graft with the Captivia® Delivery System is intended for the endovascular repair of isolated lesions (excluding dissections) of the descending thoracic aorta in patients having appropriate anatomy, including:

- iliac/femoral access vessel morphology that is compatible with vascular access techniques, devices, and/or accessories;
- non-aneurysmal aortic diameter in the range of 18 – 42mm(fusiform and saccular aneurysms/penetrating ulcers) or 18 mm to 44 mm (blunt traumatic aortic injuries); and
- non-aneurysmal aortic proximal and distal neck lengths ≥ 20mm

Contraindications

The Valiant Thoracic Stent Graft with the Captivia Delivery System is contraindicated in:

- Patients who have a condition that threatens to infect the graft.
- Patients with known sensitivities or allergies to the device materials.

Warnings and Precautions

The long-term safety and effectiveness of the Valiant Thoracic Stent Graft with the Captivia Delivery System has not been established. All patients should be advised that endovascular treatment requires lifelong, regular follow-up to assess the integrity and performance of the implanted endovascular stent graft. Patients with specific clinical findings (for example, enlarging aneurysm, endoleaks, migration, or inadequate seal zone) should receive enhanced follow-up. Specific follow-up guidelines are described in the Instructions for Use. The Valiant Thoracic Stent Graft with the Captivia Delivery System is not recommended in patients who cannot undergo, or who will not be compliant with, the necessary preoperative and postoperative imaging and implantation procedures as described in the Instructions for Use. Strict adherence to the Valiant Thoracic Stent Graft sizing guidelines as described in the Instructions for Use is expected when selecting the device size. Sizing outside of this range can potentially result in endoleak, fracture, migration, infolding, or graft wear. The safety and effectiveness of the Valiant Thoracic Stent Graft with the Captivia Delivery System has not been evaluated in some patient populations. Please refer to the product Instructions for Use for details.

MRI Safety and Compatibility

Non-clinical testing has demonstrated that the Valiant Thoracic Stent Graft is MR Conditional. It can be scanned safely in both 1.5T & 3.0T MR systems under certain conditions as described in the product Instructions for Use. For additional information regarding MRI please refer to the product Instructions for Use.

Adverse Events

Potential adverse events include, but are not limited to access failure, access site complications (e.g. spasm, trauma, bleeding, rupture, dissection), adynamic ileus, allergic reaction (to contrast, antiplatelet therapy, stent graft material), amputation, anaesthetic complications, aneurysm expansion, aneurysm rupture, angina, arrhythmia, arterial stenosis, atelectasis, blindness, bowel ischemia/infarction, bowel necrosis, bowel obstruction, branch vessel occlusion, buttock claudication, cardiac tamponade, catheter breakage, cerebrovascular accident (CVA) / stroke, change in mental status, coagulopathy, congestive heart failure, contrast toxicity, conversion to surgical repair, death, deployment difficulties / failures, dissection / perforation / rupture of the aortic vessel and/or surrounding vasculature, embolism, endoleak(s), excessive or inappropriate radiation exposure, extrusion / erosion, failure to deliver stent graft, femoral neuropathy, fistula (including aortobronchial, aortoenteric, aortoesophageal, arteriovenous, and lymph), gastrointestinal bleeding /complications, genitourinary complications, hematoma, hemorrhage / bleeding, hypotension / hypertension, infection and/or fever, insertion and removal difficulties, intercostal pain, intramural hematoma, leg /foot edema, lymphocele, myocardial infarction, neuropathy, occlusion – venous or arterial, pain / reaction at catheter insertion site, paralysis, paraparesis, paraplegia, paresthesia, peripheral ischemia, peripheral nerve injury, pneumonia, post-implant syndrome, procedural / post-procedural bleeding, prosthesis dilatation / infection / rupture / thrombosis, pseudoaneurysms, pulmonary edema, pulmonary embolism, reaction to anaesthesia, renal failure, renal insufficiency, reoperation, respiratory depression / failure, sepsis, seroma, shock, spinal neurological deficit, stent graft material failure (including breakage of the metal portion of the device / migration / misplacement / occlusion / twisting / kinking, transient ischemic attack (TIA), thrombosis, tissue necrosis, vascular ischemia, vascular trauma, wound dehiscence, wound healing complications, and/or wound infection.

Please reference product Instructions for Use for more information regarding indications, warnings, precautions, contraindications and adverse events.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

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