

Endovascular TODAY

May 2012

Endurant II



A New Level of
Confidence With EVAR.

Endurant II: A New Level of Confidence With EVAR

CONTENTS

3 THE ENDURANT STENT GRAFT

Advantages from lessons learned.

By Frank R. Arko, MD; Tzvi Nussbaum, MD; Stephen Lalka, MD;
Jerry Holleman, MD; and Tim Roush, MD

7 UNMET AAA NEEDS AND NEXT-GENERATION DEVICES

A look at the latest advances in endograft technology
and possible future developments.

By Fabio Verzini, MD, PhD

10 MEDTRONIC: FROM PIPELINE TO PATIENTS

Initiatives aimed at increasing abdominal aortic aneurysm awareness,
identifying patients, and expanding treatment options.

By L. Mariano Ferreira, MD

13 THE ENDURANT STENT GRAFT: CONSISTENT CLINICAL PERFORMANCE, TRIAL AFTER TRIAL

Overview of clinical studies and registries evaluating the Endurant stent graft system.

By Frank Vermassen, MD, PhD, and Nathalie Moreels, MD

The Endurant Stent Graft

Advantages from lessons learned.

**BY FRANK R. ARKO, MD; TZVI NUSSBAUM, MD; STEPHEN LALKA, MD;
JERRY HOLLEMAN, MD; AND TIM ROUSH, MD**

Since endovascular aneurysm repair (EVAR) was first described by Parodi near the end of the 20th century, there has been a paradigm shift from open surgical repair to EVAR for most patients. Anatomical constraints and instructions for use currently limit EVAR application to approximately 40% to 60% of patients.¹⁻³ First-generation devices have been characterized by a number of design-related issues, limiting the overall effectiveness of EVAR in certain patients.¹⁻³ These limitations have included the size of the delivery sheath with associated small-access vessels, obtaining seal in angulated and short proximal necks, and lack of conformability of early generation devices. Often, in patients with anatomic limitations, multiple adjuvant procedures would be required, including the need for conduits or placement of Palmaz stents

The Endurant stent graft was designed to allow more patients to undergo EVAR while making implantation easier and improving long-term outcomes.

(Cordis Corporation, Bridgewater, NJ) or extender cuffs proximally to achieve seal.⁴⁻⁶

Distally within the iliac system, tortuosity and ectasia can be associated with limb thrombosis and type Ib endoleaks due to kinking and poor seal/undersizing, respectively. Although safe, hypogastric artery coil embolization, when required to extend the stent graft to the external iliac artery, is associated with buttock claudication. Other limitations include stent and graft fatigue with the risk of a type III endoleak.⁵⁻⁹

To address and overcome the issues of earlier-generation stent grafts, the Endurant® stent graft (Medtronic, Inc., Minneapolis, MN) (Figure 1) was designed to allow more patients to undergo EVAR while making implantation easier and improving long-term outcomes.

DESCRIPTION OF THE ENDURANT STENT GRAFT SYSTEM

The Endurant stent graft is a self-expanding nitinol device designed for the endovascular treatment of abdominal aortic aneurysms. All stent graft components are composed of nitinol metal stents, which are sewn onto the multifilament polyester (PET [polyethylene terephthalate]) graft fabric. The suprarenal stents with anchor pins on the proximal end are laser cut from a nitinol tube. The remaining stents include seal, body, contour, and limb stents formed from nitinol wire and sewn onto the graft material. The suprarenal stents are sewn to the graft fabric using an ultra-high molecular-weight polyethylene suture that is designed to aid in better stent-to-graft attachment strength and provide a more durable proximal attachment.



Figure 1. The Endurant stent graft with a proximal M-stent design, alternating stent apex height to optimize seal in a shorter and more angulated neck through a combination of radial force and conformability.

TABLE 1. TRANSLATING DESIGN INTO PROVEN CLINICAL OUTCOMES

Endurant Technical Features and Benefits	Corresponding Clinical Outcomes
18-F low profile ^a for enhanced access	99.3% delivery and deployment success ^b
Suprarenal stent with anchor pins for migration resistance	0% migration at 2 years ^c
High-density, multifilament polyester graft material for endoleak resistance	62% of patients demonstrated significant sac shrinkage (> 5 mm) at 2 years ¹⁰
M-shaped proximal stents provide complete wall apposition and minimized infolding	0% type 1 endoleak at 2 years, ¹⁰ 98.3% freedom from sac enlargement at 2 years

^aEndurant II: 18-F crossing profile for 28-mm bifurcated device.
^bDelivery success is defined as successful vascular access and delivery of the device to the intended anatomical treatment site. Deployment success is defined as successful deployment of the device in the intended site and the successful removal of the delivery system.¹¹
^cProximal migration is observed when the stent graft covers a renal artery or moves > 10 mm. Distal migration is observed when the stent graft moves > 10 mm relative to fixed anatomic landmarks.¹⁰

Radiopaque markers are sewn onto each component of the stent graft, including limbs and extensions, to aid in visualization and to facilitate placement of each component.

ENDURANT DESIGN PROCESS

The Endurant stent graft design team, which incorporated input from more than 250 physicians, focused on creating a reliable and robust endovascular solution that focused on the following key areas:

- treatment of short and highly angulated necks
- treatment of tortuous anatomies without kinking the device
- long-term durability
- improvements in profile and deliverability.

The design optimized key performance attributes such as sealing and fixation, durability, conformability in tortuous vessels, and delivery profile. A multidisciplinary process including physician expertise, clinical imaging, computational modeling, and in vitro bench testing was utilized in the design. The subsequent sections discuss how the Endurant stent graft system was designed to meet the previously mentioned performance goals. Table 1 highlights how the design features of the Endurant stent graft system have translated to meaningful and consistent clinical outcomes.

Sealing

To treat a variety of neck anatomies and achieve maximum seal, the M-shaped proximal sealing stent of Endurant was designed to work with the suprarenal stent to enhance wall apposition and minimize the risk of graft material infolding. By maximizing the support within the seal region, a continuous circumferential coverage of the seal zone is maintained. The design of

the stent seal was selected to maximize outward radial force while ensuring that the device could be constrained to a low-profile delivery system (18 or 20 F). To address highly angulated anatomies, stent spacing and heights were optimized to achieve a high degree of conformability while maintaining the required outward radial force.

A similar design philosophy was applied to the distal limb sealing regions. The development and assessment of sealing performance included clinical imaging analysis, computational analysis, and simulated use testing. Component testing, such as radial force and simulated use testing, which was designed to represent challenging physiological conditions has shown that the seal region of the Endurant device performs with excellent results.

Fixation

Active fixation was included in the Endurant stent graft to reduce the risk of device migration. This is especially critical for the treatment of aneurysms because device migration can result in loss of sealing integrity. The fixation mechanism consists of a dual-anchor-pin configuration (two anchor pins per stent crown), which provides redundancy in the prevention of device migration. The one-piece laser-cut suprarenal stent design was selected for its enhanced structural integrity and durability. To optimize engagement of the suprarenal stent, several design attributes, such as pin angulation, pin length, tip geometry, location along the suprarenal stent, and takeoff angulation, were evaluated and optimized.

Use of the anchor pins in highly angulated neck anatomies was also taken into account. The dual-pin design allows for robust fixation in cases in which not all anchor pins may be fully engaged in the aortic wall.

The design features of the Endurant stent graft system have translated into meaningful and consistent clinical outcomes.

Evaluation of the effectiveness of aortic tissue engagement and strength (in both straight and angulated anatomies) was performed using benchtop and cadaveric tissue testing. Long-term durability testing simulating challenging physiologic loading conditions was also conducted.

Durability

Stent grafts undergo a variety of cyclic loading forces as a result of hemodynamic conditions in the aorta. Musculoskeletal motions can also result in repeated deformation of the device, potentially resulting in wear. Additionally, modular endografts can present an opportunity for overlap-related abrasion. In order to minimize the risk of fatigue and to design a graft that is extremely durable, the Endurant stent graft design underwent a rigorous battery of fatigue testing, including the evaluation of cyclic loading forces, aortic deformations, and overlapping components. Clinical imaging and physiologic data assessing neck angulation, vessel tortuosity, and cardiac and vessel wall motion were incorporated into computational analyses, as well as benchtop evaluation.

Durability testing was performed on stent graft components, including the anchor pins, stent-to-graft attachment, and nitinol stents, as well as whole device testing, to evaluate radial fatigue, aneurysm pulsatile fatigue, and overlap-related interactions.

Conformability

Incorporating conformability while eliminating the risk of kinking was one of the key components in the design of the graft. To accomplish this, the spacing between stents was optimized, and the peaks with the unique M-shaped design were offset to allow the graft to be highly conformable, even in tortuous anatomy.

Delivery System Performance

Unique anatomical challenges to EVAR are seen in women and patients with severe aortoiliac occlusive disease. The use of a conduit, with its own related morbidities, or iliac artery injury was associated with early generation devices. Lowering the profile of the stent graft delivery system is key to increasing the number

of patients who are suitable for EVAR, as well as simplifying the procedure. Graft material selection, stent design, and graft cover design and materials have made significant improvement in the delivery system profile. The Endurant stent graft component designs were also optimized, such as the creation of stent geometries that allowed for the lowest crimp profile and graft material properties. Furthermore, the reduced crossing profile and careful selection of materials allowed the Endurant delivery system to be very flexible. For example, the addition of hydrophilic coating to the surface of the sheath of the Endurant delivery system has improved the system's ability to track through challenging anatomy. The reduced force required to track the system is attributed to this lubricious hydrophilic coating.

The two-stage delivery process of the Endurant system relies on the tip-capture mechanism to facilitate accurate and reliable alignment of the proximal edge of the stent graft. The tip-capture system ensures that fixation is precisely achieved. This new design has been evaluated in multiple configurations via preclinical in vivo evaluation and in vitro benchtop testing in challenging physiological models.

ANATOMIC CRITERIA FOR THE ENDURANT SYSTEM'S INSTRUCTIONS FOR USE

Suitable candidates for EVAR require a proximal neck of ≥ 10 mm in length with nonsignificant calcification and/or nonsignificant thrombus with $\leq 60^\circ$ infrarenal and $\leq 45^\circ$ suprarenal angulation and a vessel diameter of approximately 10% to 20% smaller than the labeled Endurant diameter. Neck diameters between 19 and 32 mm can be treated, and distal fixation can be achieved in vessels between 8 and 25 mm. Distal fixation of > 15 mm is required.

CURRENT RESULTS

Current results with the Endurant stent graft have been very encouraging given the challenging anatomy

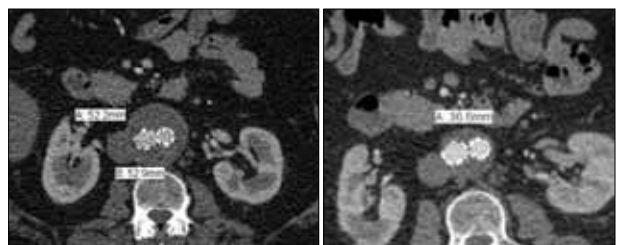


Figure 2. Example of sac shrinkage associated with the Endurant stent graft. After 6 months, the sac has decreased 16 mm in maximum diameter. At 1 year, the Endurant stent graft was associated with a 97.3% and a 100% sac shrinkage or stabilization in the European and the United States IDE trials, respectively.

set forth in the clinical trials. In a variety of studies assessing the Endurant stent graft, the number of patients enrolled ranged from 80 to 1,200.

ENGAGE (Endurant Stent Graft Natural Selection Global Postmarket Registry)* is a global, prospective, real-world postmarket registry evaluating more than 1,200 patients treated with the Endurant stent graft system. Thirty-day data have been reported on the full 1,200 patients, and 1-year data are available on 350 patients. The technical success rate of the Endurant stent graft system was 99.1%. Through 30 days, there were no instances of stent graft kinking, twisting, or bare stent fracture.¹⁰

The device received US Food and Drug Administration approval based on the Endurant US regulatory trial, which was a nonrandomized multicenter study consisting of 26 sites. A total of 150 patients were enrolled, and 2-year follow-up has been completed. Inclusion criteria included a neck length of ≥ 10 mm with $< 60^\circ$ of angulation. The mean aneurysm size was 57 mm, and the procedure was successful in 99.3% of patients. The overall operative 30-day mortality rate was 0%, and major adverse events occurred in only 4%. At 1 year, there were no type I/III endoleaks, and type II endoleaks were seen in only 8.9% of patients. No patients had sac enlargement, 50.4% of patients had a stable sac, and 49.6% of patients had sac shrinkage. Furthermore, there were no fractures, migrations, or postoperative ruptures.¹¹

As described elsewhere in this publication, the Endurant stent graft has demonstrated consistent clinical results at 2 years, with no type 1 endoleaks, migration, conversion to surgery, aneurysm-related mortality, and postoperative rupture.¹⁰

DISCUSSION

The Endurant stent graft is the newest-generation stent graft based on collaboration between engineers and physicians, designed to overcome the limitations of first-generation devices. As demonstrated by the studies to date, the device is highly effective in overcoming adverse anatomy with excellent clinical results.

The Endurant stent graft offers a low-profile delivery system to navigate and overcome significant disease of the aortoiliac segment. The smaller French sizes (18 F for 23- and 25-mm devices; 20 F for larger devices up to 36 mm) are currently available for patient implants. The addition of a hydrophilic coating should limit the need for the use of conduits, especially in women. The flexibility of the device, based on the construction of the wire-formed M-shaped body stents and the sinusoidal design distally, allows for effective access through calcified, narrowed, elongated, and kinked vessels.

Adverse proximal neck anatomy and angulation are associated with migration and type I endoleak. The Endurant stent graft appears amenable to overcoming these limitations, at least in the short term, based on current literature. The highly conformable body, which was one of the key design features, allows for sealing in a variety of neck shapes, even with significant angulation.

Results from the Endurant US IDE and CE Mark studies have been encouraging. Additional results from the ENGAGE real-world registry are also promising, showing safety and effectiveness of the device. ■

Frank R. Arko, MD, is with the Sanger Heart and Vascular Institute in Charlotte, North Carolina. Financial interest disclosure information was not available at the time of publication.

Tzvi Nussbaum, MD, is with the Sanger Heart and Vascular Institute in Charlotte, North Carolina. Financial interest disclosure information was not available at the time of publication.

Stephen Lakla, MD, is with the Sanger Heart and Vascular Institute in Charlotte, North Carolina. Financial interest disclosure information was not available at the time of publication.

Jerry Holleman, MD, is with the Sanger Heart and Vascular Institute in Charlotte, North Carolina. Financial interest disclosure information was not available at the time of publication.

Tim Roush, MD, is with the Sanger Heart and Vascular Institute in Charlotte, North Carolina. Financial interest disclosure information was not available at the time of publication.

1. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. *Ann Vasc Surg.* 1991;5:491-495.
2. EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm repair (EVAR trial 1): randomized controlled trial. *Lancet.* 2005;365:2179-2186.
3. Lederle FA, Freischlag JA, Kyriakides TC, et al. Outcomes following endovascular versus open repair of abdominal aortic aneurysm: a randomized trial. *JAMA.* 2009;302:1535-1542.
4. Sicard GA, Zwolak RM, Sidawy AN, et al; Society for Vascular Surgery Outcomes Committee. Endovascular abdominal aortic aneurysm repair: long-term outcome measures in patients at high risk for open surgery. *J Vasc Surg.* 2006;44:229-236.
5. Murray D, Ghosh J, Khwaja N, et al. Access for endovascular aneurysm repair. *J Endovasc Ther.* 2006;13:754-761.
6. Criado FJ. Iliac arterial conduits for endovascular access: technical considerations. *J Endovasc Ther.* 2007;14:630-633.
7. Sternbergh WC III, Carter G, York JW, et al. Aortic neck angulation predicts adverse outcomes with endovascular abdominal aortic aneurysm repair. *J Vasc Surg.* 2002;35:482-486.
8. Donas KP, Kafetzakis A, Umscheid T, et al. Vascular endostapling: new concept for endovascular fixation of aortic stent grafts. *J Endovasc Ther.* 2008;15:499-503.
9. Abbruzzese TA, Kwolek JC, Brewster DC, et al. Outcomes following endovascular abdominal aortic aneurysm repair (EVAR): an anatomic and device specific analysis. *J Vasc Surg.* 2008;48:19-28.
10. Endurant 2011 Annual Physician Clinical Update. Site-reported data.
11. Makaroun M. The Endurant stent graft system: results of the US Regulatory Pivotal Study. Presented at: Society of Vascular Surgery; Boston, MA; June 2010.

*Inclusion/exclusion criteria varies by trial.

Unmet AAA Needs and Next-Generation Devices

A look at the latest advances in endograft technology and possible future developments.

BY FABIO VERZINI, MD, PhD

Today, endovascular aneurysm repair (EVAR) is considered the standard treatment option for abdominal aortic aneurysms (AAAs) in appropriate candidates because it is less invasive and carries a perceived lower risk compared to open surgical repair. In 2008, a large number of elective abdominal aortic procedures were carried out via endografting: 78% of 32,382 AAA repairs utilized EVAR within the Medicare population in the United States.¹ Based on these numbers, it seems that EVAR has reached maturity and is sustained by evidence from late results of randomized trials showing equivalent survival rates after EVAR and open repair.^{2,3}

New endograft models that have been commercially introduced in the last few years have attempted to address some of the weaknesses of earlier generations. Late fixation failures, material fatigue, and modular component disconnections are rarely reported today as causative factors of reintervention, but concerns remain, particularly for the late incidence of ruptures and aneurysm-related deaths after endografting.⁴

TARGET AREAS FOR IMPROVEMENT

Deliverability

According to a thorough review of anatomic features of 1,063 patients with AAAs in a 14-year single-center experience, the second most common cause of exclusion for endografting (after short proximal aortic neck length) is the presence of small iliac access.⁵ Bilateral, small (< 6 mm) iliac lumen is more common in women than in men (47% vs 17%, respectively) and compromises EVAR access.⁵ Moreover, extensive iliac disease and calcification may increase arterial stiffness and make graft navigation impossible (Figure 1).

The availability of lower-profile devices with better



Figure 1. Multiplanar reformation. CT image of a patient with AAA and extensive iliac disease contraindicating EVAR.

navigation capabilities could increase EVAR suitability. Because most of the space in endograft delivery catheters is filled by the fabric rather than the stent, new, stronger materials with high resistance to friction and very low porosity—but reduced thickness—are being investigated. However, a decrease in device diameter must not compromise graft durability, and no attempt to make EVAR available to more patients should adversely affect late failure risks.

Sealing Stability

Proximal graft fixation and sealing has been identified as the most critical issue in long-term performance

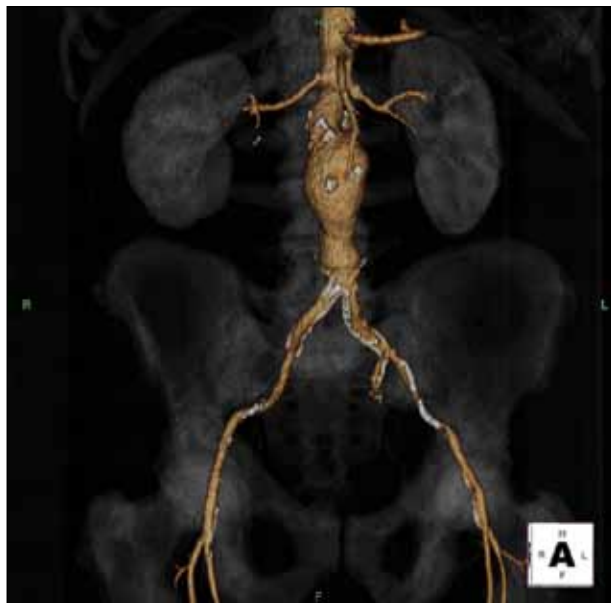


Figure 2. Three-dimensional CT reconstruction in a patient with AAA and iliac disease.



Figure 3. Three-dimensional CT reconstruction (same patient as Figure 2) after EVAR with the Endurant endograft.

of aortic endografts.⁶ With active fixation methods or suprarenal fixation of modular, tubular aortic segments, clinically significant distal migration of the proximal end of the prosthesis is quite rare in the case of adequate proximal neck anatomy. Due to displacement forces secondary to blood flow vectors, endografts are prone to movement inside the aneurysm sac, and the critical point of fixation is now represented by the distal iliac landing zones. Large aortoiliac aneurysms with short iliac necks, often ectatic, may represent the weak site for late proximal migration of the distal end of the graft. Better fixation of iliac endograft limbs is required in cases of short iliac necks. Solutions to increase iliac sealing length with the aid of bifurcated iliac grafts or improving the resistance to displacement with active iliac fixation modes could be of help.

Type II Endoleak Prevention

Even with supposed reduction of type I endoleak risks in newer-generation endografts, late aneurysm sac growth still occurs in some cases. This finding requires continued surveillance and, at times, follow-up interventions. Type II endoleak is frequently the cause of growth; it is present in 10% to 30% of cases after EVAR and requires treatment in up to 10% of patients.⁷ In a recent review from the Cleveland Clinic, incidence of sac embolization for type II endoleaks was 7.8% in 809 patients undergoing EVAR during an 11-year period.⁷ Late results showed secondary procedures were not entirely effective in preventing subsequent growth, with a

5-year freedom from sac expansion rate of 44%; the risk of a repeat embolization procedure was 24%.

Further research is needed to address this issue and prevent formation of type II endoleaks by means of innovative stent graft designs or adjunctive techniques. Sac fillers, with or without endobags inside the aneurysm, may represent a solution that is currently under clinical investigation, whereas other efforts may evaluate the potential of bioactive endografts to locally deliver drugs capable of inducing sac thrombosis or even aneurysm regression or stabilization. These solutions, however, remain unproven, and the body of clinical evidence supporting these novel concepts is still evolving.

LATEST ENDOGRAFT DEVELOPMENTS

In the last few years, all of the major aortic endograft companies have developed renewed models of grafts and/or delivery systems to cope with difficult anatomies and guarantee better delivery, more precise deployment, and improved performance. A true comparison of the results among different models is impossible due to obvious biases in anatomy selection and operator experience at different centers. Moreover, the short follow-up periods available for the newest endograft models may optimistically overestimate the favorable results of EVAR, which can present unpredicted failure modes later after implantation.

By comparison, the Endurant® stent graft (Medtronic, Inc., Minneapolis, MN) is a well-characterized device. The

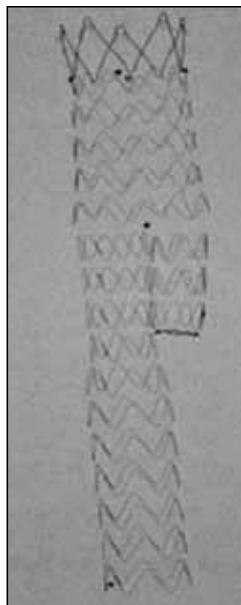


Figure 4. Radiographic image of the metallic frame of the Endurant II bifurcated graft.

Endurant stent graft has shown high success rates in clinical use in a wide variety of anatomic settings (Figures 2 and 3).⁸ One-year results in all of the published experiences reported no major migrations, failures, or AAA ruptures, and consistent results have been found across patients treated with Endurant in well-controlled approval trials as well as real-world registries, across both straight-forward and complex, challenging anatomies.⁸⁻¹⁰ In addition, Endurant has demonstrated consistent clinical outcomes between 1 and 2 years, with no incidence of type I endoleaks, migration, conversion to surgery, aneurysm-related mortality, or postoperative ruptures at 2 years.¹⁰

A new version of the graft, the Endurant® II, launched commercially in Europe in January 2012 and received FDA approval in May 2012. To facilitate deliverability, the lower-profile Endurant II delivery system in the 28-mm bifurcated device utilizes an extended hydrophilic coating length for enhanced access to tortuous and calcified iliac arteries. The 28-mm-diameter bifurcated segment is now mounted onto an 18-F outer diameter catheter due to the removal of one peak of the suprarenal stent, which is one of a few modifications made to lower the profile of the delivery system. Laboratory testing showed that migration resistance of Endurant II is comparable to that of Endurant, provided that the suprarenal pins engage the aortic wall (Medtronic in vitro bench testing. Data on file.). These innovations render the device very trackable, even in extremely difficult anatomies, and the low profile of Endurant II may also increase the number of women who can undergo minimally invasive endovascular treatment.

The Endurant II device has two new contralateral iliac limb graft lengths (156 and 199 mm) designed to enable more extensive iliac coverage. When possible, the use of fewer pieces to complete infrarenal aortoiliac exclusion may reduce the total costs of the procedure and the risks of modular disconnections.

Endurant II will continue to deliver the same consistent clinical performance, trial after trial, as that of the market-leading predecessor Endurant stent graft.

To enhance visibility of the contralateral leg of the bifurcated device, the radiopacity of the distal end of contralateral gate has been improved with the placement of a platinum-iridium markerband. This metallic reference, coupled with a lateral marker positioned on the bifurcated graft, may help in three-dimensional orientation, deployment, and limb cannulation (Figure 4). Even with these new elements, the essential components of the proven Endurant stent graft structure remain unchanged. We expect consistent performance of Endurant II in terms of proven adaptability, known sealing characteristics, and clinical efficacy. We therefore expect that Endurant II will continue to deliver the same consistent clinical performance, trial after trial, as that of the market-leading predecessor Endurant stent graft. ■

Fabio Verzini, MD, PhD, is with the Unit of Vascular and Endovascular Surgery, Hospital S. Maria della Misericordia, University of Perugia, in Perugia, Italy. He has disclosed that he has no financial interests related to this article. Dr. Verzini may be reached at +39 075 5786435; fverzini@unipg.it.

1. Sachs T, Schermerhorn M, Pomposelli F, et al. Resident and fellow experiences after the introduction of endovascular aneurysm repair for abdominal aortic aneurysm. *J Vasc Surg.* 2011;54:881-888.
2. Greenhalgh RM, Brown LC, Powell JT, et al; The United Kingdom EVAR Trial Investigators. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362:1863-1871.
3. De Bruin JL, Baas AF, Buth J, et al; DREAM Study Group. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362:1881-1889.
4. Wyss TR, Brown LC, Powell JT, Greenhalgh RM. Rate and predictability of graft rupture after endovascular and open abdominal aortic aneurysm repair. Data from the EVAR trials. *Ann Surg.* 2010;252:805-812.
5. Sweet MP, Fillinger MF, Morrison TM, Abel D. The influence of gender and aortic aneurysm size on eligibility for endovascular abdominal aortic aneurysm repair. *J Vasc Surg.* 2011;54:931-937.
6. P. Cao, F Verzini, P De Rango, et al. Device migration after endoluminal abdominal aortic aneurysm repair: analysis of 113 cases with minimum follow-up of 2 years. *J. Vasc. Surg.* 2002;35:229-235
7. Sarac TP, Gibbons C, Vargas L, et al. Long-term follow-up of type II endoleak embolization reveals the need for close surveillance. *J Vasc Surg.* 2012;55:33-40.
8. Makaroun MS, Tucheck M, Massop D, et al; Endurant US Pivotal Trial Investigators. One year outcomes of the United States regulatory trial of the Endurant stent graft system. *J Vasc Surg.* 2011;54:601-608.
9. Rouwet EV, Torsello G, de Vries JP, et al. Final results of the prospective European trial of the Endurant stent graft for endovascular abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg.* 2011;42:489-497.
10. Endurant 2011 Annual Physician Clinical Update. Site-reported data.

Medtronic: From Pipeline to Patients

Initiatives aimed at increasing abdominal aortic aneurysm awareness, identifying patients, and expanding treatment options.

BY L. MARIANO FERREIRA, MD

Over the past few years, I have instituted the following three key elements in my vascular surgery practice, resulting in more patients being treated and better perioperative and long-term outcomes: (1) an annual aneurysm screening program, (2) an imaging software system to process and clearly understand a particular anatomic situation, and (3) the use of next-generation endografts, such as the Endurant® stent graft system (Medtronic, Inc., Minneapolis, MN).

THE EVOLUTION OF EVAR

The evolution of aortic endovascular therapies over the past decade has been dramatic, especially in the imaging field. Accurate preprocedural imaging, improvements in intraoperative technology, and new endograft technologies for increased deployment accuracy and stent graft placement have established endovascular aneurysm repair (EVAR), versus open surgical repair, as the ideal procedure. More than 20 years ago, the first EVAR procedure was performed in Buenos Aires; it is encouraging to see that EVAR has passed the test of time.

Today, next-generation endografts offer new designs and features that allow treatment options for an expanded range of patient anatomies. Precise, low-profile, and more flexible off-the-shelf devices allow us to reduce the incidence of type I endoleaks in elective procedures. The M-shaped nitinol wire stents in the Endurant® stent graft system provide flexibility and conformability during deployment. The tip-capture delivery system ensures accurate, controlled release during suprarenal stent deployment. In the last 2 years, we have implanted 70 Endurant devices with a very low complication rate.

ANNUAL ANEURYSM SCREENING PROGRAM

Since 2009, we have organized a multidisciplinary program aimed at increasing the early detection of

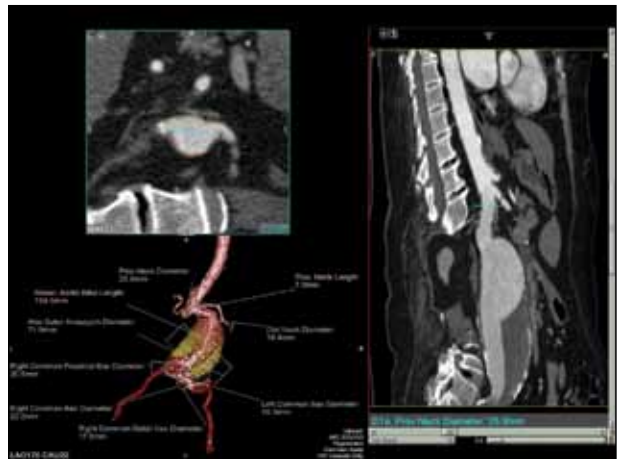


Figure 1. Preoperative planning using 3D computed tomographic angiography.

aortic aneurysms at our university hospital. To increase awareness of our program, we developed an educational website (www.aneurismadeaorta.com), and in just 4 years, we have logged more than 20 million pageviews and more than 65,000 unique visitors throughout Latin America.

We also organized *Semana del Aneurisma de Aorta* (Aortic Aneurysm Week) to invite men between 60 and 80 years of age for abdominal aortic aneurysm (AAA) screening. More than 1,500 ultrasounds were performed, identifying more than 100 AAA patients. We noted two key factors for ensuring success in our AAA screening program: (1) a high initial rate of attendance to the screening program and (2) rapid access to treatment without delays in completion of the procedure, while maintaining a low operative mortality rate. We are now expanding our focus to raise AAA disease awareness within the neighboring peripheral community. To further advance this initiative, we sought external support.

ADDRESSING AAA FROM PRODUCT PIPELINE TO PATIENT

Over the last few decades, Medtronic has made significant investments toward advancing clinical understanding of aortic aneurysms. In the past, successful investigation of a disease was often directly associated with the size of the potential patient population. Medtronic has taken a global approach toward the understanding of aortic disease, demonstrating a commitment to improving endovascular techniques and patient outcomes through investments in screening, training, imaging and innovative products and technologies.

The goal of an AAA awareness program is to reduce mortality rate through early detection. Cancer and heart disease are familiar to most people. Public awareness of aortic aneurysm disease, on the other hand, lags behind. Further, although aortic disease prevalence is high, the majority of developing countries currently do not have strategies in place to screen, detect, and treat aortic aneurysm disease. It takes great effort and time to spread the concept that one simple abdominal ultrasound provided using university, public, and/or private resources can save a life. In the last 3 years, we organized three campaigns identifying nearly 100 aneurysm patients. This is a robust start, but we know that our effort will fade if it is not spread beyond academia. Medtronic holds our shared vision and is pursuing this goal through the awareness campaign, “detectA, actúA, vivA” (detect, act, live). These campaigns are spreading throughout Latin America to fight this so-called silent killer.

Ambitious projects supported by Medtronic have been launched in Puerto Rico, the Dominican Republic, and Costa Rica, with the joint action of the medical and general communities. Medical schools, associations, media, institutions, and public and private efforts have unified to help control this disease. Research has demonstrated that offering ultrasound screening to men at age 65 could reduce the rate of premature death from ruptured AAAs by up to 50% (level Ia, recommendation A).¹⁻⁵ The objectives of the screening program are to identify eligible men and invite them for screening to accurately identify aortic aneurysms and provide patients with clear, high-quality information. The program should also minimize the adverse effects of screening, including anxiety and unnecessary investigations.

The program typically involves an ultrasound scan at community health care facilities such as hospitals, clinics, mobile units, and primary care facilities. To increase patient and community awareness of aortic disease and of the screening events, we distribute pamphlets, invita-

tion letters and posters throughout the community. Banners and posters highlighting the screening event are also prominently displayed. All of these materials are available and provided by the awareness campaign (detectA, actúA, vivA) for display in general practitioner offices, primary care facilities, and other suitable public locations. Information sheets are also available at www.detectAAA.com.

In addition to a robust aneurysm screening program, enhanced imaging tools are critical in properly diagnosing and treating aneurysm disease.

ENHANCED IMAGING TO ELEVATE AAA SCREENING

EVAR imaging technology has evolved rapidly. The gold standard for preoperative evaluation of an aortic aneurysm is computed tomography angiography. Three-dimensional (3D) reconstruction and analysis of the computed tomographic dataset is enormously helpful, and even sometimes essential, for proper sizing and planning of endovascular stent graft repair.

Medtronic's CTExpress® is a web-based document-acquisition program that enhances today's complex imaging technologies. 3D Recon (Vital Images, Inc., Minnetonka, MN) was specifically designed to rapidly transfer large digital imaging and communications in medicine (DICOM) data and provide multiplanar renderings in real time. It provides advanced post-processing techniques in 2D and 3D. The program automatically performs various image processing steps, such as bone removal and detection of an automated centerline. It offers advanced clinical tools for volumetric imaging modalities for visualization, interpretation, quantitative analysis, planning, and follow-up.

To supplement preprocedure case planning, the CTExpress (Intelemage, LLC, Cincinnati, OH) web portal allows users to manage their images and case files. This program can create and modify orders, as well as communicate with other users, allowing them to securely upload images for central laboratory technical review. It offers real-time collaboration with Medtronic experts and international Key Opinion Leaders and creates a database of stored images for individual physicians to review at later dates with no cost, allowing online access from anywhere.

In recent years, we have seen a dramatic improvement in the technology used to visualize anatomy and aneurysms. This has resulted in the creation of more flexible, adaptable, and precise endografts that conform to patient anatomy, which has in turn improved clinical outcomes. The diseased anatomy of the aorta is more important than physiological status in predicting the

Clinical evidence on the Endurant stent graft indicates that the Endurant design attributes have translated into meaningful clinical outcomes for patients.

success of endovascular intervention. The shape of the neck, the angle of the neck, and the relationship of the renal arteries to each other and their position in the neck play an important role at the time of stent graft deployment.

More complete preoperative information yields better intraoperative results. Segmentation and 3D vessel volume allow a better understanding of the anatomy, resulting in better planning, enhanced patient selection, and AAA measurement (3D double-oblique multiplanar reconstruction, 3D maximum intensity projection, or 3D curved multiplanar reconstruction). Three-dimensional branching parameters at visceral and aortic bifurcation sites, as well as blood vessel tortuosity, were determined from centerlines derived from computed tomographic angiograms (Figure 1).

Since the early days of EVAR, planning for infrarenal AAA repair has centered on anatomical assessment of the landing zones (aortic neck and iliac arteries) and access vessels. Misrepresented planar projections of branch trajectory, vessel length, and tortuosity demonstrate the importance of 3D geometric characterization. This information is useful not only for endovascular procedure case planning, but also for providing endovascular device design parameters.

PARTNERING TO ADVANCE THE PRACTICE OF EVAR

In Argentina, a recent report showed that there are 10 approved stent grafts for the treatment of AAAs. According to the National Administration of Drug, Food, and Medical Technology (ANMAT), this is more than double the figure recorded only 6 years ago. Not only has the number of available devices increased but so has the total number of aortic repairs and elective endovascular procedures.⁶ In this dynamic environment, it has become even more critical for physicians to challenge medical device manufacturers to provide solid clinical evidence to support the claims of their products. The burden of proof lies with the manufacturers to demonstrate whether changes in device design have translated to meaningful advances in clinical outcomes.

Stent graft technology is constantly evolving, and vascular specialists are gaining greater experience in treating increasingly complex pathologies. New device designs and deployment techniques have allowed treatment in the aortic arch and in the juxtarenal aorta, which was not previously possible. There is no doubt that EVAR will continue playing an increasing role in the treatment of patients with AAAs. The benefits of EVAR have been widely recognized by clinical practices, and thousands of cases are performed every year. Advances in medical imaging have also played an essential role in improving both planning and postoperative efforts.

Medtronic is recognized as the world leader in medical technology and pioneering therapies. With Endurant—designed through a multidisciplinary approach that incorporated feedback from more than 150 physicians—Medtronic has set the standard for the rigorous device design and validation process.⁷ Clinical evidence on the Endurant stent graft indicates that the Endurant design attributes have translated into meaningful clinical outcomes for patients.

By enabling research and innovation through physician partnerships, corporate sponsors like Medtronic can continue to advance EVAR therapy. Corporate collaboration expands our ability to influence development across the industry, to advance our research and work, and to deliver evidence-based practice and innovation to a growing segment of health care services. ■

L. Mariano Ferreira, MD, is vascular surgeon and endovascular specialist at the Hospital de Clínicas and ENER/Clínica La Sagrada Familia in Buenos Aires, Argentina. He has disclosed that he receives honoraria from Medtronic, Inc. for consulting, speaking, and training. Dr. Ferreira may be reached at +5411-4783-9122; drferreira@yahoo.com.

1. Scott RA, Wilson NM, Ashton HA, Kay DN. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomised controlled study. *Br J Surg*. 1995;82:1066-1070.
2. Lindholt JS, Juul S, Fasting H, Henneberg EW. Screening for abdominal aortic aneurysms: single centre randomized controlled trial. *BMJ*. 2005;330:750-753.
3. Norman PE, Jamrozik K, Lawrence-Brown MM, et al. Population based randomized controlled trial on impact of screening on mortality from abdominal aortic aneurysm. *BMJ*. 2004;329:1259-1262.
4. Multicentre Aneurysm Screening Study Group. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomized controlled trial. *Lancet*. 2002;360:1531-1539.
5. Moll FL, Powell JT, Fraedrich G, et al. Management of abdominal aortic aneurysms. Clinical practice guidelines of the European Society for Vascular Surgery. *Eur J Vasc Endovasc Surg*. 2011;41:S1-S58.
6. Comunicados de prensa, código alimentario, farmacopea y productos. Available at: <http://www.anmat.gov.ar>. Accessed April 28, 2012.
7. Arko FR, Jordan WD, Robaina S, et al. Interdisciplinary and translational innovation: the Endurant stent graft... from bedside to benchtop and back to bedside. *J Endovasc Ther*. 2011;18:779-785.

The Endurant Stent Graft: Consistent Clinical Performance, Trial After Trial

Overview of clinical studies and registries evaluating the Endurant stent graft system.

BY FRANK VERMASSEN, MD, PhD, AND NATHALIE MOREELS, MD

Twenty years after its introduction, the role of endovascular aortic aneurysm repair (EVAR) in the management of abdominal aortic aneurysms (AAAs) continues to increase. This progress was only possible thanks to the development of new stent grafts and delivery systems enabling us to perform EVAR in patients with shorter and more angulated necks, smaller and more tortuous iliacs, and overall more challenging anatomies. Insights obtained from analysis of the failure modes for previous devices led to the development of more flexible and conformable grafts and delivery systems with smaller diameters and more trackability.

Experience with the first generation of endografts also taught us to be cautious about the short- and long-term performance of these devices with regard to migration, integrity, modular disconnection, kinking, thrombosis, and late endoleaks and ruptures. Therefore, it is important to conduct thorough surveillance of implanted endografts not only in the early stages of their use, but also over the long term, and to carefully analyze the data collected. This article provides an overview of the main studies that have evaluated the Endurant® stent graft (Medtronic, Inc., Minneapolis, MN).

TRIAL RESULTS OVERVIEW

Endurant has demonstrated consistently successful clinical performance across both well-controlled trials and real-world registries, in a variety of patient types and anatomies.

The aggregated published clinical evidence highlights the consistent clinical outcomes of the Endurant stent graft system.

Prospective European Trial

The Prospective European Trial of the Endurant Stent Graft for Abdominal Aortic Aneurysm Repair (EU-trial)¹ was a prospective, single-arm, nonrandomized, multicenter trial including 80 elective patients treated in 10 European hospitals. The trial was designed to assess the clinical safety and performance of the endograft during the first year after implantation. Morphological inclusion criteria needed to be consistent with the Endurant instructions for use.

The device was successfully delivered and deployed in all cases. Only 5% needed a blood transfusion. The 30-day mortality rate was 2.5%, but none of these deaths were considered as procedure or device related. Overall, 28 endoleaks (26 type II, 2 undefined) were identified. Throughout the 1-year follow-up period, there were no type I or III endoleaks and no loss of device integrity. There was no graft migration, no conversion to open repair, and no AAA rupture. Limb thrombosis occurred in three patients but required

reintervention in only one. A total of three out of 80 patients had secondary interventions, all endovascular, to address one occlusion, one stenosis, and one procedure to extend the distal landing zone. During follow-up, two more patients died, providing a survival rate of 95% after 1 year. In only two patients a further aneurysm expansion ≥ 5 mm was observed. Both had a type II endoleak from the inferior mesenteric and lumbar arteries. A decrease of > 5 mm was seen in 43% (32/75) of the patients.

United States Regulatory Trial

The United States regulatory trial² was a prospective, single-arm, multicenter trial conducted in 26 sites in the United States and included 150 patients with AAA diameters > 5 cm, a proximal neck ≥ 10 mm, bilateral iliac landing zones ≥ 15 mm, and neck angulation $\leq 60^\circ$. The vast majority of the interventions (83%) were performed under general anesthesia. Stent graft implantation was technically successful in 99.3% (149/150). The failure was due to the inability to cannulate the contralateral gate. The problem was solved by conversion to an aorto-uni-iliac endograft with femorofemoral bypass. One patient had a neck rupture during ballooning but could still be treated successfully. Blood transfusion was required in only one patient (0.7%). Five supplementary interventions were performed during the first month, all for arterial events and all using open techniques. There was no 30-day mortality. At 1-month follow-up, endoleaks (all type II) were present in 23/143 (16%) of patients.

Through the first year of follow-up, there were no migrations, no conversions to open repair, and no ruptures. Thirteen (10%) endoleaks were found at 1 year (12 type II, 1 indeterminate). No type I or III endoleaks were identified during this first year, although one type II endoleak later proved to be a type Ib on angiography and was treated with an extension. Ten (6.7%) reinterventions were performed during the first year: four endovascular and six open. Three of these interventions were for vascular problems related to the procedure, two for the treatment of type II endoleaks (without sac enlargement), and five because of limb stenosis or occlusion. Most of these were due to compression in a small aorta or kinked iliac arteries.

Aneurysm sac diameter decreased > 5 mm at 1 year in 47% of patients and remained stable in 53%. No sac showed an increase > 5 mm.

United States Trial at 2 Years

Endurant has demonstrated consistent clinical results at 2 years.³ There were no type I endoleaks, migration, conversion to surgery, aneurysm-related mortality, and

The Endurant stent graft system has demonstrated consistently excellent clinical outcomes—in the US IDE trial and the ENGAGE real-world registry.

postoperative ruptures. Aneurysm sac diameter either decreased or remained stable in 98.3% of patients. In the second year, an additional 1.4% of patients required a second intervention (Data on file at Medtronic, Inc.). Stent graft integrity was 100%.³ These results show that at midterm follow-up (2 years), when following the instructions for use, clinical outcomes with the Endurant endograft remain excellent.

ENGAGE Registry

Trials undertaken for regulatory purposes have stringent inclusion criteria, providing the advantage of a clearly defined and homogenous study population. The disadvantage is that they often do not reflect real-world practice, and the outcomes may not be applicable to the general population.⁴

ENGAGE (Endurant Stent Graft Natural Selection Global Postmarket Registry) is a long-term, worldwide, prospective real-world postmarket study evaluating the Endurant stent graft.⁵ ENGAGE was designed to increase the knowledge base about EVAR in a complex real-world population with the use of a single, latest-generation endograft. In total, 1,262 patients were included, which makes this study the largest real-world registry for any single endograft. The implantation of the device was successful in 99.5% of patients. The all-cause mortality rate at 30 days was 1.3%. One-year follow-up is available on the first 500 patients and showed no migrations, no ruptures, and 0.6% conversions. Only one (0.2%) aneurysm-related death occurred after the 30-day period, yielding an aneurysm-related mortality rate of 1.4% at 1 year. The rate of secondary procedures to correct type I/III endoleak at 1 year was 1.2%, and the overall rate of secondary procedures was 4.6%. At 1 year, type II endoleaks were present in 8% of patients.

DISCUSSION

Although it only became commercially available in 2008, the Endurant stent graft is already one of the best characterized endografts in current use, supported by a rigorous body of clinical evidence. Pivotal trials, single-center series, and a global registry all show very

consistent results. The technical success rate in patients treated according to the morphological IFU is consistently above 99%. One-year data from the ENGAGE registry showed no type I or type IV endoleaks and no aneurysm ruptures.⁵ There were no graft migrations and only three late conversions to open repair.

Secondary vascular procedures were performed in 4.9% of the patients.⁵ The majority of these were performed for vascular access complications. Endurant has continued to demonstrate excellent clinical outcomes, and physicians are confident in the performance of the device.⁵

The clinical outcomes for Endurant—including type I/III endoleaks, conversion rates, and migration rates—are all consistently and significantly lower than what was demonstrated in older trials, such as EVAR-1 and DREAM,^{6,7} as well as the Eurostar and Lifeline registries. Similarly, the first-year reintervention rate is cut by 50% to 75% in the trials evaluating Endurant, as compared to the reintervention rates achieved in EVAR-1 and DREAM. The consistently successful clinical outcomes achieved by Endurant—across a variety of studies and various anatomies—illustrates the translation of proven endograft design concepts into excellent clinical outcomes.

CONCLUSION

The aggregated published clinical evidence highlights the consistent clinical outcomes of the Endurant stent graft system.¹⁻⁴ In several studies and a real-world regis-

try (ENGAGE), the device has consistently shown to be safe and effective, with excellent technical success rates, freedom from type I/III endoleaks, and freedom from conversion. ■

Frank Vermassen, MD, PhD, is with the Department of Vascular Surgery at Ghent University Hospital in Ghent, Belgium. He has disclosed that he has participated in clinical trials for Medtronic. Dr. Vermassen may be reached at frank.vermassen@ugent.be.

Nathalie Moreels, MD, is with the Department of Vascular Surgery at Ghent University Hospital in Ghent, Belgium. She has disclosed that she has no financial interests related to this article.

1. Rouwet EV, Torsello G, de Vries JP, et al. Final results of the prospective European trial of the Endurant stent graft for endovascular abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg.* 2011;42:489-497.
2. Makaroun MS, Tucheck M, Massop D, et al; Endurant US Pivotal Trial Investigators. One year outcomes of the United States regulatory trial of the Endurant stent graft system. *J Vasc Surg.* 2011;54:601-608.
3. Endurant 2011 Annual Physician Clinical Update. Site-reported data.
4. Böckler D, Riambau V, Fitridge R, et al. Worldwide experience with the Endurant stent graft system: Review of the literature. *J Cardiovasc Surg* 2011; 52:669-681
5. Riambau V, on behalf of ENGAGE investigators. Are contemporary results with EVAR better than in the past? Results from Engage global registry. Presented at: Leipzig Interventional Course (LINC); January 2012; Leipzig, Germany. Data on file at Medtronic, Inc.
6. The United Kingdom EVAR Trial Investigators. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362:1863-1871.
7. De Bruin J, Baas A, Buth J, et al, for the DREAM study group. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med.* 2010;362:1881-1889.

Endurant® II

AAA STENT GRAFT SYSTEM

- **Lower profile** and **extended hydrophilic coating** delivery system takes improved access a step further
- **Longer limb lengths**, now available in 156mm and 199mm limbs, provide more options
- **Improved radiopacity** of cannulation gate marker offers increased visibility

Endurant II empowers strong results for more patients. That's why
1 out of every 2 EVAR patients worldwide receives an **Endurant stent graft**.¹

For more information, please visit medtronicendovascular.com

1. Global market share data on file at Medtronic, Inc.