

# Fillable Endovascular Aneurysm Repair

An early look at a next-generation EVAR technology that may address some current limitations and improve clinical outcomes.

BY CARLOS DONAYRE, MD; GEORGE E. KOPCHOK, BS; AND RODNEY A. WHITE, MD

Approximately 19% of patients develop an endoleak or endotension within the first 18±8.2 months after endovascular repair (EVAR) of an abdominal aortic aneurysm (AAA) using current commercially available stent graft technologies, which depend solely on proximal neck sealing and fixation.<sup>1</sup> The majority of endoleaks are type II in nature,<sup>2</sup> which may be addressed through minimally invasive, catheter-based techniques with associated low complication rates. However, these secondary procedures are costly and involve patient surveillance with annual CT scans.<sup>3</sup> Furthermore, in a small percentage of these EVAR cases, which develop persistent endoleaks or endotension and continued aneurysm sac enlargement, a surgical conversion is required to prevent aneurysm rupture.<sup>2</sup> In addition, currently available commercial EVAR devices fit only 39.3% to 66%<sup>4,5</sup> of otherwise eligible patients due to the anatomical restrictions specified in their labeling. Finally, these first-generation stent grafts have a limited durability and life expectancy, which is less than that of surgical grafts.<sup>4,6,7</sup>

Presently available commercial endografts all share similar design and materials and are primarily based on bifurcated configurations. The first commercial endografts (Ancure, Guidant Corporation, Indianapolis, IN) were composed of a tube graft design with hooks at the proximal end to attach the graft to the native aorta. Reliance on proximal fixation was enhanced by adding expandable wire stents, and bifurcated systems were designed to achieve fixation in the iliac arteries. Later, stents were incorporated along the full length of the graft to create supported stent grafts, and the aortic graft bodies were lengthened to reduce the reliance on the proximal stent for sealing (AneuRx, Medtronic, Minneapolis, MN; and Powerlink, Endologix, Inc., Irvine, CA). In addition, hooks,

“... EVAR is currently limited to the treatment of AAAs with specific anatomical characteristics.”

barbs, and stents designed with increased radial force have been implemented to decrease migration, minimize endoleaks, and prevent failures (Zenith, Cook Medical, Bloomington, IN; Excluder, W. L. Gore & Associates, Flagstaff, AZ; and Talent, Medtronic). In order to address the varied aortic and iliac anatomic morphology, manufacturers developed modular stent graft component systems composed of various aortic and iliac components. These multipiece stent graft systems introduced a new failure mode classified as a type III endoleak: modular device separation as the device junctions were subjected to constant pulsation of blood flow through the graft. Furthermore, deployment of device extenders adds time, blood loss, and cost to the overall EVAR procedure.

Based on the above considerations, EVAR is currently limited to the treatment of AAAs with specific anatomical characteristics. Fenestrated and branched endografts have been introduced to shift the proximal sealing zone from the infrarenal to the suprarenal aorta, thus expanding EVAR treatment to juxta-, para-, and suprarenal aneurysms. However, fenestrated endografts require experienced operators, custom devices, and lengthy procedural times.<sup>8,9</sup>

## THE NELLIX FILLABLE EVAR TECHNOLOGY

To expand the applicability of EVAR and address the failure modes observed with current endografts, Nellix

Endovascular (Palo Alto, CA) has designed a fillable, sac-anchoring, low-profile endovascular device. The Nellix technology encompasses a fully contained, polymer-filled endobag, which conforms perioperatively to the specific shape of the patient's aneurysm while providing anchoring and sealing. The polymer is contained inside an expanded-polytetrafluoroethylene (ePTFE) bag that is lined on the inside by a metallic endoframe that forms the endoskeleton for the new lumen inside the aneurysm. The polymer itself is a proprietary formulation based on polyethylene glycol (PEG), which is biostable. PEG-based material chemistries have been approved for use in devices for vascular closure, cranial, and abdominal applications. Structural integrity of this composite device has been established through long-term in vitro and in vivo studies.

This fillable EVAR system is designed to provide aneurysm exclusion and long-term device stability, offering an exponentially larger sealing surface area compared to conventional stent grafts, as well as to possibly minimize remodeling of the aneurysm sac by eliminating lateral movement. The Nellix technology essentially "freezes" the diseased aortic sac and landing zones by filling the open spaces and gaps around the implant. The premise of this concept is that a reduction or elimination of remodeling may have a positive impact on long-term durability and reduction of endoleaks. Long-term remodeling of the aorta will be followed over time in a well-controlled clinical trial. In addition, this unique design may also eliminate migration of the endograft due to complete filling of the aneurysm sac.

## POTENTIAL BENEFITS

### Ability to Treat More Patients

The Nellix Fillable Sac Anchoring Prosthesis is designed to treat all infrarenal AAAs and aortoiliac aneurysms, including an expanded patient population with adverse neck anatomies (infrarenal neck lengths <1 cm and neck angulations >60°).

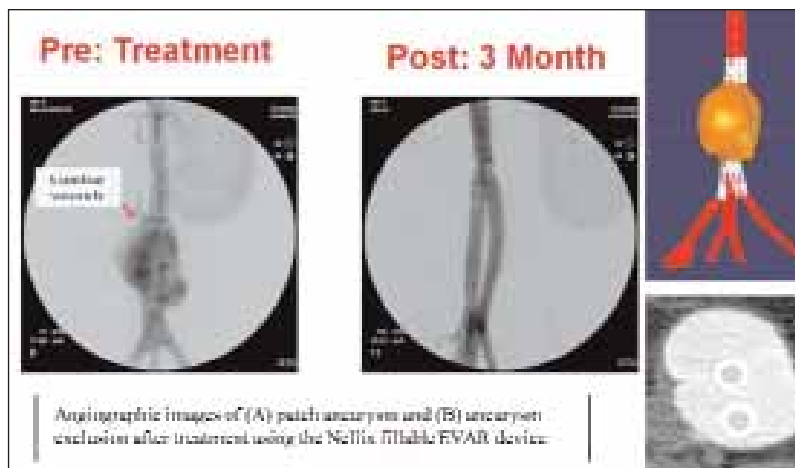


Figure 1. Angiographic and CT images of an ovine patch aneurysm treated with the Nellix fillable EVAR device pre- and postimplantation.

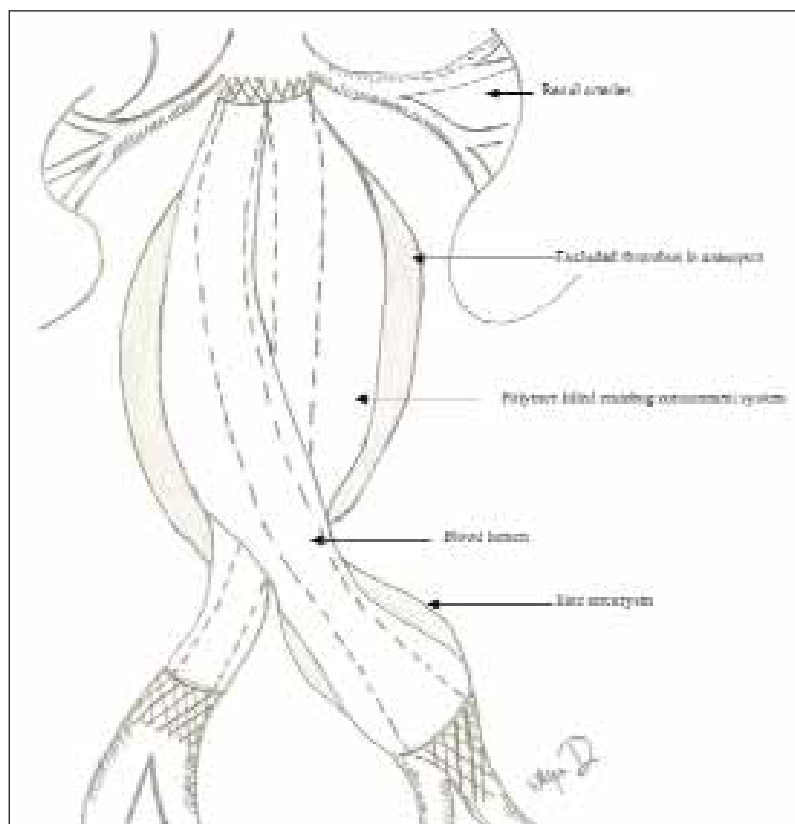


Figure 2. Fillable EVAR device preserving hypogastric flow.

### Durability

The Nellix device fills the aneurysm with a polymer using a dual endobag containment system. By filling the entire aneurysmal sac, the endobags are designed to provide complete sealing of the aneurysm at all tissue surfaces, while providing structural integrity that would pre-

(Illustration by Elynn Donayre.)

vent long-term endoleaks caused by aneurysm remodeling and separation of modular components.

## Minimizing Migration and Lateral Movement

Successful EVAR treatment by current stent graft devices is typically marked by AAA sac shrinkage. Aortic aneurysm shrinkage has been shown to increase the biomechanical forces on the proximal attachment zone over time.<sup>10</sup> This aneurysmal remodeling process may dislodge the graft from the proximal infrarenal aortic neck, resulting in a type I endoleak or component separation resulting in a type III endoleak. Lateral movement of the endograft within an aneurysm sac may also be a predictor for stent graft instability and adverse events.<sup>10</sup> In addition to potentially providing sealing in a no-neck, highly angulated aneurysm, the Nellix system is intended to completely fill the aneurysm, thereby minimizing any lateral movement or migration of the implanted device.

## PRECLINICAL STUDIES

The Nellix AAA endovascular system has been deployed in animal models to evaluate aneurysm exclusions. Dacron patch aneurysms were created surgically in an ovine model and subsequently treated using the Nellix AAA system. Study results showed safety of the Nellix device in terms of acute delivery, deployment, and aneurysm exclusion. Chronic studies, based on CT follow-up, also showed that effective long-term exclusion of AAAs with the Nellix prosthesis is feasible. Angiographic and CT images before treatment and at 3-month follow-up show patent lumens and aneurysm exclusion as evidenced by the absence of blood flow to the lumbar arteries (Figure 1). Histological examination demonstrated that implantation of the Nellix AAA endoprosthesis is associated with minimal trauma and low inflammation.

The in vivo (Dacron) patch-aneurysm studies also provided early clinical insights regarding the Nellix AAA device. Ovine models developed some mural thrombus inside patch aneurysms prior to treatment that could be identified by CT scans, similar to human AAAs. After the aneurysm was excluded, thrombus was trapped inside the Dacron patch; no sac regression was seen. Remodeling in humans, in terms of thrombus and sac regression, however, is expected to be different and will be studied in a clinical trial through periodic CT scans at follow-up. Another significant finding from the animal studies has been the total elimination of type II endoleaks, both acute and chronic, due to polymer filling and occlusion of side branch vessels (lumbar) feeding the aneurysm. Such reduction or elimination of endoleaks may reduce the need for chronic surveillance of patients treated by the Nellix fillable EVAR technology.

## CONCLUSION

As we look to the future, we can conceive of a low-profile, fillable, sac-anchoring AAA device that can address anatomical restrictions and long-term durability limitations of current EVAR endografts. By filling the aneurysm space, this platform may also reduce the occurrence of acute and chronic endoleaks. Furthermore, the fillable EVAR platform might be able to be extended to treat thoracic aneurysms and concomitant iliac aneurysms in a simplified fashion while preserving hypogastric flow as illustrated in Figure 2. As always, we must proceed with cautious optimism as new ideas invite new challenges and potential failure modes. ■

*Carlos Donayre, MD, is a vascular surgeon at the Department of Surgery, Division of Vascular Surgery, Harbor-UCLA Medical Center in Torrance, California. He has disclosed that he is a clinical advisor for Nellix, Inc., and receives research funding. Dr. Donayre may be reached at (310) 213-4878; cdonayre@cox.net.*

*George E. Kopchok, BS, is a biomedical engineer with Los Angeles Biomedical Research Institute, Harbor-UCLA Medical Center in Torrance, California. He has disclosed that he is a paid consultant to and receives grant/research funding from Nellix, Inc. Mr. Kopchok may be reached at (310) 222-3854; gkopchok@labiomed.org.*

*Rodney White, MD, is Vascular Surgery Division Chief, Vascular Surgery Fellowship Program Director and Vice Chairman of Research, Harbor-UCLA Medical Center, and Professor of Surgery, David Geffen School of Medicine at UCLA in Torrance, California. He has disclosed that he is a paid consultant to and receives grant/research funding from Nellix, Inc. Dr. White may be reached at rawhite@ucla.edu.*

1. Leurs LJ, Buth J, Laheij RJ, et al. Long-term results of endovascular abdominal aortic aneurysm treatment with the first generation of commercially available stent grafts. *Arch Surg.* 2007;142:33-41.
2. Becquemin JP, Kelley L, Zubilewicz T, et al. Outcomes of secondary interventions after abdominal aortic aneurysm endovascular repair. *J Vasc Surg.* 2004;39:298-305.
3. Brewster DC, Jones JE, Chung TK, et al. Long-term outcomes after endovascular abdominal aortic aneurysm repair – the first decade. *Ann Surg.* 2006;244:426-438.
4. Carpenter JP, Baum RA, Barker CF, et al. Impact of exclusion criteria on patient selection for endovascular abdominal aortic aneurysm repair. *J of Vasc Surg.* 2001;34:1050-1054.
5. Cotroneo AR, Iezzi R, Giancristofaro D, et al. Endovascular abdominal aortic aneurysm repair: how many patients are eligible for endovascular repair? *Radiol Med.* 2006;111:597-606.
6. Holzenbein TJ, Kretschmer G, Thurnher S, et al. Midterm durability of abdominal aortic aneurysm endograft repair: a word of caution. *J Vasc Surg.* 2001;33:S46-54.
7. Lifeline Registry of EVAR Publications Committee. Lifeline registry of endovascular aneurysm repair: long-term primary outcome measures. *J Vasc Surg.* 2005;42:1-10.
8. O'Neil S, Greenberg RK, Haddad F, et al. Prospective analysis of fenestrated endovascular grafting: intermediate-term outcomes. *Eur J Vasc Endovasc Surg.* 2006;44:115-123.
9. Muhs BE, Verhoeven EL, Zeebregts CJ, et al. Mid-term results of endovascular aneurysm repair with branch and fenestrated endografts. *J Vasc Surg.* 2006;44:9-15.
10. Rafii BY, Abilez OJ, Benharash P, et al. Lateral movement of endografts within the aneurysm sac is an indicator of stent-graft instability. *J Endovasc Ther.* 2008;15:335-343.