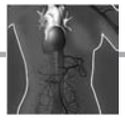
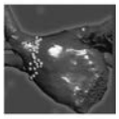
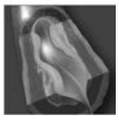

Endovascular treatment of morphologically challenging abdominal aortic aneurysms using flexible endograft

Abdominal aortic aneurysms have an incidence rate of 5–9% in men over 60 years of age. Their repair via the endovascular route is now becoming accepted as the treatment of choice. Two of the key factors determining a patient's eligibility for an endovascular repair include aneurysm neck anatomy and tortuosity of the iliac vessels. Patients who have such challenging morphology are at an increased risk of having complications such as endoleaks, graft migration and limb occlusion. Currently there is no ideal graft available for the treatment of aneurysms that are morphologically challenging. Indeed, the delivery and deployment of traditional grafts that are available for endovascular repair can be extremely challenging in these patients. This article evaluates a flexible modular self-expanding graft (Aorfix™) constructed using a circular Nitinol frame, offering considerable compliance. Its key characteristics, cost and clinical outcome data are presented.

KEYWORDS: Aorfix™ ■ aortic aneurysm ■ endovascular repair ■ stent

John Hardman[1], Kajendran Balasubramaniam[†], A Weale[2] & M Horrocks[3]

[1]Consultant Interventional Radiologist, Royal United Hospital Bath NHS Trust, Combe Park, Bath, BA1 3NG, UK
Tel.: +44 1225 428 331
john.hardman@ruh-bath.swest.nhs.uk
[2]Surgical Registrar, Royal United Hospital Bath NHS Trust, Combe Park, Bath, BA1 3NG, UK
Tel.: +44 1225 428 331
andy@weale.org.uk
[3]Professor of Vascular Surgery, Royal United Hospital Bath NHS Trust, Combe Park, Bath, BA1 3NG, UK
Tel.: +44 1225 428 331
profmhorrocks@sky.com
[†]Author for correspondence: Interventional Radiology Fellow, Royal United Hospital Bath NHS Trust, Combe Park, Bath, BA1 3NG, UK
Tel.: +44 1225 428 331
kajen1@doctors.org.uk

Endovascular repair is becoming the treatment of choice for infrarenal abdominal aortic aneurysms [1,2]. However, a significant proportion of patients are still treated by conventional open surgery due to adverse aneurysm morphology. Typical adverse features include short aneurysm neck, marked angulations or conical shape of the neck, and severe iliac tortuosity. The latter factor poses greater challenges to the delivery and deployment of standard stent graft systems. These factors are also associated with poorer clinical outcome, including type I endoleaks [3–6].

Research work carried out to overcome the above described morphological factors has resulted in the manufacture of Aorfix™ (Lombard Medical Technologies, Oxford, UK). This stent graft is an extremely flexible modular graft, in contrast to the rigid z-stent design of other commercially available stent grafts. Significantly, the device does not have a suprarenal stent that can frustrate apposition in cases with high perirenal angulation.

This article aims to provide concise information on the indications for the use of Aorfix, its key characteristics, cost, clinical outcome data and how it fits into the field of medical devices.

Overview of the market

Currently, there is no ideal graft available for the treatment of highly angulated aneurysms. A study carried out by Albertini *et al.* using a flow model confirmed the hypothesis that neck angulation increased the risk of type I endoleak and identified stent graft stiffness as a cause of failure of the seal [6].

There are a number of stent grafts currently available on the market, usually made from a Nitinol or stainless steel frame with polyester or expanded PTFE-type materials. The conformability of these grafts varies considerably, with the 'z stent' design offering greater rigidity and a spiral design allowing greater flexibility (Aorfix and Anaconda™). Rigid stent grafts are generally more challenging to deliver and deploy in patients with highly angulated aneurysms.

The Anaconda endograft (Vascutek, Terumo, Inchinnan, Scotland) is an infrarenal, trimodular stent graft that has iliac legs that are similar to Aorfix. It also has proximal rings and hooks to assist with main body fixation. The characteristics of the Anaconda graft are outlined in Tables 1 & 2.

The Eurostar registry data has shown that use of the Talent™ (Medtronic, Hertfordshire, UK), Zenith® (Cook, IN, USA) and Excluder® (Gore, AZ, USA) stent grafts in patients with severe neck angulation is associated with a more than twofold increase in both early (30 day) type I endoleak and stent migration [5]. Indeed, at 30 days, 4.9% of the 1152 patients with severe neck angulation had a type I endoleak. A recent single-center, device-specific performance study in high-angled neck aneurysms, found that the Zenith and Talent grafts had a 19 and 53% proximal type I endoleak rate, respectively [7].

future medicine part of fsg

Table 1. Currently available devices and their characteristics.

Device	Material	Configuration	Deployment	Fixation	Aortic graft diameters (mm)	Iliac graft diameters (mm)	Suprarenal stent
Aorfix™	Polyester	Modular	Self-expanding	Compression fit and hooks	24–31	10–20	No
Anaconda™	Woven polyester	Trimodular	Self-expanding	Proximal rings, hooks and compression	19.5–34	10–23	No
Endurant® (Medtronic)	Polyester	Modular	Self-expanding	Compression fit and hooks	23–36	10–28	Yes
Zenith® (Cook)	Polyester	Modular	Self-expanding	Compression fit and barbs	22–36	8–24	Yes
Excluder® (Gore)	PTFE	Modular	Self-expanding	Compression fit and anchors	23, 26, 28.5 and 31	12–14.5	No

Furthermore, whilst some authors have suggested that supra-renal fixation may reduce the adverse events associated with hostile neck anatomy, it is recognized that graft kinking may be a problem with a neck angulation of over 45° [8].

Marked tortuosity of the iliac vessels may predispose to kinking (Figures 1 & 2) and occlusion of rigid stent grafts.

Introduction to the device

■ Graft design

The Aorfix stent graft is a two-part modular implant comprising a bifurcated main body section and a straight contralateral limb section (the 'plug-in'). The self-expanding implant is fabricated from a circular Nitinol frame and a woven polyester fabric (synthetic textile), resulting in an extremely compliant graft. The Nitinol is cut flat in one continuous length, machine-sewn onto the polyester fabric, and then rolled to create a flexible seam. A continuous radiopaque marker made of Tantalum encircles both proximal and distal ends, which are connected via a seam marker.

The proximal end of the graft is 'fish mouth' shaped and incorporates four pairs of proximal Nitinol barbs (Figure 3). The device is deployed with the renal ostia in the troughs of the graft (Figure 4), thus maximizing proximal aorta–graft interaction. The main body section bifurcates into a full-length ipsilateral iliac section and a contralateral short leg mating section (termed the 'socket'). The plug-in is mated intra-operatively to the socket to form the complete bifurcated system. Each of the two components is supplied preloaded into a delivery system comprising a catheter with a built-in deployment handle.

The delivery system (Figure 5) also includes a pair of longitudinal push rods within the graft, increasing its column strength. These rods stabilize the proximal part of the graft during deployment. Once deployed, the whole graft is dilated with a moulding balloon.

The device dimensions available at the time of writing ranges from 24 to 31 mm in proximal diameter, in increments of 1 mm; and 10 to 20 mm in distal diameter in increments of 2 mm. The device is suitable for patients with an external iliac diameter of at least 7 mm. Aneurysm exclusion is achieved due to the radial expansion force of the stent graft in the sealing zones. The Nitinol hooks also assist in proximal fixation of the device.

Table 2. Indications for use of some of the currently available stent grafts.

Device	Indications for use
Aorfix™	Minimum neck length 20 mm infra-SMA; neck angle up to 90° peri-renal, 90° supra-sac; neck diameter 19–29 mm
Anaconda™	Neck diameter 16–31 mm; neck angle up to 60°; neck length 15 mm
Endurant® (Medtronic)	Neck length of at least 10 mm: Neck angle up to 45° peri-renal, 60° supra-sac; neck length of at least 15 mm: Neck angle up to 60° peri-renal, 75° supra-sac
Zenith® (Cook)	Minimum neck length 15 mm; neck diameter 18–32 mm; neck angle up to 45° peri-renal, 60° supra-sac
Excluder® (Gore)	Neck diameter 19–29 mm; minimum neck length 15 mm; neck angle up to 60° peri-renal, 60° supra-sac

SMA: Superior mesenteric artery.

■ Graft planning

Accurate planning and preparation are increasingly important in cases of greater anatomical complexity. Three dimensional CT planning tools are helpful in measuring neck angles, interpreting neck morphology and in planning access routes and landing zones.

Careful sizing of the graft is important as with many other stent devices. Consensus regarding the degree of proximal over-sizing is lacking, with some in the scientific community claiming that extensive over-sizing can lead to aneurysmal degeneration of the proximal neck and late migration of endografts. A recently published review has concluded that a 10–20% over-sizing is safe, and an over-sizing greater than 30% increased the risk of adverse outcomes [9]. In addition, the anatomy in tortuous aneurysms is more technically challenging and excessive over-sizing of greater than 30% may lead to incomplete opening of the proximal or distal fish mouth and potential luminal narrowing.

In our institution neck over-sizing of 10–15% is routinely carried out. The absence of longitudinal components in the device appears to allow the graft to fit well in conical and barrel-shaped necks.

The assessment of vessel length in tortuous anatomy is more challenging than in straight vessels, and predicting accurately the path taken by the graft through tight bends and curves can add another component of variability to length measurement.

This group prefers to select generous limb lengths as the legs can be shortened 1–2 cm during deployment. However, a range of distal extenders is available and a short device can readily be extended by these means.

■ Graft deployment

Proximal graft deployment should start high above the renal vessels with careful orientation of the fish mouth configuration of the top of the graft. This is facilitated in angulated necks by varying the obliquity and cranio-caudal angle of the image intensifier, in order to visualize the renal vessels in profile. The author's experience is such that the graft can be pulled down but not easily advanced upwards. Experience has shown that the push rods that support the proximal graft during deployment should not be advanced to dilate the proximal graft in angulated anatomy as they can distort the proximal graft.

Proximal markers are used to place the graft accurately below the renal arteries often with the peaks of the fish mouth extending superiorly to allow a degree of transrenal fixation. A minimum neck length of 15 mm is needed to achieve successful exclusion of aneurysm sac proximally. Care needs to be exercised in patients with a low origin of the superior mesenteric artery in order not to occlude this vessel origin.

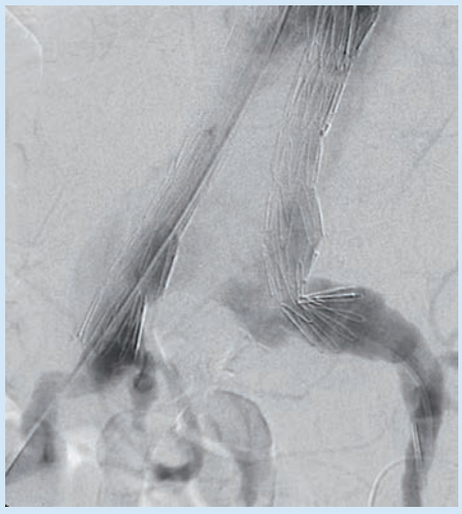

Figure 1. Angiogram showing iliac limb kinking, in a patient with tortuous anatomy.

A minimum of 10–15% over-sizing in the proximal end and at least 1 mm of over-size of the iliac limb is recommended for successful aneurysm exclusion.

■ Cost of the Aorfix™ graft

This device is priced competitively in comparison to the other commercially available grafts. The manufacturers (Lombard Medical) also provide extensive support in terms of practical

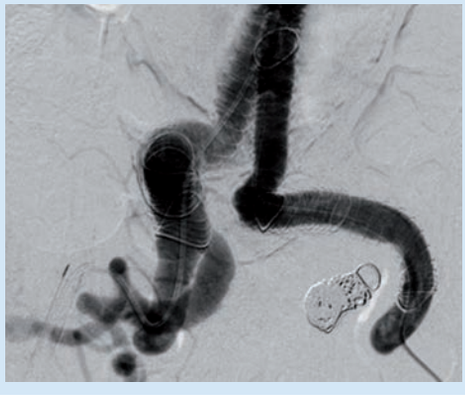

Figure 2. Angiogram showing a high degree of conformability demonstrated by the iliac limbs of Aorfix™ graft.
Image courtesy of Mr D Morrow, Consultant Vascular Surgeon, Norfolk & Norwich Hospital.

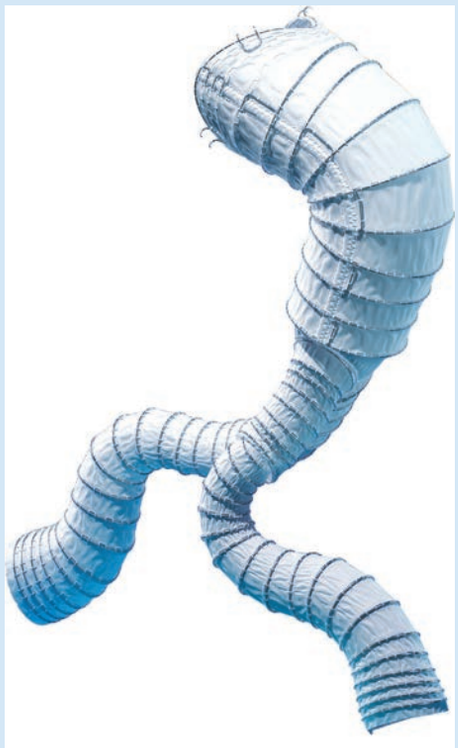

Figure 3. Aorfix™ graft, illustrating its proximal 'fish mouth' design.

workshops, assistance in graft planning and by arranging proctors to be present during the early stages of a service.

Clinical profile

A recently published study has demonstrated Aorfix to be safe and reliable in patients with complex infra-renal anatomy, giving good short- and mid-term clinical outcomes [10]. A bench test carried out to compare the endoleak rates of several stent grafts, in various degrees of neck angulations, has shown that endoleak rate was lower with Aorfix than any other graft [11]. Indeed, neck angulation had no impact on the endoleak rate with the Aorfix device.

A previous retrospective European multicenter study, conducted by Albertini *et al.*, demonstrated the utility of the Aorfix stent in patients with infra-renal neck angulation of up to 65° [12].

In the USA, Aorfix is approaching completion of an investigational device exemption study that recruited 120 patients with neck angles of 60–90°.

Data from a multicenter nonrandomized voluntary registry (Retrospective Aorfix Data Registry) also shows low rates of mortality (1.6%), endoleaks, graft limb occlusion and migration. This registry is ongoing and at the time of writing contains 753 patients with up to 6 years follow-up data.

A recently completed, yet to be published, prospective nonrandomized European multicenter study (ARBITER II) using the Aorfix device, in patients with significant neck (60–90° angulation) or iliac angulations, has provided encouraging results. In this study, 30 patients (23 males) with a mean age of 77.4 years were recruited and underwent treatment.

The mean aneurysm diameter was 69.3 mm (range: 55–109 mm), with a proximal neck length of 26.2 mm (11–40mm) and a neck diameter of 24.4 mm (19.2–29.2 mm). The mean infra-renal neck angulation was 81.2° (range: 63–110°). All patients were assessed at 72 h or discharge, 30 days and 6 months post procedure.

The level of technical success in this group of patients (90%) is comparable with the performance of other contemporary commercial devices applied to far less angulated neck anatomy – for example the Medtronic Endurant™ graft system had a success rate of 90.3% [13] in patients with neck angulation of up to 75°.

The study mortality rate of 3% is in keeping with the Eurostar registry data (2.9%). At 30 days, no patient had a type I endoleak detected and there was no evidence of any graft migration. However, at 6 months, two patients had developed very minor proximal type I endoleaks – neither have any evidence of graft migration or sac

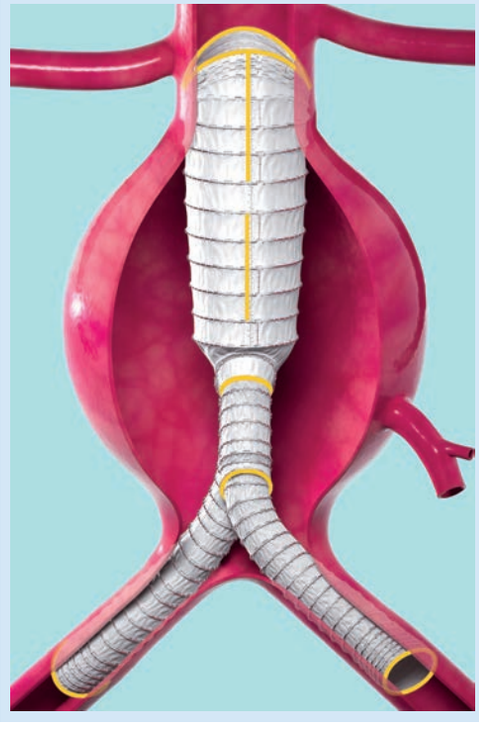

Figure 4. Positioning of the proximal 'fish mouth' in relation to the renal arteries.

expansion. Both patients had adverse neck anatomy (barrel shaped neck and short neck length of 11 mm). No interventions were required in these patients because the sacs were stable.

Although this study is small in terms of sample size, the results demonstrate that Aorfix can be used safely in the treatment of highly angulated abdominal aortic aneurysms and has allowed the Aorfix graft to obtain a CE marking/European license for use in cases up to 90°.

Figure 5. Delivery system.

Indications for use of Aorfix

This device is indicated for the endovascular repair of infra-renal abdominal aortic aneurysms with a neck of at least 20 mm (UK and Europe) or 15 mm (USA):

- With peri-renal angle of up to and including 65°;
- In patients with peri-renal angle of up to 90° in case of undue risk of open surgical repair.

Conclusion

Current evidence with regards to the safety of Aorfix is encouraging. The device's flexible design allows safe and accurate aneurysm sac exclusion in patients with highly challenging anatomy. The deployment and delivery of this device are unlike most other grafts. Some familiarity with the orientation of the proximal fish mouth configuration of the graft is essential for a successful outcome.

The introduction of this device into the market is already increasing the number of patients considered suitable for endovascular treatment who would otherwise have been excluded from this type of therapy previously.

Future perspective

The maximal diameter available for the proximal end (neck) at the time of writing is 31 mm. This device therefore is not currently offered to patients with larger aneurysm necks.

The manufacturer of Aorfix is already working on expanding the diameter range available for the proximal neck. It is conceivable to have fenestrated and branched grafts for the treatment of complex thoraco–abdominal, juxta–renal and iliac aneurysms, based on the current Aorfix platform. There are anecdotal reports of the successful use of Aorfix with 'chimney' stents in the renal arteries.

Executive summary

Background

- Highly angulated aneurysm neck and iliac angulation increase the likelihood of complications during an endovascular repair of abdominal aortic aneurysms.
- Currently there is no ideal graft available for the treatment of these morphologically challenging aneurysms.

Key characteristics of Aorfix™

- Made of circular Nitinol frame and polyester offering a highly conformable graft.
- Bifurcated modular self-expanding device.
- Can be used in neck angulations up to 90°.
- 10–30% over-sizing at the neck is recommended.
- Iliac limbs oversized by at least 1mm.
- Careful graft orientation is needed during deployment.
- In highly angulated necks, the 'push rods' may distort anatomy. In these instances, it is prudent to release the push rods and dilate the proximal end using a moulding balloon.

Cost

- Competitively priced in relation to other commercially available devices.
- Extensive support available from the manufacturer.

Clinical evidence & safety

- CE-marked for abdominal aortic aneurysm with neck angles up to 90°.
- Unlike other devices, neck angulation has no impact on the endoleak rate associated with Aorfix™.
- Already shown to be safe in patients with neck angles of up to 65°.
- Recent evidence in patients with highly challenging anatomy (neck angles up to 90°) has demonstrated technical success, with endoleak rates and mortality comparable with other devices.

Financial & competing interests disclosure

Dr John Hardman has been paid fees for consulting and speaking by Lombard Medical. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

No writing assistance was utilized in the production of this manuscript.

Bibliography

Papers of special note have been highlighted as:
- ▪ of interest
- ▪▪ of considerable interest

1 Endovascular Aneurysm Repair versus Open Repair in Patients with Abdominal Aortic Aneurysm (EVAR trial 1): randomized controlled trial. *Lancet* 365, 2179–2186 (2005).

▪▪ **Compares endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR) against open surgical repair in patients with large aneurysms using variables such as mortality, durability, cost and health-related quality of life.**

2 Prinssen M, Verhoeven EL, Buth J *et al.*: A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N. Engl. J. Med.* 351, 1607–1618 (2004).

3 Abbruzzese TA, Kwolek CJ, Brewster DC *et al.*: Outcomes following endovascular abdominal aortic aneurysm repair (EVAR): an anatomic and device-specific analysis. *J. Vasc. Surg.* 48, 19–28 (2008).

▪ **Provides follow-up results up to 5 years after EVAR, for three commercially available grafts.**

4 Abu Rahma AF, Camptell J, Stone PA *et al.*: The correlation of aortic neck length to early and late outcomes in endovascular aneurysm repair patients. *J. Vasc. Surg.* 50(4), 738–748 (2009).

5 Hobo R, Kievit J, Leurs LJ, Buth J: Influence of severe infrarenal aortic neck angulation on complications at the proximal neck following endovascular AAA repair: a EUROSTAR study. *J. Endovasc. Ther.* 14, 1–11 (2007).

6 Albertini JN, Maciere wicz JA, Yusuf SW, Wenham PW, Hopkinson BR: Pathophysiology of proximal perigraft endoleak following endovascular repair of abdominal aortic aneurysm: a study using a flow model. *Eur. J. Vasc. Endovasc. Surg.* 22, 53–56 (2001).

7 Wales L, Dunckley M, Bohm N *et al.*: Device-specific outcomes following endovascular aortic aneurysm repair. *Eur. J. Vasc. Endovasc. Surg.* 36, 661–667 (2008).

8 Robbins M, Kritpracha B, BeeBe HG, Criado FJ, Daoud Y, Comerata AJ: Suprarenal endograft fixation avoids adverse outcomes associated with aortic neck angulation. *Ann. Vasc. Surg.* 19, 172–177 (2005).

9 Van Prehn J, Schlosser FJV, Muhs BE *et al.*: Over-sizing of aortic stent grafts for abdominal aneurysm repair: a systematic review of the benefits and risks. *Eur. J. Vasc. Endovasc. Surg.* 38, 42–53 (2009).

10 Perdikides T, Georgiadis GS, Avgerinos ED *et al.*: The Aorfix stent graft to treat infrarenal abdominal aortic aneurysms with angulated necks and/or tortuous iliac arteries: midterm results. *J. Endovasc. Ther.* 16, 567–576 (2009)

11 Albertini J-N, DeMasi M-A, Maciere wicz J *et al.*: Aorfix stent graft for abdominal aortic aneurysms reduces the risk of proximal type I endoleak in angulated necks: bench-test study. *Vascular* 13, 321–326 (2005).

12 Albertini JN, Perdikidos T, Soong CV, Hinchlippe RJ, Trojanowska M, Yussup SW: Endovascular repair of abdominal aortic aneurysms in patients with severe angulation of the proximal neck using a flexible stent-graft: European Multicenter Experience. *J. Cardiovasc. Surg. (Torino)* 47, 245–250 (2006).

▪ **Highlights the utility of this graft in neck angulations up to 65°.**

13 Verhagen HJ, Torsello G, de Vries JP: Endurant stent-graft system: preliminary report on an innovative treatment for challenging abdominal aortic aneurysm. *J. Cardiovasc. Surg. (Torino).* 50, 153–158 (2009).