Supplement to

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THE NEXT CHAPTER IN TEVAR

MOVING TECHNOLOGY TOWARD PATIENT NEEDS

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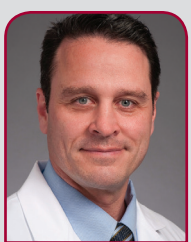

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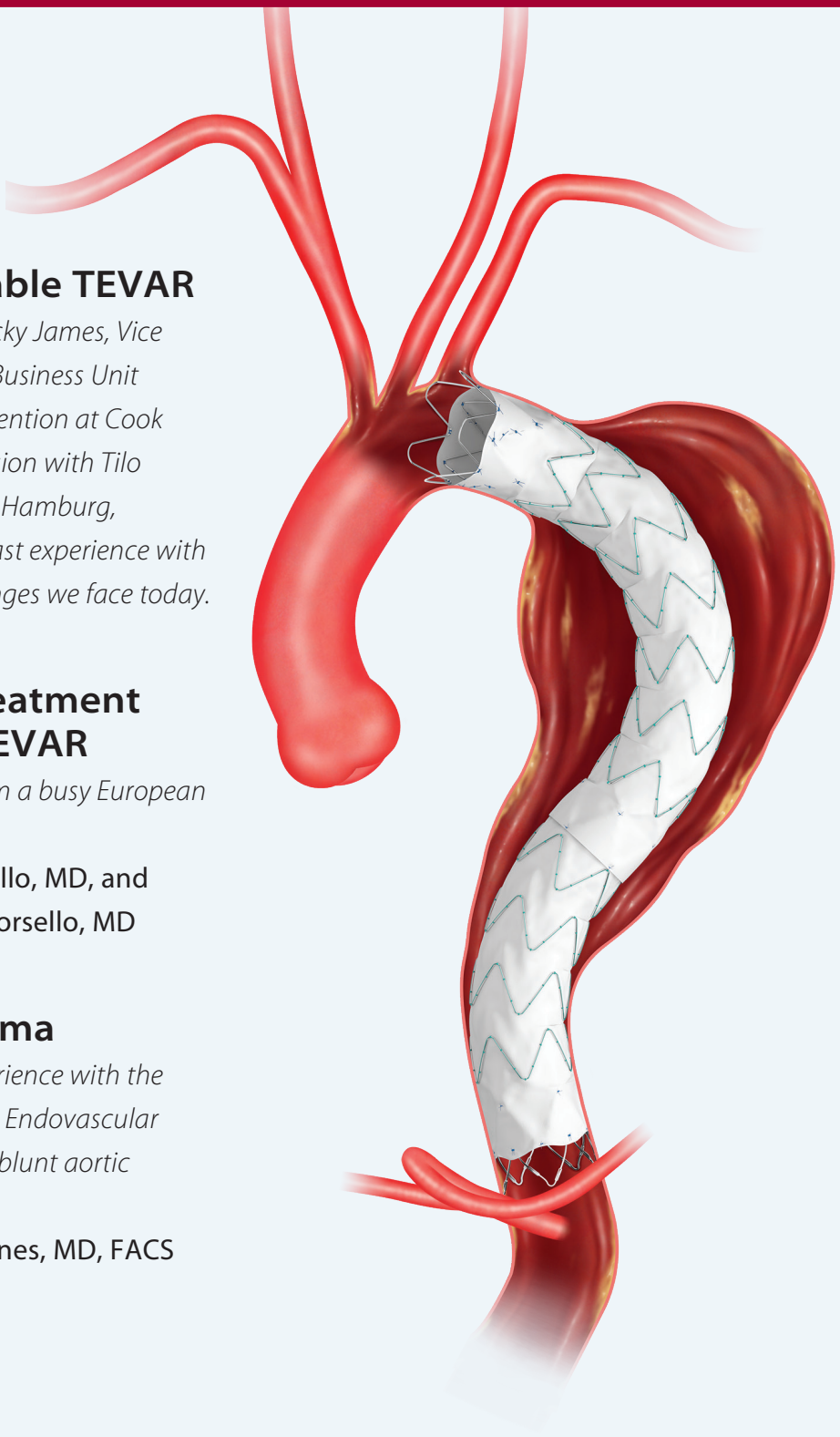

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Building Durable TEVAR

An introduction by Nicky James, Vice President and Global Business Unit Leader of Aortic Intervention at Cook Medical, and a discussion with Tilo Kölbel, MD, PhD, from Hamburg, Germany, about his vast experience with TEVAR and the challenges we face today.

We've come a long way since the first thoracic endovascular aortic repair (TEVAR) procedure in 1992.[1] Gone are the days of questioning whether open surgery is a more viable option for etiologies like aneurysms, ulcers, and transections. Equipped with a better understanding of the progressive nature of aortic disease, our approach to endovascular repair (and specifically TEVAR for this issue) must continue to evolve in order to meet the clinical needs of the patients.

We continue to ask ourselves how the technology can deliver a more durable repair to more patients. Can we improve outcomes with a smaller-bore delivery system? How do we treat emergent cases with TEVAR? What do we do with patients who present with smaller access vessels and tortuosity? In this supplement, we explore some of these key TEVAR questions.

As an introduction to this supplement, we wanted to hear the perspective of Professor Tilo Kölbel, whose extensive experience sets the context for today's challenges with TEVAR.

Tilo Kölbel, MD, PhD

Professor Kölbel, with the availability of thoracic stent grafts, more aortic etiologies are being treated by TEVAR. Where do you think TEVAR has shown the most benefit over open repair?

In recent years, TEVAR has become the unquestioned gold standard for the treatment of aortic pathologies of the descending thoracic aorta, including aneurysm, dissection, and trauma. The advantages of TEVAR—less invasiveness, instant availability, and rapidity—take fullest effect in the treatment of ruptured aortic pathologies such as transection or ruptured aneurysms. The quick procedure time, the option of local anesthesia, and no need for cardiopulmonary bypass (with necessary but potentially disastrous heparinization) have substantially decreased morbidity and mortality and enabled treatment in a group of patients who would not have survived open surgical techniques. Patients of older age and with comorbidities now have a realistic chance to survive a procedure with the use of thoracic endografts.

Another group of patients with a specific advantage are those who have undergone previous surgery; these patients combine the advantage of avoiding repeat sternotomy or thoracotomy, which multiplies open surgical risks, with the fundamental advantage of achieving a safe landing zone in the preexisting surgical graft. This becomes even more distinct in patients after previous surgery with genetic connective tissue disorders like Marfan syndrome or Loeys-Dietz syndrome. The role of endovascular repair in these high-risk patients with fragile aortic tissue is not yet defined, and I am convinced that we will see an increased utilization of endovascular techniques in the future.

What excites you most about the technology (ie, thoracic stent grafts), and what realities do you still find sobering?

Endovascular techniques for the treatment of aortic pathologies are still in their early infancy, and I am extremely excited to know that we will see substantial changes in techniques and device technology during the coming years. The materials and techniques we use today to produce endovascular grafts could essentially have been used 60 years ago. Basically, metal springs are hand-sewn onto polyester tubes and loaded into delivery sheaths. Of course, there is a lot more technology in today's grafts and their delivery systems, but this might not be obvious at first sight and is sometimes difficult to appreciate as a user. All the changes to the endografts,

delivery systems, and loading techniques have massively improved their performance during the 25 years of commercial endograft development. Still, the basic appearance and principles remain the same in current-generation endografts, with few exceptions including the polymer technologies used in recently launched endografts.

These new technologies will need to prove their safety and effectiveness in the long-term and have not yet been explored in the thoracic aorta at all. To get a glimpse into the future, we can take out our smartphones and look at the technology put into these little high-tech boxes. There is so much more to come in device technology and operating techniques in the coming years.

The most sobering fact about stent graft technology for me is the limited availability of proven devices around the world. The European Union appears as a land of bliss with regard to device availability, and we tend to forget when presenting at overseas meetings that the majority of vascular specialists and their patients around the world lack access to endografts and the adjuncts needed for their implantation.

Are we, as clinicians and industry, addressing the needs of the world's thoracic aortic disease patients? What do you see as unmet needs?

Almost all approved thoracic endografts have been certified for aneurysmal disease only. It is a clear necessity in the future to address the needs of other thoracic pathologies besides descending thoracic aortic aneurysm and to include these pathologies in the regulatory process. The different requirements of pathologies treated and the increasing utilization of endografts should grant the development of disease-specific devices.

The most important unmet need in TEVAR, from my perspective, is the unchanged high rate of cerebrovascular complications in up to 10% of patients treated with some devices. This significantly restricts endovascular treatment success despite all of the obvious advantages of endografts and should be addressed with the highest priority by interventionists and industry!

Once you've decided on a course of therapy, are you always able to get your device into place?

With all the access techniques that we have in our armamentarium today, like conduits, endoconduits, through-wires, and alternative access routes, we hardly fail to get a device into place. The reduced device profile and improved trackability of newer-generation endografts and modern imaging systems have further contributed to the fact that we rarely need to reject patients from treatment, even when they have very tortuous aortas. I expect devices of the next generation to improve the trackability further with new materials for the delivery components that allow for a better balanced allocation of stiffness throughout the length of the device.

However, this doesn't imply that we are always successful with our treatment, as there are a number of potential difficulties, especially with positioning fenestrated and branched devices and getting access to target vessels. There has been significant advancement in the planning of procedures based on the experience of interventionists worldwide and of the company specialists. The body of knowledge about what anatomy is best treated by which technique is constantly increasing and is a great example of fruitful collaboration of industry and physicians for the benefit of our patients.

What do you think TEVAR devices will look like in 5 years? 10 years?

TEVAR has proven to be a treatment option for all segments of the aorta. With branched and fenestrated techniques in the aortic arch, as well as debranching operations, TEVAR has conquered significant territory but is still considered inferior to open surgery in the aortic arch and the ascending aorta and therefore is reserved for high-risk patients. I predict that this will change within the coming 10 years for aortic arch pathologies, as we already have devices that allow endovascular treatments starting from the sinotubular junction in the ascending aorta.

However, outcomes of endovascular treatments of the complete aortic arch are still limited by adverse events. Morbidity and mortality need to be significantly reduced to allow further enforcement of these techniques. Safety is the key issue, and I am convinced that we can reduce the adverse event rate for these complex treatments of the aortic arch to under the 5% margin. Device modifications, deployment steps, and changes in the operating and monitoring techniques will allow us to overcome current limitations, and I am strongly convinced that this can only work in an environment of interdisciplinary collaboration with cardiovascular surgery and anesthesia.

With what is known today, what would you consider to be durable repair in the thoracic aorta?

A durable solution needs to be determined on an individualized basis, as the requirements for durability

differ greatly among our patients. A 25-year-old patient with Marfan syndrome requires durability for a lifetime, whereas some of our older patients are well-treated with an endovascular solution that lasts until another life-limiting disease or event strikes. Sometimes, an endovascular solution may only need to last for weeks or months to get the patient out of an acute situation and provide a treatment bridge to a more durable repair. This is the case, for example, in patients with aortic ruptures or type A aortic dissection. So, the question of durability cannot be answered collectively because of the variety of patients and diseases that we treat in the thoracic aorta. We have learned over the past 20 years that the key to a durable repair is generally the presence of a parallel-walled and nondilated landing zone, as this indicates healthy aortic wall. Given the progressive nature of aneurysmal disease, durability can only have a relative meaning because this healthy-looking aortic segment, in which we ideally choose for our endograft to land, will become diseased at a later stage. So, given this progressive nature, the best durability we can achieve is a treatment that allows for future options in extending the repair further proximal and distal into less-diseased aortic segments. Durability emerges if we calculate the natural progression of the disease in our patients and ensure a "next-step" option for treatment.

Thank you very much, Professor Kölbel for sharing your insightful thoughts on the technology.

Tilo Kölbel, MD, PhD, is with the Department of Vascular Medicine, University Heart Center in Hamburg, Germany. He has disclosed that he is an intellectual property holder of Cook Medical and has also received research and travel grants. Prof. Kölbel may be reached at t.koelbel@uke.de.

In considering the next chapter of TEVAR, as an industry, we must continue to challenge ourselves to deliver the best possible patient outcomes. At Cook Medical, we acknowledge the progressive nature of aortic disease and are working hard to find solutions that help you deliver durable repairs. We will always strive to be the responsible partner that you expect. We hope you find this supplement both useful and informative. ■

Thank you,
Nicky James
Vice President, Cook Medical
Global Business Unit Leader, Aortic Intervention

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Extending Treatment Choices for TEVAR

A large case series from a busy European endovascular center.

BY GIOVANNI B. TORSELLO, MD, AND GIOVANNI FEDERICO TORSELLO, MD

Thoracic endovascular aortic repair (TEVAR) is the standard of care in the treatment of many thoracic aortic pathologies in most clinical settings. Graft design and patient anatomy heavily influence treatment success. The Zenith Alpha Thoracic Endovascular Graft (Cook Medical) is designed to better conform to unfavorably angled aortic arches and to overcome challenging access vessel anatomy with a low-profile introduction system.

DEVICE DESCRIPTION

The Zenith Alpha Thoracic device has been described in detail elsewhere.[1] It was developed on the basis of the durable platform of the Zenith TX2 Endovascular Graft (Cook Medical), with features such as durable proximal fixation and a two-piece system, and has demonstrated safe and effective clinical performance. The first main feature of this device is the use of a braided polyester graft material with a tighter weave and self-expanding nitinol stents affixed with monofilament polypropylene sutures, resulting in a markedly reduced profile without compromising durability. The second main feature is the precurved introduction system, which, in combination with the proximal bare stent, optimizes the conformability of the graft with the inner curvature of the aorta.

CLINICAL PERFORMANCE

In this case series, we included all patients treated with Zenith Alpha at our institution from August 2010 to October 2015. In total, 112 consecutive patients were treated for penetrating aortic ulcers or thoracic aneurysms. The patient characteristics are summarized in Table 1. A considerable proportion of patients had urgent or emergency procedures (12.5% and 10.7%, respectively). In 41 patients (36.6%), access vessels were heavily calcified. The mean minimal iliac diameter was 5.98 mm (± 1.74 mm), and the mean iliac tortuosity index was 1.3 (± 0.18).[2] Most patients were treated entirely percutaneously (n = 98, 87.5%). Four patients required iliac access via a conduit (3.6%). Cerebrospinal fluid drainage was utilized in 17 cases (16%).

TABLE 1. PATIENT CHARACTERISTICS

Patient Characteristic	n (%) or mean (± SD)
Mean age	70.4 (± 9.3)
Men:women	47:58
Arterial hypertension	101 (90%)
Smoking	36 (32%)
Cerebrovascular disease	15 (13.4%)
Coronary artery disease	39 (34.8%)
Elective procedure	86 (76.8%)
Urgent procedure	14 (12.5%)
Emergency procedure	12 (10.7%)

The rate of technical success as defined by the reporting standards[3] was 99%. In one case, the graft could not be advanced into the aortic arch due to heavy calcification and severe iliac stenosis. There was no postoperative aortic rupture or device migration within 30 days. In total, there were eight access vessel complications (7.1%), including three iliac artery dissections (2.7%) that were caused by advancing the introduction system through tortuous and small access vessels and five pseudoaneurysms of the common femoral artery (4.5%) that necessitated a secondary intervention. Two patients experienced persistent spinal cord injury (1.8%); one of these patients received

intraoperative cerebrospinal fluid drainage, whereas the other one did not.

DISCUSSION

Today, it is possible to treat a variety of thoracic aortic pathologies, especially with the introduction of devices with greater trackability and flexibility. The technical success rate in this patient group correlates well with the previously published results of this and other devices.[2,4,5] The same applies to results on mortality, complication, and reintervention rates. Remaining challenges of TEVAR, such as device apposition and fixation, are increasingly addressed by Zenith Alpha and other newer-generation devices (Figure 1). However, access vessel anatomy remains a major predictor for perioperative complications, as well as a limiting factor for treatment eligibility.

Female, Asian, and young patients have an especially greater share of thoracic compared to abdominal aortic pathologies,[6] and they also represent a group of patients who commonly have smaller iliac diameters.[7] However, treating the thoracic aorta necessitates larger devices (and thus, larger-bore sheaths) compared to treating the abdominal aorta.[8] Patients with small access vessels are subject to a higher rate of access-related complications such as rupture, dissection, and pseudoaneurysm of the access vessel. The morbidity burden of these patients can be further increased by the necessity of more-invasive access methods (eg, iliac conduits).[9] Not surprisingly, the sheath size relative to the access vessel diameter determines the access vessel complication rate,[10] which ranged between 9% and 21% in the pivotal studies.[11-13] By having smaller access vessels, women tend to experience greater morbidity because of access vessel complications and more-invasive access methods.[7]

Of note, access vessel morphology was unfavorable, even in this all-comer sample of patients treated with Zenith Alpha, with a mean minimum iliac artery diameter of 5.98 mm and tortuous iliac arteries (tortuosity index, 1.3). Despite heavily calcified access vessels in 36.6% of the cases, the technical success rate of Zenith Alpha remained comparable to those of other devices in more favorable anatomy.

Applicability is an even more important consideration for this device. Although, to my knowledge, there are no sound data on the rate of patients not anatomically suitable for TEVAR due to access vessel morphology. It can be hypothesized that a considerable number of female or Asian patients cannot be treated with most grafts, simply due to prohibitively small access vessel diameters.

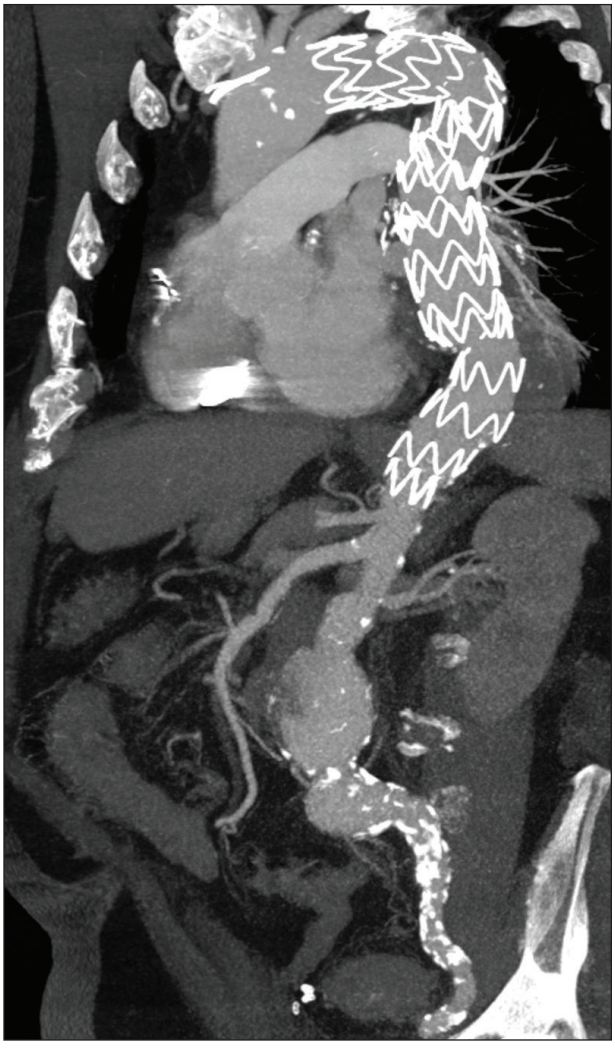

Figure 1. CT angiographic reconstruction showing the Zenith Alpha Thoracic device in a 72-year-old patient with aneurysmal disease of the thoracic, thoracoabdominal, and abdominal segments. Note the alignment of the stent graft with the tortuous aortic segments, as well as the presence of heavily calcified iliac arteries.

Furthermore, if these patients do qualify for TEVAR in terms of access vessel diameters, a considerable number of them cannot be treated due to iliac tortuosity. This is reflected in a large proportion of patients treated with Zenith Alpha Thoracic who previously underwent failed treatment attempts with other grafts.[2]

CONCLUSION

In conclusion, Zenith Alpha not only performs safely and effectively, but it also provides extended applicability to patients with challenging access vessel morphology. ■

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Treating Trauma

Case studies and experience with the Zenith Alpha Thoracic Endovascular Graft for treatment of blunt aortic injuries.

BY BENJAMIN W. STARNES, MD, FACS

Dramatic improvements have been made in the care of patients harboring vascular disease over the past 2 decades. Much of this progress has been made on the back of new device design. In 2008, the American Association for the Surgery of Trauma published results on emerging trends in the management of blunt aortic injury (BAI) and stated that, "There is a major and urgent need for improvement of the available endovascular devices."[1] Industry responded to this call for better device design with improvements that have finally arrived. In 2010, I was invited by Cook Medical to serve as Principal Investigator for TRANSFIX, the national multicenter clinical trial evaluating the Zenith TX2 low-profile endovascular graft (now called Zenith Alpha Thoracic) for the management of patients presenting with BAI. The following is a description of a few cases using this device to manage severely injured patients with aortic injury.

DISCUSSION

The Zenith Alpha Thoracic device offers what amounts to a great breakthrough in managing patients with BAI. The low-profile, hydrophilic, braided sheath delivery system; precurved inner cannula (Figure 1); and nitinol-based stent design provide for unparalleled opportunity to treat a wide variety of patients. With the lowest treatable aortic diameter (15 mm), lowest arch radius indication (20 mm), and smallest-diameter delivery system (16 F), more patients can be treated with this newer-generation device. A comparison of Zenith Alpha Thoracic with its predecessor, Zenith TX2, is depicted in Table 1.

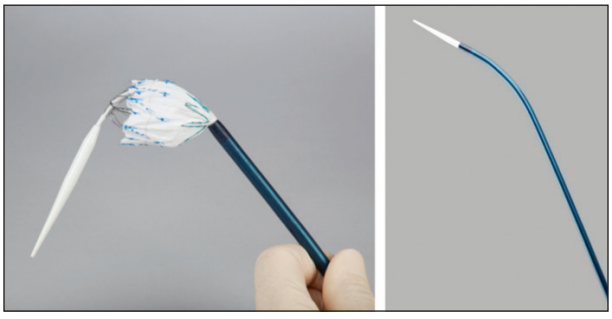


Figure 1. The precurved inner cannula.

TRANSFIX TRIAL DESIGN AND SHORT-TERM RESULTS

Fifty patients were enrolled into the prospective, nonrandomized TRANSFIX trial between January 2013 and May 2014. Patients in the trial will be followed through 5 years. The primary safety endpoint is 30-day mortality, and the primary efficacy endpoint is 30-day device success. As presented at the 2014 annual meeting of the Society for Vascular Surgery, technical success was achieved in all patients (100%), and there were no intraoperative mortalities. Short-term results

TABLE 1. COMPARISON OF ZENITH ALPHA THORACIC VERSUS ZENITH TX2 CHARACTERISTICS

Characteristics	Zenith TX2	Zenith TX2-LP (Zenith Alpha Thoracic)
Introducer sheath size	20–24 F	16–20 F
Device diameter size	22–42 mm	18–46 mm
Aortic arch radius	> 35 mm	≥ 20 mm
Stent strut metal, shape	Stainless steel, Z	Nitinol, Z
Graft material	Standard Dacron	Thinner, more tightly woven Dacron
Fixation	Covered, proximal	Bare, rounded proximal

CASE STUDY

Figures 2 through 7 are a compilation of CT images obtained from six patients who were enrolled into this trial at the author's institution between June 2013 and May 2014. All of these patients experienced blunt force trauma to the thoracic aorta by way of differing mechanisms. The images are arranged such that the preoperative axial slice (panel A) and three-dimensional reconstruction (panel B) are paired and compared with the postoperative axial slice (panel C) and relevant three-dimensional reconstruction (panel D). In Figure 4, panel E represents an alternate obliquity demonstrating good apposition of the stent graft against the aortic arch.

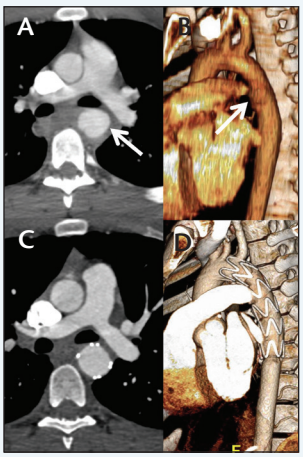
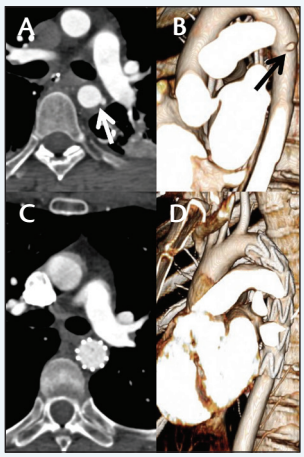


Figure 2



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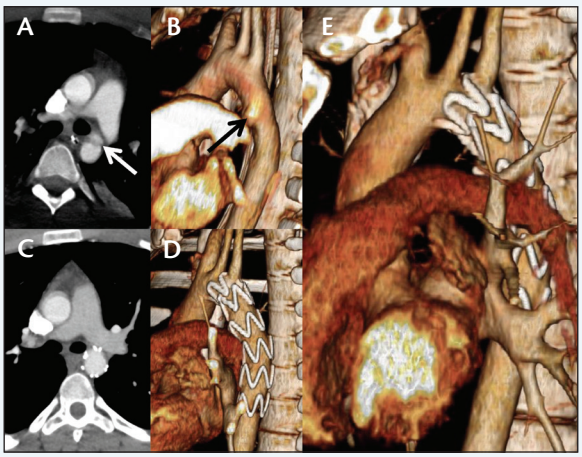

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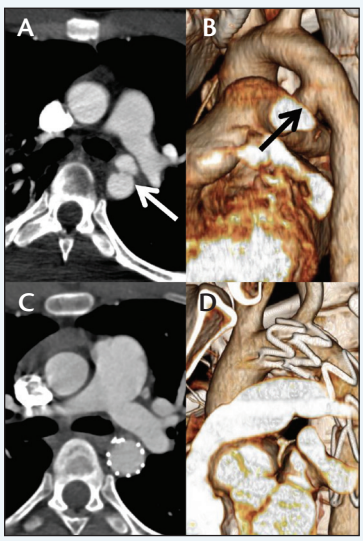

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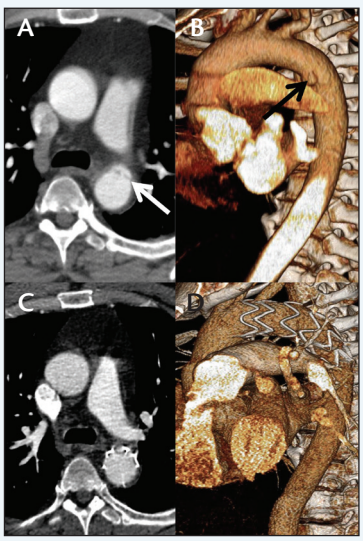

Figure 6

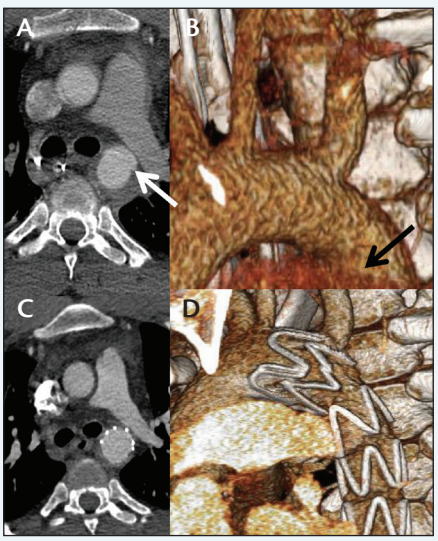

Figure 7

indicate that the Zenith Alpha Thoracic device appears safe and effective for the management of patients with BAI. As of October 2015, the Zenith Alpha Thoracic device has been approved for use by the US Food and Drug Administration.

Other than access-related complications, the most feared complication of thoracic endovascular aortic repair for BAI is either stroke or paraplegia. Modern workup includes magnetic resonance (MR) imaging of the brain or spinal cord, respectively. In the past, the presence of ferrous stent graft designs in the thoracic aorta was a contraindication to MR imaging in these scenarios. The Zenith Alpha Thoracic device has improved compatibility with MR imaging, which allows for alternative imaging in challenging clinical scenarios.

CONCLUSION

Zenith Alpha Thoracic represents a powerful tool in our armamentarium for managing aortic pathology. The management of BAI has become a percutaneous, semielective procedure that can be performed in under an hour. Thanks to better device design that includes a smaller, precurved delivery system and a nitinol frame, more patients with BAIs are candidates for this minimally invasive technology. ■

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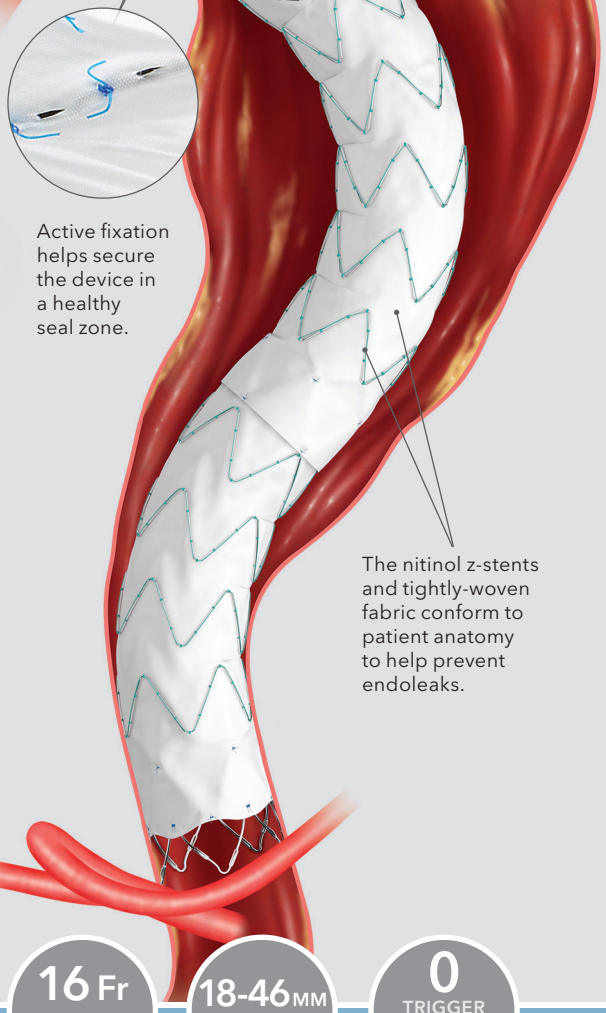
Introducing Zenith Alpha™ Thoracic

Designed to simplify device deployment so that you can deliver a durable aortic repair to more patients

A new ergonomic handle simplifies deployment without compromising precision and control.



Active fixation helps secure the device in a healthy seal zone.

The nitinol z-stents and tightly-woven fabric conform to patient anatomy to help prevent endoleaks.

16 Fr LOW PROFILE

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