Supplement to

Sponsored by Cordis Corporation

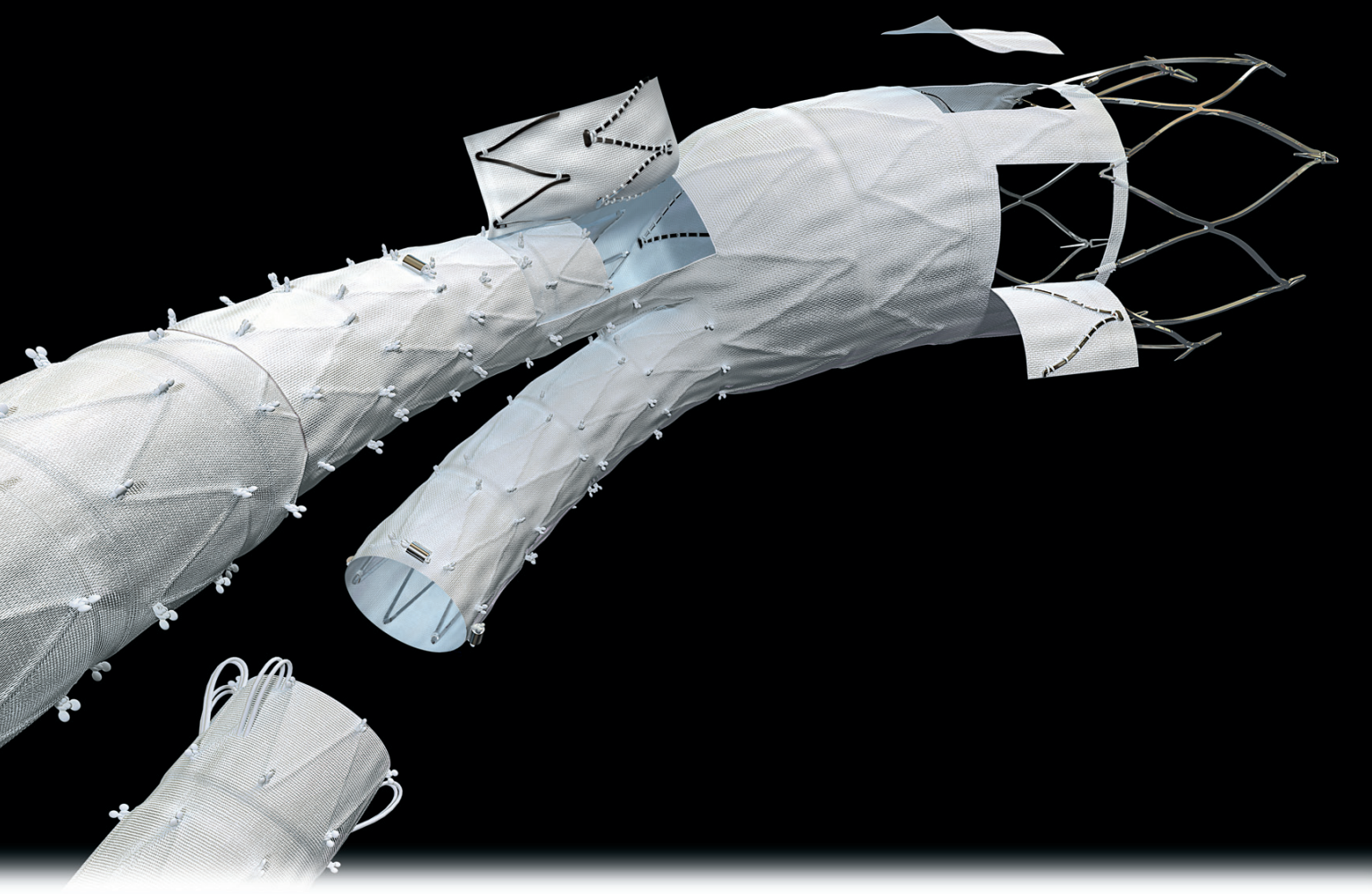
Endovascular TODAY

EUROPE

Volume 2, No. 4

Reengineering the Art of EVAR

Achieving durable, low-profile repair with the INCRAFT® AAA Stent Graft System.



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Reengineering the Art of EVAR

Achieving durable, low-profile repair with the INCRAFT® AAA Stent Graft System.

BY VINCENT RIAMBAU, MD, PHD

For the last 10 years, Cordis Corporation has labored over designing the INCRAFT® AAA Stent Graft System to make an optimal low-profile treatment option for abdominal aortic aneurysms (AAAs). In addition to creating a low-profile device, it was crucial for the INCRAFT® System to be durable and ensure good long-term outcomes. In August of 2014, the INCRAFT® System received CE Mark approval, allowing a broader range of patients to receive endovascular repair than ever before.

This supplement to *Endovascular Today* details the skillful engineering demonstrated by the INCRAFT® System through a series of articles from Cordis Corporation's own team, the physicians that guided the development process, and top interventionists who have successfully put the stent graft into practice.

To start, Cordis engineers explain the key features of the INCRAFT® System, including its long-term durability, deliverability, proximal and distal placement accuracy, and broad anatomy coverage. Paralleling the developments in other endovascular procedures, reducing the device's profile was of paramount importance to minimize invasiveness and provide the ability to treat a diverse set of anatomies, including those patients with tortuous, small, and/or highly calcified access vessels.* The team also presents two case studies in which the INCRAFT® System delivers precise repair without complications.

A key to the device's refinement was the use of a multispecialty panel of experts, consisting of opinion leaders in interventional cardiology, vascular surgery, and interventional radiology. Robert Bersin, MD; Takao Ohki, MD; and Corey Teigen, MD, share the history of the product's creation, starting with the preliminary stages and working through the rigorous testing performed to create a high quality device.

Giovanni Torsello, MD, provides insight into the device's trimodular design, a critical component in achieving precise placement and reducing the potential for unintentional anatomy coverage in the hypogastric and renal arteries. Combined with the benefits of in-situ customization and modular junction force, the initial clinical experience has proven to have excellent results.

Paralleling the developments in other endovascular procedures, reducing the device's profile was of paramount importance to minimize invasiveness and provide the ability to treat a diverse set of anatomies.

Cordis Corporation is conducting two trials for the INCRAFT® System, the INNOVATION Trial and INSPIRATION Trial. Roberto Chiesa, MD, and Ciochino Coppi, MD, detail the compelling 2-year data from the INNOVATION Trial as well as overviewing the rest of the clinical program.

Finally, Maxime Raux, MD; Prof. Jean-Pierre Becquemin, MD; and Kenneth Ouriel, MD, MBA, provide valuable perspective on type II endoleaks with a discussion on the identification, definition, and treatment of this unfortunately common complication that continues to be problematic in endovascular AAA repair.

I hope readers will discover an improved endovascular approach for AAA patients over the following pages. ■

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*Exercise caution in patients with irregular calcification and/or plaque as it may compromise the fixation and sealing of the implant, especially at the cranial and caudal sealing zones.

Durability and long-term data of the INCRAFT® AAA Stent Graft System are based on 2-year clinical follow-up and benchtop data.

The Inspiration Behind the Low-Profile, Durable, and Customizable INCRAFT® AAA Stent Graft System

The application of state-of-the-art technologies to develop an ultra-low-profile, customizable, and highly accurately placeable endograft without sacrificing durable AAA repair, anatomy coverage, or procedural complexity.

BY JAMES GROSS, MS, MBA; DAVID C. MAJERCAK, MS; AND STEFAAN VAN DER MEULEN, MS

For over a decade, Cordis Corporation has worked to reengineer and refine the conventional stent graft used for the endovascular treatment of abdominal aortic aneurysms (AAAs). This development time was necessary to achieve a stent graft design that can offer the benefits of a highly deliverable ultra-low-profile device and customization without compromising durable long-term AAA repair, broad anatomical coverage, or ease of use.

INCRAFT® CRITICAL-TO-QUALITY FEATURES

The development of the INCRAFT® AAA Stent Graft System (Cordis Corporation) focused on five critical-to-quality features:

- Long-term durability (the system completed 400 million cycles of fatigue testing under conditions representing actual clinical and physiological conditions)[1]
- Deliverability
- Proximal and distal placement accuracy
- Broad anatomy coverage
- Ease of use

Device development was not considered complete until each and every feature was achieved.

DESIGNING AN ULTRA-LOW-PROFILE DEVICE WITH LONG-TERM DURABILITY

As with the evolution of all interventional products, reducing the delivery profile is a key driver that enables higher rates of usage in a more minimally invasive fashion; a wider range of anatomies are treatable through the increased ability to reach the intended implant site. The same need holds true for AAA stent grafts, primarily due to tortuous, small, and/or highly calcified iliac arteries, but with the added need to reduce access site complications that may arise with larger-bore delivery systems.[2] The development of the INCRAFT® System sought to make a leap forward in the delivery profile of a traditional AAA endograft.

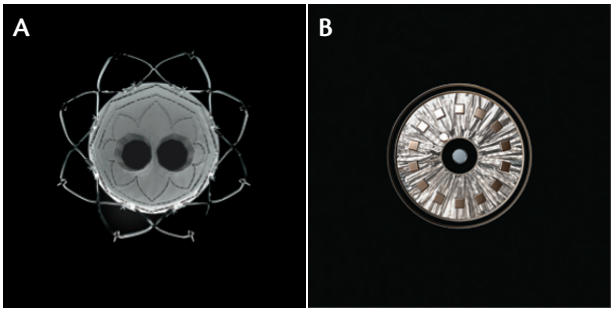

Figure 1. Fully deployed aortic bifurcate (A). Cross-sectional view illustrating the high packing efficiency of the stent graft in the ultra-low profile sheath (B).

In order to reduce the profile as significantly as possible with the INCRAFT® System, a very careful approach had to be devised that did not compromise acute performance or lead to the long-term durability issues that were observed with earlier generations of AAA endografts.[3] The key to this approach was a design that would allow the implant to be packed with high efficiency. The two main components driving this efficiency were a design that allowed an even distribution of the implant within the delivery sheath when compressed and a means to compress the materials very tightly. As was the case for most previous commercialized devices, the delivery profile was limited by localized bottlenecks, where portions of the implant were overlapped and inefficiently compressed. One key technology to overcome this

Durability and long-term data of the INCRAFT® AAA Stent Graft System are based on 2-year clinical follow-up and benchtop data.

limitation is the use of laser-cut nitinol stents that pack more efficiently than more typical wire-formed stents (Figure 1).

By far, the largest investment in time and effort in the development of the INCRAFT® System was to provide long-term device durability while lowering delivery profile. This effort entailed in-depth studies into the biomechanics of the aneurysmal environment (which has not been exhausted with the first-generation devices), careful study of the second-generation devices on the market that had promising durability, and development of a very rigorous fatigue test approach that would place devices in the most severe of environments while testing to failure. Validation of this regimen, which consisted of a battery of tests, was the replication of second-generation competitive design flaws that were addressed with subsequent iterations.

Through many rounds of this multitest, high-amplitude, mega-million-cycle testing regimen, durability was gained with seemingly small design changes. A select few areas were "durability critical" and needed the most painstaking engineering optimization and manufacturing care.[4]

A substantial portion of the profile gain was the implementation of a highly engineered catheter that is ultra-thin, yet extremely stretch-resistant in both the axial and circumferential directions. The engineering team used a variety of techniques, analytical tools, and simulations to balance the requirements of maintaining both radial and tensile force in the catheter sheath while minimizing frictional and deployment forces in the inner and outer diameter for optimal trackability through femoral access vessels.

CUSTOMIZATION AND PLACEMENT ACCURACY

Beyond the access and deliverability benefits of an ultra-low-profile delivery system, the INCRAFT® System sought to include bilateral real-time customization features that made it highly accurate to place both proximally and distally. Doing so allows the surgeon to apply control and individualize aneurysm exclusion in a wide range of vessels and associated anatomies.

Proximally, this is achieved through the ability to partially reposition the aortic main body of the stent graft during its quick, but highly controlled deployment. The barbs that offer migration resistance are held constrained against the tip of the delivery system during the initial deployment, allowing the operator to adjust positioning before using the secondary release to deploy the barbs and affix the main body within the aortic neck (Figure 2). Furthermore, the proximal sealing length of the aortic main body is maximized by a suprarenal stent design that deploys in a perpendicular fashion even in angulated vessels.

In the distal iliac vessels, the INCRAFT® System offers an in situ length customization capability that allows the operator to adjust the most caudal position of the limbs bilaterally by 2 to 3 cm during deployment by adjusting the overlap of the aortic bifurcate legs and the iliac limbs (Figure 3).

These two placement-accuracy features offer a variety of benefits to EVAR patients, their surgeons, and the institutions that provide and pay for the procedure.

Reduced Acute and Chronic Complications

Acute placement accuracy decreases the likelihood of unintentionally covering a patient's renal or internal iliac side branch vessels. Longer term, the placement accuracy offers longer seal zones, which reduce the possibility of endoleaks or device migration.

Reduced Need for Proximal or Distal Extensions

A high degree of placement accuracy significantly reduces the need for unintended extensions in the aorta and iliac vessels. When required due to an inaccurate deployment, these accessory devices result in unnecessary operative time, contrast exposure, and cost.

Few-Fits-Most Endograft Sizing

In situ length customization of the distal elements of the endograft results in far fewer device sizes and codes for the hospital to stock and manage in its inventory, without sacrificing broad anatomical coverage. The entire INCRAFT® System portfolio consists of 23 device codes to treat a wide anatomical range. There are four aortic bifurcates, all with the same length, that can treat aortic neck diameters between 17 and 31 mm. The iliac limbs are designed in five different diameters, which allow treatment of 7- to 22-mm iliac diameter distal landing zones. They are available in lengths of 80 to 140 mm, creating up to 212 mm of treatment length without the need for extensions (Figure 4).

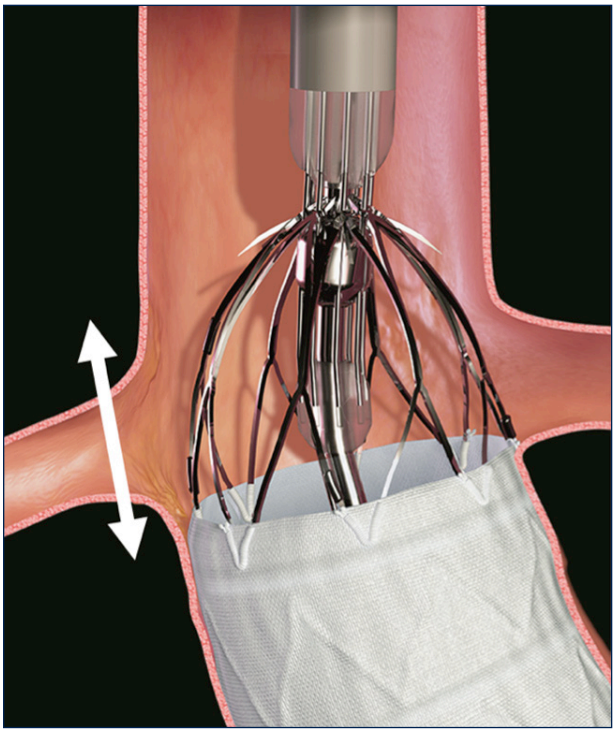

Figure 2. Proximal repositioning and perpendicular deployment.

CASE 1

MEDICAL HISTORY

An 82-year-old woman who was ASA grade III presented at the hospital with an AAA and a family history of AAA. She was elected for treatment 8 days after the initial screening.

ANATOMY

- Aortic neck diameter: 20 mm
- Neck length: 18 mm
- Neck angle: 58.6°
- AAA sac diameter: 59 mm
- Distal aorta diameter: 11 mm
- Right iliac access diameter: 5.5 mm
- Left iliac access diameter: 5.6 mm

PROCEDURE AND FOLLOW-UP

Despite very challenging access vessels and a highly calcified* and narrow distal aorta, the procedure was completed without any complications. There was very precise placement of the stent graft system in the highly angulated neck.

At 1-year follow-up, there were still no signs of migration, fractures, or graft occlusion, and the patient did not experience any aneurysm sac enlargement.

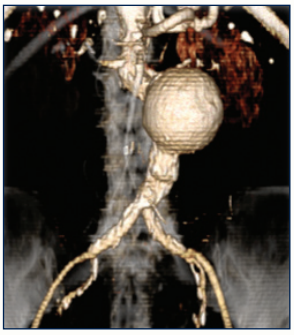

Figure 1. Preoperative image showing the highly calcified and narrow distal aorta.

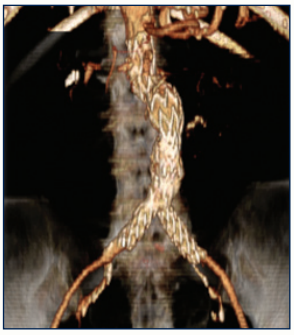

Figure 2. Postoperative image showing successful placement of the stent graft.

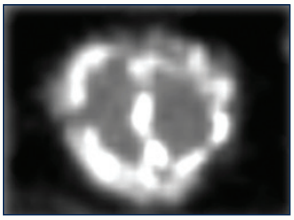

Figure 3. At the level of the distal aorta, the limbs maintain their so-called double-D configuration.

*Exercise caution in patients with irregular calcification and/or plaque as it may compromise the fixation and sealing of the implant, especially at the cranial and caudal sealing zones.

Of particular note, during the first-in-man INNOVATION study, only seven devices (two aortic bifurcates and five iliac limbs) were available, and even then, around 77% of the screened patients could be treated without any problem or need for additional device codes.[5]

Easier Preprocedural Planning

The intraoperative adjustability of the INCRAFT® System makes for an easier and more streamlined preoperative planning process because the operator can take advantage of the intraprocedural adjustability between the aortic main body and the iliac limbs.

BROAD ANATOMY COVERAGE

So far, more than 250 patients have been treated with the INCRAFT® System, most of whom were part of the INNOVATION European first-in-man trial and the INSPIRATION investigational device exemption trial, for United States and Japan approvals. Five patients have been treated through compassionate use programs in the United States and Canada, clearly demonstrating that a highly flexible, ultra-low-profile device does not just serve the current AAA population treated with endovascular repair, but can also safely expand the potentially treated population to patients who are currently in need.

During the clinical studies, patient selection and enrollment was based on the qualification of anatomical criteria as well as an independent reviewer's assessment. Core laboratory analysis of the preoperative patient's anatomy was graded using the Society for Vascular Surgery classification for challenging anatomy and demonstrates that up to 50% of the patients had multiple attributes meeting the severe hostile anatomy definition.[6] Almost half of the patients presented with access vessels smaller than 7 mm, with 5% of them smaller than 5 mm (Case 1). In addition to smaller access vessels, tortuous iliac arteries and tight distal aortas also contribute to potentially worsened patient outcomes. However, despite one-third of the first-in-man patient population having an aortic bifurcation diameter smaller than 18 mm—even as small as 11 mm in some cases—and tortuosity indices (τ) up to 2.41 (Case 2), there were no incidents in which the operator experienced difficulty gaining access during deployment, and there was only one occlusion at the 2-year follow-up time point.

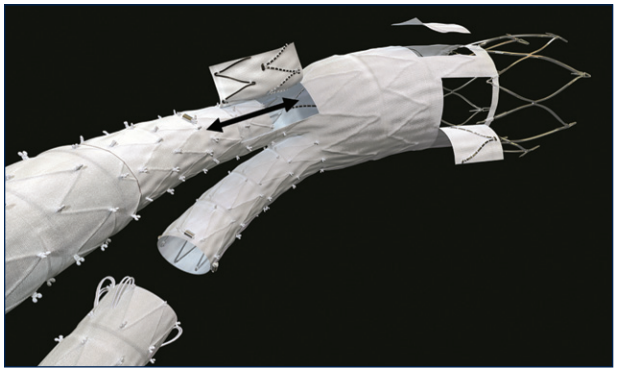

Figure 3. In situ length adjustment.

CASE 2

MEDICAL HISTORY

A 94-year-old man presented at the hospital with a symptomatic AAA. Due to his age and the size of the aneurysm, the patient was treated on the day of hospitalization.

ANATOMY

- Aortic neck diameter: 23 mm
- Neck length: 19 mm
- Neck angle: 52°
- AAA sac diameter: 101 mm
- Distal aorta diameter: 24 mm
- Right iliac tortuosity index: 1.43
- Left iliac tortuosity index: 2.41
- Right iliac access diameter: 7.9 mm
- Left iliac access diameter: 9 mm

PROCEDURE AND FOLLOW-UP

Because this was an unforeseen fourth patient treated at the study site on the same day with the INCRAFT® System, the procedure was started in the late afternoon with local anesthesia and a bilateral percutaneous approach.

Despite the extremely tortuous iliacs, the INCRAFT® System tracked very well, and the prosthesis was deployed at the desired location with nice conformability and without any adverse events or complications.

The final angiogram showed no device-related endoleaks, and the patient was discharged 3 days after the index procedure.

At 1-year follow-up, the core lab confirmed that there were no signs of migration, fractures, or graft occlusion, and the patient did not experience any aneurysm sac enlargement. The patient passed away in the second year of follow-up due to non-AAA-related events.

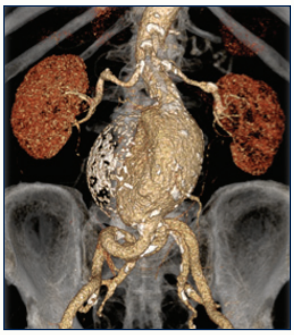

Figure 1. Preoperative image of the symptomatic AAA.

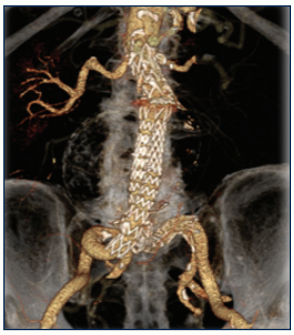

Figure 2. Postoperative image showing no device-related endoleaks.

EASE OF USE

The INCRAFT® System offers a variety of easy-to-use features above and beyond those already discussed intended to reduce the risk for adverse patient outcomes, including[4]:

- A limited number of intuitive steps without the possible allergic reaction and/or anaphylactoid response to polymers.
- An easy-to-use handle to facilitate a quick and controlled deployment.
- A built-in sheath introducer for the aortic bifurcate to eliminate the need for unnecessary sheath exchanges.
- A deployment mechanism that eliminates the need for transrenal nose cone recapturing.

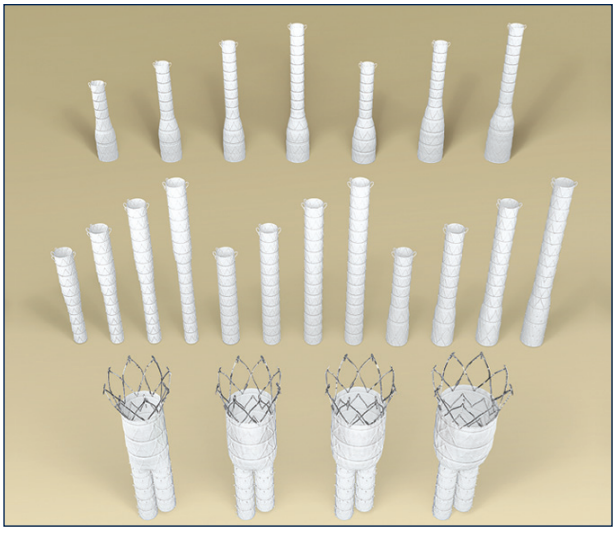

Figure 4. The INCRAFT® System portfolio of 23 codes.

CONCLUSION

The innovations and technologies embedded in the INCRAFT® System fulfill the ambitious goal set over a decade ago to evolve stent graft technology with a combination of critical-to-quality features to minimize the tradeoffs or compromises that have to be made in order to successfully treat patients with AAAs. ■

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1. Torsello G, Scheinert D, Brunkwall JS, et al. Safety and effectiveness of the INCRAFT AAA Stent Graft for endovascular repair of abdominal aortic aneurysms. J Vasc Surg. 2014 July 19. [Epub ahead of print]
2. Bastos GF, Rouwet EV, Metz R, et al. Device-specific outcomes after endovascular abdominal aortic aneurysm repair. J Cardiovasc Surg (Torino). 2010;51:515-531.
3. Hobo R, Laheij RJ, Buth J, EUROSTAR collaborators. The influence of aortic cuffs and iliac limb extensions on the outcome of endovascular abdominal aortic aneurysm repair. J Vasc Surg. 2007;45:79-85.
4. Torsello G, Brunkwall J, Scheinert D. Cordis INCRAFT ultra-low profile AAA stent-graft system. J Cardiovasc Surg (Torino). 2011;52:661-667.
5. Scheinert D, Pratesi C, Chiesa R, et al. First-in-human study of the INCRAFT endograft in patients with infrarenal abdominal aortic aneurysms in the INNOVATION trial. J Vasc Surg. 2013;57:906-914.
6. Chaikof EL, Fillinger MF, Matsumura JS, et al. Identifying and grading factors that modify the outcome of endovascular aortic aneurysm repair. J Vasc Surg. 2002;35:1061-1066.

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AAA Stent Graft System

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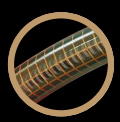
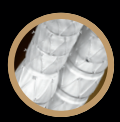
Reengineering the art of EVAR

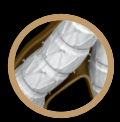


Ultra-low profile

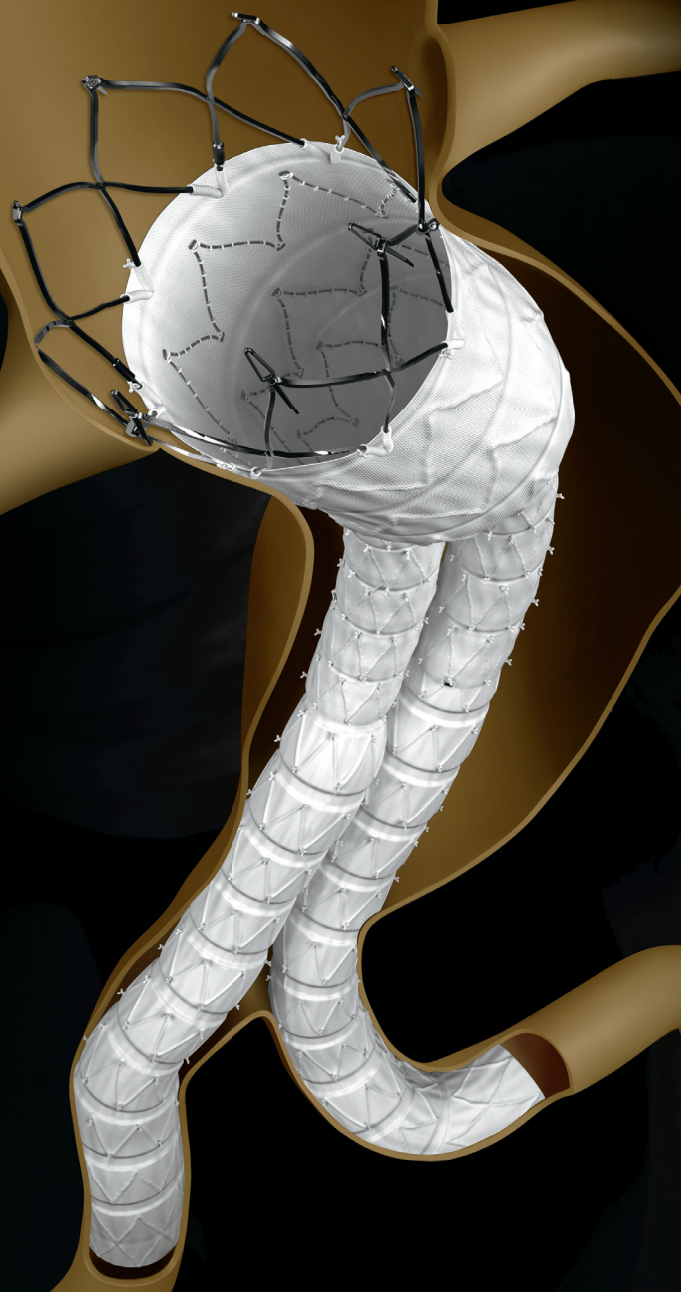


Customisable tri-modular design

Efficacy and durability without compromise[1]



Few units fit most anatomies



Talk to a Cordis representative about incorporating the INCRAFT® System into your EVAR programme.

For healthcare professionals only. Important information: Prior to use, refer to the Instructions for Use supplied with this device for indications, contraindications, side effects, suggested procedure, warnings, and precautions. As part of the Cordis policy of continuous product development, we reserve the right to change product specifications without prior notification. The INCRAFT® AAA Stent Graft System should only be used by physicians and teams trained in vascular interventional techniques, including training in the use of this device. Specific training expectations are described in the Instructions for Use.

Reference: 1. Torsello G, Brunkwall J, Scheinert D. Cordis INCRAFT™ ultra-low profile AAA stent-graft system. *J Cardiovasc Surg (Torino)*. 2011;52(5):661-667.

Contact your Cordis sales representative for availability and ordering.

Discussing the Design History of the INCRAFT® AAA Stent Graft System

The multispecialty team of expert physicians who consulted the design plan share the thoughts and experiences that led to the device's innovative development.

PARTICIPANTS:

Robert Bersin, MD
Medical Director
of Endovascular Services
Medical Director of Structural
Heart Services
Swedish Medical Center
Seattle, Washington
He has disclosed that he is a consultant to Cordis Corporation.

Takao Ohki, MD
Chariman of Surgery
Department of Surgery
Jikei University School of Medicine
Tokyo, Japan
He has disclosed that he is a consultant to Cordis Corporation.

Corey Teigen, MD
Vascular & Interventional
Radiology Department
Sanford Health
Fargo, North Dakota
He has disclosed that he is a consultant to Cordis Corporation.

When did the initial concept and design discussions for the INCRAFT® AAA Stent Graft System (Cordis Corporation) begin?

Dr. Bersin: My involvement began in 2004. Cordis had previously attempted to design a fully percutaneous stent graft some years before, and out of that came the desire to develop a next-generation percutaneous device. In the fall of 2004, a team was assembled to meet those goals and design the device.

Dr. Ohki: My involvement with the INCRAFT® System goes back to around 2004, but the seed of the percutaneous abdominal aortic aneurysm (AAA) repair was present within Cordis going back to 1997-1998.

Dr. Teigen: I was first involved with the Quantum LP graft at Cordis in the late 1990s, early 2000, and then we moved into the INCRAFT® System in 2004 when we started looking at making a graft that was small enough to meet the needs of people with smaller leg vessels.

What unmet clinical needs were you trying to solve when you embarked on the INCRAFT® System?

Dr. Bersin: There were two basic areas in which the first- and second-generation devices didn't meet all of our needs. On the access side, it was getting a lower profile, because it became clear early on that profile had a huge impact on complications and initial outcome (Figure 1).

The other area was the adverse aortic neck, the infrarenal aortic neck. This device really attempted to address the profile and be totally percutaneous and address some of the limitations of the current-generation devices as far as treating adverse necks, especially angulated necks.

Dr. Teigen: It was really about access vessels and having a low-profile graft that would treat those patients for whom the current grafts could not, especially women, people of Asian descent, and those with bad atherosclerotic disease* or small iliac vessels.

Dr. Ohki: The INCRAFT® System makes endovascular repair less invasive and gets closer to the concept that drove Cordis' innovation even in the late 1990s, which was to create a less invasive future. It's close to 20 years that we spent on creating a less invasive future.

Durability and long-term data of the INCRAFT® AAA Stent Graft System are based on 2-year clinical follow-up and benchtop data.

How would you describe the importance and the influence of having physicians from the radiology side, cardiology side, and the vascular surgery side working together as a team?

Dr. Teigen: It's absolutely necessary. We had innumerable discussions among the three of us about what would be best and all brought different skills and experiences to the table (Figure 2). I think that ultimately made the graft as great as it is.

Dr. Ohki: I think bringing the three fields together created a better, more knowledgeable team—we each have a unique strength. If you develop it just with a vascular surgeon, the surgeon would tend to give priority to the durability and give up the low-profile aspect of the stent graft. Drs. Bersin and Teigen, being interventionists, were more vocal about not giving up on low profile.

Dr. Bersin: It is crucial. Every specialty has its own perspective and experience, and that collective experience between all three major specialties proved to be an excellent mix to get consensus and question certain design elements. It worked beautifully, I think, as far as achieving the goal of getting balanced input.

What are some of the elements that have changed since the early designs? And what testing and clinical observations and animal lab observations did you perceive in order to make those changes from the initial design?

Dr. Bersin: The initial design concept centered around the idea that to get a lower profile, you had to become increasingly modular. There's just no other way to do it. The first-generation device was all-in-one,

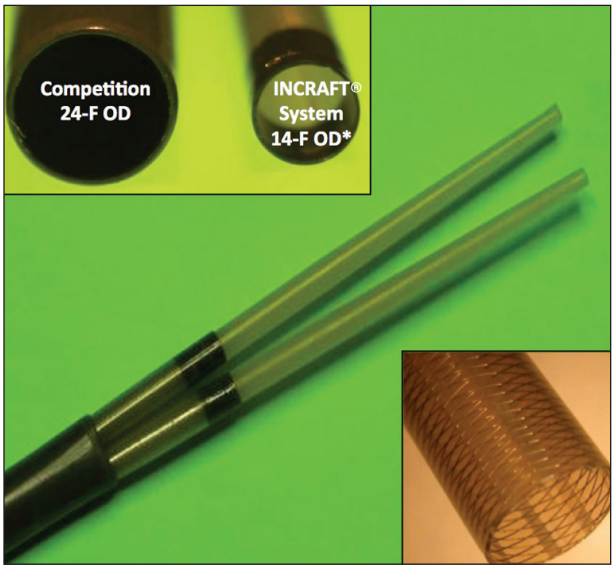


Figure 1. Comparing the profile of the INCRAFT® System aortic bifurcate delivery sheath to the profile of other major competitors. *16-F OD for the 34 mm aortic bifurcate.

Figure 2. Drs. Teigen, Bersin, and Ohki (from left to right), during some of the early deployments of the INCRAFT® System prototypes in April of 2009.

and that was the highest profile device. The current INCRAFT® System is a three-piece device (Figure 3).

Dr. Ohki: Because we wanted to create a flexible, low-profile system, the INCRAFT® System was a fairly short-pitch stent, which means that there is no support during deployment. We realized that the infrarenal design was not accurate enough, and that's when we advised the engineers to hedge risk by creating a suprarenal stent. A suprarenal stent with a mechanism to hold a top stent tip was the easiest solution to combat the windsock effect, and that's the design we have today.

Dr. Teigen: As we came up with different conflicts, we had to trade one thing for another. We pushed the engineers over and over again to solve the problem. It was a gradual process. There was a lot of durability testing, and we did a lot with the nitinol and fabric to make the stent graft last despite the fact we made it a small size.

Dr. Ohki: There is no fatigue machine that can be acquired commercially, so we had to create our own fatigue testing: pushing, pulling, twisting. The fatigue model created by the Cordis engineers compresses and twists the graft with pressured flow, and you can do 200 million cycles, accelerated. With this testing, we realized that the sharp-edge stent was no good, and if the stent was not attached to the fabric very tightly, it was prone to graft wearing.

Currently, how does the device perform for you in your patients during the INSPIRATION Trial?

Dr. Teigen: We spent 10 years working on this, so you always have some trepidation and wonder if it's really going to work—and it did; it was awesome. We enrolled 30 patients in the INSPIRATION Trial and every one of them is doing excellently. We even treated patients

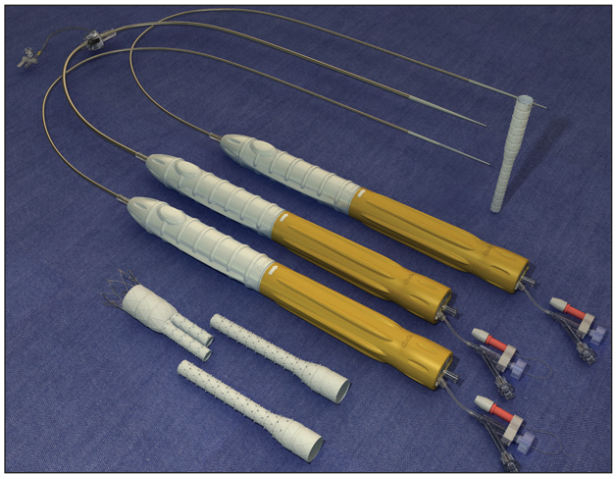


Figure 3. The trimodular design of the INCRAFT® System—implants and delivery systems.

under a compassionate use program, because there was a patient I couldn't treat any other way, and this graft treated that patient without any complication.

Dr. Bersin: The device performed excellently in the clinical trials. We could only treat up to a 60° infrarenal neck, and that was the main restriction because even small access vessels could be approached with the device's low-profile. Even up to 60° necks, this conforms as well or better than anything I have used in my experience. It truly is accurate as far as placement; we've proved that you can get within 2 mm of your intended target.[1] On an angulated neck, its ability to conform orthogonally as it's deployed is excellent because of the way the delivery system was designed.

Dr. Ohki: During the clinical trial, I performed all 30 INCRAFT® System implantations percutaneously and under local anesthesia. I was able to live up to my word that I gave my patients beforehand: the latest, state-of-the-art, cutting-edge technology. No general anesthesia, no cut down. That was a triumph. If the percutaneous success rate is 90%, then you have to worry about a one out of 10 failure, which means you have to have anesthesia backup and be prepared with a surgical kit. If you are successful with 30 out of 30 patients and have no conversion to general anesthesia, that means a lot from a clinical standpoint.

What other design elements, in your opinion, make the INCRAFT® System unique?

Dr. Bersin: I'd say number one is durability. We designed this to be durable. In our extreme bench testing, we found that this device outperformed others; freedom from frame fracture, fabric erosions, and so forth was better than any. I can say to people with confidence that this is not only lower profile, more accurate to deploy, and more orthogonal on angulated necks—it's also durable, which is quite an achievement.

The hooks for attachment (Figure 4) have more pull-out force than any other graft, so the freedom from migration is expected to be the best. The pull-out force to separate the modular limbs is expected to be the greatest.

Dr. Teigen: The low profile allows you to use it on most eligable patients. Second, the device's trackability—it goes through iliacs and aneurysms that are very tortuous.* Even in tortuous anatomies, the accuracy of placement helps you to put it right at the renal arteries where you need to. The three-piece design and being able to adjust the length of the iliacs to treat all the way down to the common iliac bifurcation have made it an excellent graft all around.

Dr. Ohki: The low profile of the INCRAFT® System allows percutaneous implantation with local anesthesia.

The in-situ customization capability of the INCRAFT® System allows you to take advantage of every millimeter of the iliac neck. With a standard stent graft, where you don't have much room on either end, you cannot make it too short or too long. The stent graft sizing would dictate the physician on where to land. With the regular, currently existing stent graft, we would land the distal end of the stent graft sometimes 1 or 2 cm away from the internal iliac artery, which means we are wasting 1 or 2 cm of neck. If we don't utilize the whole length of the distal neck, it might lead to future failure.

The other advantage was related to the flexibility of the endograft. Most stent grafts on the market straighten the aortic anatomy as they are implanted, possibly because of the stiff, large-bore delivery system. That means the aneurysm is trying to fit the endograft.

The INCRAFT® System is flexible, it goes in effortlessly and doesn't create an accordion effect. It is not intended to straighten the neck angulation. On average, we only saw about a 10% change in the infra- and suprarenal neck angulation after treatment, which supports the great conformability we observed in preclinical testing.[2]

Now, what does that mean? It might not seem bad initially, but the reality is that any aorta or aneurysm is stronger than the stent graft. With an ordinary stent graft, a 50° neck is turned into a more straightened 30° after implantation. But 6 to 12 months later, the aneurysm beats the stent graft, the 30° neck goes back to 50°, and the stent has to migrate either proximally or distally to accommodate or there is a type III endoleak.

Does the INCRAFT® System have any features that specifically help the prevention of endoleaks?

Dr. Teigen: There are several things we wanted to do to decrease the risk of endoleaks. First of all, we wanted to have an endoskeleton at the fabric on the outside have a better seal at the superior neck. We looked at having

Figure 4. The unique, sharpened, integrated nitinol barbs allows for migration-resistant suprarenal fixation of the INCRAFT® System.

Figure 5. The suture knots on the outside of the iliac limbs interlock with the endoskeletal stent struts on the inside of the aortic bifurcate legs for improved connection force in the overlap zone.

enough radial force despite the fact that it is low profile to be able to seal the proximal end zone.

We also looked at the legs and the locking mechanism between the knots and the nitinol (Figure 5). When you put the legs in, their motion is reduced, decreasing the risk of type III endoleaks. The same goes with the iliac legs—having the endoskeleton and fabric on the outside and enough radial force to seal the iliac arteries.

Is there anything that you learned about the device that makes it unique in the way that you implant it? Are there any unique deployment steps you think you would take into account when using the INCRAFT® System?

Dr. Bersin: Yes, there's actually one aspect that I found, in my opinion, to be unique about it, and it goes back to how it's designed. To be this low profile, you have to have larger and higher radial strength frame nitinol cells. You can't have as many. You can't have a tight mesh because that takes up too much room and it raises the profile. So you have to have larger cells, and to maintain the radial strength of the device, they have to be stronger. So as a result of that, the radial force of this device is quite high.

I have found that you're better off not oversizing too much because of the high radial force. Oversize this device about 10% instead of the usual 20%, and certainly not 30%.

Dr. Teigen: You want to use a relatively stiff wire. The device goes up through the iliacs and into the aorta so well. You can get it there over a floppy wire, but you really want the support of a stiffer wire when you deploy it to keep it in place because it's so accurate. You can't be too aggressive with a floppy wire.

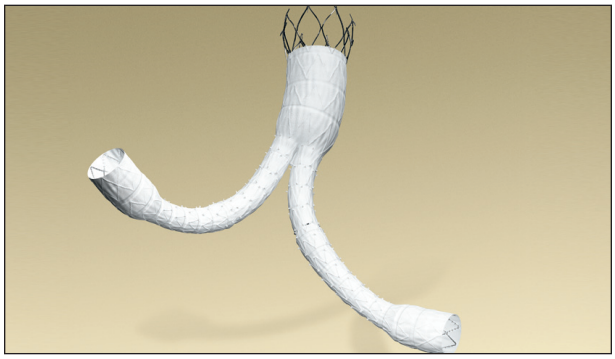


Figure 6. The INCRAFT® System, finally available after almost a decade of developmental work.

Explain to us why it took 10 years to develop the INCRAFT® System.

Dr. Bersin: Our challenge was to make this a low-profile device that is equivalent to a 12-F sheath introducer without sacrificing acute performance or durability, which is quite challenging to accomplish.

As I mentioned, you have to have fewer stent cells and higher radial force. The frames are stronger; that puts more stress on the fabric. You then have to do things in minute detail, such as change how the fabric is attached to the stent and distribute the stress force of the attachment across a broader area of fabric to prevent fabric tears and erosion.

These are very minute but important changes, and every time we made one, we did the durability testing all over again. All of the design details become exponentially more difficult as you go increasingly smaller in profile.

Dr. Ohki: The devil is in the details. Shouting, "lower profile, lower profile!" is easy, anybody can do that. But, in fact making a low-profile device with all these limitations is a conundrum—it's trying to realize two totally opposite things, and it's the engineers that made these devilish details happen.

Dr. Teigen: It's really engineering challenges. We tried to take a very large graft (originally it was 24-F) and put it down to 12- or 14 F. The engineering that it took to get it there took some time, and we wanted to make sure this was a durable graft. We put a lot of time into engineering something that was a very durable device. ■

1. Pratesi G. INCRAFT® AAA Stent Graft System 2-year clinical data from the INNOVATION Trial. Presented at: Charing Cross International Symposium. April, 2014. London, UK.
2. INNOVATION Study data on file. Cordis Corporation.

*Exercise particular care in areas that are difficult to navigate, such as areas of stenosis, intravascular thrombus, calcification, or tortuousity, or where excessive resistance is experienced, as vessel or catheter damage could occur.

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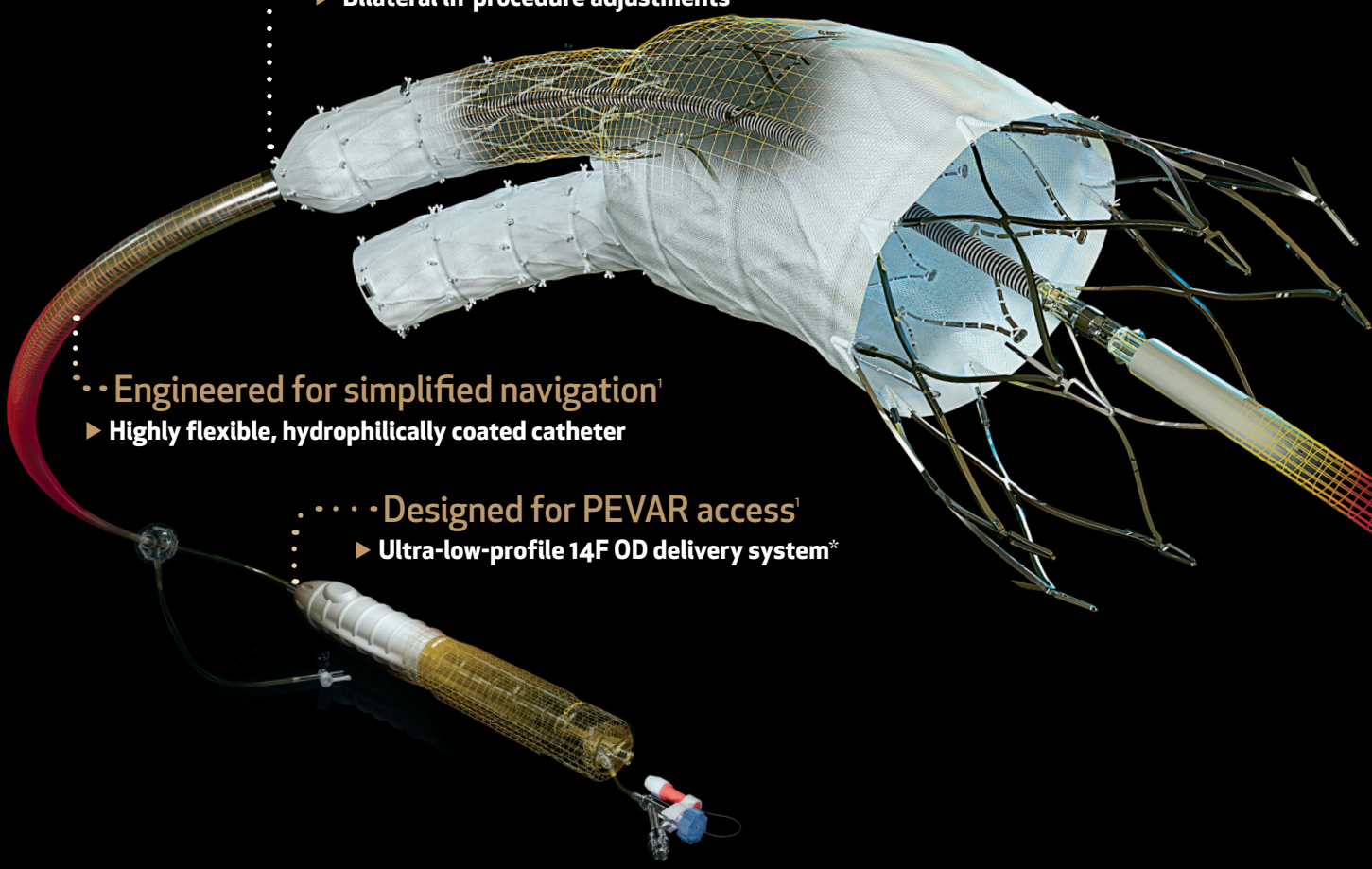
Crafted for in situ customisation[1]
- **Bilateral in-procedure adjustments**



Engineered for simplified navigation[1]
- **Highly flexible, hydrophilically coated catheter**

Designed for PEVAR access[1]
- **Ultra-low-profile 14F OD delivery system***

Talk to a Cordis representative about incorporating the INCRAFT® System into your EVAR programme.

*16F outer diameter for the 34 mm aortic bifurcate.

For healthcare professionals only. Important information: Prior to use, refer to the Instructions for Use supplied with this device for indications, contraindications, side effects, suggested procedure, warnings, and precautions. As part of the Cordis policy of continuous product development, we reserve the right to change product specifications without prior notification. The INCRAFT® AAA Stent Graft System should only be used by physicians and teams trained in vascular interventional techniques, including training in the use of this device. Specific training expectations are described in the Instructions for Use.

Reference: 1. Pratesi G. INCRAFT® AAA Stent Graft System 2-year clinical data from the INNOVATION Trial. Presented at: Charing Cross International Symposium. April 2014. London, UK.

Contact your Cordis sales representative for availability and ordering.

The Trimodular, Tailored Approach to EVAR

The benefits of incorporating proven surgical design concepts into the INCRAFT® AAA Stent Graft System design.

BY GIOVANNI TORSELLO, MD

There are two primary advantages to open surgical repair of abdominal aortic aneurysms (AAA) that result in long-term, durable outcomes: the ability to tailor-make the exclusion length based on the individual anatomical situation found during the procedure and the creation of a proximal attachment that mimics a sewn anastomosis with respect to fixation and sealing. Endovascular repair (EVAR) offers a less invasive alternative, but historically, most stent graft options have had limited anatomic applicability and can only be used in a finite range of access vessels and aortic necks. To mimic the benefits of open repair, an intuitive, low-profile endovascular system that allows introduction in a variety of iliac vessel diameters and the possibility of percutaneous introduction in some cases is crucial.

The novel INCRAFT® AAA Stent Graft System (Cordis Corporation) (Figure 1) was designed to solve the limitations of previous-generation endovascular AAA devices, particularly in regards to durability and customizability. The ultra-low-profile delivery system of the INCRAFT® System is able to navigate narrow, diseased iliac vessels and has the capability of percutaneous delivery.

In this article, the unique trimodular structure of this device will be highlighted, as well as some of the key benefits associated with this design:

- Real-time customization
- Treatment of a broad spectrum of anatomies with few units
- Enduring modular junction strength
- Placement accuracy

REAL-TIME CUSTOMIZATION

The modular components of the INCRAFT® System are designed to allow bilateral in situ length adjustment of the limb prostheses by 2 to 3 cm during implantation. This substantially improves placement accuracy, which is intended to reduce the risk of inadvertent side-branch coverage of the hypogastric and renal arteries.[1,2] With traditional systems, there is little opportunity to accommodate any needed changes after delivery system introduction, particularly with regard to potentially inaccurately measured preoperative aortoiliac dimensions. The INCRAFT® System design will fit most diameters and lengths of vessels due to the real-time customization capabilities, providing a tailored approach to EVAR.

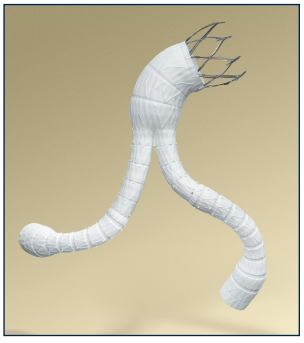


Figure 1. The INCRAFT® System provides custom deployment, optimized accuracy, and durable repair.

TREAT A BROAD SPECTRUM OF ANATOMIES WITH FEW UNITS

Another key to accommodating a wide range of aortic diameters lies in the stent structure design, which distributes the appropriate level of radial force, while maintaining conformability.

There are four aortic bifurcate sizes to treat 17- to 31-mm aortic diameters and 19 iliac limb diameters available in the INCRAFT® System portfolio, all of which are designed for in-procedure customization for coverage ranging anywhere from 10% to even 30% of oversizing.

Each iliac limb is supplied in four lengths ranging from 8 to 14 cm, allowing a total aortoiliac coverage length of between 13 and 21 cm. The combination of 23 different modular components provides the operator with highly customizable options and eases the standard complexity of device selection. Thus, fewer units create streamlined preoperative planning and inventory management and act as a benefit in both elective and emergent EVAR.

INTERLOCKING MODULAR COMPONENTS

The stent graft uses durable, biopolymer-free sealing technology, which helps to reduce modular disconnection and type III endoleaks.[1,3] There are interlocking suture knots on the limb prosthesis connecting to the Z-stents on the inside of the aortic bifurcate legs. This acts as an additional safety feature and provides a hook-and-loop-like connection between the endoskeleton stent struts of the bifurcate and the suture knots (Figure 2).

Durability and long-term data of the INCRAFT® AAA Stent Graft System are based on 2-year clinical follow-up and benchtop data.

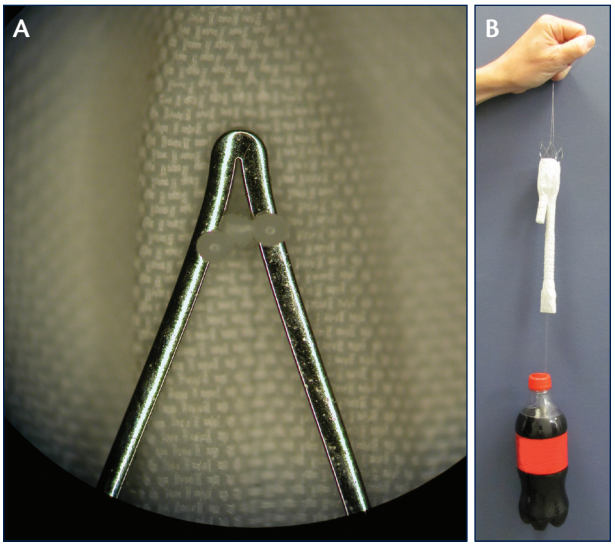


Figure 2. Increased modular junction force in the overlap zones are demonstrated by suspending a full 20 oz (591ml) soda bottle from the iliac limb ex vivo (at room temperature) (A). The modular design is enhanced by the suture knots on the exterior of the iliac limb grafts interlocking with the Z-stents on the inside of the aortic bifurcate legs (B) to reduce disconnection.

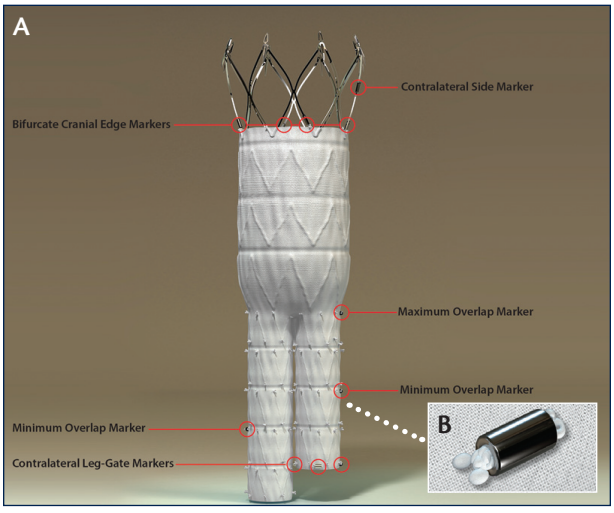


Figure 3. The locations of all the radiopaque markers on the bifurcate implant (A). Close up showing how each marker is sutured into the graft material (B).

Additionally, the seamless low-porosity polyester of the graft is kink-resistant to help mitigate perfusion of the AAA sac, and the laser-cut nitinol stents combine radial force with stent fracture resistance and are sutured to the graft in a unique way to minimize micromotion. The stent graft's stability is increased by the suprarenal fixation mechanism, composed of the laser-cut transrenal stent and integrated sharpened barbs that anchor the system.

PLACEMENT ACCURACY

Optimized proximal placement accuracy is achieved through the perpendicularly deployed aortic bifurcate and the partial repositioning of the bifurcate before full deployment, which is aided by distinctive radiopaque proximal markers (Figure 3) on the transrenal stent struts.

As noted, in-procedure bilateral in-situ adjustments of limb prostheses substantially improve distal placement accuracy and reduce the risk of inadvertent side-branch coverage.

INITIAL CLINICAL EXPERIENCE

The INNOVATION Trial is a 60-subject first-in-human trial, performed at six clinical centers in Germany and Italy. The objective of this multicenter, open-label, prospective, nonrandomized trial is to provide evidence regarding the effectiveness and safety of the INCRAFT® System in subjects with AAAs. After 2 years, no type I or III endoleaks, endograft migrations, stent fractures, or aneurysm enlargements were detected.[2] No aneurysm- or procedure-related death occurred. An average decrease of 11.4% (6 mm) was observed with ≥ 5 mm sac regression in 22 of 49 patients (45%) at 2 years. Although not statistically powered, aneurysm regression seemed to be consistent regardless of the aneurysm size. Three secondary procedures were performed: two for type I endoleak and one for limb occlusion. Three-year follow-up is still being collected.

The initial experience at Munster University Hospital showed excellent procedural results not only in straightforward anatomy, but also in patients with challenging aortoiliac anatomy, including short proximal aortic neck, neck angulation, tight distal aortic bifurcation, small access arteries, and highly tortuous iliac vessels.[1] Sac regression was 7%, 12%, and 28% after 1, 2, and 3 years, respectively. Preliminary experience confirmed the in-situ sizing ability to telescope the limb prosthesis into the sockets of the bifurcated graft, adjusting the length of the overlap between the graft components.

CONCLUSION

The INCRAFT® AAA Stent Graft System is designed to incorporate lessons learned from previous generations of endovascular technologies and mimic familiar and proven open surgical principles. The end result is a highly versatile device that offers a more individualized endovascular option to a greater number of patients with AAAs. ■

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1. Torsello G, Brunkwall J, Scheinert D. Cordis INCRAFT™ ultra-low profile AAA stent-graft system. J Cardiovasc Surg (Torino). 2011;52:661-667.
2. Torsello G, Scheinert D, Brunkwall JS, et al. Safety and effectiveness of the INCRAFT AAA Stent Graft for endovascular repair of abdominal aortic aneurysms. J Vasc Surg. 2014 July 19. [Epub ahead of print]
3. Chaikof EL, Fillinger MF, Matsumura JS. Identifying and grading factors that modify the outcome of endovascular aortic aneurysm repair. J Vasc Surg. 2002;35:1061-1066.

Innovation Without Compromise: The INCRAFT® AAA Stent Graft System

Clinical results driven by the refined features of a new device.

BY ROBERTO CHIESA, MD, AND GIOACHINO COPPI, MD

Since the first endovascular aneurysm repair (EVAR) was described by Parodi et al,[1] continued improvements have been made to stent graft design. EVAR has been shown as a safe alternative to open surgery for the treatment of abdominal aortic aneurysms (AAAs), with reduced early morbidity and mortality rates.

The EUROSTAR registry reports that the rate of secondary interventions and conversions is relatively high,[2] and the incidence of early open conversion after EVAR is mainly linked to technical misadventure, such as iliac calcification or tortuosity, technical failure during stent graft deployment, or immediate postprocedure graft thrombosis.[3]

To overcome the current limitations, manufacturers introduced new technologies to improve durability and modifications to constrain the devices in lower-profile delivery systems. Unfortunately, the balance between profile and performance is not easy, as demonstrated by some unsuccessful projects that were aborted by industry. In addition, the use of low-profile devices to treat patients with small vascular access was linked to an increased rate of early limb occlusions and thrombosis.[4]

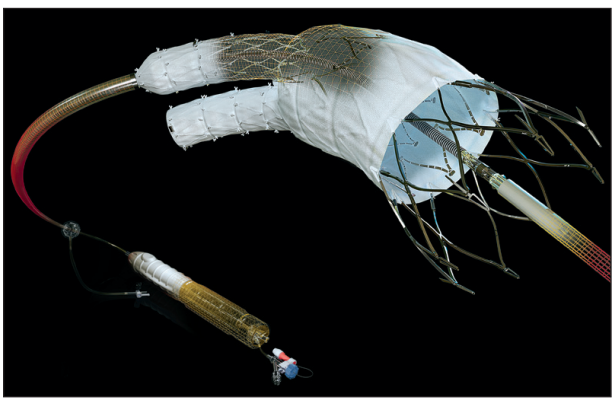

Figure 1. The Cordis INCRAFT AAA Stent Graft System bifurcate and delivery system.

As an example, clinical experience has reported an 11% rate of stenosis and a 2% rate of occlusions with recent devices (eg, Endurant, Medtronic, Inc.).[5]

Despite the progress, EVAR remains challenging in patients with small (< 10 mm), calcific, or tortuous iliac vessels, as well as in patients with hostile proximal aortic neck (< 15 mm) anatomy; this group represents 70% of the entire AAA population.[6]

The balance between innovations and the need for proven data can be challenging, too, and early promises should be supported by mid- to long-term follow-up.

AN INNOVATIVE TECHNOLOGY WITH STRONG CLINICAL DATA

The INCRAFT® AAA Stent Graft System (Cordis Corporation) (Figure 1) is an advanced EVAR technology now available for the treatment of infrarenal abdominal aneurysms. This system is the result of a long engineering history.

The INCRAFT® System is designed to address the unmet needs of current endografts by combining unique features and new refinements to existing endografts.

For the first time, a stent graft system was conceived together with its delivery system, which allows the device to be delivered through a flexible and ultra-low-profile system (equivalent to a 12-F sheath introducer for the iliac limb delivery system). The INCRAFT® System was designed to allow for increased packing efficiency without compromising on durability.[7] The remarkable radial force and flexibility of the INCRAFT® System make it conformable in challenging anatomies such as tortuous iliac arteries.

INNOVATION Trial

It is important that when a groundbreaking device is brought to market, it is backed up with solid data on midterm clinical results. S. Raffaele Hospital (Milan, Italy) and Nuovo Ospedale S. Agostino Estense (Modena, Italy) participated as investigational centers in the

Durability and long-term data of the INCRAFT® AAA Stent Graft System are based on 2-year clinical follow-up and benchtop data.

TABLE 1. INNOVATION PATIENT KEY ANATOMICAL MEASUREMENTS (CORELAB)		
	Mean (N = 60)	**Range (N = 60)**
Infrarenal angle	34.4°	6.9°–67.3°
Proximal neck diameter	22.3 mm	17–29.5 mm
Neck length	26.9 mm	5–50 mm
AAA maximum diameter	52.6 mm	35–101 mm
Minimum aortic bifurcation diameter	20.5 mm	11–33 mm
Left iliac seal zone diameter	13.3 mm	9–20 mm
Right iliac seal zone diameter	13.7 mm	8.7–23 mm
Left min. access diameter	7.1 mm	3.6–10 mm
Right min. access diameter	7.2 mm	4.3–10 mm
Preprocedural measurements were challenging and in some cases beyond the inclusion criteria, according to the core lab measurement.		

first study performed with the INCRAFT® System. The INNOVATION Trial is a multicenter, open-label, prospective, nonrandomized study of the first-in-human use of the INCRAFT® System in patients with infrarenal AAAs.[8] This trial involves six vascular centers in Germany and Italy, and 60 asymptomatic patients with AAAs were enrolled.

The aim of the INNOVATION Trial is to assess the safety and efficacy of the INCRAFT® System for the management of AAAs. The primary endpoint is technical success and patient safety through 1-month follow-up.* The 1-year safety endpoints include the absence of device- or procedure-related major adverse events, absence of type I, III, or IV endoleaks, and maintenance of device integrity through 1 year of follow-up.

The main inclusion criteria of this study are a proximal neck length of ≥ 15 mm and ≤ 27 mm in diameter, an access vessel large enough to accept the 14-F outer diameter of the delivery catheter, and an aortic bifurcation > 18 mm in diameter.

In Table 1, the key anatomical measurements are reported. Some of the patients enrolled had severe morphologies—in particular, access vessel and aortic bifurcation diameters; 33% of the patients had a bifurcation diameter inferior to 18 mm; and 45% of the patients had access vessel diameters inferior to 7 mm, according to core lab measurements.

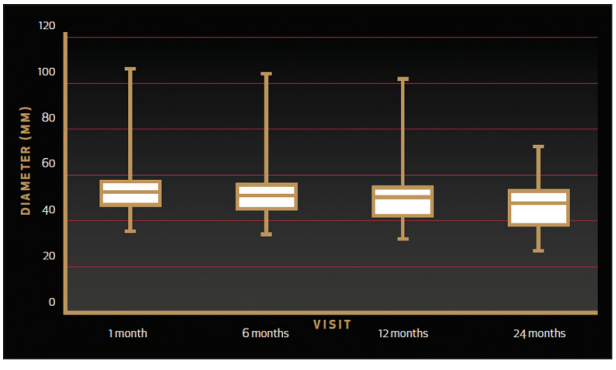

Figure 2. Mean AAA diameters at 1-, 6-, 12-, and 24-month follow-up after implantation of the INCRAFT® System.[2]

Since the first patient was enrolled in 2010, the preliminary data at 30 days[8] and the midterm data at 1 year[9] are already available, and they are very promising. The rate of technical success at 1 month was 97% (56/58 patients of the original 60 patients who were enrolled) with freedom-from-aneurysm enlargement of 100% up to 1 year and absence of both type I and III endoleaks in all patients at this time point.

These satisfactory results were confirmed at 2-year follow-up.[10] At 2-year follow-up, there were no incidences of endoleaks (type I or type III), device- or procedure-related major adverse events (death, QMI, CVA, renal failure), stent graft migrations, or stent fractures. In addition to no incidences of aneurysm sac enlargement, sac regression was observed in 45% of the patients (Figure 2). Despite the high number of patients with severe morphologies, no early limb occlusions were seen in up to 1-year follow-up (Figure 3). One patient did, however, develop a late limb occlusion at day 666 due to sac contraction and limb conformation change. There were two type I endoleaks—one found at 30-day follow-up and one found at 6-month follow-up. Both were resolved before 1-year follow-up after endovascular reintervention. Table 2 shows the summary of the acute and midterm results.

The collection of the 3-year follow-up data is now closed, and the results will be presented soon; in the meantime, the 4-year follow-up visit was performed for some patients, with confirmed motivating results.

INSPIRATION Trial

The next clinical program for the INCRAFT® System was the INSPIRATION Trial, an investigational device exemp-

TABLE 2. INNOVATION TRIAL CLINICAL OUTCOMES			
	30 Days (58/60)	**1 Year (56/60)**	**2 Years (54/60)**
Freedom from type I endoleak	96.6%[a]	100%	100%
Freedom from type III endoleak	100%	100%	100%
Stent graft patency	100%	100%	98.1%[b]
Freedom from migrations	100%	100%	100%
Freedom from fracture	100%	100%	100%
Freedom from sac enlargement	100%	100%	100%
Freedom from MAE (death, QMI, CVA, renal failure)	100%	98.2%	88.5%[c]

[a]Type I endoleak was present at 30-day follow-up and resolved after additional endovascular intervention on day 278.
[b]One patient developed a late graft occlusion at day 666 due to sac contraction and limb confirmation change.
[c]One death occurred within up to 1 year, five deaths within the 2-year time frame, all non-AAA related.
Abbreviations: AAA, abdominal aortic aneurysm; CVA, cerebral vascular accident; MAE, major adverse event; QMI, Q-wave myocardial infarction.

tion study that started in 2012 and enrolled 190 patients in the United States and Japan. At 30 days postprocedure, the INSPIRATION Trial also showed 100% (189/189) freedom from endoleaks (type I, III, IV), and 100% stent graft patency. As in the instructions for use of the product, the inclusion criteria in this trial allowed treatment of necks that were 10 mm in length.

Future Research

With such strong midterm clinical results collected in more than 250 patients across the world, along with extensive benchtop testing, the INCRAFT® System is ready to live up to its promises.

To continue building a strong reputation for the INCRAFT® System, a postmarket study, which will include an additional 150 patients throughout Europe, is currently being set up and is expected to begin enrollment in the coming months.

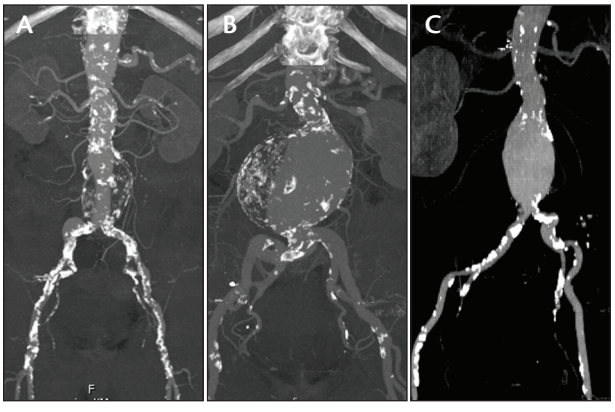

Figure 3. Examples of patients in the INNOVATION Trial: heavily calcified vessels (A), severe angulation and short neck (B), and highly tortuous iliac arteries and difficult access vessels (C).

WHAT AN ULTRA-LOW PROFILE MEANS FOR PHYSICIANS AND PATIENTS

Patients with small, tortuous, calcified access vessels account for 6% to 19% of procedures, as described in various literature.

With an ultra-low-profile device, the applicability of EVAR can be increased over a broader spectrum of the aortoiliac anatomic configurations that are encountered, as well as improve the deliverability of the device for the whole patient population. Access-related complications such as iliac rupture, dissection, and pseudoaneurysm occur in 3% to 13% of cases, and hematoma, infection, and lymphocele occur in 1% to 10% of cases.

For these reasons, the INCRAFT® System must be considered as a new referral in the EVAR technology and should not be intended as a bailout device to be used only in challenging anatomies. The profile is an important added value for all patients with an AAA.

Local anesthesia and an early discharge may be considered when performing EVAR using the INCRAFT® System.

Whether percutaneous access will ultimately be beneficial over open femoral exposure remains to be proven; however, the ultra-low profile of the INCRAFT® System allows the physicians to choose their preferred access approach to practice EVAR.

A NEW "USER-FRIENDLY" TECHNOLOGY

What is notably different with the INCRAFT® System is that it introduces an innovative concept without deviating from an already-proven stent graft approach. The INCRAFT® System is a three-piece modular system made of low-porosity polyester and segmented nitinol stents. During the procedure, surgeons follow very familiar procedural steps, but with a simplified flow, to complete the EVAR procedure without deviating too much from their current standard

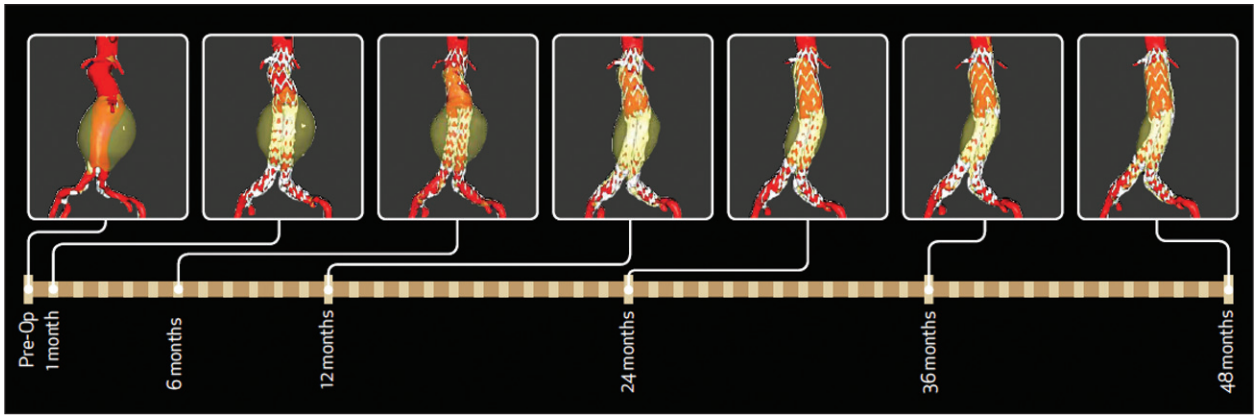

Figure 4. Long-term clinical success of one patient through 4-year follow-up after implantation of the INCRAFT® System.

practice. The integrated sheath, the hydrophilic coating of the shaft, the cap-free fixation release mechanism of the suprarenal stent, and, most importantly, the in situ length adjustment make the procedure easy, fast, and accurate.

SUMMARY

The 2-year data from the INNOVATION Trial confirm excellent results with the INCRAFT® AAA Stent Graft System. This study proves that the technology is designed to overcome the limitations of current stent grafts for the management of AAAs with alleviated concern regarding the technical compromises. With an ultra-low-profile delivery system and the ability to customize the implant during the procedure (thanks to the bilateral in situ length adjustment features and the introduction of partial proximal repositioning), this graft aims for high deliverability and placement accuracy in a durable (Figure 4) and easy-to-use system with broad anatomical coverage. ■

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1. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. Ann Vasc Surg. 1991;5:491-499.
2. Cuypers P, Leheij RJ, Buth J. Which factors increase the risk of conversion to open surgery following endovascular abdominal aortic aneurysm repair? The EUROSTAR collaborators. Eur J Vasc Endovasc Surg. 2000;20:183-189.
3. Million A, Deelchand A, Feugier P, et al. Conversion to open repair after endovascular aneurism repair: causes and results. A French multicentric study. Eur J Vasc Endovasc Surg. 2009;38:429-434.
4. Carroccio A, Faries PL, Morrissey NJ, et al. Predicting iliac limb occlusions after bifurcated aortic stent grafting: anatomic and device-related causes. J Vasc Surg. 2002;36:679e84.
5. Torsello G, Brunkwall JS, Scheinert D. Cordis INCRAFT™ ultra-low profile AAA Stent-Graft System. J Cardiovasc Surg (Torino). 2011;52:661-667.
6. Torsello G. Complex anatomy—challenges with current EVAR devices. Presented at: Charing Cross International Symposium; April 2014; London, UK.
7. Torsello G, Troisi N, Tessarek J, et al. Endovascular aortic aneurysm repair with the Endurant stent-graft: early and 1-year results from a European multicenter experience. J Vasc Interv Radiol. 2010;21:73-80.
8. Scheinert D, Pratesi C, Chiesa R, et al. First-in-human study of the INCRAFT endograft in patients with infrarenal abdominal aortic aneurysms in the INNOVATION trial. J Vasc Surg. 2013;57:906-914.
9. Coppi G, Njila M, Coppi G, et al. INCRAFT® Stent-Graft System: one-year outcome of the INNOVATION Trial. J Cardiovascu Surg. 2014;55:51-59.
10. Torsello G, Scheinert D, Brunkwall JS, et al. Safety and effectiveness of the INCRAFT AAA Stent Graft for endovascular repair of abdominal aortic aneurysms. J Vasc Surg. 2014 July 19. [Epub ahead of print]

*Technical success will be defined by the successful deployment of the stent-graft to the desired location in the absence of type I, III or IV endoleaks at the conclusion of the procedure. Safety will be defined by the absence of type I, III, or IV endoleaks and device- and/or procedural-related major adverse events (death, MI, stroke, and renal failure) within 1 month post-procedure.

Addressing Type II Endoleaks

Diagnosing and treating this continually perplexing EVAR complication.

BY MAXIME RAUX, MD; PROF. JEAN-PIERRE BECQUEMIN, MD; AND KENNETH OURIEL, MD, MBA

Over the last 15 years, EVAR has become the predominant modality of abdominal aortic aneurysm (AAA) treatment in suitable patients, gradually replacing open surgical repair (OSR).[1,2] Large, multicenter, randomized trials have highlighted benefits of EVAR over OSR as a less invasive technique, resulting in a reduction of 30-day mortality.[3,4] Notwithstanding, these benefits are lost over time.[5,6] EVAR still carries a certain rate of complications including rupture, reintervention, and conversion to open repair. Endoleaks, defined by a persistent blood flow outside the lumen of the graft but within the aneurysm sac, appear to be responsible for 60% of complications after EVAR and 45% of all reinterventions.[3] Furthermore, in a recent large-cohort study, Schanzer et al underscored that EVAR failed to prevent aneurysm sac enlargement in 41% of patients after 5 years, mainly due to the presence of any kind of endoleak.[7] Type II endoleaks are the most frequent, resulting in perfusion of the sac through collateral arteries (eg, lumbar and inferior mesenteric arteries). Type IIa endoleaks refer to simple endoleaks due to one collateral artery. Type IIb endoleaks are defined as complex, with backflow through two or more vessels. The occurrence and prevalence of this type of endoleak varies in the literature, from 7% to 44%.[8] These variations most likely result from a lack of standardization of endoleak recording. Some authors only recorded early endoleaks within the first month after EVAR placement.

IMAGING

Contrast-enhanced computed tomography (CT) scan is, so far, the gold standard to detect endoleaks; however, its sensitivity and specificity are technique-dependent and has several limitations. Directional flow cannot be accurately determined. When the endoleak is in continuity with a lumbar artery, it could be either a type II if the blood flow in the lumbar artery is retrograde, or type I if the flow is anterograde. The other counterpart is irradiation. Even if radiation exposure of a single CT scan is relatively low, repeated exposure increases cumulative dose and remains a concern.[9]

Alternative imaging modalities are magnetic resonance imaging (MRI) and duplex ultrasound. MRI poses the problem of accessibility, which is often more restrictive than a CT scan. Furthermore, MRI remains more expensive and is not recommended for ferromagnetic stent grafts, such as the Zenith® graft (Cook Medical).[10] Duplex ultrasound is less expensive and innocuous, but

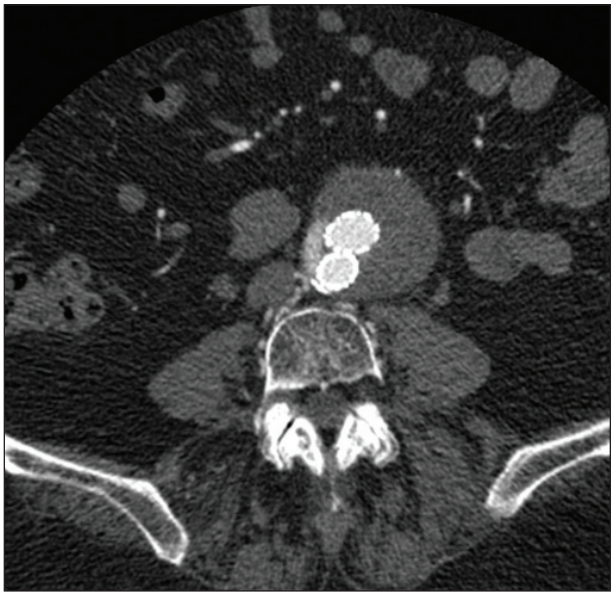

Figure 1. Type II endoleak through the lumbar artery.

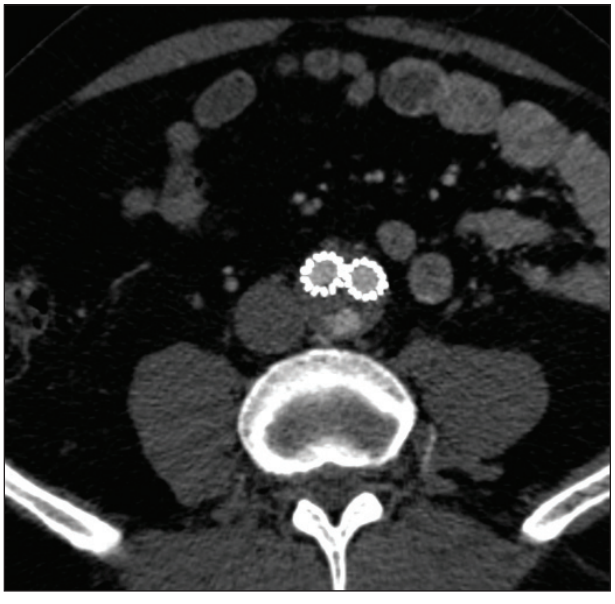

Figure 2. Type II endoleak through the lumbar artery.

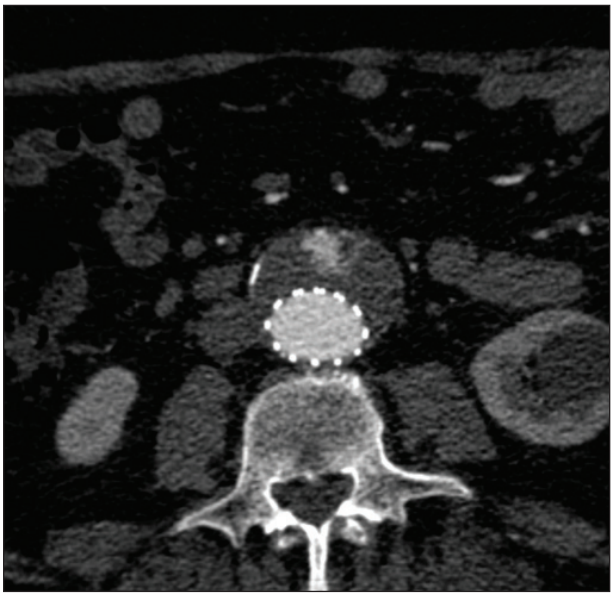

Figure 3. Type II endoleak via the inferior mesenteric artery.

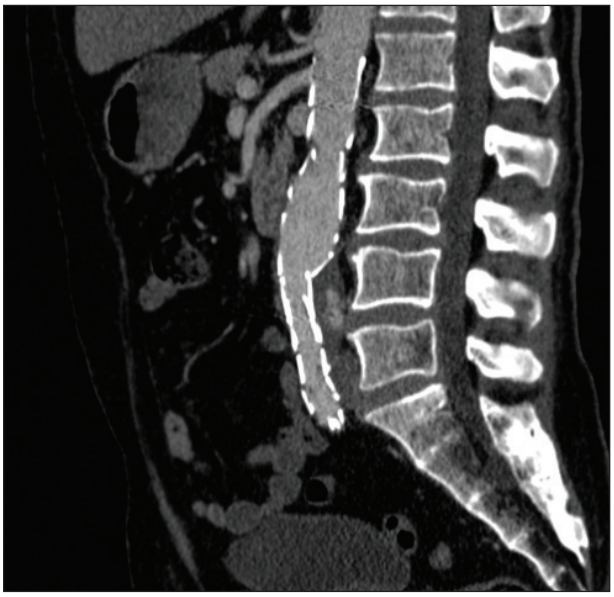

Figure 4. Type II endoleak via the inferior mesenteric artery.

is influenced by the technician's experience level and the patient's characteristics, such as obesity or gas interposition. Sandford et al showed a sensitivity of 67%, with many endoleaks present on CT scan that were not seen by ultrasound.[11]

Contrast timing is one of the key points of detecting type II endoleaks. Three phases are mandatory. The first phase is a noncontrast study to detect calcifications and thrombus remodeling. Many aneurysm sacs contain calcifications that cannot be differentiated from the contrast from an endoleak in the absence of a comparative noncontrast study. The second phase is a contrast view with early arterial acquisition. This phase usually detects type I and III endoleaks and some type II endoleaks. The third phase is acquired with delayed arterial phase images. Many lower-flow type II endoleaks are evident only on delayed acquisition.

CURRENT LITERATURE

The natural history of type II endoleaks remains poorly understood, and their management and consideration still remain controversial. A recent meta-analysis showed that type II endoleaks spontaneously resolve in 35.4% of cases within a range of 3 months to 4 years.[12] Some consider type II endoleaks as a benign condition; others hold them responsible for late ruptures, underlying a strategy of aggressive management and treatment at some centers. Several reports in the literature showed that nearly

EXPERIENCE WITH THE INCRAFT® AAA STENT GRAFT SYSTEM

The rate of endoleaks after EVAR varies between studies and devices, in part because of the disparities in definitions and the quality of the imaging studies. During the INNOVATION Trial (Cordis Corporation), 55.2% (32/58) of the patients were identified to have a type II endoleak at 1-month follow-up.[1] The number fell to 38.8% (19/49) at 2 years, one of which was newly identified between the 1- and 2-year time points. The volume of the endoleaks rarely exceeded 5 cc (2%), with more than 50% of the type II endoleaks being < 1 cc, as measured by core laboratory. Within the first 2 years of follow-up, none of the endoleaks required a reintervention.

Apart from the involvement of the core laboratory and independent clinical events committee in the identifying of endoleak type during the INNOVATION Trial, the potential cause for a higher type II endoleak detection rate could be related to the use of newer, higher-resolution CT imaging in this more recent study.

In this regard, the frequency of type II endoleaks in the recent TriVascular Ovation® trial was 34.3% (49/143; 95% CI, 26.5%–42.7%)[2], a rate that overlaps the observed point estimate of 41.5% (95% CI, 28%–56%) in the INNOVATION Trial. Additionally, there is the speculation that patients with complex and diseased anatomy, defined as narrow, tortuous, and/or calcified access vessels, might have developed more extensive collateral arterial flow and as such, could be more prone to type II endoleaks. In any event, it is unlikely that the higher incidence of type II endoleaks as seen in this study is either device- or procedure-related.

1. Torsello G, Scheinert D, Brunkwall JS, et al. Safety and effectiveness of the INCRAFT AAA Stent Graft for endovascular repair of abdominal aortic aneurysms. J Vasc Surg. 2014 July 19. [Epub ahead of print]
2. Mehta M, Valdes FE, Nolte T, et al. One-year outcomes from an international study of the Ovation Abdominal Stent Graft System for endovascular aneurysm repair. J Vasc Surg. 2014;59:65-73 e1-3.

20% of early type II endoleaks persist and account for rupture or secondary interventions.[13,14]

DEFINING TYPE II ENDOLEAKS

There are different types of type II endoleaks, with different complications. Not all of them are benign. Persistent endoleaks are defined by the absence of resolution after 6 months. Recurrent type II endoleaks correspond to the onset of a new endoleak from the same origin, independent of the resolution of the first one, regardless of delay between the two. A recent analysis of more than 750 patients during 15 years at Henri Mondor Hospital (Créteil, France) emphasized the seriousness of this complication. Incidence of type II endoleaks was 28.7%. Factors related to the onset of type II endoleaks included larger-sized aneurysms, older patients, female gender, and lumbar artery patency. Existence of a type II endoleak, regardless of its type, was associated with a higher rate of complications compared to patients without endoleak. Two main complications were related to type II endoleak: aneurysm sac enlargement (40.3% vs 16.8% for patients without endoleak; $P < .001$); and reintervention (14.9% vs. 6.6%; $P < .002$).[8]

Concerning the type of leak, persistent type II endoleak was associated with aneurysm sac enlargement ($P < .001$). Recurrent type II endoleaks were associated with higher reintervention rates, conversion to open repair, and sac enlargement ($P < .05$). These data are confirmed by multivariate analysis showing that persistent (HR 3.16; 95% CI, 2.55%–6.03%; $P < .001$) and recurrent type II endoleaks (HR 1.88; 95% CI, 1.18%–3.01%; $P = .008$) were significantly predictive of sac growth.[8] These data confirm that type II endoleaks are not benign and can deeply impact or even jeopardize outcomes after EVAR, with life-threatening complications. The data also support close follow-up with adequate imaging to detect and treat type II endoleaks in a timely manner. These data are supported by a recent long-term cohort study published by Zhou et al. This review states that delayed type II endoleaks (appearing < 12 months after EVAR implantation) are common, occurring in 41% of patients. These delayed endoleaks are significantly associated with aneurysm sac enlargement.[15]

Nevertheless, pure type II endoleak doesn't seem to increase the risk of rupture. Actually, ruptured AAA after EVAR with type II endoleak appears to be rare, occurring in less than 1% of cases in the EuroSTAR registry. Importantly, one third of ruptures occur without sac growth.[12]

The timing of treatment for type II endoleaks varies among studies, but indications such as aneurysm sac growth > 5 mm or endoleaks persisting > 6 months are well-accepted.[14,16]

TREATMENT

There are a wide variety of strategies available for treating type II endoleaks. These include transarterial embolization, gaining access through branches of the hypogastric arteries for lumbar endoleaks, or through branches of the superior mesenteric arteries for endoleaks originating from the inferior mesenteric arteries. Translumbar embolization of the sac and its feeding branches has also been employed with success, as has open or laparoscopic ligation of inflow arteries. Occasionally, open surgical reinterventions with aneurysm sac placation or open conversions are necessary.

CONCLUSION

In summary, type II endoleak after EVAR is a commonly encountered finding. While the frequency of aneurysm sac regression is lower in the presence of a type II endoleak, the vast majority of such leaks are of no clinical consequence to the patient. Occasionally, however, type II endoleaks can be associated with sac enlargement or symptoms, and in these cases, treatment with transarterial embolization or other reinterventions are indicated. ■

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1. Giles KA, Pomposelli F, Hamdan A, et al. Decrease in total aneurysm-related deaths in the era of endovascular aneurysm repair. J Vasc Surg. 2009;49:543-550; discussion 550-551.
2. Schwarze ML, Shen Y, Hemmerich J, Dale W. Age-related trends in utilization and outcome of open and endovascular repair for abdominal aortic aneurysm in the United States, 2001-2006. J Vasc Surg. 2009;50:722-729 e722.
3. EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. Lancet. 2005;365:2179-2186.
4. Blankensteijn JD, de Jong SE, Prinssen M, et al. Two-year outcomes after conventional or endovascular repair of abdominal aortic aneurysms. N Engl J Med. 2005;352:2398-2405.
5. Greenhalgh RM, Brown LC, Powell JT, et al. Endovascular versus open repair of abdominal aortic aneurysm. N Engl J Med. 2010;362:1863-1871.
6. De Bruin JL, Baas AF, Buth J, et al. Long-term outcome of open or endovascular repair of abdominal aortic aneurysm. N Engl J Med. 2010;362:1881-1889.
7. Schanzer A, Greenberg RK, Hevelone N, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. Circulation. 2011;123:2848-2855.
8. El Batti S, Cochennec F, Roudot-Thoraval F, Becquemin JP. Type II endoleaks after endovascular repair of abdominal aortic aneurysm are not always a benign condition. J Vasc Surg. 2013;57:1291-1297.
9. Brenner DJ, Hall EJ. Computed tomography—an increasing source of radiation exposure. N Engl J Med. 2007;357:2277-2284.
10. Hiramoto JS, Reilly LM, Schneider DB, et al. The effect of magnetic resonance imaging on stainless-steel Z-stent-based abdominal aortic prosthesis. J Vasc Surg. 2007;45:472-474.
11. Sandford RM, Bown MJ, Fishwick G, et al. Duplex ultrasound scanning is reliable in the detection of endoleak following endovascular aneurysm repair. Eur J Vasc Endovasc Surg. 2006;32:537-541.
12. Sidloff DA, Stather PW, Choke E, et al. Type II endoleak after endovascular aneurysm repair. Br J Surg.2013;100:1262-1270.
13. 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.
14. Jones JE, Atkins MD, Brewster DC, et al. Persistent type 2 endoleak after endovascular repair of abdominal aortic aneurysm is associated with adverse late outcomes. J Vasc Surg. 2007;46:1-8.
15. Zhou W, Blay E Jr., Varu V, et al. Outcome and clinical significance of delayed endoleaks after endovascular aneurysm repair. J Vasc Surg. 2014;59:915-920.
16. Chaikof EL, Brewster DC, Dalman RL, et al. SVS practice guidelines for the care of patients with an abdominal aortic aneurysm: executive summary. J Vasc Surg. 2009;50:880-896.

INCRAFT® AAA Stent Graft System

INDICATIONS FOR USE

The **INCRAFT® AAA Stent Graft System** is intended for the endovascular treatment of patients with infrarenal abdominal aortic aneurysms (AAA) with the following characteristics:
Femoral access vessels should be adequate to fit the selected delivery system
Proximal neck length ≥ 10 mm
Aortic neck diameters ≥ 17 mm and ≤ 31 mm
Aortic neck suitable for suprarenal fixation
Infrarenal and suprarenal neck angulation ≤ 60°
Iliac fixation length ≥ 15 mm
Iliac diameters ≥ 7 mm and ≤ 22 mm
Minimum overall AAA treatment length (proximal landing location to distal landing location) ≥ 128 mm
Morphology suitable for aneurysm repair

CONTRAINDICATIONS

The **INCRAFT® AAA Stent Graft System** is contraindicated for:
Patients with a known allergy or intolerance to nickel titanium (nitinol), polyethylene terephthalate (PET), or polytetrafluoroethylene (PTFE).
Patients with a known contraindication to undergoing angiography or anticoagulation.

Durability and long-term data of the INCRAFT® AAA Stent Graft System are based on 2-year clinical follow-up and benchtop data.

For healthcare professionals only. Important information: Prior to use, refer to the Instructions for Use supplied with this device for indications, contraindications, side effects, suggested procedure, warnings, and precautions.

As part of the Cordis policy of continuous product development, we reserve the right to change product specifications without prior notification.

The INCRAFT® AAA Stent Graft System should only be used by physicians and teams trained in vascular interventional techniques, including training in the use of this device. Specific training expectations are described in the Instructions for Use.

Contact your Cordis sales representative for availability and ordering. Cordis Medical Affairs may be reached at RA-CRDUS-CordisMedAf@ITS.JNJ.com.

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