

First-in-human study of the INCRAFT endograft in patients with infrarenal abdominal aortic aneurysms in the INNOVATION trial

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Objective: This multicenter, prospective, nonrandomized trial was undertaken to evaluate the first-in-human experience with the INCRAFT endograft (Cordis Corporation, Bridgewater, NJ), an ultralow-profile trimodular bifurcate device for the repair of abdominal aortic aneurysms.

Methods: Patients with asymptomatic infrarenal abdominal aortic aneurysms were eligible for enrollment in the trial. Anatomic eligibility criteria included a proximal aortic neck at least 15 mm in length and up to 27 mm in diameter, and an aortic bifurcation ≥ 18 mm in diameter. Iliofemoral access vessels were required to be large enough to accept the 14F (4.7 mm) outer diameter of the delivery system. The primary efficacy end point was technical success, defined by successful device deployment during the conclusion of the procedure at the desired location without a type I, III, or IV endoleak. The primary safety end point was defined by the absence of a type I, III, or IV endoleak or a device- or procedure-related major adverse event at the 1-month follow-up point.

Results: Over a 16-month period divided into two different phases, 57 men and three women with a mean age of 74.4 ± 6.9 years were enrolled at three German and three Italian centers. A percutaneous approach was used in 36 patients (60%). Successful graft deployment at the desired location was achieved in 59 patients (98%). A single patient had successful deployment of the device although it was located more distally than planned. Technical success was achieved in 54 patients (90%); one patient had a type I endoleak, four had type IV endoleaks, and one had an endoleak of undetermined origin. The primary safety end point was met in 56 of the 58 patients (97%) with complete core laboratory data at 1 month; two patients had type I endoleaks. There were no type III or IV endoleaks and no device or procedure-related major adverse events at 1 month. No limb thromboses or stent fractures were noted on postoperative imaging studies and no patient required rehospitalization, a secondary procedure, or open surgical conversion through 1 month of follow-up.

Conclusions: The INCRAFT endograft device holds promise as an innovative alternative to currently marketed devices and broadens the eligibility for endovascular aneurysm repair. More definitive observations will be generated as longer-term data from this trial become available. (*J Vasc Surg* 2013;57:906-14.)

Historically, open surgical repair has been the gold standard method for preventing rupture of abdominal aortic aneurysms (AAAs).¹⁻³ Endovascular aneurysm repair (EVAR) evolved in the early 1990s as a minimally invasive treatment option. The use of EVAR increased over time, and more than 50% of elective AAA repairs are now

performed with this approach.⁴ The widespread applicability of EVAR, however, is limited by current device technology such that patients with challenging arterial anatomy are either unsuitable for a minimally invasive approach or have an increased risk of device-related complications over time.⁵⁻⁸ Further, preprocedure imaging studies can only estimate the aortoiliac length and diameter measurements encountered with conformational changes that occur during device implantation. Many commercially available devices have limited ability for length adjustment on a real-time basis to reliably conform to the specific anatomic configurations encountered intraprocedurally in an individual patient.⁹⁻¹¹

INCRAFT (Cordis Corporation, Bridgewater, NJ) is a highly customizable, ultralow-profile stent graft that can be efficiently deployed and accurately placed over a wide range of vessel sizes and configurations.¹² The device employs an integrated delivery system with a 13F inner diameter and 14F outer diameter (OD) to improve deliverability through tortuous or small access vessels and reduce the risk of delivery-related complications. The device has radiopaque maximum and minimum overlap marker bands to facilitate precise in situ length adjustment during

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deployment of the iliac limbs, accommodating the broad spectrum of anatomic variability encountered during a procedure. Herein, we report the first in-human experience with the INCRAFT device, assessing periprocedural outcome in the first 60 treated patients.

METHODS

The INNOVATION study (multicenter, open-label, prospective, nonrandomized study of INCRAFT in subjects with AAAs) is a multicenter, prospective, nonrandomized evaluation of the first in-human experience with the INCRAFT device. Patients were enrolled in two phases. The first phase of the trial included 25 patients at three German sites, enrolled between March and November 2010. To comply with regulatory requests for a larger sample size, the protocol was revised to increase the study to 60 patients, and three Italian sites were added. Between March and June 2011, 35 additional patients were enrolled in the second phase of the trial. The trial was registered on ClinicalTrials.gov (NCT01106391) and Competent Authority approval was obtained. The study was conducted in accordance with the International Conference on Harmonization Guidelines, Good Clinical Practices, Declaration of Helsinki, ISO 14155-1, ISO 14155-2, and ethics committee requirements, and all patients gave written informed consent prior to participation.

On the basis of on site-determined measurements and driven by the limited INCRAFT sizes available during this study, patients were eligible for inclusion if the aneurysm was ≥ 4.5 cm in diameter in women or ≥ 5.0 cm in men, or ≥ 4.0 cm in either sex but had increased in diameter by ≥ 0.5 cm over the prior 6 months. Patients were also eligible if the aneurysm sac was ≥ 1.5 times the diameter of the reference aortic diameter measured 15 mm inferior to the distal main renal artery or if the aneurysm was of saccular morphology. The iliofemoral access arteries needed to be suitable to accommodate a 14F profile delivery system (4.7 mm) and patients were excluded if the aortic bifurcation was ≤ 18 mm in diameter. Major inclusion and exclusion criteria are listed in Table I. Overall, 78 patients were consented and screened, and 18 failed to meet the eligibility criteria (23%), leaving 60 patients who underwent device implantation and constituted the study population.

Device and the delivery system. The INCRAFT AAA Stent graft System is a trimodular (one aortic bifurcate prosthesis main body and two iliac limb prostheses), bifurcated, endovascular graft (Fig 1) that is preloaded into a delivery system. The device is typically assembled from the three components: the aortic bifurcate prosthesis main body and the two iliac limb prostheses. If distal extension is desired, additional iliac limb prostheses can be deployed. The endograft is constructed of a seamless, low-porosity, woven polyester fabric tube, supported by a series of electropolished, laser-cut, self-expanding nitinol stent rings along its entire length, each sutured to the inner surface of the graft material. Radiopaque markers are affixed to the device to facilitate fluoroscopic positioning. The aortic bifurcate prosthesis has a short infrarenal sealing endoskeleton and a proximal transrenal bare

Table I. Major eligibility criteria

Inclusion criteria	
Age	≥ 18 years
Candidacy for open surgical repair of an AAA	
AAA	
Diameter	≥ 4.5 cm in women or ≥ 5 cm in men, or Diameter >4 cm that has increased in size by 0.5 cm within 6 months, or Diameter ≥ 1.5 times aortic diameter measured 15 mm distal to lowermost main renal artery, or Saccular configuration
Access vessel size	compatible to a 14F (4.7 mm) outer diameter delivery system
Proximal neck length	≥ 15 mm
Proximal neck diameter	20-27 mm
Iliac landing zone length	≥ 10 mm
Iliac landing sites diameter	9-18 mm
Length from lowest renal artery to distal landing zone	of ≥ 140 mm
Exclusion criteria	
Aortic dissection	
Inflammatory aneurysm	
Ruptured aneurysm	
Pararenal aneurysm	
Suprarenal aorta	2 cm above lowest renal artery that is not more than the nominal diameter of the aortic bifurcate prosthesis
Suprarenal or infrarenal angulation	of $>60^\circ$
Aortic bifurcation	≤ 18 mm in diameter
Aortic length (lowest renal artery origin to the aortic bifurcation)	<8.7 cm
Circumferential thrombosis and/or calcification	$\geq 50\%$ in the suprarenal aorta, proximal aortic neck, or iliac landing zones

AAA, Abdominal aortic aneurysm.

stent with eight laser-cut barbs near the cranial apex of each bare stent. The modular endograft components use suture knots on the outer surface of the limb prostheses, acting as an interlocking mechanism to decrease the risk of limb disunion. The maximum and minimum radiopaque marker bands facilitate precise fluoroscopic visualization and allow intraprocedural length adjustment 2 to 3 cm between interlocking modular components. At the time of the study, the aortic bifurcate device was supplied in 26- and 30-mm diameters to accommodate a range of aortic diameters from 20.0 to 22.9 mm and from 23.0 to 26.9 mm, respectively. Iliac graft limbs were available in diameters of 13, 16, and 20 mm, accommodating iliac vessels from 9.0 to 10.9, 11.0 to 13.9, and 14.0 to 17.9 mm in diameter, respectively.

There are two variations of the delivery system; one for the aortic bifurcate prostheses and one for the iliac limb prostheses. The delivery system for the aortic bifurcate prosthesis has an inner diameter of 13F (14F OD) integrated sheath introducer and does not employ a cap, simplifying the deployment procedure. The delivery system for the iliac limb prosthesis is similar to that of the aortic bifurcate prosthesis, except that it is smaller in diameter (12.5F OD) and does not have an integrated sheath introducer. The delivery system facilitates controlled deployment at the intended location (Fig 2). The prostheses are deployed by turning the handle of the delivery system until the sheath begins to retract. The barbs are unsheathed at the beginning of deployment,

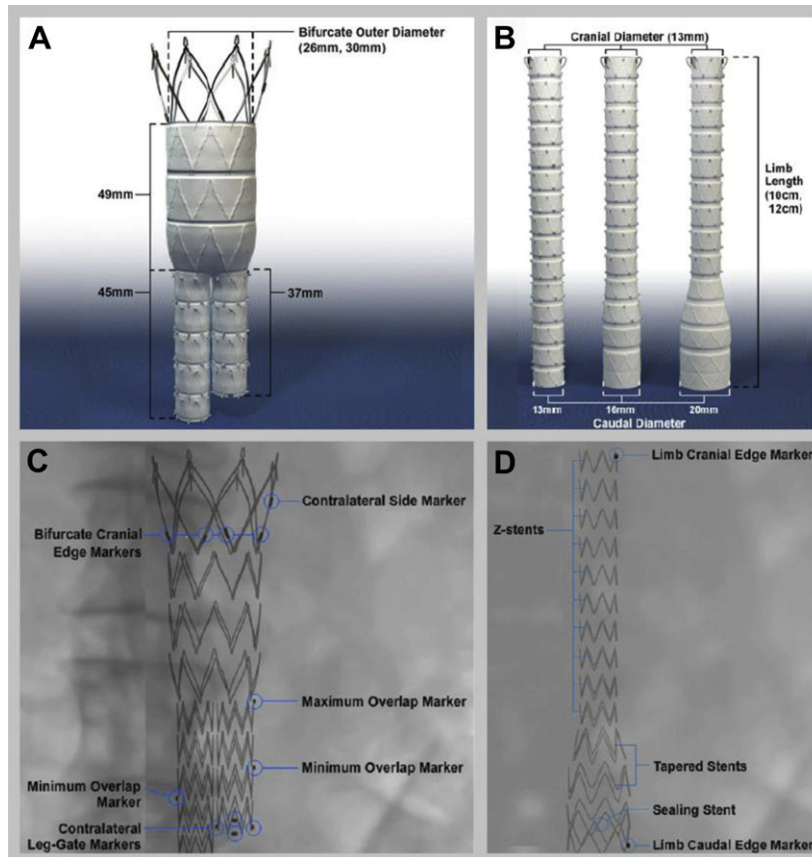


Fig 1. INCRAFT endograft. **A** and **B**, Abdominal bifurcate and limb diameter and length. **C** and **D**, Radiographs showing stent components and radiopaque markers.

but remain constrained, and adjustment of the proximal position of the main body device is possible. Repositioning remains possible until the graft is unsheathed beyond the contralateral side markers and the fixation release wire is pulled to fully unconstrain the cranial aspect of the transrenal stents.

Study end points. The study was designed with primary efficacy and primary safety end points. The primary efficacy end point was technical success, defined by successful device deployment at the desired location without a type I, III, or IV endoleak at the conclusion of the procedure. This definition is similar to that of the Society for Vascular Surgery reporting standards, except that type IV endoleaks and device deployment at other than the intended location were included in the current study.¹³ Major adverse events were defined as any death, myocardial infarction, stroke, or occurrence of renal failure. The primary safety end point was defined by the absence of a type I, III, or IV endoleak or device- or procedure-related major adverse event (death, myocardial infarction, stroke, or renal failure) at 1 month. Secondary end points were measured at 1 month and included stent fracture, graft thrombosis, and device explanation. The length of intensive care unit stay, if any, as well as the postprocedure and total length of hospital stay, was recorded.

Follow-up assessments. Vital signs and medications were recorded at discharge and 1 month. Subsequent follow-up visits will occur at 6 months, 12 months, and annually thereafter up to 5 years and will be the subject of subsequent communications, as data become available. Follow-up imaging at 1 month included abdominal computed tomography (CT), adding plain-film radiography when the CT scan was inadequate to assess stent graft integrity or stent fracture. Accuracy of endograft placement was assessed by core laboratory measurement of the distance between the graft edge marker of the aortic bifurcate prosthesis and the lowest renal ostium on the 1-month CT scan. Any reinterventions or rehospitalizations were tabulated through 1 month, as were adverse events categorized by relatedness to the device or to the procedure, severity (mild, moderate, or severe), and whether they were serious or unanticipated.

Data analysis. No formal hypothesis testing was implemented in this feasibility study; rather, descriptive statistics alone were used. Patient source documentation was fully monitored by site-independent clinical research associates and assessed for completeness and accuracy. Any discrepancies were resolved by queries with the site investigator or designee. All CT images, plain film abdominal radiographs, and procedure arteriograms were reviewed by the independent core laboratory. Clinical events were adjudicated by

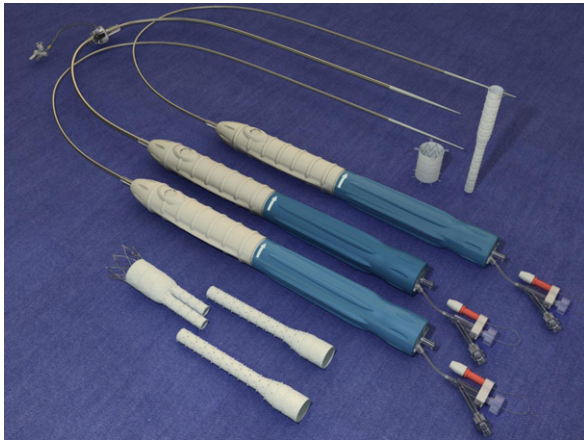


Fig 2. INCRAFT delivery system.

a Clinical Events Committee (CEC) composed of three independent experts not participating as investigators in the trial. The CEC adjudicated all protocol-defined major adverse events and type I, III, and IV endoleaks. Type II endoleaks were adjudicated only when there was a discrepancy between the site and the core laboratory assessment. A Data and Safety Monitoring Board consisting of the three CEC members was also established. The Data and Safety Monitoring Board reviewed the data on a periodic basis to determine the necessity of protocol modifications or, if major safety issues arose, to recommend discontinuation of the trial. Core laboratory and CEC-adjudicated data are specified throughout, unless otherwise noted.

RESULTS

The 57 men and three women were an average of 74.4 ± 6.9 years of age. Patient baseline clinical characteristics are summarized in Table II. Anatomic characteristics are summarized in Table III. Mean aneurysm diameter was 52.6 ± 9.2 mm, with a median of 52.2 mm (range, 34.7-101 mm). Patients were enrolled for aneurysms, ≥ 45 mm if female and ≥ 50 mm if male, in 30 cases (50%); for AAAs ≥ 1.5 times the diameter of the reference aorta in 26 cases (43%); for AAAs that enlarged by ≥ 5 mm over 6 months in two cases (3%); and for saccular AAAs in two cases (3%). The maximum AAA diameter was less than 40 mm in one patient (2%), 40-49 mm in 21 patients (35%), 50-59 mm in 31 patients (52%), 60-69 mm in six patients (10%), and ≥ 70 mm in one patient (2%). The configuration of the proximal neck was parallel in 58 patients (97%), conical in one patient (2%), and reverse-tapered in another patient (2%). Using the Society for Vascular Surgery grading classification for morphological risk, 45% of patients had hostile anatomy that met criteria for the "severe" classification (Table IV; Fig 3).¹⁴

The aortic bifurcate was introduced from the right side in 54 patients (90%). Percutaneous access with Perclose devices (Abbott Vascular, Redwood City, Calif) was employed in 36 of 60 patients (58%), bilaterally in 34 patients (94%), and unilaterally in two patients (6%), and the devices were

successfully delivered in all cases. A standard trimodular configuration was used in 56 patients (93%), whereas four patients (6.7%) had additional iliac extensions placed as planned procedures to reach the desired distal landing location. All 60 patients had successful deployment of the endografts without open surgical conversion or unintentional renal or hypogastric artery occlusion. The endografts were deployed at the intended aortic location in 59 patients (98%); a single patient had successful deployment of the aortic bifurcate prosthesis, although 10 mm distal to the lowest renal artery, and an aortic extension cuff was used to obtain additional sealing length. Additional endovascular procedures were performed in seven patients (12%). Self-expanding nitinol stent placement into a graft limb was attempted in four patients (7%), each to prevent future problems within a diseased or tortuous iliac artery; none of the stented limbs had stenosis or kinking evident at the time of deployment. Among the four stents, three were actually deployed; one dislodged prior to deployment and was retrieved without subsequent placement of another stent. Therapeutic embolization of side branches was performed in two patients (3%), one on the inferior mesenteric artery and one on the hypogastric artery. A renal stent was placed in one patient in whom preexisting 80% renal artery stenosis worsened after angioplasty. The median postprocedure length of hospital stay was 5 days (range, 2-55 days). Additional technical details of the procedures and hospitalizations are provided in Table V.

Endografts were placed with a high degree of accuracy, with a mean distance between lowest renal artery and the proximal graft edge markers of 3 mm (range, -4 to 15 mm, without renal coverage). A core laboratory measurement value of -4 mm was recorded, measuring the distance on CT from the caudal point of the lowest renal ostium to the caudal end of the second cranial graft-edge marker. Although this measurement is accurate, it does not take into account that the graft is positioned perpendicular to the centerline and that the graft itself starts 0.0-1.0 mm below the marker. The postdeployment images do not reveal any renal artery obstruction in this patient. The patient with deployment 15 mm below the lowest renal artery had the device placed at this location because of unfavorable anatomy in the cranial aspect of the proximal aortic neck. Distally, the distance between the caudal graft-edge markers and the hypogastric orifices averaged 12.2 mm, with mean common iliac artery coverage of 79% by length. At the conclusion of the procedure, 55 patients (92%) had no evidence of type I, III, or IV endoleak (Table VI). With the additional patient with graft deployment 10 mm below the renal level, the primary efficacy end point of technical success was achieved in 54 of 60 patients (90%; 95% confidence interval [CI], 80%-96%).

The primary safety end point was met in 56 of 58 patients (97%; 95% CI, 88%-100%) with core laboratory imaging available within the 1-month window. No patient experienced a device- or procedure-related major adverse event and 56 patients were free from type I, III, or IV endoleaks at 1 month (Table VI). Type I endoleaks were noted in two patients (3.3%). One patient had extensive aortic and

Table II. Patient baseline characteristic

Characteristic	Mean \pm SD [95% CI] or % (number/total) [95% CI]
Age (mean), years	74.4 \pm 6.9 [72.6, 76.2]
Proportion male	95% (57/60) [86%, 99%]
Body mass index	26.7 \pm 3.1 [25.9, 27.5]
Smoking history	
Current smoker	10% (6/60) [4%, 21%]
Former smoker	75% (16/25) [62%, 85%]
Diabetes	
Insulin-dependent diabetes	5% (6/60) [1%, 14%]
Non-insulin-dependent diabetes	17% (10/60) [8%, 29%]
Hypertension	95% (57/60) [86%, 99%]
Hyperlipidemia	70% (42/60) [57%, 81%]
Renal status	
Creatinine level, mg/dL	1.0 \pm 0.3 [1.0, 1.1]
<1.5 mg/dL	92% (55/60) [82%, 97%]
1.5-2.0 mg/dL	7% (4/60) [2%, 16%]
>2.0 mg/dL	2% (1/60) [0%, 9%]
Pulmonary status	
No clinically evident lung disease	70% (42/60) [57%, 81%]
Clinically evident lung disease (COPD)	25% (15/60) [15%, 38%]
Other	7% (4/60) [2%, 16%]
Ischemic heart disease ^a	
Asymptomatic, normal ECG	55% (33/60) [42%, 68%]
History of arrhythmia	22% (13/60) [12%, 34%]
History of angina	13% (8/60) [6%, 25%]
History of myocardial infarction	25% (15/60) [15%, 38%]
Previous CABG	15% (9/60) [4%, 21%]
PTCA \pm stent	10% (6/60) [0%, 9%]
Carotid/cerebral vascular disease	
No disease	64% (38/59) [51%, 76%]
Asymptomatic stenosis	22% (13/59) [12%, 35%]
Transient ischemic attack	10% (6/59) [4%, 21%]
Completed stroke	3% (2/59) [0%, 12%]
Malignancy	15% (9/60) [7%, 27%]
Lower extremity arterial disease	8% (5/60) [3%, 18%]

CABG, Coronary artery bypass graft; CI, confidence interval; COPD, chronic obstructive pulmonary disease; ECG, electrocardiogram; PTCA, percutaneous transluminal coronary angioplasty; SD, standard deviation.

^aA single patient had unknown coronary status.

iliac calcification on preoperative CT imaging studies. This patient had evidence of a type I endoleak on completion arteriography, and placement of a Palmaz XL stent (Cordis Corporation) into the proximal aortic neck diminished but did not resolve the endoleak. The endoleak remained evident on the 1-month CT imaging study, but was subsequently treated successfully after reintervention with balloon inflation at the proximal attachment site. A type I endoleak in a second patient was initially reported as a type II endoleak by the site, but was subsequently adjudicated as a type I endoleak by the CEC. This endoleak resolved after placement of an aortic extender cuff and chimney graft to the left renal artery, with endostapling at the proximal attachment site. These two secondary interventions were performed after the 1-month follow-up point.

Among the 60 enrolled patients, five procedure-related serious adverse events occurred in four patients (7%). These events included bleeding or hematoma formation at an access site in two patients, one external iliac dissection, and one lymphorrhea (Table VII). The iliac dissection occurred on the side of main body introduction and was treated with the deployment of an endograft limb to exclude the area of

injury. There were five serious adverse events in four patients that were not related to the device or the procedure. There were no protocol-specified major adverse events, no device-related serious adverse events, and no unanticipated adverse device effects through 1 month of follow-up. Similarly, no patient underwent open surgical conversion, and there were no limb occlusions, endograft migrations, secondary procedures, or rehospitalization through 1 month of follow-up. Eight access-related adverse events occurred in seven patients (three percutaneous, four open), including four bleeding events (three percutaneous, one open), three lymphatic complications (all open), and one false aneurysm formation (percutaneous). Among 54 patients with plain abdominal radiographs evaluated at 1 month by the core laboratory, no stent fractures or barb separations were observed.

DISCUSSION

Although EVAR has become a desirable alternative to traditional open surgical repair of AAAs, clinical outcome continues to be suboptimal in patients with complex aortoiliac anatomy. Challenges for current devices fall into two

Table III. Anatomic characteristics on the initial CT imaging study (Core Laboratory determinations)

<i>Anatomic measurement</i>	<i>Mean ± SD (range) [95% CI]</i>
Suprarenal aortic diameter, mm	24.2 ± 2.0 (19.5-29.5) [23.7, 24.8]
Proximal neck diameter, cranial, mm	22.3 ± 2.2 (17.0-29.5) [21.7, 22.8]
Proximal neck diameter, caudal, mm ^a	23.0 ± 2.4 (18.0-29.1) [22.4, 23.7]
Proximal neck length, mm	26.9 ± 11.3 (5.0-49.8) [24.0, 29.8]
Suprarenal neck angulation, degrees (°)	14 ± 8.3 (0.7-51) [12, 16]
Infrarenal neck angulation, degrees (°)	34 ± 14 (7-67) [31, 38]
Maximum aneurysm diameter, mm	52.6 ± 9.2 (34.7-101) ^b [50.2, 55.0]
Aortic bifurcation diameter, mm	20.6 ± 4.6 (11.0-33.0) [19.4, 21.7]
Right distal iliac landing site diameter, mm	13.2 ± 1.8 (9.0-18.0) [12.7, 13.6]
Left distal iliac landing site diameter, mm	13.9 ± 2.5 (9.3-20.5) [13.2, 14.5]
Right access vessel minimum diameter, mm	7.2 ± 1.3 (4.3-10.1) [6.9, 7.5]
Left access vessel minimum diameter, mm	7.1 ± 1.5 (3.6-10.0) [6.8, 7.5]

CI, Confidence interval; CT, computed tomography; SD, standard deviation.

^aMeasured 15 mm distal to the inferiormost main renal artery.

^bA single patient had a 34.7-mm aneurysm that was measured by the site to be 41 mm and ≥1.5 times the reference aortic diameter.

Table IV. Proportion of patients with severe morphology as determined by core Laboratory measurements^a

<i>Anatomic measurement</i>	<i>Threshold for severe grade^b</i>	<i>Proportion with severe grade</i>
Infrarenal neck angulation	≥60°	5%
Proximal neck diameter	>28 mm	2%
Proximal neck length	<10 mm	17%
Right iliac artery sealing zone	<10 mm	10%
Left iliac artery sealing zone	<10 mm	13%
Right access artery diameter	<7 mm	44%
Left access artery diameter	<7 mm	46%

^aPatients are enrolled based on site-determined measurements. These measurements may differ from core laboratory measurements, accounting for enrollees with certain core laboratory determinations outside of the inclusion/exclusion criteria.

^bAs defined by grade 3 (severe) anatomy, Ad Hoc Committee for Standardization Reporting Practices in Vascular Surgery of the Society for Vascular Surgery/American Association for Vascular Surgery.

general categories: safe access through compromised access vessels, and reliable fixation and sealing within nonideal proximal or distal attachment sites.¹⁵ These limitations explain the continued necessity for open surgical repair in approximately one-third of candidates.¹⁶ Long-term failures of sealing and fixation and graft limb patency issues continue to occur in patients in whom the anatomic eligibility indications for EVAR have been stretched.¹⁷ Lastly, most marketed devices lack flexibility for intraprocedural adjustments to accommodate inaccurate aortoiliac length and diameter measurements from preoperative imaging studies, requiring the use of additional components such as iliac extender limbs and adjunctive stents to achieve satisfactory aneurysm exclusion.¹⁰ The use of such adjuvant components not only increases the duration and cost of the procedure, but also increases the risk of early and late device-related complications.¹⁸

Smaller, tortuous, and atherosclerotic iliofemoral access vessels represent challenges to current devices. Navigation

through such vessels can be associated with arterial injury, intuitively more risky with larger-bore devices but still common with even the newest devices.¹⁹⁻²³ As well, whether percutaneous access will ultimately be proven to be beneficial over open femoral exposure, the approach has been preferred by some physicians and can be more difficult when the access vessels are small in relation to the delivery system.²⁴⁻²⁶ The introducer sheath for the Cook Zenith Flex device (Cook Medical, Bloomington, Ind) ranges from 21F OD for the smallest-diameter main body devices to 24.5F OD for the largest-diameter devices. The Excluder trunk (W. L. Gore, Flagstaff, Ariz) is delivered through a sheath similar in size to the Zenith: either 20.5F OD for the smaller-size device or 23F OD for the larger device. The Endologix AFX system (Endologix, Irvine, Calif) uses a 19F OD sheath, whereas the original Endologix Powerlink system used a 22F OD sheath. The Cook Zenith Low Profile endograft (Cook Medical), currently unavailable in the United States, is an 18F OD system. Lastly, the Medtronic Endurant (Medtronic Inc, Minneapolis, Minn) main body uses a somewhat smaller sheathless delivery system, ranging from 18F OD for the smaller sized devices to 20F OD for the larger devices.

Maximal coverage of the aorta within the proximal aortic neck and common iliac arteries is desirable to decrease the risk of endograft migration.^{27,28} It has long been known that the proximal sutured anastomosis of a surgically placed aortic graft should be placed as close to the renal orifices as feasible; failure to do so is associated with an increased risk of aneurysm formation above the level of the original graft.²⁹ Compared with that after open surgical repair, the outcome after endovascular repair may be more sensitive to changes in vessel diameter.³⁰ Whereas the danger of neck dilation after open repair does not become evident until the vessel dilates to a size where rupture is possible, even 2 or 3 mm of aortic neck dilatation was associated with a requirement for reinterventions in two studies.^{31,32} Although coverage of the aortoiliac segment from the renal arteries to hypogastric orifices is desirable, current devices are limited by the

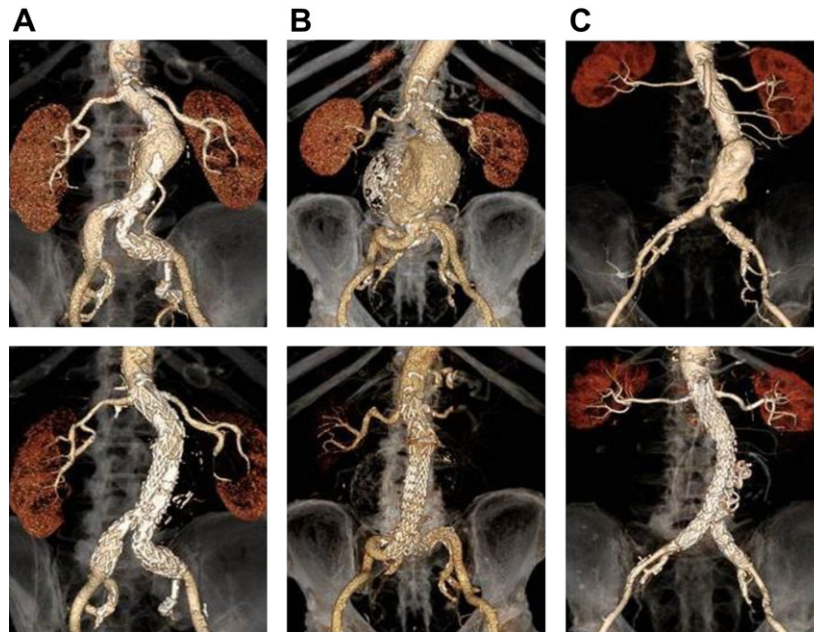


Fig 3. Treated patients who fell within the severe morphological classification (screening study at top, post-treatment on bottom). **A,** Severe neck angulation. **B,** Iliac tortuosity. **C,** Small external iliac arteries. Images were created with the ImagineSCT medical imaging system for clinical trials.

Table V. Details of the procedure and hospitalization

<i>Characteristic</i>	<i>Mean ± SD [95% CI]</i>
Total procedure time, minutes	118 ± 37 [109, 128]
Time to deploy device, minutes	42 ± 23 [36, 48]
Fluoroscopy time, minutes	21 ± 13 [18, 24]
Contrast administered, cc	127 ± 67 [110, 145]
Procedural estimated blood loss, cc	213 ± 170 [165, 261]
Postprocedure length of hospital stay, days	5.7 ± 6.8 [3.9, 7.4]

CI, Confidence interval; SD, standard deviation.

accuracy with which they can be delivered to the precise intended location. Imprecise delivery increases the need for additional endograft components. In the standard risk cohort of the Cook Zenith Investigational Device Exemption (IDE) trial, ipsilateral and contralateral iliac limb extensions were used in 9.5% and 11% of patients, respectively.³³ In the Ovation IDE trial, four or more components were implanted in 18.6% of patients.³⁴

The INCRAFT device was designed to address some limitations of currently available devices. The device has an ultralow-profile integrated delivery system with a 13F inner diameter and 14F OD that can fit through tortuous and small access vessels, improving the ease and speed of navigation and potentially reducing delivery-related complications. The lower profile of the delivery system is of particular value in patients with small or diseased iliofemoral access vessels, and facilitates percutaneous introduction when desired. The inability to accurately assess aortoiliac dimensions on

preoperative imaging studies is, in part, addressed by a broad spectrum of length and diameter applicability for relatively few sizes of graft components. As well, the portfolio of available device sizes was broadened after enrollment of the current series of patients, and current INCRAFT devices now accommodate proximal aortic necks ranging from 17 to 31 mm in diameter. The INCRAFT delivery mechanism allows for in situ customized length adjustment features to provide an individualized approach for patients. The INCRAFT device has a partial repositioning feature to improve proximal stent graft placement and fixation. The Gore C3 delivery system has a repositioning feature, whereas the Cook Zenith device does not offer this feature and the Medtronic Endurant has only limited repositioning capabilities.^{35,36}

For the first 60 patients treated with the INCRAFT device, feasibility and excellent periprocedural outcome were documented. The primary efficacy and safety end points were uniformly met, and the rate of endoleaks was acceptable. The accuracy of device deployment was high, with delivery of the INCRAFT aortic bifurcate prosthesis an average of 3 mm below the lowermost renal artery and deployment at the intended location in 98% of patients. The use of additional iliac extension limbs was necessary in only 7% of cases, likely a function of placement accuracy and the broad range of device overlap within the gate that provides the capacity for intraprocedural length adjustment. The lower-profile delivery system facilitated percutaneous access in the majority of patients, without conversion to open femoral exposure in any case. This outcome was achieved despite the particularly large number of patients with small access vessels compared

Table VI. Incidence of endoleaks^a

Type	Procedure (n = 60)	1 month (n = 58)			
		Still evident	Resolved	New	Total ^b
I	1	1	0	1	2
II	13	11	2	21	32
III	0	0	0	0	0
IV	4	0	4	0	0
Undetermined	1	0	1	0	0

^aEndoleaks at the conclusion of the procedure are site reported. Endoleaks at 1 month are Core Laboratory reported and adjudicated by the Clinical Events Committee.

^bTotal endoleaks = number still evident – number resolved + new endoleaks.

Table VII. Serious adverse events within 30 days of implantation

Category of serious adverse event	No. (%) of patients	No. of events
Procedure related	4 (7)	5
Hematoma or bleeding at puncture site	2 (3)	2
Pleural effusion	1 (2)	1
Lymphorrhoea	1 (2)	1
External iliac artery dissection	1 (2)	1
Device related	0	0
Neither procedure nor device related	4 (7)	5
Hypertension	1 (2)	1
Myocardial infarction	1 (2)	1
Dyspnea	1 (2)	1
Lymphocele	1 (2)	1
Claudication	1 (2)	1

with what is observed in the real-world setting. The mean external iliac diameter was only 7 mm, a size that is at the lower threshold specified by the instructions for use for most currently marketed devices.^{17,37} Studies of other devices report an increased risk of iliac graft limb thrombosis when smaller-diameter graft limbs are used.⁷ As well, limb occlusion rates have been high with newer, smaller-bore devices. The Medtronic Endurant graft had limb occlusion rates of 1.3% at 30 days and 2.7% at 12 months,³⁸ and a 7.7% thrombosis rate was observed at 12 months with the Cook Zenith AAA Low Profile endograft.³⁹ It remains unclear whether these limb problems relate to a trade-off between device profile and stent radial force or to an expansion of use to patients with more challenging iliac anatomy.^{38,40} Although 50% of limb occlusions have been reported to occur within 30 days of endovascular repair,^{7,38} the absence of INCRAFT limb complications must be confirmed by longer-term observations.

The 90% technical success rate observed in the current study was less than what has been characteristic of recent series, even when the series included patients with challenging anatomy.^{8,41-43} Although most reports use the Society for Vascular Surgery Reporting Standards definition of technical success, the current study added device

deployment at the desired location and type IV endoleak to the list of events that define success.¹³ Using the Society for Vascular Surgery definition for technical success, one patient with device deployment inferior to the intended site and four patients with type IV endoleaks would not have triggered the end point, resulting in a technical success rate of 98%, quite similar to that of other contemporary reports.³⁸ This difference in the definition of technical success, in large part, accounts for the differences between this study and prior reports. The 7% observed rate of type IV endoleaks in this study is higher than one might expect, but is similar to the 12% rate reported in the Endurant US IDE trial. Whether the higher rate of type IV leak in this study and in the Endurant trial relates to greater rigor in postdeployment angiography, better imaging equipment, or the fabric remains undefined, but clinical sequelae have not been observed.

CONCLUSIONS

In summary, this feasibility study confirms excellent short-term results with the INCRAFT device. The results, however, must be considered within the context of the short-term follow-up and the small study cohort of this first in-human experience. Confirmation that the device meets expectations must await the availability of longer-term data in a larger group of patients. Nevertheless, the findings suggest that the INCRAFT device holds promise as an innovative alternative to currently marketed devices and broadens the eligibility for EVAR. More definitive observations will be generated as longer-term data from this study become available, as well as after the completion of other INCRAFT investigational trials currently in progress in the United States and Japan and planned for Australia, New Zealand, and Europe.

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AUTHOR CONTRIBUTIONS

Conception and design: DS, AC

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