thoraflex™ hybrid

Instructions for Use

Rx only

TERUMO Aortic

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1 Device Description

Thoraflex™ Hybrid is designed for the open surgical repair of aneurysms and/or dissections in the aortic arch and descending aorta with or without involvement of the ascending aorta. There are two types of Thoraflex™ Hybrid implants, namely the Plexus 4 and the Ante-Flo versions. Each patient receives one Thoraflex™ Hybrid device (either the Plexus 4 or Ante-Flo). For patients that need additional length for repair of their lesions, the Relay®Pro Non-Bare Stent (NBS) Thoracic Stent Graft System can be used to extend the repair. If a Relay®Pro NBS Thoracic Stent Graft System is to be used, please refer to the Relay®Pro NBS Thoracic Stent Graft System IFU for additional information on that device.

Thoraflex™ Hybrid Device

The Thoraflex™ Hybrid device is a gelatin coated vascular graft combined with a distal stented graft, supplied pre-loaded in a single use delivery system. The entire implant is coated with gelatin, loaded into a delivery system and terminally sterilized. The Thoraflex™ Hybrid implant, once placed in the aorta, provides an alternative conduit for blood flow while excluding the lesion. Thoraflex™ Hybrid is designed to perform the Frozen Elephant Trunk (FET) procedure in which a diseased aortic arch/ascending aorta is replaced by a surgical graft and a stented graft is placed in the descending thoracic aorta (DTA). FET allows for more of the aorta to be treated from a smaller opening in the chest than a conventional Elephant Trunk (ET) procedure.

Thoraflex™ Hybrid Implant

The Thoraflex™ Hybrid implant consists of a proximal vascular graft section, a collar, and a distal stented graft section. Each of these aspects of the implant are described in **Figure 1** below.

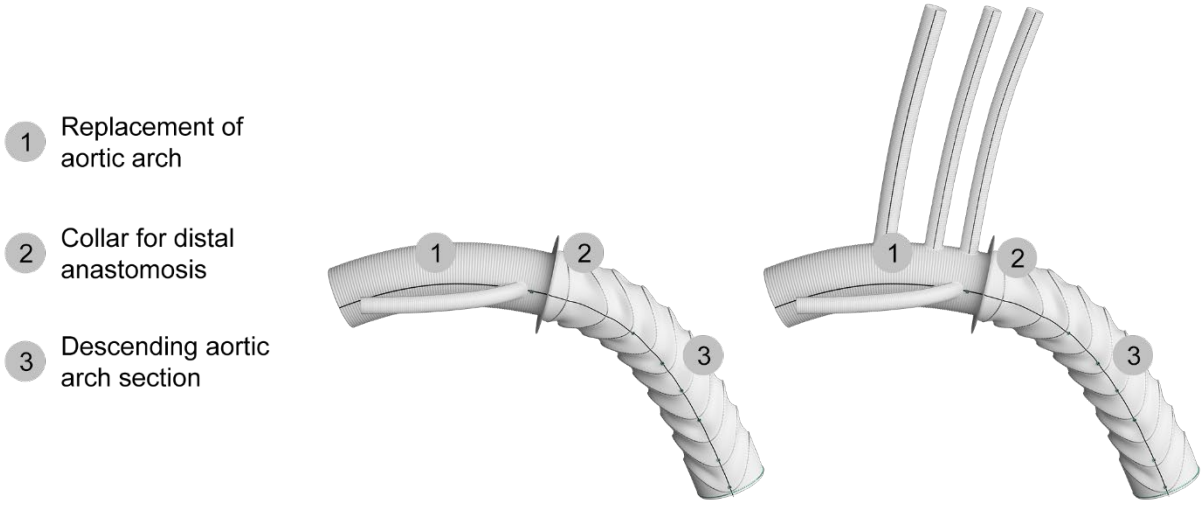


Figure 1 – Key Aspects of a Thoraflex™ Hybrid Device

The implant is comprised of a woven polyester graft material that is gelatin coated. Radiopaque tantalum markers aid visualization.

The proximal graft section is crimped. The distal stented graft section is comprised of self-expanding nitinol stents sutured to the woven polyester fabric using polyester sutures. The stent scaffold is a series of springs stacked in a tubular configuration. These stents are externally spaced along the length of the graft fabric to provide radial support and allow for the self-expansion of the distal stented graft section. For visualization when extending the Thoraflex™ Hybrid device, there are radiopaque tantalum markers located at approximately 20mm increments starting from the most distal end of the device and covering a total length of 100mm.

The design of the distal stented graft section of the Thoraflex™ Hybrid device can be considered in two main zones (**Figure 2**): Zone 1 (the proximal part) and Zone 2 (the distal part). Zone 1 is designed to be flexible in order to conform to the aortic arch anatomy, as well as to have column stiffness to maintain its form in the straight section of the vessel. The proximal part of the stented section is attached to the vascular graft section and is designed to provide a seal comparable to the permeability of the rest of the device. Zone 2 is the sealing/docking zone designed to create a blood flow conduit between the proximal vascular graft section and the healthy vessel in the region of the distal landing zone. The distal stent rings are designed to provide distal sealing or alternatively, a docking zone for landing a Relay®Pro NBS Thoracic Stent Graft System in patients that need an extension procedure.

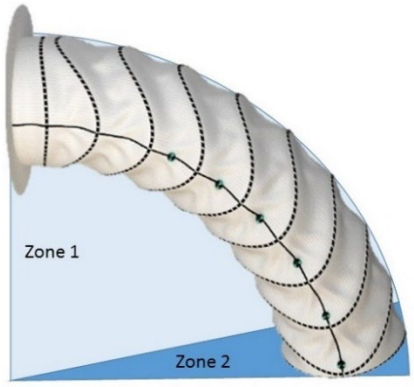


Figure 2 - Structure of the Distal Stented Graft Section

The collar is designed to facilitate the anastomosis of the graft to the native vessel. The anastomosis also provides proximal fixation of the distal stented graft section of the device.

The Thoraflex™ Hybrid device is available in two configurations, which differ only in the proximal vascular graft section, which are the Plexus 4 and Ante-flo versions. The Plexus 4 version (**Figure 3**) includes three branches for attachment to the great vessels and an Ante-Flo branch to aid cannulation and perfusion. The Ante-Flo version (**Figure 4**) contains only a single Ante-Flo branch.

The Thoraflex™ Hybrid device is tapered between the proximal vascular graft section and the distal stented graft section. For each configuration, the proximal vascular graft section is available in 22 – 32 mm diameters, and the distal stented graft section is available in 24 - 40 mm diameters. The distal stented section is available in 100 mm and 150 mm lengths. The branches are available in 8 - 12 mm diameters dependent on the graft configuration.

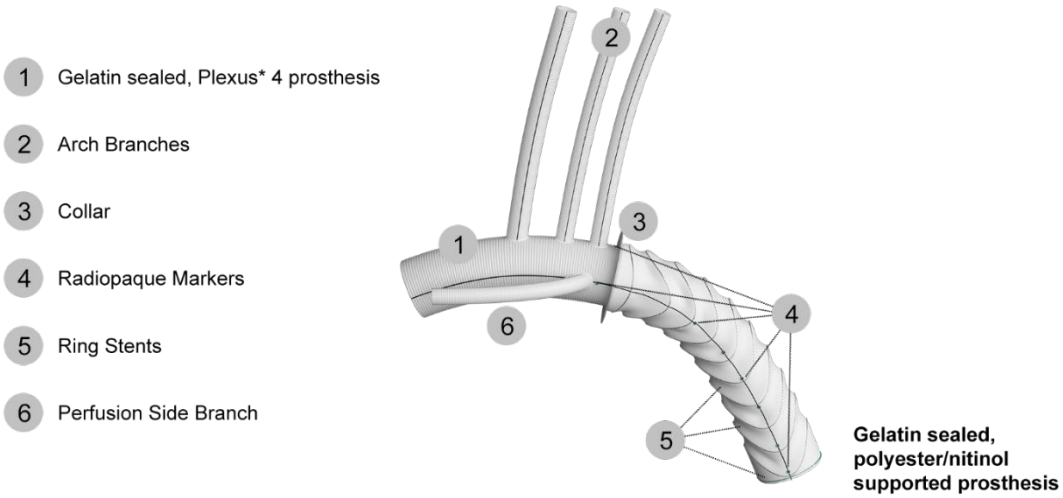


Figure 3 - Thoraflex™ Hybrid Plexus 4 implant

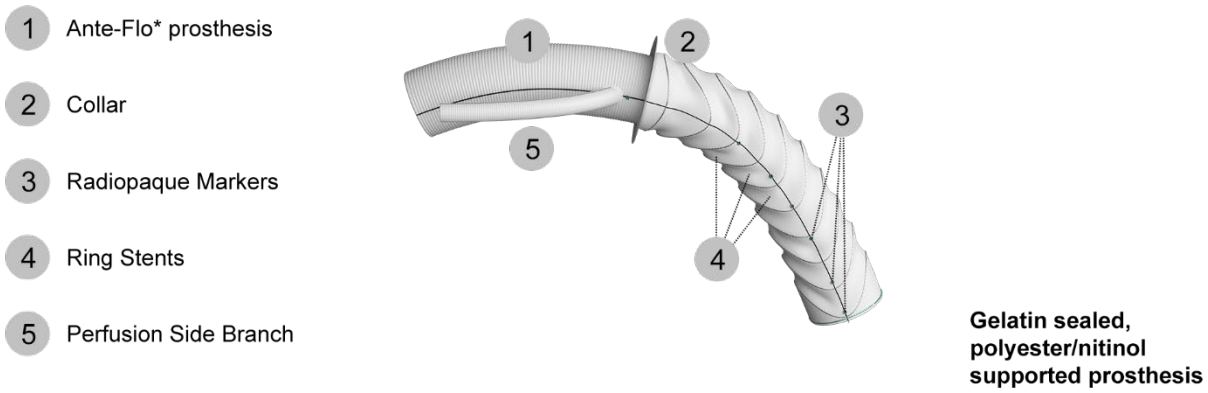


Figure 4 - Thoraflex™ Hybrid Ante-Flo implant

Table 1 provides a summary of Thoraflex™ Hybrid materials.

Table 1 - Thoraflex™ Hybrid Materials of Construction

Implant Component	Material
Stent	Nitinol
Graft	Gelatin Impregnated Polyester
Radiopaque Markers	Tantalum
Sutures	Polyester
Collar	Polyester
Eyelets	Polyethylene Terephthalate (PET) Monofilament

Thoraflex™ Hybrid Delivery System

The Thoraflex™ Hybrid device is supplied pre-loaded in a delivery system (**Figure 5**) which is designed to facilitate delivery and accurate deployment in the patient's descending aorta. The delivery systems for the Plexus and Ante-Flo configurations are identical. The general design provides a delivery aid for the user and provides the device in a compacted state. The distal stented portion of the device is compacted into a PTFE sheath, while the proximal vascular graft section remains largely uncompacted. This allows the distal stented portion to be inserted into the descending aorta while the proximal vascular graft section retains its crimped form. As the device is unsheathed to release the distal stented portion into the descending aorta, the delivery system causes the sheath to split around the proximal vascular graft section to leave it unaffected.

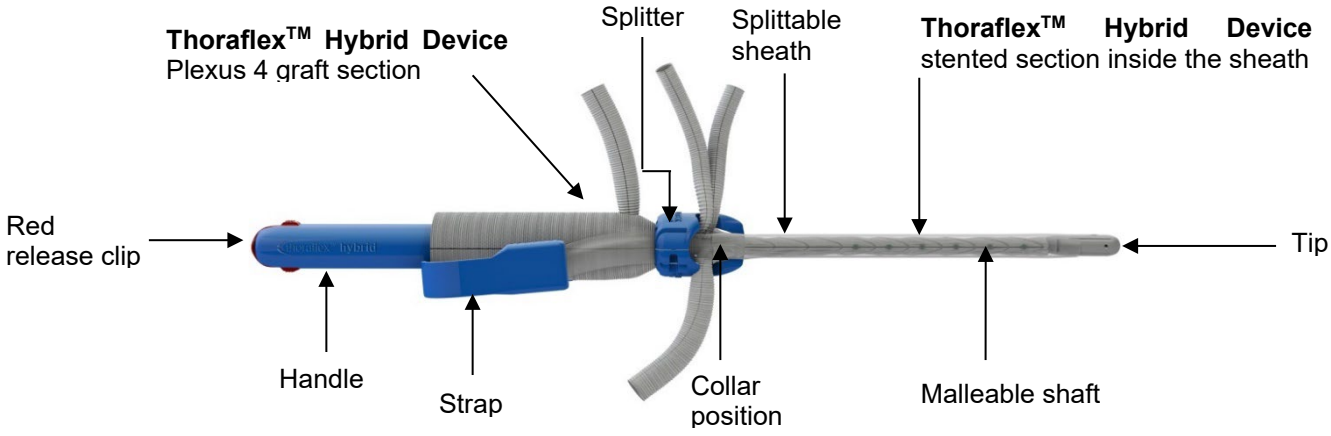


Figure 5 - Thoraflex™ Hybrid Delivery System

An atraumatic tip at the distal end of the delivery system has a profile that is designed to guide the delivery system, with or without a guide wire, into the descending aortic arch. The tip has two guide wire ports that can be used at the discretion of the surgeon, dependent on the particular anatomy being treated.

The shaft, to which the device is attached via the tip, is comprised of a malleable stainless-steel section that allows the surgeon to manipulate the curvature of the delivery system to treat a particular patient anatomy. The distal stented graft section is attached to the tip of the delivery system via a release wire. The entire graft is also held in place by the splitter, which inhibits rotational and longitudinal movement of the device relative to the delivery system and also assists in splitting the sheath during deployment.

2 Indications for Use

The Thoraflex™ Hybrid device is intended for the open surgical repair or replacement of damaged or diseased vessels of the aortic arch and descending aorta with or without involvement of the ascending aorta in cases of aneurysm and/or dissection.

3 Contraindications for Use

The Thoraflex™ Hybrid device is contraindicated in the following:

1. Patients with a known allergy or intolerance to device materials (Polyester, Nitinol, tantalum, or materials of bovine origin)
2. Patients with a condition that threatens to infect the graft

4 Warnings and Precautions

Caution: Read all instructions carefully. Failure to properly follow the instructions, warnings, and precautions may lead to serious consequences or injury to the patient.

4.1 General

- All physicians should be trained in the use of Thoraflex™ Hybrid before using it, as per the requirements in **Section 11.1**.
- Thoraflex™ Hybrid should only be used by physicians and teams trained in cardiovascular techniques and in the use of this device.
- The vascular graft material is based on a woven structure and therefore must be cut with a cautery to minimize fraying.
- **NOTE: IMMERSION OF THE DEVICE IN A SALINE SOLUTION IMMEDIATELY PRIOR TO USE WILL PREVENT FOCAL BURNING WHICH MAY RESULT DURING CAUTERISATION.** The device must be immersed in a saline solution (approximately 700ml) for 5 minutes. Failure to rinse for 5 minutes could lead to the graft being more susceptible to leakage when implanted. Vascutek does not recommend that the device is soaked for longer than 5 minutes as the onset of gelatin hydrolysis may start to occur which may have an impact on clinical performance. The device must not be allowed to dry out after soaking.
- **DO NOT PRECLOT.** These devices contain a gelatin sealant and must not be pre-clotted.
- **DO NOT USE BEYOND THE INDICATED EXPIRATION DATE.** The gelatin impregnation may not meet the design specification after the expiration date.
- **DO NOT RESTERILIZE. FOR SINGLE USE ONLY.** Do not reuse, reprocess or re-sterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in deterioration of health or death of patients. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross infection, including but not limited to the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient end-user.

- The implant is made from gelatin sealed Gelweave polyester material. Due to its use in conjunction with a delivery system, the proximal vascular graft section may suffer some slight initial blood loss when compared to a standard gelatin sealed Gelweave graft.
- Store in a cool dry place out of direct sunlight.
- Clamping may damage the prosthesis. Atraumatic clamps, ideally with soft shod jaws, should be used with a minimum application of force. Excessive force should be avoided as it will damage the polyester fibers and the gelatin impregnation.
- Excessive tension on the prosthesis should be avoided.
- Round body taper point needles should be used when implanting the device to minimize fiber damage.
- If de-airing is required, then the smallest needle possible should be used. A 19 gauge needle is normally sufficient. Hypodermic needles have a cutting point which may result in blood leakage and require repair by suturing.
- The manufacturing process for gelatin sealed vascular grafts uses the cross-linking agent formaldehyde to achieve the graft performance. All gelatin sealed grafts are thoroughly rinsed with Reverse Osmosis (RO) water to reduce residual formaldehyde; however, residual amounts may be present in the finished graft. Formaldehyde is also found at low levels naturally in the body, some of which is derived from food. Formaldehyde is known to be mutagenic and carcinogenic. The risks of these potential harms from the product have not been established clinically.
- The number of patients with acute dissection or rupture treated in the IDE study was limited.

4.2 Patient and Device Selection

- Strict adherence to the sizing guidelines in **Sections 8.2 and 12.7** is expected. Sizing outside these guidelines could result in endoleak, migration, stent-graft separation, infolding, or device damage.
- Key anatomic features that may adversely impact successful exclusion of the lesion include tortuosity, short landing zone, and thrombus or calcium formation at the implantation sites.
- Care should be taken with respect to occlusion of intercostals/spinal cord arteries.
- Patients should be monitored on a regular basis for adverse events, for example endoleaks and aneurysm growth.
- When using an extension device, the minimum recommended amount of overlap between devices is three overlapping covered stents (approximately 50mm). Less than this amount of overlap may result in endoleak (with or without component separation). Device lengths should be selected accordingly.
- This device contains nitinol, an alloy of nickel and titanium. Persons with allergic reactions to these metals may suffer an allergic reaction to this implant. Prior to implantation, patients should be counseled on the materials contained in the device, as well as potential for allergy/hypersensitivity to these materials.
- Significant or circumferential calcification or mural thrombus in the landing zone may adversely impact sealing.
- Vascutek Ltd does not have sufficient data available to show compatibility of Thoraflex™ Hybrid with distal extension devices other than Relay®Pro NBS Thoracic Stent Graft System.

The Thoraflex™ Hybrid device has not been evaluated in the following patient situations and/or populations:

- Pregnancy
- Children
- Known sensitivity to polyester, nitinol, or materials of bovine origin
- Active endocarditis or an active infective disorder of the aorta
- Active systemic infection
- Uncorrectable bleeding anomaly
- Renal failure (defined as dialysis dependent or serum creatinine ≥2.5mg/dL)
- Known sensitivity to radiopaque contrast agents that cannot be adequately pre-treated

4.3 Prior to Implant Procedure

- Preoperative planning for access and placement should be performed prior to opening device packaging.
- Before use, carefully inspect all packaging for damage or defects. If the product or package has been damaged or the sterility of the contents is compromised, do not use the device. The product is provided double-pouched inside a foil bag. If the foil bag or outer pouch are opened, damaged, or missing, the product should not be used. Always handle devices with care.
- Note product “Use By” date and do not use if the date has been exceeded.

4.4 During the Implant Procedure

- A seal zone less than recommended in **Sections 8.2 and 12.7** could increase the risk of endoleak or migration of the implant.
- It is of particular importance that the stented section is pre-soaked as advised in **Section 12.1** as this will greatly reduce the force required to deploy the device.
- Excess delivery system angulation will cause more kinking of the sheath and therefore require an increased deployment force.
- Maintain guidewire position during delivery system insertion.
- When manipulating catheters, wires and sheaths within the thoracic aorta, use caution as this activity can cause rupture or dislodge fragments of thrombus or plaque which may lead to proximal/distal embolization.
- Stop advancing the guidewire or delivery system if resistance is encountered. Assess the source of the resistance before proceeding to avoid vessel or catheter damage.
- **IF A GUIDEWIRE WAS USED DURING THE DEPLOYMENT OF THE DEVICE, IT MUST BE REMOVED FROM THE DELIVERY SYSTEM BEFORE THE RELEASE WIRE IS REMOVED – See Section 12.5.3.**
- Oversize the stent-graft per the sizing guidelines in **Sections 8.2 and 12.7**.
- Care should be taken when using the device in areas of stenosis, thrombosis, or calcified and tortuous vessels. This may lead to dislodgement of material during positioning or lead to inadequate exclusion or vessel damage after placement.
- When excluding an aneurysm, the distal stented graft section of the Thoraflex™ Hybrid device must be landed in healthy tissue. Healthy tissue is non-aneurysmal and is without evidence of circumferential thrombus, intramural hematoma, dissection, or ulceration. Failure to place the distal stented graft of the Thoraflex™ Hybrid in healthy tissue could lead to inadequate exclusion or vessel damage, including perforation.
- In dissection cases, additional care must be taken during the insertion and removal of the delivery system in order to minimize the risk of trauma to the vessel wall.
- Delivery system removal - if the system is introduced around a curve, it must be removed following an identical path in order to avoid moving the device or causing trauma to the vessel.
- Some movement of the distal ring of the implant may occur following re-perfusion of the thoracic aorta.
- Endoleaks detected at the conclusion of the procedure and not corrected should be carefully monitored after implantation.
- Deploying the device in a portion of the aorta with a different diameter than planned when selecting the graft size may potentially result in inadequate sizing and therefore migration, endoleak, aneurysm growth, or increased risk of thrombosis.
- Institutional practices should be observed regarding systemic anticoagulation. Alternate anticoagulation should be used when heparin is contraindicated.
- The use of a balloon expandable stent to treat an endoleak may result in abrasion of the graft material leading to graft failure or fatigue.
- If balloon modeling is desired, use a compliant balloon. Balloon inflation should not exceed 1 atm. Inflate the balloon inside the covered portion of the stent-graft. Failure to do so could lead to aortic rupture, atherosclerotic plaque embolization or other complications. Over inflation of a semi or non-compliant balloon can cause graft tears and/or vessel dissection or rupture.

- When expanding the prostheses, there is an increased risk of vessel injury and/or rupture, and possible patient death, if the compliant balloon's proximal and distal radiopaque markers are not completely within the covered (graft fabric) portion of the prosthesis. Ballooning outside the covered portion could cause aortic rupture, atherosclerotic plaque embolization, or other complications.
- The implantation procedure for extension with Relay®Pro NBS Thoracic Stent Graft System should follow the manufacturer's IFU, describing an endovascular retrograde implantation approach. Compatibility of extension devices deployed from the antegrade approach has not been assessed.
- Adjunctive devices with barb or hook features which would be positioned in the overlap region should not be used.
- Care should be taken to ensure the implant is in its intended position prior to extension device deployment. Close monitoring of position and alignment of both devices should be performed during extension deployment.
- During non-clinical bench testing, distal extension devices with proximal bare stents in a supported overlap region showed a risk of compromising the integrity of the primary device fabric.
- Excessive overlap length between Thoraflex™ Hybrid and the Relay®Pro NBS Thoracic Stent Graft System should be avoided, and the extension device's proximal edge must not be advanced beyond the radiopaque marker on the graft portion of the Thoraflex™ Hybrid device

4.5 Treatment and Follow-up

- The long-term performance of Thoraflex™ Hybrid has not yet been established.
- Vascutek has no long-term data regarding the compatibility of the Thoraflex™ Hybrid Device with a secondary or extension stent-graft.
- Any endoleak left untreated during the implantation procedure must be carefully monitored after implantation.
- All patients should undergo periodic imaging to evaluate the lesion size, occlusion of vessels in the treatment area and distal extension stent-graft. Significant lesion-expansion, the appearance of a new endoleak, false lumen perfusion, thrombosis, evidence of peri graft flow, or distal extension stent-graft migration should prompt further investigation and may indicate the need for additional intervention.
- Patients experiencing reduced blood flow through the surgical graft or the distal extension stent-graft or due to endoleaks may be required to undergo secondary interventions or surgical procedures.
- Additional treatment including endovascular treatment or surgical procedure should be strongly considered in the following cases:
    - Aortic dilation > 5mm, with or without endoleak,
    - false lumen perfusion
    - persistent Type I/III endoleak,with or without aortic dilation,
    - persistent Type II endoleak with aortic dilation, and/or
    - distal extension stent-graft migration.
- Following treatment, spinal cord ischemia (SCI) may result in a rare complication of paraplegia or paraparesis. Cerebrospinal fluid (CSF) drain is advised if spinal cord ischemia is suspected.

5 Magnetic Resonance Imaging (MRI) Safety Information

Nonclinical testing has demonstrated that the Thoraflex™ Hybrid and Relay®Pro NBS Thoracic Stent Graft System are MR Conditional. They can be scanned safely in both 1.5T and 3.0T MR systems only, with the parameters specified in **Section 14**. Additional MRI safety information is also provided in **Section11.6**.

6 Adverse Events

6.1 Potential Adverse Events

Adverse events that may occur in conjunction with surgery for thoracic aortic pathologies include, but are not limited to, those listed in the following section. For specific adverse events that occurred in the clinical study, please see **Section 7.**

Table 2 - Potential Adverse Events

Anaemia	Hepatic failure
Allergic reaction to device materials	Infection of the prosthesis / wound site
Aneurysm enlargement	Lymphatic complications e.g. lymph fistula
Aneurysm/Lesion Rupture	Multi-system organ failure
Aortic damage, including perforation, dissection, bleeding, aortic rupture	Neointimal Hyperplasia
Arterial or venous thrombosis	Neurological local or systematic complications e.g. confusion, stroke, transient ischemia attack (TIA), paraplegia, paraparesis, paralysis, spinal cord injury, peripheral neuropathy, altered mental status, temporary post-operative delirium, altered consciousness, coma, new onset seizures
Aorto-bronchial fistula, aorto-esophageal fistula, arterial or venous fistula, arteriovenous fistula,	Prosthesis dilatation
Bleeding, blood loss, hematoma, coagulopathy, re-opening, thrombocytopenia,	Prosthesis occlusion
Bowel complications e.g. aortoenteric fistula, bowel obstruction, bleeding, infection, ileus, perforation, transient ischemia, infarction, necrosis, mesenteric ischemia, hepatic complications	Pseudoaneurysm
Cardiac complications e.g. Angina, arrhythmia (e.g. atrial or ventricular fibrillation) congestive heart failure, hypotension, hypertension shock, cardiac tamponade, valve insufficiency, myocardial infarction, murmur of aortic insufficiency and pulse deficits, embolization (micro and macro) with transient or permanent ischemia or infarction, pericardial effusion, intramural hematoma, occlusion, downstream reintervention for aortic complications	Renal complications e.g. acute kidney injury, renal insufficiency, renal dysfunction, artery occlusion, failure, infarction, transient or permanent increase in serum creatinine, urinary tract infection
Device deficiencies e.g. Stented Section: improper component placement; incomplete component deployment; component migration and/or separation; suture break; occlusion; infection; stent fracture; graft material wear; graft twisting/kinking; dilatation; erosion; puncture; perigraft flow; and corrosion	Respiratory complications e.g. breathing difficulties, pneumonia, pulmonary edema, pulmonary embolism, post-operative respiratory insufficiency (defined as requiring prolonged intubation (>72 hours), reintubation, or ventilatory support requiring tracheostomy), pleural effusion, exacerbation of COPD
Death	Sepsis
Edema	Stenosis
Endoleak	Surgical complications: sternal instability, swelling, rash, pain, compartment syndrome, recurrent laryngeal nerve damage/paralysis
Fever & localized inflammation	Vascular trauma, spasm, damage and access site complications (infection, pain, hematoma, pseudoaneurysm, arteriovenous fistula, ilio-femoral vessel dissection, bleeding, rupture, deep vein thrombosis)
Genitourinary complications e.g. ischemia, erosion, fistula, incontinence, hematuria, infection, impotence	Wound complications e.g. dehiscence, infection, hematoma, seroma, cellulitis, pain, sacral ulcer/pressure sore and any commonly recognized complications associated with the following adverse events: paraplegia/paraparesis, coma and spinal cord injury (for example pressure sores/sacral ulcer resulting from paraplegia)

6.2 Adverse Event Reporting

Any adverse event involving a Thoraflex™ Hybrid device should be immediately reported to Vascutek using either the email address complaintsUK@terumoaortic.com or via your local distributor.

7 Summary of Clinical Study

7.1 Introduction

The primary objectives of the pivotal study were to evaluate the safety and effectiveness of the Thoraflex™ Hybrid device in subjects with aneurysms and/or dissections in the aortic arch and descending thoracic aorta with or without involvement of the ascending aorta. The study was a multi-center, prospective, two arm, clinical study. Sixty-five (65) subjects were treated in the main study arm and nine (9) subjects were treated in the aortic rupture arm. Subjects were treated between August 22, 2016 and May 29, 2018 at 12 investigational sites in the United States and followed at discharge/30-days, 3 months, 12 months, 2 years, and 3 years. All subjects have completed the study and data lock occurred on July 31, 2021.

7.2 Endpoints

7.2.1 Primary Endpoint

The primary endpoint was defined as the proportion of subjects with freedom from the following composite of Major Adverse Events (MAEs) occurring ≤ 1-year post-procedure:

- Permanent stroke defined as any confirmed new neurological deficit of abrupt onset caused by a disturbance in blood supply to the brain that did not resolve prior to subject being discharged from the hospital.
- Permanent paraplegia/paraparesis defined as complete/partial or incomplete loss of lower limb motor function (paralysis), related to spinal cord ischemia and not relating to stroke.
- Unanticipated aortic related re-operation (excluding re-operation for bleeding) defined as any surgical re-intervention to address complications with the Thoraflex™ Hybrid device, which were not specified pre-operatively or intra-operatively as being required.
- All-cause mortality

The primary endpoint was compared to a performance goal of 57.4%. The performance goal was derived from the frequency of these events in a historical cohort of subjects who underwent an Elephant Trunk (ET) procedure for treatment of aortic aneurysm or aortic dissection. These MAE frequencies were as follows: 6.5% permanent stroke; 5.4% permanent paraplegia/paraparesis; 28.1% mortality at one year; 2.7% unanticipated aortic related re-operation. The proportion of patients in the historical cohort with 1 or more MAE at one year was 35.7%. The proportion of patients MAE-free at one year was 64.3% (95% CI 57.4% to 71.2%).

Furthermore, data were extrapolated from a Frozen Elephant Trunk (FET) meta-analysis (Tian et al, 2013) of 17 studies and 1,675 patients (both aneurysm and dissection) that reported 4.9% stroke; 5.1% paraplegia/paraparesis and 15.3% mortality at one year.

Based on these data and assuming a re-operation rate of 2.7%, a cumulative total of 28% is achieved. However, as patients often have more than one MAE, this figure was adjusted using the ratio of MAEs per patient observed in the historical cohort (1.2 events per patient), resulting in an overall anticipated rate of 23.4% of FET patients experiencing one or more MAE. Consequently, it can be anticipated that 76.6% of patients will be free from MAE. This figure has been used together with the performance goal of 57.4% from the historical cohort to derive the study sample size.

The hypothesis tested for the primary endpoint at a one-sided alpha level of 0.025 was:

Null hypothesis: H_0: $p \leq 0.574$

Alternative hypothesis: H_1: $p > 0.574$

where p represents the probability of being free from the defined composite MAEs in the population under study.

The primary endpoint will be met if the upper limit of the 95% one-sided exact confidence interval of the 12-month endpoint were above 57.4%.

7.2.2 Sample Size

The sample size for the Thoraflex™ Hybrid pivotal study was driven by the primary endpoint.

Primary Endpoint:

The expected rate of freedom from the defined composite MAEs was 76.6%. Therefore a total of fifty-two (52) subjects would provide 90% power to reject the null hypothesis using a one-sided test and a significance level of α=0.025. To accommodate an anticipated dropout rate of 20%, 65 subjects were enrolled in the main study arm.

Secondary Endpoints (evaluated at discharge/30 days, and 3, 12, 24, and 36 months follow-up):

- Incidence of the individual components of the composite primary endpoint
- Incidence of any paraplegia/paraparesis
- Incidence of myocardial infarction
- Incidence of respiratory failure (ventilator dependence greater than 48 hours)
- Incidence of renal failure requiring dialysis
- Incidence of thromboembolic adverse events
- Incidence of bowel ischemia
- Incidence of failed patency, defined as a reduction in blood flow through the device as determined through imaging analysis and requiring surgical intervention
- Incidence of aortic disease related mortality
- Incidence of all re-interventions in the downstream aorta
- Incidence of change in aortic size in the grafted segment > 5 mm from the discharge/30 day CT. This was defined as an increase in diameter >5 mm measured along the major axis. Maximum aortic diameter is measured inner diameter to inner diameter
- Incidence of pseudoaneurysm
- Incidence of aortic rupture. Aortic rupture was defined as leakage of blood from the blood vessel into a body cavity or adjacent organ as determined from imaging
- Incidence of significant failure of device integrity, defined as wear or tear in the fabric or wire breakage resulting in a compromised seal and blood leakage or movement of the device
- Incidence of device migration. Migration was evaluated based on the position of the device at discharge/30 days; migration will be considered as a change >10mm from this position. First-stage procedures where the device cannot be adequately placed in the distal landing zone will be reported separately
- Endoleaks
    - Incidence of all endoleaks
    - Incidence of secondary procedures to correct endoleaks
- Incidence of thrombosis of the lumen (perigraft lumen, false lumen)
- Endpoints specific to extension procedures:
    - Incidence of any failure of device-extension integrity (e.g., wear or tear in the fabric or wire breakage) resulting in a compromised seal and blood leakage or movement of the device
    - Incidence of Type III endoleak
    - Incidence of failed patency of the device-extension overlap
    - Incidence of MAE at 30 days post-extension
    - Incidence of secondary procedures related to the extension
- Procedural outcomes which include procedure times (e.g., total operation time, bypass time), intraoperative blood loss, anesthesia type and time, intraoperative management (e.g., lowest core temperature, spinal drainage), device information and performance, length of ICU stay, length of hospital stay, discharge destination, concomitant procedures
- Incidence of hypersensitivity reactions
- Post-operative outcomes: return to normal activities – employment, household activities, social life and hobbies and Health Related Quality of Life Measure (HRQoL) - EQ-5D
- Non-serious and serious adverse events

Composite Secondary Endpoints:
Device Technical Success (at exit from OR) defined as:

- Successful delivery and accurate placement of the intraluminal part of the graft at the intended implantation site and retrieval of the device delivery system, and
- Patency of the graft (including branches) and absence of device deformations (e.g., kinks) requiring unplanned placement of additional devices within the graft, and
- No need for unanticipated or emergency surgery (e.g., return to bypass after initial removal of aortic cannula or reversal of heparin) or re-intervention (e.g., placement of additional unplanned endoluminal devices within the frozen segment) related to the device or procedure.

Procedural Success defined as Device Technical Success, with absence of the following at discharge/30 days:

- Death
- Major adverse ischemic events: paraplegia / paraparesis, disabling stroke, new ischemia (i.e., not evident at the time of the index procedure) due to branch vessel compromise (malperfusion of organ including bowel, upper limb, or lower limb), distal procedure-related thromboembolic adverse event
- Aortic and valve complications: aortic rupture, Increase in aortic regurgitation grade of greater than 1 (i.e., on 0 – 4 scale)
- General procedure related complications: peri-procedural myocardial infarction (biomarker increase > 10×ULN first 72 hours) or need for urgent or emergent percutaneous coronary interventions (PCI)/ coronary artery bypass grafting (CABG), new onset renal failure requiring dialysis, renal dysfunction or volume overload requiring ultrafiltration, bowel ischemia requiring surgery or intervention, life-threatening bleed, severe Heart Failure (HF) or hypotension requiring pressors or IV inotrope > 24 hr or mechanical circulatory support (MCS), prolonged Intubation > 48 hours, pseudoaneurysm of any graft surgical suture line, additional unplanned surgical or interventional procedures related to the device since completion of the original procedure

Treatment Success (Discharge/30 days and all post-procedural intervals) defined as Device Technical Success, with absence of the following at discharge/30 days and at all post-procedural intervals:

- Aortic enlargement >0.5cm between scheduled post-operative imaging (that is performed in the region encompassed by the initial lesion), aortic rupture, fistula formation, lesion-related mortality, loss of device integrity (e.g., wireform fracture that could affect fixation or seal, graft fabric hole or tear, collapse), residual or new Type III endoleak,
- The subset of major adverse events of disabling stroke within 30 days of the procedure and paraplegia/paraparesis (defined as permanent if persisting at 12 months post procedural follow up)

Individual Subject Success (1 year) defined as Treatment Success at one year, post-operative return to normal activities – employment, household activities, social life, and hobbies, and Improved Health Related Quality of Life Measure (HRQoL) - EQ-5D.

7.3 Subjects

7.3.1 Main Study Arm

Subjects aged 18 or older enrolled in the main study arm of the pivotal study met the following criteria:

- Acute aortic dissection that required repair or replacement of damaged or diseased vessels of the aortic arch (with or without involvement of the ascending aorta), and the descending aorta requires replacement, or, in the opinion of the investigator, the subject would derive clinical benefit from prophylactic treatment of the descending aorta.

- Chronic aortic dissection that required repair or replacement of damaged or diseased vessels of the aortic arch and descending aorta with or without involvement of the ascending aorta, with one or more of the following criteria:
    - An aortic sinus, or ascending aorta, or aortic arch, or descending aorta diameter ≥5.5 cm (including if asymptomatic), or
    - An aortic diameter <5.5 cm and growth rate ≥0.5 cm/year (including if asymptomatic), or
    - An ascending aorta diameter ≥4.5 cm and required valve repair or replacement
- Aortic aneurysm (including connective tissue disorders) that:
    - required repair or replacement of damaged or diseased vessels of the aortic arch and descending aorta with or without involvement of the ascending aorta, with one or more of the following criteria:
    - An aortic sinus, or ascending aorta, or aortic arch, or descending aorta diameter ≥5.5cm (including if asymptomatic), or
    - An aortic diameter <5.5cm and growth rate ≥0.5cm/year (including if asymptomatic), or
    - An ascending aorta diameter ≥4.5cm and requires valve repair or replacement, or
    - Marfan syndrome or other genetically mediated disorders with aortic sinus, or ascending aorta, or arch diameter ≥4.5cm, or the ratio of the maximal ascending or aortic root area (Π r2) in cm^2 divided by the subject's height in meters exceeds 10

Subjects were excluded from enrollment in the main study arm of the pivotal study if they had any of the following anatomic or physiologic characteristics:

- Unfitness for open surgical repair involving circulatory arrest
- Known sensitivity to polyester, nitinol, or materials of bovine origin
- A ruptured aorta
- Active endocarditis or an active infective disorder of the aorta
- Active systemic infection that, in the opinion of the investigator, would compromise the outcome of the surgical procedure.
- Participation in another active study and has received an investigational product (device, pharmaceutical or biologic) within 6 months prior to the date of the implant or had not reached the primary endpoint of the study
- Pregnant, or planned pregnancy during the course of the study.
- Uncorrectable bleeding anomaly
- Renal failure (defined as dialysis dependent or serum creatinine ≥2.5mg/dL)
- Known sensitivity to radiopaque contrast agents that cannot be adequately pre-treated
- Co-morbidity causing expected survival to be less than 1 year
- Any other medical, social or psychological problems that in the opinion of the investigator preclude them from study treatment and the procedures and evaluations pre and post procedure

7.3.2 Rupture Arm: Subjects with Ruptured Aorta Only

Subjects enrolled in the aortic rupture arm of the pivotal study met the following criteria

- 18 years or over on the date of consent
- Subject or their legally authorized representative is able and willing to give consent to the subject's enrollment in the study.
- Either a ruptured thoracic aorta, or, in the experience of the treating surgeon is at high risk of imminent rupture of the thoracic aorta

Subjects were excluded from enrollment in the aortic rupture arm of the pivotal study if they had any of the following anatomic or physiologic characteristics:

- Chronic dissection or aneurysmal disease which, in the opinion of the investigator, could be treated electively

All subjects enrolled in the study met the selection criteria based on site-reported imaging.

7.4 Study Results

7.4.1 Subject Accountability and Follow-up

Eighty-six subjects were screened for the study: four subjects were consented and screen failed before assignment to a treatment arm (not included in the table below) and six subjects screen failed after treatment assignment (five to the main study arm, one to the aortic rupture arm). Reasons for screen failure included insurance issues, device availability, withdrawal of consent and medical/social/psychological problems. Of the 74 subjects implanted (Enrolled) in the pivotal study, there were 65 in the main study arm and 9 in the aortic rupture arm.

At datalock, 56 of 65 treated subjects in the main study arm had one-year follow-up data available; 7 (10.8%) had died and 2 (3.1%) had no visit. At three-year follow-up, 46 subjects were assessed: 6 (9.2%) further mortalities, 5 (7.7%) were lost to follow-up, and 4 (6.2%) subjects withdrew before completing the study. **Table 3** provides a summary subject disposition.

Table 3 - Subject Disposition (All Enrolled Subjects) – Overall

Characteristic	Main Study Arm n (%)	Aortic Rupture Arm n (%)
Total Subjects Screened[a]	72	10
Screen Failure[b]	5 (6.9)	1 (10.0)
Implant surgery (Enrolled)	65	9
Intent-to-Treat Population	65 (100.0)	9 (100.0)
Per-Protocol Population	63 (96.9)	7 (77.8)
Exclusions from the Per Protocol Population[c]		
Lost to follow-up	1 (1.5)	2 (22.2)
Subject withdrawal	1 (1.5)	0 (0.0)
Completed study per protocol	47 (72.3)	5 (55.6)
Reason for early study discontinuation		
Premature closure of study site	0 (0.0)	0 (0.0)
Subject withdrawal	4 (6.2)	0 (0.0)
Investigator withdrew subject	0 (0.0)	0 (0.0)
Lost to follow-up	1 (1.5)	2 (22.2)
Death	13 (20.0)	2 (22.2)
Device Explant	0 (0.0)	0 (0.0)
Ongoing	0 (0.0)	0 (0.0)

a – Screened subjects and screen failures are summarized by planned treatment arm. All other categories are summarized by actual treatment arm.
b – 9 total screen failures, including 4 subjects not assigned to any treatment arms. Two subjects (neither treated) were not listed as screen failures but withdrawals; one subject had other CRF data entered, so this subject appears here as the single screen failure.
- Percentage of screen failures are based on the total number of subjects screened. All other percentages are based on the number of subjects enrolled.
c- Exclusions from the per protocol population – lost to follow-up: one subject (Main Study Arm), two subjects (Aortic Rupture Arm); Subject withdrawal: One subject (Main Study Arm)
Intent-to-Treat Population – includes all subjects who are enrolled and meet all selection criteria for the main study arm and are treated with the Thoraflex™ Hybrid Device. The Intent-to-Treat Population for the main study arm is the primary analysis population.
Per Protocol Population – includes all subjects who are enrolled and are evaluated for the primary endpoint at one year post-procedure without any major protocol violations.

The post procedure follow-up regimen for both the main study and aortic rupture arms involved evaluations at hospital discharge/30day, 3 month, 12, 24 and 36 months. All visits were comprehensive visits requiring physical examination, vital signs, laboratory tests (including assessment of serum creatinine and eGFR), adverse event assessment, additional interventions, health related quality of life measure and assessment of return to normal activities and imaging. Subject follow-up visit information including CT data, could be obtained from the subject's local medical records if appropriate medical release forms were collected and if the follow up visit was not conducted at the research site where the implant occurred. Telephone follow up direct with the subject could be completed for the 3-month, 24-month and 36-month visits if the subject was unable to be return to the implanting site or a local site. At the discharge or 30-day visit (if the subject remained hospitalized at the time or if the subject was unfit for contrast enhanced CT scan at the time of discharge), the first series of post procedure imaging data was collected for submission and analysis by the Core Lab.

In the event that the subject was deemed to be not medically fit by the investigator for contrast enhanced CT scan, the scan could be delayed by up to 30 days at all follow-up timepoints, or it could be omitted if the subject was not fit for the scan after 30 days. Discharge contrast enhanced CT scans could be also delayed until 30 days post-surgery if the investigator deemed the subject was not fit to complete imaging. If the subject was not fit after 30 days post-surgery, then the CT scan could be omitted on the grounds of subject safety. If a contrast enhanced CT scan was delayed or omitted, then the investigator documented and justified the reason for the delay or omission.

CT results from the investigator's assessment were entered onto the eCRF in a separate imaging database. Anonymized copies of all CT scans were sent to the study Core Laboratory for independent analysis. In the event that the investigator and the Core Laboratory did not agree on the analysis, the CEC adjudicated. Adjudication was only performed for endoleak, patency and device migration.

These data provided the baseline measurements for aneurysm enlargement and migration, against which all subsequent visits were compared. **Table 4** summarizes the visit windows as defined in the protocol. In some instances, subjects could return for follow-up visits outside the protocol-defined windows in order to obtain as much safety and effectiveness data. If a subject's visits occurred outside of the protocol-defined visit window, a protocol deviation was entered in the case report forms.

Table 4 - Follow-Up Interval Summary and Visit Windows

Interval	Protocol Visit Window	Analysis Window
Implant	Day 0	Procedure date
Discharge or within 30 days Follow-up	30 days +/- 7 weeks	Day 1 through Day 37
3-Month Follow-up	13 weeks +/- 4 weeks	Day 38 through Day 175
12-Month Follow-up	52 weeks +/- 8 weeks	Day 176 through Day 420
24-Months Follow-up	104 weeks +/- 8 weeks	Day 421 through Day 784
36-Months Follow-up	156 weeks +/- 8 weeks	Day 785 through Day 1148
Extension additional follow-up procedure: Additional follow-up at 3 months after extension procedures, unless this visit falls within 6 weeks of a visit scheduled as part of the primary follow-up protocol, in which case the additional extension related data will be collected at the scheduled primary study visit.		

Subject visit compliance and Core Laboratory imaging follow-up for all enrolled subjects are presented in **Table 5** Summary of Visit Compliance and Core Laboratory Imaging Follow Up for the Main Study Arm and

Table 6 for the Aortic Rupture Arm.

Patency, rupture, endoleak, and migration are evaluated by Core Laboratory review of CT imaging. Imaging was considered adequate to assess the parameter if a response for the parameter was documented by the Core Laboratory. Although evaluations of endoleak and fracture are conducted during the procedure, these evaluations are made using intraoperative angiography rather than CT or x-ray. As such, imaging during the operative period is listed as "Not Applicable."

In the main study arm, 65 subjects were implanted with Thoraflex™ Hybrid and seen through discharge.

The primary analysis population for the primary endpoint (freedom from MAE) is the Intent-to-Treat population (ITT) defined as all patients who were enrolled and met all selection criteria for the main study arm and treated with the ThoraflexTM Hybrid device. Additional analysis was performed on the Per-Protocol Population defined as all patients enrolled and evaluated for the primary endpoint at one year post-procedure without any major protocol violations.

Table 5 and **Table 6** show the patient follow up, imaging adequacy and patient status at each follow up time point for the main and aortic rupture study arm, respectively.

Table 5 - Summary of Visit Compliance and Core Lab Imaging Follow-Up: Main Study Arm

Visit	Subject Follow-Up					Adequate Imaging to Assess the Parameter†					Subject Status			
	Eligible	Data for Visit	No Visit [1]	Still in Window [2]	CT Scan	Patency	Size Increase	Rupture	Migration	Endoleak	Death	Lost to Follow up [3]	Early Withdrawal [4]	Not Due for Next Visit [5]
0	65	65/65 (100%)	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0/65 (0.0%)	0/65 (0.0%)	0/65 (0%)	0/65 (0.0%)
30D	65	65/65 (100%)	0	0/65 (0%)	55/65 (84.6%)	54/65 (83.0%)	55/65 (84.6%)	55/65 (84.6%)	N/A	54/65 (83.0%)	5/65 (7.6%)	2/65 (3.1%)	1/65 (1.5%)	0/65 (0%)
3M	58	58/58 (100%)	0	0/58 (0%)	55/58 (94.8%)	52/58 (89.6%)	55/58 (94.8%)	55/58 (94.8%)	53/58 (91.3%)	52/58 (89.6%)	2/58 (3.4%)	0/58 0%	0/58 (0%)	0/58 (0%)
1Y	56	56/56 (100%)	0	0/56 (0%)	54/56 (96.4%)	52/56 (92.8%)	54/56 (96.4%)	54/56 (96.4%)	53/56 (94.6%)	52/56 (92.8%)	4/56 (7.1%)	3/56 (5.4%)	3/56 (5.4%)	0/56 (0%)
2Y	49	49/49 (100%)	0	0/49 (0%)	36/49 (73.5%)	35/49 (71.4%)	36/49 (73.5%)	36/49 (73.5%)	36/49 (73.5%)	35/49 (71.4%)	2/49 (4.1%)	0/49 (0%)	0/49 (0%)	0/49 (0%)
3Y	47	46/47 (91.5%)	1	0/47 (0%)	33/47 (70.2%)	30/47 (63.8%)	33/47 (70.2%)	33/47 (70.2%)	33/47 (70.2%)	30/47 (63.8%)	0/47 (0%)	0/47 (0%)	0/47 (0%)	0/47 (0%)

N/A: not applicable; CT: Contrast or non-contrast CT scans. The numbers in the table are the numbers of subjects in the specified category. "Data for Visit" means that any data were collected for the follow-up time point.

[1] Subjects who did not have a visit within the window or subjects who did not have a visit but have not yet reached the end of the analysis window.
[2] Subjects still within follow-up window, but data not yet available.
[3] Lost to follow-up includes all Early Withdrawal [4] subjects.
[4] Early withdrawal includes both subject withdrawal and investigator withdrew of subject.
[5] Not due for next visit includes subjects who had visits within the specified window but were not eligible at the start of the next window due to death, surgical conversion, or early withdrawal.

Table 6 - Summary of Visit Compliance and Core Lab Imaging Follow-Up: Aortic Rupture Arm

Visit	Subject Follow-Up					Adequate Imaging to Assess the Parameter†					Subject Status			
	Eligible	Data for Visit	No Visit [1]	Still in Window [2]	CT Scan	Patency	Size Increase	Rupture	Migration	Endoleak	Death	Lost to Follow up [3]	Early Withdrawal [4]	Not Due for Next Visit [5]
0	9	9/9 (100%)	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0/9 (0%)	0/9 (0%)	0/9 (0%)	0/9 (0%)
30D	9	9/9 (100%)	0	0/9 (100%)	6/9 (66.6%)	6/9 (66.6%)	6/9 (66.6%)	6/9 (66.6%)	N/A	6/9 (66.6%)	1/9 (11.1%)	1/9 (11.1%)	0/9 (0%)	0/9 (0%)
3M	7	7/7 (100%)	0	0/7 (0%)	5/7 (71.4%)	5/7 (71.4%)	5/7 (71.4 %)	5/7 (71.4%)	5/7 (71.4%)	5/7 (71.4%)	0/7 (0%)	1/7 (14.2%)	0/7 (0%)	0/7 (0%)
1Y	6	6/6 (100%)	0	0/6 (0%)	5/6 (83.3%)	5/6 (83.3%)	5/6 (83.3%)	5/6 (83.3%)	5/6 (83.3%)	5/6 (83.3%)	1/6 (16.6%)	0/6 (0%)	0/6 (0%)	0/6 (0%)
2Y	5	5/5 (100%)	0	0/5 (0%)	3/5 (60%)	2/5 (40%)	3/5 (60%)	3/5 (60%)	3/5 (60%)	2/5 (40%)	0/5 (0%)	0/5 (0%)	0/5 (0%)	0/5 (0%)
3Y	4	4/4 (100%)	0	0/0 (0%)	4/4 (100%)	4/4 (100%)	4/4 (100%)	4/4 (100%)	4/4 (100%)	4/4 (100%)	0/4 (0%)	0/4 (0%)	0/4 (0%)	0/4 (0%)

N/A: not applicable; CT: Contrast or non-contrast CT scans. The numbers in the table are the numbers of subjects in the specified category. "Data for Visit" means that any data were collected for the follow-up time point.

[1] Subjects who did not have a visit within the window or subjects who did not have a visit but have not yet reached the end of the analysis window.
[2] Subjects still within follow-up window, but data not yet available.
[3] Lost to follow-up includes all Early Withdrawal [4] subjects.
[4] Early withdrawal includes both subject withdrawal and investigator withdrew of subject.
[5] Not due for next visit includes subjects who had visits within the specified window but were not eligible at the start of the next window due to death, surgical conversion, or early withdrawal.

7.4.2 Subject Demographics and Comorbidities

In the main study arm, 66.2% of the subjects were male (43/65) and 33.8% were female (22/65). The average age at screening was 64.6 years. The majority of the subjects in the main study arm were White (44/65, 67.7%) and non-Hispanic or Latino (57/65, 87.7%) with 43.1% (28/65) of the main study arm being ex-smokers and 40% (26/65) non-smokers.

In the aortic rupture arm, 7 subjects (77.8%) were males and 2 (22.2%) were females. Subjects had an average age of 63.2 years at the time of screening. The majority of the aortic rupture arm were White (7/9, 77.8%) and 22.2% (2/9) were Hispanic. Five subjects (5/9, 55.6%) were ex-smokers and three (33.3%) were non-smokers. **Table 7** summarizes the subject demographics and baseline characteristics for the intent-to-treat population for both the main study arm and aortic rupture arm.

Table 7 - Summary of Subject Demographics & Baseline Characteristics (Intent-to-Treat Population)- Overall

Characteristic	Main Study Arm (N=65)	Aortic Rupture Arm (N=9)
Gender, n (%)		
Male	43 (66.2)	7 (77.8)
Female	22 (33.8)	2 (22.2)
Age at screening		

Characteristic	Main Study Arm (N=65)	Aortic Rupture Arm (N=9)
N	65	9
Mean	64.6	63.2
SD	12.74	16.32
Minimum	31	31
Median	68.0	70.0
Maximum	86	79
Ethnicity, n (%)		
Hispanic or Latino	5 (7.7)	2 (22.2)
Not Hispanic or Latino	57 (87.7)	7 (77.8)
Not Reported	2 (3.1)	0 (0.0)
Unknown	1 (1.5)	0 (0.0)
Race, n (%)		
Asian	6 (9.2)	0 (0.0)
American Indian or Alaska Native	0 (0.0)	0 (0.0)
Black or African American	12 (18.5)	2 (22.2)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)
White	44 (67.7)	7 (77.8)
Other	3 (4.6)	0 (0.0)
Baseline Height (cm)		
N	65	9
Mean	172.62	172.54
SD	10.29	6.28
Minimum	152.40	165.10
Median	172.72	170.2
Maximum	195.6	185.4
Baseline Weight (Kg)		
N	65	9
Mean	86.29	81.28
SD	19.45	14.62
Minimum	50.35	60.70
Median	83.0	82.1
Maximum	142.40	99.79

Characteristic	Main Study Arm (N=65)	Aortic Rupture Arm (N=9)
Baseline BMI (kg/m^2)		
N	65	9
Mean	28.85	27.32
SD	5.34	4.96
Minimum	19.9	21.0
Median	28.07	26.39
Maximum	43.3	36.1
ASA Grade		
I	0 (0.0)	0 (0.0)
II	3 (4.6)	0 (0.0)
III	7 (10.8)	1 (11.1)
IV	55 (84.6)	7 (77.8)
V	0 (0.0)	0 (0.0)
Missing	0 (0.0)	1 (11.1)
Smoker		
Yes	11 (16.9)	1 (11.1)
No	26 (40.0)	3 (33.3)
Ex-smoker	28 (43.1)	5 (55.6)

N = Number of subjects in the given cohort in the population and is used as the denominator for percentage calculations.
n = Number of subjects with a value.
Baseline is defined as the pre-procedure measurement.
BMI = body mass index.

In the main study arm, 92.3% (60/65) had hypertension, 56.9% (37/65) had hyperlipidemia, 38.5% (25/65) had coronary artery disease, 16.9% (11/65) had renal insufficiency, 15.4% (10/65) had chronic obstructive pulmonary disease (COPD), and 13.8% (9/65) had a stroke. The surgical histories for the main study arm include the following: 32.3% (21/65) had a previous aortic dissection repair, 18.5% (12/65) had an aortic valve replacement or repair, 10.8% (7/65) had coronary artery bypass grafting and 10.8% (7/65) had an aortic aneurysm repair.

In the aortic rupture arm, 100% (9/9) had hypertension, 44.4% (4/9) had hyperlipidemia, 22.2% (2/9) had coronary artery disease and 22.2% (2/9) had chronic obstructive pulmonary disease. **Table 8** includes the medical and surgical histories of all enrolled subjects.

Table 8 - Summary of Medical & Surgical History (All Enrolled Subjects) – Overall

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Cardiac Medical History		
Other	47 (72.3)	4 (44.4)
Coronary Artery Disease - CAD	25 (38.5)	2 (22.2)

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Congestive Heart Failure - CHF	10 (15.4)	1 (11.1)
Angina	3 (4.6)	0 (0.0)
Myocardial Infarction - MI	5 (7.7)	1 (11.1)
Cardiac Surgical History		
Aortic Dissection Repair	21 (32.3)	2 (22.2)
Other	13 (20.0)	1 (11.1)
Aortic Valve Replacement or Repair	12 (18.5)	1 (11.1)
Aortic Aneurysm Repair	7 (10.8)	1 (11.1)
Coronary Artery Bypass Graft - CABG	7 (10.8)	1 (11.1)
Coronary Angioplasty or Stent	4 (6.2)	0 (0.0)
Pacemaker	2 (3.1)	0 (0.0)
Endocrine Medical History		
Hypertension	60 (92.3)	9 (100.0)
Hyperlipidemia	37 (56.9)	4 (44.4)
Hypothyroid	9 (13.8)	1 (11.1)
Other	7 (10.8)	2 (22.2)
Diabetes	6 (9.2)	0 (0.0)
Cancer	5 (7.7)	0 (0.0)
Hyperthroid	1 (1.5)	0 (0.0)
Neurological Medical History		
Other	10 (15.4)	0 (0.0)
Stroke	9 (13.8)	0 (0.0)
Transient Ishemic Attack - TIA	4 (6.2)	0 (0.0)
Seizure	2 (3.1)	0 (0.0)
Nerve Damage	1 (1.5)	0 (0.0)
Neuromuscular Disease	1 (1.5)	0 (0.0)
Paraplegia	1 (1.5)	0 (0.0)
Pulmonary Medical History		
Other	27 (41.5)	3 (33.3)
Chronic Obstructive Pulmonary Disease-COPD	10 (15.4)	2 (22.2)
Asthma	8 (12.3)	2 (22.2)
Pulmonary Hypertension	3 (4.6)	0 (0.0)
Emphysema	2 (3.1)	0 (0.0)

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Bronchitis	1 (1.5)	0 (0.0)
Other Medical History	50 (76.9)	6 (66.7)
Renal Medical History		
Renal Insufficiency	11 (16.9)	1 (11.1)
Renal Failure	2 (3.1)	0 (0.0)
Vascular Surgical History		
Endovascular Stent-graft	5 (7.7)	1 (11.1)
Other	5 (7.7)	0 (0.0)
Non-Coronary Bypass	4 (6.2)	0 (0.0)
Non-Coronary Angioplasty – with/without Stenting	3 (4.6)	0 (0.0)
Surgical Aneurysm Repair	2 (3.1)	1 (11.1)
Embolization	1 (1.5)	0 (0.0)
N = Number of subjects in the given study arm and is used as the denominator for percentage calculations.		

7.4.3 Summary of Indication for Surgery

The Thoraflex™ Hybrid Device is intended for the open surgical repair or replacement of damaged or diseased vessels of the aortic arch and descending aorta, with or without involvement of the ascending aorta, in cases of aneurysm and/or dissection. A summary of indication for surgery for all enrolled subjects is presented in **Table 9**. Note that some subjects presented with multiple pathologies.

In the main study arm, 59 subjects (90.8%, 59/65) had an aneurysm as an indication for surgery; 40% (26/65) had aneurysm only. Many subjects also presented with dissection: 38 (58.5%, 38/65) of the dissections were chronic and a single dissection was acute (1.5% (1/65)). Of the 59 subjects in the main study arm with an aneurysm, 32 (54.2%, 32/59) of those subjects also had a chronic dissection.

In the aortic rupture arm, 5 subjects (55.6%, 5/9) had an aneurysm and 7 subjects (77.8%) had an acute dissection. Two (22.2%) had aneurysm only. Three (33.3%) had both aneurysm and dissection indications. One subject had an indication of aortic rupture when enrolled. The remaining subjects in this arm were included if the treating surgeon considered the subject a high risk of imminent rupture of the thoracic aorta.

In the entire study, five subjects with a connective tissue disorder were enrolled 4 (6.2%) in the main study arm and 1 (11.1%) in the aortic rupture arm. Twenty-one subjects with atherosclerosis were enrolled; 19 (29.2%) in the main study arm and 2 (22.2%) in the aortic rupture arm.

Table 9 - Summary of Indication for Surgery (All Enrolled Subjects)

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Dissection		
Acute	1 (1.5)	7 (77.8)
Chronic	38 (58.5)	0 (0.0)
Aneurysm		

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Yes	59 (90.8)	5 (55.6)
Aneurysm only (no dissection)	26 (40.0)	2 (22.2)
No	6 (9.2)	4 (44.4)
Aortic Rupture		
Yes	0 (0.0)	1 (11.1)
No*	65 (100.)	8 (88.9)*
Degenerative Condition		
Atherosclerosis	19 (29.2)	2 (22.2)
Connective Tissue Disorder	4 (6.2)	1 (11.1)
Marfan Syndrome	0 (0.0)	0 (0.0)
Other	4 (6.2)	1 (11.1)

N = Number of subjects in the study arm and is used as the denominator for percentage calculations.
Some subjects had multiple pathologies; of the 59 subjects in the main study arm with an aneurysm, 32 (54.2%, 32/59) also had a chronic dissection. In the aortic rupture arm. Three (33.3%) of those subjects had both indications.
** High risk of imminent rupture.*

7.4.4 Thoraflex™ Hybrid Devices Implanted

A total of 74 Thoraflex™ Hybrid devices were implanted in the study. The Plexus 4 model device was more commonly used, with 56 implanted in both arms compared to 18 Ante-Flo. Forty-eight of the 56 Plexus 4 model devices and 17 of the Ante-Flo devices were implanted in the main study arm. In the aortic rupture arm, there were 8 Plexus 4 devices and 1 Ante-Flo device implanted. The 150mm device length was the length used most often, with 37 devices used compared to 28 of the 100mm devices.

The summary of device type and device configuration are shown below.

Table 10 - Summary of Device Type (Intent-to-treat Population)

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Configuration		
Ante-Flo	17 (26.2)	1 (11.1)
Plexus 4	48 (73.8)	8 (88.9)
Sizes (mm)		
Short stent-graft section	28 (43%)	4 (44%)
22×24×100	0 (0.0)	0 (0.0)
24×26×100	1 (1.5)	0 (0.0)
26×28×100	7 (10.8)	1 (11.1)
28×30×100	5 (7.7)	0 (0.0)
30×32×100	1 (1.5)	1 (11.1)
30×34×100	4 (6.2)	2 (22.2)
30×36×100	0 (0.0)	0 (0.0)
30×38×100	3 (4.6)	0 (0.0)
30x40×100	6 (9.2)	0 (0.0)
32×40×100	1 (1.5)	0 (0.0)
Long stent-graft section	37 (57%)	5 (56%)
22×24×150	0 (0.0)	0 (0.0)
24×26×150	1 (1.5)	0 (0.0)

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
26×28×150	5 (7.7)	1 (11.1)
28×30×150	4 (6.2)	0 (0.0)
30×32×150	6 (9.2)	3 (33.3)
30×34×150	5 (7.7)	0 (0.0)
30×36×150	3 (4.6)	0 (0.0)
30x38×150	5 (7.7)	1 (11.1)
30×40×150	7 (10.8)	0 (0.0)
32×40×150	1 (1.5)	0 (0.0)
Measurements are: proximal (graft) diameter × distal (stent-graft) diameter × stent-graft length. Denominator is either total number of implants or number of specific size used.		

7.4.5 Procedural Outcomes

Information and observations about the implantation procedure were documented by physicians on case report forms. General anesthesia was utilized in all subjects in both study arms. The mean total operative time was longer in the main study arm (main study arm: 555.5 min, aortic rupture arm: 492.2 min). The aortic cross-clamp time was 127.8 min in the main study arm and 112.4 min in the aortic rupture arm. The lowest core temperature mean was similar in both arms (main study arm: 68.87°F, aortic rupture arm: 69.42°F). Spinal drainage was used prophylactically in 11 subjects (16.9%) in the main study arm and was not utilized for any subjects in the aortic rupture arm.

The mean lengths of ICU and hospital stay for the main study arm were 6.4 days and 14.5 days, respectively and for the aortic rupture arm were 8.8 days and 17.5 days, respectively. Of the 62 subjects in the main study arm who survived to be discharged, 39 (62.9%) were discharged home, 14 (22.6%) to a rehabilitation center and 5 (8.1%) to a nursing home. Four subjects (50%, 4/8) in the aortic rupture arm were discharged home (one subject died prior to discharge), one subject was discharged to a rehabilitation center, three discharge destinations were not recorded. Procedural outcomes are summarized in **Table 11**.

Table 11 - Summary of Procedural Outcomes (Intent-to-Treat Population) – Overall

Characteristic	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Total Operation Time (min)		
N	65	9
Mean	555.5	492.2
SD	152.25	89.32
Minimum	270	419
Median	529.0	468.0
Maximum	1034	701
Anesthesia type, n (%)		
General	65 (100.0)	9 (100.0)
Other	0 (0.0)	0 (0.0)
Cardio-pulmonary bypass time (min)		
N	65	9
Mean	202.6	193.9
SD	81.61	39.28
Minimum	41	143
Median	198.0	200.0
Maximum	430	246
Aortic cross-clap time (min)		
N	65	9
Mean	127.8	112.4
SD	73.37	27.73
Minimum	11	72
Median	120.0	105.0

Characteristic	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Maximum	349	164
Hypothermic circulatory arrest time (min)		
N	65	9
Mean	51.7	40.8
SD	36.24	27.64
Minimum	0	3
Median	50.0	44.0
Maximum	235	82
Selective cerebral perfusion, n (%)		
Retrograde	11 (16.9)	0 (0.0)
Antegrade	54 (83.1)	9 (100.0)
Perfusion time (min)		
N	63	9
Mean	61.8	47.1
SD	35.55	25.88
Minimum	3	7
Median	57.0	54.0
Maximum	246	82
Rewarming time (min)		
n	64	9
Mean	85.7	87.6
SD	44.73	30.83
Minimum	24	39
Median	73.5	82.0
Maximum	313	140
Lower body ischemia time (min)		
n	64	9
Mean	51.9	40.7
SD	42.28	27.56
Minimum	0	3
Median	47.5	44.0
Maximum	242	82
Blood Loss (mL)		
N	48	7
Mean	1034.0	628.6
SD	936.05	815.91
Minimum	2	0
Median	800.0	250.0
Maximum	3650	2400
Anesthesia duration (min)		
N	65	9
Mean	606.4	552.4
SD	160.63	102.49
Minimum	235	424
Median	572.0	533.0
Maximum	999	721
Lowest core temperature (F)		
n	65	9
Mean	68.874	69.416
SD	6.5269	6.5718
Minimum	53.60	59.00
Median	68.000	68.000
Maximum	83.84	80.60
Spinal drainage duration (day)		
n	11	0
Mean	3.27	0

Characteristic	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
SD	1.834	0
Minimum	1.0	0
Median	3.10	0
Maximum	8.0	0
Length of ICU stay (day)		
N	62	8
Mean	6.4	8.8
SD	7.03	10.00
Minimum	1	2
Median	4.5	4.5
Maximum	38	32
Length of hospital stay (day)		
N	62	8
Mean	14.5	17.5
SD	11.34	12.51
Minimum	5	6
Median	11.0	11.0
Maximum	64	39
Discharge destination, n (%)		
N*	62*	8*
Home	39 (60.0)	4 (44.4)
Rehabilitation Center	14 (21.5)	1 (11.1)
Other hospital	1 (1.5)	0 (0.0)
Nursing home	5 (7.7)	0 (0.0)
Other	3 (4.6)	3 (33.3)
N=number of subjects in ITT population ** Three subjects in the Main Study Arm and 1 subject in the Aortic Rupture Arm died before discharge.*		

7.4.6 Intraoperative Graft Adjustments

Each subject was treated with a Thoraflex™ Hybrid device in accordance with the device instructions for use (IFU) and standard of care. The size of the device was selected based on pre-operative imaging and taking into account the sizing recommendations in the IFU. The graft portion of the device could be trimmed to fit the subject's anatomy using standard surgical techniques. Shortening the main body of the graft portion of the device or shortening any of the branch vessels on a Plexus-4 version of the device was expected as this is consistent with standard surgical practice and data was not collected. Any other adjustments which were made to the proximal graft portion of the device in order for the device to achieve best fit to the subject's anatomy was recorded in the eCRFs. **Table 12** provides data reported by the sites of intraoperative graft adjustments in the intent to treat population.

Table 12 - Summary of Intraoperative Graft Adjustments (Intent-to-Treat Population)

Adjustment Type	Main Study Arm (N =65) n (%)	Aortic Rupture Arm (N = 9) n (%)
Any graft adjustment	22 (33.8)	6 (66.7)
Non-anatomical implantation of branches	4 (6.2)	0 (0.0)
Attachment of additional grafts or native vessels directly onto the graft	9 (13.8)	1 (11.1)
Altering location of the 'cut-down' and subsequent attachment of the collar	9 (13.8)	3 (33.3)
Use of pledglets, cuffs, or other felt products to reinforce collar/vessel	7 (10.8)	2 (22.2)
Other graft adjustments	1 (1.5)*	1 (11.1)**

Adjustment Type	Main Study Arm (N =65) n (%)	Aortic Rupture Arm (N = 9) n (%)
*For this "other" reported, the Investigator stated that the subclavian branch was removed and ligated because the Investigator was unable to dissect the subclavian artery due to heavy scar tissue from previous surgery. ** For this "other" reported, a hole was made in the graft and an anastomosis between the graft and the right coronary button was constructed with 5 0 prolene continuous suture.		

7.4.7 Concomitant Procedures

Concomitant procedures include any procedures that occurred during index procedure: CABG (7 procedures), valve surgery (9 procedures), and other (16 procedures) for both study arms. The other procedures included pacemaker insertion, aortic root replacement, chest re-exploration, planned second stage elephant completion, and planned pseudoaneurysm repair.

Two subjects in the aortic rupture arm underwent 4 concomitant procedures, which included 1 CABG, 1 valve surgery, and 2 others. **Table 13** provides a summary of the concomitant procedures required by subjects in both the Main Study and Aortic Rupture Arms.

Table 13 - Concomitant Procedures (Intent-to-Treat Population) - Overall

Timepoint Procedure	Main Study Arm (N = 65) n (%) e	Aortic Rupture Arm (N = 9) n (%) e
n	**65**	**9**
Planned Concomitant Procedures		
CABG	**6 (9.2) 6**	**1 (11.1) 1**
Urgent	0 (0.0) 0	1 (11.1) 1
Emergent	0 (0.0) 0	0 (0.0) 0
Elective	6 (9.2) 6	0 (0.0) 0
Valve Surgery	**6 (9.2) 7**	**0 (0.0) 0**
Aortic	6 (9.2) 6	0 (0.0) 0
Mitral	1 (1.5) 1	0 (0.0) 0
Tricuspid	0 (0.0) 0	0 (0.0) 0
Other	**5 (7.7) 9**	**1 (11.1) 1**
Unplanned Concomitant Procedures		
CABG	**0 (0.0) 0**	**0 (0.0) 0**
Urgent	0 (0.0) 0	0 (0.0) 0
Emergent	0 (0.0) 0	0 (0.0) 0
Elective	0 (0.0) 0	0 (0.0) 0
Valve Surgery	**1 (1.5) 1**	**1 (11.1) 1**
Aortic	1 (1.5.) 1	1 (11.1) 1
Mitral	0 (0.0) 0	0 (0.0) 0
Tricuspid	0 (0.0) 0	0 (0.0) 0
Other	**5 (7.7) 5**	**1 (11.1) 1**
*- N=number of subjects in ITT population; n=number of subjects in specified category; %=100*n/N, e=total number of procedures*		

7.4.8 Aborted Procedures

No procedures were aborted.

7.4.9 Primary Endpoint

The primary endpoint was defined as the proportion of subjects with freedom from athe following composite Major Adverse Events (MAEs) occurring ≤ 1 year post procedure: permanent stroke, permanent

paraplegia/paraparesis, unanticipated aortic related re-operation (excluding reoperation for bleeding), and all-cause mortality.

The primary endpoint was compared to a performance goal of 57.4%. The rate of freedom from composite MAEs occuring ≤ 1 year post procedure was 76.9% (50/65, 95% CI 66.7% to 87.2%) in the main study arm. The lower bound of the 95% confidence interval was above 57.4% indicating that the Performance Goal was met. A total of 18 events were observed in a total of 13 subjects. In addition, two (2) subjects were imputed as failures as their status was unknown at 1 year. Events reported include 5 permanent strokes, 3 cases of permanent paralysis/paraplegia, 7 deaths, and 3 unanticipated aortic related re-operations. **Table 14** shows the analysis of major adverse events (MAEs) within one year of implant among the intent-to-treat population.

Table 14 – Primary Endpoint Failure within One Year of Implant by Study Arm (Intent-to-Treat Population)

Study Arm Overall	Event	Subjects with Event n (%)	Subjects Event-Free n (%)	95% Confidence Interval for Event-Free (%)
Main Study Arm (N' = 65)	Any failure	15 (23.1%)	50 (76.9%)	(66.7, 87.2)
	Permanent Stroke	5 (7.7%)	60 (92.3%)	(85.8, 98.8)
	Permanent Paraplegia/Paraparesis	3 (4.6%)	62 (95.4%)	(90.3, 100)
	Mortality	7 (10.8%)	58 (89.2%)	(81.7, 96.8)
	Unanticipated Aortic Related Re-operation	3 (4.6%)	62 (95.4%)	(90.3, 100)
Aortic Rupture Arm (N' = 9)	Any failure	4	5	(23.1, 88.0)
	Permanent Stroke	2	7	(50.6, 100)
	Permanent Paraplegia/Paraparesis	1	8	(68.4, 100)
	Mortality	1	8	(68.4, 100)
	Unanticipated Aortic Related Re-Operation	0	9	(100, 100)

All MAEs were adjudicated by the Clinical Events Committee (CEC)
N' = number of subjects within each study arm; n=number of subjects in specified category; p=n/N'.
NOTE: If the lower bound of the 95% confidence interval is >0.574 for Any MAE in the Main Study Arm, the study has demonstrated that the proportion of subjects in this population treated with the Thoraflex™ Hybrid Device meets the performance goal.
NOTE: For this analysis, two subjects whose status at Year 1 was unknown are considered primary endpoint failures.
NOTE: Unanticipated aortic related re-operation excluded any planned extension procedure with its need identified prior to or during the implantation of the device. Non-permanent paraplegia/paraparesis are excluded from MAEs.

7.4.10 Poolability

The summary below of MAEs within 1-year of implant evaluates the comparability and poolability of the investigational sites. Elimination of each investigational site in turn produced only minor changes in the proportion and confidence interval of the primary outcome. In summary, (i) no individual site has undue influence upon the proportion and (ii) the lower confidence interval remains above the performance goal regardless of which site is eliminated.

7.4.11 Secondary Endpoints

7.4.11.1 Composite Secondary Endpoints

Composite secondary endpoints include device technical success (at exit from the operating room), procedural success at discharge and treatment success.

For the main study arm, device technical success was 98.5% (64/65). Procedural success was 67.7% (44/65) at discharge/30 days. Treatment success was 91.1% (51/56) at 12 months, 95.9% (47/49) at 2-years and 95.7% (44/46) at 3-years.

For the aortic rupture arm, 88.9% (8/9) of subjects achieved device technical success. Procedural success was 55.6% (5/9) at discharge/30 days. Treatment success was 83.3% (5/6) at 12 months, 60% (3/5) at 24 months and 50% (2/4) at 36 months. **Table 15** provides a summary for both the main study and aortic rupture arms.

Table 15 - Summary of Composite Secondary Endpoints (Intent-to-Treat Population) – Overall

Endpoint Timepoint	Main Study Arm (N = 65) n/N´ (%)	Aortic Rupture Arm (N = 9) n/N´ (%)
Device Technical Success (at exit from OR)	64/65 (98.5%)	8/9 (88.9%)
Successful delivery achieved	64/65 (98.5%)	9/9 (100.0%)
Patency of graft	65/65 (100.0%)	9/9 (100.0%)
No re-intervention	65/65 (100.0%)	8/9 (88.9%)
Procedural Success (at discharge/30 days)	44/65 (67.7%)	5/9 (55.6%)
Death	2/65 (3.1%)	1/9 (11.1%)
Major adverse ischemic events	8/65 (12.3%)	2/9 (22.2%)
Aortic and valve complications	0/65 (0.0%)	0/9 (0.0%)
General procedure-related complications	17/65 (26.2%)	3/9 (33.3%)
Treatment Success		
Discharge/30 days	57/65 (87.7%)	7/9 (77.8%)
3 Months	52/58 (89.7%)	6/7 (85.7%)
12 months	52/56 (92.9%)	5/6 (83.3%)
24 months	47/49 (95.9%)	3/5 (60.0%)
36 months	44/46 (95.7%)	2/4 (50.0%)

- N=number of subjects in the ITT population; n=number of subjects in specified category; Percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each arm.
In one case, the Thoraflex™ Hybrid device did not deploy as described in the Instructions-For-Use; the investigator removed the device and successfully implanted a different device. Failure to remove the guidewire prior to removing the handle was the most likely cause of incorrect deployment.
Major adverse ischemic events comprised: New ischemia (i.e., not evident at the time of the index procedure) due to branch vessel compromise (malperfusion of organ including bowel, upper limb, or lower limb), Disabling stroke, Paraparesis,
General procedure-related complications comprised: prolonged intubation (>48h), and new onset renal failure requiring dialysis, Renal dysfunction or volume overload requiring ultrafiltration, Severe Heart Failure (HF) or hypotension requiring pressors or IV inotrope > 24hr or mechanical circulatory support (MCS), Peri-procedural myocardial infarction (biomarker increase > 10x ULN first 72 hours) or need for urgent or emergent PCI/CABG, Additional unplanned surgical or interventional procedures related to the device since completion of the original procedure, and Peri-procedural myocardial infarction (biomarker increase > 10×ULN first 72 h) or need for urgent or emergent PCI/CABG

7.4.11.2 All-Cause Mortality

There were 7 deaths (10.8%) through one year in the main study arm. There were six more deaths in the main study arm after one year (20% in total to three years, 13/65).

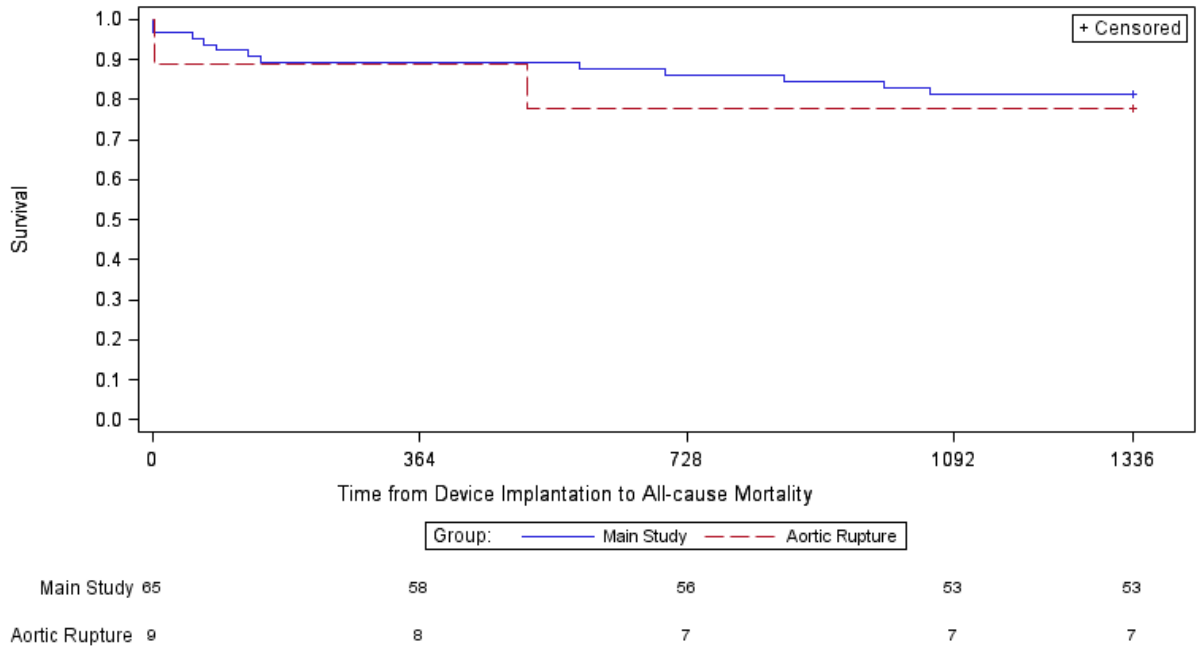
Three deaths were adjudicated as aortic-disease related (see preceding section). Four deaths were adjudicated by the CEC as possibly device-related, three as procedure-related, four as possibly procedure-related; and five as neither device or procedure related. The Kaplan-Meier estimate of the freedom from all-cause mortality rates in the main study arm at one year is 89.2% (95% CI, 78.7-94.7). The Kaplan-Meier estimate of the freedom from all-cause mortality is 81.5% (95% CI, 69.8-89.1) out to 3 years for the main study arm.

There were 2 events of all-cause mortality in the aortic rupture arm through 3 years. One death was adjudicated as related to procedure and one death as unknown due to the lack of information and details provided to the Investigator by the next of kin. The Kaplan-Meier estimate of the freedom from all-cause mortality rates in the aortic rupture arm is 88.9% (95% CI, 43.3-98.4) at one year. The Kaplan-Meier estimate of the freedom from all-cause mortality is 77.8% (95% CI 36.5-93.9) out to 3 years for the aortic rupture arm.

Table 16 - All-cause mortality: Intent-to-Treat Population

Secondary Endpoint	Discharge/30 days	3 Month	12 Months	24 Months	36 Months	Total
Number of subjects eligible (Main/Aortic Rupture Arm) - *N´*	65/9	60/7	57 § /6	50/5	48/4	65/9
Main Study Arm n (%) ‡	2 (3.1)	3 (5.0)	2 (3.5)	3 (6.0)	2 (4.8)	12 (18.5)‡
Aortic Rupture Arm n (%)	1 (11.1)	0 (0.0)	0 (0.0)	1 (20.0)	0 (0.0)	2 (22.2)

N=number of subjects enrolled; n=number of subjects in specified category; Percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each subgroup.
‡ Total number of deaths in the main study arm is 13: one subject is not listed in the follow-up timepoints because AE start date/end dates were missing and could not be assigned to a visit (but were after one year).
§ One subject was excluded from denominator because death was POD 147 and there was no 12M visit.



	POD	Events	Event free (%)	95% lower CI	95% upper CI
Main Study	0	0	1.000	1.000	1.000
	1	2	0.969	0.883	0.992
	55	3	0.954	0.864	0.985
	69	4	0.938	0.844	0.976
	87	5	0.923	0.825	0.967
	130	6	0.908	0.806	0.957
	147	7	0.892	0.787	0.947
	582	8	0.877	0.769	0.936
	697	9	0.862	0.751	0.925
	860	10	0.846	0.733	0.914
	997	11	0.831	0.715	0.902
	1058	12	0.815	0.698	0.891
	1336	12	0.815	0.698	0.891
Aortic Rupture	0	0	1.000	1.000	1.000
	3	1	0.889	0.433	0.984
	509	2	0.778	0.365	0.939
	1336	2	0.778	0.365	0.939

Figure 6 - Kaplan-Meier Time from Implantation to All-Cause Mortality (Intent-to-Treat Population)

7.4.11.3 Aortic-Disease Related Mortality

Aortic-Disease Related Mortality is defined as death due to aortic disease or complications from aortic disease and incidence was collected throughout follow-up. The CEC adjudicated all deaths to determine those that meet the aortic-disease related mortality definition.

There were 3 subjects (3/65, 4.6%) in the main study arm that were adjudicated with aortic-disease related morality. One subject had an unplanned TEVAR at day 1 post-implant with a date of death on day 2 post-implant; the cause of death was multiorgan complications from unanticipated aortic-related reoperation. The investigator initially reported the event as aortic rupture; the CEC adjudicated this event as unanticipated aortic-related reoperation. The second subject had an unplanned endovascular repair of the descending thoracic aorta due to rapid aneurysm growth at 23 days post-implant with a date of death at 69 days post implant; the cause of death was rupture (aortic-disease related). The third subject had a sudden and unexplained death caused by a witnessed cardiac arrest at 147 days post-implant.

There were no aortic-disease related mortalities in the aortic rupture arm.

Table 17 - Incidence of Aortic Disease Related Mortality – Intent-To-Treat Population

Secondary Endpoint	Discharge/ 30 days	3-Month	12-Months	24-Months	36 Months	Total
Number of Subjects Eligible (Main/Aortic Rupture Arm) - *N′*	65/9	58/7	56/6	47/4	46/4	65/9
Main Study Arm n (%)	1 (1.5)	1 (1.7)	1 (1.8)	0 (0.0)	0 (0.0)	3 (4.6)
Aortic Rupture Arm n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

N=number of subjects enrolled; n=number of subjects in specified category; Percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each subgroup.

7.4.11.4 Aortic Rupture

Aortic rupture is defined as the leakage of blood from the blood vessel into a body cavity or adjacent organ and determined by the investigator from appropriate imaging. There were no cases of CEC adjudicated aortic rupture in either study arm. The CEC reviewed core lab findings. The Core Laboratory did not report any rupture. One site-reported rupture was adjudicated by the CEC instead as unanticipated aortic-related reoperation.

7.4.11.5 Permanent Stroke

In the main study arm, there were 5 MAEs of permanent disabling stroke (5/65, 7.7%), 4 were ischemic and one was hemorrhagic and fatal, which was also the only one that occurred post-discharge (at 3 months). One stroke resolved without sequelae, one resolved with sequelae, one improved but remained ongoing, and one remained unchanged.

In the aortic rupture arm, there were two MAEs of permanent ischemic and disabling stroke (2/9, 22.2%) within 30 days: One subject subsequently died; a second subject's event was procedure-related, device-unrelated, moderate in severity and resolved with sequelae. A third subject had a stroke that was unrelated to the device or procedure on POD 1283: combined events of Type B intramural hematoma, paraparesis, ischemic stroke, hemorrhagic stroke, respiratory failure, and cocaine vasculopathy were severe and unresolved at the time of the last study visit.

Table 18 - Summary of Permanent Stroke -Intent-to-Treat Population

Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Subjects Eligible N'	65/9	58/7	55/6	47/4	46/4	65/9
Main Study Arm n (%)	4 (6.2)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	5 (7.7)
Aortic Rupture Arm n (%)	2 (22.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	3 (33.3)

- N=number of subjects enrolled; n=number of subjects in specified category; Percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each subgroup.
Permanent stroke is defined as any confirmed new neurological deficit of abrupt onset caused by a disturbance in blood supply to the brain that did not resolve prior to subject being discharged from the hospital. The diagnosis must be confirmed by at least one of the following: Neurologist or neurosurgical specialist; Neuroimaging procedure (CT scan or brain MRI), but stroke could be diagnosed on clinical grounds alone.
Ischemic Stroke: Acute episode of focal cerebral, spinal, or retinal dysfunction caused by infarction of central nervous system tissue.
Hemorrhagic Stroke: Acute episode of focal or global cerebral or spinal dysfunction caused by intraparenchymal, intraventricular, or subarachnoid hemorrhage.
Disabling Stroke: Modified Rankin Score (mRS) score of 2 or more at 90 days and an increase in at least one mRS category from an individual's pre-stroke baseline.
.
The Total column number is the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.

7.4.11.6 Unanticipated Aortic-related Re-Operation

In the main study arm, one re-operation occurred in one subject (1/65 1.5%) at the discharge/30 day follow up and two re-operations in two subjects (2/58 3.4%) at the 3-month follow-up. None of the events were device related. Kaplan-Meier estimates of freedom from unanticipated aortic-related re-operation in the main study arm were 96.9% at 30 days and 95.4% at 90 days through 1 year.

Two unanticipated aortic-related re-operations were emergent TEVARs (second-stage procedures that were planned but had to be brought forward). One subject died before discharge; a second was discharged but later died. The third case was due to a new abdominal aortic dissection and was treated successfully by open repair of infrarenal abdominal aorta.

In the aortic rupture arm, there were no cases of unanticipated aortic-related re-operation (excluding re-operation for bleeding).

7.4.11.7 Paraplegia/Paraparesis

In the main study arm, there were 5 reported cases of paraplegia/paraparesis and one reported case of spinal cord ischemia (SCI). Three were adjudicated as permanent, 2 of which persisted until death. All 3 cases that were considered permanent received a 150mm distal stented graft section. None of these 3 subjects received further extension with an additional endovascular graft. Including the event reported as

SCI, the incidence at Discharge/30 days is 6.2% (4/65). This SCI event was not reported as paraplegia/paraparesis as this subject had prior history of lower extremity weakness. This subject received a 150 mm device and was found POD 1 to have bilateral lower extremity weakness but could ambulate. A CSF drain was placed, and the patient improved to baseline by POD 13. The CEC adjudicated this event as not an MAE and not permanent as the SCI resolved prior to 12 months.

In the aortic rupture arm, there was one case adjudicated by the CEC as permanent paraplegia/paraparesis. One other event within 30-days was reported as Brown-Sequard Syndrome. The CEC did not consider this an MAE and not permanent paraplegia/paraparesis and is not presented in the table below.

Table 19 - Summary of Select Secondary Endpoints: Paraplegia/Paraparesis -Intent-to-Treat Population

	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Subjects Eligible N'	65/9	58/7	55/6	48/4	46/4	65/9
Any paraplegia/paraparesis						
Main Study Arm n (%)	3 (4.6) *	1 (1.7)	0 (0.0)	1 (2.1)	0 (0.0)	5 (7.7) *
Aortic Rupture Arm n (%)	1 (11.1) †	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	2 (22.2) †
Permanent paraplegia/paraparesis persisting at 12 months						
Main Study Arm (N=65) n (%)						3 (4.6) ‡
Aortic Rupture Arm (N=9) n (%)						1 (11.1)
Permanent paraplegia/paraparesis persisting at death						
Main Study Arm (N=65) n (%)						2 (3.1) §
Aortic Rupture Arm (N=9) n (%)						0 (0.0)

** 4 (6.2%) at 30 days and 6 (9.2%) total with the event reported as SCI.*
† 2 (22.2%) at 30 days and 3 (33.3%) total with the event reported as Brown-Sequard Syndrome.
- N=number of subjects enrolled; n=number of subjects in specified category; percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each group.
**‡ Three subjects met this primary endpoint MAE.*
§ One subject expired POD 103 and another expired POD 130.

The Total column number is the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.
Paraplegia/paraparesis is defined as complete/partial or incomplete loss of lower limb motor function (paralysis), related to spinal cord ischemia and not relating to stroke. Where paraplegia/paraparesis is reported at discharge/30 days and persists at 12 months the term will be updated to permanent paraplegia/paraparesis. Where a subject dies prior to 12-month follow-up, the term will be updated to paraplegia/paraparesis persisting at time of death.

7.4.11.8 Myocardial Infarction

In the main study arm, there was one (1/48, 2.1%) myocardial infarction reported at the 24-month follow-up. This subject had a myocardial infarction on post-operative day 698 with an elevated troponin level of 9.13 ng/ml (normal range 0.04 ng/ml) after undergoing an Extent 1 Thoracoabdominal aortic aneurysm replacement (30 mm Gelweave) using a stage II elephant trunk technique with celiac reimplantation in which a chronic aorto-esophageal fistula was also noted.

There were no reported cases of myocardial infarction in the aortic rupture arm.

Table 20 - Incidence of Myocardial Infarction

	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Subjects Eligible (Main/Aortic Rupture Arm) - *N´*	65/9	57/7	55/6	48/4	46/4	65/9
Main Study Arm n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	0 (0.0)	1 (1.5)
Aortic Rupture Arm n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

- N=number of subjects enrolled; n=number of subjects in specified category; percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each arm.
The Total column number is the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.
Myocardial infarction (MI) was defined as evidence of myocardial necrosis (either changes in cardiac biomarkers or post-mortem pathological findings) and supporting information derived from the clinical presentation, electrocardiographic changes, or the results of myocardial or coronary artery imaging.

7.4.11.9 Respiratory Failure

In the main study arm, 15 subjects (15/65, 23.1%) experienced respiratory failure at discharge/30 days, 2 (2/58, 3.4%) at 3 months follow-up, 1/55 (1.8%) at 12 months, 1/48 (2.1%) at 24 months, and 3/47 (6.4%) at 36-month follow-up. Of the 15 respiratory failures reported at discharge/30-day visit, 93.3% (14/15) resolved by the 3 month visit. The other subject's respiratory failure resolved during the 3 month follow up visit on post-operative day (POD) 55.

The subject's respiratory failure event was newly reported at the 3-month follow-up visit and remained unchanged until the time of death on POD 103.

There were two late cases of respiratory failure reported at 12 and 24 months related to subsequent thoracoabdominal aneurysm repairs.

In the aortic rupture arm, one (11.1%, 1/9) subject experienced respiratory failure at discharge/30 days, and one (11.1%, 1/7) experienced respiratory failure at 3-month follow up. The respiratory failure reported at discharge/30-day visit remained unchanged at the time of death. There was one (11.1%) reported respiratory failure at 3-month follow up which was moderate in intensity and resolved on POD 72. The CEC adjudicated this event as not related to device but related to procedure.

Table 21 - Incidence of Respiratory Failure: Intent-to-Treat Population

	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Subjects Eligible (Main/Aortic Rupture Arm) - *N´*	65/9	58/7	55/6	48/4	47/4	65/9
Main Study Arm n (%)	15 (23.1)	2 (3.4)	1 (1.8)	1 (2.3)	3 (6.4)	21 (32.3)
Aortic Rupture Arm n (%)	1 (11.1)	1 (14.3)	0 (0.0)	0 (0.0)	1 (25 .0)	3 (33.3)

- N=number of subjects enrolled; n=number of subjects in specified category; percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each arm.
The Total column number is the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.
Respiratory failure is defined as ventilator dependence greater than 48 hours.

7.4.11.10 Renal Failure

In the main study arm, 4 subjects (4/65, 6.2%) were reported with renal failure at discharge/30 days. All 4 incidences of renal failure were treated with hemodialysis and occurred within 1-2 days from the implant surgery. There was one (2.1%) more event at 36 months in a subject who subsequently died.

In the aortic rupture arm, renal failure was reported in 1 subject at discharge/30 days. This acute kidney injury was due to ischemic acute tubular necrosis post-operatively resulting in gross fluid overload. The subject was treated with continuous veno-venous hemodialysis (CVVHD). The event remained unchanged at the time of death (POD 4).

Table 22 - Incidence of Renal Failure

	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Subjects Eligible (Main/Aortic Rupture Arm) - *N´*	65/9	57/7	55/6	47/4	47/4	65/9
Main Study Arm n (%)	4 (6.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	5 (7.7)
Aortic Rupture Arm n (%)	1 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)

- N=number of subjects enrolled; n=number of subjects in specified category; percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each subgroup.
The Total column number is the N' of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.
Renal failure is defined as dialysis dependent or serum creatinine ≥2.5mg/dL.

7.4.11.11 Bowel Ischemia

In the main study arm, bowel ischemia was reported in one subject at discharge/30 days, and a second subject at 3-months through the 12-month follow-up visit. These cases are briefly discussed below.

- One subject had ischemic colitis at the discharge/30 day visit, intensity was reported as mild and unchanged at the time from withdrawing from the study. This event was CEC adjudicated as not related to the device and related to the procedure.
- The second subject had bowel ischemia at 3-month follow-up. It continued through the 12 month visit and was severe in intensity but resolved POD 333. The CEC adjudicated as not related to the device and not related to the procedure.

No instances of bowel ischemia were reported in the aortic rupture arm.

Table 23 - Incidence of Bowel Ischemia

	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Subjects Eligible (Main/Aortic Rupture Arm) - N	65/9	57/7	55/6	47/4	46/4	65/9
Main Study Arm n (%)	1 (1.5)	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	2 (3.1)
Aortic Rupture Arm n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

- N=number of subjects enrolled; n=number of subjects in specified category; percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each arm.
The Total column number is the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.
Bowel ischemia is defined as inadequate flow of oxygenated blood to the intestines.

7.4.11.12 Device-related Adverse Events

Adverse events adjudicated by the CEC as device-related are summarized in **Table 24**. This table includes both AEs and SAEs and is sorted by MedDRA (Medical Dictionary for Regulatory Activities) system organ class (SOC) and preferred term (PT). In the main study arm, 33.8% (22/65) of subjects experienced a device-related adverse event. For the Aortic Rupture Arm, 33.3% (3/9) subjects experienced a device-related adverse event.

The device-related events for this group are summarized below.

Table 24 - Summary of Device-Related Adverse Events SOC/PT – Intent-to-Treat Population (Overall)

MedDRA SOC/PT	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Any Device-Related Adverse Event	22 (33.8)	3 (33.3)
General disorders and adminisration site conditions	7 (10.8)	1 (11.1)
Systemic inflammatory response syndrome	2 (3.1)	1 (11.1)
Stent-graft endoleak	2 (3.1)	0 (0.0)
Pain	1 (1.5)	0 (0.0)
Death	1 (1.5)	0 (0.0)
Vascular stent thrombosis	1 (1.5)	0 (0.0)
Vascular disorders	6 (9.2)	1 (11.1)
Embolism	2 (1.5)	1 (11.1)
Aortic Dissection	1 (1.5)	0 (0.0)
Aortic aneurysm rupture	1 (1.5)	0 (0.0)
Iliac artery embolism	1 (1.5)	0 (0.0)
Shock	1 (1.5)	0 (0.0)
Nervous system disorders	5 (7.7)	1 (11.1)
Cerebrovascular accident*	2 (3.1)	0 (0.0)
Paraparesis	1 (1.5)	1 (11.1)
Paralysis	1 (1.5)	0 (0.0)
Paraplegia	1 (1.5)	0 (0.0)
Surgical and medical procedures	5 (7.7)	0 (0.0)
Aortic surgery	3 (4.6)	0 (0.0)
Aortic stent insertion	2 (3.1)	0 (0.0)
Injury, poisoning and procedural complications	2 (3.1)	1 (11.1)
Spinal cord injury	2 (3.1)	1 (11.1)
Gastrointestinal disorders	1 (1.5)	0 (0.0)
Abdominal pain	1 (1.5)	0 (0.0)

MedDRA SOC/PT	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Nausea	1 (1.5)	0 (0.0)
Vomiting	1 (1.5)	0 (0.0)
Infections and infestations	1 (1.5)	0 (0.0)
Gangrene	1 (1.5)	0 (0.0)
Cardiac disorders	1 (1.5)	0 (0.0)
Arrhythmia	1 (1.5)	0 (0.0)
Renal and urinary disorders	1 (1.5)	0 (0.0)
Renal failure	1 (1.5)	0 (0.0)
Skin and subcutaneious tissue disorders	1 (1.5)	0 (0.0)
Decubitus ulcer	1 (1.5)	0 (0.0)

- Adverse events are collected from the time of device implant. All adverse events are coded using MedDRA version 18.1.
- Relatedness includes both "related" and "possibly related".
- N = number of subjects in the ITT population; n=number of subjects in specified category; Percentages are based on number of subjects within each arm
**Both strokes were moderate in severity. One was CEC adjudicated as an MAE. The second was not adjudicated as an MAE, possibly related to device and related to procedure.*

7.4.11.13 Significant Failure of Device Integrity

Significant failure of device integrity is defined as wear or tear in the fabric or wire breakage resulting in a compromised seal and blood leakage or movement of the device. There have been no reported failures of device integrity in the main study arm.

One subject in the aortic rupture arm was reported with “left subclavian artery disconnected from graft with associated leak” at 36 months. This does not appear to be due to a device integrity failure as tified the subject was implanted using the island technique, so the LSA was not directly anastomosed to the Thoraflex™ Hybrid proximal vascular graft section.

7.4.11.14 Failed Patency

Incidence of failed patency is defined as a reduction in blood flow through the device as determined through imaging analysis and requiring surgical intervention.

7.4.11.15 Thrombosis of the Lumen

The presence of thrombus in the distal neck or within the descending thoracic aneurysm was evaluated. If present, it was sub-classified as complete or incomplete thrombosis. Thrombosis of the perigraft lumen was captured. Complete thrombosis is defined as occluding the entire lumen while incomplete thrombosis is a partial occlusion.

In the main study arm, false lumen thrombosis was reported in 27 subjects (27/54, 50.0%) at discharge/30 days and 25 subjects (25/52,48.1%) at 3 months; in 11 (16.9%) false lumen thrombosis was complete. In dissection subjects (n=38 chronic and n=1 acute), 78.8% (26/33) and 70.1% (24/34) were reported with early false lumen thrombosis (discharge and 3 months, respectively). Thrombosis external to the graft and within the true lumen was reported, but this was aneurysm thrombosis (not inside the graft).

In the aortic rupture arm, 5 subjects (5/6, 83.3%) at the discharge/30 days discharge were reported to have thrombosis of the false lumen, 4 subjects (4/5, 80.0%) continued with this incidence at the 3-month follow up, and 2 subjects (2/4 50.0%) were reported at 12-month follow-up.

Table 25 - Incidence of Thrombosis of the Lumen Intent-To-Treat-Population

	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months
Number of Subjects Eligible - N´	54/6	52/5	50/5	34/2	29/4
Thrombosis of the false lumen n (%)					
Main Study Arm	27 (50.0)	25 (48.1)	11 (22.0)	2 (5.9)	0 (0.0)
Aortic Rupture Arm	5 (83.3)	4 (80.0)	2 (40.0)	0 (0.0)	0 (0.0)
Thrombosis of the true lumen n (%)					
Main Study Arm	4 (7.4)	3 (5.8)	2 (4.0)	3 (8.8)	0 (0.0)
Aortic Rupture Arm	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thrombosis of the false lumen (dissection only, acute & chronic) n (%)					
Number of Subjects Eligible - N´	33/5	34/4	30/4	19/2	16/3
Main Study Arm	26 (78.8)	24 (70.1)	11 (36.7)	2 (10.1)	0 (0.0)
Aortic Rupture Arm	4 (80.0)	3 (75.0)	2 (50.0)	0 (0.0)	0 (0.0)
Thrombosis of the true lumen (dissection only, acute & chronic) n (%)					
Main Study Arm	0 (0.0)	1 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)
Aortic Rupture Arm	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

N=number of subjects enrolled; n=number of subjects in specified category; percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each arm.

7.4.11.16 Device Migration

Migration is defined as a change of >10mm from the discharge/30 days position. There were no Core Lab or site-reported device migrations for either study arm.

7.4.11.17 Endoleaks

Endoleak is defined as blood flow outside of the stent-graft and insdie the aneurysm sac. Endoleaks are classified according to the source of the blood flow. Data was collected and is reported on the following endoleak types.

- Type I endoleaks have blood flow that originates from a stent-graft attachment site. Separation occurs between the stent-graft and the native arterial wall creating flow between the aneurysm sac and arterial circulation. Type I endoleaks are the most common after thoracic aortic aneurysm repair.
    - Type I endoleaks are further subclassified as Type Ia, which has a proximal source, and Type Ib which has a distal source.
- Type III endoleaks occur after a structural failure of the stent-graft, which can include fractures or rip or holes in the fabric.
- Type IV endoleaks result from porosity of the stent-graft. Usually seen at the time of implantation when the subject is anticoagulated. After restoration of the normal anticoagulation system, the endoleak resolves.

Type Ib endoleaks are anticipated in certain cases where the Thoraflex™ Hybrid device is not long enough to exclude the aneurysm in a single stage procedure, in such cases extension of the Thoraflex™ Hybrid device is required to exclude the aneurysm. Subjects who have a pre-planned extension of the Thoraflex™ Hybrid device may have a Type Ib endoleak after implantation of the Thoraflex™ Hybrid device and prior to the extension procedure being performed and were considered anticipated. Type Ib endoleak in these instances will therefore not be considered an adverse event. These events were recorded as pre-planned

secondary interventions. All subjects were assessed by the Investigator as requiring a planned extension procedure. Unanticipated endoleaks are those that were not planned (that is, a deliberate treatment strategy not to completely exclude the lesion and allow perfusion, typically with the intention to reduce the risk of SCI). These are a subset of the respective category of endoleak.

The Investigator reviewed all images and the Core Laboratory independently assessed for endoleaks. In the event the Investigator and Core Laboratory disagreed on the specific field for endoleak in the imaging eCRFs, the CEC was provided CT scans for adjudication. The CEC's determination was be recorded in the Core Laboratory EDC system.

Table 26 below contains a summary of endoleaks in the main study arm. In the main study arm, 14 subjects (14/54, 25.9%) at 30-days were observed with a Type Ib endoleak, 11 (11/52, 21.2%) at 3-months (8 persistent), and 6 (6/52, 11.5%) were observed at 12 months (3 persistent and continued at 24 months). There were 3 subjects who experienced an unanticipated Type Ib endoleak: 2 at 12-months and 1 at 36-months.

In the aortic rupture arm, there was 1 anticipated Type Ib endoleak observed at the 3-month visit that persisted to the 12-month visit. The numbers of subjects with adequate imaging to determine endoleaks were: 6 (30 days); 5 (3 months); 5 (1 year); 2 (2 years); 4 (3 years).

There were no Type Ia endoleaks, Type III endoleaks, or Type IV endoleaks reported at any timepoint in the either study arm.

Table 26 - Summary of Endoleaks: Main Study Arm

Endoleak n (%)	30 Days	3 Months	12 Months	24 Months	36 Months	Total
Adequate imaging	54	52	52	35	30	60
Type Ia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Type Ib						
New	14 (25.9)	3 (5.8)	3 (5.8)	0 (0.0)	1 (3.3)	-
Persistent	0 (0.0)	8 (15.4)	3 (5.8)	3 (8.6)	2 (6.7)	-
New/persistent	14 (25.9)	11 (21.2)	6 (11.5)	3 (8.6)	3 (10.0)	21 (35.0)
Type III	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Type IV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Un**anticipated Type Ia**	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unanticipated Type Ib						
New	0 (0.0)	0 (0.0)	2 (3.8)	0 (0.0)	1 (3.3)	-
Persistent	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-
New/persistent	0 (0.0)	0 (0.0)	2 (3.8)	0 (0.0)	1 (3.3)	3 (5.0)

Unanticipated endoleaks are those that were not planned (that is, a deliberate treatment strategy not to complete exclude the lesion and allow perfusion, typically with the intention to reduce the risk of SCI). These are a subset of the respective category of endoleak.
- N = number of subjects enrolled; n=number of subjects in specified category; Percentages are based on number which is the number of subjects who have adequate data to assess the parameter within each arm.
New endoleaks include any events that are newly reported during a study visit, from both EDC and CEC adjudication. Persistent endoleak include any events that are continued from prior study visits.
The Total column number is the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.

Summary of Type Ib Endoleaks
Note that Type Ib endoleaks are anticipated in certain cases where the Thoraflex™ Hybrid device is not long enough to exclude the aneurysm in a single stage procedure; in such cases, extension of the Thoraflex™ Hybrid device is required to exclude the aneurysm.

In the main study arm, there were 14 subjects reported with a new Type Ib endoleak at discharge/30-days, 3 new at 3 months, 3 new at 12 months, no new at 24 months, and 1 new at 36 months. Three (4.6%) were unanticipated. All 14 with a Type Ib endoleak at discharge/30-days were assessed by the Investigator either preoperatively or intraoperatively as needing a planned extension procedure and 11 subjects eventually received an extension procedure. Of the three subjects who did not have an extension; one subject had partial thrombosis of the false lumen at 30 days and the Type Ib endoleak was residual at that point and absent at one year; the Type Ib endoleaks of the other two subjects were absent at one year follow-up.

In the aortic rupture arm, there was one Type Ib endoleak reported at 3 month follow-up that persisted at the 12 month follow-visit; this subject was anticipated to need extension. Change in Aortic Size in the Grafted Segment

Incidence of change in the aorta is defined as an increase in diameter >5mm measured along the major axis from the discharge/30-day CT. Maximum aortic diameter is measured inner diameter to inner diameter.

The Core Laboratory reported enlargement only for one subject (1.5%, 1/65) in the grafted segment in the descending thoracic aorta along with Type Ib endoleak that the CEC adjudicated as residual; the subject later had unplanned second-stage TEVAR extension.

7.4.11.18 Thromboembolic Adverse Events
Thromboembolic events are defined as:

- Thromboembolism: Formation in a blood vessel of a clot (thrombus) that breaks loose and is carried by the blood stream to plug another vessel. This can be either arterial or venous.
- Pulmonary embolism: Thrombus arising within the circulatory system and obstructing pulmonary blood flow in the pulmonary artery or any of its branches.

In the main study arm, two (3.1%, 2/65) subjects were reported to have thromboembolic adverse events (arterial and pulmonary, respectively) at the discharge/30 day visit and one (pulmonary) at 36 months.

In the aortic rupture arm, one (14.3%) subject was reported to have a arterial thromboembolic adverse event at the 3-month follow-up.

Table 27 - Incidence of Thromboembolic Adverse Events

	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Subjects Eligible (Main/Aortic Rupture Arm) - N´	65/9	57/7	55/6	47/4	47/4	65/9
Main Study Arm n (%)	2 (3.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	3 (4.6)
Aortic Rupture Arm n (%)	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)

- N=number of subjects enrolled; n=number of subjects in specified category; percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each arm.
The Total column number is the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.

7.4.11.19 Pseudoaneurysm

Pseudoaneurysm is defined as a false aneurysm classified as either procedure related (e.g., associated with graft suture line, or graft infection) or non-procedure related (e.g., caused by trauma). The CEC adjudicated all pseudoaneurysms.

There have been no pseudoaneurysms of any surgical suture line related to the Thoraflex™ Hybrid device in the main study arm. Pseudoaneurysms were reported for three subjects in the main study arm (2 at 12-months and 1 at 36 months); however, these pseudoaneurysms were not in the treated segment of the aorta.

There have been no instances of pseudoaneurysms reported in the aortic rupture arm in the treated or non-treated segment of the aorta.

7.4.11.20 Hypersensitivity Reactions

In the main study arm, there have been three hypersensitivity reactions reported, namely contrast allergy, pruritus, and contact dermatitis at the 12-month follow-up visit.

No instances of hypersensitivity were reported for the aortic rupture arm.

7.4.11.21 Extension Procedures

Investigators were asked to assess requirements for a future extension pre-operatively and post-implant. The timing of any extension procedure was at the discretion of the treating surgeon and could be amended (performed on an earlier or later date) by the surgeon if it was in the best interest of the subject. A second-stage procedure included an extension to the Thoraflex™ Hybrid device performed during the initial (study) implant procedure.

Although 47 subjects (72.3%, 47/65) in the main study arm were initially assessed prior to implant as requiring an extension procedure, 32 subjects (49.2%) received extensions; 28 (43.1%) of which received an endovascular extension (using commercially available thoracic stent-grafts; three with the Relay®Plus Thoracic Stent Graft System, none with the Relay®Pro NBS Thoracic Stent Graft System) and 5 (7.7%) of which received a surgical extension (one subject had both endovascular and surgical extensions) with Gelweave grafts. There were no device complications or deficiencies intra-operatively during the extension procedures. One subject received two separate endovascular extensions (one within one year and one at three years). There were no device complications or deficiencies during the extension procedures. Two of the 28 subjects with endovascular extensions had their procedures performed on an unanticipated basis within 30 days of the study procedure. Per protocol, any unanticipated aortic interventions were classified as MAEs, consequently these two subjects were reported as a failures of the primary endpoint.

Three subjects (33.3%) in the aortic rupture arm were initially assessed prior to implant as requiring an extension procedure, but none actually received the extension.

There was no failure of device-extension integrity (e.g., wear or tear in the fabric or wire breakage) resulting in a compromised seal and blood leakage or movement of the device, no Type III endoleak, no failed patency of the device-extension overlap, and no secondary procedures related to the extension at any point in the study.

Table 28 - Summary of Extension Procedures

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Pre-operative Timepoint		
Extension procedure required	47 (72.3)	3 (33.3)
Extension procedure not required	17 (26.2)	6 (66.7)
Extension assessment not performed	1 (1.5)	0 (0.0)
Implant Timepoint		
Extension procedure required	42 (64.6)	3 (33.3)

Extension procedure not required	19 (29.2)	5 (55.6)
Extension assessment not performed	4 (6.2)	1 (11.1)
Actual Extension Procedures Performed		
Number of subjects with adequate data (N´)	29	0
Performed at any timepoint	29 (100.0)	0 (0.0)
Performed within one year of implantation	26 (89.7)	0 (0.0)
Performed more than one year after implantation	3 (10.3)	0 (0.0)
Any Intra-operative Device Complications/Device Deficiencies during Extension Procedures		
No	29 (100.0)	0 (0.0)
Yes	0 (0.0)	0 (0.0)
Any Aortic Insufficiency during Extension Procedure		
No	25 (86.2)	0 (0.0)
Yes	4 (13.8)	0 (0.0)
Grade 1	4 (100.0)	0 (0.0)
Grade 2	0 (0.0)	0 (0.0)
Grade 3	0 (0.0)	0 (0.0)
Grade 4	0 (0.0)	0 (0.0)
N = Number of subjects in the ITT population; n=number of subjects in a specified category; Percentages are based on N´ which is the number of subjects who have adequate data to assess the parameter within each subgroup. *Note: Requirements for extension procedure are based on PI assessment*		

7.4.11.22 Reinterventions in the Downstream Aorta

Reintervention in the downstream aorta is defined as all reinterventions in the downstream aorta, including unanticipated aortic-related re-operation, but excluding planned extensions of the Thoraflex™ Hybrid device classified by location: ascending aorta, arch, descending thoracic aorta, abdominal aorta.

Three reinterventions in the downstream aorta were reported for two subjects (2/55 3.6%) in the main study arm at the 12-month visit and one of those subjects (1/47, 2.1%) had a second reintervention at the 24-month visit. The reason for the reinterventions were to treat aneurysm enlargement (TEVAR), aortic dissection/rupture (open surgical repair) and SMA-duodenal fistula (partial duodenal resection, infected graft removal, duodeno-jejunostomy, and cryoartery graft placement).

In the aortic rupture arm, no reinterventions in the downstream aorta were reported.

7.4.11.23 Other Reinterventions

In the main study arm, 4 other secondary reinterventions were reported in 4 subjects (6.1%, 4/65) which are different interventions than those reported above (not related to the device in any case, related to the procedure in two cases, unrelated in two). One of the secondary interventions occurred within the discharge/30 day follow up while the remaining three occurred within the 12-month follow up. These secondary reinterventions included treatment for post-operative bleeding (suturing and cauterizing the site of the anastomosis), atelectasis (left chest washout), renal artery occlusion (angioplasty and right renal stent placement) and a protruding sternal wire (debridement).

In the aortic rupture arm, no other secondary reinterventions were reported.

7.4.11.24 Unanticipated/Emergency Surgery or Reintervention

In the main study arm, 3 unanticipated/emergency surgery or reinterventions were reported in 2 subjects. These events were reported at discharge/30-day and 3-month follow up for one subject (drainage of pericardial effusion, drainage of left pleural effusion and electrical cardioversion to resolve atrial flutter and sternal wound infection at the ascending aorta) and at the 12-month follow-up visit for the second subject, specifically repair of ruptured thoracoabdominal aneurysm. The 3 events were considered not related to the device.

In the aortic rupture arm, no unanticipated/emergency surgery or reinterventions were reported.

7.4.12 Individual Subject Success

Individual subject success is defined as treatment success at one year as well as Post-Operative return to normal activities and Improved Health related Quality of Life measure (HRQoL) EQ-5D. Individual subject success is only 8.9% despite 92.9% treatment success and 41.1% with improved health-related quality of life. The low overall value may be linked to only one quarter of subjects who were able to return to normal activities (23.2%).

Subject success is consistent with expectations for subjects who have undergone a major open surgical procedure for aortic arch pathology (Lohse F, Lang N, Schiller W, et al. Quality of Life after Replacement of the Ascending Aorta in subjects with True Aneurysms. Tex Heart Inst J. 2009;36(2):104-110.)

Table 29 - Individual Subject Success at 1-Year

Endpoint Timepoint	Main Study Arm n/N' (%)	Aortic Rupture Arm n/N' (%)
Individual Subject Success at 1-year	5/56 (8.9)	0/6 (0.0)
Treatment Success	52/56 (92.9)	5/6 (83.3)
Post-operative return to normal activities	13/56 (23.2)	0/6 (0.0)
Improved Health Related Quality of Life Measures	23/56 (41.1)	0/6 (0.0)
N = number of subjects in the ITT population; n=number of subjects in specified category; Percentages are based on N' which is the number of subjects who have adequate data to assess the parameter within each subgroup.		

7.5 Relay®Pro NBS Thoracic Stent Graft System Thoracic Stent-Graft System Experience

Clinical data from a US pivotal study is available regarding the endovascular repair of subjects with aneurysms and penetrating atherosclerotic ulcers (PAUs) in the descending thoracic aorta (DTA). Please refer to the Instructions for Use for the Relay®Pro NBS Thoracic Stent Graft Systemfor the details regarding the clinical information available from that study.

The Relay®Pro NBS Thoracic Stent Graft Systemis also being evaluated in the endovascular repair of subjects with dissections in the DTA; please refer to the Relay®Pro NBS Thoracic Stent Graft System IFU for the currently approved indications for use. This US pivotal study began enrollment on September 7, 2017, and the last subject was enrolled on September 3, 2021. A total of 56 subjects have been enrolled with data available on 54 subjects. Forty-eight (48) subjects have a visit performed at 30-days, 32 subjects at 6-months, 27 subjects at 12-months, 14 subjects at 2-years, and 4 subjects at 3-years. The study is continuing active follow-up at 6-months, 1-year, and annually through 5-years.

The primary endpoint is the rate of all-cause mortality. There was one dissection-related mortality on POD 8. The freedom from dissection-related mortality at 1-year is 98.0% and freedom of from all-cause mortality at 1 year is 85.6%.

Technical success at the index procedure, based on site reported data was achieved for all enrolled subjects (100%, 54/54). All subjects had the primary entry tear covered (100%, 54/54). Regarding additional events and observations through all available follow-up, there was 1 aortic rupture (CEC adjudicated, not Core Laboratory reported), 1 new Type Ia endoleak (1.9%, 1/54), 3 new migrations (5.6%, 3/54), 2 new retrograde dissections (3.7%, 2/54), and 2 new aortic expansions (3.7%, 2/54). There have been no ruptures of the dissection septum, fistula formation, component separation, losses of stent graft patency, stent-graft stenosis (> 50%) kinking, twisting, misalignment/birdbeaking, loss of device integrity, or stent fracture in the attachment zone.

There is limited clinical information available on the use of Thoraflex™ Hybrid with the Relay®Pro NBS Thoracic Stent Graft System distal extension. Additional clinical data is to be collected in a post-market study. The labeling will be updated with data from the post-market study when it becomes available.

8 Patient Selection and Treatment

8.1 Patient Selection

Physicians should evaluate each patient to determine if the Thoraflex™ Hybrid device would be appropriate to treat their lesion according to the criteria as specified in the Indications for Use, including:

- Adequate access compatible with the delivery system.
- For aneurysms: a distal landing zone in healthy vessel with an inside diameter of 19mm – 34mm and a length of ≥ 40mm
- For dissections: a distal landing zone with an inside diameter of 20mm – 38mm and a length of ≥ 40mm
- For treatments involving planned Relay®Pro NBS Thoracic Stent Graft System extension a distal landing zone with inside diameter of 20mm – 38mm and a length of 25mm or 30mm depending on device diameter. Refer to **Section 12.7** for further sizing information.

Additional considerations for patient selection when considering FET may include the following:

- Age and life expectancy
- Comorbidities such as cardiac, pulmonary, renal insufficiency, morbid obesity)
- Patient's suitability for open surgical repair
- Ability to tolerate general anesthesia
- The device should not be used in patients unwilling or unable to comply with the recommended post procedure clinical and imaging follow-up

8.2 Device Sizing

8.2.1 Aneurysm Sizing (single stage)

This section discusses the recommended sizing for the Thoraflex™ Hybrid device for aneurysm treatment, when landed distally in healthy vessel of the descending thoracic aorta, as illustrated in **Figure 9**. The Thoraflex™ Hybrid Aneurysm Sizing Chart incorporates a suitable oversize of ring stent diameter to aortic diameter. Aortic diameter is based on inner vessel diameter (ID) measurements; therefore, no further oversize is required. If outside vessel diameters (OD) are measured, then an allowance for the vessel wall thickness must be made before using the sizing chart for device selection.

A minimum of 40 mm in length for the distal landing zone is recommended (**Table 30, Figure 7, Figure 8, Figure 9)**.

NOTE: The diameter of the sheath measures 10mm.

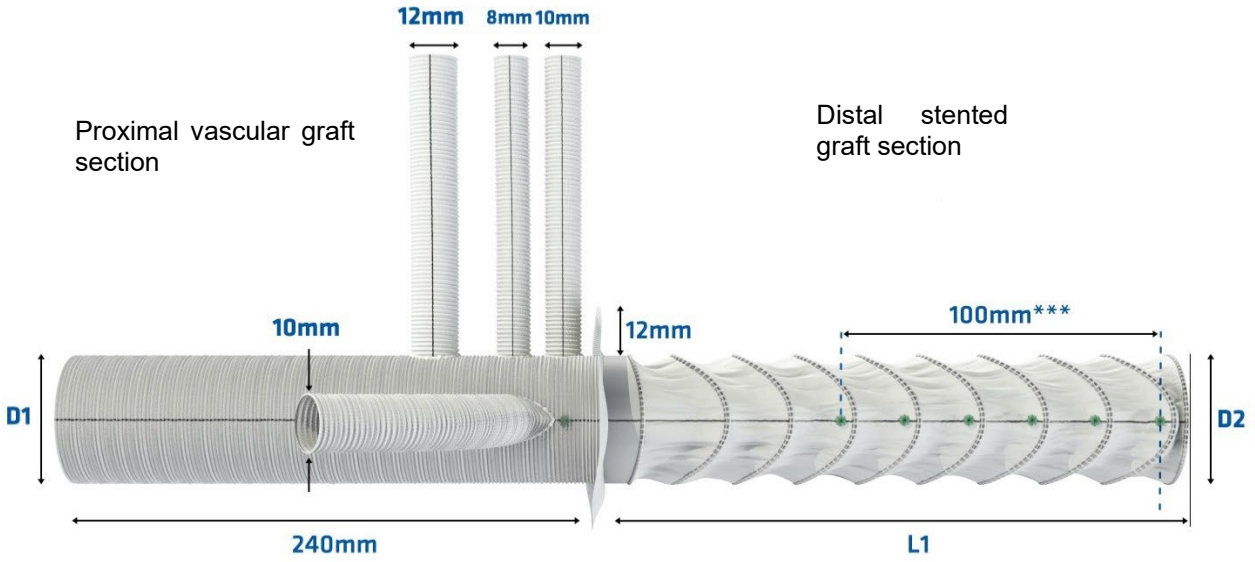
Table 30 - Thoraflex™ Hybrid Device Aneurysm Sizing Chart

Catalog No. (Plexus)	Catalog No. (Ante-Flo)	D1 Graft ID (mm)	D2 Stent-graft OD (mm)	D3 Descending Landing Zone Vessel ID (mm)	Branch Configuration IA, LCC, LSA Diameters (mm)	L1* Stent-graft Nominal Length (mm)
THP2224X100A	THA2224X100A	22	24	19 - 21	10, 8, 8	100
THP2426X100A	THA2426X100A	24	26	20 - 22	10, 8, 8	100
THP2628X100A	THA2628X100A	26	28	22 - 24	12, 8, 10	100
THP2830X100A	THA2830X100A	28	30	24 - 26	12, 8, 10	100
THP3032X100A	THA3032X100A	30	32	25 - 27	12, 8, 10	100
THP3034X100A	THA3034X100A	30	34	27 - 29	12, 8, 10	100
THP3036X100A	THA3036X100A	30	36	29 - 31	12, 8, 10	100
THP3038X100A	THA3038X100A	30	38	30 - 33	12, 8, 10	100
THP3040X100A	THA3040X100A	30	40	32 - 34	12, 8, 10	100
THP3240X100A	THA3240X100A	32	40	32 - 34	12, 8, 10	100
THP2224X150A	THA2224X150A	22	24	19 - 21	10, 8, 8	150
THP2426X150A	THA2426X150A	24	26	20 - 22	10, 8, 8	150
THP2628X150A	THA2628X150A	26	28	22 - 24	12, 8, 10	150
THP2830X150A	THA2830X150A	28	30	24 - 26	12, 8, 10	150
THP3032X150A	THA3032X150A	30	32	25 - 27	12, 8, 10	150
THP3034X150A	THA3034X150A	30	34	27 - 29	12, 8, 10	150
THP3036X150A	THA3036X150A	30	36	29 - 31	12, 8, 10	150
THP3038X150A	THA3038X150A	30	38	30 - 33	12, 8, 10	150
THP3040X150A	THA3040X150A	30	40	32 - 34	12, 8, 10	150
THP3240X150A	THA3240X150A	32	40	32 - 34	12, 8, 10	150

***Nominal length quoted.**

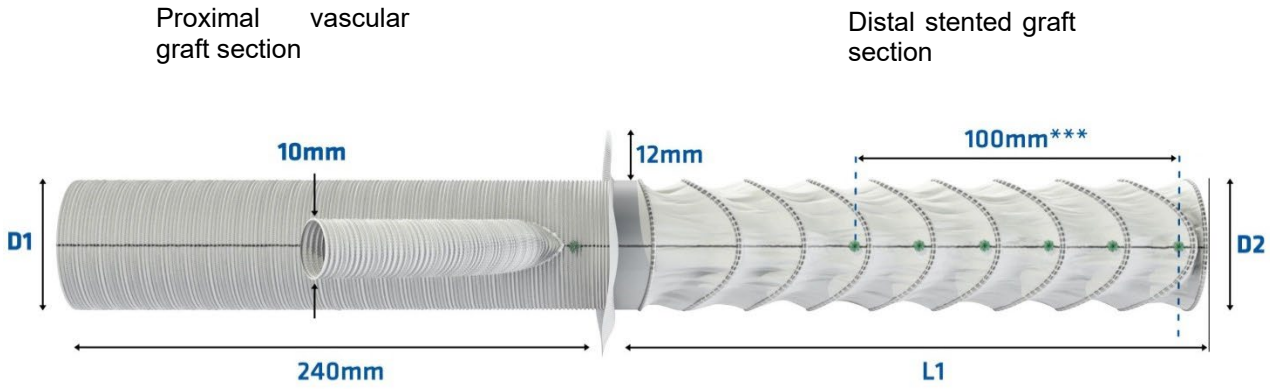
ID, inner diameter; OD, outer diameter.

When measuring length, it should be considered that the device will take the outer curve of the aorta. Refer to **Figure 9**.



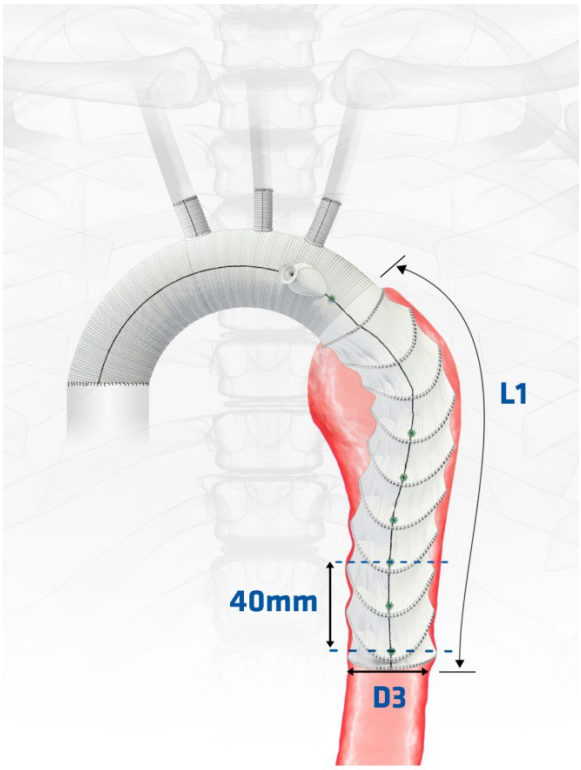
***Length shown to indicate overall marker positions. The distance between each marker is approximately 20mm but varies from 17.5mm-22mm depending on the ring stent configuration, which varies with stented section diameter and length.

Figure 7 - Thoraflex™ Hybrid Plexus 4 Device Dimensions



***Length shown to indicate overall marker positions. The distance between each marker is approximately 20mm but varies from 17.5mm-22mm depending on the ring stent configuration, which varies with stented section diameter and length.

Figure 8 - Thoraflex™ Hybrid Ante-Flo Device Dimensions



Stent ring oversizing and landing zone guidelines are applicable to all designs.

Figure 9 - Device Sizing

Some movement of the distal ring of the Thoraflex™ Hybrid device may occur following re-perfusion of the thoracic aorta. Excessive aortic tortuosity may result in inability to properly position the stent-graft, or stent-graft kinking with thrombus formation. If balloon modelling is desired (e.g., for endoleak, stent-graft kinking or stenosis), use a compliant balloon equal in size to the largest target vessel's diameter. Balloon inflation should not exceed 1 atm.

8.2.2 Aneurysm Sizing (two stage)

Thoraflex™ Hybrid is indicated to be extended using a Relay®Pro NBS Thoracic Stent Graft System to exclude aneurysms longer than the standard Thoraflex™ Hybrid device. In these cases, the distal stented graft of the Thoraflex™ Hybrid will be within the aneurysm sac, and there will be no distal seal until the Relay®Pro NBS Thoracic Stent Graft System has been implanted. Sizing of the Thoraflex™ Hybrid device should be based on the complete treatment and take into account the size of the distal landing zone of the compatible Relay®Pro NBS Thoracic Stent Graft System, e.g., if a 34mm Relay®Pro NBS Thoracic Stent Graft System has been selected for the distal treatment then the compatible Thoraflex™ Hybrid device would be 32mm – see **Section 12.7** for further information on extension device sizing.

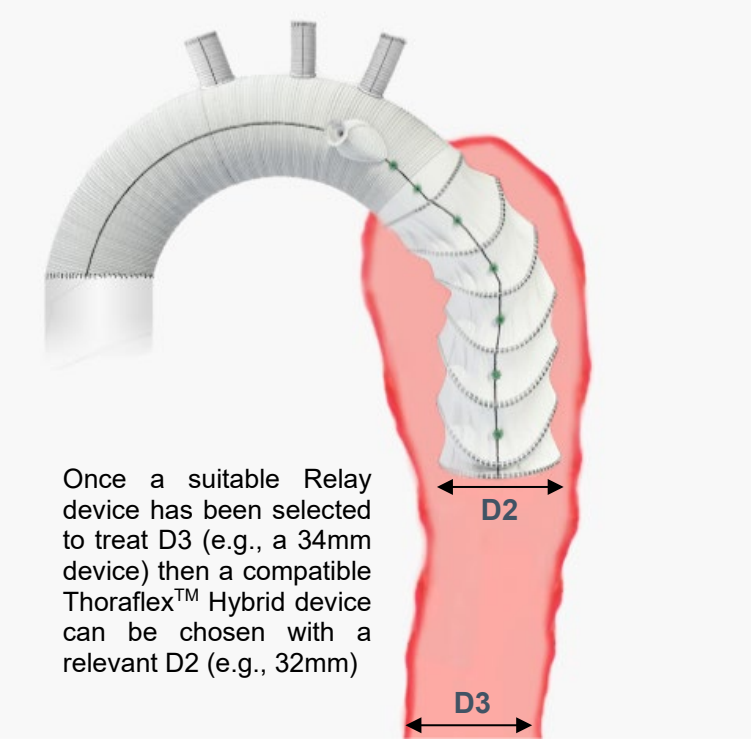


Figure 10 – Thoraflex™ Hybrid Distal Stent within the Aneurysm Sac

In these cases where the Thoraflex™ Hybrid does not create a complete distal seal, using larger device

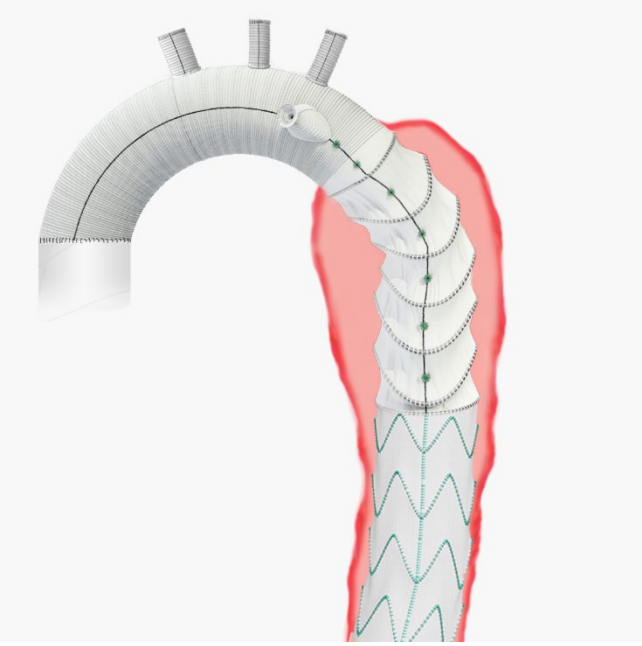


Figure 11 - Thoraflex™ Hybrid Extended with a RelayPro NBS Stent-Graft

diameters than required will increase the complexity of sizing the extension device and may additionally increase the risk of thrombus generation until completion of the therapy. See Section 12.7 for instructions on how to select device size if a distal extension is planned.

8.2.3 Dissection Sizing (single stage)

This section discusses the recommended sizing for the Thoraflex™ Hybrid device for dissection treatment, when landed distally in dissected vessel of the descending thoracic aorta. When oversizing in a dissection, clinical judgement must be used on an individual patient basis, using the Thoraflex™ Hybrid Dissection Sizing Chart (**Table 31**) as a guideline. The Thoraflex™ Hybrid Dissection Sizing Chart incorporates a suitable oversize of ring stent diameter to aortic diameter.

It is recommended that a minimum 40mm distal landing zone length is used.

NOTE: The diameter of the sheath measures 10mm.

NOTE: Excessive aortic tortuosity may result in inability to properly position the stent-graft, or stent-graft kinking with thrombus formation. If balloon modelling is desired (e.g., for treatment of endoleak, stent-graft kinking or stenosis observed intraoperatively), use a compliant balloon equal in size to the largest target vessel's diameter. Balloon inflation should not exceed 1 atm.

Table 31 - Thoraflex™ Hybrid Device Dissection Sizing Chart

Catalog No. (Plexus)	Catalog No. (Ante-Flo)	D1 Graft ID (mm)	D2 Stent-graft OD (mm)	D3 Descending Landing Zone Vessel ID (mm)	Branch Configuration IA, LCC, LSA Diameter (mm)	L1* Stent-graft Nominal Length (mm)
THP2224X100A	THA2224X100A	22	24	20 – 22.5	10, 8, 8	100
THP2426X100A	THA2426X100A	24	26	21.5 – 24.5	10, 8, 8	100
THP2628X100A	THA2628X100A	26	28	23.5 – 26.5	12, 8, 10	100
THP2830X100A	THA2830X100A	28	30	25 – 28.5	12, 8, 10	100
THP3032X100A	THA3032X100A	30	32	26.5 – 30	12, 8, 10	100
THP3034X100A	THA3034X100A	30	34	28.5 – 32	12, 8, 10	100
THP3036X100A	THA3036X100A	30	36	30 – 34	12, 8, 10	100
THP3038X100A	THA3038X100A	30	38	32 – 36	12, 8, 10	100
THP3040X100A	THA3040X100A	30	40	34 - 38	12, 8, 10	100
THP3240X100A	THA3240X100A	32	40	34 - 38	12, 8, 10	100
THP2224X150A	THA2224X150A	22	24	20 – 22.5	10, 8, 8	150
THP2426X150A	THA2426X150A	24	26	21.5 – 24.5	10, 8, 8	150
THP2628X150A	THA2628X150A	26	28	23.5 – 26.5	12, 8, 10	150
THP2830X150A	THA2830X150A	28	30	25 – 28.5	12, 8, 10	150
THP3032X150A	THA3032X150A	30	32	26.5 – 30	12, 8, 10	150
THP3034X150A	THA3034X150A	30	34	28.5 – 32	12, 8, 10	150
THP3036X150A	THA3036X150A	30	36	30 – 34	12, 8, 10	150
THP3038X150A	THA3038X150A	30	38	32 – 36	12, 8, 10	150
THP3040X150A	THA3040X150A	30	40	34 - 38	12, 8, 10	150
THP3240X150A	THA3240X150A	32	40	34 - 38	12, 8, 10	150

*Nominal length quoted.

ID, inner diameter; OD, outer diameter.

8.2.4 Dissection Sizing (two stage)

Thoraflex™ Hybrid is indicated to be extended using a Relay®Pro NBS Thoracic Stent Graft System to exclude dissections longer than the standard Thoraflex™ Hybrid device. In these cases, the distal stented graft of the Thoraflex™ Hybrid will likely be oversized within the dissected vessel and not expanded to its maximum diameter. Sizing of the Relay®Pro NBS Thoracic Stent Graft System should be based on the nominal size of the distal stented graft of the Thoraflex™ Hybrid device and not the measured size of the vessel, e.g., if a Thoraflex™ Hybrid with a 34mm distal stented graft has selected for the treatment of a 30mm vessel then the compatible Relay®Pro NBS Thoracic Stent Graft System would also be 34mm – see **Section 12.7** for further information on extension device sizing.

9 Patient Counseling

The clinician should review all associated risks and benefits when counseling the patient about this vascular prosthesis and all associated procedures.

It is recommended that the clinician inform the patient of all associated risks and benefits, in written form. These include but are not limited to:

- patient age and life expectancy
- risks and benefits related to the procedure
- risks related to non-interventional treatment or medical management or alternative surgical options
- long term monitoring requirements
- possibility that subsequent endovascular or open surgical repair of the lesion may be required
- the long-term safety and effectiveness of Thoraflex™ Hybrid has not been established
- long-term, regular follow-up by a specialist with periodic imaging is needed to assess patient health status and device performance
- patients with specific clinical findings (e.g. endoleaks, enlarging aneurysms) should be monitored closely
- symptoms of aortic rupture

Details regarding risks occurring during or after implantation of the device are provided in **Section 6.1** Potential Adverse Events.

Please instruct the patient as to proper postoperative care, including limiting movement of the affected area during the convalescent period.

10 Additional Information

10.1 Origin of Gelatin

The Thoraflex™ Hybrid device uses gelatin manufactured from animals native to, and exclusively raised in the United States of America. The United States of America is classified as a negligible BSE risk country according to the OIE categorization (referenced in FDA guidance “Medical Devices Containing Materials Derived from Animal Sources (Except for In Vitro Diagnostic Devices)”). The gelatin is hydrolyzed within approximately 14 days and is replaced by normal tissue incorporation.

10.2 Sterilization

These systems have been sterilized using Ethylene Oxide and are supplied sterile. The Tyvek seal on both intermediate and inner pouches must be intact. Any damage to the pouches renders the system non-sterile.

Note: In the event of damage to the primary packaging (Tyvek pouches), the product must not be used and should be returned immediately to the supplier. If the sterile packaging is unintentionally opened before use or exposed to environmental conditions out with those specified, then the device should be discarded as per **Section 10.5**.

CAUTION: THE THORAFLEX™ HYBRID SYSTEM MUST NOT BE RE-STERILIZED. Thoraflex™ Hybrid is provided sterile for single-use only. Do not re-sterilize any components of the system.

CAUTION: DO NOT USE BEYOND THE INDICATED EXPIRATION DATE.

10.3 Packaging

Each device is pre-loaded in its individual delivery system and packaged using a double pouch system with peel-open end seals. Each package contains a label describing the device details such as catalog number, diameter, length, delivery system size, etc.

Tyvek pouches are enclosed in a foil pouch that serves as a vapor barrier and preserves optimal system characteristics. A sachet containing a desiccant is included to aid this purpose. Store the packaged Thoraflex™ Hybrid in a cool, dry place to avoid exposure to extreme temperatures and humidity.

Note: The foil pouch and outer Tyvek pouch are not sterile. Only the innermost pouch and tray can be introduced to the sterile field. If the sterile packaging is unintentionally opened before use or exposed to environmental conditions out with those specified, then the device should be discarded as per **Section 10.5.**

The product is supplied with the following model designation identified on the label as shown in **Table 32**.

Table 32 - Product Designation

Internal Code	Identifier	Open Graft Diameter	Stent Diameter*	Stent Length**	Device Designation
TH	P: Plexus A: Ante-Flo	XX	XX	XXX	A: Standard Catalog Product for US
** Stent diameter is for distal diameter of the stented section.* *** Stent length is for covered length from the collar to the distal stent.*					

10.4 Additional Labels

Additional labels are enclosed for use on patient records.

10.5 Disposal of the Thoraflex™ Hybrid Delivery System

At the end of the procedure, care must be taken to ensure safe disposal of the Thoraflex™ Hybrid delivery system. Each operating team must ensure local and national regulatory requirements for the disposal of contaminated clinical waste products are adhered to.

10.6 Returning a Thoraflex™ Hybrid Delivery System or Device

Any explanted devices (along with their delivery systems) should be returned to Vascutek for analysis as soon as possible. In the event of a used delivery system/device needing to be returned, it is a requirement to have the delivery system/device, and any other items used in the procedure to be returned in an explants box which can be obtained from the Quality Assurance Department. If required, explant kits can be requested at complaintsUK@terumoaortic.com or through your local distributor and will be provided for the retrieval and preservation of the explanted device and/or delivery system or other components for transit.

11 Clinical Use Information

11.1 Physician Training Requirements

All physicians should be trained in the use of Thoraflex™ Hybrid before using it.

Caution: Thoraflex™ Hybrid should only be used by physicians and teams trained in Cardiovascular techniques and in the use of this device.

1. Knowledge of natural history of arch and thoracic aortic repair, as well as the comorbidities associated with these conditions
2. Experience with CT and/or MRI image interpretation for sizing and case planning
3. Experience with cardiothoracic surgical techniques such as: sternotomy, cardiopulmonary bypass and perfusion systems and techniques.
4. Experience in repair/replacement of the thoracic aorta

11.2 Case Planning and Individualization of Treatment

Practitioners using Thoraflex™ Hybrid should have a thorough understanding of open surgical and endovascular procedures and techniques. In particular, Thoraflex™ Hybrid should only be used by physicians and teams with experience and training in cardiovascular techniques, including, but not limited to, training on the use of Thoraflex™ Hybrid, as described in the preceding section. Selecting the proper graft with the appropriate length and diameter is paramount to the successful exclusion of aneurysm/lesion and to minimize endoleaks and SCI. Measure all parameters needed for proper sizing of the stent-graft carefully. Vascutek Ltd. recommends evaluation of all imaging studies available, i.e., angiograms, CT scans, MRI scans, MRA scans and plain radiographs. Each imaging modality offers additional information to the sizing process. The physical characteristics of the vessel should be evaluated in addition to its size. Factors such as stenosis, atherosclerotic disease, ectasia and tortuosity may affect device selection and placement strategy. **The final device selection will be the responsibility of the physician.**

11.3 Device Inspection Prior to Use

Inspect the system packaging for tears, punctures, breaks, or openings that would compromise the system sterility.

Note: The device should not be opened until correct size has been selected and ready to use.

Warning: Do not use the system if the outer pouch has any punctures, tears or opening as this may have affected system sterility.

11.4 Devices, Supplies and Equipment Required

- Thoraflex™ Hybrid implants of appropriate sizes.
- Minimum 260cm Guidewire/0.035” [0.89mm] (Super Stiff)
- Arterial puncture needles 18G or 19G
- Syringes
- Saline solution
- Sterile gauze pads
- Cautery
- Selection of surgical clamps
- Suture

11.5 Supportive/Supplementary Equipment

- Vascular balloons, catheters of the appropriate size

11.6 Magnetic Resonance Imaging (MRI) Safety

MRI Safety Information

MR Conditional

A person with the Thoraflex™ Hybrid alone or in combination with the Relay®Pro NBS Thoracic Stent Graft System may be safely scanned under the following conditions. Failure to follow these conditions may result in injury.

Device Name	Thoraflex™ Hybrid and Relay®Pro NBS Thoracic Stent Graft System
Static Magnetic Field Strength (B_o)	1.5T or 3.0T
Maximum Spatial Field Gradient	40 T/m (4,000 gauss/cm)
RF Excitation	Circularly Polarized (CP)
RF Transmit Coil Type	There are no Transmit Coil restrictions
Operating Mode	Normal Operating Mode
Maximum Whole-Body SAR	2 W/kg (Normal Operating Mode)
Maximum Head SAR	3.2 W/kg (Normal Operating Mode)
Scan Duration and Wait Time	15 continuous minutes of scan duration with 5 minutes wait time before additional scanning.
MR Image Artifact	In non-clinical testing, the image artifact caused by the device extends approximately 6mm from the Thoraflex™ Hybrid and Relay®Pro NBS Thoracic Stent Graft System when imaged with a gradient echo pulse sequence and a 3.0 T MR system.

12 Instructions for Implantation of the Thoraflex™ Hybrid Device

12.1 Preparation of the Thoraflex™ Hybrid Delivery System

Once in the sterile field, the entire Thoraflex™ Hybrid delivery system must be immersed in a saline solution (approximately 700ml) for 5 minutes. Failure to rinse for 5 minutes could lead to the graft being more susceptible to leakage when implanted. Vascutek does not recommend that the device is soaked for longer than 5 minutes as the onset of gelatin hydrolysis may start to occur, which may have an impact on clinical performance.

Note: The delivery system and the implant must not be allowed to dry out after soaking. Pre-soaking will reduce the force necessary to unsheath the distal stented graft section of the device.

12.2 Forming of the Thoraflex™ Hybrid Delivery System

The distal stented graft section of the Thoraflex™ Hybrid delivery system can be shaped to resemble the anatomy of the aorta in the area of the stent-graft only (**Figure 12**).

CAUTION: DO NOT BEND THE DISTAL STENTED GRAFT SECTION WITHIN 10MM OF THE SPLITTER OR WHILE HOLDING THE HANDLE OF THE SYSTEM.

CAUTION: IF THE SYSTEM IS FORMED INTO AN ANGLE OF GREATER THAN 50° A HIGHER FORCE WILL BE NEEDED TO DEPLOY THE STENT.

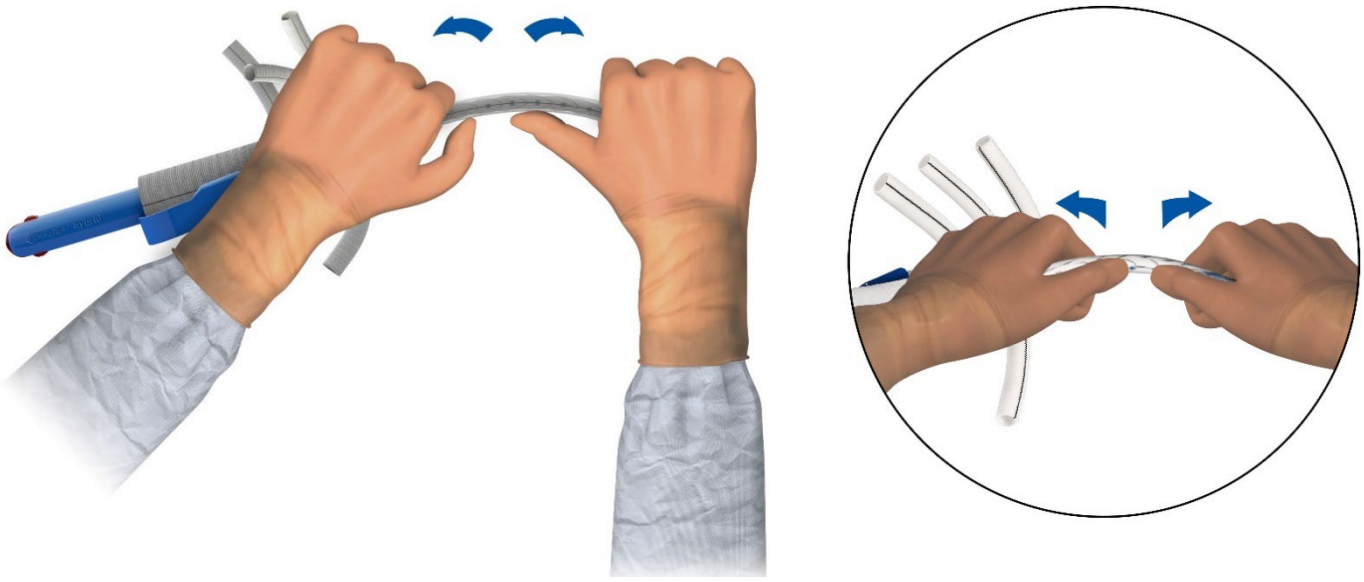


Figure 12 - Shaping of the Stented Section of the System

If any major sheath kinking is evident after shaping the delivery system, then local pressure should be applied to the kinks in order to reduce the sheath folding and remove any sharp points (**Figure 13**).

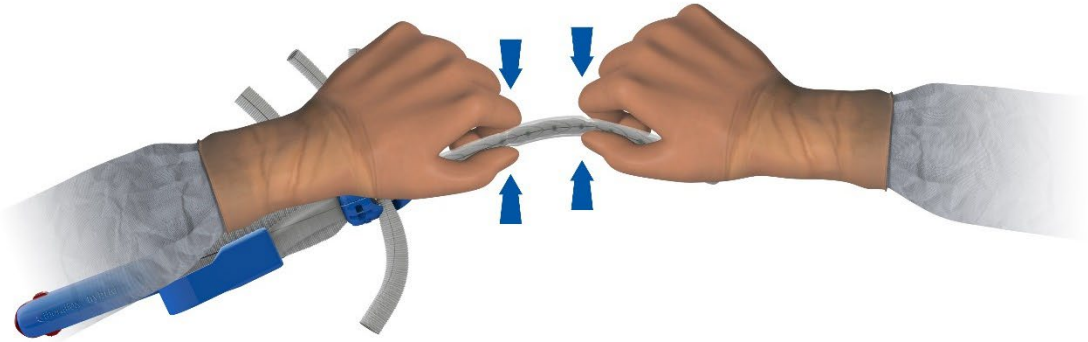


Figure 13 - Removal of Kinks in the Sheath

12.3 Introduction of the Thoraflex™ Hybrid Delivery System Using a Guide Wire

It is recommended that the Thoraflex™ Hybrid delivery system is used with a guide wire (**Figure 14**). The tip contains a choice of two guide wire access ports (**Figure 15**). The guide wire can be fed through either port and then along the outside of the sheath. The delivery system can then be moved along it into position.

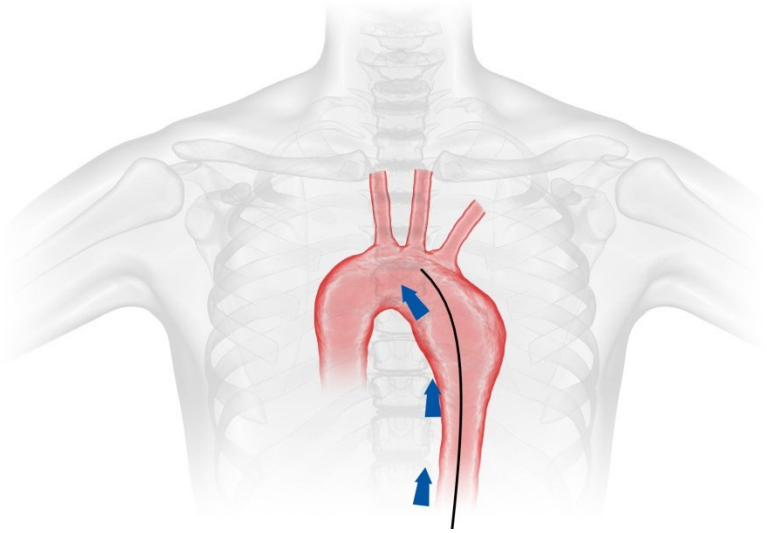


Figure 14 - Guide Wire Use in the Aorta

12.4 Positioning the Thoraflex™ Hybrid Delivery System

The Thoraflex™ Hybrid delivery system must be placed through the opened aortic arch into the descending thoracic aorta. This should be done over a guide wire in order to ensure that the correct lumen is being treated, for example in cases of dissection (**Figure 16**). When positioning the delivery system, ensure that the splitter release clip is accessible, and the collar is positioned correctly in relation to the anastomotic site.

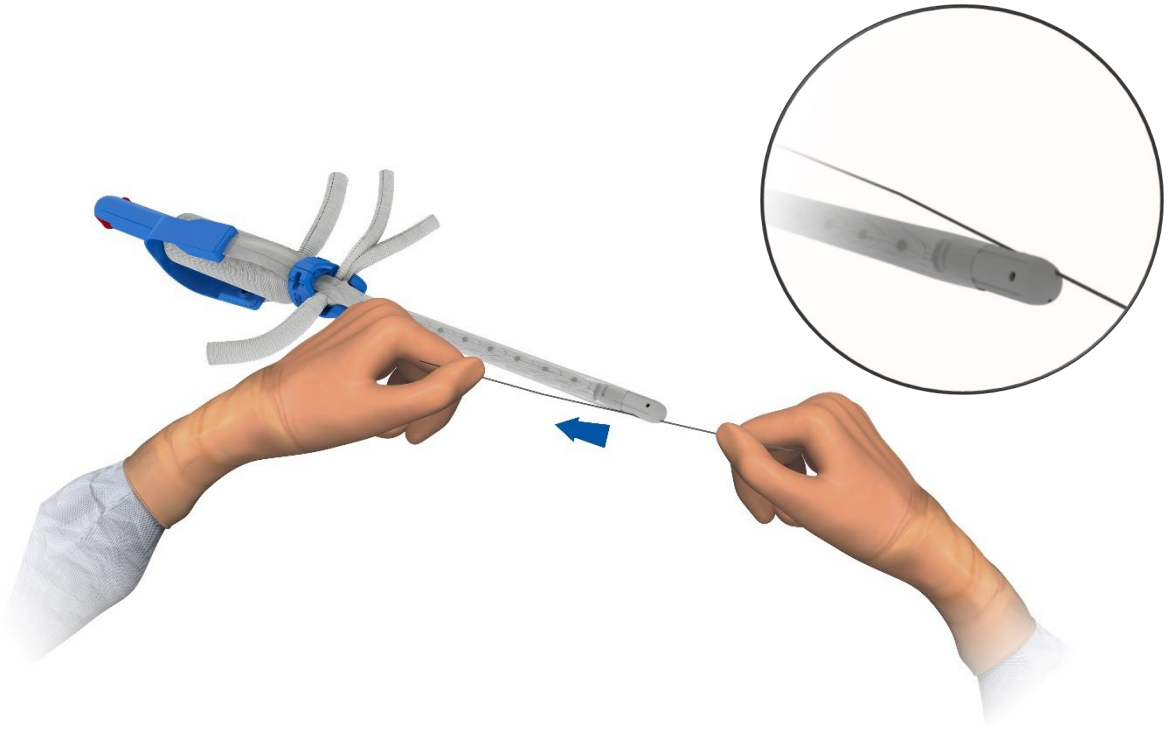


Figure 15 - Insertion of the Guide Wire Through Tip Guide Wire Access Ports

The splitter should be positioned in the distal aorta so that when the device is deployed the collar is in the correct position (**Figure 16**). For the Thoraflex™ Hybrid Plexus 4 version, the delivery system should be orientated so that the device branches and aortic arch vessels are aligned.

Note: Excessive aortic tortuosity may result in inability to properly position the stent-graft, or stent-graft kinking with thrombus formation. If balloon modelling is desired (i.e. for endoleak, stent-graft kinking or stenosis), use a compliant balloon equal in size to the largest target vessel's diameter. Balloon inflation should not exceed 1 atm.

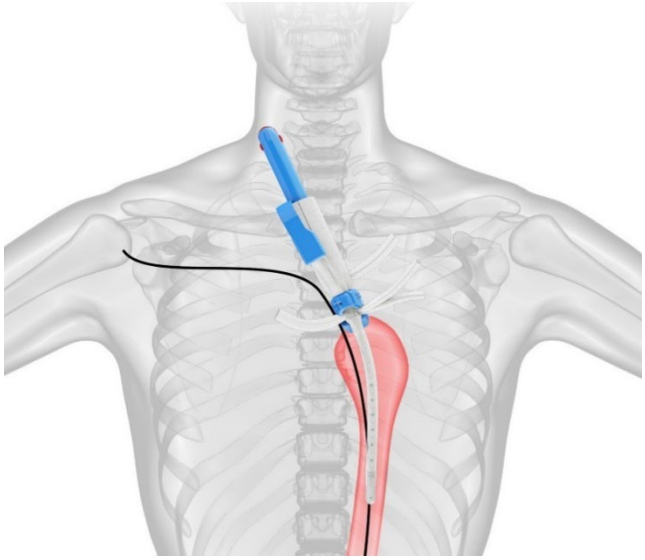


Figure 16 - Positioning of the Thoraflex™ Hybrid Delivery System

12.5 Deployment Sequence for the Thoraflex™ Hybrid Device

12.5.1 Sheath Retraction (Device Release Stage I)

When the optimum orientation and position has been achieved, the delivery system should be unsheathed. In order to unsheath the implant, firmly stabilize the handle with one hand and with the other hand pull back the strap in-line with the handle (**Figure 17 to Figure 19**). This will simultaneously retract and split the sheath, allowing it to be completely removed from the delivery system. The complete stented section of the device will now be unsheathed.

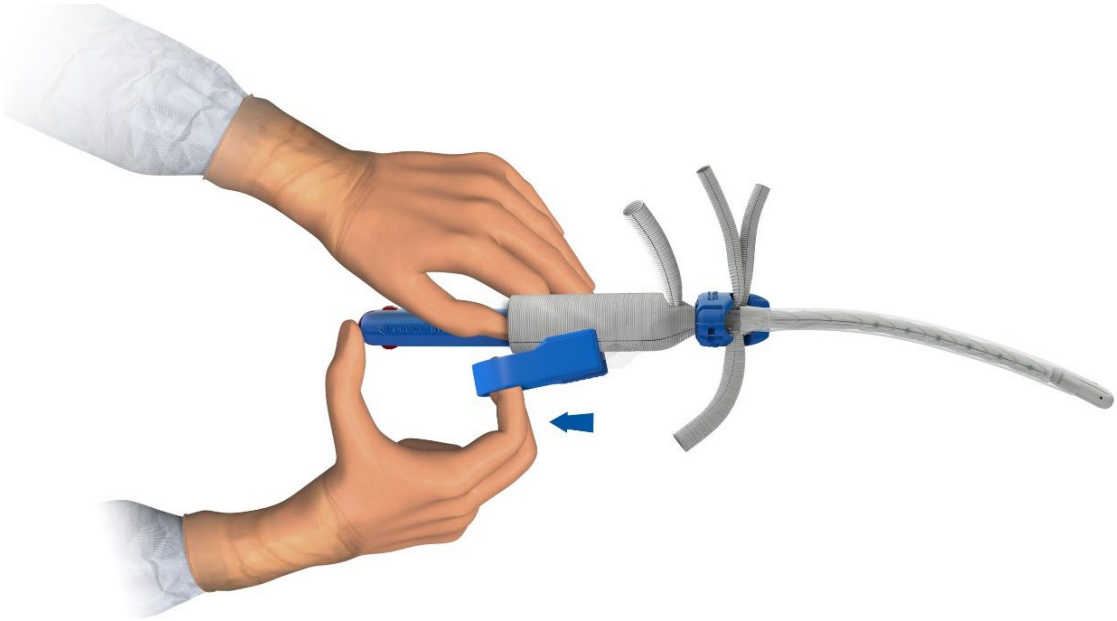


Figure 17 - Sheath Retraction

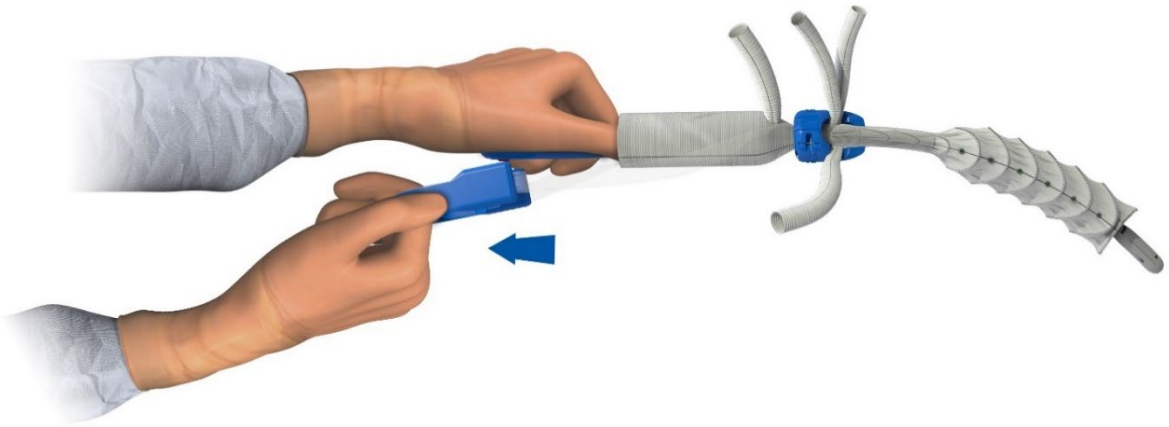


Figure 18 - Sheath Retraction

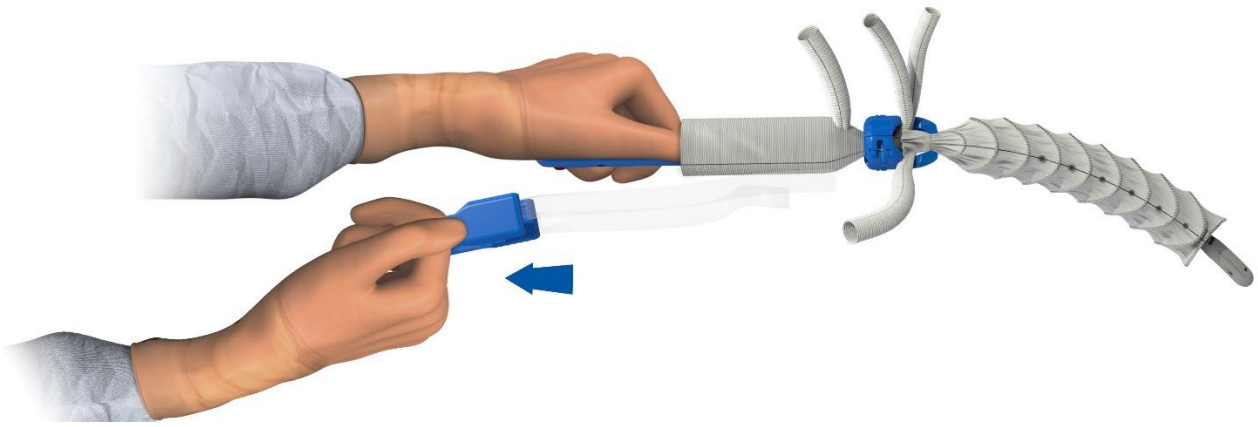


Figure 19 - Sheath Retraction

12.5.2 Removal of the Sheath Splitter (Device Release Stage II)

Once the sheath has been removed, the splitter is detached from the delivery system by cutting the suture (**Figure 20**). Ensure the graft fabric under the splitter is opened up to facilitate the removal of the handle (**Figure 21**).

Figure 20 - Remove Splitter by Cutting the Suture

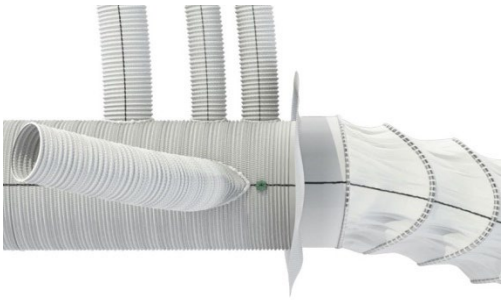


Figure 21 - Graft Fabric Opened Around the Collar

12.5.3 Guide Wire Removal

CAUTION: IF A GUIDE WIRE WAS USED DURING THE DEPLOYMENT OF THE DEVICE, IT MUST BE REMOVED FROM THE SYSTEM BEFORE THE RELEASE WIRE IS REMOVED (Figure 22). This step enables the guide wire to be removed while the device remains held in position by the system thereby preventing movement of the stented section.

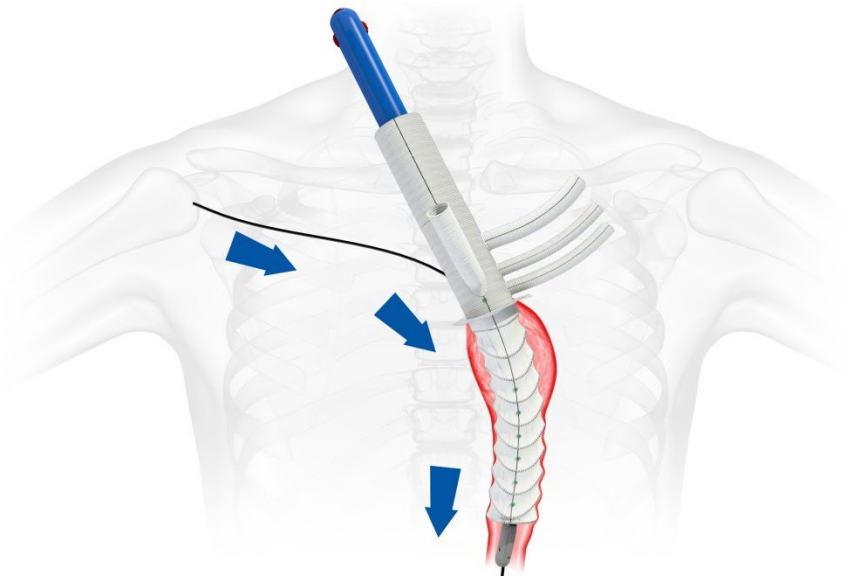


Figure 22 - Guide Wire Removal

12.5.4 Release Wire Removal (Device Release Stage III)

In order to fully release the device from the delivery system, pull the red release clip and attached wire out of the delivery system handle (**Figure 23**). The release wire should be pulled out proximally, in line with the delivery system handle. The distal end of the stent-graft will now be released from the delivery system (**Figure 23**).

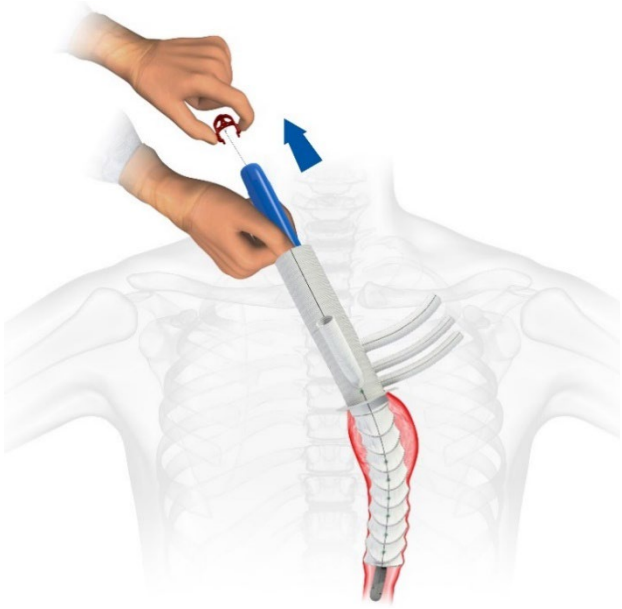


Figure 23 - Release Wire Removal

12.5.5 Delivery System Removal

Once the device has been released from the delivery system, the remaining handle assembly must be removed from the device. This is removed by gently pulling the handle proximally ensuring that the device is sufficiently loose around the shaft to allow removal without disturbing the graft. If the delivery system was introduced around a curve, as shown in **Figure 24**, it must be removed following the identical path in order to avoid moving the device or causing trauma to the vessel.

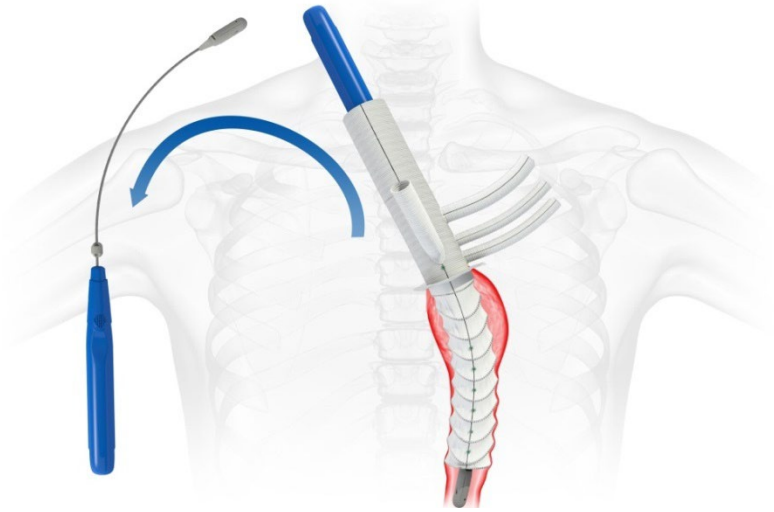


Figure 24 - Delivery System Removal

12.5.6 Use of The Thoraflex™ Hybrid Device Perfusion Side Branch

Initiation of Antegrade Perfusion: The bypass catheter should be placed in the side branch of the Plexus 4 or Ante-Flo device and securely attached.

Completion of Antegrade Perfusion: Once bypass is complete, the cannula side branch of the Plexus 4 or Ante-Flo device should be cut off and the remaining stump over-sewn using standard surgical technique.

12.5.7 Thoraflex™ Hybrid Device Anastomoses

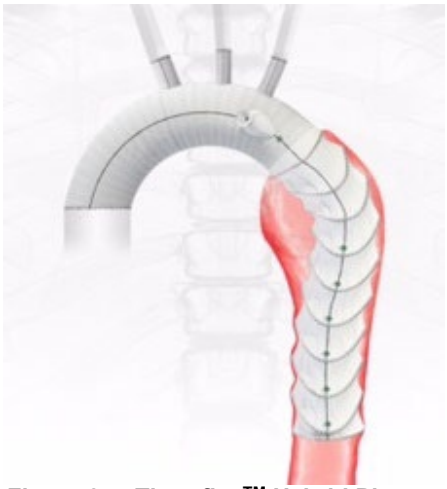


Figure 25 - Thoraflex™ Hybrid Plexus 4 Device Anastomoses

Once the delivery system has been removed, the collar should be sutured to the native aortic vessel in order to provide fixation and stability to the device. The exact technique used is at the discretion of the surgeon implanting the device; however, a circumferential anastomosis is required to ensure that the implant is sealed correctly (**Figure 25**). The remaining supra aortic vessel and graft anastomoses are now carried out.

Note: Some movement of the distal ring of the Thoraflex™ Hybrid device may occur following re-perfusion of the thoracic aorta.

12.6 Device Tracking Information

The Thoraflex™ Hybrid device is packaged with the following:

- **Implant Information Form.** This form must be completed by the hospital staff and sent to Vascutek (c/o Bolton Medical Inc) for the purposes of tracking all patients who receive a Thoraflex™ Hybrid device (as required by U.S. Federal Regulation).

- **Patient Implant Card.** This card must be completed by the hospital staff by attaching the provided device information label to the patient implant card and providing this card to the patient. Patients should be instructed by their physician to keep this card with them at all times. Patients should refer to the card when visiting other healthcare practitioners, and especially when visiting MR imaging facilities since the card provides specific information on the safe imaging of the Thoraflex™ Hybrid device via MR.

12.7 Use of Extension Devices

The Thoraflex™ Hybrid device can be extended using a Relay®Pro NBS Thoracic Stent Graft System. A Relay®Pro NBS Thoracic Stent Graft System reference number can be decoded as follows:

Table 33 - Relay®Pro NBS Thoracic Stent Graft System Product Designation

Internal Code	Identifier	Proximal Diameter (mm)	Family Length* (mm)	Distal Diameter (mm)	Device Designation	French Size
28	**N4:** Non-Bare Stent Configuration	XX	XXX	XX	**U:** Standard Catalog Product for US	(XX Fr)
*Family lengths listed. Final lengths to be listed on product labeling (Tolerance of ±10 mm).						

Notes:
- If the lesion requires use of an endovascular extension, only a Relay®Pro NBS Thoracic Stent Graft System configuration should be used.
- Adjunctive devices with barb or hook features which would be positioned in the overlap region should not be used.

The implantation procedure for Relay®Pro NBS Thoracic Stent Graft System devices should follow the manufacturer's IFU, describing an endovascular retrograde implantation approach. Compatibility of extension devices deployed from the antegrade approach has not been assessed.

12.7.1 Extension Sizing – Unsupported Junction (Aneurysm)

The minimum recommended amount of overlap between a Relay®Pro NBS Thoracic Stent Graft System device and a Thoraflex™ Hybrid device is three overlapping covered stents (approximately 50mm). Less than this amount of overlap may result in endoleak (with or without component separation). Relay®Pro NBS Thoracic Stent Graft System device lengths should be selected accordingly. Excessive overlap length should be avoided, and the extension device's proximal edge must not be advanced beyond the radiopaque marker on the graft portion of the Thoraflex™ Hybrid device.

For modular, unsupported junctions (i.e., where the Thoraflex™ Hybrid distal stent-graft region is within an aneurysm sac), a Relay®Pro NBS Thoracic Stent Graft System device with a proximal outer diameter 2mm greater than the nominal outer diameter of the in-situ Thoraflex™ Hybrid must be used. In these cases, the distal stent graft of the Thoraflex™ Hybrid will be within the aneurysm sac, and there will be no distal seal until the Relay®Pro NBS Thoracic Stent Graft System device has been implanted. This may increase the risk of thrombus generation until completion of the therapy. Sizing of the Thoraflex™ Hybrid device should be based on the complete treatment and take into account the size of the distal landing zone of the compatible Relay®Pro NBS Thoracic Stent Graft System device, e.g. if a 34mm Relay®Pro NBS Thoracic

Stent Graft System device has been selected for the distal treatment, then the compatible Thoraflex™ Hybrid device would be 32mm – see **Section 8.2** for further information on Thoraflex™ Hybrid device sizing.

Table 34 – Thoraflex™ Hybrid Device with Relay®Pro NBS Thoracic Stent Graft System Extension – Unsupported Junction Sizing Chart

Catalog No. (Plexus)	Catalogue No. (Ante-Flo)	Thoraflex™ Hybrid Stent-Graft OD (mm)	Relay®Pro Stent Graft Proximal OD (mm)
THP2224X100B	THA2224X100B	24	26
THP2426X100B	THA2426X100B	26	28
THP2628X100B	THA2628X100B	28	30
THP2830X100B	THA2830X100B	30	32
THP3032X100B	THA3032X100B	32	34
THP3034X100B	THA3034X100B	34	36
THP3036X100B	THA3036X100B	36	38
THP3038X100B	THA3038X100B	38	40
THP3040X100B	THA3040X100B	40	42
THP3240X100B	THA3240X100B	40	42
THP2224X150B	THA2224X150B	24	26
THP2426X150B	THA2426X150B	26	28
THP2628X150B	THA2628X150B	28	30
THP2830X150B	THA2830X150B	30	32
THP3032X150B	THA3032X150B	32	34
THP3034X150B	THA3034X150B	34	36
THP3036X150B	THA3036X150B	36	38
THP3038X150B	THA3038X150B	38	40
THP3040X150B	THA3040X150B	40	42
THP3240X150B	THA3240X150B	40	42

In cases of aneurysm, extension procedures should be planned and performed to ensure that the combined devices take the outer curve between the proximal anastomosis above the aneurysm and the distal neck below the aneurysm. This is consistent with the existing guidance for planning and implantation of the Thoraflex™ Hybrid Device. When extending Thoraflex™ Hybrid with a Relay®Pro NBS Thoracic Stent Graft System, the distal end of the Relay®Pro NBS Thoracic Stent Graft System should be landed in healthy vessel within the descending thoracic aorta according to the Relay®Pro NBS Thoracic Stent Graft System distal sizing chart below (note that this sizing follows the sizing guidance within the Relay®Pro NBS Thoracic Stent Graft System IFU).

Table 35 – Relay®Pro NBS Thoracic Stent Graft System Extension – Distal Sizing Chart

Relay®Pro Stent Graft Distal OD (mm)	Descending landing zone vessel ID (mm)	Distal landing zone length (mm)
24	20-21	25
26	22-23	
28	24-25	
30	26-27	
32	28-29	
34	30-31	
36	32-33	
38	34	
40	35-36	30
42	37-38	

12.7.2 Extension Sizing – Supported Junction (e.g. Dissection)

The minimum recommended amount of overlap between a Relay®Pro NBS Thoracic Stent Graft System device and a Thoraflex™ Hybrid device is three overlapping covered stents (approximately 50mm). Less than this amount of overlap may result in endoleak (with or without component separation). Relay®Pro NBS Thoracic Stent Graft System device lengths should be selected accordingly. Excessive overlap length should be avoided, and the extension device's proximal edge must not be advanced beyond the radiopaque marker on the graft portion of the Thoraflex™ Hybrid device.

For modular, supported junctions (for example where the Thoraflex™ Hybrid distal stent-graft region is within dissection), a Relay®Pro NBS Thoracic Stent Graft System device with a proximal outer diameter equal to the nominal outer diameter of the in-situ Thoraflex™ Hybrid must be used.

Table 36 – Thoraflex™ Hybrid Device with Relay®Pro NBS Thoracic Stent Graft System Extension – Supported Junction Sizing Chart

Catalog No. (Plexus)	Catalog No. (Ante-Flo)	Thoraflex™ Hybrid Stent-Graft OD (mm)	Relay®Pro Stent Graft Proximal OD (mm)
THP2224X100B	THA2224X100B	24	24
THP2426X100B	THA2426X100B	26	26
THP2628X100B	THA2628X100B	28	28
THP2830X100B	THA2830X100B	30	30
THP3032X100B	THA3032X100B	32	32
THP3034X100B	THA3034X100B	34	34
THP3036X100B	THA3036X100B	36	36
THP3038X100B	THA3038X100B	38	38
THP3040X100B	THA3040X100B	40	40
THP3240X100B	THA3240X100B	40	40
THP2224X150B	THA2224X150B	24	24
THP2426X150B	THA2426X150B	26	26
THP2628X150B	THA2628X150B	28	28
THP2830X150B	THA2830X150B	30	30
THP3032X150B	THA3032X150B	32	32
THP3034X150B	THA3034X150B	34	34
THP3036X150B	THA3036X150B	36	36
THP3038X150B	THA3038X150B	38	38
THP3040X150B	THA3040X150B	40	40
THP3240X150B	THA3240X150B	40	40

Sizing outside these guidelines could result in endoleak, migration, stent-graft separation, infolding or device damage.

Axial Positioning during Extension Procedure

It is possible for some axial displacement of the distal section of the Thoraflex™ Hybrid device to occur during insertion and positioning of guide wires, catheters and delivery systems, and during deployment of the extension device. Care should be taken to ensure the Thoraflex™ Hybrid Device is in its intended position prior to extension device deployment. Close monitoring of position and alignment of both devices should be performed during extension deployment.

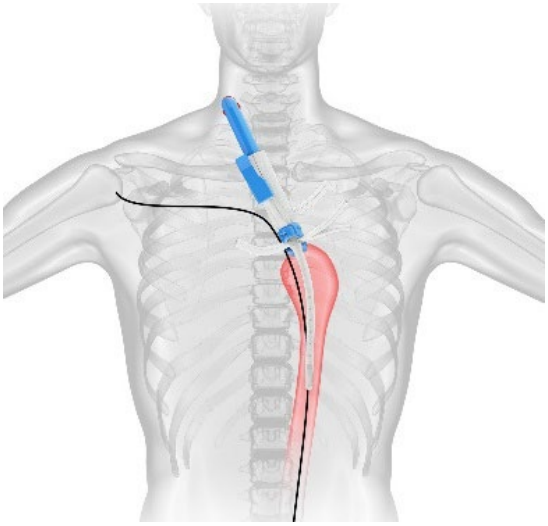
13 Troubleshooting Guide

13.1 Difficulty Advancing the Delivery System to the Intended Deployment Site

Potential Causes

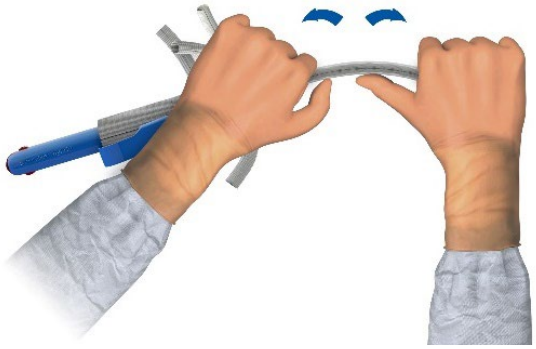
A. The level of angulation of the sheath/ malleable shaft may not be compatible with the aortic anatomy.

B. During introduction the system does not follow the path of the guide wire.



Recommended Actions

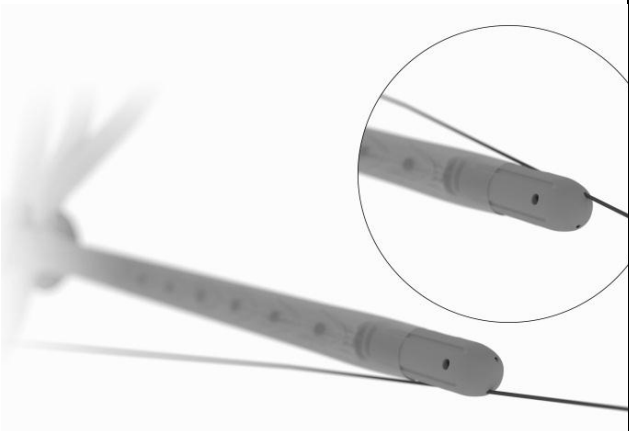
A.1. Remove the delivery system, check the degree of angulation of the delivery system shaft is suitable for the anatomy.



B.1. Feed the guide wire through the other tip guide wire port. This should minimize the effect of this issue.

Note: The guide wire does not travel through the center of the delivery system. As a result, consideration must be taken of the appropriate angle when advancing the system.

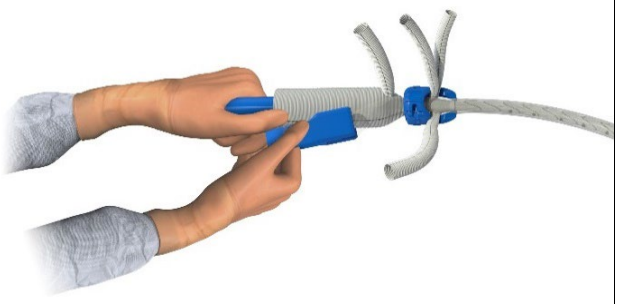
B.2. If A1 and B1 do not work, then use another device.



13.2 Sheath Retraction - A High Force is Required to Retract the Sheath and Deploy the Implant

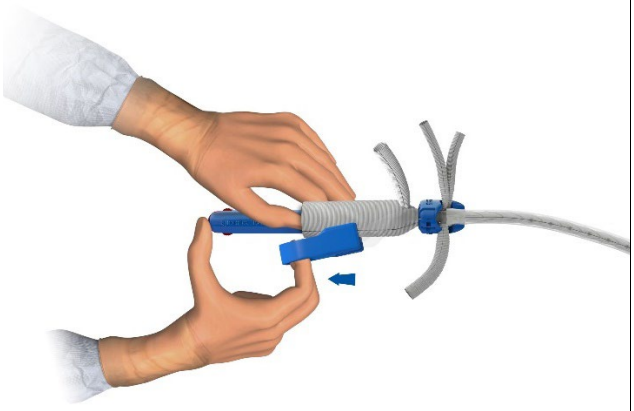
Potential Cause

High level of angulation of the sheath and malleable shaft may result in excessive kinking of the sheath. This can lead to higher deployment forces being experienced during sheath retraction.



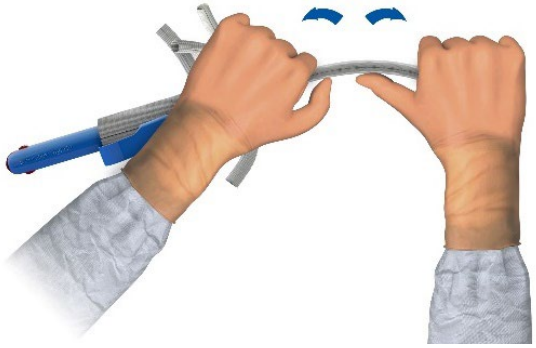
Recommended Actions

Where high deployment forces are experienced, applying a syringe like grip to the system can provide greater control for the initial stage of the retraction process.



The following steps may also resolve this issue.

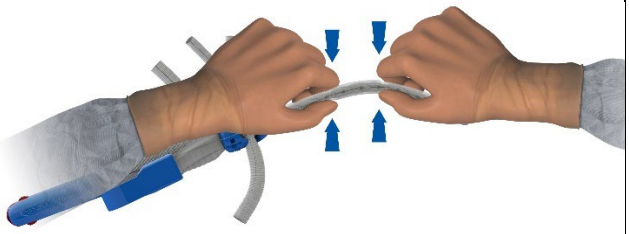
1. Remove the system and inspect the sheath for any excessive kinking.



2. Where possible, straighten the delivery system to remove the kinks.

3. Kinks can also be removed from the sheath by using localized compression of the affected area.

4. Repeat steps 1-3 until the deployment force required has been reduced.

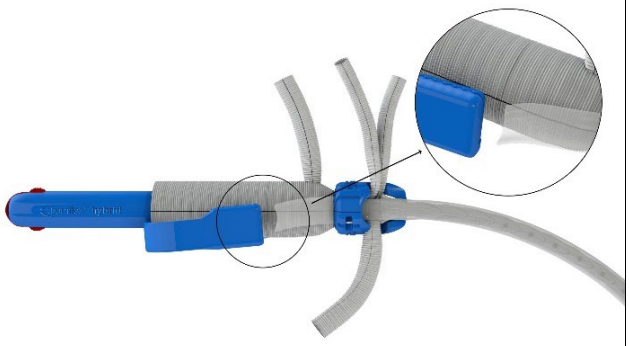


Note: Ensure one hand stabilizes the handle. The graft section should be moved forward thus providing a longer length of handle to hold.

13.3 Sheath Retraction - The Strap Becomes Detached from the Delivery Sheath

Potential Cause

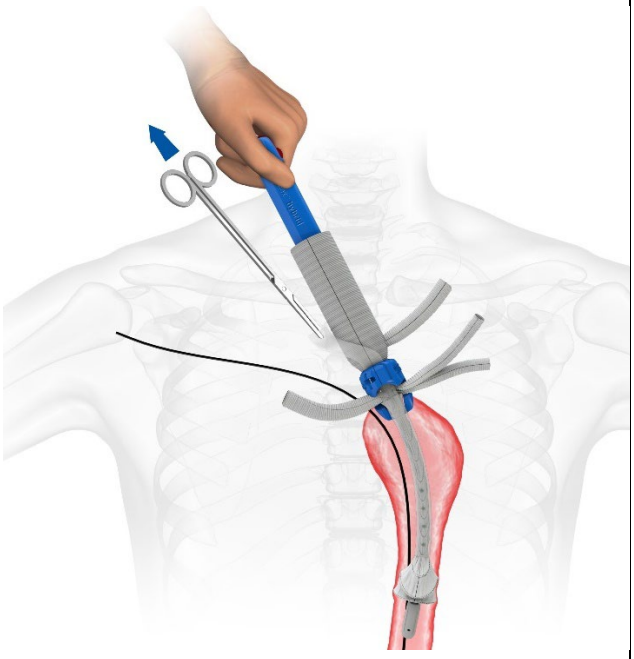
Excessively high deployment forces or poor strap to sheath attachment strength may result in the detachment of the strap from the sheath.



Recommended Actions

1. Attach one pair of atraumatic artery forceps to each side of the sheath.
2. Ensure the handle is stabilized.
3. With the handle stabilized, pull the forceps to retract both parts of the sheath simultaneously.

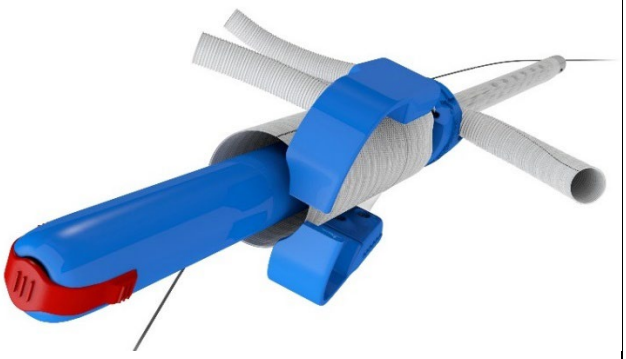
Note: Both parts of the sheath must be pulled back simultaneously to ensure the correct unsheathing of the stented section of the implant.



13.4 Sheath Retraction - The Strap Handle Breaks in Two

Potential Cause

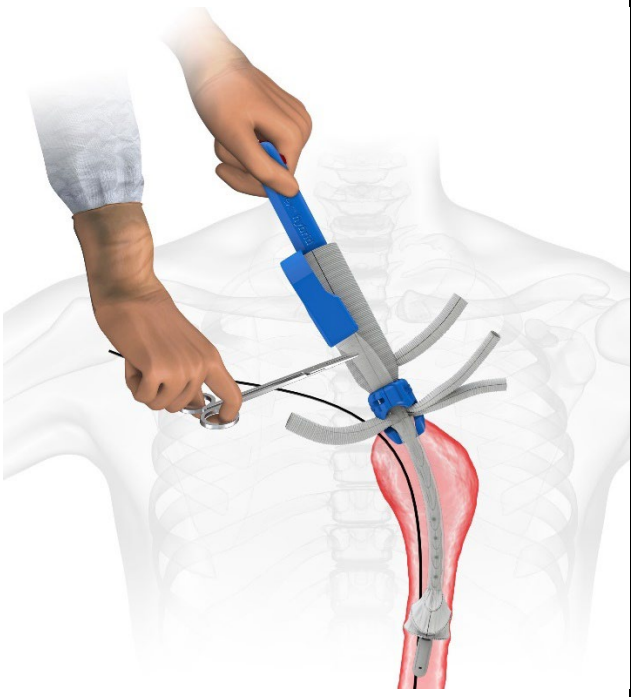
An excessive deployment force can contribute to the potential fracture and/or weakening of the strap. This may cause it to break during the device deployment.



Recommended Actions

1. Gather both halves of the strap in one hand.
2. Stabilize the handle of the delivery system.
3. Retract both halves of strap together thus splitting the sheath in two.

Note: This process could be completed using atraumatic artery forceps as described in **Section 12.5.1** Sheath Retraction - The strap becomes detached from the delivery sheath.



13.5 The Splitter is Detached During / Prior to Deployment

Potential Cause

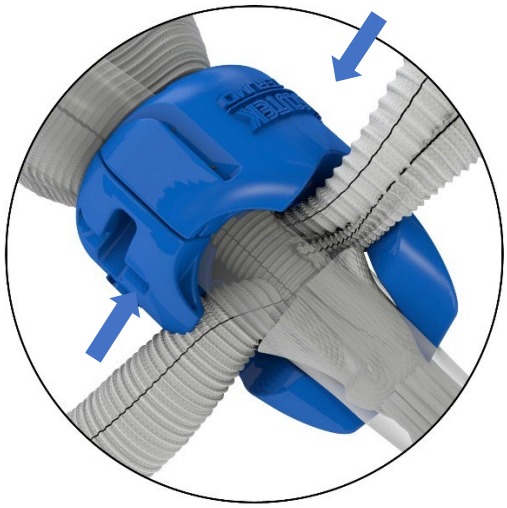
Splitter suture is loose or unfastened during use.

Recommended Actions

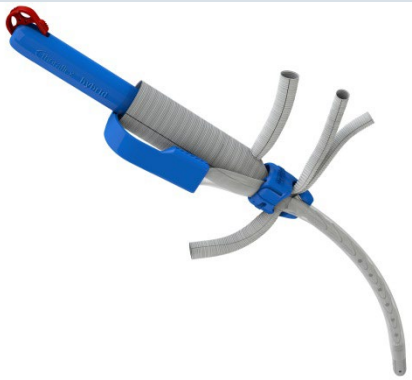
1. The splitter can be manually closed and held during deployment or if partially open can be reattached.
2. Ensure that the fabric of the graft is not caught in the splitter when re-attaching.
3. Push both sides of the splitter together until they click together.
4. The splitter should be held closed during the sheath retraction element of the procedure.

Note: If the hinge of the splitter breaks, care must be taken to ensure that both parts of the splitter are removed from the chest cavity after use.

Note: The splitter is not essential to deploy the implant.



13.6 The Handle Release Clip is not Attached to the Delivery System Handle

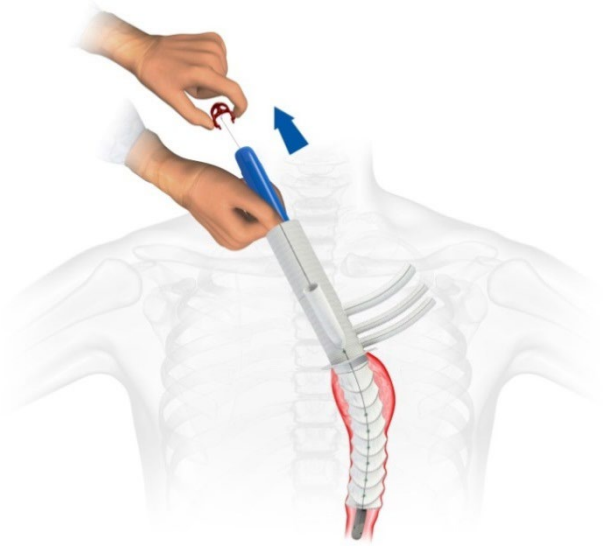


Potential Causes

A. The red release clip has become loose, but is still attached to the handle, either during transit or use.

B. The red release clip is no longer attached to the release wire

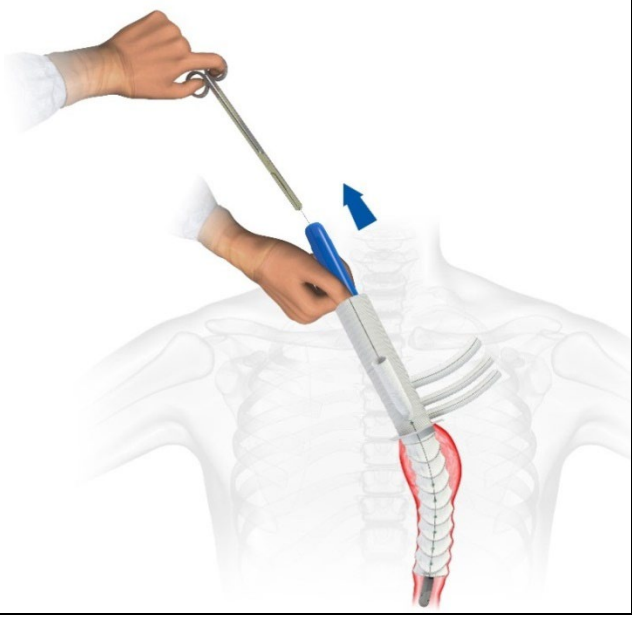
Recommended Actions



A.1. Check that the red release clip is still attached to its release wire by gently pulling it to ensure that tension can still be felt.

A.2. If still attached, the red release clip can be pushed back into its housing in the handle.

A.3. The red release clip can be removed and retracted as per the IFU **Section 12.5.4**.



B.1. Remove the release wire.

B.2. The release wire should be retracted as described in the IFU **Section 12.5.4** using atraumatic artery forceps. The atraumatic artery forceps should be attached to the release wire and retracted.

Note: Only one wire is present in the delivery system

13.7 Difficulty Removing the Guide Wire

Potential Cause

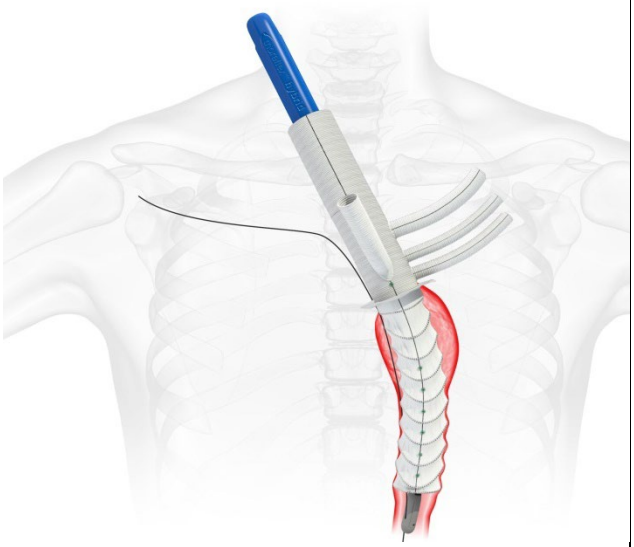
The combination of delivery system manipulation and the guide wire port used has prevented the easy removal of the guide wire from the delivery system.

Recommended Actions

1. Ensure that the handle is stabilized during guide wire removal to avoid compromising the position and stability of the stented section of the implant.

2. Try to remove the guide wire in the opposite direction to how it was inserted i.e. distal removal not proximal / proximal removal not distal.

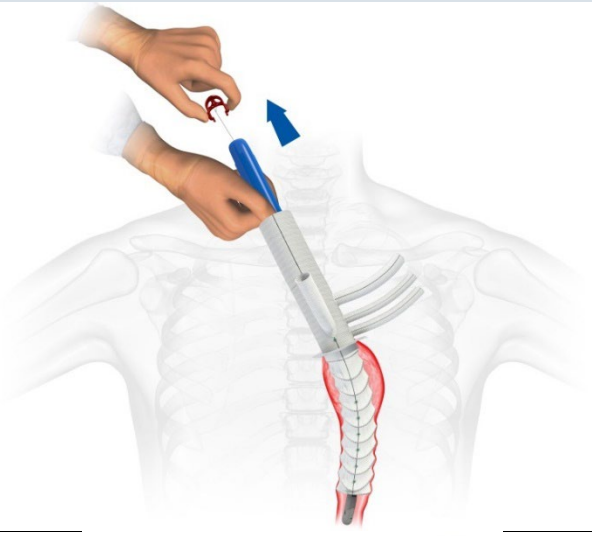
Note: The direction of guide wire removal may be compromised by the anatomy.



13.8 Difficulty Removing the Release Wire from the Delivery System

Potential Cause

If resistance is felt by the operator when removing the release wire, there is the possibility that the release wire has become kinked and/or snapped within the implant. The snapped portion of the release wire must be removed before the deployment can be completed.



Recommended Actions

1. The release wire should be inspected once it has been removed from the system. Look for any sign of fracture, damage or shortened length.

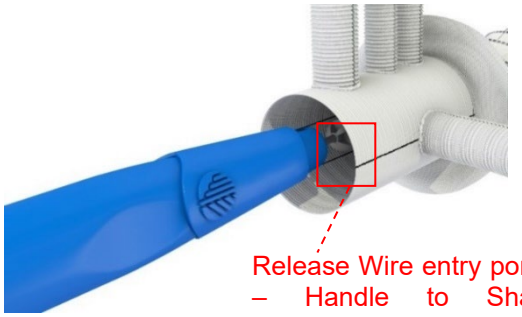
Final length should be approximately:

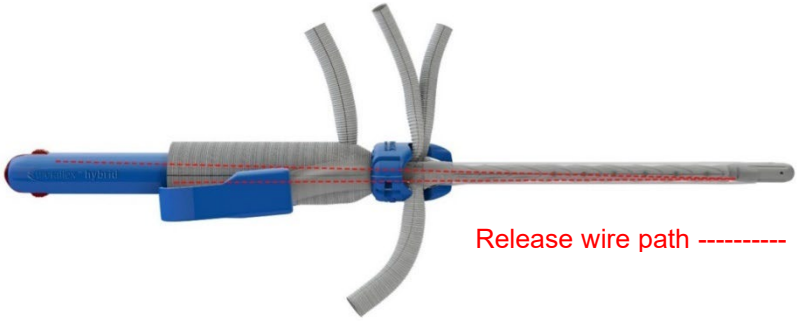
- Cat No. TH…..X100A = 530mm
- Cat No. TH…..X150A = 630mm

2. Check the wire entry ports on the handle of the delivery system. If a piece of wire is still there, remove it using forceps.

The release wire runs from the release clip to the tip of the delivery system and terminates back inside the handle.

If no wire is present on either side of the handle, then the implant should have been freed from the delivery system. Any difficulty experienced must be due to the angulation of the system. See **Section 13.9**.

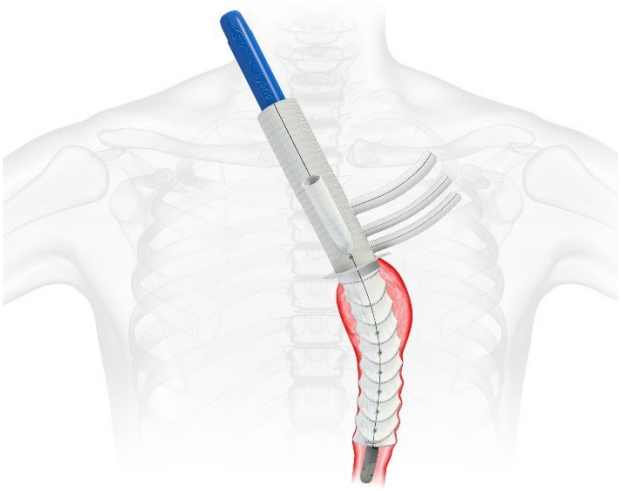




13.9 Difficulty Removing the Delivery System – High Angulation

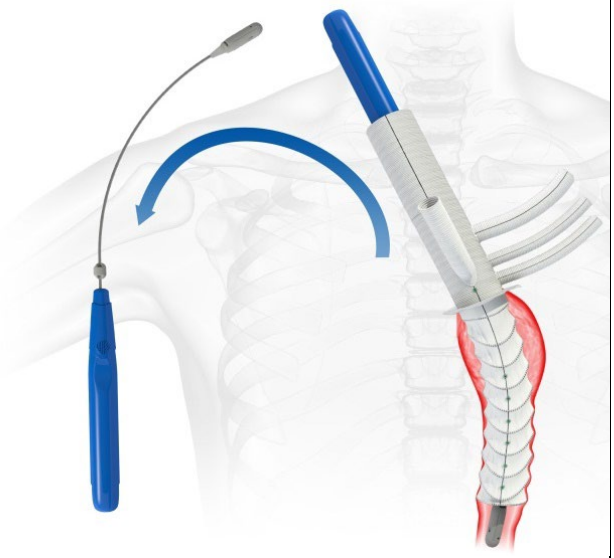
Potential Issue

The level of angulation applied to the delivery system is causing difficulty during handle removal.



Recommended Actions

1. Take account of the curvature applied to the delivery system before application, the removal may have to follow a similar path.
2. Remove gently.



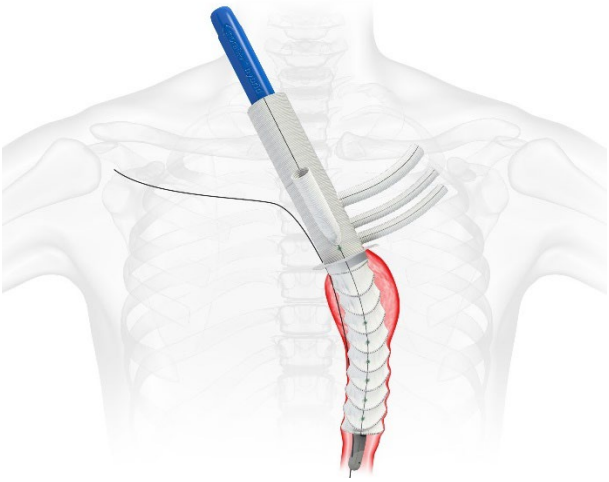
13.10 Difficulty Removing the Delivery System – Release Wire and Guide Wire

Potential Causes

A. The delivery system is still attached to the implant.

B. The delivery system is still attached to the guide wire.

Note: If the handle is removed whilst still attached to the guide wire, the stented section of the implant will become dislodged.

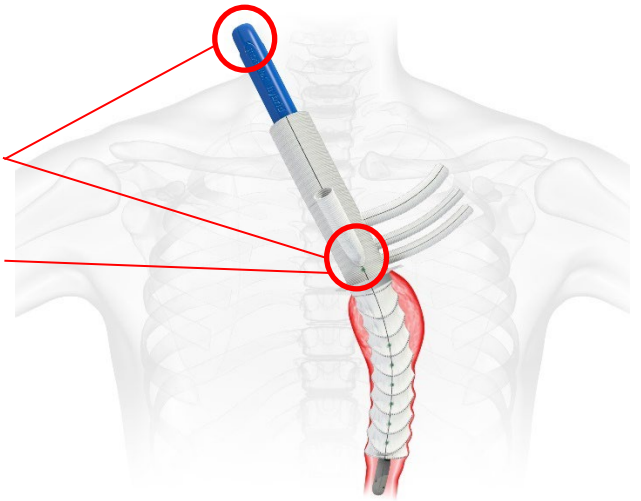


Recommended Actions

A.1. Check that the release wire and splitter have been removed.

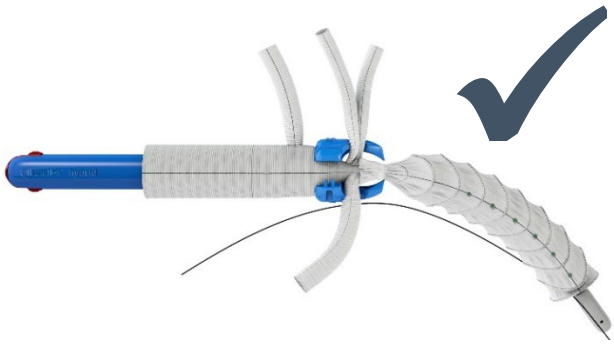
A.2. Ensure the graft has been unfolded in the area where the splitter was.

A.3. Gently move the handle distally before removing.

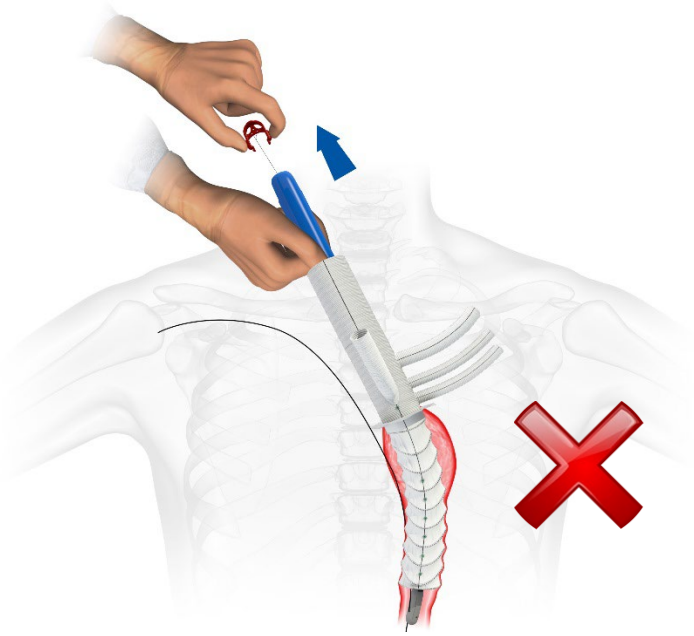


B.1. If the implant is positioned correctly (sheathed or unsheathed) and is still connected to the delivery system, the guide wire can be removed without dislodging the implant.

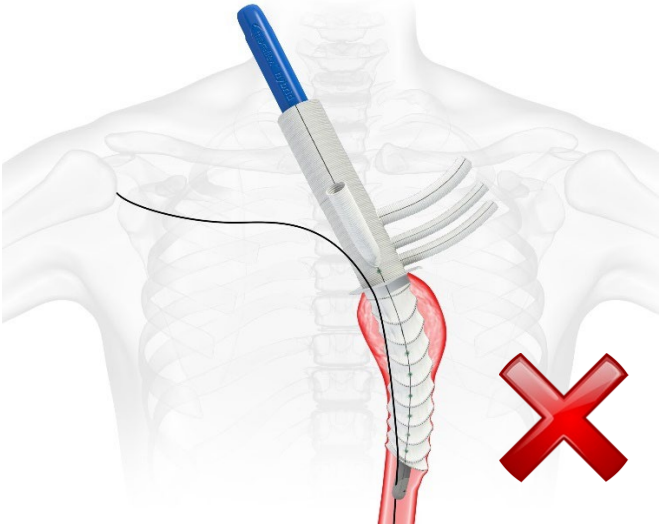
Note: This is the last point in the procedure where the guide wire can be removed without significant consequence or detrimental effect to the implant.



B.2. After removal of the release wire, the implant is no longer attached to the delivery system, hence removal of the guide wire may dislodge the implant if not previously removed.



B.3. If the handle is removed while attached to the guide wire, this may cause the implant to be moved from the deployment site. The effects may be detrimental without secondary intervention.



14 Follow-up Procedure

The follow-up recommendations described in this section are applicable to Thoraflex™ Hybrid only. If a Relay®Pro NBS Thoracic Stent Graft System is used to distally extend a Thoraflex™ Hybrid, please refer to Section 13 of the Relay®Pro NBS Thoracic Stent Graft System IFU for specific follow-up recommendations.

14.1 General

All patients should be advised that Frozen Elephant Trunk (FET) treatment requires lifelong, regular follow-up to assess their health and the performance of the device. Patients with specific clinical findings (such as, endoleaks, enlarging aneurysms, enlarging false lumens, or changes in the structure or position of the endovascular graft) should receive additional follow-up. Patients should be counseled on the importance of adhering to the follow-up schedule, both during the first year and at yearly intervals thereafter. Patients should be informed that regular and consistent follow-up is a critical part of ensuring the ongoing safety and effectiveness of FET repair. Physicians should evaluate patients on an individual basis and prescribe follow-up relative to the needs and circumstances of each individual patient.

Current recommended imaging of stent-graft patients includes X-ray and CT, with and without contrast medium. Alternative imaging modalities such as magnetic resonance imaging should be used in patients with impaired renal function or intolerance to contrast media that cannot be adequately premedicated. Imaging should be decided based upon the physician's clinical assessment of the patient pre- and post-implantation of the implant. After implant, patients should be regularly monitored for perigraft flow, disease progression or changes in the structure or position of the implant. At a minimum, baseline post-procedure imaging within 30 days following implant along with annual imaging is recommended, including contrast and non-contrast CT to examine aneurysm changes, perigraft flow, patency, tortuosity and progressive disease. If renal complications or other factors preclude the use of image contrast media, duplex ultrasound, or MRI/MRA may provide alternative means of providing some of this information.

14.2 CT with Contrast

Contrast-enhanced CT should be used to assess fixation, deformation, apposition to the vessel wall at distal fixation site, device migration, patency (e.g., occlusion of branch vessels), and endoleak (including source and type if present). A pre-contrast scan is suggested to determine if there are calcifications or areas where metal artifacts may be misinterpreted as endoleak. Arterial and venous phase spiral CT scans and overlapping images with coverage from the celiac artery to the aortic valve are recommended. The venous phase scan may also be performed with thicker collimation.

It is recommended that the source data set be archived in case specialized evaluation is needed later (volume measurements, 3-dimensional reconstruction, or computer-aided measurement software). If the aortic pathology is not remodeling adequately or progressing distally within the first year, volume measurements may be obtained as a more sensitive indicator of size using 3-dimensional software. Patients who are allergic to contrast should be pre-medicated 12-24 hours prior to receiving the drug.

14.3 Non-Contrast CT

For patients with impaired renal function or those who are allergic to contrast medium, a spiral CT without contrast may be considered to assess device fixation, deformation, apposition to the vessel wall at distal fixation site, device migration, occlusion of vessels, and the extent of the disease, diameter, length and volume measurements.

14.4 Duplex Ultrasound

For patients with impaired renal function or those who are allergic to contrast medium, a color duplex ultrasound may be considered to assess extent of the disease, endoleaks, and device occlusion and stenosis.

14.5 MRI or MRA

Patients with impaired renal function, i.e., renal insufficiency, may also be considered for magnetic resonance imaging or angiography (MRI, MRA) in facilities that have expertise in this area. Artifact may occur related to the stent, and care should be used to ensure adequate imaging of the outer aneurysm wall to assess size. Volume measurement may be helpful if the aneurysm is not clearly shrinking. If there are concerns regarding imaging of calcified areas, fixation sites, or the outer wall of the aorta, adjunctive CT without contrast may be needed.

14.6 Supplemental Imaging

Note: Additional radiological imaging may be necessary to further evaluate the device *in situ* based on findings revealed by one of the surveillance programs. The following recommendations may be considered:

- If there is evidence of poor or irregular position of the device, severe angulation, kinking or migration of the device on X-ray, a spiral CT should be performed to assess the lesion and the presence or absence of an endoleak.
- If a new endoleak or disease progression is observed by spiral CT, adjunctive studies such as 3-D reconstruction or angiographic assessment of the stent-graft and native vasculature may be helpful in further evaluating any changes of the stent-graft or aorta.
- Spiral CT without contrast, MRI or MRA may be considered in select patients who cannot tolerate contrast media or who have renal function impairment. For centers with appropriate expertise, gadolinium or CO2 angiography may be considered in patients with renal function impairment requiring angiographic assessment.

14.7 Additional Surveillance and Treatment

Additional endovascular repair or open surgical aneurysm repair should be considered for patients with malperfusion, an increase in aneurysm size of more than 5mm or evidence of sub-optimal fixation, distal endoleak, junction endoleak, or unknown origin of perigraft flow. Consideration for adjunctive procedures or reintervention should include the attending physician's assessment of an individual patient's comorbidities, life expectancy, and the patient's personal choices. Patients should be counseled that subsequent adjunctive procedures or reintervention may become necessary after a FET repair.

15 Disclaimer of Warranty

Many factors are outside Vascutek Ltd's supervision and control after sale of Thoraflex™ Hybrid and accessory instruments described in these instructions. Vascutek Ltd has no control over the conditions under which the device is used, the diagnosis of the patient or the methods or procedures used for implantation. Therefore, Vascutek Ltd makes no warranty or guaranty, expressed or implied, of Thoraflex™ Hybrid and accessory instruments other than the warranty that at the time of manufacture, reasonable care was used in their manufacture of these devices.

This warranty is in lieu of any warranty expressed or implied. Any warranty or representation by any other person or firm is void. No warranty of merchantability or fitness for a particular purpose will apply. Vascutek Ltd neither assumes, nor authorizes any other person to assume for it any other liability in connection with sale of these devices. Vascutek Ltd will not be liable for any incidental or consequential loss, damage or expense arising directly or indirectly from the use of these devices.

Some jurisdictions do not allow the exclusion of or limitations on an implied warranty. Similarly, some jurisdictions do not allow the exclusion or limitations of incidental or consequential damages. Therefore, some of the above exclusions may not apply. This warranty gives specific legal rights. The patient may also have their rights which vary from jurisdiction to jurisdiction.

16 Symbols Glossary

The below symbols have been used on the device labeling. The table below shows the symbol, its title and a reference to the relevant international standard the symbol has been taken from. The full designations and titles of the standards listed below are:

- ISO 15223-1:2021 - Medical devices - Symbols to be used with information to be supplied by the manufacturer - Part 1: General requirements
- ASTM F2503 - 20 Standard Practice for Marking Medical Devices and Other Items for Safety in the Magnetic Resonance Environment

Symbol	Meaning	Ref	Symbol	Meaning	Ref
	Use-by Date	ISO 15223-1 5.1.4		Latex-free	N/A
	Batch Code	ISO 15223-1 5.1.5		Catalogue Number	ISO 15223-1 5.1.6
	Serial Number	ISO 15223-1 5.1.7		Sterilized using ethylene oxide	ISO 15223-1 5.2.3
	Do not re-use	ISO 15223-1 5.4.2		Consult electronic instructions for use	ISO 15223-1 5.4.3
	Diameter	N/A		Usable Length	N/A
	Date of Manufacture	ISO 15223-1 5.1.3		Manufacturer	ISO 15223-1 5.1.1
	Do not use if package is damaged and consult instructions for use	ISO 15223-1 5.2.8		Double sterile barrier system	ISO 15223-1 5.2.12
	Do not resterilize	ISO 15223-1 5.2.6		MR Conditional	ASTM F2503 Figure 5
	Unique Device Identifier	ISO 15223-1 5.7.10		Contains biological material of animal origin	ISO 15223-1 5.4.8
	Medical Device	ISO 15223-1 5.7.7		Keep away from sunlight	ISO 15223-1 5.3.2
	Keep dry	ISO 15223-1 5.3.4		Caution	ISO 15223-1 5.4.4
	CAUTION: Federal Law restricts this device to sale by or on the order of a physician.	CFR Title 21 § 801.109			

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