Summary of Safety and Effectiveness Data (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Endovascular Graft
Device Trade Name:	Valiant® Thoracic Stent Graft with the Captivia Delivery System
Device Procode:	MIH
Applicant's Name and Address:	Medtronic Vascular 3576 Unocal Place Santa Rosa, CA 95403 USA
Premarket Approval Application Number:	P100040/S008
Date of Panel Recommendation:	None
Date of Notice of Approval to Applicant:	October 26, 2012
Expedited:	Not Applicable

The original PMA (P100040) was approved on April 1, 2011 and is indicated for the endovascular repair of fusiform aneurysms and saccular aneurysms/penetrating ulcers of the descending thoracic aorta in patients having appropriate anatomy, including: iliac or femoral artery access vessel morphology that is compatible with vascular access techniques, devices, or accessories; and nonaneurysmal aortic diameter in the range of 18 mm to 42 mm; nonaneurysmal aortic proximal and distal neck lengths ≥20 mm. The SSED to support the indication is available on the CDRH website and is incorporated by reference here. The current supplement was submitted to expand the indication for the Valiant® Thoracic Stent Graft with the Captivia Delivery System.

PMA supplement P100040/S008 was submitted to obtain approval to market the Valiant® Thoracic Stent Graft with the Captivia Delivery System for the endovascular repair of isolated lesions of the descending thoracic aorta (DTA), excluding dissections. The data presented below support the use of the device for the treatment of aortic transections. These data, in combination with the data provided previously in this PMA, are adequate to demonstrate that the device is a safe and effective treatment option for an expanded indication for use, that is, isolated lesions of the DTA. This broader indication, which excludes the treatment of dissections, includes the treatment of all types of isolated lesions in the DTA, such as, saccular and fusiform aneurysms, penetrating ulcers, isolated hematomas, and transections. Because of the significant challenges in conducting a study that would capture data on each of the lesion types, the broader indication is supported by the data for the most challenging lesion type to treat endovascularly (i.e., aneurysms) and the other relatively common isolated lesion treated endovascularly (i.e., transections).

II. INDICATIONS FOR USE

The Valiant® Thoracic Stent Graft with the Captivia Delivery System is intended for the endovascular repair of isolated lesions (excluding dissections) of the descending thoracic aorta in patients having appropriate anatomy, including:

- iliac or femoral artery access vessel morphology that is compatible with vascular access techniques, devices, or accessories;
- nonaneurysmal aortic diameter in the range of 18 to 42 mm (fusiform and saccular aneurysms/penetrating ulcers) or 18 mm to 44 mm (blunt traumatic aortic injuries); and
- nonaneurysmal aortic proximal and distal neck lengths $\geq$ 20 mm.

III. CONTRAINDICATIONS

The Valiant Thoracic Stent Graft with the Captivia Delivery System is contraindicated in the following clinical scenarios:

- Patients who have a condition that threatens to infect the graft.
- Patients with known sensitivities or allergies to the device materials.

Physicians should also consider the information in Patient Selection (Section 4.2 of the Instructions for Use).

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Instructions for Use for the Valiant Thoracic Stent Graft with Captivia Delivery System.

V. DEVICE DESCRIPTION

A. Valiant Thoracic Stent Graft with the Captivia Delivery System

The Valiant Thoracic Stent Graft with the Captivia Delivery System is comprised of two components:

- Valiant Thoracic Stent Graft
- Captivia Delivery System

The Valiant Thoracic Stent Graft is intended to be delivered endoluminally via access through the femoral or iliac artery to the site of the lesion using the Captivia Delivery System. The stent graft is inserted and constrained by the delivery system outer sheath (graft cover). The pre-loaded stent graft is advanced to the lesion location over a guidewire. Upon deployment, the stent graft self-expands due to the superelastic properties of the nitinol stent. The proximal and distal ends of the stent graft are intended to conform to the shape and size of the proximal and distal seal zones of the targeted lesion due to the radial force of the stents.

1. Valiant Thoracic Stent Graft

   The Valiant Thoracic Stent Graft is a self-expanding, tube endoprosthesis composed of a polyester graft fabric and a spring scaffold made from nitinol wire. The metal scaffolding is composed of a series of serpentine springs stacked in a tubular configuration. The springs are sewn onto a polyester fabric with non-absorbable sutures.

   Platinum-Iridium radiopaque markers are sewn to the fabric to facilitate radiographic visualization of the edge of the graft material and the minimum overlap required when multiple stent grafts are used. The four proximal **Figur8** markers (shaped as a figure 8), and the two distal **Zer0** markers (shaped as a Zero), indicate the extremities of the covered stent graft. The single **Figur8** "mid-marker" indicates the minimum amount of overlap required for multiple components.

   During manufacturing, the Valiant Thoracic Stent Graft is preloaded into a delivery system.

   See **Figure 5-1** for a drawing of the Valiant Thoracic Stent Graft.

   Valiant Thoracic Stent Graft Configuration and Placement

   The Valiant Thoracic Stent Graft is a modular device that accommodates the use of additional sections depending on the configuration of the anatomy where single or multiple components may be required to achieve sufficient coverage of the lesion.

   If the vessel diameter and condition require variable proximal and distal diameter devices, the smallest diameter stent graft should be placed first, either at the proximal or distal end of the lesion, as appropriate. The additional section is to be deployed within the primary piece following the

oversizing requirements, as will be detailed in the Instructions for Use (IFU) manual.

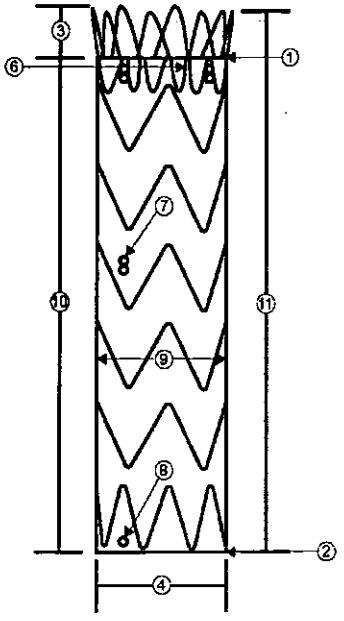
If the vessel diameter and condition require the same proximal and distal diameter devices, the primary section should be placed at the proximal end of the lesion. To achieve the same final diameter with the proximal and distal sections, a tapered configuration is required for the distal section. The flare of the tapered graft permits the over sizing requirements between components.

Different end configurations are available to further accommodate anatomical dimensions. The proximal end comes in two configurations: FreeFlo or Closed Web (**Figure 5-1**). Devices with a FreeFlo proximal end configuration have a bare spring extending beyond the edge of the fabric at the proximal end of the stent graft and should be implanted in the most proximal position only. The Closed Web proximal end configuration, which has a covered spring at the proximal end of the stent graft, is implanted distally. The distal end configurations of the stent grafts are Closed Web or Bare Spring. The Closed Web distal end configuration has a covered spring at the distal end of the stent graft. The Bare Spring distal end configuration has a bare spring at the distal end of the stent graft that extends beyond the edge of the fabric. **Table 5-1** provides the configurations and sizes of the Valiant Stent Graft.

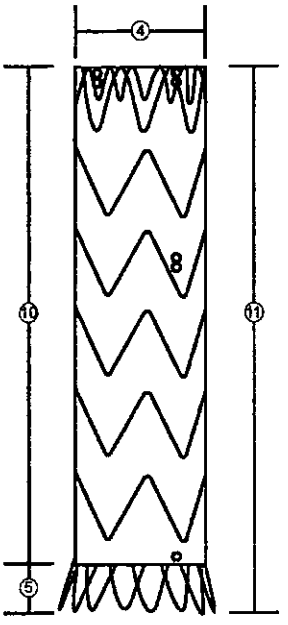
Table 5-1: Valiant Thoracic Stent Graft Configurations

Stent Graft Type	Proximal Diameter, Configuration	Distal Diameter, Configuration	Approx. Covered Lengths (mm)	Delivery System Diameter (Fr)
Proximal FreeFlo Straight – Proximal Component (distal diameter is equal to proximal diameter)	22 mm-28 mm FreeFlo	22 mm-28 mm Closed Web	100, 150	22
	30 mm-32 mm (increments of 2 mm), FreeFlo	30 mm-32 mm (increments of 2 mm), Closed Web	100, 150, 200	22
	34 mm-40 mm (increments of 2 mm), FreeFlo	34 mm-40 mm (increments of 2 mm), Closed Web	100, 150, 200	24
	42 mm-46 mm (increments of 2 mm), FreeFlo	42 mm-46 mm (increments of 2 mm), Closed Web	100, 150, 200	25
Proximal Closed Web Straight – Distal Component (distal diameter is equal to proximal diameter)	22 mm-28 mm Closed Web	22 mm-28 mm Closed Web	100, 150	22
	30 mm-32 mm (increments of 2 mm), Closed Web	30 mm-32 mm (increments of 2 mm), Closed Web	100, 150, 200	22
	34 mm-40 mm (increments of 2 mm), Closed Web	34 mm-40 mm (increments of 2 mm), Closed Web	100, 150, 200	24
	42 mm-46 mm (increments of 2 mm), Closed Web	42 mm-46 mm (increments of 2 mm), Closed Web	100, 150, 200	25
Closed Web Tapered – Distal Component (distal diameter is 4 mm less than proximal diameter)	26 mm – 32 mm (increments of 2 mm), Closed Web	22 mm – 28 mm (increments of 2 mm), Closed Web	150	22
	34 mm – 40 mm (increments of 2 mm), Closed Web	30 mm – 36 mm (increments of 2 mm), Closed Web	150	24
	42 mm – 46 mm (increments of 2 mm), Closed Web	38 mm – 42 mm (increments of 2 mm),	150	25

Stent Graft Type	Proximal Diameter, Configuration	Distal Diameter, Configuration	Approx. Covered Lengths (mm)	Delivery System Diameter (Fr)
		Closed Web		
Distal Bare Spring Straight – Distal Component (distal diameter is equal to proximal diameter)	22 mm – 32 mm (increments of 2 mm), Closed Web	22 mm – 32 mm (increments of 2 mm), Bare Spring	100	22
	34 mm – 40 mm (increments of 2 mm), Closed Web	34 mm – 40 mm (increments of 2 mm), Bare Spring	100	24
	42 mm – 46 mm (increments of 2 mm), Closed Web	42 mm – 46 mm (increments of 2 mm), Bare Spring	100	25



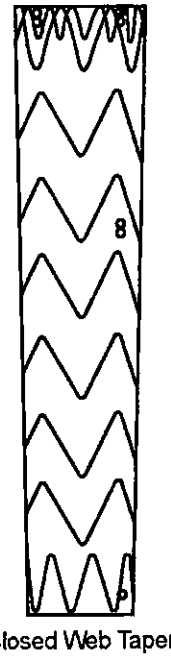
FreeFlo Straight
(Proximal Component)



Distal Bare Spring
Straight (Distal Component)

1. Proximal End
2. Distal End
3. FreeFlo
4. Closed Web
5. Bare Spring
6. Mini Support Spring
7. Figure8 Marker
8. Zer0 Marker
9. Diameter
10. Covered Length
11. Total Length

Closed Web Straight
(Distal Component)



Closed Web Taper
(Distal Component)

Figure 5-1: Valiant Thoracic Stent Graft End Configurations

NOTE: This and all other product graphics appearing in this summary are not drawn to scale, are for graphical representation only, and may appear differently under fluoroscopy.

2. Captivia Delivery System

The Captivia Delivery System consists of a single use, disposable catheter with an integrated handle to provide the user with controlled deployment. The Captivia Delivery System (**Figure 5-2**) is the generic name for the following two delivery system configurations:

- The FreeFlo Stent Graft Delivery System (Tip Capture)
- The Closed Web Stent Graft Delivery System (non-Tip Capture)

a) *FreeFlo Stent Graft Delivery System*

The FreeFlo Stent Graft Delivery System is used with the FreeFlo Straight configuration, the stent graft configuration that is implanted in the most proximal position. The delivery system features a tip capture mechanism from which the proximal stent graft is deployed in two stages:

(1) Deployment of the stent graft with the apices of the bare stent of the FreeFlo configuration still constrained by the tip capture mechanism; and

(2) Release of the proximal bare spring portion of the stent graft.

b) *Closed Web Stent Graft Delivery System*

The Closed Web Stent Graft Delivery System is used with the Closed Web Straight, Distal Bare Spring Straight, and Closed Web Tapered configuration stent grafts. Because these devices do not have a bare spring configuration at the proximal end of the stent graft, the Closed Web Delivery System does not include a tip capture mechanism. As a result, deployment using the Closed Web Delivery System is accomplished in a single step when the outer sheath is removed from the stent graft.

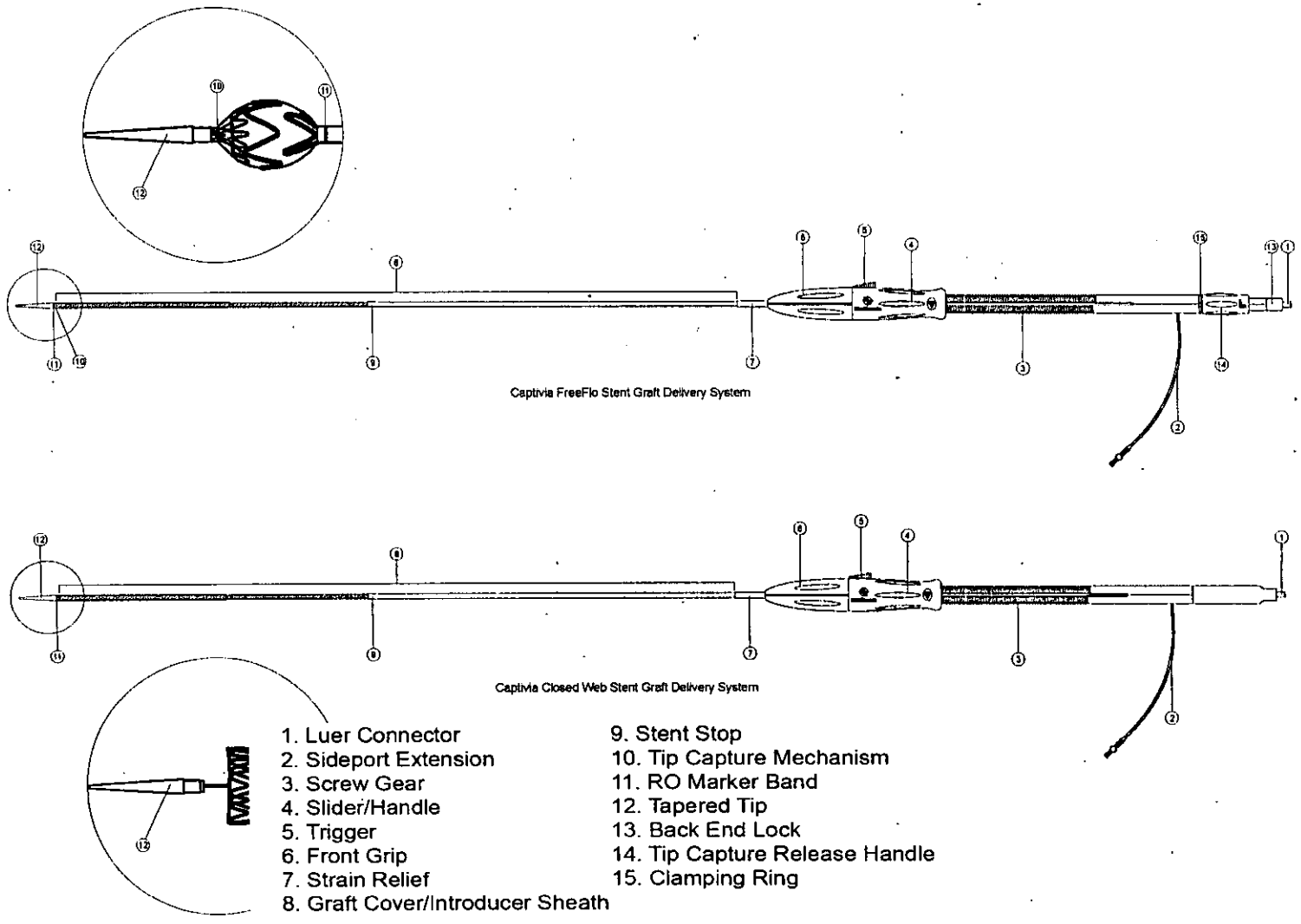


Figure 5-2: Captivia Delivery System
(The FreeFlo Stent Graft Delivery System on Top, Closed Web Stent Graft Delivery System on Bottom)

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of isolated lesions of the descending thoracic aorta (DTA) including endovascular repair using another endovascular grafting system, surgical implantation of a synthetic graft within the aortic vessel, and medical management. Each alternative has its own advantages and disadvantages. The physician should fully discuss these alternatives with his/her patient to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Valiant Thoracic Stent Graft with the Captivia Delivery System originally received premarket approval for use in the treatment of aneurysms of the DTA on April 1, 2011.

The Valiant Thoracic Stent Graft with the Captivia Delivery System has been commercially available for distribution outside of the United States including regions in the European Union, Asia, Africa, Middle East, Latin America, Australia, and New Zealand since September 2009.

The Valiant Thoracic Stent Graft with the Captivia Delivery System has not been withdrawn from the market for any reason related to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Adverse events or complications associated with the use of the Valiant Thoracic Stent Graft with the Captivia Delivery System that may occur and may require intervention include, but are not limited to, to those listed in **Table 8-1**.

Table 8-1: Potential Adverse Effects

• Access failure	• Endoleaks	• Procedural bleeding
• Access site complications (e.g. spasm, trauma, bleeding, rupture, dissection)	• Excessive or inappropriate radiation exposure	• Prosthesis dilatation
• Adynamic Ileus	• Extrusion/erosion	• Prosthesis infection
• Allergic reaction (to contrast, anti-platelet therapy, stent graft material)	• Failure to deliver the stent graft	• Prosthesis rupture
• Amputation	• Femoral neuropathy	• Prosthesis thrombosis
• Anesthetic complications	• Fistula (aortobronchial, aortoenteric, aortoesophageal arteriovenous, and lymph)	• Pseudoaneurysm
• Aneurysm expansion	• Gastrointestinal bleeding/complications	• Pulmonary edema
• Aneurysm rupture	• Genitourinary complications	• Pulmonary embolism
• Angina	• Hematoma	• Reaction to anaesthesia
• Arrhythmia	• Hemorrhage/bleeding	• Renal failure
• Arterial stenosis	• Hypotension/hypertension	• Renal insufficiency
• Atelectasis	• Infection or fever	• Reoperation
• Blindness	• Insertion or removal difficulty	• Respiratory depression or failure
• Bowel ischemia/infarction	• Intercostal pain	• Sepsis
• Bowel necrosis	• Intramural hematoma	• Seroma
• Bowel obstruction	• Leg edema/foot edema	• Shock
• Branch vessel occlusion	• Lymphocele	• Spinal neurological deficit
• Buttock claudication	• Myocardial infarction	• Stent graft material failure (including breakage of metal portion of device)
• Cardiac tamponade	• Neuropathy	• Stent graft migration
• Catheter breakage	• Occlusion – Venous or Arterial	• Stent graft misplacement
• Cerebrovascular accident (CVA)/Stroke	• Pain/Reaction at catheter insertion site	• Stent graft occlusion
• Change in mental status	• Paralysis	• Stent graft twisting or kinking
• Coagulopathy	• Paraparesis	• Transient-ischemic attack (TIA)
• Congestive heart failure	• Paraplegia	• Thrombosis
• Contrast toxicity	• Paresthesia	• Tissue necrosis
• Conversion to surgical repair	• Peripheral ischemia	• Vascular ischemia
• Death	• Peripheral nerve injury	• Vascular trauma
• Deployment difficulties/ failures	• Pneumonia	• Wound dehiscence
• Dissection, perforation, or rupture of the aortic vessel & surrounding vasculature	• Post-implant syndrome	• Wound healing complications
• Embolism	• Post-procedural bleeding	• Wound infection

IX. SUMMARY OF PRE-CLINICAL STUDIES

The SSED containing the pre-clinical studies to support the aneurysm indication for the original Valiant Thoracic Stent Graft PMA (P100040) is available on the CDRH website. Additional pre-clinical testing conducted to support the blunt thoracic aortic injury (BTAI) indication is discussed below.

A. Laboratory Studies

In Vitro Bench Testing

Medtronic conducted fatigue and Finite Element Analysis (FEA) testing to ensure that the Valiant Thoracic Stent Graft with the Captivia Delivery System will accommodate the unique *in vivo* conditions associated with a transected aorta. A summary of the fatigue and FEA testing is provided in **Table 9-1.**

Table 9-1: Summary of Tests Performed related to Functionality of the Valiant Thoracic Stent Graft with the Captivia Delivery System

Test	Test Purpose	Acceptance Criteria	Pass/Fail
Finite Element Analysis	Quantify levels of strain of 8-peak and 5-peak springs when subjected to in-vivo fatigue conditions. Furthermore, use fatigue life data to present estimates of fatigue safety factors.	Fatigue safety factors to be > 1 based on endurance limit determined through endurance life testing.	PASS All of the computed fatigue safety factors were > 1.
Spring Component Fatigue	To evaluate the spring durability following 10 years simulated (400 million cycles) accelerated *in vitro* testing under clinically-relevant loading conditions.	The device, due to the integrity of its sample components (i.e. stents, sutures, and graft fabric) must be able to maintain patency over 10 years simulated (400 million cycles) accelerated pulsatile durability testing.	PASS The device satisfied the acceptance criteria for 10-year device integrity.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

One primary clinical study was conducted to support the expanded indication of isolated lesions of the DTA for the Valiant Thoracic Stent Graft with the Captivia Delivery System. This study evaluated the safety and effectiveness of the Valiant Thoracic Stent Graft in subjects with blunt thoracic aortic injuries (BTAI) in the RESCUE trial and is summarized in **Table 10-1**. The safety and effectiveness of the Valiant Thoracic Stent Graft for isolated lesions of the DTA was not based on the RESCUE clinical study alone, but rather on all available data for the Valiant Thoracic Stent Graft to date, including data from the aneurysm clinical study (VALOR II) that was reviewed under PMA (P100040). As supplemental clinical information, the literature was reviewed and compared to the clinical outcomes in the RESCUE trial.

Table 10-1: Summary of Primary Clinical Studies

Clinical Study	Study Design	Objective	Number of Sites with Enrollments	Number of Subjects
RESCUE (Blunt Thoracic Aortic Injury study)	Prospective, non-randomized, multicenter study to evaluate the clinical performance of Valiant Captivia for treatment of BTAI. The primary and secondary endpoints were assessed using descriptive statistics.	To evaluate the safety and effectiveness of Valiant Captivia in subjects with BTAI as determined by all-cause mortality within 30-days of the index procedure.	20	50

A. Study Design

The RESCUE study (G090201) was a prospective, non-randomized, multicenter study to evaluate the clinical performance of the Valiant Thoracic Stent Graft for treatment of BTAI. The primary objective was to evaluate the safety and effectiveness of the Valiant Thoracic Stent Graft in the treatment of BTAI.

1. Clinical Inclusion and Exclusion Criteria

   The study investigators were responsible for ensuring the subjects met the inclusion and exclusion criteria for the trial. Pre-treatment evaluation included a contrast-enhanced CT angiogram (CTA) of the chest and abdomen for assessment of the aortic morphology and vascular characteristics. A physical exam was conducted to assess medical history, Injury Severity Score (ISS) and the inclusion/exclusion criteria below.

   a) *Inclusion Criteria*

   - Subject had a blunt thoracic aortic injury which:

- was confirmed, at a minimum, by diagnostic contrast-enhanced CTA and/or contrast-enhanced magnetic resonance angiogram (MRA)
- occurred no more than 30 days prior to the stent implant procedure

- Subject was ≥ 18 years of age
- Subject or subject's legally authorized representative signed an IRB approved informed consent
- Subject was hemodynamically stable
- Subject's anatomy was required to meet all of the following anatomical criteria:
  - Aortic diameter (adventitia to adventitia) of the proximal and distal landing zones was between 18 mm and 44 mm
  - Subject had patent iliac or femoral arteries or could tolerate an iliac conduit that allowed endovascular access to the injury site with the delivery system of the appropriate sized device
  - The centerline distance from the distal margin of left common carotid artery (LCC) to the injury was ≥ 20 mm

b) *Exclusion Criteria*

- Planned placement of the COVERED portion of the stent graft over the celiac axis or the LCC, or in cases of bovine anatomy, innominate artery
- Subject had systemic infection
- Subject was pregnant
- Subject had received a previous stent or stent graft or previous surgical repair in the DTA
- Subject had a history of bleeding diathesis, coagulopathy, or refuses blood transfusion
- Subject was participating in an investigational drug or device clinical trial which would interfere with the endpoints and/or follow-ups of this study
- Subject had a known allergy or intolerance to the device components
- Subject had a known hypersensitivity or contraindication to anticoagulants or contrast media, which is not amenable to pre-treatment
- Subject was in extremis, *defined as subject has non-survivable injury/condition*
- Subject had a cerebral vascular accident (CVA) within two (2) months prior to implant procedure

c) *Enrollment*

Once satisfying the eligibility criteria, the subject was enrolled at the time of arterial access with intent to implant the Valiant Thoracic Stent Graft.

2. Follow-up Schedule and Evaluations

In addition to pre-treatment evaluations, data was collected during the procedure, post-operatively and at hospital discharge. After discharge, subjects were required to comply with follow-up visits and evaluations that occur at one, six, and 12 months and annually for five years post-implant. At each follow-up, a physical exam, CTA or MRA, and x-ray were performed per the protocol schedule.

a) *External Evaluation Groups*

There were three external evaluation groups that independently reviewed data for this study. These groups were a Clinical Events Committee (CEC), a Data Monitoring Committee (DMC) and an imaging core laboratory.

(1) *Clinical Events Committee (CEC)*

The CEC was a group of physicians, independent of the clinical study with expertise and experience in the endovascular repair of descending thoracic aortic pathologies. The CEC met to review and adjudicate all deaths and UADEs (there were no UADEs identified in this study) for relatedness to the aorta, device and procedure. The CEC will continue to review and adjudicate deaths and UADEs out to five years.

(2) *Data Monitoring Committee (DMC)*

The DMC was composed of at least five members, four physicians from the fields of vascular or cardiovascular surgery and interventional radiology or interventional cardiology and one biostatistician, none of whom were involved in the conduct of the study. The DMC met to review trial conduct and study data after the first 20 subjects reached the 30-day follow-up time point, and recommended that the clinical trial continue without modifications.

(3) *Core Laboratory (Core lab)*

The Core lab provided independent verification of imaging findings after images were transferred by the sites, as required by protocol. Medical Image & Data Management Services Inc. (M2S) served as the independent image core lab for this study. Detailed analysis of study imaging utilizing three-dimensional reconstructions was undertaken in order to provide critical and comprehensive data evaluation during the pre- and post-operative periods. Investigational sites submitted contrast-enhanced/non-contrast computerized tomography (CT) or

contrast-enhanced magnetic resonance (MR) imaging to the core lab for three-dimensional reconstructions at baseline, 1 month, 6 months and 12 months. Chest x-rays were also submitted to the core lab for analysis at 12 months.M2S technology processes and systems were GMP/GCP, HIPAA, and 21 CFR Part 11 compliant and were provided within an ISO 13485 certified facility which adheres to all applicable federal regulations.

3. Clinical Endpoints

The primary safety endpoint was all-cause mortality within 30-days of the index procedure. Additional secondary objectives evaluated the acute safety and effectiveness by reporting the following outcomes, all occurring within 30-days:

- Aortic related mortality (defined as death caused by the underlying thoracic aortic injury and/or from any procedure intended to treat the aortic injury)
- Device, procedure and/or aortic related adverse events
- Successful delivery and deployment of the stent graft

The primary objective and set of secondary objectives were assessed descriptively and there was no formal hypothesis testing. The sample size of 50 subjects was planned without a formal statistical sample size calculation and selected based on precision around the estimated 30-day mortality.

Medtronic designed the RESCUE trial to show that the Valiant Thoracic Stent Graft did not introduce any new concerns for the safety and effectiveness of the device for the treatment of BTAI. The study design was deemed appropriate because the effectiveness of the device was studied in the clinical trial for aneurysm subjects and expected to perform no worse than the results in that trial, unless a device-related issue was identified during the clinical trial due to different patient populations. For safety considerations, a mortality-related performance goal could not be established due to (1) deaths within the BTAI patient population being related to concomitant injuries and not the BTAI treatment and (2) the absence of deaths in the aneurysm trial that were related to device failure.

B. Accountability of PMA Cohort

Subjects were screened and enrolled per the protocol. A total of 69 subjects were screened for eligibility for the RESCUE trial and 19 subjects were excluded from the study (**Figure 10-1**). Reasons for exclusion are provided in **Table 10-2.**

Table 10-2: Subject Screening

Reason for Exclusion	# of Subjects Excluded from the Study
Appropriate device size not available at site in enough time to treat subject	4
Unable to obtain IC	2
Opted surgical treatment	2
Medically managed	2
Aortic diameter is 15 mm	1
Proximal landing zone centerline distance < 20mm	1
BCBC Insurance would not cover	1
Patient died just after being consented	1
Emergency unstable	1
Patient declined participation in the study	1
Contraindication to anticoagulants	1
Patient was pregnant	1
Surgery>30 days after consent	1
TOTAL	**19**

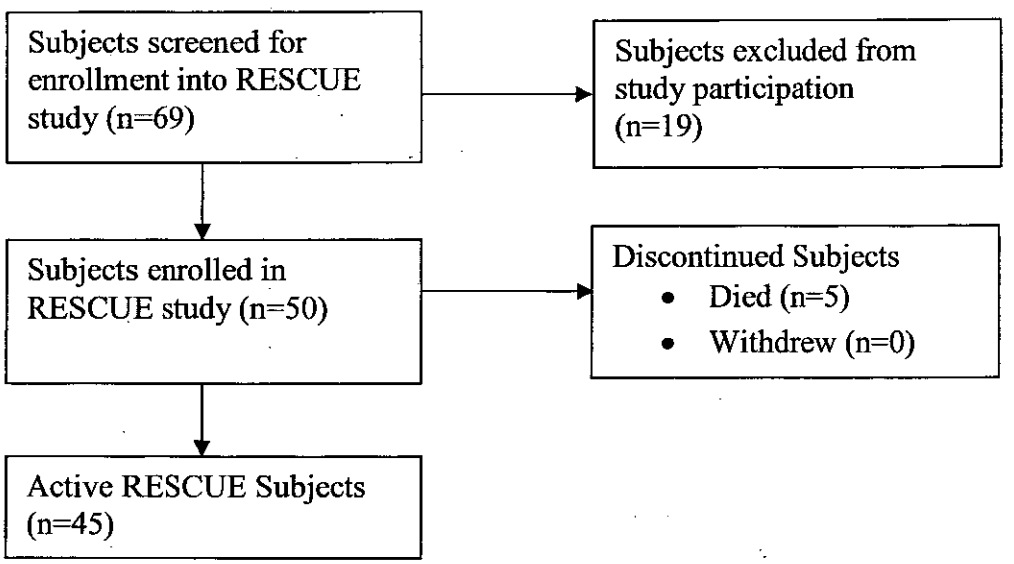


Figure 10-1: Enrollment Flowchart

Fifty subjects (50) were enrolled in this study between April 2010 and January 2012 at 20 investigational sites. All enrolled subjects underwent endovascular repair with the Valiant Thoracic Stent Graft. **Table 10-3** summarizes the subject accountability and compliance by study interval.

Four (4) subjects died within 30-days of the index procedure. One (1) of these subjects had a 1-month follow-up and imaging visit completed before death. Of the 47 subjects eligible for 1-month clinical and imaging follow-up, the clinical follow-up compliance was 97.9% and the image follow-up compliance was 95.7%. No subjects were discontinued, lost to follow-up, withdrew consent or were converted to surgery.

Table 10-3: RESCUE Trial Subject Follow-up, Imaging and Accountability (Site Reported)

	Subject Follow-up % (m/n)[2]			Subject Imaging % (m/n)[2]			Patients with Adequate Imaging to Assess the Parameter % (m/n)[2]			Subject Accountability N					
Implant and Follow-up	**Eligible[1]**	**Clinical Follow-up**	**Imaging Follow-up**	**CT/MR Imaging**	**Chest X-Ray**	**Additional Imaging Modalities**	**Endoleak**	**Migration from 1-Month**	**Integrity**	**Enrolled but not Implanted**	**Withdrawal**	**Conversion to Surgery**	**Death**	**Lost to Follow-up**	**Not Due for Next Visit**
Implant	50														
Events Between Implant and 1-Month										0	0	0	4[3]	0	0
1-Month	47[3]	97.9% (46/47)	95.7% (45/47)	95.7% (45/47)		0.0% (0/47)	93.6% (44/47)		97.9% (46/47)						
Events Between 1-Month and 6-Month											0	0	1[3]	0	18
6-Month	27	85.2% (23/27)	81.5% (22/27)	81.5% (22/27)		0.0% (0/27)	81.5% (22/27)	81.5% (22/27)	81.5% (22/27)						
Events Between 6-Month and 12-Month											0	0	0	0	13
12-Month	14	85.7% (12/14)	85.7% (12/14)	85.7% (12/14)	85.7% (12/14)	0.0% (0/14)	85.7% (12/14)	85.7% (12/14)	85.7% (12/14)						
Events Between 12-Month and 2-Year											0	0	0	0	14
2-Year	0	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)		0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)						
									Total	0	0	0	5	0	
									Deaths Post Conversion to Surgery				0		

	Subject Follow-up % (m/n)[2]			Subject Imaging % (m/n)[2]			Patients with Adequate Imaging to Assess the Parameter % (m/n)[2]			Subject Accountability N					
Implant and Follow-up	**Eligible[1]**	**Clinical Follow-up**	**Imaging Follow-up**	**CT/MR Imaging**	**Chest X-Ray**	**Additional Imaging Modalities**	**Endoleak**	**Migration from 1-Month**	**Integrity**	**Enrolled but not Implanted**	**Withdrawal**	**Conversion to Surgery**	**Death**	**Lost to Follow-up**	**Not Due for Next Visit**
													Total Deaths	5	

[1]Eligible at implant are all subjects enrolled by snapshot date. Eligible (E_T) for time intervals post implant is eligible from the previous interval (E_{PI}) less the sum of enrolled but not implanted (ENI) plus withdrawal (W) plus conversion to surgery (CTS) plus death (D) plus lost to follow-up (LTF) plus not due for next visit (NDNV) subjects. $E_T = E_{PI} - (ENI + W + CTS + D + LTF + NDNV)$.

[2] Percentages are based on number of all subjects enrolled by snapshot date and include subjects that have a completed clinical/imaging follow-up form for the time point, divided by number of eligible subjects. To be considered within window, a subject must have at a minimum, the clinical follow-up or the imaging follow up occurring within the follow-up window.

[3] There were 4 deaths within 30 days and 47 subjects were eligible at 1-month follow-up visit instead of 46 subjects since one subject that died had completed the 1-month follow-up visit prior to death. This subject is included under the eligible subjects at 1-month follow-up time point in the table.

m = number of subjects in category, n = number of subjects with available data.

Site Reported Table.

C. Subject Population Demographics and Baseline Parameters

Baseline parameters of the study subjects include demographics, medical history, associated injuries to the BTAI, pre-treatment risk using the ISS, and radiological aortic assessment.

Table 10-4 provides a summary of demographic data. The median age of the study population was 39.5 years (ranging from 18 to 76). The majority of the subjects were male (76.0%). Hispanic or Latino ethnicity constituted 20.0% of the study population. The subjects had a race distribution of 68.0% White, 20.0% African American and 4.0% Asian.

Table 10-4: Subject Demographics

Age (years)	
n	50
Mean ± SD	40.7 ± 17.4
Median	39.5
Min, Max	18, 76
Sex % (m/n)	
Male	76.0% (38/50)
Female	24.0% (12/50)
Weight (lbs)	
n	50
Mean ± SD	189.3 ± 39.3
Median	186.1
Min, Max	115, 324
Ethnicity % (m/n)	
Hispanic or Latino	20.0% (10/50)
Not Hispanic or Latino	72.0% (36/50)
Not Available	8.0% (4/50)
Race % (m/n)	
White	68.0% (34/50)
Black or African American	20.0% (10/50)
Asian	4.0% (2/50)
Native Hawaiian or Other Pacific Islander	0.0% (0/50)
American Indian or Alaska Native	0.0% (0/50)
Other	4.0% (2/50)
Not Available	4.0% (2/50)

m = number of subjects in category, n = number of subjects enrolled in this study.
Site Reported Table.

Subject medical history is presented in **Table 10-5**. Hypertension was the most common pre-existing condition and reported in 24.0% of the subjects. One subject presented with paraplegia that was a result of the subject's associated injuries prior to treatment. Medical conditions, such as cardiac risk factors and comorbid conditions were uncommon in the study population. Approximately half of the subjects (46.0%) reported with other medical conditions that were varied and not amenable to grouping.

Table 10-5: Subject Medical History

Subject Medical History	% (m/n)
Hypertension	
Yes	24.0% (12/50)
No	74.0% (37/50)
Unknown	2.0% (1/50)
COPD	
Yes	4.0% (2/50)
No	94.0% (47/50)
Unknown	2.0% (1/50)
Congestive Heart Failure	
Yes	2.0% (1/50)
No	96.0% (48/50)
Unknown	2.0% (1/50)
Paraplegia	
Yes	2.0% (1/50)
No	96.0% (48/50)
Unknown	2.0% (1/50)
Diabetes	
Yes	2.0% (1/50)
No	96.0% (48/50)
Unknown	2.0% (1/50)
GI Conditions	
Yes	2.0% (1/50)
No	94.0% (47/50)
Unknown	4.0% (2/50)
MI	
Yes	0.0% (0/50)
No	98.0% (49/50)
Unknown	2.0% (1/50)
Coronary Artery Bypass Grafting (CABG)	
Yes	0.0% (0/50)
No	98.0% (49/50)
Unknown	2.0% (1/50)

Subject Medical History	% (m/n)
Renal Insufficiency	
Yes	0.0% (0/50)
No	98.0% (49/50)
Unknown	2.0% (1/50)
Stroke/Cerebrovascular Accident (CVA)	
Yes	0.0% (0/50)
No	98.0% (49/50)
Unknown	2.0% (1/50)
Paraparesis	
Yes	0.0% (0/50)
No	98.0% (49/50)
Unknown	2.0% (1/50)
Bleeding Disorder	
Yes	0.0% (0/50)
No	98.0% (49/50)
Unknown	2.0% (1/50)
Other Important Medical Conditions	
Yes	46.0% (23/50)
No	54.0% (27/50)

m = number of subjects in category, n = number of subjects enrolled in this study.
Site Reported Table.

The subject injury characteristics are summarized in **Table 10-6**. Motor vehicle and motorcycle accidents accounted for the injuries in the majority of subjects (82.0%). Most subjects presented with associated injuries and were treated within a day of their BTAI. Commonly reported injuries were lung injuries, abdominal injuries, head injuries and various fractures. Each subject was assigned an ISS that represents the pre-treatment risk to the subject.

The site-reported measurements are summarized in **Table 10-7** and **Table 10-8** (with the exception of length of stent graft coverage, which is reported by the core lab). The mean diameter at the proximal landing zone (D2) was 24.3 ± 3.9 mm (minimum of 18 mm and a maximum of 35 mm). The recommended proximal landing zone, measured from the LCC to the aortic injury (L1) is at least 20 mm. All subjects met this requirement. The mean L1 reported by the site was 30.0 ± 8.2 ranging from 20 mm to 52 mm.

In summary, the demographics and baseline parameters show that subjects that suffer BTAI are generally younger and healthier than subjects with aneurysmal disease. Subjects with BTAI present with associated injuries that add to their surgical risk. The thoracic aortas of these subjects have localized injuries and are generally smaller than the aortas of older, aneurysmal subjects.

Table 10-6: Subject Injury Characteristics

Subject Injury Characteristics	
Duration from Injury to Procedure (days)	
n	50
Mean ± SD	1.8 ± 4.0
Median	1.0
Min, Max	0, 23
Assigned ISS	
n	50
Mean ± SD	37.6 ± 14.3
Median	35.0
Min, Max	13, 75
Mechanism of Blunt Injury % (m/n)	
Motor Vehicle Accident	60.0% (30/50)
Motorcycle Accident	22.0% (11/50)
Pedestrian Hit by Motor Vehicle	10.0% (5/50)
Fall	4.0% (2/50)
Other	4.0% (2/50)
Associated Traumatic Injuries % (m/n)	
Head Injury	48.0% (24/50)
Long Bone Fracture	38.0% (19/50)
Pelvic Fracture	40.0% (20/50)
Scapula Fracture	8.0% (4/50)
Unstable C/T/L Spine Fractures	14.0% (7/50)
Abdominal Injury (solid organ, bowel, bladder, or diaphragm injury)	58.0% (29/50)
Lung Injury	70.0% (35/50)
Neurologic Deficits	12.0% (6/50)
Rib Fracture	64.0% (32/50)
Sternum Fracture	6.0% (3/50)
Other	50.0% (25/50)
Location of Aortic Injury % (m/n)	
Isthmus (just distal to the left subclavian artery to the third intercostals artery)	84.0% (42/50)
Distal Descending Thoracic Aorta	16.0% (8/50)
Extent of Aortic Injury % (m/n)[1]	
Grade 1 - Intimal Tear	18.0% (9/50)
Grade 2 - Intramural Hematoma	12.0% (6/50)
Grade 3 - Aortic Pseudoaneurysm	68.0% (34/50)

Grade 4 - Free Rupture	2.0% (1/50)

m = number of subjects in category, n = number of subjects enrolled in this study.
Site Reported Table.
[1]*Azizzadeh A, Keyhani K, Miller CC, Coogan SM, Safi HJ, Estrera AL: Blunt traumatic aortic injury: Initial experience with endovascular repair. J Vasc Surg 2009; 49: 1403-8.*

Table 10-7: Site Reported Thoracic Aortic Measurements – Diameters (mm)

D1: Aortic Diameter at Left Common Carotid Artery	
n	50
Mean ± SD	24.2 ± 5.0
Median	24.0
Min, Max	10, 40
D2: Aorta Diameter (2 cm proximal to injury)	
n	50
Mean ± SD	24.3 ± 3.9
Median	23.5
Min, Max	18, 35
D3: Maximum Descending Thoracic Aorta Diameter	
n	50
Mean ± SD	26.5 ± 6.6
Median	25.5
Min, Max	18, 42
D4: Aorta Diameter (2 cm distal to the injury)	
n	50
Mean ± SD	22.5 ± 4.1
Median	21.0
Min, Max	18, 34
D5: Aortic Diameter at Celiac Axis	
n	49[1]
Mean ± SD	20.5 ± 3.5
Median	20.0
Min, Max	14, 28
Right Common Iliac Diameter	
n	49[1]
Mean ± SD	10.0 ± 1.7
Median	10.0
Min, Max	6, 13
Left Common Iliac Diameter	
n	49[1]
Mean ± SD	10.0 ± 1.8
Median	10.0
Min, Max	6, 15
Right External Iliac Diameter	

n	49[1]
Mean ± SD	8.1 ± 1.5
Median	8.0
Min, Max	3, 11
Left External Iliac Diameter	
n	49[1]
Mean ± SD	8.1 ± 1.7
Median	8.0
Min, Max	3, 12
Right Femoral Diameter	
n	47[2]
Mean ± SD	8.2 ± 1.4
Median	8.0
Min, Max	5, 13
Left Femoral Diameter	
n	47[2]
Mean ± SD	8.0 ± 1.6
Median	8.0
Min, Max	4, 14

[1] The images taken for some subjects did not cover the celiac axis region.

[2]There were three cases in which the pre-implant image was insufficient and the access was assessed during the procedure. There were no access issues or any adverse events related to the procedure in these subjects.

Site Reported Table.

Table 10-8: Thoracic Measurements – Lengths (mm)

L1: Distance from LCC to Injury (pre-implant)	
n	50
Mean ± SD	30.0 ± 8.2
Median	29.5
Min, Max	20, 52
L2: Distance from LSA to Injury (pre-implant)	
n	50
Mean ± SD	15.0 ± 9.4
Median	13.5
Min, Max	0, 36
L3: Distance from Injury to Celiac Axis (pre-implant)	
n	42[1]
Mean ± SD	175.1 ± 50.9
Median	182.5
Min, Max	17, 300

[1] The images taken for some subjects did not cover the celiac axis region.
Site Reported Table.

1. Valiant Thoracic Stent Graft Usage and Acute Procedural Data

The technical success was 100% in this study as shown in **Table 10-9**. Vessel access was obtained in all subjects and the device was successfully delivered and deployed in all the subjects in this study population. As summarized in **Table 10-10**, most subjects (58.0%) received a device in zone 2 of the aorta. One subject who had a bovine arch had a device implanted in zone 1.

Table 10-9: Technical Success

Technical Success	**% (m/n)**
Vessel Access Success	100.0% (50/50)
Delivery Success	100.0% (50/50)
Deployment Success	100.0% (50/50)

m = number of subjects in category, n = number of subjects enrolled in this study.
Site Reported Table.

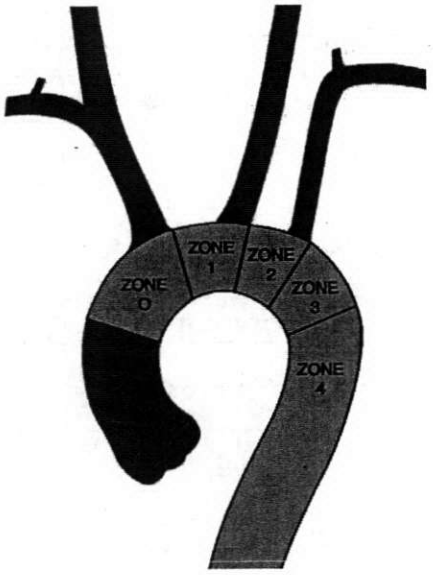


Figure 10-2: Diagram of Thoracic Arch Zones

Table 10-10: Implanted Zone (Implanted)

Implanted Zone of Proximal Piece	% (m/n)
Zone 1	2.0% (1/50) [1]
Zone 2	58.0% (29/50)
Zone 3	36.0% (18/50)
Zone 4	4.0% (2/50)

[1] One subject had a bovine arch.
m = number of subjects in category, n = number of subjects enrolled in this study.
Site Reported Table.

Table 10-11 summarizes the device usage by quantity. All but two (2) subjects received a single device. Both of the remaining subjects received two (2) stent grafts. One (1) subject received two (2) Valiant Thoracic Stent Grafts of 100 mm in length each. The second subject received a Valiant Thoracic Stent Graft as the proximal piece and the second device was a Talent Thoracic Stent Graft as the distal piece. The Talent Thoracic Stent Graft was used due to the emergent nature of the procedure and the lack of an appropriately sized Valiant Thoracic Stent Graft distal piece in stock at the site. A distribution of the type of device components of the Valiant Thoracic Stent Graft system implanted is shown in **Table 10-12**. A FreeFlo Straight proximal component was used in 98% of cases. A closed web tapered device was implanted in one (1) subject and a protocol deviation was reported. No complications resulted from the implant.

The Valiant Thoracic Stent Graft was available in a wide set of sizes ranging from 22 mm to 46 mm in diameter allowing physicians to treat aortic diameters between 18 mm to 44 mm. As summarized in **Table 10-13**, the majority of the proximal devices used were 28 mm or less in diameter. The largest diameter device implanted was a 38 mm device. These results show

that the subjects with BTAI generally have smaller aortas and require a short area of coverage, as compared to larger aortas of diffuse length as seen in subjects with aneurysmal disease. As reported by the core lab, the mean total length of coverage (shown in **Table 10-14**) after the procedure was 130.4 mm ± 21.3 mm ranging from 90 mm to 179 mm.

Table 10-11: Number of Devices Implanted

Number of Devices Implanted[1]	Subjects % (m/n)
1	96.0% (48/50)
2	4.0% (2/50)[2]

[1]Number of devices implanted includes devices implanted at initial procedure.
[2]One subject had one Talent Thoracic Stent Graft implanted distal to the Valiant Thoracic Stent Graft.
m = number of subjects in category, n = number of subjects enrolled in this study.
Site Reported Table.

Table 10-12: Valiant Devices Implanted by Type

Valiant Device Type	% (m/n)
FreeFlo Straight (Proximal Component)	98.0% (50/51)
Closed Web Straight (Distal Component)	0.0% (0/51)
Distal Bare Spring Straight (Distal Component)	0.0% (0/51)
Closed Web Tapered (Distal Component)	2.0% (1/51)

m = number of Valiant devices in category, n = total number of Valiant devices implanted in all subjects.
Site Reported Table.

Table 10-13: Proximal Valiant Device Diameters Implanted at Initial Procedure

Valiant Device Diameter	Number of Devices Implanted
22	11
24	8
26	8
28	11
30	6
32	1
34	3
36	2
38	1
40	0

Valiant Device Diameter	Number of Devices Implanted
42	0
44	0
46	0
Site Reported Table.	

Table 10-14: Length of Stent Graft Coverage

Total Length of Coverage (post-implant) (mm)	
N	45[1]
Mean ± SD	130.4 ± 21.3
Median	136.2
Min, Max	90, 179

[1]This is core lab reported data. Core lab did not receive adequate imaging from all sites.
Core Lab Reported Table.

The details of the implant procedure are summarized in **Table 10-15**. The Left Subclavian Artery (LSA) was covered in 29 subjects (58.0% of study population). LSA coverage was intentional in all cases and resulted in partial coverage in nine (9) subjects (31.0% of LSA covered population) and complete coverage in 20 subjects (69.0% of LSA covered population). Revascularization of the LSA prior to the procedure occurred in only one (1) subject (3.4% of LSA covered population). After the procedure, one (1) subject had LSA revascularization within 30-days of the index procedure as an intervention for an adverse event. Two (2) additional subjects had an LSA revascularization procedure beyond 30-days as an intervention for an adverse event. Five (5) subjects (10.0%) had some form of spinal protection during the procedure. Accessed sites are summarized in **Table 10-16**.

A summary of the acute measures at implant are summarized in **Table 10-17**. The median hospital stay after endovascular treatment was 11 days. All subjects had an ICU stay, of which the median length of time in the ICU was 141 hours (5.9 days). Hospital survival was 94.0%.

Table 10-15: Implant Procedure

Type of Anesthesia Used	% (m/n)
General	100.0% (50/50)
Spinal	0.0% (0/50)
Regional	0.0% (0/50)
Local	0.0% (0/50)
Systemic Heparinization	**80.0% (40/50)**
Spinal CSF Drainage Used	**4.0% (2/50)**

Any Other Spinal Protective Measure Used	**6.0% (3/50)**
LSA Coverage	
None	42.0% (21/50)
Partial	18.0% (9/50)
Complete	40.0% (20/50)
Subjects with LSA Coverage	**58.0% (29/50)**
LSA Covered subjects with pre-implant adjunctive procedure[1]	2.0% (1/50)

[1]Procedures involving LSA by-pass/LSA revascularization/LSA debranching/LSA transposition.
m = number of subjects in category, n = number of subjects enrolled in this study.
Site Reported Table.

Table 10-16: Arterial Access Entry Site

Access Site Used to Deliver the Device	% (m/n)
Femoral Artery	92.0% (46/50)
Iliac Artery	6.0% (3/50)
Abdominal Aortic Conduit	2.0% (1/50)
Iliac Conduit	0.0% (0/50)
Additional Vascular Access Achieved Via:	
Femoral Artery	83.3% (40/48)
Iliac Artery	0.0% (0/48)
Abdominal Aortic Conduit	2.1% (1/48)
Iliac Conduit	0.0% (0/48)
NA	14.6% (7/48)

m = number of subjects in category, n = number of subjects with available data.
Site Reported Table.

Table 10-17: Acute Measurement at Implant

Duration of Implant Procedure (min)	
n	50
Mean ± SD	102.2 ± 57.0
Median	90.5
Min, Max	35, 311
Contrast Volume (ml)	
n	47[1]
Mean ± SD	120.8 ± 49.1
Median	110.0
Min, Max	31, 230
Total Fluoroscopic Time (mins)	
n	44[1]
Mean ± SD	11.0 ± 10.1
Median	8.7
Min, Max	3, 66
Blood Loss During Procedure (ml)	
n	49[1,2]
Mean ± SD	123.4 ± 152.9
Median	50.0
Min, Max	10, 900
Subjects Requiring Blood Transfusion % (m/n)[3]	**18.0% (9/50)**
Hospital Survival % (m/n)	**94.0% (47/50)**
Overall Hospital Stay (days)	
n	49[1]
Mean ± SD	14.7 ± 12.6
Median	11.0
Min, Max	1, 58
Time in Intensive Care Unit From Admission to Discharge (hours)	
n	49[4]
Mean ± SD	201.7 ± 194.3
Median	140.8

Min, Max	3, 976

[1]Most of the subjects were treated emergently in the middle of the night; measurements like contrast volume, total fluoroscopic time, etc. may not be captured in the research coordinator's absence.
[2]Subject's blood loss information was not reported by the site but was reported that no blood transfusion was required.
[3]Not limited to blood transfusion required as a result of blood loss during the procedure.
[4]Subject was not discharged at the time of data snapshot date.
m = number of subjects in category, n = number of subjects with available data.
Site Reported Table.

D. Safety and Effectiveness Results

1. Safety Results:

a) *Primary and Secondary Endpoint Analysis*

The primary endpoint included all enrolled subjects and was measured by the all-cause mortality rate within 30-days. As shown in

Table 10-18, four (4) subjects died within 30 days of the index procedure. This result demonstrates a 30-day all-cause mortality rate of 8.0% for BTAI subjects treated with the Valiant Thoracic Stent Graft.

There were a total of five (5) subject deaths that occurred throughout the course of the study. Based on the CEC adjudication, there were two (2) deaths in this trial that met the aortic-related mortality definition per the protocol (death caused by the underlying thoracic aortic injury and/or from any procedure intended to treat the aortic injury). This resulted in an aortic-related mortality of 4.0% (2/50). Neither of these deaths was reported by the sites to be aortic related, as presented in **Table 10-19**.

Table 10-18: Primary Endpoint

Primary Endpoint	% (m/n)
30-day All-Cause Mortality	8.0% (4/50)

m = number of subjects in category, n = number of subjects enrolled in this study.
Site and CEC Adjudicated Reported Table.

Table 10-19: Deaths

Subject ID	Procedure Date	Death Date	Time to Death (days)	Cause of Death Site Reported	Death Relatedness Site Reported	Death Relatedness CEC Adjudicated
00018-001	01/25/2011	01/26/2011	1	Hemothorax	Not Related	Aortic Related[1]
00182-001	10/06/2010	10/07/2010	1	Traumatic Brain Injury	Not Related	Not Related
00344-003	01/26/2011	01/31/2011	5	Arrhythmia	Not Related	Not Related
00059-002	08/26/2011	09/17/2011	22	Complications of Multiple Blunt Force Injuries	Device Relation Not Evaluable, Aortic Relation Not Evaluable, Not Related to Procedure	Device Related, Procedure Related, Aortic Related[2]
00340-004	04/10/2011	09/26/2011	169	Infection	Not Related	Not Related

Site and CEC Adjudicated Reported Table.

[1] A 22 year-old male, thrown from a horse into a tree, arrived with bilateral hemothoraces and a myocardial contusion (ISS=30, Grade III aortic injury). The patient underwent prompt and successful thoracic endovascular aneurysm repair (TEVAR), with the post-procedural aortogram demonstrating successful exclusion of BTAI and no extravasation or endoleak. While the left sided hemothorax subsided after TEVAR, the patient expired on the next day from continued right-sided massive hemothorax. An autopsy was performed on this patient and showed no evidence of an additional aortic injury. The CEC adjudicated this death to be related to the aortic injury and unrelated to the device or procedure.

[2] Sudden unexplained death day 22 in acute care facility, with limited information and no autopsy. Subject had a history of atrial fibrillation and recent pulmonary embolus on Coumadin. Imaging taken one week before death showed complete exclusion of pseudoaneurysm and good graft position. Due to unknown cause of death the CEC conservatively adjudicated the event to be related to the device, procedure, and aorta.

b) *Summary of All Adverse Events (AEs)*

As stated in the protocol, only those adverse/serious adverse events that are related to the device, to the implant procedure and/or to the aorta and serious adverse events (SAEs) that lead to death, regardless if they are related to the device, procedure or the aorta, were reported by the sites. SAEs are defined as any adverse event that:

- led to a death;
- led to a serious deterioration in the health of the subject that:
- resulted in life threatening illness or injury;
- resulted in a permanent impairment of a body structure or a body function;
- required in-patient hospitalization or prolongation of existing hospitalization; or
- resulted in medical or surgical intervention to prevent permanent impairment to a body structure or a body function; or
- led to fetal distress, fetal death or a congenital abnormality or birth defect.

The AEs reported during this study are identified in **Table 10-20**. Of note is that no subject had a stroke/cerebrovascular accident, spinal cord ischemia, paraparesis or paraplegia.

Adverse events that occurred within 30-days of the procedure and were related to the procedure, aorta or device were reported by the study sites in six (6) subjects (12.0%). Of these adverse events, procedure related adverse events were reported in five (5) subjects (10.0%), and an aorta related adverse event was reported in one (1) subject (2.0%). The CEC, that adjudicated events associated with deaths, adjudicated one additional SAE as being related to the aorta. There were no adverse events reported to be related to the device by the sites, however the CEC adjudicated one death from unknown causes as related to the procedure, device and aorta, as described above. A listing of all AEs, including those SAEs that led to death, whether or not they were related to the device, procedure or the aorta, is shown in **Table 10-20.**

Table 10-20: All Adverse Events Within 30 Days

Adverse Event	Relatedness Site Reported	Relatedness CEC Adjudicated
Any Procedure, Aorta or Device Related AE	**12.0% (6/50)**	**N/A**
Any Procedure Related AE	**10.0% (5/50)**	**N/A**
Any Aorta Related AE	**2.0% (1/50)**	**N/A**
Any Device Related AE	**0% (0/50)**	**N/A**
SAEs Leading to Death[1]		
Hemothorax	Not Related	Aortic Related
Traumatic Brain Injury	Not Related	Not Related
Arrhythmia	Not Related	Not Related

Adverse Event	Relatedness Site Reported	Relatedness CEC Adjudicated
Complications of Multiple Blunt Force Injuries	Not Evaluable Device Related, Not Evaluable Aortic Related; Not Related to Procedure	Device Related, Procedure Related, Aortic Related
SAEs Not Leading to Death		
Femoral Artery Dissection[2]	Procedure Related	N/A
Anoxic Encephalopathy[3]	Aortic Related	N/A
Left Arm Ischemia[4,5]	Procedure Related	N/A
Left Arm Claudication[6]	Procedure Related	N/A
Additional AEs		
Hematoma[7]	Procedure Related	N/A
Incision Site Erythema[8]	Procedure Related	N/A

[1] Information on patients who died and had SAEs is provided in **Table 10-19**. These are the only events adjudicated by the CEC, as the CEC is only responsible for adjudicating deaths and UADE's.
[2] Subject had a right common femoral artery focal dissection during index procedure. Subject underwent a thrombectomy and patch angioplasty and the event recovered the same day.
[3] Subject developed an anoxic brain injury related to the rupture on the day of the procedure. This subject's discharge summary notes mentioned that "the patient's course was complicated by hypoxic-ischemic encephalopathy secondary to significant hypotension and hypoxia after the accident as well as intra-operatively" prior to the deployment of the stent graft. Additionally this subject experienced another SAE: infection, on day 169 post procedure that led to death (refer to Table x).
[4] Subject had peripheral ischemia on day seven (7), LSA was intentionally (partially) covered during initial procedure. Subject underwent a left carotid to subclavian bypass on day eight and the ischemia resolved the next day.
[5] Subject experienced upper left limb ischemia on day 36 post procedure, related to the procedure. During the procedure, the physician intentionally completely covered the left subclavian artery (LSA). The subject eventually developed signs of upper left extremity ischemia. This subject underwent a left carotid to subclavian bypass on day 36 post procedure that led to resolution of the event on the day of the bypass.
[6] Subject experienced left arm claudication on day 30, LSA was intentionally (completely) covered during initial procedure. Subject underwent left carotid to subclavian bypass on day 103 and the event has since resolved.
[7] Subject developed a right groin hematoma on the day of the index procedure. The event resolved without treatment four days post procedure.
[8] Subject developed erythema at right groin incision on day four (4) from the index procedure. The site reported this event to be related to the procedure. This event resolved the following day with medication.

In addition to the events listed above, there was one subject that experienced peripheral arm ischemia on day 36 post-procedure. That same day a left carotid-to-subclavian by-pass procedure was performed and the peripheral arm ischemia was resolved on the day of the procedure. The site reported this as procedure related. There was also one subject that experienced no palpable radial pulse on day 39 post-procedure. The site reported this event to be related to the procedure and was 'unresolved, not treating' as of the data cut-off date for the data presented. There was also one death reported after 30-days as described in **Table 10-19**. There were no additional adverse events reported during this study.

2. Effectiveness Results

To assess the effectiveness of the Valiant Thoracic Stent Graft, the RESCUE trial collected information on the success of device delivery and deployment. Information was also collected on technical observations including endoleaks, stent graft kinking, stent graft twisting, misaligned deployment, stent graft fracture, loss of stent graft integrity, loss of stent graft patency, migration and if the traumatic injury was covered by the stent.

In addition, the following device assessments were collected by the sites and verified by the independent core laboratory:

- Loss of stent graft patency
- Total length of the stented segment
- Stent graft migration
- Presence and type of endoleaks

As shown in **Table 10-21**, after gaining vessel access at procedure, the investigators reported that the device was delivered and deployed successfully in all 50 subjects.

There were no Type I or Type III endoleaks reported in this study population. There were two (2) subjects reported to have a Type II endoleak at the end of procedure by the site, both of these endoleaks resolved without treatment by the 1-month visit. No other technical observations were reported from the 1-month follow-up CTA/MRA images. The stent graft integrity was maintained in 100% of the cases. There were no reports of stent graft twisting, kinking, or fracture, and all stent grafts remained patent as reported by the sites and the core lab.

There were no occurrences of Unanticipated Adverse Device Effects (UADEs) in this trial.

Table 10-21: Secondary Efficacy Endpoint

Secondary Efficacy Endpoint	% (m/n)
Successful Delivery and Deployment of the Stent Graft	100.0% (50/50)

m = number of subjects in category, n = number of subjects enrolled in this study.
Site and CEC Adjudicated Reported Table.

There were no cases of endovascular re-intervention or conversion to open surgery reported. There was one (1) subject within 30-days and two (2) subjects between 31 and 365 days that required LSA bypass to correct left arm ischemia. These events are captured under the 'Other' category **Table 10-22** below.

Table 10-22: Secondary Procedures

Secondary Procedure	0 to 30 Days % (m/n)	31 to 365 Days % (m/n)	366 to 731 Days % (m/n)	732 to 1096 Days % (m/n)	1097 to 1461 Days % (m/n)	1462 to 1826 Days % (m/n)
Conversion to Open Repair	0.0% (0/50)	0.0% (0/43)	0.0% (0/11)	N/A	N/A	N/A
Additional Endovascular Device Placed	0.0% (0/50)	0.0% (0/43)	0.0% (0/11)	N/A	N/A	N/A
Other[2]	2.0% (1/50)	4.7% (2/43)	0.0% (0/11)	N/A	N/A	N/A

m = number of subjects in category, n = number of subjects with study stent implanted who experienced an event or who were followed at least until the lower endpoint of the interval. For example, for column '0-30 Days', '31-365 Days', '366-731 Days', '732-1096 Days', '1097-1461 Days' and '1462-1826 Days', a subject had to be followed respectively for at least 0 day, 31 days, 366 days, 732 days, 1097 days and 1462 days in order to be included in the denominator, unless he/she experienced an event in the corresponding interval.
Site Reported Table.
[2] One subject had peripheral ischemia on day seven, LSA was intentionally (partially) covered during initial procedure. Subject underwent a left carotid to subclavian bypass on day eight and the ischemia resolved the next day.
Another subject experienced left arm claudication on day 30, LSA was intentionally (completely) covered during initial procedure. Subject underwent left carotid to subclavian bypass on day 103 and the event has since resolved.
A third subject experienced peripheral arm ischemia on day 36. On that same day a left carotid-to-subclavian by-pass procedure was performed and the peripheral arm ischemia was resolved on the day of the procedure.

3. Subgroup Analysis (Gender)

Out of the 50 subjects that were enrolled in this study, 38 subjects (76%) were male and 12 subjects (24%) were female. In the literature, Dake et al[1], reported on endograft management of traumatic thoracic aortic transections at 30-days and 1-year from five (5) physician sponsored investigational device exemption clinical trials from 2002-2008 and demonstrated a similar percentage of males in the male cohort (68.3% of the 60 subjects with traumatic aortic transections).

In the RESCUE trial, the 30-day all-cause mortality rate was similar between males and females, with a rate of 7.9% in the male cohort and rate of 8.3% in the female cohort.

Adverse event rates between genders were reported at 13.2% and 8.3% in the male and the female cohorts, respectively. There was one (1) subject in each cohort that met the definition for aortic related mortality (defined as: death caused by the underlying thoracic aortic injury and/or from any procedure intended to treat the

[1] Dake MD, White RA, Diethrich EB, et al. Report on endograft management of traumatic thoracic aortic transections at 30 days and 1 year from a multidisciplinary subcommittee of the Society for Vascular Surgery Outcomes Committee. J Vasc Surg. 2011 Apr;53(4):1091-6.

aortic injury). Sufficient patient numbers are not available to determine whether there is a difference in outcomes between male and female subjects.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A review of the contemporary literature was performed to identify supplemental clinical information and outcomes of the endovascular treatment of BTAI, as shown in **Table 11-1**. Information was identified for series of patients treated with thoracic endovascular aneurysm repair (TEVAR) alone as well as for series of patients treated with TEVAR compared to open repair (OR). Several meta-analyses published on endovascular treatment of BTAI have concluded that endovascular repair is associated with lower mortality and paraplegia rates than open repair; by their analyses these rates may be halved[2,3,4,5] The baseline characteristics of age and ISS were comparable in these reports.[1,2,3,4,5] In this meta-analysis, the mean early mortality rate was lower with TEVAR, at 9% versus 19% and the rate of spinal cord ischemia was 3% with TEVAR compared to 9% with OR.2 Stroke has been reported in TEVAR subjects at a rate of 0.9%.[3] Studies have found a generally lower rate of CVA related to TEVAR, including the meta-analysis performed by Xenos et al, which found an operative risk of stroke of 0.86 for the OR group.[4] Endoleak was reported to be 4.2% in patients undergoing TEVAR.[3] The largest prospective study that compared TEVAR to OR, reported by Demetriades et al, found aortic mortality to be 7.2% in TEVAR versus 23.5% in OR and procedure-related paraplegia to be 0% in TEVAR versus 2.9% in OR.[5] In comparison to these published results, the outcomes for the Valiant Thoracic Stent Graft from the RESCUE trial are comparable to those reported for TEVAR.

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[2] Murad MH, Rizvi AZ, Malgor R, et al. Comparative effectiveness of the treatments for thoracic aortic transection. J Vasc Surg 2011; 53; 193-199.

[3] Hoffer EK, Forauer AR, Silas AM and Gemery JM. Endovascular stent-graft or open surgical repair for blunt thoracic aortic trauma: Systematic review. J Vasc Interv Radiol 2008;19:1153-1164.

[4] Xenos ES, Abeidi NN, Davenport DL, et al. Meta-analysis of endovascular vs open repair for traumatic descending thoracic aortic rupture. J Vasc Surg 2008;48:1343-51.

[5] Demetriades D, Velmahos GC, Scalea TM, et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: Results of an American Association for the Surgery of Trauma multicenter study. J Trauma 2008;64:561-71.

Table 11-1: Literature Review

Publication [ref.]	Sample of Subjects	Analysis Method	Subject Characteristics				Outcomes					
			Age		ISS		Mortality		Paraplegia		Stroke	
			TEVAR	OR	TEVAR	OR	TEVAR	OR	TEVAR	OR	TEVAR	OR
Dake et al1	60 subjects from 5 studies including TEVAR	Observational, single-arm, prospective study	46		39		8%		2%		10%	
Murad et al2	7,768 subjects from 139 studies including TEVAR, OR and non-operative	Meta-analysis of literature	39	39	40	34	9%	19%	N/A	N/A	3%	3%
Hoffer et al3	262 TEVAR and 376 OR subjects from 19 studies. Pooled analysis of 667 TEVAR survivors from 50 reports.	Meta-analysis of nonrandomized retrospective studies	40	38	40	38	8.4%	20.2%	0.8%	5.7%	N/A	N/A
Xenos et al4	589 subjects (369 OR, 220 TEVAR) from 17 studies	Meta-analysis of nonrandomized retrospective studies	38.8	38.8	42.4	37.4	8%	20%	0%	7%		OR subjects: Operative risk of 0.86
Demetriades et al5	193 subjects (68 OR, 125 TEVAR)	Prospective, nonrandomized multicenter studies	42.2	34.1	39.4	38.9	7.2%	23.5%	0.8%	2.9%	N/A	N/A

XII. PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. OVERALL CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The safety and effectiveness of the Valiant Thoracic Stent Graft for isolated lesions of the DTA were not based on the RESCUE clinical study alone, but rather on all available data for the Valiant Thoracic Stent Graft to date, including pre-clinical data and data from the aneurysm clinical study (VALOR II), reviewed under PMA P100040.

A. Effectiveness Conclusions

All devices in the 50 subjects were successfully delivered and deployed. The traumatic injury was successfully covered in 100% of the cases. There were no reports of misaligned deployment, aortic perforation, retrograde Type A dissection or conversion to open surgery. There were no occurrences of Unanticipated Adverse Device Effects (UADEs) in this trial. In addition, there were no conversions to surgery and no endovascular secondary procedures. There was one (1) subject within 30-days and two (2) subjects between 31 and 365 days that required LSA bypass to correct left arm ischemia/claudication.

There were no Type I or Type III endoleaks reported in this study population. There were two (2) subjects reported to have a Type II endoleak at the end of procedure, both of these endoleaks resolved without treatment by the 1-month visit. Stent graft integrity was maintained in 100% of the cases. There were no reports of stent graft twisting, kinking, or fracture, and all stent grafts remained patent as reported by the sites and the core lab.

The RESCUE trial effectiveness outcomes were comparable to the literature. Specifically, the early endoleak rate was 4% in RESCUE, versus 1.3% to 4.2% in the literature; and there was 100% technical success in RESCUE (Type II endoleaks), versus the range of 96.5% to 100% in the literature.

B. Safety Conclusions

Non-Clinical

Non-clinical safety information was reviewed under the original Valiant PMA P100040. This information also supports the broader indication of treatment of isolated lesions of the DTA.

In addition to the leveraged data from the original Valiant PMA, Medtronic conducted fatigue and durability assessments with FEA and bench-testing studies to evaluate the Valiant Thoracic Stent Graft under the *in vivo* conditions seen in patients with BTAI. Testing was performed in accordance with applicable guidance documents and national and international standards. The testing confirmed that the Valiant Thoracic Stent Graft met performance and design specifications. These studies further support the safety of this device for the treatment of isolated lesions of the DTA.

Clinical

The primary objective for the RESCUE trial was assessed by the primary endpoint of all-cause mortality within 30-days of treatment. In this trial there were four (4) deaths within 30-days, which resulted in an all-cause mortality rate of 8.0% within 30-days of treatment for BTAI with the Valiant Thoracic Stent Graft. This rate is comparable to the rate of 6% to 10% as reported in the literature.[1,2,3,4,5] There were two deaths that were adjudicated by the CEC to be aortic-related, resulting in an aortic-related mortality of 4.0% (2/50).

Adverse events that occurred within 30-days of the procedure and were related to the procedure, aorta or device were reported in six (6) subjects (12.0%). Of these adverse events, procedure related adverse events were reported in five (5) subjects (10.0%), and an aorta related adverse event was reported in one (1) subject (2.0%). There were no adverse events reported to be related to the device by the sites, however CEC adjudicated one death from unknown causes as related to the procedure, device and aorta. The CEC adjudicated one additional death as related to the aorta. In addition, there were no reports of spinal cord ischemia, paraplegia or cerebrovascular accidents/strokes, which are reported adverse events in the literature with rates of 0.83% for paraplegia and 1.7% for cerebrovascular accidents/strokes.[4]

C. Benefit-Risk Conclusions

The probable benefits on the expanded indications of the device are based on data collected in a clinical study conducted to support PMA approval along with supplementary data, as described above. The probable benefit of the Valiant® Thoracic Stent Graft with the Captivia Delivery System is improving outcomes in patients with isolated lesions of the DTA (excluding dissections), as compared to open surgical repair.

To demonstrate the long-term performance of the device, data was leveraged from a clinical study for the most challenging lesion type to treat endovascularly (i.e., aneurysms). Since any differences resulting from the expanded indication were expected to be seen in the short-term, the broader indication is supported by 30-day safety and effectiveness data on the other relatively common isolated lesion treated endovascularly (i.e., transections). Both studies providing the clinical safety and effectiveness evidence were multi-center and were conducted in the United States and Canada. Important clinical outcomes, such as all-cause mortality and endoleaks occurred at an acceptable frequency. There are no reasons to expect that the results of these studies will differ from "real world" performance.

Alternative treatments, including the use of other endovascular grafts, open surgical repair, and medical management, were carefully considered. Endovascular repair is often highly valued by patients because it is less invasive than open surgical repair. The risks and benefits of the Valiant® Thoracic Stent Graft with the Captivia Delivery System were found to be similar to the risks and benefits of other approved endovascular grafts. Patient risk is minimized by limiting use of the device in patients suitable for endovascular repair and to operators who have the necessary training to use the device safely and effectively.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks when the Valiant® Thoracic Stent Graft with the Captivia Delivery System is used to repair isolated lesions of the descending thoracic aorta (excluding dissections), and the device provides an additional treatment option for these patients.

D. Overall Conclusions

Medtronic has previously studied the Valiant Thoracic Stent Graft and shown it is safe and effective in subjects with aneurysmal disease. To study a broader patient population, Medtronic designed the RESCUE trial to demonstrate that the Valiant Thoracic Stent Graft would not introduce any new concerns of safety or effectiveness in the treatment of BTAI subjects. The patient population with BTAI differs from the degenerative aneurysm patient population by being relatively younger, having generally healthy aortas and having an aortic lesion caused by traumatic injury, frequently accompanied with concomitant injuries. In contrast, the aortic aneurysm patients often have co-morbid diseases rather than injuries, such as pulmonary disease or renal insufficiency, which are less prevalent in the BTAI patient population. These co-morbid diseases add substantially to the open surgical risk of the patient. Although differences exist between the aneurysm and BTAI patient populations, the TEVAR device and procedure for both types of thoracic aortic lesions are similar. Specifically, hemodynamic seal of the lesion within the thoracic aorta is achieved through the same access and deployment techniques.

The primary objectives for safety and effectiveness were achieved in the trials that studied the Valiant Thoracic Stent Graft in aneurysm patients and separately in BTAI patients. Based on the totality of evidence presented, this application supports the reasonable assurance of safety and effectiveness of the Valiant Thoracic Stent Graft in the expanded indication of isolated lesions of the DTA (excluding dissections) for subjects who have appropriate vascular anatomy and who are candidates for endovascular treatment. Patients who have known allergies to the device materials or who have an increased risk of device infection should not be treated with the device.

XIV. CDRH DECISION

CDRH issued an approval order on October 26, 2012. The final conditions of approval cited in the approval order are described below.

The applicant currently provides a clinical update to physician users at least annually with current information regarding the Valiant device. Future clinical updates are to also include information from the RESCUE (transection) clinical study. At a minimum, the information to be included regarding RESCUE will include a summary of the number of patients for whom data are available, with the rates of death, secondary endovascular procedures, conversion to open surgical repair, major device events, endoleak, prosthesis migration, losses of device integrity, aortic rupture and patency. Reports of losses of device integrity, reasons for secondary interventions and conversions to open surgical repair, and causes of death that may be associated with the lesion treated (e.g., death within 30 days of a secondary procedure to treat the index lesion and death from bleeding through the index lesion) are to be described. A summary of any explant analysis findings is to be included. Additional relevant information from commercial experience within and outside of the US is also to be included. The clinical updates for physician users and the information supporting the updates must be provided in the Office of Device Evaluations (ODE) annual report.

XV. APPROVAL SPECIFICATIONS

Directions for Use: See device labeling.

Hazards to Health from Use of Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post Approval Requirements and Restrictions: See approval order.