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

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P100040/S012

Date of FDA Notice of Approval: January 22, 2014

Priority Review: Not Applicable

The Valiant® Thoracic Stent Graft with the Captivia® Delivery System original PMA (P100040) was approved on April 1, 2011 for the endovascular repair of fusiform aneurysms and saccular aneurysms/penetrating ulcers of the descending thoracic aorta (DTA). The indications for use were expanded to include the treatment of isolated lesions (excluding dissections) of the DTA in patients who have appropriate anatomy via P100040/S008 on October 26, 2012, based on the submission of data for the treatment of traumatic transections. The Summaries of Safety and Effectiveness Data (SSED) to support the original approval and the expanded indication are available on the CDRH website and are incorporated by reference here. The current supplement was submitted to further expand the indication for the Valiant® Thoracic Stent Graft with the Captivia® Delivery System to include the treatment of all lesions of the DTA, including Type B dissections.

II. INDICATIONS FOR USE

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

- iliac/femoral access vessel morphology that is compatible with vascular access techniques, devices, and/or accessories;
- non-aneurysmal aortic diameter in the range of 18–42 mm (fusiform and saccular aneurysms/penetrating ulcers), 18 mm to 44 mm (blunt traumatic aortic injuries) or 20 mm to 44 mm (dissections) and

- non-aneurysmal aortic proximal and distal neck lengths ≥ 20 mm (fusiform and saccular aneurysms/penetrating ulcers), landing zone ≥20 mm proximal to the primary entry tear (BTAI, dissection). The proximal extent of the landing zone must not be dissected.

III. CONTRAINDICATIONS

The Valiant thoracic stent graft with the Captivia delivery system is contraindicated in the following patient populations:

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

IV. WARNINGS AND PRECAUTIONS

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

V. DEVICE DESCRIPTION

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 loaded into 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.

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 polyester 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 1** for a drawing of the Valiant Thoracic Stent Graft.

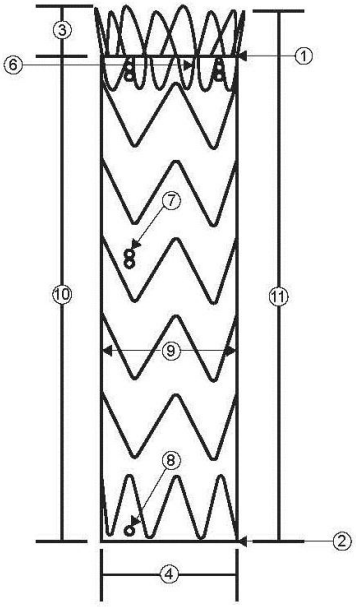
Valiant Thoracic Stent Graft Configuration and Placement

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.

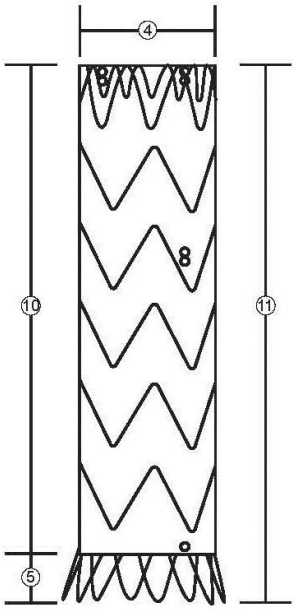
If the vessel diameter and condition require variable proximal and distal diameter devices, the smallest diameter stent graft should be placed first, either at the proximal or distal end of the lesion, as appropriate. The additional section is to be deployed within the primary piece following the oversizing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

Different end configurations are available to further accommodate anatomical dimensions. The proximal end comes in two configurations: FreeFlo or Closed Web (**Figure 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.

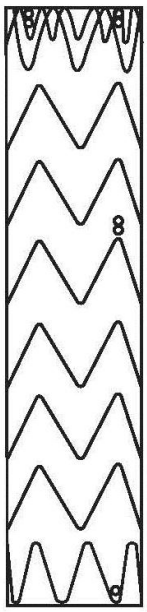


FreeFlo Straight
(Proximal Component)

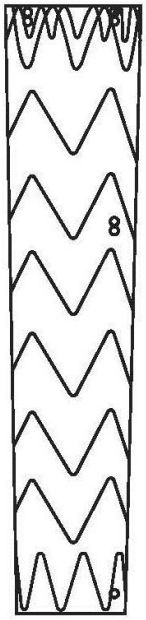


Distal Bare Spring
Straight (Distal Component)

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 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.

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 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)

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 spring of the FreeFlo configuration still constrained by the tip capture mechanism; and

(2) Release of the proximal bare spring.

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. The Closed Web Delivery System does not include a tip capture mechanism because these devices do not have a bare spring configuration at the proximal end of the stent graft. 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.

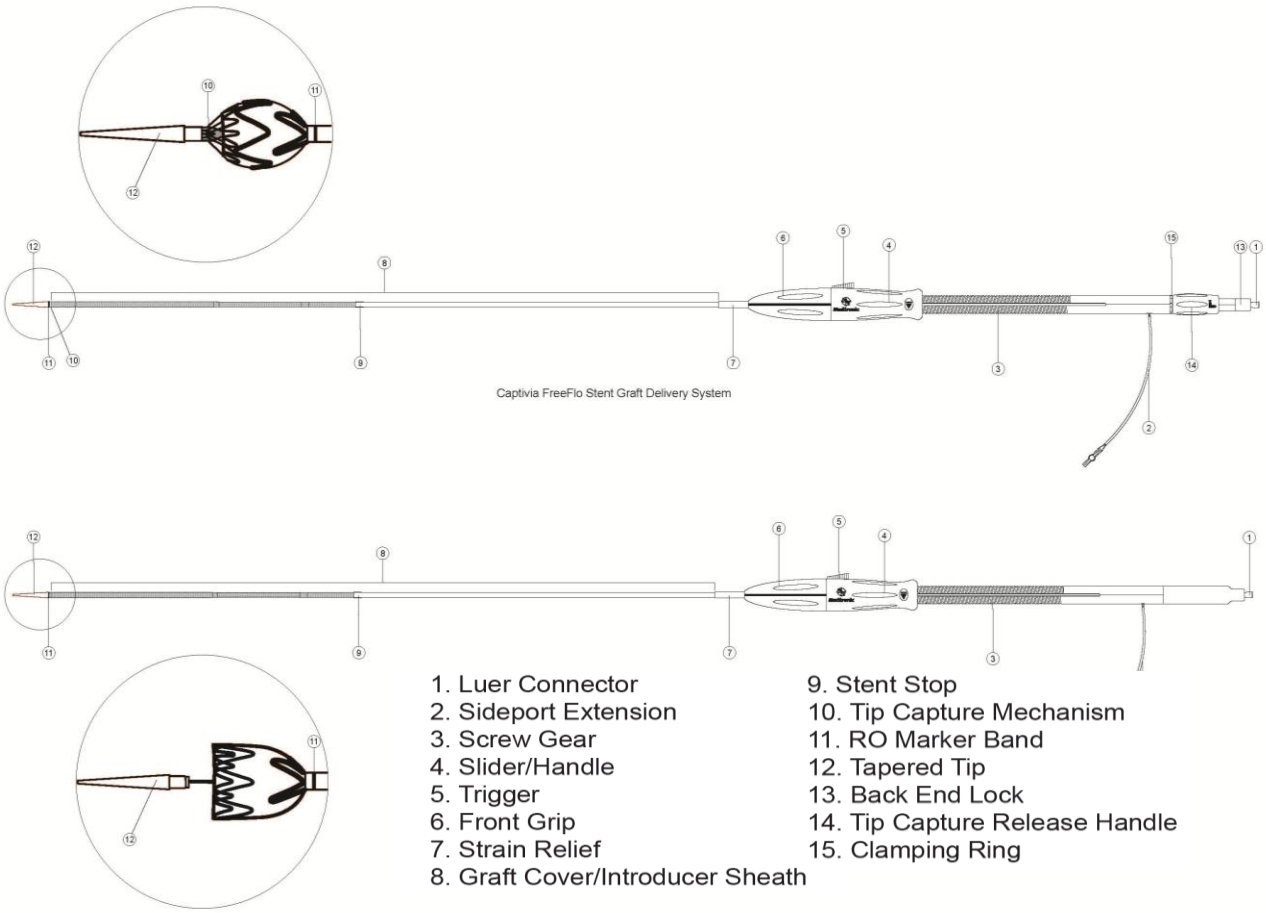


Figure 2. Captivia Delivery System

(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 treatment of the descending thoracic aorta 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. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

Alternative practices and procedures used in the treatment of Type B aortic dissection can involve an open surgical thoracic aortic graft repair, interventional or surgical flap fenestration and true lumen stenting, catheter reperfusion or extra-anatomic surgical bypass. The goal of both thoracic endovascular aortic repair (TEVAR) and open surgical treatment is to seal, or resect the intimal tear, thus depressurizing and shrinking the false lumen with subsequent aortic remodeling and aortic stabilization. Due to high mortality rates and associated complications with the alternative practices listed above, the treatment of acute complicated dissections has shifted to thoracic endovascular aortic repair (TEVAR).

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. Subsequently, the Valiant Thoracic Stent Graft with Captivia Delivery system received FDA approval for the endovascular repair of isolated lesions of the DTA (excluding dissections) on October 26, 2012.

The Valiant Thoracic Stent Graft with the Captivia Delivery System has been commercially available for distribution outside of the United States since October 2009. It is commercially available in Argentina, Australia, Belarus, Belize, Bosnia-Herzegovina, Brazil, Canada, Chile, China, Colombia, Costa Rica, Croatia, Dominican Republic, Ecuador, Egypt, El Salvador, the European Union, Guatemala, Honduras, Hong Kong, Hungary, India, Israel, Japan, Kazakhstan, Kuwait, Macedonia, Malaysia, Mexico, Montenegro / Serbia, New Zealand, Nicaragua, Panama, Peru, Puerto Rico, Romania, Russia, Saudi Arabia, Serbia, Singapore, Slovakia, Slovenia, South Africa, South Korea, Taiwan, Thailand, Turkey, Ukraine, Uruguay, US, Venezuela and Vietnam.

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

Below is a list of the potential adverse effects (e.g., complications) that may be associated with the use of the device.

Table 1. Potential Adverse Effects

Access failure	Endoleaks	Post-procedural bleeding
Adynamic Ileus	Excessive or inappropriate radiation exposure	Procedural bleeding
Allergic reaction (to contrast, anti-platelet therapy, stent graft material)	Extrusion/erosion	Prosthesis dilatation
Amputation	Failure to deliver the stent graft	Prosthesis infection
Anesthetic complications	Femoral neuropathy	Prosthesis rupture
Aortic expansion (e.g.	Fistula (aortoenteric,	Prosthesis thrombosis

aneurysm, false lumen)	arteriovenous, aortoesophageal, aortobronchial)	
Aneurysm rupture	Gastrointestinal bleeding/complications	Pseudoaneurysm
Angina	Genitourinary complications	Pulmonary edema
Arrhythmia	Hematoma	Pulmonary embolism
Arterial Stenosis	Hemorrhage/bleeding	Reaction to anaesthesia
Atelectasis	Hypotension/hypertension	Renal failure
Blindness	Infection or fever	Renal insufficiency
Bowel ischemia	Insertion or removal difficulty	Reoperation
Bowel necrosis	Intercostal pain	Respiratory depression or failure
Bowel obstruction	Intramural hematoma	Retrograde Type A dissection
Branch vessel occlusion	Leg edema/foot edema	Sepsis
Breakage of the metal portion of the device	Lymphocele	Seroma
Buttock claudication	Myocardial infarction	Shock
Cardiac tamponade	Nerve injury	Spinal neurological deficit
Catheter breakage	Neuropathy	Stent graft migration
Cerebrovascular accident (CVA)	Occlusion – Venous or Arterial	Stent graft misplacement
Change in mental status	Pain/Reaction at catheter insertion site	Stent graft occlusion
Coagulopathy	Paralysis	Stent graft twisting or kinking
Congestive heart failure	Paraparesis	Transient-ischemic attack (TIA)
Contrast toxicity	Paraplegia	Thrombosis
Conversion to surgical repair	Paresthesia	Tissue necrosis
Damage to the vessel which may require a conversion to open repair	Perfusion of the false lumen	Vascular ischemia
Death	Peripheral ischemia	Vascular trauma
Deployment difficulties/ failures	Peripheral nerve injury	Wound healing complications
Dissection, perforation, or rupture of the aortic vessel & surrounding vasculature	Pneumonia	Wound infection
Embolism	Post-implant syndrome	Wound dehiscence

IX. SUMMARY OF PRECLINICAL STUDIES

The SSEDs containing the pre-clinical studies to support the aneurysm indication (the original Valiant Thoracic Stent Graft PMA (P100040)) and the indication for isolated lesions (excluding dissections) (P100040/S008) are available on the CDRH website.

Medtronic is seeking approval of an expanded indication using the same commercially approved Valiant Thoracic Stent Graft with the Captivia delivery System. No changes

have been made to the product design or specifications. All pre-clinical studies previously provided in P100040 and P100040/S008 are applicable to and support the use of the Valiant Thoracic Stent Graft with the Captivia Delivery System in the endovascular treatment of Type B dissection of the DTA under this Supplement.

X. SUMMARY OF PRIMARY CLINICAL STUDY

One primary clinical study (the Medtronic Dissection Trial) was conducted to support the expansion of the Valiant Captivia indications for use to include all lesions of the descending thoracic aorta (DTA), under IDE G090199. Key characteristics of the clinical study are provided in **Table 2**.

The safety and effectiveness of the Valiant Thoracic Stent Graft for lesions of the DTA was not based on the Medtronic Dissection Trial alone, but rather on all available data for the Valiant Thoracic Stent Graft to date, including data from the aneurysm clinical study (VALOR II), reviewed under PMA P100040, and the blunt traumatic aortic injury (BTAI) clinical study (RESCUE), reviewed under PMA-S P10040/S008. Further discussion of the supplementary information considered along with relevant factors regarding the patient populations covered under the indication of all lesions of the DTA will be provided subsequently along with clinical background information on Type B dissections.

Table 2. Summary of Clinical Study

Clinical Study	Study Design	Objective	Number of Sites with Enrollments	Number of Subjects
Medtronic Dissection Trial	Prospective, non-randomized, multicenter study to evaluate the clinical performance of Valiant Captivia in the treatment of acute, complicated Type B dissection. The primary endpoint was all-cause mortality within 30 days of the index procedure. Several secondary observations of safety and effectiveness were assessed using descriptive statistics.	To evaluate the safety and effectiveness of Valiant Captivia in the treatment of subjects with acute, complicated Type B dissection, as determined by all-cause mortality within 30 days of the index procedure.	16	50

A. Study Design

The Medtronic Dissection Trial was a was a prospective, non-randomized, multicenter study to evaluate the clinical performance of the Valiant Thoracic Stent Graft for treatment of acute, complicated Type B dissection. Patients were treated between June 25, 2010 and May 8, 2012. The database for this summary reflected

data collected through May 30, 2013 and included 50 patients. There were 16 investigational sites. The primary objective was to evaluate the safety and effectiveness of the Valiant Thoracic Stent Graft in the treatment of acute, complicated Type B dissection, as determined by all-cause mortality within 30 days of the index procedure.

The primary hypothesis of the study was that all-cause mortality through 30 days post-treatment met the performance goal of 25%. An adaptive design was utilized such that additional subject enrollment (up to 84 subjects total) would be allowed as necessary to meet the performance goal. However, the performance goal was met after evaluation of the primary endpoint for the initial 50 subjects.

Statistical Methods of Analysis

H_0: $P_{DISSECTION} \geq P_{PG} = 25\%$

H_A:$P_{DISSECTION} < P_{PG} = 25\%$

$P_{DISSECTION}$ = 30-day mortality rate in targeted population

P_{PG} = Performance Goal (PG) for 30-day mortality rate.

Expected 30-day mortality rate = 11%

1-sided alpha error (α) = 5%

Power of the test = 80%

Sample size (n): 50 subjects

The primary endpoint was analyzed using the exact test method based on a binomial distribution. The null hypothesis will be rejected if the upper limit of the one-sided 95% confidence interval on the 30-day mortality rate is less than 25%. The one-sided upper 95% confidence interval on the 30-day mortality rate will be calculated based on a binomial distribution.

Additionally, separate secondary analyses were performed for all-cause mortality within 30 days for the groups of subjects with the two complicating factors of rupture and ischemia. Secondary endpoints are presented descriptively.

The Performance Goal was set at 25% after considering the mortality rates from 1) the Society for Vascular Surgery (SVS) Master Access File (MAF) of 85 acute, complicated dissection subjects; 2) the recent literature on open surgical repair and 3) the recent literature on TEVAR treated dissection patients. The performance goal allowed for reasonable variances due to the low rate of occurrence, the low baseline sample size in the literature and MAF and for variances in outcomes due to both a potential difference in patient complicating factors and a broader selection of physicians implanting the device in this study.
The primary endpoint analysis set included all enrolled subjects who had at least one (1) study stent graft implanted. The Intent-to-Treat (ITT) analysis set included all enrolled subjects who had an intra-arterial access procedure with intent to receive the study device.

All 50 subjects enrolled in the study received the study stent graft and therefore the two (2) analysis sets defined above are identical. The primary endpoint and secondary observations were analyzed with all 50 ITT subjects.

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.

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 for relatedness to the aorta, device and procedure. There were no UADEs identified in this study.

Data Monitoring Committee (DMC)

The DMC was composed of at least five members, including four physicians from the fields of vascular surgery, cardiothoracic surgery, interventional radiology or interventional cardiology and one biostatistician, none of whom were involved in the conduct of the study. The DMC reviewed the 30-day data for the first 20 subjects and for the first 30 subjects. The committee recommended that the clinical trial could continue without modifications.

Core Laboratory (Core Lab)

In order to provide independent verification of imaging findings, images required by protocol were sent by the sites to a central imaging core lab. Medical Image & Data Management Services Inc. (M2S) served as the independent image core lab for this study. 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. Three-dimensional reconstruction was undertaken in order to provide critical and comprehensive data evaluation during the pre- and post-operative periods. Chest x-rays were also submitted to the core lab for analysis. M2S technology processes and systems are GMP/GCP, HIPAA, and CFR 21 Part 11 compliant and are provided within an ISO 13485 certified facility which adheres to all applicable federal regulations.

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 CTA/MRA for assessment of the aortic morphology and vascular characteristics. A physical exam was conducted and medical history and the inclusion/exclusion criteria below were assessed.

Enrollment in the Medtronic Dissection Trial was limited to patients who met the following inclusion criteria:

- Subject signed an informed consent.
- Subject is at least 18 years old.
- Subject has an acute, complicated Type B aortic dissection with evidence of at least one of the following:
  - Malperfusion (visceral, renal, spinal cord and/or lower limb ischemia)
    - Visceral ischemia measured by either radiographic or clinical evidence.
    - Renal ischemia measured by either radiographic or clinical evidence.
    - Spinal cord ischemia measured by either radiographic or clinical evidence.
    - Lower limb ischemia measured by either radiographic or clinical evidence.
  - Rupture – Measured by radiographic or clinical evidence.
- Subject is hemodynamically stable.
- Subject's anatomy must meet all of the following anatomical criteria:
  - Proximal landing zone aortic diameter must be between 20 mm and 44 mm;
  - Centerline distance from distal margin of left CCA or in cases of bovine anatomy, innominate artery, to start of most proximal tear must be $\geq$ 20 mm;
  - Subject has patent iliac or femoral arteries or can tolerate an iliac conduit that allows endovascular access to the dissection site with the delivery system of the appropriate sized device.
- Thoracic aortic dissection is confirmed, at a minimum, by diagnostic contrast-enhanced computerized tomography angiogram (CTA) with 3-D reconstruction, and/or contrast enhanced magnetic resonance angiogram (MRA) obtained prior to the implant procedure.

Patients were <u>not</u> permitted to enroll in the Medtronic Dissection Trial if they met any of the following exclusion criteria:

- Planned placement of the covered portion of the stent graft over the left carotid artery, or the celiac trunk.
- Subject has systemic infection.
- Subject is pregnant.

- Subject has received a previous stent or stent graft or previous surgical repair in the DTA.
- Subject has had a cerebral vascular accident (CVA) within 2 months.
- Subject has a history of bleeding diathesis, coagulopathy, or refuses blood transfusion.
- Subject has a history of Marfan Syndrome or other connective tissue disorder.
- Subject is currently participating in an investigational drug or device clinical trial which would interfere with the endpoints and follow-ups of this study.
- Subject has a known allergy or intolerance to the device components.
- Subject has a known hypersensitivity or contraindication to anticoagulants or contrast media, which is not amenable to pre-treatment.
- Subject has a co-morbidity causing expected survival to be less than 1 year.

2. Follow-up Schedule

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, CT with and without contrast, or an MRA and x-ray were performed per the protocol schedule.

Table 3. Overview of the study procedures and data collection requirements

Data	Screening / Baseline	Procedure	Pre-Hospital Discharge	1-month FU ± 14 days	6-Month FU ± 60 days	12-Month FU ± 90 days	2 - 5 Year FU ± 16 weeks
Informed Consent	✓						
Vital Signs, ABI, Pulse	✓		✓	✓	✓	✓	✓
Pregnancy test (if applicable)	✓						
Medical History	✓						
Device & Procedure Information		✓					
Angiogram		✓					
Laboratory Tests Serum Creatinine, GFR	✓						
CT w/out contrast & CTA/MRA	✓		✓	✓	✓	✓	✓
Chest X-Ray				✓	✓	✓	✓
Adverse Event Assessment		✓	✓	✓	✓	✓	✓

3. Clinical Endpoints

The primary hypothesis of the study was that all-cause mortality through 30 days post-treatment met the performance goal of 25%. The performance goal was justified based on historical data, including the Society for Vascular Surgery (SVS) Master Access File (MAF) of 85 acute, complicated dissection subjects and the open surgical repair and endovascular repair literature.

Additional secondary objectives evaluated the safety and effectiveness by reporting the following outcomes:

Acute Observations (to 30 days)

- Successful delivery and deployment of the stent graft
- Coverage of proximal entry tear
- Aortic remodeling
- Serious Adverse Events (SAE)
- Rupture

Late Observations

- Aortic remodeling at 6 and 12 month visit
- Secondary procedures within 12 months
- Continuing or new false lumen (FL) perfusion
- SAEs within 12 months

- Rupture within 12 months
- All-cause mortality within 12 months

Although the primary and secondary effectiveness endpoints were not hypothesis driven, they are clinically meaningful in assessing the effectiveness of treatment of acute complicated Type B dissections. These effectiveness endpoints were qualitatively compared to historical endovascular literature and were found to be comparable.

With regard to success/failure criteria, the overall Medtronic Dissection Trial was considered successful if the primary safety endpoint result met the pre-specified performance goal. No individual subject success/failure criteria were defined in the protocol.

B. Accountability of PMA Cohort

Fifty subjects (50) were enrolled in this study between June 2010 and May 2012, at 16 investigational sites. All enrolled subjects underwent endovascular repair with the Valiant Captivia to treat acute complicated Type B aortic dissection. Subjects enrolled in the Medtronic Dissection Trial were required to return for follow-up visits as described in **Table 3**.

A total of 89 subjects were screened for enrollment in the study. The reasons for exclusion were lack of malperfusion or rupture (n=10), presence of chronic dissection >14 days (n=7), inability to consent (n=3), no indication for intervention (n=3), inclusion criteria not met (n=2), fenestrated (n=2), intramural hematoma without dissection (n=2), <20 mm proximal landing zone (n=2), unreliable for follow-up (n=1), patient refused (n=1), previous repair (n=1), medically managed (n=1), history of aortic repair (n=1), unstable for surgery (n=1), Marfan's Syndrome (n=1), and retrograde extension to LCC (n=1).

Four (4) subjects died within 30 days of the index procedure. Of the 46 subjects eligible for 1-month follow-up, the clinical and imaging compliance was 97.8%. One (1) subject voluntarily withdrew from the study between the 1-month and 6-month visit. One (1) subject was lost to follow-up after the 1-month visit.

In the interval between 1 month and 6 months post-procedure, three (3) additional subjects died. During the same period, one (1) subject was lost to follow up and one (1) subject withdrew from the study. Of the 41 subjects eligible for the 6-month follow-up visit, 36 subjects completed the clinical follow-up visit and 34 subjects completed the imaging, resulting in a compliance of 87.8% and 82.9% respectively.

One subject died on day 432 post-procedure, within the 12-month visit window. However, because the subject died after the statistical analysis window of 365 days; this subject death is not counted in the 12-month mortality tables. There were 40 subjects eligible for the 12-month follow-up visit. The clinical and imaging

compliance at this follow-up visit were 90.0% and 85% respectively. There were no subjects lost to follow-up, withdrawals or conversion to open surgery between the 6 month and the 1 year interval.

Table 4. Subject Follow up, Imaging and Accountability

	Subject Follow-up % (m/n)[2]			Subject Imaging % (m/n)[2]			Subjects with Adequate Imaging to Assess the Parameter % (m/n)[2]					Subject Events Occurring Before Next Visit					
Implant and Follow-up	Eligible[1]	Clinical Follow-up	Imaging Follow-up	CT/MR Imaging	Chest X-Ray	Additional Imaging Modalities	Max DTA Diameter	Change in Max DTA Diameter from Discharge[3]	Endoleak	Migration	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 Discharge												0	0	0	3	0	0
Discharge	47	97.9% (46/47)	80.9% (38/47)	76.6% (36/47)[4]		2.1% (1/47)	76.6% (36/47)		68.1% (32/47)		78.7% (37/47)						
Events Between Discharge and 1-Month													0	0	1	0	0
1-Month	46	97.8% (45/46)	97.8% (45/46)	97.8% (45/46)	91.3% (42/46)	0.0% (0/46)	95.7% (44/46)		87.0% (40/46)	97.8% (45/46)	95.7% (44/46)						
Events Between 1-Month and 6-Month													1	0	3	1	0
6-Month	41	87.8% (36/41)	82.9% (34/41)	80.5% (33/41)	68.3% (28/41)	0.0% (0/41)	80.5% (33/41)	80.5% (33/41)	78.0% (32/41)	78.0% (32/41)	78.0% (32/41)						
Events Between 6-Month and 12-Month													0	0	1	0	0
12-Month	40	90.0% (36/40)	85.0% (34/40)	85.0% (34/40)	75.0% (30/40)	0.0% (0/40)	85.0% (34/40)	85.0% (34/40)	85.0% (34/40)	85.0% (34/40)	85.0% (34/40)						
											Total	0	1	0	8	1	
											Deaths Post Conversion to Surgery				0		
											Total Deaths				8		

[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 for eligible subjects are based on number of all subjects enrolled by snapshot date and for clinical and site reported imaging follow-up are based on number of subjects who had follow-up visit within window divided by number of eligible subjects. Within window visits are defined as: for discharge: day 0 to the day of discharge, for 1 month: 16-44 days, for 6 months: 123-243 days, for 12 months: 275-455 days, for 2 years: 619-843 days, for 3 years: 984-1208 days, for 4 years: 1349-1573 days, for 5 years: 1714-1938 days.

[3] The first post-implant image will be used as the baseline image for measuring the change in DTA diameter and migration.

[4] 36 subjects had CTs and 2 subjects had X-ray imaging only. X-ray imaging was not required at pre-discharge and thus these two patients do not show up under the X-ray column.

m = number of subjects in category, n = number of subjects with available values

C. Study Population Demographics and Baseline Parameters

Baseline parameters of the study subjects included demographics, medical history, American Society of Anesthesiologists (ASA) Physical Status Classification and initial dissection assessment via imaging at presentation.

Because data on subjects with acute complicated type B dissections in the SVS MAF was used to calculate the PG, a comparison of the SVS MAF and Medtronic Dissection Trial subjects has been provided in the results tables where data was available.

Demographics

Table 5 below presents comparative demographic data between the SVS MAF subjects and the Medtronic Dissection Trial subjects. The mean subject age was approximately 57.2 ± 12.9 years in the Dissection subjects and 58.3 ± 15.4 years in the SVS MAF subjects. Dissection subjects were predominantly male (80%) and Caucasian (62%), with African American (22%), Asian (12%) and other races (4%) represented. The SVS MAF subjects were also predominantly male (72.9%) and Caucasian (52.9%), with African American (27.1%), Asian (3.5%) and other races (2.4%) represented. While the data on the subject's race was available on all the 50 Dissection subjects, the data was unavailable on 14.1% of the SVS MAF subjects.

Table 5. Subject Demographics

Subject Demographic	SVS MAF Subjects	Dissection Subjects[1]
Age (years)		
n	85	50
Mean ± SD	58.3 ± 15.4	57.2 ± 12.9
Median	59.0	56.5
Min, Max	25, 88	18, 83
Sex % (m/n)		
Male	72.9% (62/85)	80.0% (40/50)
Female	27.1% (23/85)	20.0% (10/50)
Ethnicity % (m/n)		
Hispanic or Latino	14.3% (12/84)	10.0% (5/50)
Not Hispanic or Latino	85.7% (72/84)	88.0% (44/50)
Not Available	--	2.0% (1/50)
Refuses to answer	NA	--
Race % (m/n)		

Table 5. Subject Demographics

Subject Demographic	SVS MAF Subjects	Dissection Subjects[1]
Caucasian	52.9% (45/85)	62.0% (31/50)
Black or African American	27.1% (23/85)	22.0% (11/50)
Asian	3.5% (3/85)	12.0% (6/50)
Native Hawaiian or Other Pacific Islander	1.2% (1/85)	--
American Indian or Alaskan Native	1.2% (1/85)	--
Other	--	4.0% (2/50)
Not Available	14.1% (12/85)	--

[1]Based on number of ITT subjects with available data. ITT subjects are all enrolled subjects.
m = number of subjects in category, n = number of subjects with available values

Medical History

Table 6 summarizes the medical history of the subjects with available data. Among the Medtronic Dissection Trial subjects, conditions that are common to cardiovascular disease are represented; specifically, hypertension (90.0%), current tobacco use (43.8%), hyperlipidemia (32.7%), peripheral vascular disease (14.0%), coronary artery disease (12.0%), abdominal aortic aneurysm (12.0%) and ascending thoracic aneurysm (8.0%).

Similar to the Medtronic Dissection Trial subjects, the SVS MAF subjects had a high incidence of hypertension (83.5%) and current tobacco use (32.5%). Information among other categories such as hyperlipidemia, peripheral vascular disease, coronary artery disease, abdominal aortic aneurysm and ascending thoracic aneurysm was unavailable for the SVS MAF subjects.

Among the SVS MAF subjects, 11.8% had vascular disorders as compared to 44% in the Medtronic Dissection Trial group and 7.1% of the SVS MAF subjects had GU/Renal disorders, as compared to 38% in the Medtronic Dissection Trial group.

Table 6. Subject Medical History

Subject Medical History	SVS MAF Subjects % (m/n)	Dissection Subjects % (m/n)[1]	p-value[2]
Cardiac	89.4% (76/85)	90.0% (45/50)	>0.999
Congestive Heart Failure	10.6% (9/85)	8.0% (4/50)	0.767
Hypertension	83.5% (71/85)	90.0% (45/50)	0.443

Table 6. Subject Medical History

Subject Medical History	SVS MAF Subjects % (m/n)	Dissection Subjects % (m/n)[1]	p-value[2]
MI	11.8% (10/85)	6.0% (3/50)	0.371
Arrhythmia	11.8% (10/85)	8.0% (4/50)	0.571
Angina	NA	14.0% (7/50)	NA
Coronary Artery Disease	NA	12.0% (6/50)	NA
Coronary Artery Bypass Grafting (CABG)	NA	2.0% (1/50)	NA
Percutaneous Coronary Intervention	NA	4.0% (2/50)	NA
Other Cardiac	NA	4.0% (2/50)	NA
Vascular	11.8% (10/85)	44.0% (22/50)	<0.001
Abdominal Aortic Aneurysm	NA	12.0% (6/50)	NA
Ascending Thoracic Aneurysm	NA	8.0% (4/50)	NA
Family History of Aneurysms	NA	4.3% (2/47)[2]	NA
Peripheral Vascular Disease	NA	14.0% (7/50)	NA
Carotid Artery Disease	NA	4.1% (2/49)[2]	NA
Lower Extremity Claudication	NA	6.1% (3/49)[2]	NA
Lower Extremity Rest Pain	NA	6.0% (3/50)	NA
Lower Extremity Ulcers	NA	4.0% (2/50)	NA
DVT	NA	6.0% (3/50)	NA
Pulmonary Embolus	NA	--	NA
Other Vascular	NA	14.0% (7/50)	NA
Pulmonary	12.9% (11/85)	18.0% (9/50)	0.458
COPD	10.6% (9/85)	4.0% (2/50)	0.212
Mechanical Ventilation (for > 24 hrs)	NA	6.0% (3/50)	NA
Other Chronic Pulmonary Disease	2.4% (2/85)	12.0% (6/50)	0.051
Cerebrovascular/Neurological	7.1% (6/85)	8.0% (4/50)	>0.999
Transient Ischemic Attack (TIA)	--	--	NA
Stroke/Cerebrovascular Accident (CVA)	3.5% (3/85)	4.0% (2/50)	>0.999
Paraplegia	2.4% (2/85)	--	0.530
Paraparesis	1.2% (1/85)	2.0% (1/50)	>0.999
Other Cerebrovascular/Neurological	--	2.0% (1/50)	0.370
GU/Renal	7.1% (6/85)	38.0% (19/50)	<0.001

Table 6. Subject Medical History

Subject Medical History	SVS MAF Subjects % (m/n)	Dissection Subjects % (m/n)[1]	p-value[2]
Hemodialysis	NA	2.0% (1/50)	NA
Chronic Renal Failure	NA	--	NA
Renal Insufficiency	NA	24.0% (12/50)	NA
Other GU/Renal	NA	16.0% (8/50)	NA
Connective Tissue Disease	4.7% (4/85)	--	0.296
Marfan Syndrome	NA	--	NA
Ehlers Danlos	NA	--	NA
Other Connective Tissue Disease	NA	--	NA
Diabetes Mellitus	12.9% (11/85)	8.0% (4/50)	0.572
Insulin Dependent	NA	2.0% (1/50)	NA
Cancer	9.4% (8/85)	14.0% (7/50)	0.412
Liver Disease	--	--	NA
GI Conditions	NA	22.4% (11/49)[2]	NA
Bleeding Disorder	NA	--[2]	NA
Hyperlipidemia	NA	32.7% (16/49)[2]	NA
Other Systemic Conditions	NA	4.1% (2/49)[2]	NA
History of EtOH Abuse	NA	4.0% (2/50)	NA
Tobacco Use			0.355
Current Smoker	32.5% (27/83)	43.8% (21/48)[2]	
Former Smoker	37.3% (31/83)	35.4% (17/48)[2]	
Never Smoked	30.1% (25/83)	20.8% (10/48)[2]	
Other Medical History	NA	40.0% (20/50)	NA

[1]Based on number of ITT subjects with available data

[2] Not all subjects answered every medical history question and that is reflected in the denominator for each category. In cases where the data was missing, the sites were queried and the data was unavailable.

m = number of subjects in category, n = number of subjects with available values. A subject may have more than one condition; hence, number of subjects at higher level may not be equal to the total at lower level.

[2]Fisher's exact test

Clinical Symptoms

A summary of the clinical symptoms that the subjects reported at onset and at presentation are summarized in **Table 7**. The most common symptoms for the Medtronic Dissection Trial subjects at onset were back/chest pain (88.0%),

hypertension (52.0%), abdominal pain (36.0%), nausea/vomiting (24.0%) and paraparesis (12.0%). There were minimal differences between the clinical symptoms of the subjects at onset and presentation. Of the 50 subjects enrolled in the study

- 40 subjects (80%) experienced malperfusion with no rupture,
- 7 subjects (14%) experienced rupture with no malperfusion and
- 3 subjects (6%) experienced both malperfusion and rupture

The most common symptoms for the SVS MAF subjects at onset were pain (76.5%), hypertension (43.5%) and bleeding (8.2%).

Table 7. Clinical Symptoms

	SVS MAF Subjects	**Dissection Subjects[1]**	**p-value[2]**
Rupture % (m/n)	31.8% (27/85)	20.0% (10/50)	0.165
Malperfusion % (m/n)	71.8% (61/85)	86.0% (43/50)	0.089
Visceral Ischemia % (m/n)	14.1% (12/85)	40.0% (20/50)	0.001
Renal Ischemia % (m/n)	25.9% (22/85)	42.0% (21/50)	0.058
Lower Limb Ischemia % (m/n)	40.0% (34/85)	40.0% (20/50)	>0.999
Spinal Cord Ischemia % (m/n)	2.4% (2/85)	6.0% (3/50)	0.359
Ischemia (Other) % (m/n)	5.9% (5/85)	2.0% (1/50)	0.412
At Onset			
Duration from Onset to Presentation (days)			
n	NA	50	
Mean ± SD	NA	1.4 ± 2.4	NA
Median	NA	0.0	
Min, Max	NA	0, 10	
Duration from Onset to Procedure (days)			
n	85	50	
Mean ± SD	2.9 ± 3.4	4.7 ± 4.5	0.015
Median	1.0	3.0	
Min, Max	0, 14	0, 23	
Hypertension % (m/n)	43.5% (37/85)	52.0% (26/50)	0.375
Pain % (m/n)	76.5% (65/85)	94.0% (47/50)	0.009
Abdominal Pain % (m/n)	NA	36.0% (18/50)	NA
Back/Chest Pain % (m/n)	NA	88.0% (44/50)	NA
Bleeding % (m/n)	8.2% (7/85)	2.0% (1/50)	0.257

Table 7. Clinical Symptoms

	SVS MAF Subjects	Dissection Subjects[1]	p-value[2]
Paraplegia % (m/n)	NA	4.0% (2/50)	NA
Paraparesis % (m/n)	NA	12.0% (6/50)	NA
Headache % (m/n)	NA	4.0% (2/50)	NA
Syncope/Altered Consciousness % (m/n)	NA	--	NA
Nausea/Vomiting % (m/n)	NA	24.0% (12/50)	NA
At Presentation			
Duration from Presentation to Procedure (days)			
n	NA	50	
Mean ± SD	NA	3.3 ± 3.6	NA
Median	NA	1.5	
Min, Max	NA	0, 14	
Hypertension % (m/n)	NA	60.0% (30/50)	NA
Pain % (m/n)	NA	92.0% (46/50)	NA
Abdominal Pain % (m/n)	NA	42.0% (21/50)	NA
Back/Chest Pain % (m/n)	NA	78.0% (39/50)	NA
Bleeding % (m/n)	NA	2.0% (1/50)	NA
Paraplegia % (m/n)	NA	4.0% (2/50)	NA
Paraparesis % (m/n)	NA	14.0% (7/50)	NA
Headache % (m/n)	NA	4.0% (2/50)	NA
Syncope/Altered Consciousness % (m/n)	NA	2.0% (1/50)	NA
Nausea/Vomiting % (m/n)	NA	18.0% (9/50)	NA
New Medications After Admission			
Inotropic Support % (m/n)	NA	16.0% (8/50)	NA
Anti-Hypertensives % (m/n)	NA	84.0% (42/50)	NA

[1]Based on number of ITT subjects with available data
m = number of subjects in category, n = number of subjects with available values
[2]A t-test was performed on duration measures; Fisher's exact test was carried out on other parameters.

Initial Dissection Assessment

The initial dissection assessment information is summarized in **Table 8**. Dissection originated at the LSA in 37 (74%) of the subjects and at greater than 2 cm distal to the

LSA in 11(22%) of the 50 subjects. The extent of the initial dissection was available on 49 of the 50 subjects. In only three (3) cases (6.1%) was the dissection limited to the thoracic aorta. Thirty five (71.4%) of the 49 subjects had a dissection that extended to or past the aortic bifurcation into the iliac or femoral arteries.

The proximal entry tear was located in the proximal descending aorta in the majority (90%) of the subjects, in the mid descending aorta in 6% and in the distal descending aorta in 4% of the subjects. There were no visible re-entry tears in 24 of the 50 subjects.

Table 8. Initial Dissection Assessment

Initial Dissection Assessment	**% (m/n)[1]**
Site of Proximal Entry Tear	
Proximal Descending Aorta	90.0% (45/50)
Mid Descending Aorta	6.0% (3/50)
Distal Descending Aorta	4.0% (2/50)
Visible Re-entry Tears	
None	48.0% (24/50)
One Tear	10.0% (5/50)
Two Tears	14.0% (7/50)
Three Tears	8.0% (4/50)
Four Tears	14.0% (7/50)
Five Tears	6.0% (3/50)
Most Proximal Aspect of Dissection	
At LSA	74.0% (37/50)
Greater Than 2 cm Distal to LSA	22.0% (11/50)
Mid Descending Aorta	4.0% (2/50)
Most Distal Aspect of Dissection	
Thoracic Aorta	6.1% (3/49)
Celiac Trunk	2.0% (1/49)
Superior Mesenteric Artery	--
Abdominal Aorta (Suprarenal)	--
Abdominal Aorta (Infrarenal)	20.4% (10/49)

Table 8. Initial Dissection Assessment	
Initial Dissection Assessment	**% (m/n)[1]**
Aortic Bifurcation	6.1% (3/49)
Common Iliac	28.6% (14/49)
Internal Iliac	4.1% (2/49)
External Iliac	20.4% (10/49)
Femoral Artery	12.2% (6/49)

[1]Based on number of ITT subjects with available data
m = number of subjects in category, n = number of subjects with available data

ASA Physical Classification

Based on the medical history and physical condition, the subjects were stratified into four (4) different classes according to the American Society of Anesthesiologists (ASA) Physical Status Classification System as reported in **Table 9**. The majority of the Medtronic Dissection Trial subjects and the SVS MAF subjects were Class III with severe systemic disease or Class IV with severe systemic disease that was a constant threat to life. The distribution of subjects across the different ASA Physical Status classifications was similar in the Dissection and the SVS MAF groups.

Table 9. ASA Physical Classification		
ASA Physical Classification	**SVS MAF Subjects % (m/n)**	**Dissection Subjects % (m/n)[1]**
I	--	--
II	2.4% (2/85)	6.0% (3/50)
III	22.4% (19/85)	22.0% (11/50)
IV	64.7% (55/85)	66.0% (33/50)
V	10.6% (9/85)	6.0% (3/50)
Not assessed	--	--

[1]Based on number of ITT subjects with available data
m = number of subjects in category, n = number of subjects with available values

Dissection Characteristics

Pre-procedural imaging was used to measure the vessel dimensions. In many cases

when CT imaging was insufficient, both angiography and IVUS were used for initial measurements by the sites.

The baseline vessel diameters are presented in **Table 10** below. The protocol required the proximal landing zone aortic diameter to be between 20 mm and 44 mm.

Table 10. Aortic and Iliac Measurements at Presentation: Diameters

Thoracic Aortic Measurements: Diameters (mm)[1]	Site Reported
AD1: Maximum Thoracic Aortic Centerline Diameter	
N	50
Mean ± SD	40.6 ± 7.5
Median	40.0
Min, Max	18, 60
AD2: Maximum True Lumen Diameter at AD1	
N	50
Mean ± SD	19.9 ± 9.9
Median	20.0
Min, Max	3, 52
AD3: Maximum False Lumen Diameter at AD1	
N	50
Mean ± SD	23.0 ± 8.9
Median	23.5
Min, Max	0, 40
D1: Diameter of Distal Margin of L CCA (Long Axis of Ellipse)	
N	50
Mean ± SD	32.0 ± 4.3
Median	32.0
Min, Max	20, 44
Diameter at Proximal Landing Zone if Different from D1	
N	50
Mean ± SD	31.4 ± 3.1
Median	31.0
Min, Max	22, 38
Right External Iliac Artery Diameter	
N	49
Mean ± SD	10.2 ± 2.6

Table 10. Aortic and Iliac Measurements at Presentation: Diameters	
Thoracic Aortic Measurements: Diameters (mm)[1]	**Site Reported**
Median	10.0
Min, Max	5, 18
Left External Iliac Artery Diameter	
N	49
Mean ± SD	10.0 ± 3.0
Median	10.0
Min, Max	0, 18
[1]Based on number of ITT subjects with available data	

The baseline vessel lengths are presented in **Table 11** below. The protocol required that the centerline distance from distal margin of left CCA or in cases of bovine anatomy, innominate artery, to the start of the most proximal tear must be greater than or equal to 20 mm. All of the enrolled subjects met this inclusion criterion.

Table 11. Aortic Measurements at Presentation: Lengths	
Thoracic Aortic Measurements: Lengths (mm)[1]	**Site Reported**
L1: Landing Zone (Distal Margin of LCCA to Primary Entry Tear)	
N	50
Mean ± SD	39.7 ± 34.0
Median	29.5
Min, Max	20, 223
L2: Total Length of Aortic Dissection (Thoracic and Abdominal)	
N	46
Mean ± SD	376.4 ± 111.4
Median	378.0
Min, Max	50, 580
L3: Total Thoracic Aortic Length (L CCA to Celiac)	
N	47
Mean ± SD	278.4 ± 63.6
Median	271.0

Table 11. Aortic Measurements at Presentation: Lengths	
Thoracic Aortic Measurements: Lengths (mm)[1]	**Site Reported**
Min, Max	190, 580

[1]Based on number of ITT subjects with available data

Summary of Study Population Demographics and Baseline Parameters

In summary, the subjects treated in the Medtronic Dissection Trial presented with a complicated morbid disease. They were characterized by demographics, medical history and clinical symptoms and were compared to subjects in the SVS MAF group, where data was available. Subject demographics, history and symptoms were comparable between the two study groups, although it appeared that the Medtronic Dissection Trial subjects' history showed more extensive systemic disease.

Acute Procedural Data

The technical success was 100% in this study as shown in **Table 12**. The device was successfully delivered and deployed and the proximal entry tear was successfully covered in all subjects.

As summarized in **Table 13**, the most proximal device was implanted in either Zone 2 or Zone 3 in 46 of the 50 subjects. In three (3) subjects, the proximal device was placed in Zone 4 and in one (1) subject, the proximal device was placed in Zone 1. One (1) subject had a bovine arch with a common takeoff of the innominate & LCA. The stent graft was deployed with the covered portion at the distal margin of the common trunk covering the LSA.

Table 12. Technical Success	
Technical Success[1]	**% (m/n)**
Vessel Access Success	100.0% (50/50)
Delivery Success	100.0% (50/50)
Deployment Success	100.0% (50/50)

[1]Based on number of ITT subjects with available data
m = number of subjects in category, n = number of subjects with available values

Table 13. Implanted Zone at Initial Procedure	
Implanted Zone of Proximal Stent Graft	**% (m/n)[1]**
Zone 1	2.0% (1/50)
Zone 2	58.0% (29/50)
Zone 3	34.0% (17/50)
Zone 4	6.0% (3/50)

[1]Based on number of implanted subjects with available data
m = number of subjects in category, n = number of subjects with available data

Table 14. Entry Tear Coverage at Implant	
	% (m/n)[1]
Proximal Entry Tear Covered	100.0% (50/50)

[1]Based on number of ITT subjects with available data
m = number of subjects with successful events, n = number of subjects with available values

Stent Graft Usage and Oversizing

All subjects successfully received one (1) or more devices. There were no device malfunctions reported. Thirty one of the 50 subjects enrolled received a single device. Sixteen of the remaining subjects received two (2) stent grafts and three (3) subjects received three (3) stent grafts at the initial procedure.

Table 15 below contains the information regarding the average number of devices implanted per subject at initial procedure. **Table 16** contains information regarding the types of devices implanted.

Table 15. Number of Devices Implanted at Initial Procedure	
Number of Devices Implanted	**Subjects % (m/n)[1]**
1	62.0% (31/50)
2	32.0% (16/50)
3	6.0% (3/50)

[1]Based on number of implanted subjects with available data
m = number of subjects in category, n = number of subjects with available values

Table 16. Devices Implanted by Type at Initial Procedure

Device Type	% (m/n)[1]
FreeFlo Straight (Proximal Component)	75.0% (54/72)
Closed Web Straight (Distal Component)	9.7% (7/72)
Distal Bare Spring Straight (Distal Component)	--
Closed Web Tapered (Distal Component)	15.3% (11/72)

[1]Based on total number of devices implanted in all subjects
m = number of devices in category, n = total number of devices implanted in all subjects

The Valiant Stent Graft was available in a wide set of sizes ranging from 22 mm to 46 mm in diameter, treating subjects with proximal landing zone diameter from 25 mm to 38 mm. The diameter of the majority of the devices implanted was between 32 mm and 40 mm. This data is summarized in **Table 17** below.

Table 17. Proximal Diameters of Implanted Proximal Devices at Initial Procedure

Device Diameter (mm)[1]	Number of Devices Implanted (n)
22	0
24	0
26	1
28	0
30	1
32	13
34	13
36	7
38	10
40	4
42	1
44	0
46	0

[1]Based on number of implanted subjects with available data

Table 18 provides the breakdown of the number of devices of different lengths that were used at the initial procedure. Forty six of the 72 devices implanted at the initial procedure were 150 mm in length.

Table 18. Device Lengths at Initial Procedure

Device Length (mm)[1]	Number of Devices Implanted (n)
100	4
150	46
200	22

[1]Based on total number of devices implanted in all subjects

As reported by the core lab, the mean total length of coverage (reported in **Table 19** below) after the procedure was 196.9 mm ± 67.1 mm ranging from 93 mm to 346 mm.

Table 19. Core Lab Reported Length of Coverage at Baseline

Length of Coverage at Baseline[1, 2] (mm)	
n	47
Mean ± SD	196.9 ± 67.1
Median	170.9
Min, Max	93, 346

[1]Baseline image is the first post-procedure image.
[2]Based on number of implanted subjects with available data
Core Lab Reported Table

Table 20 provides information on the device oversizing. The median oversizing for this population was 11.5 %. In one (1) subject, three (3) stent grafts were implanted in the descending thoracic aorta using the distal-to-proximal implantation technique. The diameter of the primary (most distal) device implanted was 34 mm. The first device placed proximal to the primary device was oversized by 2 mm and the second device placed proximal to the first device was further oversized by 2 mm per the IFU. This successive oversizing resulted in the most proximal piece having an oversizing measurement of 52%.

Table 20. Device Oversizing at Initial Procedure	
Device Oversizing[1] (%)	
n	50
Mean ± SD	12.0 ± 10.3
Median	11.5
Min, Max	-9, 52

[1]Based on number of implanted subjects with available data
Device oversizing (%) = 100*(device diameter - diameter at proximal landing zone)/(diameter at proximal landing zone).

Perioperative Data

All cases were performed under general anesthesia. Systemic heparin was administered in 98.0% of the subjects. Heparin was not administered in one (1) subject at the physician's discretion.

Cerebrospinal fluid (CSF) drainage and other spinal protective measures were used in 32.0% and 24.0% of the subject population respectively. No cases of spinal cord ischemia, paraplegia or paraparesis at the index procedure were reported.

The LSA was covered in 60.0% of the subjects (complete coverage: 44.0% and partial coverage: 16.0%).

Table 21. Implant Procedure	
Implant Procedure	**% (m/n)**
Heparin Administered During Implant	98.0% (49/50)
Type of Anesthesia Used	
General	100.0% (50/50)
Spinal	4.0% (2/50)
Epidural	--
Local	--
Spinal Protective Measure	54.0% (27/50)
Spinal CSF Drain	32.0% (16/50)
Maintenance of controlled hypertension following placement	6.0% (3/50)
Monitoring of evoked potentials	18.0% (9/50)
LSA Coverage	
None	40.0% (20/50)
Partial	16.0% (8/50)

Table 21. Implant Procedure

Implant Procedure	% (m/n)
Complete	44.0% (22/50)
Subjects with LSA Coverage	
LSA Covered Subjects with Any Pre-implant Adjunctive Procedure[1]	10.0% (3/30)
LSA Covered Subjects with Any Post-implant Adjunctive Procedure[2]	23.3% (7/30)

m = number of subjects in category, n = number of subjects with available data.
For Subjects with LSA Coverage, the denominator is based on those with LSA coverage or partial coverage.
[1]These included carotid to subclavian bypass, left renal stent, left iliac stent, right iliac stent.
[2]These included carotid to subclavian bypass, femfem bypass, SMA stent, left iliac stent, right iliac stent and other.

The most commonly used access entry site was the femoral artery in 98.0% of the subjects. The brachial artery was used in 22.0% of the subjects for additional vascular access.

Table 22. Arterial Access Entry Site

Arterial Access Entry Site	% (m/n)[1]
Access Site Used to Deliver the Device	
Femoral Artery	98.0% (49/50)
Iliac Artery	--
Abdominal Aortic Conduit	--
Iliac Conduit	2.0% (1/50)
Additional Vascular Access Achieved Via	
Femoral Artery	58.0% (29/50)
Iliac Artery	--
Abdominal Aortic Conduit	--
Iliac Conduit	--
Brachial Artery	22.0% (11/50)
Other	8.0% (4/50)[2]
NA	12.0% (6/50)

[1]Based on number of ITT subjects with available data
m = number of subjects in category, n = number of subjects with available values
[2] All subjects had right radial artery access

The median duration of the implant procedure was reported as 108.5 minutes. One subject had a procedure time of 920 minutes. This subject had significant

comorbidities and underwent several adjunct procedures. These factors contributed to the procedure lasting longer than usual.

Overall, the procedures required a median of 115.0 ml of contrast agent. The median reported blood loss during the procedure was 100.0 ml.

The duration of the overall hospital stay ranged from 1 to 124 days with a median of 9 days. Two (2) subjects experienced much longer times in the intensive care unit (ICU) and longer hospital stays than the other subjects enrolled. One of these subjects was in the ICU for 2,737 hours and hospitalized for 124 days. This subject was never discharged from the hospital and died secondary to cardiac arrest on post-operative day 124. The other subject was in the ICU for 1,040 hours and hospitalized for 72 days. This subject died secondary to pneumonia 87 days post-operatively. Time in intensive care was not reported for the subject who died during the implant procedure.

Additional measurements at implant are presented in the tables below.

Table 23. Acute Measurements at Implant

Acute Measurements at Implant[1]	
Duration of Implant Procedure (min)	
n	50
Mean ± SD	142.9 ± 125.6
Median	108.5
Min, Max	45, 920
Contrast Volume (ml)	
n	47
Mean ± SD	122.2 ± 72.1
Median	115.0
Min, Max	20, 300
Total Fluoroscopic Time (min)	
n	42
Mean ± SD	17.1 ± 25.7
Median	12.2
Min, Max	4, 175
Blood Loss During Procedure (ml)	
n	49
Mean ± SD	180.1 ± 223.6
Median	100.0

Table 23. Acute Measurements at Implant	
Acute Measurements at Implant[1]	
Min, Max	10, 1400
Subjects Requiring Blood Transfusion % (m/n)	40.0% (20/50)
Time in ICU (hours)	
n	49
Mean ± SD	211.4 ± 429.2
Median	76.0
Min, Max	5, 2737
Overall Hospital Stay (days)	
n	50
Mean ± SD	14.1 ± 19.9
Median	9.0
Min, Max	1, 124

[1]Based on number of ITT subjects with available data
m = number of subjects in category, n = number of subjects with available values

Table 24 lists the 7 (seven) adjunctive procedures performed prior to and twenty three (23) adjunctive procedures performed after deployment of the study device. Three (3) subjects had an LSA-Carotid bypass procedure before the implant and one (1) subject underwent the bypass as an adjunctive procedure after the implant.

Table 24. Adjunctive Procedures Performed		
Adjunctive Procedures Performed	**Prior to Deployment % (m/n)[1]**	**After Deployment % (m/n)[2]**
Intervention location: Aortic arch	6.0% (3/50)	2.0% (1/50)
Carotid to Subclavian Bypass	6.0% (3/50)	2.0% (1/50)
Intervention location: Mesenteric vessels	--	2.0% (1/50)
SMA Stent	--	2.0% (1/50)
Intervention location: Renal vessels	2.0% (1/50)	2.0% (1/50)
Left Renal Stent	2.0% (1/50)	--
Right Renal Stent	--	2.0% (1/50)
Intervention location: Iliac vessels	4.0% (2/50)	16.0% (8/50)
Left Iliac Stent	4.0% (2/50)	12.0% (6/50)

Table 24. Adjunctive Procedures Performed		
Adjunctive Procedures Performed	**Prior to Deployment % (m/n)[1]**	**After Deployment % (m/n)[2]**
Right Iliac Stent	2.0% (1/50)	8.0% (4/50)
Intervention location: Femoral vessels	--	6.0% (3/50)
Fem-Fem Bypass	--	6.0% (3/50)
Other (Listed in Error! Reference source not found. below)	--	14.0% (7/50)
No. of Subjects with Adjunctive Procedures[4]	6.0% (3/50)	28.0% (14/50)

[1]Based on number of ITT subjects with available data
[2]Based on number of implanted subjects with available data
m = number of subjects in category, n = number of subjects with available data
[4]Some subjects had multiple adjunctive procedures.

A listing of the seven (7) other adjunctive procedures that were performed after deployment is included in **Table 25.**

Table 25. List of Other Adjunctive Procedures
Other Adjunctive Procedures
Thoracentisis/abd endoscopy
Thrombectomy left common/external IA, interposition graft L CFA
Laparotomy by General Surgery
Right common femoral exposure, false lumen thrombectomy and obliteration, patch angioplasty with bovi
Endovascular repair of abdominal aortic dissection
Right external iliac thrombectomy and stenting and fasciotomy of the right calf
Right axilla-femoral bypass and right sided calf fasciotomy

D. Safety and Effectiveness Results

1. Safety Results

The primary endpoint analysis of all-cause mortality at 30 days was based on a cohort of 50 patients. Other safety outcomes are presented for 0 to 30 days post-implant procedure and 31 to 365 days post-implant procedure. The key safety outcomes for this study are presented below in Tables 26 to 37. Adverse events are reported in Tables 31 to 37.

Primary Endpoint Analysis

The primary endpoint for this trial was the all-cause mortality within 30 days of the index procedure. The Medtronic Dissection Trial met its primary endpoint with a 30-day all-cause mortality rate of 8.0%. The null hypothesis was rejected since the upper limit of the one-sided 95.0% confidence interval on the 30-day mortality rate was 17.4%, which was less than the performance goal of 25.0%. One (1) subject did not meet the inclusion criteria for an acute Type B aortic dissection. Table 34 shows the primary endpoint analysis on all enrolled subjects for all-cause mortality within 30 days. Table 35 shows the sensitivity analysis on the primary endpoint by excluding this subject from the ITT population. In either analysis (PP or ITT), the dissection trial met its primary endpoint.

Four (4) subjects died within 30 days of the study procedure.

- One subject died from *cardiac tamponade* on the day of the procedure
- One subject died from *mesenteric ischemia in totalis* on day 1 post-procedure
- One subject died from *sepsis* on day 9 post-procedure
- One subject died from a *pulmonary embolism* on day 26 post-procedure

Table 26. Primary Endpoint - All-Cause Mortality within 30 Days

	% (m/n) [95% UCL][1, 2, 3]
30-day All-Cause Mortality	8.0% (4/50) [17.4%]

[1]95% Upper Confidence Limit (UCL) was calculated using an exact method based on the binomial distribution.
[2]Based on the number of evaluable subjects. Subjects will be considered unevaluable if they are withdrawn before the lower limit of the 30-day follow-up window (16 days) or they are lost to follow-up before the lower limit of the 30-day follow-up window (16 days) and had no contact thereafter.
[3]Based on CEC adjudicated data

All-cause mortality within 30 days for Medtronic Dissection Trial subjects with the complicating factor of rupture was 0.0% (0 out of 10 subjects) as reported in **Table 27** and all-cause mortality within 30 days for subjects with the complicating factor of ischemia was 10% (4 out of 40 subjects) as reported in **Table 28**.

Table 27. All-Cause Mortality within 30 Days for Medtronic Dissection Trial Subjects with the Complicating Factor of Rupture

	% (m/n) [95% UCL][1, 2, 3]
30-day All-Cause Mortality	0.0% (0/10) [25.9%]

[1]95% Upper Confidence Limit (UCL) was calculated using an exact method based on the binomial distribution.
[2]Based on the number of evaluable subjects. Subjects will be considered unevaluable if they are withdrawn before the lower limit of the 30-day follow-up window (16 days) or they are lost to follow-up before the lower limit of the 30-day follow-up window (16 days) and had no contact thereafter.
[3]Based on CEC adjudicated data

Table 28. All-Cause Mortality within 30 Days for Medtronic Dissection Trial Subjects with the Complicating Factor of Ischemia Only

	% (m/n) [95% UCL][1, 2, 3]
30-day All-Cause Mortality	10.0% (4/40) [21.4%]

[1]95% Upper Confidence Limit (UCL) was calculated using an exact method based on the binomial distribution.
[2]Based on the number of evaluable subjects. Subjects will be considered unevaluable if they are withdrawn before the lower limit of the 30-day follow-up window (16 days) or they are lost to follow-up before the lower limit of the 30-day follow-up window (16 days) and had no contact thereafter.
[3]Based on CEC adjudicated data

Secondary Observations

The device was delivered and deployed successfully in all 50 subjects (100.0%) enrolled in the Medtronic Dissection Trial. The proximal entry tear was successfully covered in all subjects. There were no incidents of post-operative rupture. The all-cause mortality was 14.6% at 12 months. Four (4) subjects underwent secondary endovascular procedures within 12 months. Twenty three (23) subjects (23/49, 46.9%) had a serious adverse event reported within 12 months.

The trial data demonstrated favorable remodeling of the stented segment of the aorta after TEVAR. Beyond the stented segment, a trend towards positive remodeling was seen.

Of the nine (9) subjects who had perfusion of the false lumen at the 12-month visit, seven (7) were cases of continuing perfusion and one (1) was a case of new false lumen perfusion. The type of perfusion could not be ascertained in one (1) subject.

Table 29. Secondary Observations	
	% (m/n)
Successful Delivery and Deployment of the Stent Graft[1]	100.0% (50/50)
Coverage of Proximal Entry Tear at Implant[1]	100.0% (50/50)
Adverse Events within 30 Days[1]	52.0% (26/50)
Non-serious Adverse Events	16.0% (8/50)
Device related	--
Procedure related	16.0% (8/50)
Dissection related	4.0% (2/50)
Serious Adverse Events	38.0% (19/50)
Device related	4.0% (2/50)
Procedure related	20.0% (10/50)
Dissection related	28.0% (14/50)
Rupture within 30 Days[1]	--
Secondary Procedures within 12 Months[2]	
Secondary Endovascular Procedures related to the Dissection[3]	6.3% (3/48)
Secondary Endovascular Procedures not related to the Dissection[4]	2.1% (1/48)
Open Repair of Retrograde Type A Dissection	4.2% (2/48)
Conversion to Open Repair for Descending Dissection	--
LSA Bypass	4.2% (2/48)
Adverse Events within 12 Months[2]	59.2% (29/49)
Non-serious Adverse Events	16.7% (8/48)
Device related	--
Procedure related	16.7% (8/48)
Dissection related	4.2% (2/48)
Serious Adverse Events	46.9% (23/49)
Device related	6.3% (3/48)
Procedure related	20.8% (10/48)
Dissection related	34.7% (17/49)
Rupture within 12 Months[2]	--
All-Cause Mortality within 12 Months[2, 5]	14.6% (7/48)
Continuing or New False Lumen (FL) Perfusion at 6 Month Visit[6]	
Core Lab Reported	39.4% (13/33)
Continuing or New False Lumen (FL) Perfusion at 12 Month Visit[6]	

Table 29. Secondary Observations	
	% (m/n)
Core Lab Reported	27.3% (9/33)

[1]Based on number of ITT subjects with available data
[2]Based on the number of evaluable subjects. Subjects will be considered unevaluable if they are withdrawn b efore the lower limit of the 12 months follow-up window (275 days) or they are lost to follow-up before the lower limit of the 12 months follow-up window (275 days) and had no contact thereafter.
[3]Additional endovascular device placed
[4]LSA plug
[5]Based on CEC adjudicated data
[6]Based on the number of subjects with evaluable imaging at follow-up visit
Site Reported and Core Lab Reported Table

Summary of Deaths

Table 30 below summarizes the eight (8) deaths that have occurred to date in this subject population. Four (4) of the deaths occurred within 30 days of the procedure. Seven (7) occurred in the first 12 months and a single death has occurred post 365 days.

Table 30. Listing of Deaths

Implant to Death (days)	Cause of Death Site Reported	Death Relatedness[1] Site Reported	Death Relatedness[1] CEC Adjudicated
0	Cardiac Tamponade[2]	Procedure Related	Device Related, Procedure Related, Dissection Related
1	Mesenteric Ischemia In Totalis[3]	Dissection Related	Dissection Related
9	Sepsis[4]	Not Related	Procedure Related, Dissection Related
26	Pulmonary Embolism[5]	Not Related	Procedure Related, Dissection Related
71	Cardiac Arrest[6]	Not Related	Not Related
87	Pneumonia[7]	Not Related	Dissection Related
124	Cardiac Arrest[8]	Not Related	Procedure Related

Table 30. Listing of Deaths

Implant to Death (days)	Cause of Death Site Reported	Death Relatedness[1] Site Reported	Death Relatedness[1] CEC Adjudicated
432	Natural Causes[9]	Not Related	Not Related

[1]Relationship to Device/Procedure/Dissection Site and CEC Adjudicated Reported Table

[2]The subject had a large pericardial effusion with acute cardiac tamponade most likely due to injury by a guidewire or catheter. Underlying causes /conditions were listed as cardiac arrest, ascending aortic dissection and ascending aortic aneurysm.
[3]The subject was diagnosed with mesenteric ischemia in totalis. Immediate cause of death was identified as multi-system organ failure due to or as a consequence of an acute complicated Type B dissection.
[4]The subject's immediate cause of death was sepsis, with contributing causes listed as pneumonia, respiratory failure and descending aortic aneurysm. In addition, CT data was suggestive of a stroke. See Table 37 for additional information.
[5]The subject had pulmonary embolism due to or as a consequence of a DVT and AAA repaired with stents.
[6]The subject had a sudden cardiac arrest in spite of gradual improvement following treatment.
[7]The subject experienced fever, abdominal pain and abnormal LFTs prior to death whose cause was reported to be pneumonia.
[8]The subject's immediate cause of death was identified as cardiac arrest due to or as a consequence of abdominal sepsis with a contributing cause of sacral decubitus ulcer.
[9]In addition to aortic dissection, the subject experienced CHF, COPD, DVT and RA.

Adverse events that occurred in the PMA clinical study

Only those adverse events and serious adverse events that were related to the device, to the implant procedure and/or to the aortic disease and serious adverse events that lead to death, regardless if they are related to the device, procedure or the aortic disease, were reported by the sites. Thirty eight percent of eligible subjects experienced an SAE within 30 days and 19.6% experienced an SAE between 31 and 365 days. **Error! Reference source not found.** lists the number of subjects who experienced one or more SAEs. In addition to the SAEs reported by the sites, those adverse events that did not meet the criteria of an SAE were reported as AEs. Sixteen percent of eligible subjects experienced an AE (excluding SAEs) within 30 days where as 2.2% experienced an AE between 31 and 365 days. These events are listed in **Table 31**. A subject may have experienced multiple adverse events, and in different subcategories; therefore, the number of subjects in each category may not be the sum of those in each subcategory. Each subject was only counted once in each subcategory. An adverse event may have been reported as related to one or more of the following: device, dissection or procedure. In cases where the AE was reported to be related to more than one category, it was included in all applicable AE tables. Therefore, the same event may appear in the device-related, procedure-related or dissection-related SAE tables.

All AEs and SAEs are further categorized based on the relatedness to the device, procedure or dissection in the following section.

Table 31. Subjects with Serious Adverse Events by Date of Onset

Category	0 to 30 Days % (m/n)[1]	31 to 365 Days % (m/n)[1]
Subjects experiencing one or more SAE[2]	38.0% (19/50)	19.6% (9/46)
Cardiac Disorders	2.0% (1/50)	4.3% (2/46)
Cardiac Arrest	--	4.3% (2/46)
Cardiac Tamponade	2.0% (1/50)	--
Gastrointestinal Disorders	4.0% (2/50)	--
Ileus	2.0% (1/50)	--
Intestinal Ischaemia	2.0% (1/50)	--
General Disorders And Administration Site Conditions	--	2.2% (1/46)
Death	--	--
Continued Perfusion from a Branch Vessel requiring Treatment	--	2.2% (1/46)
Infections	2.0% (1/50)	2.2% (1/46)
Pneumonia	2.0% (1/50)	2.2% (1/46)
Sepsis	2.0% (1/50)	--
Procedural Complications	8.0% (4/50)	--
Incision Site Pain	2.0% (1/50)	--
Nerve Injury	2.0% (1/50)	--
Stent-Graft Endoleak	4.0% (2/50)	--
Wound	2.0% (1/50)	--
Abnormal Lab Values	2.0% (1/50)	--
White Blood Cell Count Increased	2.0% (1/50)	--
Musculoskeletal And Connective Tissue Disorders	4.0% (2/50)	--
Muscular Weakness	2.0% (1/50)	--
Rhabdomyolysis	2.0% (1/50)	--
Nervous System Disorders	10.0% (5/50)	--
Cerebral Ischaemia	2.0% (1/50)	--
Cerebrovascular Accident	6.0% (3/50)	--
Monoplegia	2.0% (1/50)	--
Paralysis	2.0% (1/50)	--
Paraplegia	2.0% (1/50)	--
Spinal Cord Ischaemia	2.0% (1/50)	--
Renal And Urinary Disorders	6.0% (3/50)	2.2% (1/46)
Renal Failure Acute	6.0% (3/50)	2.2% (1/46)
Respiratory, Thoracic And Mediastinal Disorders	4.0% (2/50)	--
Haemothorax	2.0% (1/50)	--

Pulmonary Embolism	2.0% (1/50)	--
Vascular Disorders	10.0% (5/50)	10.9% (5/46)
Aortic Aneurysm	--	4.3% (2/46)
Retrograde Type A Aortic Dissection	2.0% (1/50)	2.2% (1/46)
Deep Vein Thrombosis	2.0% (1/50)	--
Haemorrhage	2.0% (1/50)	--
Hypertension	--	2.2% (1/46)
Intermittent Claudication	--	2.2% (1/46)
Peripheral Vascular Disorder	2.0% (1/50)	--
Subclavian Artery Embolism	2.0% (1/50)	--

[1]m = number of subjects experiencing one or more serious adverse events in a category, n = number of subjects who experienced a serious adverse event or who died during the interval, or who were followed at least until the lower endpoint of the interval.
[2]A subject may report multiple adverse events and in different categories; hence, number of subjects in each category may not be the sum of those in each subcategory. Each subject was only counted once in each category.

A comparison of rates of particular 30-day SAEs provided in the SVS MAF to those in the Medtronic Dissection Trial is presented in Table 10-30. Overall, 30-day SAE rates in the Medtronic Dissection Trial group were comparable to or lower than those in the SVS MAF group. Stroke was reported in three (3) subjects in the Medtronic Dissection Trial group. One resolved without treatment and two (2) were unresolved at the time of the patients' deaths. Paralysis was reported in three (3) subjects. One was unresolved at the time of the patient's death, one resulted in above the knee amputation and remained unresolved and one remains unresolved and is not being treated any further by the physician.

Table 32. Selected 30 Day SAE Results from Valiant Captivia and the SVS MF

	SVS MAF Subjects % (m/n)[1]	**MDT Dissection Subjects % (m/n)[1]**
Any Event[2]	37.6% (32/85)	16.0% (8/50)
Death	10.6% (9/85)	8.0% (4/50)
MI	1.2% (1/85)	--
Stroke	9.4% (8/85)	6.0% (3/50)
Renal Failure (+Dialysis)	9.4% (8/85)	2.0% (1/50)
Respiratory Failure	2.4% (2/85)	--
Paraplegia/Paraparesis[3]	9.4% (8/85)	6.0% (3/50)

Table 32. Selected 30 Day SAE Results from Valiant Captivia and the SVS MF

	SVS MAF Subjects % (m/n)[1]	MDT Dissection Subjects % (m/n)[1]
Bowel Ischemia	3.5% (3/85)	2.0% (1/50)

[1]m = number of subjects experienced the event in question, n = number of evaluable subjects in the cohort.
[2]A subject may report multiple events; hence, number of subjects with any events may not be the sum of those in each event. Each subject was only counted once in each category.
[3]Includes one event of monoplegia and two events of paraplegia.

Table 33. Subjects with Adverse Events (Excluding SAEs) by Date of Onset

Category	0 to 30 Days % (m/n)[1]	31 to 365 Days % (m/n)[1]
Subjects Experiencing One or More AEs (Excluding SAEs)[2]	16.0% (8/50)	2.2% (1/46)
Blood And Lymphatic System Disorders	4.0% (2/50)	--
Haemorrhagic Anaemia	2.0% (1/50)	--
Heparin-Induced Thrombocytopenia	2.0% (1/50)	--
General Disorders And Administration Site Conditions	2.0% (1/50)	--
Malaise	2.0% (1/50)	--
Infections	2.0% (1/50)	--
Urinary Tract Infection	2.0% (1/50)	--
Procedural Complications	2.0% (1/50)	--
Seroma	2.0% (1/50)	--
Abnormal Lab Values	--	2.2% (1/46)
Weight Decreased	--	2.2% (1/46)
Metabolism And Nutrition Disorders	2.0% (1/50)	--
Hyperglycaemia	2.0% (1/50)	--
Musculoskeletal And Connective Tissue Disorders	2.0% (1/50)	2.2% (1/46)
Back Pain	2.0% (1/50)	--
Pain In Extremity	--	2.2% (1/46)
Nervous System Disorders	4.0% (2/50)	--
Headache	2.0% (1/50)	--
Monoplegia	2.0% (1/50)	--

Table 33. Subjects with Adverse Events (Excluding SAEs) by Date of Onset

Category	0 to 30 Days % (m/n)[1]	31 to 365 Days % (m/n)[1]
Psychiatric Disorders	--	2.2% (1/46)
Depression	--	2.2% (1/46)
Mental Status Changes	--	2.2% (1/46)
Respiratory, Thoracic And Mediastinal Disorders	6.0% (3/50)	--
Pleural Effusion	4.0% (2/50)	--
Pulmonary Oedema	2.0% (1/50)	--
Respiratory Failure	2.0% (1/50)	--
Skin And Subcutaneous Tissue Disorders	2.0% (1/50)	--
Skin Ulcer	2.0% (1/50)	--
Vascular Disorders	2.0% (1/50)	2.2% (1/46)
Aortic Disorder	--	2.2% (1/46)
Hypertension	2.0% (1/50)	--
Peripheral Arterial Occlusive Disease	2.0% (1/50)	--

[1]m = number of subjects experiencing one or more non-serious adverse events in a category, n = number of subjects who experienced a non-serious adverse event or who died during the interval, or who were followed at least until the lower endpoint of the interval.
[2]A subject may report multiple adverse events and in different categories; hence, number of subjects in each category may not be the sum of those in each subcategory. Each subject was only counted once in each subcategory and category.

Summary of Device-Related, Procedure-Related and Dissection-Related Adverse Events

The device-related AEs and SAEs are listed in **Table 34**. Four (4) percent of eligible subjects experienced a device-related AE/SAE within 30 days and 2.2% experienced a device-related AE/SAE between 31 and 365 days. Three (3) serious adverse events were reported as related to the device: retrograde Type A aortic dissection, CVA and continued perfusion from a branch vessel.

The number of subjects experiencing one or more procedure-related adverse events is listed in **Table 35.** Thirty four percent of eligible subjects experienced a procedure-related AE/SAE within 30 days and 4.3% experienced a procedure-related AE/SAE between 31 and 365 days. The following procedure-related adverse events which were observed in the trial are considered to be of greatest importance with endovascular treatment: cerebral ischemia, CVA, monoplegia, transient spinal cord ischemia, intermittent claudication and seroma. None of these occurred at rates that were unexpected or that were outside those reported in the literature.

The number of subjects experiencing one or more dissection-related adverse events is listed in **Table 36**. Thirty percent of eligible subjects experienced a dissection-related AE/SAE within 30 days and 10.9% experienced a dissection-related AE/SAE between 31 and 365 days. Retrograde Type A dissection was reported in one subject on day 5 and in another subject on day 56 post-procedure. Both subjects underwent open repair the following day, resolving the SAE. Stroke was reported in two (2) subjects. In one subject, it occurred on day 1 post-procedure and was unresolved at the time of the patient's death. In the second subject it occurred on day 7 and was resolved without treatment. Paralysis was reported in three (3) subjects. One was unresolved at the time of the patient's death, one resulted in above the knee amputation and remained unresolved and one remains unresolved and is not being treated any further by the physician.

Results for serious adverse events of interest in the treatment of Type B dissection are listed in **Table 37**.

Table 34. Subjects with Device Related Adverse Events within 365 Days

	SAE		AE (Non-Serious)	
Category	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**
Subjects Experiencing One or More AEs[2]	4.0% (2/50)	2.2% (1/46)	--	--
General Disorders And Administration Site Conditions	--	2.2% (1/46)	--	--
Continued Perfusion from a Branch Vessel requiring treatment	--	2.2% (1/46)	--	--
Nervous System Disorders	2.0% (1/50)	--	--	--
Cerebrovascular Accident	2.0% (1/50)	--	--	--
Vascular Disorders	2.0% (1/50)	--	--	--
Retrograde Type A Aortic Dissection	2.0% (1/50)	--	--	--

[1]m = number of subjects experiencing one or more device related adverse events in a category, n = number of subjects who experienced a device related adverse event or who died during the interval, or who were followed at least until the lower endpoint of the interval.
[2]A subject may report multiple adverse events and in different categories; hence, number of subjects in each category may not be the sum of those in each subcategory. Each subject was only counted once in each subcategory and category.

Table 35. Subjects with Procedure Related Adverse Events within 365 Days

	SAE		AE (Non-Serious)	
Category	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**
Subjects Experiencing One or More AEs[2]	20.0% (10/50)	2.2% (1/46)	16.0% (8/50)	2.2% (1/46)

Table 35. Subjects with Procedure Related Adverse Events within 365 Days

	SAE		AE (Non-Serious)	
Category	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**
Blood And Lymphatic System Disorders	--	--	4.0% (2/50)	--
Haemorrhagic Anaemia	--	--	2.0% (1/50)	--
Heparin-Induced Thrombocytopenia	--	--	2.0% (1/50)	--
Cardiac Disorders	2.0% (1/50)	--	--	--
Cardiac Tamponade	2.0% (1/50)	--	--	--
General Disorders And Administration Site Conditions	--	--	2.0% (1/50)	--
Malaise	--	--	2.0% (1/50)	--
Infections And Infestations	2.0% (1/50)	--	2.0% (1/50)	--
Pneumonia	2.0% (1/50)	--	--	--
Urinary Tract Infection	--	--	2.0% (1/50)	--
Procedural Complications	6.0% (3/50)	--	2.0% (1/50)	--
Incision Site Pain	2.0% (1/50)	--	--	--
Nerve Injury	2.0% (1/50)	--	--	--
Seroma	--	--	2.0% (1/50)	--
Stent-Graft Endoleak	2.0% (1/50)	--	--	--
Wound	2.0% (1/50)	--	--	--
Metabolism And Nutrition Disorders	--	--	2.0% (1/50)	--
Hyperglycaemia	--	--	2.0% (1/50)	--
Musculoskeletal And Connective Tissue Disorders	2.0% (1/50)	--	2.0% (1/50)	2.2% (1/46)
Back Pain	--	--	2.0% (1/50)	--
Pain In Extremity	--	--	--	2.2% (1/46)
Rhabdomyolysis	2.0% (1/50)	--	--	--
Nervous System Disorders	8.0% (4/50)	--	4.0% (2/50)	--
Cerebral Ischaemia	2.0% (1/50)	--	--	--
Cerebrovascular Accident	6.0% (3/50)	--	--	--
Headache	--	--	2.0% (1/50)	--
Monoplegia	2.0% (1/50)	--	2.0% (1/50)	--
Transient Spinal Cord Ischaemia	2.0% (1/50)	--	--	--
Respiratory, Thoracic And Mediastinal Disorders	--	--	6.0% (3/50)	--
Pleural Effusion	--	--	4.0% (2/50)	--

Table 35. Subjects with Procedure Related Adverse Events within 365 Days

	SAE		AE (Non-Serious)	
Category	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**
Pulmonary Oedema	--	--	2.0% (1/50)	--
Respiratory Failure	--	--	2.0% (1/50)	--
Skin And Subcutaneous Tissue Disorders	--	--	2.0% (1/50)	--
Skin Ulcer	--	--	2.0% (1/50)	--
Vascular Disorders	6.0% (3/50)	2.2% (1/46)	--	--
Deep Vein Thrombosis	2.0% (1/50)	--	--	--
Haemorrhage	2.0% (1/50)	--	--	--
Intermittent Claudication	--	2.2% (1/46)	--	--
Subclavian Artery Embolism	2.0% (1/50)	--	--	--

[1]m = number of subjects experiencing one or more procedure related adverse events in a category, n = number of subjects who experienced a procedure related adverse event or who died during the interval, or who were followed at least until the lower endpoint of the interval.
[2]A subject may report multiple adverse events and in different categories; hence, number of subjects in each category may not be the sum of those in each subcategory. Each subject was only counted once in each subcategory and category.

Table 36. Subjects with Dissection Related Adverse Events within 365 Days

	SAE		AE (Non-Serious)	
Category	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**
Subjects Experiencing One or More AEs[2]	28.0% (14/50)	10.9% (5/46)	4.0% (2/50)	2.2% (1/46)
Gastrointestinal Disorders	4.0% (2/50)	--	--	--
Ileus	2.0% (1/50)	--	--	--
Intestinal Ischaemia	2.0% (1/50)	--	--	--
General Disorders And Administration Site Conditions	--	2.2% (1/46)	2.0% (1/50)	--
Malaise	--	--	2.0% (1/50)	--
Continued Perfusion from a Branch Vessel requiring Treatment	--	2.2% (1/46)	--	--
Procedural Complications[3]	4.0% (2/50)	--	--	--
Nerve Injury	2.0% (1/50)	--	--	--
Stent-Graft Endoleak	2.0% (1/50)	--	--	--

Table 36. Subjects with Dissection Related Adverse Events within 365 Days

	SAE		AE (Non-Serious)	
Category	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**
Abnormal Lab Values	2.0% (1/50)	--	--	2.2% (1/46)
Weight Decreased	--	--	--	2.2% (1/46)
White Blood Cell Count Increased	2.0% (1/50)	--	--	--
Musculoskeletal And Connective Tissue Disorders	4.0% (2/50)	--	--	2.2% (1/46)
Muscular Weakness	2.0% (1/50)	--	--	--
Pain In Extremity	--	--	--	2.2% (1/46)
Rhabdomyolysis	2.0% (1/50)	--	--	--
Nervous System Disorders	10.0% (5/50)	--	--	--
Cerebral Ischaemia	2.0% (1/50)	--	--	--
Cerebrovascular Accident	4.0% (2/50)	--	--	--
Monoplegia	2.0% (1/50)	--	--	--
Paralysis	2.0% (1/50)	--	--	--
Paraplegia	2.0% (1/50)	--	--	--
Psychiatric Disorders	--	--	--	2.2% (1/46)
Depression	--	--	--	2.2% (1/46)
Mental Status Changes	--	--	--	2.2% (1/46)
Renal And Urinary Disorders	6.0% (3/50)	2.2% (1/46)	--	--
Renal Failure Acute	6.0% (3/50)	2.2% (1/46)	--	--
Respiratory, Thoracic And Mediastinal Disorders	2.0% (1/50)	--	--	--
Haemothorax	2.0% (1/50)	--	--	--
Vascular Disorders	8.0% (4/50)	8.7% (4/46)	2.0% (1/50)	2.2% (1/46)
Aortic Aneurysm	--	4.3% (2/46)	--	--
Aortic Disorder	--	--	--	2.2% (1/46)
Retrograde Type A Aortic Dissection	2.0% (1/50)	2.2% (1/46)	--	--
Haemorrhage	2.0% (1/50)	--	--	--
Hypertension	--	2.2% (1/46)	2.0% (1/50)	--
Peripheral Arterial Occlusive Disease	--	--	2.0% (1/50)	--
Peripheral Vascular Disorder	2.0% (1/50)	--	--	--

Table 36. Subjects with Dissection Related Adverse Events within 365 Days

	SAE		AE (Non-Serious)	
Category	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**	**0 to 30 Days % (m/n)[1]**	**31 to 365 Days % (m/n)[1]**
Subclavian Artery Embolism	2.0% (1/50)	--	--	--

[1]m = number of subjects experiencing one or more dissection related adverse events in a category, n = number of subjects who experienced a dissection related adverse event or who died during the interval, or who were followed at least until the lower endpoint of the interval.
[2]A subject may report multiple adverse events and in different categories; hence, number of subjects in each category may not be the sum of those in each subcategory. Each subject was only counted once in each subcategory and category.
[3]Listed as dissection-related as per site reports.

Additional Adverse Event Information

In order to provide further clarity on adverse events of particular interest in the setting of endovascular treatment of acute complicated Type B aortic dissection, further detailed information has been compiled on stroke, spinal cord ischemia, and aortic dissection events subsequent to the initial endovascular procedure and reported in **Table 37**.

Stroke was reported in 3 subjects in the Medtronic Dissection Trial (6%): all occurring within the first 30 days after treatment. These were classified as serious events and were reported in **Tables 31, 32, 35** and **37** as cerebrovascular accidents. Events classified as stroke could have been identified by clinical symptoms that may or may not have included a follow-up evaluation by a neurologist, radiographic imaging or a combination of both types of assessments (unless otherwise noted). As opposed to cerebrovascular ischemia, where a narrowing of a vessel is seen on imaging, a CVA is an infarct where there is no flow through the vessel.

One transient spinal cord ischemia event was observed in the Medtronic Dissection Trial.

A total of three paraplegia/monoplegia events were observed in the Medtronic Dissection Trial.

Progressive aortic dissection (retrograde type A dissection) was reported in a total of two subjects in the Medtronic Dissection Trial.

Table 37. SAEs of Interest in the Treatment of Type B Aortic Dissection

Subject ID	Days to AE	AE Term	Outcome

Stroke			
00059-001	7	Cerebrovascular accident	Resolved without treatment
00141-001	1	Cerebrovascular accident	Unresolved at time of subject's death
00005-008	2	Cerebrovascular accident	Unresolved at time of subject's death
Spinal Cord Ischemia			
00332-002	5	Transient spinal cord ischemia	Resolved with medication
Paraplegia/Monoplegia/Paraparesis			
00005-008	2	Paralysis	Unresolved at time of subject's death
00223-001	1	Monoplegia	Above the knee amputation, Event remains unresolved
00328-003	27	Paraplegia	Unresolved, not being treated further
Retrograde Type A Dissection			
00020-002	5	Aortic dissection	Open repair of retrograde type A dissection, Recovered with treatment
00059-004	56	Aortic dissection	Open repair of retrograde type A dissection, Recovered with treatment

2. Effectiveness Results

To assess the performance of the Valiant Thoracic Stent Graft, the Medtronic Dissection Trial collected information on the secondary observations summarized above. In addition, the following device assessments were collected by the sites and verified by the independent core laboratory:

- False lumen thrombosis status
- Aortic remodeling
- Endoleaks
- Technical observations at follow-up

This section includes summary information on these secondary observations and additional information on continuing or new false lumen perfusion.

False Lumen Thrombosis Status

The false lumen thrombosis status was measured by the core lab in three (3) aortic segments: stented segment (V1), bottom of the stent to the celiac artery (V2) and celiac artery to the aortic bifurcation (V3). Baseline measurements were obtained from the first post-operative images, not from pre-treatment images. Core lab and site reported false lumen thrombosis status are listed in **Tables 38** and **39**.

Over the stented aortic segment (V1), the core lab reported partial or complete thrombosis of the false lumen in 87.5% of the subjects at the first post-procedural CT (partial in 45.0% and complete in 42.5%). This number increased to 97.0% (partial in 36.4% and complete in 60.6%) and 90.9% (partial in 18.2% and complete in 72.7%) of the subjects at the 6 and 12-month visits. Thrombosis status reported by the sites indicated 65.1% of the subjects had a partially or a completely thrombosed false lumen at

the first post-procedural CT (partial in 30.2% and complete in 34.9%). The percentage remained high at more than 79% at both the 6 and 12-month visits (partial in 30.3% and complete in 45.5% at 6 months; partial in 14.7% and complete in 64.7% at 12 months).

Over the aortic segment between the distal end of the stent-graft and the ostium of the celiac trunk (V2), the core lab and the sites reported a partial or complete thrombosis of the false lumen in 41.7% and 37.5% at the first post-procedural CT respectively. At 6 months, the core lab and the sites reported that 61.3% and 40.6% of the subjects had a completely or partially thrombosed false lumen. Both the core lab and the sites reported complete or partial thrombosis in more than 60% of the subjects at 12 months.

Over the segment between the ostium of the celiac trunk and the aortic bifurcation (V3), the core lab and the sites reported a partial or complete thrombosis of the false lumen in 39.5% and 24.4% of the subjects respectively. At 6 months, 51.7% and 42.0% of the subjects had a completely or partially thrombosed false lumen as reported by the core lab and the sites respectively. These numbers were reported as 48.2% and 46.9% at the 12-month visit for the core lab and the sites respectively.

Thirty five of the 49 subjects (in whom the data was available) had a dissection that extended to or past the aortic bifurcation into the iliac or femoral arteries. Among these subjects, 18 subjects had at least one re-entry tear, 10 of whom had three (3) or more re-entry tears. Not all re-entry tears were covered in these subjects. This may have contributed to the false lumen remaining patent in a higher percentage of subjects outside the stented region. Changes in the false lumen volume also followed similar trends in the areas outside the stented region.

Table 38. Core Lab Reported False Lumen Thrombosis Status

Thrombosis Status[1]	**Baseline[2] % (m/n)**	**6-Month Follow-up % (m/n)**	**12-Month Follow-up % (m/n)**
Stented Segment (V1)			
Patent	12.5% (5/40)	3.0% (1/33)	9.1% (3/33)
Partially Thrombosed	45.0% (18/40)	36.4% (12/33)	18.2% (6/33)
Thrombosed	42.5% (17/40)	60.6% (20/33)	72.7% (24/33)
Bottom of Stent to the Celiac Artery (V2)			
Patent	58.3% (21/36)	38.7% (12/31)	35.5% (11/31)
Partially Thrombosed	27.8% (10/36)	32.3% (10/31)	25.8% (8/31)
Thrombosed	13.9% (5/36)	29.0% (9/31)	38.7% (12/31)
Celiac to Bifurcation (V3)			
Patent	60.5% (23/38)	48.3% (14/29)	51.7% (15/29)
Partially Thrombosed	26.3% (10/38)	37.9% (11/29)	31.0% (9/29)

Table 38. Core Lab Reported False Lumen Thrombosis Status

Thrombosis Status[1]	Baseline[2] % (m/n)	6-Month Follow-up % (m/n)	12-Month Follow-up % (m/n)
Thrombosed	13.2% (5/38)	13.8% (4/29)	17.2% (5/29)

[1] Based on number of ITT subjects with available data
V1= the stented segment of the aorta
V2= the aortic segment between the distal end of the stent graft and the ostium of the celiac trunk
V3= the segment between the ostium of the celiac trunk and the aortic bifurcation
[2] Baseline image is the first post-procedure image
m = number of subjects in category, n = number of subjects with available values
Core Lab Reported Table

Table 39. Site Reported False Lumen Thrombosis Status

Thrombosis Status[1]	Baseline[2] % (m/n)	6-Month Follow-up % (m/n)	12-Month Follow-up % (m/n)	2-Year Follow-up % (m/n)	3-Year Follow-up % (m/n)	4-Year Follow-up % (m/n)	5-Year Follow-up % (m/n)
Stented Segment (V1)							
Patent	34.9% (15/43)	24.2% (8/33)	20.6% (7/34)	35.7% (5/14)	--	NA	NA
Partially Thrombosed	30.2% (13/43)	30.3% (10/33)	14.7% (5/34)	21.4% (3/14)	--	NA	NA
Thrombosed	34.9% (15/43)	45.5% (15/33)	64.7% (22/34)	42.9% (6/14)	100.0% (1/1)	NA	NA
Bottom of Stent to the Celiac Artery (V2)							
Patent	62.5% (25/40)	59.4% (19/32)	38.7% (12/31)	38.5% (5/13)	--	NA	NA
Partially Thrombosed	27.5% (11/40)	28.1% (9/32)	32.3% (10/31)	38.5% (5/13)	100.0% (1/1)	NA	NA
Thrombosed	10.0% (4/40)	12.5% (4/32)	29.0% (9/31)	23.1% (3/13)	--	NA	NA
Celiac to Bifurcation (V3)							
Patent	75.6% (31/41)	58.1% (18/31)	53.1% (17/32)	42.9% (6/14)	100.0% (1/1)	NA	NA
Partially Thrombosed	17.1% (7/41)	35.5% (11/31)	37.5% (12/32)	50.0% (7/14)	--	NA	NA

Table 39. Site Reported False Lumen Thrombosis Status

Thrombosis Status[1]	Baseline[2] % (m/n)	6-Month Follow-up % (m/n)	12-Month Follow-up % (m/n)	2-Year Follow-up % (m/n)	3-Year Follow-up % (m/n)	4-Year Follow-up % (m/n)	5-Year Follow-up % (m/n)
Thrombosed	7.3% (3/41)	6.5% (2/31)	9.4% (3/32)	7.1% (1/14)	--	NA	NA

[1]Based on number of ITT subjects with available data
V1 = the stented segment of the aorta
V2 = the aortic segment between the distal end of the stent graft and the ostium of the celiac trunk
V3 = the segment between the ostium of the celiac trunk and the aortic bifurcation
[2]Baseline image is the first post-procedure image
m = number of subjects in category, n = number of subjects with available values

Aortic Remodeling

For purposes of all diameter and volume changes, baseline measurements are obtained from the first post-operative images, not from pre-treatment images. All cases reported complete coverage of the primary tear with a patent graft at the conclusion of the procedure. Thus the changes in true and false lumen (diameter and/or volume) may not be as significant as a comparison between pre- and post-stent graft implant procedure.

The maximum true and false lumen diameters were measured at the same location as the maximum overall aortic diameter within the stented region. However, the location of the maximum aortic diameter over the stent graft may vary from one visit to the next. Tables 10-38 and 10-39 list Core Lab and site reported aortic remodeling based on 5mm change.

Increase in True Lumen Diameter: Both the sites and the core lab reported that the true lumen diameter remained stable or increased (by at least 5.0 mm) compared to baseline in more than 90% of the subjects at 6 and 12-month visits.

Decrease in False Lumen Diameter: Both the sites and the core lab reported that the false lumen remained stable or decreased (by at least 5.0 mm) compared to baseline in at least 75% of the subjects at 6 and 12-month visits.

Change in Total Aortic Diameter: The sites and the core lab reported that the total aortic diameter remained either stable or decreased (by at least 5.0 mm) compared to baseline in more than 75% of subjects at the 6-month visit and in 85.3% (site reported) and 78.1% (core lab reported) of the subjects at the 12-month visit.

In those subjects with a decrease in the true lumen diameter at 6 or 12 months, the true lumen volume over the stented region increased by more than 10% per the core lab. No clinical issues were reported.

Table 40. Core Lab Reported Aortic Remodeling Based on 5mm Change

Thoracic Dissection Measurements[1]	Baseline[2] % (m/n)	6-Month Follow-up % (m/n)	12-Month Follow-up % (m/n)
Change from Baseline[2] in the Maximum True Lumen Diameter over the Length of the Stent Graft			
Decrease[3]	NA	6.7% (2/30)	6.9% (2/29)
Stable	NA	60.0% (18/30)	58.6% (17/29)
Increase	NA	33.3% (10/30)	34.5% (10/29)
Change from Baseline[2] in the Maximum False Lumen Diameter over the Length of the Stent Graft			
Decrease[3]	NA	40.0% (12/30)	44.8% (13/29)
Stable	NA	46.7% (14/30)	31.0% (9/29)
Increase	NA	13.3% (4/30)	24.1% (7/29)
Change from Baseline[2] in the Maximum Total Descending Thoracic Aortic Diameter (mm)			
Decrease[3]	NA	18.2% (6/33)	25.0% (8/32)
Stable	NA	63.6% (21/33)	53.1% (17/32)
Increase	NA	18.2% (6/33)	21.9% (7/32)
False Lumen Thrombosis over the Length of the Stent Graft			
Completely Thrombosed	42.5% (17/40)	60.6% (20/33)	72.7% (24/33)
Partially Thrombosed	45.0% (18/40)	36.4% (12/33)	18.2% (6/33)
Patent	12.5% (5/40)	3.0% (1/33)	9.1% (3/33)

[1]Based on number of ITT subjects with available data
[2]Baseline image is the first post-procedure image
[3]Decrease is defined as a 5mm or greater decrease from baseline in measured diameter, increase is defined as a 5mm or greater increase from baseline in measured diameter
m = number of subjects in category, n = number of subjects with available values
Core Lab Reported Table

Table 41. Site Reported Aortic Remodeling Based on 5mm Change

Thoracic Dissection Measurements[1]	Baseline[2] % (m/n)	6-Month Follow-up % (m/n)	12-Month Follow-up % (m/n)
Change from Baseline[2] in the Maximum True Lumen Diameter over the Length of the Stent Graft			
Decrease[3]	NA	6.1% (2/33)	5.9% (2/34)
Stable	NA	54.5% (18/33)	47.1% (16/34)
Increase	NA	39.4% (13/33)	47.1% (16/34)
Change from Baseline[2] in the Maximum False Lumen Diameter over the Length of the Stent Graft			
Decrease[3]	NA	36.4% (12/33)	50.0% (17/34)
Stable	NA	39.4% (13/33)	32.4% (11/34)
Increase	NA	24.2% (8/33)	17.6% (6/34)
Change from Baseline[2] in the Maximum Total Descending Thoracic Aortic Diameter (mm)			
Decrease[3]	NA	35.3% (12/34)	32.4% (11/34)
Stable	NA	41.2% (14/34)	52.9% (18/34)
Increase	NA	23.5% (8/34)	14.7% (5/34)
False Lumen Thrombosis over the Length of the Stent Graft			
Completely Thrombosed	34.9% (15/43)	45.5% (15/33)	64.7% (22/34)
Partially Thrombosed	30.2% (13/43)	30.3% (10/33)	14.7% (5/34)
Patent	34.9% (15/43)	24.2% (8/33)	20.6% (7/34)

[1]Based on number of ITT subjects with available data
[2]Baseline image is the first post-procedure image
[3]Decrease is defined as a 5mm or greater decrease from baseline in measured diameter, increase is defined as a 5mm or greater increase from baseline in measured diameter
m = number of subjects in category, n = number of subjects with available values
Site Lab Reported Table

Changes in aortic diameter at the celiac artery

Increase in True Lumen Diameter: The core lab reported that the true lumen diameter remained stable or increased (by at least 5.0 mm) compared to baseline in 96.6% of the subjects at 6 months and in 93.1% at the 12-month visit.

Decrease in False Lumen Diameter: The core lab reported that the false lumen remained stable or decreased (by at least 5.0 mm) compared to baseline

in 72.4% of the subjects at 6-months and in 79.3% of the subjects at the12-month visit.

Change in Total Aortic Diameter: The core lab reported that the total aortic diameter remained either stable or decreased (by at least 5.0 mm) compared to baseline in 74.2% of subjects at the 6-months and in 67.7% of the subjects at the 12-month visit.

Changes in aortic diameter at the distal renal artery

Increase in True Lumen Diameter: The core lab reported that the true lumen diameter remained stable or increased (by at least 5.0 mm) compared to baseline in more than 93.1% of the subjects at 6 months and in 92.6% of the subjects at the 12-month visit.

Decrease in False Lumen Diameter: The core lab reported that the false lumen remained stable or decreased (by at least 5.0 mm) compared to baseline in more than 79.3% of the subjects at 6 months and in 74.1% of the subjects at the 12-month visit.

Change in Total Aortic Diameter: The core lab reported that the total aortic diameter remained either stable or decreased (by at least 5.0 mm) compared to baseline in 96.7% of subjects at the 6-month visit and in 82.1% of the subjects at the 12-month visit.

Changes in aortic diameter over the length of the aorta

Maximum diameter was measured anywhere along the thoracic aorta. The maximum true and false lumen diameters were measured at the same location as the maximum aortic diameter as the inner wall to inner wall distance along the minor axis and major axis, respectively.

The location of the maximum aortic diameter may have varied from one visit to the next. Although the true lumen, false lumen and maximum aortic diameters are compared across time points, it is important to note that they may not have been measured at the same location in the aorta over time.

Subjects whose location of maximum aortic diameter occurred in the stented region at baseline:

Increase in True Lumen Diameter: Both the sites and the core lab reported that the true lumen diameter remained stable or increased (by at least 5.0 mm) compared to baseline in 86.7% (site reported) and 92.3% (core lab reported) of the subjects at the 12-month visit.

Decrease in False Lumen Diameter: The sites and the core lab reported that false lumen diameter remained either stable or decreased (by at least 5.0 mm) compared to baseline in more than 75% (both sites and core lab) of the subjects at the 12-month visit.

Change in Total Aortic Diameter: The sites and the core lab reported that the total aortic diameter remained either stable or decreased (by at least 5.0

mm) compared to baseline in 93.3% (site reported) and 78.6% (core lab reported) of the subjects at the 12-month visit.

Subjects whose location of maximum aortic diameter occurred outside the stented region at baseline:

Increase in True Lumen Diameter: The core lab reported that the true lumen diameter remained stable or increased (by at least 5.0 mm) compared to baseline in two (2) of the three (3) subjects at the 12-month visits. The sites reported that the true lumen diameter remained stable or increased (by at least 5.0 mm) compared to baseline in two (2) of the four (4) subjects at the 12-month visit.

Decrease in False Lumen Diameter: The core lab reported that the false lumen diameter remained stable or decreased (by at least 5.0 mm) compared to baseline in 1 (one) of the 3 (three) subjects at the 12-month visit. The sites reported that the false lumen diameter remained stable or decreased (by at least 5.0 mm) compared to baseline in one (1) of the four (4) subjects at the 12-month visit.

Change in Total Aortic Diameter: The core lab reported that the total aortic diameter remained stable or decreased (by at least 5.0 mm) compared to baseline in two (2) of the four (4) subjects at the 12-month visit. The sites reported that the total aortic diameter remained stable or decreased (by at least 5.0 mm) compared to baseline in one (1) of the four (4) subjects at the 12-month visit.

Change in True and False Lumen Volume

The volumes of the false and true lumens were measured by the core lab over the entire aorta (from LSA to aortic bifurcation) and in three (3) aortic segments: stented segment (V1), bottom of the stent to the celiac artery (V2) and celiac artery to the aortic bifurcation (V3). **Table 42** lists Core Lab reported 10% change in false and true lumen volumes at six and twelve months. It should be noted that the core lab was unable to obtain volume measurements in many cases because of incomplete anatomy, inability to combine CTs with even slightly different slice thicknesses and / or information from CTs on different dates.

Volume Regression of the False Lumen: Over the length of the stent graft (V1), the volume of the false lumen decreased (by at least 10%) in 94.4% of the subjects at 12 months. The false lumen volume over V2 and the entire aortic segment remained stable or decreased (by at least 10%) in more than 80% of the subjects at 12 months. The false lumen volume over V3 remained stable or decreased (by at least 10%) in 50% of the subjects at the 12-month visit.

Volume Expansion of the True Lumen: Over the length of the stent graft (V1), the true lumen volume remained stable or increased (by at least 10%) in 100% of the subjects at 12 months. The true lumen volumes over V2, V3 and the segment from the LSA to the aortic bifurcation followed similar trends in that each

remained stable or increased (by at least 10%) in more than 84% of the subjects at the 12-month visit.

This continued expansion of the true lumen and the regression of the false lumen demonstrate favorable remodeling of the aorta.

Table 42. Core Lab Reported 10% Change in False and True Lumen Volumes

Change in False and True Lumen Volume[1]	6 Month Change from Baseline[2] % (m/n)	12 Month Change from Baseline[2] % (m/n)
False Lumen (FL)		
FL Volume from LSA to Aortic Bifurcation		
Decrease[3]	56.5% (13/23)	61.9% (13/21)
Stable	8.7% (2/23)	19.0% (4/21)
Increase	34.8% (8/23)	19.0% (4/21)
FL Volume of Stented Segment (V1)		
Decrease[3]	85.0% (17/20)	94.4% (17/18)
Stable	--	--
Increase	15.0% (3/20)	5.6% (1/18)
FL Volume Aortic Segment Stent to Celiac Artery (V2)		
Decrease[3]	61.9% (13/21)	77.3% (17/22)
Stable	9.5% (2/21)	13.6% (3/22)
Increase	28.6% (6/21)	9.1% (2/22)
FL Volume Aortic Segment Celiac Artery to Bifurcation (V3)		
Decrease[3]	30.4% (7/23)	36.4% (8/22)
Stable	13.0% (3/23)	13.6% (3/22)
Increase	56.5% (13/23)	50.0% (11/22)
True Lumen (TL)		
TL Volume from LSA to Aortic Bifurcation		
Decrease[3]	--	4.2% (1/24)
Stable	7.7% (2/26)	8.3% (2/24)
Increase	92.3% (24/26)	87.5% (21/24)
TL Volume of Stented Segment (V1)		
Decrease[3]	--	--
Stable	3.4% (1/29)	--
Increase	96.6% (28/29)	100.0% (29/29)
TL Volume Aortic Segment Stent to Celiac Artery (V2)		
Decrease[3]	8.0% (2/25)	16.0% (4/25)
Stable	8.0% (2/25)	4.0% (1/25)
Increase	84.0% (21/25)	80.0% (20/25)
TL Volume Aortic Segment Celiac to Bifurcation (V3)		
Decrease[3]	11.1% (3/27)	12.0% (3/25)
Stable	66.7% (18/27)	36.0% (9/25)

Table 42. Core Lab Reported 10% Change in False and True Lumen Volumes		
Change in False and True Lumen Volume[1]	**6 Month Change from Baseline[2] % (m/n)**	**12 Month Change from Baseline[2] % (m/n)**
Increase	22.2% (6/27)	52.0% (13/25)

[1]Based on number of ITT subjects with available data
[2]Baseline image is the first post-procedure image
[3]Decrease is defined as a 10% or greater decrease from baseline in measured volume, increase is defined as a 10% or greater increase from baseline in measured volume
m = number of subjects in category, n = number of subjects with available values
Core Lab Reported Table

Continuing or New False Lumen (FL) Perfusion over the Stented Segment

The false lumen was completely thrombosed in 72.7% of the subjects at 12 months. Of the nine (9) subjects who had perfusion of the false lumen at the 12-month visit, seven (7) were cases of continuing perfusion and one (1) was a case of new false lumen perfusion. The type of perfusion could not be ascertained in one (1) subject. False lumen perfusion sources included intercostal arteries and the distal aorta or its branches. In more than 25% of the subjects, the source was not identified at the 12-month visit.

Endoleaks

A summary of the endoleaks reported by both the sites and the core lab from implant through 12 months is reported in **Table 43** and **Table 44.**

Table 43. Core Lab Reported Endoleaks				
Endoleaks[1]	**Discharge Follow-up % (m/n)**	**1-Month Follow-up % (m/n)**	**6-Month Follow-up % (m/n)**	**12-Month Follow-up % (m/n)**
Type Ia (proximal end)	--	--	6.1% (2/33)	--
Type Ib (distal end)	--	--	--	--
Type II	--	--	--	--
Type III	--	--	--	--
Type IV	--	--	--	--
Endoleak Type Undetermined	--	--	--	3.0% (1/33)

[1]Based on number of implanted subjects with available data
m = number of subjects in category, n = number of subjects with available values
Core Lab Reported Table

Table 44. Site Reported Endoleaks

Endoleaks[1]	Procedure[2] % (m/n)	Discharge Follow-up % (m/n)	1-Month Follow-up % (m/n)	6-Month Follow-up % (m/n)	12-Month Follow-up % (m/n)
Type Ia (proximal end)	--	6.1% (2/33)	10.0% (4/40)	3.0% (1/33)	--
Type Ib (distal end)	--	--	--	--	--
Type II	6.0% (3/50)	3.0% (1/33)	2.5% (1/40)	--	--
Type III	--	--	--	--	--
Type IV	--	--	--	--	--
Endoleak Type Undetermined	--	3.0% (1/33)	--	3.1% (1/32)	--

[1]Based on number of implanted subjects with available data
[2]Unresolved endoleaks only
m = number of subjects in category, n = number of subjects with available values

Technical Observations

Imaging for subjects that completed the discharge, one-month, six-month and twelve-month follow-up intervals were reviewed for technical observations by both the core lab and the sites. Site and Core Lab reported technical observations by device imaging assessment are listed in **Table 45** and **Table 46**. The stent graft maintained patency and integrity at all of the time intervals. In addition, there was no evidence of misaligned deployment, stent graft twisting, stent graft kinking, or stent graft fracture.

Table 45. Site Reported Technical Observations by Device Imaging Assessments

Technical Observations[1]	Discharge Follow-up % (m/n)	1-Month Follow-up % (m/n)	6-Month Follow-up % (m/n)	12-Month Follow-up % (m/n)	2-Year Follow-up % (m/n)	3-Year Follow-up % (m/n)	4-Year Follow-up % (m/n)	5-Year Follow-up % (m/n)
Stent Graft Kinking	--	--	--	--	--	--	NA	NA
Stent Graft Twisting	--	--	--	--	--	--	NA	NA
Evidence of Misaligned Deployment	--	--	--	--	--	--	NA	NA
Stent Graft Fracture	--	--	--	--	--	--	NA	NA
Loss of Integrity	--	--	--	--	--	--	NA	NA
Loss of Patency	--	--	--	--	--	--	NA	NA

Table 45. Site Reported Technical Observations by Device Imaging Assessments

Technical Observations[1]	Discharge Follow-up % (m/n)	1-Month Follow-up % (m/n)	6-Month Follow-up % (m/n)	12-Month Follow-up % (m/n)	2-Year Follow-up % (m/n)	3-Year Follow-up % (m/n)	4-Year Follow-up % (m/n)	5-Year Follow-up % (m/n)
Migration > 10mm from Baseline[2]	NA	--	--	--	--	--	NA	NA
Proximal Migration	NA	--	--	--	--	--	NA	NA
Distal Migration	NA	--	--	--	--	--	NA	NA

[1]Based on number of ITT subjects with available data
[2]Baseline image is the first post-procedure image
m = number of subjects in category, n = number of subjects with available values

Table 46. Core Lab Reported Technical Observations by Device Imaging Assessments

Technical Observations[1,2]	Discharge Follow-up % (m/n)	1-Month Follow-up % (m/n)	6-Month Follow-up % (m/n)	12-Month Follow-up % (m/n)
Stent Graft Kinking	0.0% (0/8)	0.0% (0/39)	0.0% (0/26)	0.0% (0/27)
Stent Graft Twisting	0.0% (0/8)	0.0% (0/39)	0.0% (0/26)	0.0% (0/27)
Stent Graft Fracture	0.0% (0/7)	0.0% (0/38)	0.0% (0/26)	0.0% (0/27)
Loss of Integrity	0.0% (0/7)	0.0% (0/32)	0.0% (0/24)	0.0% (0/27)
Loss of Patency	0.0% (0/34)	0.0% (0/39)	0.0% (0/33)	0.0% (0/32)

[1]Based on number of ITT subjects with available data
[2] No current definition for Migration in a dissection population has been published. The Core Lab and the Sponsor have agreed that the migration definition for an aneurysm population is not appropriate, therefore migration has not been reported in this table.
m = number of subjects in category, n = number of subjects with available values
Core Lab Reported Table

3. Gender Analysis

Eighty percent of the subjects enrolled in the Medtronic Dissection Trial were male. The mean subject age was approximately 56.6 ± 11.2 years in the male subjects and 59.7 ± 18.6 years in the female subjects.

Primary Endpoint

All-cause mortality within 30 days by gender in the Medtronic Dissection Trial subjects was 10.0% in males and 0% in females compared to 11.3% in males and 8.7% in females in the SVS MAF group.

Secondary Observations

The device was delivered and deployed successfully in all 50 subjects (100%) enrolled in the Medtronic Dissection Trial. The proximal entry tear was successfully covered in all subjects. There were no incidents of post-operative rupture through 12 months.

Forty of the 50 subjects enrolled in the study were male. Four (4) male subjects underwent secondary endovascular procedures within 12 months. All the reported deaths and secondary endovascular procedures occurred in male subjects. Both subjects who underwent open repair for retrograde Type A dissections and both subjects who underwent LSA bypass as a secondary procedure were male.

In addition, 18 of the 19 subjects who experienced an SAE at 30 days and 22 of the 23 subjects who experienced an SAE at 12 months were male. There were seven (7) deaths in the study within 12 months. All deaths occurred in male subjects. Of the nine (9) subjects who had perfusion of the false lumen at the 12-month visit, seven (7) were male.

4. Data Post 12 Months

As of the data cut-off date (May 30, 2013), seventeen subjects (17) had been followed through 2 years and one (1) subject has been followed through 3 years. Twenty three (23) subjects had not reached their 2-year visit. One (1) subject died on day 432 due to natural causes. The death was adjudicated by the CEC to be not related to the device, procedure or dissection. No ruptures, conversions to surgical repair, stent graft occlusions, or SAEs related to the device, procedure or aortic disease have been reported past 12 months. In one (1) subject, the site reported an endoleak, type undetermined. One subject underwent an additional endovascular procedure for continued perfusion of the false lumen, at which time two (2) additional stent grafts were implanted. The site reported the event as resolved at the time of the data cut-off for this summary.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 59 investigators at 16 active sites, none of whom were full-time or part-time employees of the sponsor and 5 investigators had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below: (Please note that Financial Disclosure Forms from investigators either from sites that were closed or that have exited the study (without participating in implants for any of the subjects enrolled in Medtronic Dissection Trial) have not been collected.)

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 5
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A. Medtronic is aware of three studies of endovascular repair of Type B dissection using the Valiant device outside the US.

The VIRTUE study enrolled 100 subjects, of which 50 had acute dissection, 24 had sub-acute dissection and 26 had chronic dissection. Subjects have been followed to the 36-month post-implantation interval.

The Valiant Captivia OUS post-market registry had 100 subjects enrolled as of August 13, 2012. Of the 100 subjects, 49 were enrolled with aneurysm, 23 had chronic dissection, 19 had acute/sub-acute dissection and nine (9) had other indications. These subjects have been followed for 12 months.

The TRAVIATA study (a retrospective review of data on all subjects treated with Valiant at 4 German centers, who had at least 12 month follow up) enrolled 92 total subjects, 52 subjects had degenerative aneurysm, 32 subjects had aortic dissection, and four subjects had traumatic aortic injury.

The three studies/registries account for approximately 175 subjects who received the Valiant device for dissection. Of these, 100 subjects were followed for three years and the rest were followed for at least one year. These were observational studies intended to collect clinical performance and safety data for Type B dissection subjects treated with the Valiant stent graft.

Retrograde Type A dissection occurred in two (2) acute Type B dissection subjects in the VIRTUE Registry, one (1) acute and one (1) chronic Type B dissection subject in the Valiant Captivia OUS Registry and one (1) acute Type B dissection subject in the TRAVIATA Registry. Paralysis occurred in two (2) acute and one (1) chronic Type B dissection subjects in the VIRTUE Registry and none of the subjects in the Valiant Captivia OUS Registry or TRAVIATA Registry. Stroke occurred in five (5) acute Type

B dissection subjects in the VIRTUE Registry and none of the subjects in the Valiant Captivia OUS Registry or TRAVIATA Registry.

No new safety concerns have been identified in any of these studies and most patients continue to be followed under the clinical study or as the standard of care of patients with aortic endograft with a yearly CT scan. Table 47 below provides a summary of the major outcomes for patients in these registries.

Table 47. Major Outcomes for Dissection Patients in VIRTUE, Valiant Captivia OUS and TRAVIATA Registries

	VIRTUE Registry - Major Outcomes (36 months of follow-up)			Valiant Captivia OUS Registry – Major Outcomes (12 months of follow-up)		TRAVIATA Registry – Major Outcomes (patients were followed for at least 1 year)
	Acute Type B Dissection	**Sub-Acute Type B Dissection**	**Chronic Type B Dissection**	**Acute Type B Dissection**	**Chronic Type B Dissection**	**Acute Type B Dissection**
No. of subjects	50	24	26	19	23	32
Retrograde Type A Dissection	2	0	0	1	1	1
Deaths	9	1	6	4	3	0
Paralysis	2	0	1	0	0	0 (30-day)
Stroke	5	0	0	0	0	0 (30-day)
Rupture	1	0	1	0	0	1 (30-day)
Conversion to open repair	0	0	1	0	0	0
Spinal cord Ischemia	1	0	2	0	0	1 (30-day)
# of subjects needing dissection related re-interventions	12	7	11	4	4	4

B. Justification for Indication

Diseases or injuries of the descending thoracic aorta can be classified as either isolated lesions or Type B dissections. The Valiant Captivia is currently approved for the treatment of isolated lesions (excluding dissections) of the descending thoracic aorta (P100040/S008). This PMA supplement expands the indications for use to include treatment of all lesions of the descending thoracic aorta including dissections.

There are two types of Type B dissections: acute and chronic. Acute dissections have historically been defined as dissections that are diagnosed within 14 days of symptom onset. Acute dissections can be sub-divided into complicated and uncomplicated dissections. Acute complicated dissections require intervention in order to resolve emergent complications that cannot be managed with medication alone, such as malperfusion or rupture, while acute uncomplicated dissections are treated in order to resolve less emergent conditions, such as uncontrollable pain, chronic hypertension, or impending rupture. The treatment goal for all acute Type B dissections is to cover the primary entry tear, repressurize and expand the true lumen, and depressurize the false lumen, which promotes false lumen thrombosis in the treated length.

The safety and effectiveness of the Valiant Captivia Device for the treatment of acute complicated Type B dissections was established with the Medtronic Dissection Trial. Because the Valiant Captivia Device was evaluated in a more compromised patient population as compared to patients with uncomplicated dissections and there was no suggestion that the device would be less safe or effective in the uncomplicated population, this information can be extrapolated to address the safety and effectiveness of the broader population of patients with acute dissections.

Chronic dissections have historically been defined as dissections that are diagnosed more than 14 days after symptom onset; chronic dissections started as acute uncomplicated dissections that were medically managed only or untreated. The primary reason for intervention is often aneurysmal dilation of the false lumen (impending rupture), uncontrollable pain, or acute extension of dissection (acute or chronic) leading to acute phase complications such as malperfusion. As aneurysmal dilation of the false lumen is the most common reason for intervention of chronic dissections, the conditions that lead to intervention are often similar to aneurysms. These conditions include a total aortic diameter of $\geq$ 5.5cm, rapid growth or impending rupture of the false lumen, or a symptomatic aneurysmal false lumen. The treatment goal for chronic Type B dissections is the same as for acute Type B dissections: cover the primary entry tear, repressurize and expand the true lumen, and depressurize the false lumen, which promotes false lumen thrombosis in the treated length. When treating chronic Type B dissections with endovascular devices, many of the considerations during treatment are similar to those of aneurysm patients as well as acute Type B dissection patients, including the risk of endoleaks leading to repressurization of the false lumen, distal tears allowing continued perfusion of the false lumen, and sufficient length of coverage to optimize exclusion of arterial flow to the lesion. The cumulative data from the aneurysm clinical study (VALOR II) and the Medtronic Dissection Trial provide physicians with significant knowledge that will assist with treatment of chronic Type B dissections including IFU warnings and precautions around treatment of these patients generated from the conclusions of these studies. This study data, combined with peer reviewed literature, supplements known safety information regarding the endovascular treatment of chronic Type B dissections. Table 48 shows a selection of peer reviewed articles with longer-term follow-up on endovascular treatment of patients with chronic Type B dissections. These data are consistent with other published literature on endovascular treatment of chronic Type B dissections and show low perioperative mortality rates and high mid-term survival rates for this patient population. Reasonable assurance of

effectiveness of the treatment of chronic Type B dissections can be inferred from the VALOR II and the Medtronic Dissection Trial data. In addition, reasonable assurance of safety of the treatment of chronic Type B dissections can be inferred from a combination of the VALOR II and the Medtronic Dissection Trial data as well as from peer reviewed literature.

Table 48. Literature Review for Endovascular Treatment of Chronic Type B Dissections

Publication	N	Follow-up	Operative Mortality	Mid-term Survival
Mani [26]	58	48 months	5%	57%
Sayer[27]	40	30 months	7.5%	66.5%
Parsa[28]	51	60 months	0	78%
Oberhuber[29]	19	13 months	0	N/A
Manning[30]	10	56 months	0	100%

Data from multiple studies (VALOR II, Valiant Captivia OUS post-market registry, and TRAVIATA) have demonstrated reasonable assurance of safety in the endovascular treatment of descending thoracic aortic aneurysms. The RESCUE traumatic transection study extended the assurance of safety to isolated lesions of the descending thoracic aorta; the Medtronic Dissection Trial and VIRTUE study further extended the assurance of safety to include Type B dissections. The data from the combination of these studies, supported and substantiated with peer reviewed literature, demonstrate reasonable assurance of safety in the endovascular treatment of all lesions of the descending thoracic aorta.

Effectiveness of the treatment of aneurysms, traumatic transections, and acute complicated Type B dissections was also established with all of the studies that were completed to demonstrate a reasonable assurance of safety. Given the similarities in reasons for treatment and treatment goals, there is reasonable assurance of effectiveness for the treatment of all other descending thoracic aortic diseases and injuries.

In total, clinical experience has shown that a thoracic stent graft can be safely introduced and delivered in patients with various types of aortic pathologies, however; some pathologies (e.g., dissection, rupture) carry additional inherent risk. The clinical experience also shows that thoracic stent grafts can perform their intended purpose in a reliable fashion without causing significant detriment to the patient both in the short and mid-term following intervention. A general indication for the treatment of all lesions of the descending thoracic aorta allows physicians to choose endovascular repair with an on-label indication if they feel it is the best option for their patients based on available safety and effectiveness data.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

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. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The safety and effectiveness of the Valiant Thoracic Stent Graft for lesions of the descending thoracic aorta (DTA) are not based on the Medtronic Dissection Trial alone, but rather on all available data for the Valiant Thoracic Stent Graft to date, including pre-clinical data, data from the aneurysm clinical study (VALOR II), reviewed under PMA P100040, and data from the RESCUE clinical study, reviewed under PMA P100040/S008.

A. Primary Endpoint Conclusion from the Medtronic Dissection Trial

The primary objective was achieved in the Medtronic Dissection Trial, which 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 was less than the performance goal of 25.0%. This compares favorably to both the outcomes reported in the SVS MAF reference group (11.7% at 30-days) and recent literature reports for in-hospital or 30-day open surgical mortality (17.4% to 33.3%)[1,2,3]. There were three (3) additional deaths that occurred within 31 to 365 days of the index procedure. One additional death at day 432 has been reported.

B. Effectiveness Conclusions

All devices in the 50 subjects were successfully delivered and deployed. No misaligned deployment was reported. The proximal entry tear was covered in 100% of the subjects. No migrations were reported by the sites.

Two (2) subjects with reported endoleaks required a secondary endovascular procedure. Retrograde Type A dissection was reported in two (2) subjects. Both were resolved after the subjects underwent open ascending thoracic repair. Stroke was reported in three (3) subjects, one (1) major, one (1) minor and one (1) whose severity was unknown. (The patient was sedated throughout hospitalization; CT data suggested a stroke but the patient died before recovering consciousness.)

Paraplegia was reported in one (1) subject, monoplegia was reported in one (1) subject and paralysis was reported in one (1) subject.

The Medtronic Dissection Trial data demonstrated favorable remodeling of the stented segment of the aorta after TEVAR. There was consistent increase in true lumen diameter and volume and consistent decrease in the false lumen diameter and volume over the endograft segment. Beyond the stented segment, a trend towards positive remodeling was seen.

Of the nine (9) subjects who had perfusion of the false lumen at the 12-month visit, seven (7) were cases of continuing perfusion and one (1) was a case of new false lumen perfusion. The type of perfusion could not be ascertained in one (1) subject.

There were no occurrences of Unanticipated Adverse Device Effects (UADEs). Four (4) subjects required additional secondary endovascular procedures, three (3) involved placing additional endovascular devices and one, an LSA plug.

There were no reported incidents of rupture or conversions to open repair of the descending thoracic aorta.

Investigational sites did not report any device events from the categories of fracture, extrusion/erosion, lumen obstruction, device compression or thrombus. The Core Lab confirmed that none of these device events had occurred. There was no site reported device migration.

The results of the Medtronic Dissection Trial suggest that the Valiant Captivia Device is an effective treatment option for acute complicated Type B aortic dissection.

Information reviewed under separate PMA supplements P100040 and P100040/S008 provided the additional information needed to support the effectiveness of the broader indication of treatment of the descending thoracic aorta.

C. Safety Conclusions

The risks of the device are based on data collected in a clinical study conducted to support PMA approval as described above.

The primary safety endpoint was all-cause mortality at 30 days and the performance goal was met as described above.

Of the adverse events (AEs and SAEs) that occurred within 30 days of the procedure, device-related adverse events were reported in two (2) subjects (4.0%), procedure-related adverse events were reported in seventeen (17) subjects (34%), and dissection-related adverse events were reported in fifteen (15) subjects (30.0%).

Of the adverse events (AEs and SAEs) that occurred within 31 to 365 days of the procedure, device-related adverse events were reported in one (1) subject (2.2%), procedure-related adverse events were reported in two (2) subjects (4.3%), and dissection-related adverse events were reported in five (5) subjects (10.9%).

The rates of conversion to open repair, retrograde Type A dissections, stroke and secondary endovascular procedures observed in the Medtronic Dissection Trial appear to be acceptable for patients presenting with this disease.

Additional safety information was reviewed under the original Valiant PMA P100040 and in supplement P100040/S008 in support of the broader indication of treatment of lesions of the DTA.

D. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above.

Patients diagnosed with descending thoracic aortic dissection are generally managed with a complication-specific approach. Traditionally, dissections associated with no or minimal impact on body systems are treated with a medical regimen focused on strict blood pressure control with the treatment goal to prevent any further

progression of the dissection. However, a recent randomized controlled clinical study published in Circulation Cardiovascular Interventions, concluded that the use of aortic endografts in addition to optimal medical therapy was associated with improved 5-year aorta-specific survival and delayed disease progression. Therefore, the use of endografts in stable Type B dissection with suitable anatomy may be considered to improve late outcome.

For dissections with significant impact on body systems, also referred to as complicated dissections, an intervention is necessary. The types of interventions available for complicated dissections are either open surgical repair, which includes an open thoracotomy that carries significant mortality and morbidity, or endovascular repair.

In the presence of rupture or malperfusion, acute aortic dissection is a real vascular emergency that requires immediate intervention and which has one of the highest mortality rates of the cardiovascular diseases. Conventional open surgical and medical therapies continue to be associated with significant mortality risk which is reported to be as high as 50%. Although open surgery can be performed to repair the dissection entry tear, the operation itself is technically challenging due to the fact that the aortic tissues are very fragile which make it difficult to sew a synthetic graft with adequate anastomosis. Therefore, there are no good alternative treatments for patients presenting with acute complicated Type B aortic dissection.

Patients that survive the acute dissection episode become chronic dissections. Chronic dissections tend to be more like descending thoracic aneurysm in the sense that the indications for interventions are oftentimes related to the size of the aorta. Long-term prognosis of chronic Type B dissection is sobering, with just 60% to 80% survival estimates at 5 years using conservative management because complications and aneurysm expansion are likely. Once the aortic diameter exceeds 5.5 to 6.0 cm, the risk of rupture is estimated at 30% per year. Even if medical therapy is considered the best option for uncomplicated Type B aortic dissection, the effect of medical therapy may delay the expansion of the descending aorta, but would not enhance the remodeling process. Late interventions are often performed in chronic Type B aortic dissection for development of complications, such as aneurysm expansion, progressive/new dissection, and other related adverse events from the unresolved dissection process. Recurrence of symptoms, aneurysmal dilation (total aortic diameter $\geq$ 5.5 cm), or a yearly increase (>4mm) of aortic diameter should be considered signs of instability in the chronic phase and indication for thoracic endovascular repair, or in unsuitable anatomy, indication for open surgery, as the early mortality in complicated chronic Type B aortic dissection is lower with TEVAR compared with open surgery.

Clinical benefit to the acute dissection patient is the immediate restoration of circulation to ischemic tissues or exclusion of an aortic rupture site. Chronic patients will be eligible for a less invasive procedure and enjoy the peri-operative benefits commonly described in a descending aneurysm population. Following endovascular

treatment, patients are able to resume their normal daily activities in a more rapid fashion as compared to patients treated with open surgical repair. Stabilized patients can enter a maintenance phase with their follow-up physician concentrating on blood pressure management and serial observation of the dissection for potential continued progression in other parts of the aorta. Residual risks to the patient remain after Valiant Captivia implant due to the aortic dissection disease process and its potential negative impact on the vascular system. As with all thoracic stent grafts, risks are monitored with serial follow-up evaluations and active physician oversight.

In conclusion, the information presented above and the published medical literature support that the benefits outweigh the risks for using the Valiant Captivia Device for the treatment of aortic dissections and therefore support the modification to the current indications for the device.

E. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

The safety and effectiveness of the treatment of aneurysms, traumatic transections, and acute complicated Type B dissections with the Valiant Captivia has been established with the VALOR II, RESCUE and Medtronic Dissection Trials, respectively. Given the similarities in reasons for treatment and treatment goals, there is reasonable assurance of safety and effectiveness for the treatment of all other descending thoracic aortic diseases and injuries.

The addition of the treatment of dissections in the indications for the Valiant Captivia will provide an on-label, less-invasive treatment option for patients. Based on the available data, it can be assumed that patients will benefit from this treatment option, given the low mortality rate observed in the clinical study.

Based on all data presented, the Valiant Captivia has demonstrated a reasonable assurance of safety and effectiveness in the endovascular repair of the descending thoracic aorta in patients with appropriate vascular anatomy who are candidates for endovascular treatment. However, 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 January 22, 2014. The final conditions of approval cited in the approval order.

In addition to the annual reporting conditions outlined in the approval order, the sponsor has agreed to conduct a post-approval study (PAS) to evaluate freedom from dissection-related mortality in patients followed through 5 years post implantation as described below:

Valiant Dissection Post-Approval Study: The study will be a prospective, single arm registry of patients treated for thoracic dissection, consecutively enrolled at multiple investigational centers treated with the Valiant Captivia device or any other thoracic endovascular grafts. The study will consist of all patients treated at centers that agree to participate in the 5-year follow-up PAS.

The primary objective for the Post-Approval Study is to evaluate freedom from dissection-related mortality through 5-years post-implantation in patients treated for acute or chronic dissection with thoracic endovascular grafts.

The primary safety endpoint of the study is freedom from dissection-related mortality post implantation at 5 years. The primary effectiveness endpoints will include device technical success at the time of the procedure and device procedural success at 30 days.

Secondary endpoints through 5-years include additional dissection-related intervention, dissection treatment success, the individual elements of the composite endpoint dissection treatment success, all-cause mortality, false lumen patency, endovascular device penetration of the aortic wall, and loss of device integrity.

Patients treated with the Valiant Captivia device will be part of a total of 200 acute patients and 200 chronic patients treated with thoracic endovascular grafts. This sample size will provide sufficiently narrow 95% confidence intervals to estimate a 5-year primary endpoint rate of 5% (1.98 - 8.02) to 40% (33.21- 46.79). A minimum of 60 patients with acute dissection and 60 patients with chronic dissection treated with the Valiant Captivia device will be included in the study.

Data will be analyzed and presented separately for the acute and chronic study arms. These data will be provided in post-approval study reports that are separate from the ODE annual reports.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

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