VALIANT® THORACIC STENT GRAFT WITH THE CAPTIVIA® DELIVERY SYSTEM

2015 ANNUAL PHYSICIAN CLINICAL UPDATE

MARCH, 27 2015

Medtronic
Further, Together

Abstract

Medtronic presents the fourth edition of the Valiant® Thoracic Stent Graft with the Captivia® Delivery System Clinical Update. The purpose of this report is to provide physicians with current information on the clinical trial and commercial experience with the Valiant Thoracic Stent Graft System. The Valiant® Thoracic Stent Graft with the Captivia® Delivery System has been commercially distributed worldwide since it received its CE Mark in September 2009. On April 1, 2011, the system received FDA approval for sale in the United States.

Data from three US clinical studies, VALOR II, RESCUE and Medtronic Dissection Trial, is presented in this report.

The VALOR II study is comprised of 160 subjects. These subjects have now been followed through five years after implantation as part of the Post Approval Study for the Valiant Thoracic Stent Graft with the Captivia Delivery System. The clinical data results support the safety and effectiveness of the Valiant Thoracic Stent Graft System when used for the endovascular repair of fusiform aneurysms and saccular aneurysms / penetrating ulcers of the descending thoracic aorta in patients having appropriate anatomy. As of October 24, 2014, a 94.8% freedom from Aneurysm-Related Mortality was achieved, with one surgical conversion and two thoracic aortic aneurysm ruptures observed. All study visits have now been completed and all the data has been monitored. The final study report was submitted to the FDA on January 22, 2015.

In October 2012, FDA approval was received to expand the indications for use to include the endovascular repair of blunt traumatic injuries of the descending thoracic aorta. In the associated RESCUE IDE study, 50 subjects with blunt thoracic aortic injury (BTAI) were enrolled between April 14, 2010 and January 17, 2012 at 20 sites, and are being followed through five years after implantation. The primary objective of the RESCUE trial was to assess the safety of the Valiant Thoracic Stent Graft with the Captivia Delivery System in the treatment of BTAI subjects, determined by the rate of all-cause mortality within 30 days from the index procedure, using descriptive statistics. The blunt aortic injuries in this subject cohort included intimal tear, intramural hematoma, pseudoaneurysm and rupture. The RESCUE trial met its primary objective with a 30-day all-cause mortality rate of 8.0%, which was within the expected mortality rate derived from the literature. The Valiant Thoracic Stent Graft with the Captivia Delivery System was approved for the endovascular treatment of isolated lesions (excluding dissections) of the descending thoracic aorta.

In January 2014, FDA approval was received to expand the indications for use to include endovascular repair of Type B dissections. In the associated Medtronic Dissection Trial IDE Study, 50 subjects with acute, complicated Type B dissections were enrolled between June 25, 2010 and May 8, 2012 at 16 sites, and are being followed through five years after implantation. The primary endpoint of the Medtronic Dissection trial was to evaluate the safety of the Valiant Thoracic Stent Graft with the Captivia Delivery System in the treatment of acute, complicated Type B thoracic aortic dissections subjects, determined by the rate of all-cause mortality within 30 days from the index procedure. This cohort included subjects with acute, complicated Type B aortic dissections with evidence of at least malperfusion (visceral, renal, spinal cord and/or lower limb ischemia) and/or rupture. The Medtronic Dissection trial met its primary objective with a 30-day all-cause mortality rate of 8.0%.

The safety and effectiveness of the Valiant Thoracic Stent Graft with the Captivia Delivery System has been established via the Medtronic Dissection Trial for treatment of acute, complicated Type B dissection, which carries significantly higher mortality and morbidity than chronic dissection. This treatment was therefore also considered appropriate for chronic Type B dissection, where there are fewer complications and co-morbidities.

As of January 22, 2014, the Valiant Thoracic Stent Graft with the Captivia Delivery System is approved for treatment of all lesions of the descending thoracic aorta.

The Valiant Captivia European Registry and Talent Captivia Study were conducted to provide confirmatory clinical information to support the evaluation of the Captivia Delivery System.

Commercial complaint data for the Valiant Thoracic Stent Graft System with the Captivia Delivery System have been collected for over 55,000 devices distributed worldwide as of December 31, 2014. For complaints collected between January 1, 2014 and December 31, 2014, nine post-implant ruptures, 14 surgical conversions, 38 aneurysm-related deaths, 20 device integrity issues, six migrations and one misaligned deployment were reported.

Medtronic's hope is that the information provided in this report helps physicians make informed decisions regarding patients with lesions of the descending thoracic aorta who have or may be considering the Valiant Stent Graft as potential treatment. Based on the results published in this report, the Valiant Thoracic Stent Graft provides a safe and effective option for appropriately selected patients.

Device Description

The Valiant Thoracic Stent Graft with the Captivia Delivery System is indicated for the endovascular repair of all lesions of the descending thoracic aorta. When placed within the target lesion, the stent graft provides an alternative conduit for blood flow within the patient's vasculature by excluding the lesion from blood flow and pressure.

The Valiant Thoracic Stent Graft with the Captivia Delivery System is comprised of two components: an implantable stent graft and a disposable delivery system. The stent graft is preloaded into the delivery system, which is inserted endoluminally via the femoral or iliac artery and tracked through the patient's vasculature to deliver the stent graft to the target site. 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 may be used as a single, primary stent graft if its size is sufficient to provide desired coverage, or it may be used in combination with additional stent graft sections, which increase the graft length either distal or proximal to the primary section. The Valiant Thoracic Stent Graft is available in five configuration options:

- FreeFlo Straight (Proximal Component)
- FreeFlo Tapered (Proximal Component)
- Closed Web Straight (Distal Component)
- Distal Bare Spring Straight (Distal Component)
- Closed Web Tapered (Distal Component)

The Valiant Thoracic Stent Graft is a self-expanding, tube endoprosthesis composed of a self-expanding, spring scaffold made from nitinol wire sewn to a fabric graft with non-resorbable sutures. The metal scaffolding is composed of a series of serpentine springs stacked in a tubular configuration. Radiopaque markers are sewn onto each component of the stent graft to aid in visualization and to facilitate accurate placement. The nitinol stents are also visible under fluoroscopy. See **Figure 1** for the Valiant Thoracic Stent Graft Configurations.

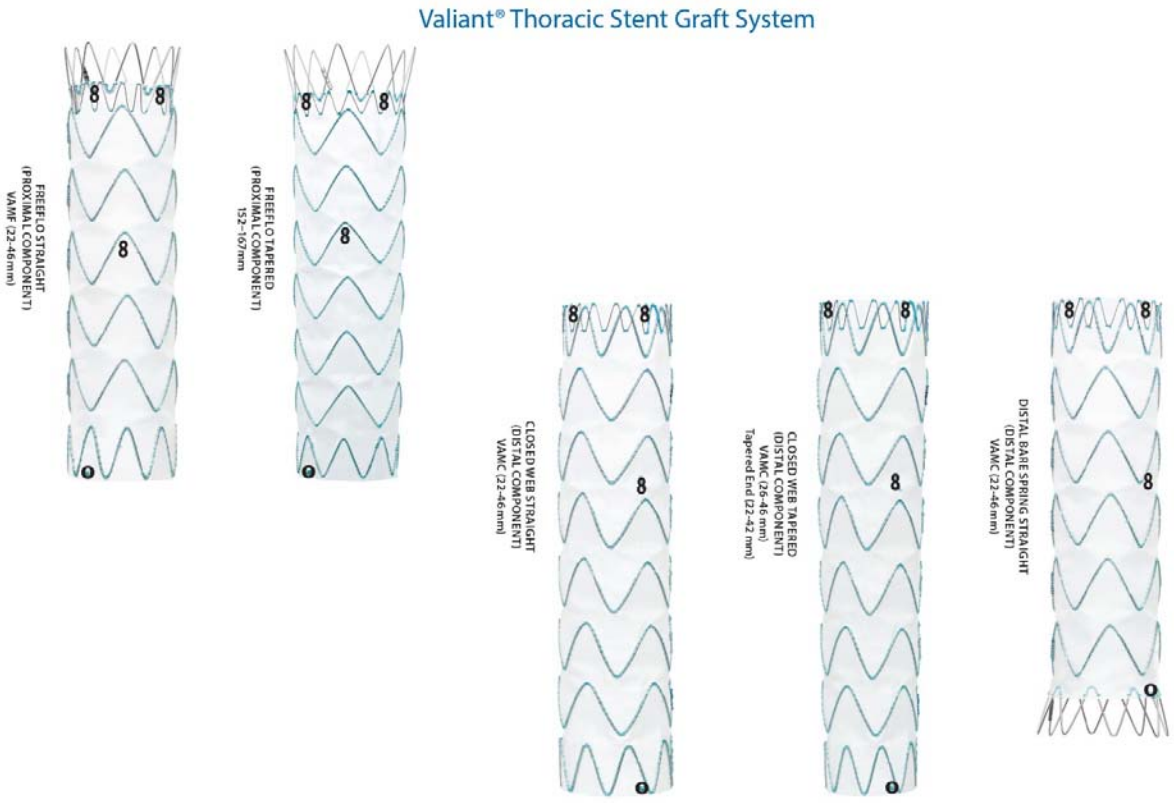
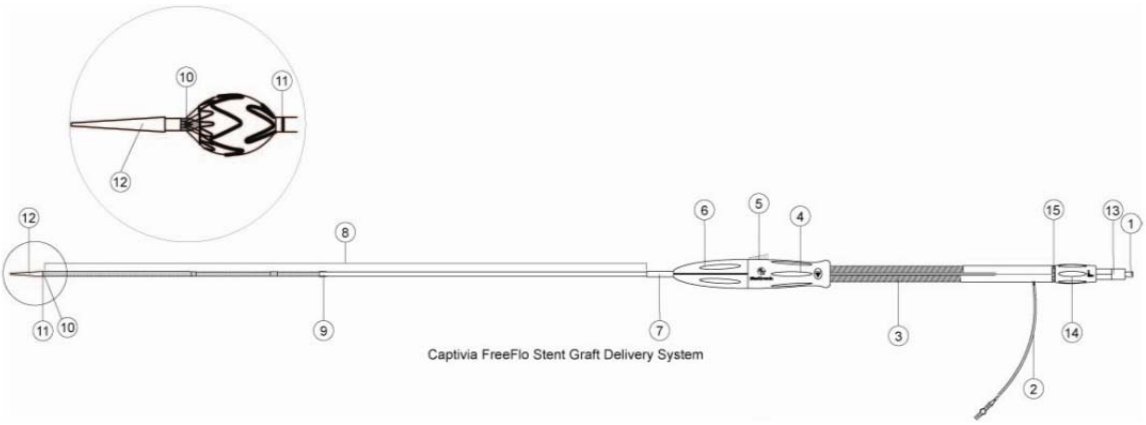


Figure 1: Valiant Thoracic Stent Graft Configurations

Captivia Delivery System

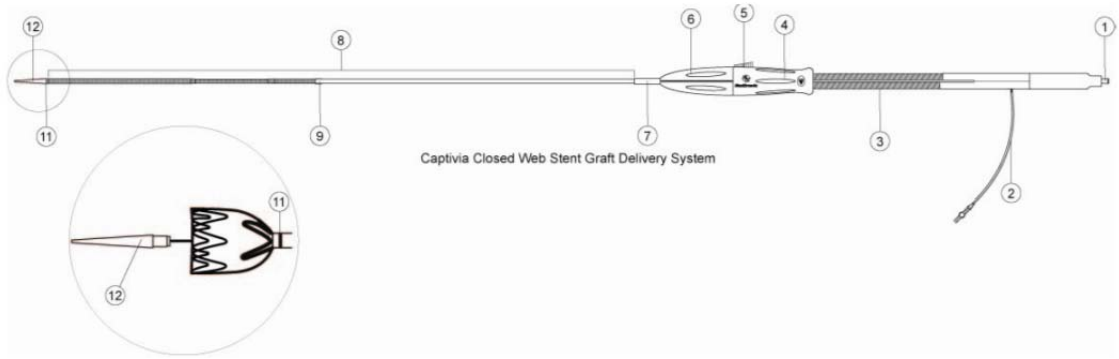
The Captivia Delivery System is a single use, disposable catheter with an integrated handle to provide the user with controlled deployment. The Captivia Delivery System is the generic name for the following 2 delivery system configurations:

- FreeFlo Stent Graft Configuration (Tip Capture) – Enhanced control of the proximal end of the stent graft using stent graft tip capture. This configuration will be used to deploy the Valiant FreeFlo Stent Grafts. See **Figure 2**.
- Closed Web Stent Graft Configuration (Non-tip Capture) – Standard control system without tip-capture. This configuration will be used to deploy the Valiant Closed Web, Distal Bare-Spring, and Closed Web Tapered Stent Grafts. See **Figure 3**.



1. Luer Connector	2. Sideport Extension	3. Screw Gear
4. Slider/Handle	5. Trigger	6. Front Grip
7. Strain Relief	8. Graft Cover/Introducer Sheath	9. Stent Stop
10. Tip Capture Mechanism	11. RO Marker Band	12. Tapered Tip
13. Back End Lock	14. Tip Capture Release Handle	15. Clamping Ring

Figure 2: Valiant FreeFlo Stent Graft Captivia Delivery System (with Tip Capture)



1. Luer Connector	2. Sideport Extension	3. Screw Gear
4. Slider/Handle	5. Trigger	6. Front Grip
7. Strain Relief	8. Graft Cover/Introducer Sheath	9. Stent Stop
10. Tip Capture Mechanism (not included in Closed Web system)	11. RO Marker Band	12. Tapered Tip

Figure 3: Valiant Closed Web Stent Graft Captivia Delivery System (without Tip Capture)

Introduction

Medtronic is committed to keeping physicians informed about product performance and product improvements. We hope that the information presented in this update will help physicians make informed decisions regarding their patients with lesions of the descending thoracic aorta. Based on the results published in this report, the Valiant Thoracic Stent Graft provides a safe and effective therapy option for treating appropriately selected patients.

This report is divided into five sections. A brief description of each of the five sections is provided below:

Section 1.0 contains information about the three US studies for the Valiant Thoracic Stent Graft System: VALOR II, RESCUE and the Medtronic Dissection Trial. The clinical data for each study includes key safety endpoints (e.g., subject mortality, rupture, surgical conversion) as well as effectiveness measures (e.g., endoleaks, migrations, aneurysm size, device specific events). This report includes information collected and analyzed as of October 24, 2014 for the VALOR II study and January 7, 2015 for the RESCUE study and the Medtronic Dissection Trial. Summary information is also provided on two studies conducted to support the evaluation of the Captivia Delivery System, Valiant Captivia European Registry and Talent Captivia US study, both of which have completed enrollment and follow up.

Section 2.0 provides a summary of the worldwide commercial experience of the Valiant Thoracic Stent Graft with the Captivia Delivery System. This section includes important safety information, such as ruptures, conversion, aneurysm related mortality, etc., reported to Medtronic and analyzed for the time period between January 1, 2014 and December 31, 2014.

Section 3.0 summarizes the analysis of explanted Valiant Thoracic Stent Graft devices returned to Medtronic as of December 31, 2014.

Section 4.0 provides notes to clinicians and discusses patient selection criteria and follow-up guidelines for the commercial use of the Valiant Thoracic Stent Graft System.

Section 5.0 provides a summary of indications for use, contraindications, warnings and precautions regarding the Valiant Thoracic Stent Graft with the Captivia Delivery System.

Device Development History

The Valiant Thoracic Stent Graft was initially introduced to the market with the Xcelerant® Delivery System. This iteration was CE marked in 2005 and was only commercially available outside of the United States. The Valiant Thoracic Stent Graft with Xcelerant Delivery System was used in the VALOR II investigational study in the United States to evaluate the treatment of descending thoracic aneurysms of degenerative etiology.

In 2009, a second iteration of the Valiant Thoracic Stent Graft delivery system, the Captivia Delivery System, was developed. The Captivia Delivery System differs from the Xcelerant Delivery System in the following:

- Tip capture feature for the FreeFlo Stent Graft configurations intended to enhance control of deployment and deployment accuracy
- Hydrophilic coating intended to facilitate deliverability
- Optimized internal components
- Simplified external handle design

Although modifications were made to the delivery system, the Valiant Thoracic Stent Graft did not change and remains identical to the one used with the Xcelerant Delivery System.

Valiant Thoracic Stent Graft with Captivia Delivery System, subject of this Clinical Update, received CE mark in 2009 and FDA approval in April 2011.

Table of Contents

List of Tables

List of Figures

1.0 Clinical Study Experience

1.1 Introduction

The clinical evidence supporting the safety and effectiveness of the Valiant Thoracic Stent Graft with the Captivia Delivery System is from a combination of five clinical studies:

- Valiant Thoracic Stent Graft US Pivotal Study (VALOR II)
- Valiant Captivia European Registry
- Talent Captivia IDE Study
- RESCUE IDE Study
- Medtronic Dissection Trial (IDE)

The purpose of the VALOR II pivotal clinical study was to demonstrate the safe and effective use of the Valiant Thoracic Stent Graft for the treatment of fusiform aneurysms and saccular aneurysms/penetrating ulcers of the descending thoracic aorta in subjects who were candidates for endovascular repair.

Subsequent to the enrollment in the pivotal stent graft study presented above, the delivery system was updated from the Xcelerant to the Captivia Delivery System. The Captivia Delivery System is a design iteration of the Xcelerant Delivery System. The primary difference between the 2 delivery systems is the incorporation of a tip capture mechanism designed to constrain the proximal bare springs of the FreeFlo stent graft until proper positioning has been obtained.

The Valiant Captivia European Registry and Talent Captivia Study were conducted to provide confirmatory clinical information to support the evaluation of the Captivia Delivery System.

The RESCUE IDE study was conducted to evaluate the safety and effectiveness of the Valiant Captivia in the treatment of blunt thoracic aortic injury (BTAI) subjects, determined by the rate of all-cause mortality within 30-days from the index procedure.

The Medtronic Dissection Trial IDE study was conducted to evaluate the safety and effectiveness of the Valiant Captivia in the treatment of acute, complicated Type B thoracic aortic dissection subjects, determined by the rate of all-cause mortality within 30-days from the index procedure.

Summaries of the five aforementioned studies are provided below.

VALOR II: Valiant Thoracic Stent Graft Pivotal Study

A total of 160 subjects were enrolled in the Valiant US study (VALOR II) at 24 investigational sites from December 2006 to September 2009. The Valiant Thoracic Stent Graft with Captivia Delivery System was approved by the FDA in the United States in April 2011. Approval was received based on the 1-year follow-up data. As a condition of approval for the Valiant Thoracic Stent Graft System, FDA requested Medtronic to conduct a post-approval study to evaluate the longer term safety and effectiveness of the Valiant Stent Graft through 5 years of implantation. All of the study visits have been completed and all data has

been monitored. The final post-approval study report was approved by FDA on April 21, 2105.

Valiant Captivia European Registry

The Valiant Captivia European post-market registry study is a multi-center, post-market, non-interventional, single-arm study that collected and evaluated mid-term clinical performance data of the Valiant Thoracic Stent Graft with the Captivia Delivery System, following market approval in the European Union. Subjects who were diagnosed with either thoracic aortic aneurysm or aortic dissection were enrolled into the study for treatment with Valiant Captivia and were followed for 1 year after implantation. Enrollment was completed on December 9, 2010 and the follow-up visits are complete.

The primary endpoint for the 30-day analysis was defined as successful delivery and deployment of the stent graft (assessed intraoperatively). This parameter is achieved by deployment of the Valiant Thoracic Stent Graft in the planned location; without unintentional coverage of the left subclavian artery, left common carotid artery, and/or brachiocephalic artery; and with the removal of the delivery system. Successful delivery and deployment of the Valiant Thoracic Stent Graft using the Captivia Delivery System was achieved in all 100 subjects (100% success rate).

Talent Captivia US Study

In the Talent Captivia Delivery System IDE study, 20 subjects were enrolled in a modified open arm of the US IDE evaluation of the Talent Thoracic Stent Graft System in the treatment of patients with thoracic aortic disease. Disease etiologies included fusiform aneurysms and saccular aneurysms / penetrating ulcers of the descending thoracic aorta. The data collected from this evaluation was considered relevant to the Valiant Thoracic Stent Graft with the Captivia Delivery System, as the delivery systems used with Talent and Valiant stent grafts are the same in design and principles of operation. Enrollment was completed on August 10, 2010 and the follow-up visits are complete.

The primary endpoint of this study was successful delivery and deployment, which was defined as: a) attaining vessel access to insert the delivery catheter, and b) deployment of the graft to the intended treatment site. A total of 19 out of the 20 enrolled subjects had successful delivery and deployment of the stent graft at the initial implant procedure, resulting in a 95% success rate.

RESCUE IDE Study

In the RESCUE IDE study, 50 subjects with blunt thoracic aortic injury (BTAI) in the descending thoracic aorta were enrolled between April 14, 2010 and January 17, 2012 at 20 sites. The primary endpoint of the RESCUE trial was to evaluate the safety and effectiveness of the Valiant Captivia in the treatment of BTAI subjects, determined by the rate of all-cause mortality within 30 days from the index procedure. The blunt aortic injuries in this subject cohort included intimal tear, intramural hematoma, pseudoaneurysm and rupture. The RESCUE trial met its primary objective with a 30-day all-cause mortality rate of 8.0%. Follow up for this study is ongoing.

Medtronic Dissection Trial IDE Study

In the Medtronic Dissection Trial IDE study, 50 subjects with acute, complicated Type B thoracic aortic dissections were enrolled between June 25, 2010 and May 8, 2012 at 16 sites. The primary endpoint was to evaluate the safety and effectiveness of the Valiant Captivia in the treatment of acute, complicated Type B thoracic aortic dissections subjects, determined by the rate of all-cause mortality within 30 days from the index procedure. This cohort included subjects with acute, complicated Type B aortic dissections with evidence of malperfusion (visceral, renal, spinal cord and/or lower limb ischemia) and/or rupture. The Medtronic Dissection trial met its primary objective with a 30-day all-cause mortality rate of 8.0%. Follow up for this study is ongoing.

1.2 VALOR II Clinical Study Data

Medtronic enrolled 160 subjects in the VALOR II study and has followed the subjects through the final 5-year follow-up visit. The final data snapshot occurred on October 24, 2014. This study has had all follow-up visits completed and all case report forms monitored. This section provides the following clinical data:

- Subject Accountability
- Aneurysm Related Mortality
- Aneurysm Rupture
- Secondary Endovascular Procedures
- Conversion to Open Surgery
- Major Adverse Events
- Endoleaks
- Aneurysm Enlargement
- Migration
- Device Patency
- Device Integrity

1.2.1 Subject Accountability

Subject accountability for VALOR II is summarized in **Table 1-1**. No procedure or pre-discharge imaging was required per study protocol.

As shown in **Table 1-1**, the number of subjects that have completed clinical follow-up is 140 for 1-month, 109 for 12- month, 95 for 2-year, 84 for 3-year, 70 for 4-year, and 68 for the 5-year follow-up.

As for follow-up imaging, also shown in **Table 1-1**, 152 subjects were eligible for 1-month, of which 147 (96.7%) completed any type of follow-up imaging. At 12 months, 139 were eligible, of which 114 (82%) completed any type of follow-up imaging. At the 2-year follow-up, 125 were eligible, of which 91 (72.8%) completed any type of follow-up imaging. At the 3-year follow-up, 117 were eligible, of which 90 (76.9%) completed any type of follow-up

imaging. At the 4-year follow-up, 103 were eligible, of which 74 (71.8%) completed any type of follow-up imaging. At the 5-year follow-up, 93 subjects were eligible, of which 69 (74.2%) completed any type of follow-up imaging.

Table 1-1: VALOR II - Subject Accountability and Imaging Compliance[1]

	Patient follow-up # (%)			Patients with Imaging (at each time interval) # (%)			Patients with adequate imaging to assess the parameter # (%)					Patient events occurring before next visit # (%) [2]					
Treatment / Follow-up Interval	Eligible	Treatment or Clinical f/u	Imaging f/u	CT/MR Imaging	Chest X-Ray	Additional Imaging modalities	Max ANR Diameter	Change in ANR diameter (from 1 month)	Endo-leak	Migration (from 1 month)	Integrity	Intent to Treat but Not implanted	Con-version to Surgery	Death	With-drawal	LTF	Not due for next visit
Implant	160	160 (100.0%)															
Events between implant and pre-discharge[3]												3	0	0	0	0	0
Pre-discharge	157	157 (100.0%)	67 (42.7%)	25 (15.9%)	59 (37.6%)	0 (0.0%)	25 (15.9%)		24 (15.3%)		59 (37.6%)						
Events between pre-discharge and 1 month follow-up visit													0	5	0	0	0
1 month	152	140 (92.1%)	147 (96.7%)	143 (94.1%)	133 (87.5%)	0 (0.0%)	143 (94.1%)		136 (89.5%)		133 (87.5%)						
Events between 1 month and 6 months follow-up visit													0	4	0	0	0
6 month	148	112 (75.7%)	115 (77.7%)	111 (75.0%)	97 (65.5%)	0 (0.0%)	111 (75.0%)	108 (73.0%)	101 (68.2%)	114 (77.0%)	98 (66.2%)						

	Patient follow-up # (%)			**Patients with Imaging (at each time interval) # (%)**			**Patients with adequate imaging to assess the parameter # (%)**					**Patient events occurring before next visit # (%)** [2]					
Treatment / Follow-up Interval	Eligible	Treatment or Clinical f/u	Imaging f/u	CT/MR Imaging	Chest X-Ray	Additional Imaging modalities	Max ANR Diameter	Change in ANR diameter (from 1 month)	Endo-leak	Migration (from 1 month)	Integrity	Intent to Treat but Not implanted	Con-version to Surgery	Death	With-drawal	LTF	Not due for next visit
Events between 6 months and 12 months follow-up visit													0	9	0	0	0
12 month	139	109 (78.4%)	114 (82.0%)	112 (80.6%)	105 (75.5%)	0 (0.0%)	112 (80.6%)	105 (75.5%)	97 (69.8%)	114 (82.0%)	105 (75.5%)						
Events between 12 months and 2 year follow-up visit													0	10	4	0	0
2 year	125	95 (76.0%)	91 (72.8%)	88 (70.4%)	77 (61.6%)	0 (0.0%)	87 (69.6%)	81 (64.8%)	78 (62.4%)	91 (72.8%)	77 (61.6%)						
Events between 2 year and 3 year follow-up visit													0	8	0	0	0
3 year	117	84 (71.8%)	90 (76.9%)	84 (71.8%)	83 (70.9%)	0 (0.0%)	83 (70.9%)	79 (67.5%)	70 (59.8%)	90 (76.9%)	83 (70.9%)						
Events between 3 year and 4 year follow-up visit													1	10	1	2	0

	Patient follow-up # (%)			Patients with Imaging (at each time interval) # (%)			Patients with adequate imaging to assess the parameter # (%)					Patient events occurring before next visit # (%) [2]					
Treatment / Follow-up Interval	Eligible	Treatment or Clinical f/u	Imaging f/u	CT/MR Imaging	Chest X-Ray	Additional Imaging modalities	Max ANR Diameter	Change in ANR diameter (from 1 month)	Endo-leak	Migration (from 1 month)	Integrity	Intent to Treat but Not implanted	Con-version to Surgery	Death	With-drawal	LTF	Not due for next visit
4 year	103	70 (68.0%)	74 (71.8%)	71 (68.9%)	62 (60.2%)	0 (0.0%)	70 (68.0%)	66 (64.1%)	61 (59.2%)	74 (71.8%)	62 (60.2%)						
Events post 4 year follow-up visit													0	8	0	2	0
5 year	93	68 (73.1%)	69 (74.2%)	67 (72.0%)	61 (65.6%)	0 (0.0%)	67 (72.0%)	56 (60.2%)	59 (63.4%)	69 (74.2%)	61 (65.6%)						
Totals												3	1	54	5	4	
Death post conversion to surgery														0			
Total Deaths														54			

[1]The information in this table represents monitored data collected as of October 24, 2014. Information presented in this table may differ from that presented in either the Summary of Safety and Effectiveness Data (SSED) or labeling, given that the data were obtained at different time periods.

[2] Results for the following categories have a hierarchical relationship in this order: *Intent to Treat but not-Implanted, Conversion to surgery, Death, Withdrawal, Lost to follow-up and Not yet due for follow-up*. A hierarchical structure facilitates tracking of eligibility, imaging, and follow-up.

[3] "*Events between implant and pre-discharge*" includes events that took place at implant. Similarly, "*Events between 1 month and 6 months follow-up*" includes events that occurred at the 1 month follow-up visit. The same principle applies to subsequent intervals.

1.2.2 Aneurysm Related Mortality (ARM)

In VALOR II, ARM is defined as deaths occurring within 30 days from initial implantation or occurring as a consequence of an aneurysm rupture, a conversion to open repair, or a secondary procedure intended to treat the aneurysm that was originally treated by the Valiant Thoracic Stent Graft System. Any death within 30 days of a procedure intended to treat the aneurysm was presumed to be aneurysm-related.

There have been eight aneurysm-related deaths reported in this study. **Table 1-2** summarizes the information on aneurysm-related mortality events.

Table 1-2: VALOR II - Aneurysm-Related Mortality Details

Date of Implant	Time to Aneurysm-Related Mortality (Days)	Cause of Death (Investigator Assignment)	Cause of Aneurysm-Related Mortality (CEC Assignment)	Device Relatedness (Investigator Assignment)	Device Relatedness (CEC Assignment)	Procedure Relatedness (Investigator Assignment)	Procedure Relatedness (CEC Assignment)
12/07/2007	0	Aortic rupture[1]	Death related to aneurysm	Unrelated	Related	Related	Related
03/19/2007	3	Aortic dissection[2]	Death related to aneurysm	Unknown	Related	Related	Related
09/11/2007	3	Multi-organ failure	Death related to aneurysm	Unknown	Unrelated	Unknown	Related
03/25/2009	12	Pneumonia	Death, Non-Cardiac, Non-Neuro	Unrelated	Unrelated	Unknown	Related
02/21/2008	21	Respiratory failure	Death, Non-Cardiac, Non-Neuro	Unrelated	Related	Related	Related
05/22/2008	80	Ventricular arrhythmia/cardiac standstill	Death related to aneurysm	Unknown	Related	Unknown	Related
03/31/2008	163	Aortic dissection[3]	Death related to aneurysm	Unknown	Related	Unknown	Unrelated
07/23/2008	1,067	Aneurysm rupture	Death related to aneurysm	Related	Related	Unrelated	Unrelated

[1]During index procedure the implanting physician reported difficulties encountered due to tortuous anatomy and prior endograft repair of infra-renal abdominal aortic aneurysm. The subject became hypotensive and subsequent exploratory laparoscopy identified perforation of the aorta at the level of the crus of the diaphragm. Attempts to stabilize were unsuccessful. Subject expired due to exsanguination and aortic rupture.
[2]Type II endoleak unresolved at end of index procedure. Subject experienced peri-operative non-ST segment elevation myocardial infarction (NSTEMI) one day post-op. No further complications, subject discharged 3 days post-op. Subject returned to emergency room later that same day with severe radiating chest pain. Subject experienced seizure, became apneic and bradycardic. Death certificate states immediate cause of death as Cardiac Arrest with underlying causes of Cardiac Tamponade, Aortic Dissection and Aortic Aneurysm.
[3]Subject presented to emergency room 157 days post-op due to weakness and dizziness. CT scan revealed "obvious Type A aortic dissection starting at the aortic valve and extending into the arch". Subject refused surgical intervention and expired 163 days post-op.

1.2.3 Kaplan-Meier: Freedom from ARM within 5 Years

The Kaplan-Meier estimate for freedom from aneurysm-related mortality within five years for this study is 94.8%, with a standard error of plus or minus 1.8%.

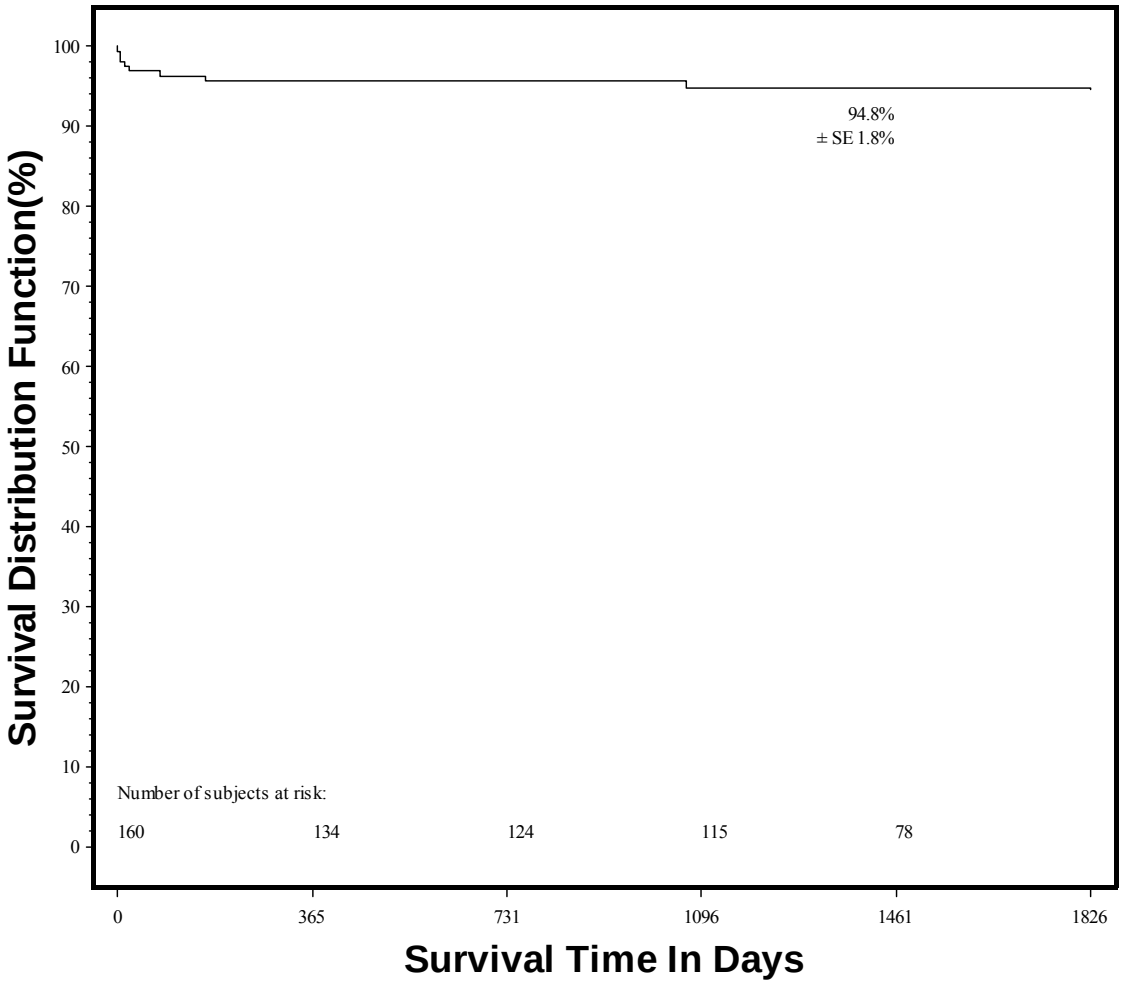


Figure 1-1: VALOR II - Kaplan-Meier Curve of Freedom from ARM within 5 Years

Table 1-3: VALOR II - Kaplan-Meier Estimates of Freedom from ARM within 5 Years

	0 to 30 days	31 to 183 days	184 to 365 days	366 to 731 days	732 to 1096 days	1097 to 1461 days	1462 to 1826 days
No. at Risk[1]	160	155	151	135	125	116	100
No. of Events	5	2	0	0	1	0	0
No. Censored[2]	0	2	16	10	8	16	100

	0 to 30 days	31 to 183 days	184 to 365 days	366 to 731 days	732 to 1096 days	1097 to 1461 days	1462 to 1826 days
Kaplan-Meier Estimate[3]	96.9%	95.6%	95.6%	95.6%	94.8%	94.8%	94.8%
Standard Error[3]	1.4%	1.6%	1.6%	1.6%	1.8%	1.8%	1.8%

[1] Number of subjects at risk at the beginning of an interval.
[2] Subjects are censored because their last follow-up has not reached the end of the time interval. Censored subjects will include those who withdraw, are lost to follow-up, or who die from non-aneurysm related causes.
[3] Kaplan-Meier Estimate and Standard Error were calculated at the end of time interval.

1.2.4 Aneurysm Ruptures

In the VALOR II study, 1.3% of subjects (2/160) experienced aneurysm ruptures. **Table 1-4** provides details for both events.

Table 1-4: VALOR II - Aneurysm Rupture Details (Site Reported)

Date of Implant	Time to Aneurysm Rupture (days)	Cause of Aneurysm Rupture (Investigator Assignment)	Summary
01/31/2008	605	Multiple endoleaks / TAA growth	Subject was an 86 y.o. male treated with the Valiant graft in January 2008. An endoleak type II was reported at discharge. TAA growth was not observed at the six-month visit. At the 12-month visit in February 2009, an endoleak type I and TAA growth of 10 mm were identified. Subject underwent a secondary procedure via deployment of additional stent graft within the primary prosthesis. Seven months later in September 2009, subject was admitted to hospital for chest pain. Imaging showed continuing aneurysm expansion with a semi-emergent, TAA ruptured condition. An endoleak type V/ unknown was reported and the subject underwent an additional endovascular procedure via deployment of additional stent grafts within the primary prosthesis. At the 24-month visit in February 2010, aneurysm size remained unchanged relative to the size measured at discharge in October 2009. Subject was non-compliant with his 36-month follow-up visit though site spoke with subject in March 2011. Subject died in August 2011, before the 48-m visit. Source documents indicate cause of death was an abdominal aortic aneurysm rupture. The CEC adjudicated death as being unrelated to the thoracic aortic aneurysm, to the device, or to the procedure.
7/23/2008	1,062	Type III or Type IV Endoleak	Subject was an 86 y. o. female who had a secondary procedure in August 2009 with a Valiant device to correct a Type Ib endoleak (distal). She missed the next follow-up interval (September 2010). On 6/20/2011, subject was

Date of Implant	Time to Aneurysm Rupture (days)	Cause of Aneurysm Rupture (Investigator Assignment)	Summary
			admitted into non-study hospital due to a ruptured thoracic aortic aneurysm. On 6/22/2011, hospital tried to treat her. Attempts to implant an additional graft were unsuccessful due to iliac tortuosity. Alternative routes of insertion were ruled out. Procedure was aborted and subject was transferred to ICU. Subject died the next day, on 6/23/2011. Investigator assigned cause of death to potential aneurysm rupture caused by a likely type III or type IV endoleak (reported as type V/unknown). The CEC adjudicated death as being related to the thoracic aortic aneurysm.

1.2.5 Secondary Endovascular Procedures

In VALOR II, secondary endovascular procedures are defined as additional procedures required to achieve successful treatment of the aneurysm at a time beyond initial implantation, including deployment of a secondary graft within the primary graft or balloon dilatation of anchor zones. All secondary procedures are shown in **Table 1-5** below. A total of 13 secondary procedures were performed in 11 subjects. Nine subjects had a single secondary procedure. Two subjects had two secondary procedures each. In all secondary procedures, subjects were treated via deployment of additional stent graft(s) within the primary prosthesis.

Table 1-5: VALOR II - Secondary Procedure Details (Site Reported)

Date of Implant	Time to Secondary Procedure (days)	Cause of Secondary Procedure (Investigator Assignment)[1]
01/19/2009	9	Type I endoleak
01/31/2008[2]	375	Type I endoleak
	608	aneurysm expansion
07/23/2008[3]	392	Type I endoleak
	1,064	aneurysm rupture
12/20/2007	791	Type I endoleak
02/27/2007	811	other endoleak(s)
07/02/2008	811	aneurysm expansion
07/24/2008	1,152	Type I endoleak
05/16/2008	1,214	Type I endoleak
06/17/2008	1,415	Type I endoleak
10/05/2007	1,467	Type I endoleak
05/24/2007	1,586	aneurysm expansion

[1] Data was obtained from a drop-down field in the case report form in which only one option can be chosen. A physician chose "resolve endoleak" as reason for treatment, even though the subject may have also had aneurysm enlargement. As a result, the table shows only two subjects with aneurysm enlargement, even though aneurysm enlargement was reported for additional subjects as discussed in **Section 1.2.8.5**.
[2]Subject had two secondary procedures; one at day 375 and one at day 608.
[3]Subject had two secondary procedures; one at day 392 and one at day 1,064.

1.2.6 Conversions to Surgery

In VALOR II, there has been one reported case of conversion to surgery. A narrative for this event is provided below.

> The subject is a 73 y.o. female originally treated with the Valiant stent graft in September 2008. Aneurysmal sac growth was detected during the 36-month follow-up visit in June 2011. No endoleaks were found. No additional device-specific adverse events were identified and the treatment option was as per the Investigator's discretion. Subject underwent conversion in October 2011. No complications were reported.

Table 1-6: VALOR II - Conversion to Surgery Details

Date of Implant	Time to Conversion (days)	Cause of Conversion (Investigator Assessment)
09/16/2008	1112	Aneurysm Expansion

1.2.7 Major Adverse Events

In VALOR II, the Major Adverse Event (MAE) construct was originally designed to allow for comparison to open surgical repair; therefore, MAEs are defined as those events that are relevant to the surgical treatment of thoracic aortic aneurysms. MAEs within 12 months and after 12 months are presented in **Table 1-7** and **Table 1-8**, respectively. Data for **Table 1-7** was adjudicated by the Clinical Events Committee, whereas data for **Table 1-8** was obtained from a composite based on site-reported events.

It is possible for a subject to experience multiple and/or persistent MAEs at more than one time period, so the same subject may appear across multiple timeframes and MAE categories.

There have been nine major adverse events in six subjects reported as related to the study device. Eight of these events took place within 365 days; one after 365 days. Details about these events are footnoted in **Table 1-7** and **Table 1-8**.

Table 1-7: VALOR II - Major Adverse Events within 12 Months (CEC Adjudicated)

Category[1]	0-30 days % (m/n)[2]	31-365 days % (m/n)[3]
Any MAE	38.1% (61/160)	22.7% (35/154)
Respiratory Complications	9.4% (15/160)	6.5% (10/154)
Respiratory failure	4.4% (7/160)	2.6% (4/154)
Pneumonia	3.8% (6/160)	1.9% (3/154)
Atelectasis	1.3% (2/160)	0.6% (1/154)
Pulmonary embolism	1.3% (2/160)	1.3% (2/154)
Pulmonary edema	1.9% (3/160)	1.9% (3/154)
Renal Complications	5.0% (8/160)	5.2% (8/154)
Renal insufficiency	2.5% (4/160)	1.9% (3/154)
Renal failure	2.5% (4/160)	3.2% (5/154)
Cardiac Complications	15.0% (24/160)	7.8% (12/154)
Myocardial Infarction	1.9% (3/160)	0.6% (1/154)
Unstable angina	0.6% (1/160)	0.6% (1/154)
New arrhythmia / Cardiac arrest	11.9% (19/160)	1.9% (3/154)
Exacerbation of CHF	1.9% (3/160)	5.2% (8/154)
Neurological Complications	5.0% (8/160)	5.2% (8/154)
Stroke/CVA	2.5% (4/160)	3.9% (6/154)

Category[1]	0-30 days % (m/n)[2]	31-365 days % (m/n)[3]
Transient Ischemic Attack	-	1.3% (2/154)
Paraplegia	0.6% (1/160)	-
Paraparesis	1.9% (3/160)	-
Gastrointestinal Complications	1.3% (2/160)	1.3% (2/154)
Bowel ischemia	1.3% (2/160)[4]	1.3% (2/154)
Major Bleeding Complications	6.9% (11/160)	0.6% (1/154)
Major bleeding event, procedural or post-procedure	5.0% (8/160)[5]	-
Coagulopathy	2.5% (4/160)	0.6% (1/154)
Vascular Complications	20.6% (33/160)	3.9% (6/154)
AV fistula	-	0.6% (1/154)
Hematoma	6.3% (10/160)[6]	0.6% (1/154)
Non-aortic vessel rupture/dissection	5.0% (8/160)[7]	-
Aortic rupture/dissection	1.9% (3/160)	2.6% (4/154)
Embolism (not CVA/TIA/Pulmonary)	1.9% (3/160)	-
Arterial Occlusion	2.5% (4/160)[8]	0.6% (1/154)
Retroperitoneal bleed	1.9% (3/160)	-
Thrombosis	0.6% (1/160)	-
Pseudoaneurysm	3.8% (6/160)	-
Vessel Disruption	1.9% (3/160)	-
Aneurysm Rupture	-	-

For ease of review, a dash symbol "-" has replaced 0.0% in this table where the numerator is 0 and denominator can be found in the first row of the table.

[1] Category "All-cause mortality" and sub-category "Aneurysm-related mortality" were not included in table, as these are included in **Table 1-1** and **Table 1-2**, respectively.

[2] m is the number of subjects experiencing a certain event within 30 days; n is the ITT population.

[3] m is the number of subjects experiencing a certain event in the interval 31-365 days, n is the number of subjects who experienced at least one MAE in the interval, underwent a secondary procedure within 365 days or are followed for at least 337 days.

[4] One of the two bowel ischemia events was determined to be related to the device. Event took place at procedure and was caused by coverage of the celiac artery by study device, causing permanent sequelae.

[5] Two of the eight bleeding complications were reported as being related to the device. One of these events was a procedural bleeding with EBL of 1000 cc caused by the right iliac artery being torn (an additional MAE); in the other event, a subject received five units of blood four days after the procedure. Both events were recovered with treatment.

[6] One of the 10 hematomas was attributed to the device. It was observed two weeks after the procedure, on insertion area. Recovered with treatment thereafter.

[7] Three of the eight non-aortic vessel rupture/dissections were reported as being device-related. The three of them took place during the procedure and involved tearing of an access vessel. Recovered with treatment.

[8] One of the arterial occlusions was reported as being device-related. The stent graft covered the left subclavian artery causing left arm weakness. Per Case Report Form (CRF), event was recovered without treatment.

Table 1-8: VALOR II - Major Adverse Events after 12 Months (Site Reported)

Category[1]	366-731 days % (m/n)[2]	732-1096 days % (m/n)[3]	1097-1461 days % (m/n)[4]	1462-1826 days % (m/n)[5]
Any MAE	28.6% (38/133)	21.8% (27/124)	28.1% (32/114)	23.5% (23/98)
Respiratory Complications	7.5% (10/133)	6.5% (8/124)	8.8% (10/114)	7.1% (7/98)
Respiratory failure	1.5% (2/133)	2.4% (3/124)	1.8% (2/114)	-
Pneumonia	4.5% (6/133)	0.8% (1/124)	2.6% (3/114)	2.0% (2/98)
Atelectasis	-	-	0.9% (1/114)	1.0% (1/98)
Pulmonary embolism	-	0.8% (1/124)	-	-
Pulmonary edema	-	0.8% (1/124)	1.8% (2/114)	-
Renal Complications	2.3% (3/133)	3.2% (4/124)	2.6% (3/114)	1.0% (1/98)
Renal insufficiency	1.5% (2/133)	-	1.8% (2/114)	-
Renal failure	0.8% (1/133)	1.6% (2/124)	0.9% (1/114)	-
Cardiac Complications	12.8% (17/133)	11.3% (14/124)	8.8% (10/114)	8.2% (8/98)
Myocardial Infarction	1.5% (2/133)	1.6% (2/124)	1.8% (2/114)	2.0% (2/98)
Unstable angina	5.3% (7/133)	0.8% (1/124)	1.8% (2/114)	1.0% (1/98)
New arrhythmia / Cardiac arrest	3.0% (4/133)	5.6% (7/124)	0.9% (1/114)	4.1% (4/98)
Exacerbation of CHF	2.3% (3/133)	3.2% (4/124)	2.6% (3/114)	-
Multi-organ Failure[6]	-	-	0.9% (1/114)	-
Neurological Complications	3.0% (4/133)	3.2% (4/124)	2.6% (3/114)	4.1% (4/98)
Stroke/CVA	0.8% (1/133)	0.8% (1/124)	0.9% (1/114)	1.0% (1/98)
TIA	-	0.8% (1/124)	-	-
Paraplegia/ Paraparesis[7]	0.8% (1/133)	-	-	-
Gastrointestinal Complications	3.8% (5/133)	4.8% (6/124)	5.3% (6/114)	3.1% (3/98)
Bowel ischemia	-	-	-	-
Major Bleeding Complications	3.0% (4/133)	3.2% (4/124)	5.3% (6/114)	2.0% (2/98)
Major bleeding event, procedural or post-procedure	0.8% (1/133)	-	0.9% (1/114)	-
Coagulopathy	1.5% (2/133)	0.8% (1/124)	0.9% (1/114)	-
Vascular Complications	8.3% (11/133)	4.8% (6/124)	4.4% (5/114)	5.1% (5/98)
AV fistula	0.8% (1/133)	-	-	-
Hematoma	0.8% (1/133)	-	1.8% (2/114)	1.0% (1/98)

Category[1]	366-731 days % (m/n)[2]	732-1096 days % (m/n)[3]	1097-1461 days % (m/n)[4]	1462-1826 days % (m/n)[5]
Vessel (including aorta) rupture/dissection[8]	-	0.8% (1/124)	-	-
Embolism (not CVA/TIA/Pulmonary)	0.8% (1/133)	-	-	-
Arterial Occlusion	-	-	-	-
Retroperitoneal bleed	-	-	-	-
Thrombosis	-	-	-	-
Pseudoaneurysm	-	0.8% (1/124)	-	-
Vessel Disruption	-	-	-	-
Aneurysm Rupture	0.8% (1/133)	0.8% (1/124)[9]	-	-

For ease of review, a dash symbol "-" has replaced 0.0% in this table where the numerator is 0 and denominator can be found in the first row of the table.

[1] Category "All-cause mortality" and sub-category "Aneurysm-related mortality" were not included in table, as these are included in **Table 1-1** and **Table 1-2**, respectively.

[2] m is the number of subjects who experienced a certain event between 366 and 731 days; n is the number of subjects who experienced at least one MAE or who underwent a secondary procedure in this interval, or who were followed for at least 674 days

[3] m is the number of subjects who experienced a certain event between 732-1096 days; n is the number of subjects who experienced at least one MAE or who underwent a secondary procedure in this interval, or who were followed for at least 1039 days

[4] m is the number of subjects who experienced a certain event between 1097-1461 days; n is the number of subjects who experienced at least one MAE or who underwent a secondary procedure in this interval, or who were followed for at least 1404 days

[5] m is the number of subjects who experienced a certain event between 1462-1826 days; n is the number of subjects who experienced at least one MAE or who underwent a secondary procedure in this interval, or who were followed for at least 1769 days

[6] Sites captured multi-organ failures using a single adverse event code. Multi-organ failure events are included in this table as they can involve respiratory or renal failure. In this table, multi-organ failure events were not counted in either respiratory complications or renal complications fields to avoid reporting same events multiple times.

[7] Spinal cord ischemia is related to either partial (paraparesis) or total paralysis of lower extremities (paraplegia). As a result, site-reported events of spinal cord ischemia, paraplegia, and paraparesis were merged into the same field.

[8] Sites captured vessel rupture / dissections and aortic dissections using the same adverse event code. As a result, these fields were merged.

[9] The aneurysm rupture that occurred 1,062 days after procedure was reported and adjudicated as being related to the device. Subject died as a result. Details about this event are presented in the second narrative of **Section 1.2.4.**

1.2.8 Endoleaks and Other Device-Specific Safety Measures

Table 1-9 summarizes endoleaks and device-specific safety measurements reported at VALOR II clinical sites. It is possible for a subject to experience multiple types of endoleaks

or a persistent endoleak at more than one time period, so the same subject may appear across multiple timeframes and endoleak categories.

Table 1-9: VALOR II - Safety Measurements at Follow-Up (Site Reported)[1]

Event	Through 1-month visit % (m/n)	> 1-month visit to 12-month visit % (m/n)	> 12-month visit to 24-month visit % (m/n)	> 24-month visit to 36-month visit % (m/n)	> 36-month visit to 48-month visit % (m/n)	> 48-month visit to 60-month visit % (m/n)
Any Endoleak Type	17.9% (25/140)	6.7% (9/134)	6.1% (6/98)	5.2% (4/77)	4.1% (3/73)	1.7% (1/60)
Type I	3.6% (5/140)	2.2% (3/134)	3.1% (3/98)	2.6% (2/77)	2.7% (2/73)	0.0% (0/60)
Type Ia (proximal)	0.7% (1/140)	0.7% (1/134)	0.0% (0/98)	0.0% (0/77)	0.0% (0/73)	0.0% (0/60)
Type Ib (distal)	2.9% (4/140)	1.5% (2/134)	3.1% (3/98)	2.6% (2/77)	2.7% (2/73)	0.0% (0/60)
Type II	10.7% (15/140)	4.5% (6/134)	1.0% (1/98)	0.0% (0/77)	0.0% (0/73)	1.7% (1/60)
Type III	0.7% (1/140)	0.0% (0/134)	0.0% (0/98)	0.0% (0/77)	0.0% (0/73)	0.0% (0/60)
Type IV	1.4% (2/140)	0.0% (0/134)	0.0% (0/98)	0.0% (0/77)	0.0% (0/73)	0.0% (0/60)
Type V/Unknown	1.4% (2/140)	0.7% (1/134)	2.0% (2/98)	2.6% (2/77)	1.4% (1/73)	0.0% (0/60)
Loss of patency	0.0% (0/140)	0.0% (0/134)	0.0% (0/98)	0.0% (0/77)	0.0% (0/73)	0.0% (0/60)
Migration (> 10mm from 1-month)	N/A	0.0% (0/144)	0.0% (0/111)	0.0% (0/98)	0.0% (0/83)	0.0% (0/70)
Loss of integrity	0.0% (0/147)	0.0% (0/138)	0.0% (0/99)	0.0% (0/92)	0.0% (0/69)	0.0% (0/61)

[1] Throughout this table, m is the number of subjects who experienced events; n is the number of evaluable subjects who had imaging in the interval or who experienced the event.

1.2.8.1 Endoleaks

In VALOR II, as shown in **Table 1-9** above, 13 subjects experienced 15 type I endoleak events. Of these events, 13 were distal and two were proximal. Two of these type I endoleaks have been reported to be resolved without treatment. Eight type I endoleaks have been reported as resolved with treatment. Endoleaks of any type in nine subjects were treated via secondary endovascular procedures as discussed in **Section 1.2.8.5**. Two subjects with continuing type I endoleaks exited the study. Three subjects with continuing type I endoleaks died due to causes unrelated to the aneurysm (as adjudicated by the CEC).

Additionally, two subjects experienced type IV endoleaks. Both occurred during the procedure and were resolved without treatment by the first month with no adverse sequelae.

One subject experienced a single event of type III endoleak. The cause/type of this type III endoleak was unknown and it resolved without treatment.

One subject with a reported Type V (unknown) endoleak at day 1,064 expired due to aneurysm rupture at day 1,067. Investigator assigned cause of death due to potential aneurysm rupture caused by a likely Type III or Type IV endoleak.

1.2.8.2 Migration

In VALOR II, no stent graft migration events have been reported by clinical sites.

1.2.8.3 Stent Graft Patency

In VALOR II, no stent graft loss of patency events have been reported by clinical sites.

1.2.8.4 Device Integrity

In VALOR II, no loss of stent graft integrity events have been reported by clinical sites.

1.2.8.5 Aneurysm Enlargement

In VALOR II, aneurysm enlargement is defined as an increase greater than 5 mm in maximum aneurysm diameter as measured by appropriate imaging, as compared to the 1-month follow-up imaging.

As shown in **Table 1-10** below, aneurysm expansion greater than 5 mm has been reported by clinical sites in two subjects at the 6-month timeframe, four at the 1-year, five at the 2-year, three at the 3-year, four at the 4-year, and in six subjects at the 5-year interval. It is possible for a site to report an aneurysm enlargement event in a single subject across multiple intervals.

Overall, there were 24 thoracic aneurysm enlargement events in 12 subjects. Endoleaks have been reported in four of those 12 subjects: three subjects experienced type I endoleaks, of which one also experienced type V/unknown endoleak and one subject experienced a type V/unknown endoleak. This latter subject also experienced weakness and decreased pulse on the left hand, which was determined to be device-related as the left subclavian artery was covered by the device.

Of the 12 subjects that experienced aneurysm enlargement:

- One subject had a secondary procedure for a Type I endoleak, then experienced a thoracic aortic aneurysm rupture that was treated successfully by an additional endovascular procedure. Subject subsequently expired due to abdominal aortic aneurysm rupture.
- One subject had a secondary procedure for an ‘other endoleak’ (Type V). Subject subsequently expired due to causes unrelated to the aneurysm.
- One subject had a secondary procedure for a Type I endoleak and completed study-required follow-up.
- Two subjects had a secondary procedure for aneurysm expansion and completed study-required follow-up.
- Three subjects had no other device-related events (e.g., secondary procedure, rupture) and expired due to causes unrelated to the aneurysm.

- Four subjects had no other device-related events (e.g., secondary procedure, rupture) and completed study-required follow-up.

Measurements were taken from visits within protocol-defined windows. If there were multiple records within one visit interval, the visit closest to the target date was used. The target dates are 30 days from the initial implant procedure for the one-month visit; 183 days for the 6-month visit; 365 days for the 12-month visit, etc.

Table 1-10: VALOR II - Changes to Aneurysm Diameter during Follow-up (Site Reported)

Change	Increase >5mm % (m/n)[1]	No Change ±5mm % (m/n)[1]	Decrease >5mm % (m/n)[1]
1-month to 6-month	1.9% (2/108)	72.2% (78/108)	25.9% (28/108)
1-month to 12-month	3.8% (4/105)	60.0% (63/105)	36.2% (38/105)
1-month to 24-month	6.2% (5/81)	48.1% (39/81)	45.7% (37/81)
1-month to 36-month	3.8% (3/79)	49.4% (39/79)	46.8% (37/79)
1-month to 48-month	6.1% (4/66)	39.4% (26/66)	54.5% (36/66)
1-month to 60-month	10.7% (6/56)	41.1% (23/56)	48.2% (27/56)

[1] Throughout this table, m = number in category; n = number of known values

1.2.9 Conclusion

In summary, the information above provides the clinical data from the 160 subjects enrolled in the Valiant US study, VALOR II, which has completed the follow-up period.

A total of 54 deaths were reported in the VALOR II study. Eight of them have been adjudicated to be aneurysm-related. In addition, 15 type I and one type III endoleak events have been reported. Some of these endoleaks have been reported for the same subjects across intervals. Endoleaks in nine subjects, thoracic aortic aneurysm growth in three subjects, and one thoracic aortic aneurysm rupture have been treated via 13 secondary procedures. There have been two reports of aneurysm rupture and one of conversion to surgery. The percentages of subjects that experienced Major Adverse events are as follows: 38.1% within 30 days after implant, 22.7% between 31 days and 12 months, 28.6% between 12 and 24 months, 21.8% between 24 and 36 months, 28.1% between 36 and 48 months, and 23.5% between 48 and 60 months. There have been no site reported events of stent graft kinking, migration, or stent graft loss of patency.

Based on the VALOR II data analyzed in this section, no new safety and effectiveness concerns have been identified for the Valiant Thoracic Stent Graft System.

1.3 RESCUE IDE Clinical Study Data

This section provides clinical information on the RESCUE IDE subjects that has been entered into the Medtronic database as of January 7, 2015. The following clinical data are presented for the subjects:

- Subject Accountability
- Subject Deaths
- Aortic Rupture
- Secondary Endovascular Procedures
- Conversion to Open Surgery
- Device Related Serious Adverse Events
- Endoleaks
- Migration

1.3.1 Subject Accountability

The post-implant subject and imaging accountability for the 50 enrolled subjects is summarized in **Table 1-11** below. This data was current as of the data cut-off date, January 7, 2015. Subject accountability for the study at 1-month, 6-month, 12-month, 2 year, 3 year, 4 year and 5 year follow up time frames is summarized in **Table 1-11**. No imaging was required for pre-discharge follow-up. This table is based on case report forms completed as of January 7, 2015, and includes monitored and unmonitored data. As shown in **Table 1-11**, the number of subjects that completed clinical follow-up were 46 for 1-month, 37 for 6-month, 38 for 1-year, 31 for 2-year, 22 for 3-year and 4 for the 4-year visit.

As for follow-up imaging, also shown in **Table 1-11**, 47 subjects were eligible for 1-month, of which 45 (95.7%) completed any type of follow-up imaging. At 6 months, 44 were eligible, of which 36 (81.8%) completed any type of follow-up imaging. At the 1-year follow up, 44 were eligible, of which 35 (79.5%) completed any type of follow-up imaging. At the 2-year follow up, 44 were eligible, of which 26 (59.1%) completed any type of follow-up imaging. At the 3-year follow-up, 30 were eligible, of which 19 (63.3%) completed any type of follow-up imaging. At the 4-year follow-up, 6 were eligible, of which 2 (33.3%) completed any type of follow-up imaging.

Table 1-11: RESCUE - Subject Follow-up, Imaging and Accountability[1]

	Subject Follow-up % (m/n)[2]			Subject Imaging % (m/n)[2]			Patients with Adequate Imaging to Assess the Parameter % (m/n)[2]			Subject Accountability N					
Implant and Follow-up	**Eligible[3]**	**Clinical Follow-up**	**Imaging Follow-up**	**CT/MR Imaging**	**Chest X-Ray**	**Additional Imaging Modalities**	**Endoleak**	**Migration from 1 Month**	**Integrity**	**Enrolled but not Implanted**	**Withdrawal**	**Conversion to Surgery**	**Death**	**Lost to Follow-up**	**Not Due for Next Visit**
Implant	50														
Events Between Implant and 1-Month										0	0	0	3[4]	0	0
1-Month	47	97.9% (46/47)	95.7% (45/47)	95.7% (45/47)		0.0% (0/47)	93.6% (44/47)		97.9% (46/47)						
Events Between 1-Month and 6-Month											0	0	3[4]	0	0
6-Month	44	84.1% (37/44)	81.8% (36/44)	81.8% (36/44)		0.0% (0/44)	79.5% (35/44)	81.8% (36/44)	81.8% (3/44)						
Events Between 6-Month and 12-Month											0	0	0	0	0
12-Month	44	86.4% (38/44)	79.5% (35/44)	79.5% (35/44)	63.6% (28/44)	0.0% (0/44)	77.3% (34/44)	77.3% (34/44)	77.3% (34/44)						

	Subject Follow-up % (m/n)[2]			Subject Imaging % (m/n)[2]			Patients with Adequate Imaging to Assess the Parameter % (m/n)[2]			Subject Accountability N					
Implant and Follow-up	**Eligible[3]**	**Clinical Follow-up**	**Imaging Follow-up**	**CT/MR Imaging**	**Chest X-Ray**	**Additional Imaging Modalities**	**Endoleak**	**Migration from 1 Month**	**Integrity**	**Enrolled but not Implanted**	**Withdrawal**	**Conversion to Surgery**	**Death**	**Lost to Follow-up**	**Not Due for Next Visit**
Events Between 12-Month and 2-Year											0	0	0	0	0
2-Year	44	70.5% (31/44)	59.1% (26/44)	59.1% (26/44)		0.0% (0/ 44)	56.8% (25/44)	59.1% (26/44)	59.1% (26/44)						
Events Between 2-Year and 3-Year											0	0	1	0	13
3-Year	30	73.3% (22/30)	63.3% (19/30)	63.3% (19/30)	56.7% (17/30)	0.0% (0/30)	60.0% (18/30)	60.0% (18/30)	63.3% (19/30)						
Events Between 3-Year and 4-Year											0	0	0	0	24
4-Year	6	66.7% (4/6)	33.3% (2/6)	33.3% (2/6)		0.0% (0/6)	33.3% (2/6)	33.3% (2/6)	33.3% (2/6)						
Events Between 4-Year and 5-Year											0	0	0	0	6

	Subject Follow-up % (m/n)[2]			Subject Imaging % (m/n)[2]			Patients with Adequate Imaging to Assess the Parameter % (m/n)[2]			Subject Accountability N					
Implant and Follow-up	**Eligible[3]**	**Clinical Follow-up**	**Imaging Follow-up**	**CT/MR Imaging**	**Chest X-Ray**	**Additional Imaging Modalities**	**Endoleak**	**Migration from 1 Month**	**Integrity**	**Enrolled but not Implanted**	**Withdrawal**	**Conversion to Surgery**	**Death**	**Lost to Follow-up**	**Not Due for Next Visit**
5-Year	0	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)						
									Total	0	0	0	7	0	
												Deaths Post Conversion to Surgery	0		
													Total Deaths	7	

[1] The information in this table represents unmonitored and monitored data collected as of January 7, 2015. Information presented in this table may differ from that presented in either the Summary of Safety and Effectiveness Data (SSED) or labeling, given that the data were obtained at different time periods.
[2] Percentages are based on number of all subjects enrolled by snapshot date and include subjects that have a completed clinical/imaging follow up form for the timepoint, divided by number of eligible subjects. To be considered within window, a subject must have at a minimum, the clinical follow up or the imaging follow up occurring within the follow up window.
m = number of subjects in category, n = number of subjects with available data.
[3] Eligible at implant are all subjects enrolled by snapshot date. Eligible (ET) for time intervals post implant is eligible from the previous interval (EPI) 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. ET = EPI – (ENI + W + CTS + D + LTF + NDNV).
[4] There were 4 deaths within 30 days and 47 subjects were eligible at 1-month follow-up visit instead of 46 subjects since one subject that died had completed the 1-month follow-up visit prior to death. This subject is included under the eligible subjects at 1-month follow-up time point in the table.

1.3.2 Subject Deaths

Four subjects died within 30 days of their initial procedure. Of the four deaths, two deaths were adjudicated as not related to the device, procedure and/or to the aorta per the CEC. One death due to hemothorax was adjudicated as related to the aorta per the CEC. Another death, which was due to complications from multiple injuries, was adjudicated as related to the procedure, device and to the aorta due to the vague nature of the cause of death.

Beyond 30-days, there have been three deaths. One subject died due to infection on day 169 post- procedure. The CEC adjudicated this death to be unrelated to the device, procedure and/or to the aorta.

One subject died on day 59 post procedure. The subject's cause of death as reported by the site was respiratory failure secondary to pseudomonas pneumonia, staphylococcus aureus with underlying COPD exacerbated by a motor vehicle accident and stage III lung cancer. The CEC adjudicated this death to be unrelated to the device, procedure and/or to the aorta.

One additional subject died on day 1086 post-procedure. The subject's cause of death as reported by the site was seizure secondary to brain metastasis presumably from Stage IV prostate cancer. The CEC adjudicated the death to be unrelated to the device, procedure and/or to the aorta.

Table 1-12 summarizes information on subject deaths and relatedness.

Table 1-12: RESCUE - Mortality Details

Date of Implant	Time to Death (days)	Cause of Death (Investigator Assignment)	Death Relatedness (Investigator Assignment)	Death Relatedness (CEC Adjudicated)
01/25/2011	1	Hemothorax	Not related	Aortic related
10/06/2010	1	Traumatic brain injury	Not related	Not related
01/26/2011	5	Arrhythmia	Not related	Not related
08/26/2011	22	Complications of multiple blunt force injuries	Unknown	Device related, procedure related, aortic related
01/07/2012	59	Respiratory failure	Not related	Not related
04/10/2011	169	Infection	Not related	Not related
08/25/2010	1086	Seizure (secondary to brain metastasis presumably from Stage IV prostate cancer	Not related	Not related

1.3.3 Aortic Ruptures

There have been no post-procedure ruptures reported in this study.

1.3.4 Additional Procedures

There were no cases of additional endovascular procedures. Four subjects required secondary non-endovascular procedures, all of which were LSA bypass, to treat ischemia and pain symptoms, as shown in **Table 1-13** below.

Table 1-13: RESCUE – Secondary Procedure Details (Site Reported)

Date of Implant	Time to Secondary Procedure (days)	Procedure Performed	Cause of Secondary Procedure (Investigator Assignment)
06/08/2011	8	Other - left carotid to subclavian bypass	Peripheral ischemia
10/31/2010	36	Other – left carotid to subclavian bypass	Upper left limb ischemia
12/24/2011	103	Other – revascularization left carotid to left subclavian bypass	Left arm claudication
10/08/2011	784	Other - LSA bypass	Left arm pain

1.3.5 Conversions to Surgery

There have been no site reported cases of conversion to surgery.

1.3.6 Device Related Serious Adverse Events

There have been no site reported device related adverse events in the study.

1.3.7 Endoleaks and Other Device-Specific Safety Measures

1.3.7.1 Endoleaks

There were no Type I or Type III endoleaks reported by the sites in this study population. There were two subjects that were reported by the sites to have a Type II endoleak at the end of the procedure. Both of these endoleaks resolved without treatment by the 1-month visit. There have been no site reported events of endoleaks from the 1-month visit onwards.

1.3.7.2 Migration

There have been no site reported events of stent graft migration.

1.3.7.3 Stent Graft Patency

There have been no site reported events of stent graft loss of patency.

1.3.7.4 Device Integrity

There have been no site reported events of stent graft loss of device integrity.

1.3.8 Conclusion

In summary, the information above provides the most current clinical follow-up data on the RESCUE study. This data represents 50 subjects enrolled in the RESCUE Study.

As of January 7, 2015, the data cut-off date for this report, there have been seven deaths in the subject population. Two deaths were adjudicated to be aortic-related, with one of the two also noted as procedure and device related. Four subjects have been treated with four secondary non-endovascular procedures, of which all were LSA bypass. There were no cases of endovascular re-intervention, conversion to open surgery or ruptures reported. Two subjects experienced Type II endoleaks at the end of the procedure but both were resolved without treatment by the 1-month visit. No other subject has experienced an endoleak. There have been no site reported events of stent graft kinking, migration, or stent graft loss of patency.

Based on the longer term follow-up data, no new safety and effectiveness concerns have been identified for the Valiant Thoracic Stent Graft System.

1.4 Medtronic Dissection Trial IDE Clinical Study Data

This section provides clinical information on the Medtronic Dissection Trial IDE subjects that has been entered into the Medtronic database as of January 7, 2015. The following clinical data are presented for the subjects:

- Subject Accountability
- Subject Deaths
- Aortic Rupture
- Additional Endovascular Procedures
- Conversion to Open Surgery
- Serious Adverse Events
- Device-Specific Safety Measures
    - Aortic Enlargement
    - Technical Observations

1.4.1 Subject Accountability

The post-implant subject and imaging accountability for the 50 enrolled subjects is summarized in **Table 1-14** below. This data was current as of the data cut-off date, January 7, 2015. Subject accountability for the study at 1-month, 6-month, 12-month, 2 year, 3 year, 4 year and 5 year follow up time frames is summarized in **Table 1-14**. This table is based on case report forms completed as of January 7, 2015, and includes monitored and unmonitored data. As shown in **Table 1-14**, the number of subjects that completed clinical follow-up was 45 for 1-month, 36 for 6- month, 34 for 1-year, 27 for 2-years, 17 for 3-years and 1 for the 4-year visit.

As for follow-up imaging, also shown in **Table 1-14**, 46 subjects were eligible at 1-month, of which 45 (97.8%) completed any type of follow-up imaging. At 6 months, 41 were eligible,

of which 34 (82.9%) completed any type of follow-up imaging. At the 1-year follow-up, 37 were eligible, of which 33(89.2%) completed any type of follow-up imaging. At the 2-year follow up, 35 were eligible, of which 27 (77.1%) completed any type of follow-up imaging. At the 3-year follow-up, 18 were eligible, of which 17 (94.4%) completed any type of follow-up imaging. At the 4-year follow-up, 2 were eligible, of which 1 (50.0%) completed any type of follow-up imaging.

Table 1-14: MEDTRONIC DISSECTION TRIAL - Subject Follow up, Imaging and Accountability[1]

	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[3]**	**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[4]**	**Endo-leak**	**Migration from Discharge**	**Integrity**	**Enrolled but not Implant-ed**	**With-drawal**	**Con-version 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)[5]	76.6% (36/47)		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													0	0	3	0	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	1	0

	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[3]**	**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[4]**	**Endo-leak**	**Migration from Discharge**	**Integrity**	**Enrolled but not Implant-ed**	**With-drawal**	**Con-version to Surgery**	**Death**	**Lost to Follow-up**	**Not Due for Next Visit**
12-Month	37	91.9% (34/37)	89.2% (33/37)	89.2% (33/37)	78.4% (29/37)	0.0% (0/37)	89.2% (33/37)	89.2% (33/37)	89.2% (33/37)	89.2% (33/37)	89.2% (33/37)						
Events Between 12-Month and 2-Year													0	0	1	1	0
2-Year	35	77.1% (27/35)	77.1% (27/35)	77.1% (27/35)	71.4% (25/35)	0.0% (0/35)	77.1% (27/35)	77.1% (27/35)	74.3% (26/35)	77.1% (27/35)	77.1% (27/35)						
Events Between 2-Year and 3-Year													0	0	0	1	16
3-Year	18	94.4% (17/18)	94.4% (17/18)	94.4% (17/18)	83.3% (15/18)	0.0% (0/18)	88.9% (16/18)	88.9% (16/18)	77.8% (14/18)	88.9% (16/18)	94.4% (17/18)						
Events Between 3-Year and 4-Year													0	0	0	0	16
4-Year	2	50.0% (1/2)	50.0% (1/2)	50.0% (1/2)	50.0% (1/2)	0.0% (0/2)	50.0% (1/2)	50.0% (1/2)	50.0% (1/2)	50.0% (1/2)	50.0% (1/2)						

	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[3]**	**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[4]**	**Endo-leak**	**Migration from Discharge**	**Integrity**	**Enrolled but not Implant-ed**	**With-drawal**	**Con-version to Surgery**	**Death**	**Lost to Follow-up**	**Not Due for Next Visit**
Events Between 4-Year and 5-Year													0	0	0	0	2
5-Year	0	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)						
Total												0	1	0	10	5	
Deaths Post Conversion to Surgery															0		
Total Deaths															10		

[1] The information in this table represents unmonitored and monitored data collected as of January 7, 2015. Information presented in this table may differ from that presented in either the Summary of Safety and Effectiveness Data (SSED) or labeling, given that the data were obtained at different time periods.

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

[3] Eligible at implant are all subjects enrolled by snapshot date. Eligible (ET) for time intervals post implant is eligible from the previous interval (EPI) 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. ET = EPI – (ENI + W + CTS + D + LTF + NDNV) ET = EPI – (ENI + W + CTS + D + LTF + NDNV) ET = EPI – (ENI + W + CTS + D + LTF + NDNV)

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

[5] 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.

1.4.2 Subject Deaths

Table 1-15 below summarizes the ten deaths that occurred as of the data cut-off date, January 7, 2015. All deaths have been adjudicated by the CEC.

Four of the deaths occurred within 30 days of the procedure. Of the four, one death secondary to cardiac tamponade was adjudicated by CEC as related to the device, procedure and dissection. Two deaths caused by sepsis and pulmonary embolism were adjudicated by CEC as related to the procedure and to the dissection. One death secondary to mesenteric ischemia in totalis was adjudicated by CEC as dissection related.

Four deaths occurred between 30 and 365 days. One death was secondary to cardiac arrest on day 71 post-procedure. The CEC adjudicated the death as unrelated to the device, procedure or dissection. There was one death secondary to pneumonia 87 days post-procedure adjudicated as dissection related by the CEC. One subject died from cardiac arrest on day 124 post-procedure. The CEC adjudicated this death as procedure related. Another subject died on day 315 post procedure due to respiratory failure. The CEC adjudicated this death as unrelated to the device, procedure or the dissection.

Between the 1-year and 2-year follow-up, one death reported as due to natural causes on day 432 was adjudicated by the CEC as not related to the device, procedure or dissection.

Beyond 2 years, one subject died on day 812 post-procedure. Cause of death was sepsis and this was adjudicated by the CEC as unrelated to the device, procedure or dissection.

Table 1-15: Dissection – Mortality Details

Procedure Date	Death Date	Implant to Death (days)	Cause of Death Site Reported	Death Relatedness[1] Site Reported	Death Relatedness[1] CEC Adjudicated
10/29/2010	10/29/2010	0	Cardiac Tamponade	Procedure Related	Device Related, Procedure Related, Dissection Related
02/16/2012	02/17/2012	1	Mesenteric Ischemia In Totalis	Dissection Related	Dissection Related
03/18/2012	03/27/2012	9	Sepsis	Dissection Related	Procedure Related, Dissection Related
06/25/2010	07/21/2010	26	Pulmonary Embolism	Not Related	Procedure Related, Dissection Related
02/14/2012	04/25/2012	71	Cardiac Arrest	Not Related	Not Related
08/09/2011	11/04/2011	87	Pneumonia	Not Related	Dissection Related
10/28/2010	03/01/2011	124	Cardiac Arrest	Not Related	Procedure Related
05/04/2012	03/15/2013	315	Respiratory Failure	Not Related	Not Related
09/15/2011	11/20/2012	432	Natural Causes	Not Related	Not Related
03/19/2011	06/08/2013	812	Sepsis	Not Related	Not Related

[1]Relationship to Device/Procedure/Dissection

1.4.3 Aortic Ruptures

There have been no post-index procedure ruptures reported in this study.

1.4.4 Additional Procedures

Additional endovascular procedures performed that are related to the dissection and not related to the dissection are listed in **Table 1-16**. Related to the dissection, three subjects underwent a total of five procedures that involved the placement of an additional endovascular device: One subject required one additional endovascular procedure for placement of an additional stent graft due to a Type I endoleak that occurred 9 days post-index procedure. One subject required one additional endovascular procedure for placement of an additional endovascular device to treat a descending thoracic aneurysm 246 days post-index procedure. One subject required LSA bypass due to false lumen perfusion on day 87 post-index procedure and three additional endovascular procedures for placement of additional endovascular devices to treat continued perfusion of the false lumen on post-index procedure days 164, 367 and 538. Also related to the dissection, one additional subject underwent a coil embolization and embolization using a liquid embolic agent on day 1279 to treat a Type Ia endoleak.

One subject had an additional endovascular procedure that was not related to the dissection. This subject had a Type Ia Endoleak on day 3 post-implant. The subject had an LSA plug placed on day 9 that was reported as related to the procedure but not related to the dissection by the site.

Table 1-16: Additional Endovascular Procedures

	0 to 30 Days % (m/n)[1]	**31 to 365 Days % (m/n)[1]**	**366 to 731 Days % (m/n)[1]**	**732 to 1096 Days % (m/n)[1]**	**1097 to 1461 Days % (m/n)[1]**	**1462 to 1826 Days % (m/n)[1]**
Additional Endovascular Procedure Related to the Dissection	2.0% (1/50)	4.3% (2/46)	2.7% (1/37)	0.0% (0/32)	7.7% (1/13)	0.0% (0/1)
Additional Endovascular Device Placed	2.0% (1/50)	4.3% (2/46)	2.7% (1/37)	0.0% (0/32)	0.0% (0/13)	0.0% (0/1)
Coil Embolization	0.0% (0/50)	0.0% (0/46)	0.0% (0/37)	0.0% (0/32)	7.7% (1/13)	0.0% (0/1)
LSA Plug	0.0% (0/50)	0.0% (0/46)	0.0% (0/37)	0.0% (0/32)	0.0% (0/13)	0.0% (0/1)
Other	0.0% (0/50)	0.0% (0/46)	0.0% (0/37)	0.0% (0/32)	7.7% (1/13)	0.0% (0/1)
Additional Endovascular Procedure Not Related to the Dissection	2.0% (1/50)	0.0% (0/46)	0.0% (0/37)	0.0% (0/32)	0.0% (0/13)	0.0% (0/1)

[1]m = number of subjects in category. For overall number of subjects underwent secondary endovascular procedures, n = number of implanted subjects who experienced an event or who were followed at least until the lower endpoint of the interval. For example, for column ‘0-30 Days', ‘31-365 Days', ‘366-731 Days',’732-1096 Days','1097-1461 Days' and '1462-1826 Days', a subject had to be followed respectively for at least 0 days, 31 days, 366 days, 732 days, 1097 days and 1462 days in order to be included in the denominator, unless he/she experienced an event in the corresponding interval.

Other secondary non-endovascular procedures performed are listed in **Table 1-17**. Two subjects required open repairs of retrograde Type A dissections. A subject was observed to have a retrograde type A dissection during the discharge CTA on day 5 post-index procedure and subsequently had open surgical repair on day 6. The investigator reported this event as procedure-related. The second subject presented to the hospital with a retrograde type A dissection involving the ascending aorta on day 56 post-index procedure and was repaired by open surgical repair on day 57 post-index procedure. The investigator reported this event as dissection-related. There were no conversions to open repairs of the descending dissection. Two subjects required LSA bypass secondary procedures. One subject required LSA bypass due to false lumen perfusion on day 87 post-index procedure. One subject required LSA bypass due to left arm claudication on day 53 post-index procedure.

Table 1-17: Additional Secondary Non-Endovascular Procedures

Additional Secondary Non-Endovascular Procedures	0 to 30 Days % (m/n)[1]	31 to 365 Days % (m/n)[1]	366 to 731 Days % (m/n)[1]	732 to 1096 Days % (m/n)[1]	1097 to 1461 Days % (m/n)[1]	1462 to 1826 Days % (m/n)[1]
Open Repair of Retrograde Type A Dissection	2.0% (1/50)	2.2% (1/46)	0.0% (0/37)	0.0% (0/32)	0.0% (0/13)	0.0% (0/1)
Conversion to Open Repair for Descending Dissection	0.0% (0/50)	0.0% (0/46)	0.0% (0/37)	0.0% (0/32)	0.0% (0/13)	0.0% (0/1)
LSA Bypass	0.0% (0/50)	4.3% (2/46)	0.0% (0/37)	0.0% (0/32)	0.0% (0/13)	0.0% (0/1)

[1]m = number of subjects in category, n = number of implanted subjects who experienced an event or who were followed at least until the lower endpoint of the interval. For example, for column '0-30 Days', '31-365 Days', '366-731 Days', '732-1096 Days', '1097-1461 Days' and '1462-1826 Days', a subject had to be followed respectively for at least 0 days, 31 days, 366 days, 732 days, 1097 days and 1462 days in order to be included in the denominator, unless he/she experienced an event in the corresponding interval.

1.4.5 Conversions to Surgery

There have been no site reported cases of conversion to surgery.

1.4.6 Serious Adverse Events

As per the study protocol, only those serious adverse events (SAEs) that are related to the device, to the implant procedure, and/or to the aortic disease are reported by the sites.

Table 1-18 lists the number of subjects who experienced one or more SAEs. A subject may report multiple adverse events, and in different subcategories; hence, the number of subjects in each category may not be the sum of those in each subcategory.

Rates of particular events most relevant to Dissection subjects are provided in **Table 1-19**.

Regarding SAEs, 38.0% (19/50) of subjects had one or more SAE within 30 days and 19.6% (9/46) of subjects had one or more SAE within one year. Regarding neurological events, stroke was reported in three subjects in the Medtronic Dissection Trial. One resolved without treatment and two were unresolved at the time of the subjects' deaths. One subject experienced a cerebrovascular ischemic event and lower limb extremity paralysis that required above the knee amputation. This subject experienced paralysis of the left lower extremity that prohibited healing, resulting in infection and ulceration that required treatment with an above-the-knee amputation. One additional subject had paralysis that was unresolved at the time of the subject's death. A second subject has paraplegia.

Of note regarding vascular disorders, two subjects experienced retrograde Type A dissections requiring open surgical repair and an additional two subjects were reported with aortic aneurysm: One subject had TAA requiring secondary endovascular treatment and one subject had AAA requiring open surgical repair.

Table 1-18: Subjects with Serious Adverse Events by Date of Onset

Category	0 to 30 Days % (m/n)[1]	31 to 365 Days % (m/n)[1]	366 to 731 Days % (m/n)[1]	732 to 1096 Days % (m/n)[1]	1097 to 1461 Days % (m/n)[1]	1462 to 1826 Days % (m/n)[1]
Subjects experiencing one or more SAE[2]	38.0% (19/50)	19.6% (9/46)	2.7% (1/37)	3.1% (1/32)	7.7% (1/13)	0.0% (0/1)
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)	2.7% (1/37)	-	-	-
Death[3]	-	-	2.7% (1/37)	-	-	-
Continued perfusion from a branch vessel requiring treatment[4]	-	2.2% (1/46)	-	-	-	-
Infections And Infestations	2.0% (1/50)	2.2% (1/46)	-	-	-	-
Pneumonia	2.0% (1/50)	2.2% (1/46)	-	-	-	-
Sepsis	2.0% (1/50)	-	-	3.1% (1/32)	-	-
Injury, Poisoning And Procedural Complications	8.0% (4/50)	-	-	-	7.7% (1/13)	-
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)	-	-	-	-	-
Investigations	2.0% (1/50)	-	-	-	-	-

Category	0 to 30 Days % (m/n)[1]	31 to 365 Days % (m/n)[1]	366 to 731 Days % (m/n)[1]	732 to 1096 Days % (m/n)[1]	1097 to 1461 Days % (m/n)[1]	1462 to 1826 Days % (m/n)[1]
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	12.0% (6/50)	-	-	-	-	-
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)	2.2% (1/46)	-	-	-	-
Haemothorax	2.0% (1/50)	-	-	-	-	-
Pulmonary Embolism	2.0% (1/50)	-	-	-	-	-
Respiratory Failure	-	2.2% (1/46)	-	-	-	-
Vascular Disorders	10.0% (5/50)	10.9% (5/46)	-	-)	-	-
Aortic Aneurysm	-	4.3% (2/46)	-	-	-	-
Retrograde Type A 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)	-	-	-	-	-

Category	0 to 30 Days % (m/n)[1]	31 to 365 Days % (m/n)[1]	366 to 731 Days % (m/n)[1]	732 to 1096 Days % (m/n)[1]	1097 to 1461 Days % (m/n)[1]	1462 to 1826 Days % (m/n)[1]
Subclavian Artery Embolism	2.0% (1/50)	-	-	-	-	-

For ease of review, a dash symbol "-" has replaced 0.0% in this table where the numerator is 0 and denominator can be found in the first row of the table.

[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.

[3] One SAE was reported as "Death" by the site as the subject died of natural causes. Events in this category do not include SAEs that resulted in death.

[4] The adverse event wording was taken from the CRF. MedDra coding currently does not have a code for continued perfusion requiring treatment; hence this event is placed in the General Disorders category. Continued false lumen perfusion observed in one subject was treated with additional devices and was therefore reported as a serious adverse event.

Table 1-19: Subjects with Selected Events by Date of Onset

	0 to 30 Days % (m/n)[1]	31 to 365 Days % (m/n)[1]	366 to 731 Days % (m/n)[1]	732 to 1096 Days % (m/n)[1]	1097 to 1461 Days % (m/n)[1]	1462 to 1826 Days % (m/n)[1]
Any Event	16.0% (8/50)	8.7% (4/46)	2.7% (1/37)	3.1% (1/32)	0.0% (0/13)	0.0% (0/1)
Death[2]	8.0% (4/50)	8.7% (4/46)	2.7% (1/37)	3.1% (1/32)	-	-
MI	-	-	-	-	-	-
Stroke	6.0% (3/50)	-	-	-	-	-
Renal Failure (+Dialysis)	2.0% (1/50)	-	-	-	-	-
Respiratory Failure	-	2.2% (1/46)	-	-	-	-
Paralysis/Paraparesis	6.0% (3/50)	-	-	-	-	-
Bowel Ischemia	2.0% (1/50)	-	-	-	-	-

For ease of review, a dash symbol "-" has replaced 0.0% in this table where the numerator is 0 and denominator can be found in the first row of the table.
[1]m = number of subjects experiencing one or more events in a category, n = number of subjects who experienced an event or who died during the interval, or who were followed at least until the lower endpoint of the interval.
[2] This represents all deaths irrespective of the event that caused it.

1.4.6.1 Device Related Adverse Events

The device-related AEs are listed in **Table 1-20**. Two subjects had device-related AEs, both of which were SAEs. One subject had a CVA requiring intubation on postoperative day 1. This event was unresolved at the time of the subject's death on day 124. The second subject experienced continued perfusion of the false lumen that was reported on day 83 post-index procedure and the subject underwent an LSA bypass on day 87. The perfusion of the false lumen persisted and the subject underwent a secondary endovascular procedure on day 164 post-procedure, at which time a proximal graft was placed. The perfusion continued to persist and the subject underwent an additional endovascular procedure on day 367 post-implant, at which time two additional stent grafts were implanted, one proximal and one distal. This subject required an additional secondary endovascular procedure to place an additional stent graft on day 538 and the site reported that the subject recovered with treatment.

Table 1-20: Subjects with Device Related Adverse Events by Date of Onset

Category	0 to 30 Days % (m/n)[1]	31 to 365 Days % (m/n)[1]	366 to 731 Days % (m/n)[1]	732 to 1096 Days % (m/n)[1]	1097 to 1461 Days % (m/n)[1]	1462 to 1826 Days % (m/n)[1]
Subjects Experiencing One or More AEs	2.0% (1/50)	2.2% (1/46)	0.0% (0/37)	0.0% (0/32)	0.0% (0/13)	0.0% (0/1)
General Disorders And Administration Site Conditions[2]	-	2.2% (1/46)	-	-	-	-
Continued perfusion from a branch vessel requiring treatment[3]	-	2.2% (1/46)	-	-	-	-
Nervous System Disorders	2.0% (1/50)	-	-	-	-	-
Cerebrovascular Accident	2.0% (1/50)	-	-	-	-	-

For ease of review, a dash symbol "-" has replaced 0.0% in this table where the numerator is 0 and denominator can be found in the first row of the table.
[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] MedDra coding currently does not have a code for continued perfusion requiring treatment; hence this event is placed in the General Disorders category.
[3] The adverse event wording was taken from the CRF.

1.4.7 Device-Specific Safety Measures

1.4.7.1 Aortic Enlargement

For this study, several measures of aortic remodeling were taken, including the following:

- Change, from baseline in the maximum true lumen (TL) diameter over the length of the stent graft
- Change, from baseline in the maximum false lumen (FL) diameter over the length of the stent graft
- Change, from baseline in the maximum total descending thoracic aortic diameter
- FL thrombosis over the length of the stent graft

The first image taken after the procedure was used as the baseline image. Site-reported results for changes in aortic diameter over the length of the stent graft are presented in **Table 1-21**. It includes information on subjects whose diameter remained stable, or increased or decreased by more than 5 mm. 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.

Increase in True Lumen Diameter Over the Length of the Stent Graft:

The sites 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 follow-up visits. Over 85% of subjects at 2 years of follow-up and 100% of subjects at 3-year follow-up had a true lumen diameter that remained stable or increased (by at least 5.0 mm) compared to baseline.

Decrease in False Lumen Diameter Over the Length of the Stent Graft:

The sites reported that the false lumen diameter remained stable or decreased (by at least 5.0 mm) compared to baseline in at least 75% of the subjects at the 6-month visit, and at least 80% at the 12-month visit. In over 75% of subjects completing 2 years of follow-up and 80% of subjects at 3-year follow-up, the false lumen remained stable or decreased (by at least 5.0 mm) compared to baseline.

Change in Total Aortic Diameter:

The sites 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, in more than 85% of the subjects at the 12-month visit. In over 75% of subjects completing 2 and 3 years of follow-up, the total aortic diameter remained stable or decreased (by at least 5.0 mm) compared to baseline.

False Lumen Thrombosis Status Over the Length of the Stent Graft:

The sites reported a partial or complete thrombosis of the false lumen in more than 65.0% of the subjects at the first post-procedural CT, in more than 75% of the subjects at the 6 and 12-month visits, more than 70% of the subjects at 2 years and more than 85% of subjects at 3-year follow-up.

Two subjects with a partially thrombosed false lumen experienced SAEs. One subject experienced a stroke and paralysis on day 2. The second subject experienced cardiac arrest on day 71 that resulted in the subject's death.

Table 1-21: 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)	2-Year Follow-up % (m/n)	3-Year Follow-up % (m/n)	4-Year Follow-up % (m/n)	5-Year 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)	14.3% (4/28)	0.0% (0/15)	0.0% (0/1)	NA

Thoracic Dissection Measurements[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)
Stable	NA	54.5% (18/33)	47.1% (16/34)	46.4% (13/28)	46.7% (7/15)	100.0% (1/1)	NA
Increase	NA	39.4% (13/33)	47.1% (16/34)	39.3% (11/28)	53.3% (8/15)	0.0% (0/1)	NA
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)	53.6% (15/28)	33.3% (5/15)	100.0% (1/1)	NA
Stable	NA	39.4% (13/33)	32.4% (11/34)	25.0% (7/28)	46.7% (7/15)	0.0% (0/1)	NA
Increase	NA	24.2% (8/33)	17.6% (6/34)	21.4% (6/28)	20.0% (3/15)	0.0% (0/1)	NA
Change from Baseline[2] in the Maximum Total Descending Thoracic Aortic Diameter (mm)							
Decrease[3]	NA	35.3% (12/34)	32.4% (11/34)	35.7% (10/28)	31.3% (5/16)	100.0% (1/1)	NA
Stable	NA	41.2% (14/34)	52.9% (18/34)	42.9% (12/28)	43.8% (7/16)	0.0% (0/1)	NA
Increase	NA	23.5% (8/34)	14.7% (5/34)	21.4% (6/28)	25.0% (4/16)	0.0% (0/1)	NA
False Lumen Thrombosis over the Length of the Stent Graft							
Completely Thrombosed	34.9% (15/43)	45.5% (15/33)	64.7% (22/34)	51.9% (14/27)	71.4% (10/14)	0.0% (0/1)	NA
Partially Thrombosed	30.2% (13/43)	30.3% (10/33)	14.7% (5/34)	18.5% (5/27)	14.3% (2/14)	0.0% (0/1)	NA
Patent	34.9% (15/43)	24.2% (8/33)	20.6% (7/34)	29.6% (8/27)	14.3% (2/14)	100.0% (1/1)	NA

[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.

1.4.7.2 Technical Observations

Stent graft integrity was maintained and there have been no site reported events of stent graft twisting, kinking or fracture.

1.4.8 Conclusion

In summary, the information above provides the most current clinical follow-up data from the Medtronic Dissection Trial. The data represents the results for the 50 subjects enrolled in this study.

As of January 7, 2015, the data cut-off date for the Medtronic Dissection Trial in this report, there have been 10 deaths in the subject population. One death secondary to cardiac tamponade was adjudicated by the CEC as device, procedure and dissection related. Two deaths caused by sepsis and pulmonary embolism were CEC adjudicated as procedure and dissection related. One death secondary to mesenteric ischemia in totalis and another death secondary to pneumonia were adjudicated as dissection related. One death due to cardiac arrest was adjudicated as procedure related, and four deaths due to cardiac arrest, natural causes, respiratory failure and sepsis were adjudicated as not related to the device, procedure or dissection.

Regarding SAEs, 38.0% (19/50) of subjects had one or more SAE within 30 days and 19.6% (9/46) of subjects had one or more SAE within one year. There were two SAEs reported as device related: One was a cerebrovascular accident and one was continued perfusion of the false lumen. The remaining SAEs were reported as procedure or aortic disease related. Regarding neurological events, three subjects experienced CVAs all within 7 days of the procedure. One subject experienced a cerebrovascular ischemic event and lower limb extremity paralysis that required above the knee amputation. Of note regarding vascular disorders, two subjects experienced retrograde Type A dissections requiring open surgical repair and an additional two subjects were reported with aortic aneurysm: One subject had TAA requiring secondary endovascular treatment and one subject had AAA requiring open surgical repair.

For events that were dissection-related, three subjects required additional endovascular devices placed to treat events that included a subject with TAA, a subject with Type I endoleak and a subject with continued perfusion of the false lumen from a branch vessel. One additional subject required an endovascular procedure that involved coil embolization to treat Type I endoleak. Also for dissection-related events, two subjects required non-endovascular procedures, which included one subject that required an open repair of retrograde Type A dissection and one subject that required a LSA bypass.

There were no cases of conversion to open surgery or ruptures reported. There have been no site reported events of stent graft kinking, migration, or loss of patency.

Based on the available follow-up data, no new safety and effectiveness concerns have been identified for the Valiant Thoracic Stent Graft System.

2.0 Worldwide Commercial Experience

As of December 31, 2014, approximately 55,000 units of the Valiant Thoracic Stent Graft with Captivia Delivery System have been distributed worldwide.

Medtronic performs a rigorous analysis of all product complaints received, including complaints from US/OUS clinical trials, post market trials/registries, and commercial use of Medtronic Vascular products.

Although complaints from both clinical trials and commercial experience are reviewed, the analyses presented below are derived from commercial data only (i.e., post market trials/registries, and commercial use of Medtronic Vascular products).

The data presented in **Table 2-1** summarizes the adverse events reported for the time period from January 1, 2014 to December 31, 2014, for devices in commercial use. Additional information regarding each of these events is presented in the sections following this table.

Table 2-1: Summary of Reported Adverse Events from Worldwide Commercial Experience

Adverse Event Type	US	International
Ruptures (Post-implant)	5	4
Surgical Conversion	10	4
Aneurysm-Related Death	31	7
Integrity	4	16
Migration	3	3
Misaligned Deployment	1	0

Summary of Aneurysm-Related Mortality Events

A total of 37 aneurysm related deaths have been reported worldwide in subjects treated with the Valiant Thoracic Stent Graft System. Of these aneurysm related deaths, 29 were associated with treatment of aneurysm/PAU and eight were associated with treatment of dissections.

Table 2-2: Summary of Aneurysm-Related Mortality

Cause for Aneurysm Related Mortality[1]	Number of Cases
Pre Implant Aortic Rupture	6
Post Implant Aortic Rupture[2]	5
Procedure-Related • Other complications[3] • Pulmonary embolism • Vessel perforation • MI • Stroke • Blood Loss	22 (10) (1) (1) (3) (1) (2)

Cause for Aneurysm Related Mortality[1]	Number of Cases
• Post Implant Type A Dissection • Cardiac Arrest • Embolic Event	(2) (1) (1)
Unknown[4]	4

[1] Aneurysm-related mortality is defined as any death, irrespective of the pathology being treated, occurring within 30 days of the index procedure, or due to a rupture, conversion or secondary procedure.
[2] Details on post implant aortic ruptures can be found in the section following this table.
[3] Complications related to pre-existing medical conditions, i.e., bowel ischemia, pre-operative dissection/Type A dissection, pre-existing aortic root tear, patient reaction to anti-coagulant, colon infarct, brain death, etc.
[4] Cause of death was unknown due to insufficient information received.

Summary of Post-Implant Aortic Ruptures

There have been a total of nine post-implant aortic ruptures reported to Medtronic, as shown in the **Table 2-3**. Of these nine post-implant aortic ruptures, five were associated with the treatment of an aneurysm and four were associated with treatment of dissections.

Of the five ruptures associated with the treatment of aneurysms, one event occurred due to ballooning, which moved the graft proximally causing the distal portion of the stent graft to contact the aneurysm wall leading to rupture. One rupture occurred due to damage of the stent graft during lung surgery, which led to a type V/unknown endoleak and rupture. One rupture was due to a Type I endoleak. For the remaining two aneurysm ruptures, one of which involved the rupture of an abdominal aneurysm, the exact cause could not be determined due to inadequate information.

Of the four ruptures observed during treatment of dissections, one event was related to the treatment of a type A dissection, the exact cause could not be determined due to inadequate information. One event was due to a Type II endoleak from the intercostal artery. One event was due to a break in the front grip of the delivery system during the procedure leading to an inaccurate deployment of the stent graft in the aorta. This led to an elective secondary intervention of conversion to open surgery during which the false lumen ruptured and the patient expired. Investigation into the break of the front grip determined the root cause to be associated with a step in the manufacturing process and measures are being taken to prevent future occurrences. For the remaining rupture, the exact cause could not be determined due to inadequate information.

Out of nine events, five of the patients with aortic rupture expired as indicated in **Table 2-2**. The four other ruptures occurred post-index procedure, one of which was repaired via open surgical repair and the others via secondary endovascular procedures.

Table 2-3 lists the causes of ruptures and **Table 2-4** lists the timeframe of each rupture.

Table 2-3: Summary of Post-Implant Aortic Ruptures

Causes of Ruptures	Number of Cases[1]
Endoleaks • Type I Endoleak • Type II (Intercostal Artery) • Type V/Unknown Endoleak	 1 1 1
Ballooning	1
Broken Delivery System[3]	1
Unknown[2]	4

[1] Total of five post implant rupture cases led to aneurysm related mortality summarized in **Table 2-2**.
[2] Includes events where adequate information is not available in order to determine the cause of rupture.
[3] Inaccurate delivery resulted from front grip break during deployment and elective secondary intervention of open conversion was performed (instead of endovascular intervention).

Table 2-4: Timeframes for Ruptures[1]

Time Period	Within 1 year post implant	1 year post implant	2 years post implant	3 years post implant	4 years post implant	5 years post implant	6 years post implant	Time Unknown
Number of ruptures	7	-	-	-	-	-	-	2

[1] The timeframes are calculated from initial endovascular repair.

Summary of Conversions

In the time period from January 1, 2014 to December 31, 2014, conversion to open repair has been reported in 14 subjects treated with the Valiant Thoracic Stent Graft with Captivia Delivery System. The primary causes of these conversions are listed in the table below.

Table 2-5: Summary of Conversions

Cause for Conversions	Number of cases
Type A Dissection	6
Pre-Existing Infection	2
Post-Operative Rupture	1
User Error	1
Deployment Difficulties	1
Aortic Perforation[1]	3

[1]Two aortic perforations were associated with perforation of the aorta by proximal bare springs, and one aortic perforation occurred in which the delivery system perforated the aorta during treatment of a ruptured pseudoaneurysm.

The table below provides an overview of the timeframes in which the conversions took place. The majority of the conversions took place within 1 year post-implant.

Table 2-6: Timeframe for Conversions

Time Period	Within 1 year post implant	1 year post implant	2 years post implant	3 years post implant	4 years post implant	5 years post implant	>5 years post implant	Time Unknown
Number of Conversions	13	-	-	-	-	-	-	1

Device Integrity

There were 20 events reported for device integrity issues. As shown in **Table 2-7**, six out of the 20 device integrity events were related to Type III endoleaks. The six type III endoleak events were due to unknown causes and did not lead to any patient death. Twelve events were due to breaks observed in the delivery system and two events were related to stent fractures. The exact cause of these events could not be determined upon further investigation.

One out of the 20 device integrity events led to patient death. This event involved a break in the front grip of the delivery system during the procedure leading to an inaccurate deployment of the stent graft in the aorta. This led to an elective secondary intervention of conversion to open surgery, during which the false lumen ruptured and the patient expired. Investigation into the break of the front grip determined the root cause to be associated with a step in the manufacturing process and steps are being taken to prevent future occurrences.

For the remaining nineteen cases, there was either no patient impact (damaged device not used or used without any issue) or the patient was treated via a secondary procedure using another Medtronic or competitor stent graft.

Table 2-7: Summary of Device Integrity Issues

Device Integrity Issue	Number of cases
Break in Delivery System[1]	12
Leak, Type III, Fabric	6
Stent Fracture	2

[1] Includes damage to the delivery system components i.e. broken hand switch, broken screw gear, broken sideport, detached front grip, hole in sheath housing.

Migration

For purposes of the commercial adverse event information, “stent graft migration” is defined as any movement from the original point of placement of the stent graft, post implantation.

Between the time period of January 1, 2014 and December 31, 2014, there were six events related to device migration reported to Medtronic. Five of the six events were associated with aneurysm treatment and one was associated with a dissection treatment.

Of the six migrations, four had unknown contributing factors and two were due to aneurysm growth. Five of the migrations were corrected using secondary endovascular procedure and one was treated with surgical conversion.

Misaligned Deployment

One subject experienced misaligned deployment between January 1, 2014 and December 31, 2014. The Closed Web stent graft configuration, which does not have the tip capture mechanism, was utilized. This event was considered Severity 1 misaligned deployment, as there were no clinical sequelae. The exact cause of the misaligned deployment could not be determined.

Misaligned Deployment and the associated clinical severities are described below:

Misaligned deployment can occur when the proximal stent apices of a deployed stent graft remain significantly non-parallel to the wall of the aorta after deployment has been completed. Potential clinical sequelae of misaligned deployment range from negligible to significant and may present either acutely or chronically.

- Severity 1: No clinical impact- unresolved mild asymmetry or stent apex protrusion into the aortic wall without clinical impact, including no evidence of endoleak, graft narrowing/occlusion or perforation.
- Severity 2: Clinical impact- unresolved asymmetry or stent apex protrusion into the aortic wall with clinical impact, including evidence of endoleak or luminal narrowing of the endograft.

3.0 Explant Analysis

Medtronic Vascular has collected and analyzed the Valiant Thoracic Stent Graft devices (both Xcelerant and Captivia Delivery System configurations) that were implanted and subsequently explanted and returned to Medtronic, either during conversion to open surgical repair or in conjunction with an autopsy.

As of December 31, 2014, Medtronic Vascular has completed explant analyses on 13 cases from patients who were implanted with a Valiant stent graft as the main device, between October 2005 and November 2012. There were no explants received by Medtronic for the reporting period of the report (January 1, 2014 through December 31, 2014). Data from the explant program are used to guide ongoing product development, design improvement, and training programs.

Table 3-1: Sources of Explanted Devices

Source of Explants	Total Number
IDE Clinical Study	4
Commercial Sales Outside of the United States	8
Commercial Sales Within the United States	1
Total	**13**

Each explanted device received by Medtronic Vascular is evaluated by internal personnel and by outside technical experts when appropriate. The detailed findings are then analyzed in conjunction with the patient-specific clinical information in order to assess the potential clinical significance, if any, of the device findings. Patient anatomy and the procedural technique used by the physician are also assessed.

Summary of Explant Observations

The histogram in **Figure 3-1** shows the distribution of implant duration for the 13 explants analyzed. The devices explanted had been implanted for an average of 2.4 months (72 days). Nine of the 13 explants (69%) had been implanted for less than 30 days. The remaining 4 explants were implanted for duration of 3.3, 5.4, 7.6, and 13.5 months.

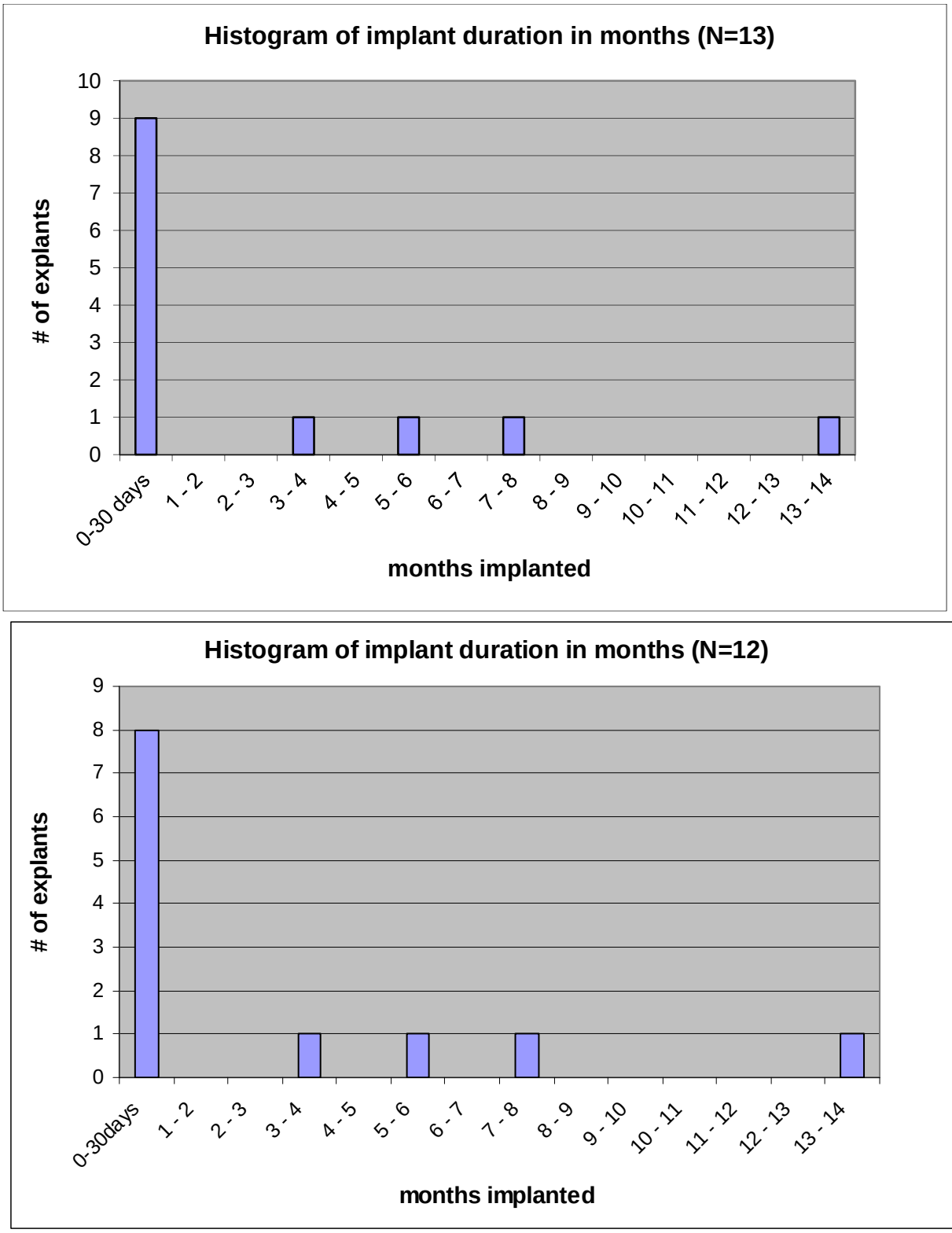


Figure 3-1: Histogram of Implant Duration

Explanted Device Observations

The Medtronic explant program provides important information that helps to guide decisions regarding device design and implantation technique improvements.

As part of the analysis of each explanted device, the integrity of the components of the stent graft is examined (including the stents, graft material, and sutures). Of these 13 explanted thoracic cases, there were 23 total stent grafts implanted.

Of the 13 explant cases returned for examination, a total of 3 cases were not examined for device integrity. Two of these were incidental autopsy cases (awaiting possible examination at a later date), and one of these was a thoracic specimen cut by the pathologist in order to perform histology. A summary of the primary and secondary reasons for explant determined by the explanting physicians for the 13 explant cases is presented in **Table 3-2**. Note that secondary reasons were not reported by the explant physicians in every case.

Table 3-2: Summary of Explanting Physician's Primary and Secondary Reason for Explant

Explant #	Primary cause	Secondary cause	Secondary cause	Secondary cause
1	Incidental autopsy			
2	Rupture, post-implant			
3	Implantation difficulties			
4	Incidental autopsy	Type 2 endoleak	Type 1 endoleak, proximal	Rupture
5	Rupture, post-implant			
6	Implantation difficulties			
7	Implantation difficulties			
8	Incidental autopsy	Symptomatic TAA		
9	Incidental autopsy			
10	Rupture, pre-implant	Type 3 endoleak, transgraft		
11	Increase in aneurysm diameter	Type 1 endoleak, proximal	Leak of unknown etiology	
12	Thrombosis			
13	Rupture, post-implant			

Stent Observations

From the 10 examined cases, no fatigue fractures were observed. Two explant cases (4 components) showed a total of 10 cuts located on the covered stent ring (N=5), support spring (N=4), and bare spring (N=1), all likely occurring from excision of the stent graft during the surgical conversion procedure, and not related to stent fatigue.

Graft Material Observations

From the 10 examined explant cases, a total of 5 stent graft wear-related holes were seen with 2 cases (2 stent grafts). The average size of the holes was 0.41mm in length, and varied in length from 0.3 – 0.6 mm. The primary cause of these holes was determined to be abrasion related. Eight explant cases (10 components) showed a total of 27 fabric cuts, all likely occurring from excision of the stent graft during the surgical conversion procedure, and not related to graft material wear.

Type III transgraft endoleaks are attributed to microscopic holes and fabric wear. However a majority of these endoleaks can resolve on their own by clotting. Of these 13 explant cases returned, transgraft endoleak was not identified as the reason for explant by the primary physician, but was reported as a possible secondary reason for 1 explant case.

4.0 Notes to Clinicians

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

- Iliac or femoral artery access vessel morphology that is compatible with vascular access techniques, devices, or accessories;
- non-aneurysmal aortic diameter in the range of 18 – 42mm (fusiform and saccular aneurysms/penetrating ulcers) or 18 – 44mm (blunt traumatic aortic injuries) or 20 mm to 44 mm (dissections); and
- non-aneurysmal aortic proximal and distal neck lengths ≥ 20mm (fusiform and saccular aneurysms/penetrating ulcers), landing zone ≥ 20 mm proximal to the primary entry tear (blunt traumatic aortic injuries, dissections). The proximal extent of the landing zone must not be dissected.

All patients should be advised that endovascular treatment requires life-long, regular follow-up to assess their health and the performance of their endovascular graft. Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms/ false lumens, or changes in the structure or position of the endovascular graft) should receive additional follow-up. Patients should be counseled on the importance of adhering to the follow-up schedule, both during the first year and at yearly intervals thereafter. Patients should be informed that regular and consistent follow-up is a critical part of ensuring the ongoing safety and effectiveness of endovascular treatment of lesions of the descending thoracic aorta.

Physicians should evaluate patients on an individual basis and prescribe follow-up relative to the needs and circumstances of each individual patient.

Annual imaging follow-up may include chest X-ray and computed tomography angiogram (CTA), with and without contrast.

- The combination of contrast and non-contrast CT imaging provides information on aneurysm diameter change, endoleak, patency, tortuosity, progressive disease, fixation length and other morphological changes
- The chest X-rays provide information on device integrity (separation between components and stent fracture)

Table 4-1 lists the recommended imaging follow-up for patients with the Valiant Thoracic Stent Graft. Ultimately, it is the physician's responsibility, based on previous clinical results and the overall clinical picture, to determine the appropriate imaging schedule for a particular patient.

Table 4-1: Recommended Imaging Schedule for Endovascular Graft Patients

Interval	Angiogram	CTA/MRA[2,3]	Chest X-ray[2]
Pre-procedure	X (optional)	X[1]	
Procedural	X		
1 Month		X[4]	X
12 Months (annually thereafter)		X[4]	X

[1] Pretreatment assessment should be done within 3 months prior to treatment.
[2] A 6 month follow-up with CT Scan and Chest X-ray are recommended if an endoleak is reported at 1 month after the procedure.
[3] Magnetic resonance angiogram (MRA) may be used in patients with impaired renal function or intolerance to contrast media at the discretion of the physician.
[4] If a Type I or III endoleak is present, prompt intervention and additional follow-up post-intervention is recommended.

Adverse Event Reporting

Below are the instructions for reporting of adverse events:

1. Any adverse event (clinical incident) involving the Valiant Thoracic Stent Graft System should be reported to Medtronic Vascular immediately. To report an incident, call (800) 465-5533 (in the US). To report an incident outside the US, please contact your Medtronic Sales Representative. This information may also be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088), fax (1-800-FDA-0178) or to the MedWatch website at www.fda.gov/medwatch. Form 3500 should be used for reporting adverse events.
2. Forward patient films, explant data and explanted stent to Medtronic Vascular.
3. For additional information, contact your local Medtronic Vascular representative, or call 1-800-678-2500.

5.0 Brief Summary of Indications for Use, Warnings and Precautions

Indications

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

- Iliac or femoral artery access vessel morphology that is compatible with vascular access techniques, devices, or accessories;
- non-aneurysmal aortic diameter in the range of 18 – 42mm (fusiform and saccular aneurysms/penetrating ulcers) or 18 – 44mm (blunt traumatic aortic injuries) or 20 mm to 44 mm (dissections); and
- non-aneurysmal aortic proximal and distal neck lengths ≥ 20mm (fusiform and saccular aneurysms/penetrating ulcers), landing zone ≥ 20 mm proximal to the primary entry tear (blunt traumatic aortic injuries, dissections). The proximal extent of the landing zone must not be dissected.

Contraindications

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

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

Warnings and Precautions

The long-term safety and effectiveness of the Valiant Thoracic Stent Graft with the Captivia Delivery System has not been established. All patients should be advised that endovascular treatment requires lifelong, regular follow-up to assess the integrity and performance of the implanted endovascular stent graft. Patients with specific clinical findings (for example, enlarging aneurysm/ false lumen, endoleaks, migration, or inadequate seal zone) should receive enhanced follow-up. Specific follow-up guidelines are described in the *Instructions for Use*. The Valiant Thoracic Stent Graft with the Captivia Delivery System is not recommended in patients who cannot undergo, or who will not be compliant with, the necessary preoperative and postoperative imaging and implantation procedures as described in the *Instructions for Use*. Strict adherence to the Valiant Thoracic Stent Graft sizing guidelines as described in the *Instructions for Use* is expected when selecting the device size. Sizing outside of this range can potentially result in endoleak, fracture, migration, infolding, or graft wear. The safety and effectiveness of the Valiant Thoracic Stent Graft with the Captivia Delivery System has not been evaluated in some patient populations. Please refer to the product *Instructions for Use* for details.

MRI Safety and Compatibility

Non-clinical testing has demonstrated that the Valiant Thoracic Stent Graft is MR Conditional. It can be scanned safely in both 1.5T & 3.0T MR systems under certain conditions as described in the product *Instructions for Use*. For additional information regarding MRI please refer to the product *Instructions for Use*.

Adverse Events

Potential adverse events include, but are not limited to access failure, access site complications (e.g., spasm, trauma, bleeding, rupture, dissection), adynamic ileus, allergic reaction (to contrast, antiplatelet therapy, stent graft material), amputation, anaesthetic complications, aortic expansion (e.g. aneurysm, false lumen), aneurysm rupture, angina, aortic vessel rupture, arrhythmia, arterial stenosis, atelectasis, blindness, bowel ischemia/infarction, bowel necrosis, bowel obstruction, branch vessel occlusion, buttock claudication, cardiac tamponade, catheter breakage, cerebrovascular accident (CVA) / stroke, change in mental status, coagulopathy, congestive heart failure, contrast toxicity, conversion to surgical repair, death, deployment difficulties / failures, dissection / perforation / rupture of the aortic vessel and/or surrounding vasculature, embolism, endoleaks, excessive or inappropriate radiation exposure, extrusion / erosion, failure to deliver stent graft, femoral neuropathy, fistula (including aortobronchial, aortoenteric, aortoesophageal, arteriovenous, lymph), gastrointestinal bleeding /complications, genitourinary complications, hematoma, hemorrhage / bleeding, hypotension / hypertension, infection or fever, insertion and removal difficulty, intercostal pain, intramural hematoma, leg /foot edema, lymphocele, myocardial infarction, neuropathy, occlusion – venous or arterial, pain / reaction at catheter insertion site, paralysis, paraparesis, paraplegia, perfusion of false lumen, paresthesia, peripheral ischemia, peripheral nerve injury, pneumonia, post-implant syndrome, procedural / post-procedural bleeding, prosthesis dilatation / infection / rupture / thrombosis, pseudoaneurysms, pulmonary edema, pulmonary embolism, reaction to anaesthesia, renal failure, renal insufficiency, reoperation, respiratory depression / failure, sepsis, seroma, shock, spinal neurological deficit, stent graft material failure (including breakage of the metal portion of the device / migration / misplacement / occlusion / twisting / kinking, transient ischemic attack (TIA), thrombosis, tissue necrosis, vascular ischemia, vascular trauma, wound dehiscence, wound healing complications, and/or wound infection.

Please reference product *Instructions for Use* for more information regarding indications, warnings, precautions, contraindications and adverse events.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician.

Medtronic

Medtronic
3576 Unocal Place
Santa Rosa, CA 95403
USA

Product Services Support Center
Tel: 888.283.7868
Fax: 800.838.3103

CardioVascular LifeLine Customer Support
Tel: 877.526.7890
Tel: 763.526.7890

medtronic.com
aortic.medtronicendovascular.com