- Secondary endovascular procedures for primary device failures (including Type I/III endoleaks, aneurysm expansion, aneurysm/aortic rupture, and BSG occlusion)
- Rupture
- Endoleaks
- Maximum aneurysm diameter change from baseline*
- Exclusion of aneurysm
- Exclusion of penetrating aortic ulcer (PAU)
- Stent graft patency
- Stent graft integrity
- Conversion to surgery
- Surgical revascularization of the LSA
- Paraparesis
- Adverse events including serious adverse events and device, procedure, and/or disease-related Adverse Events
- For CTBD, these additional observations will be evaluated:
    - Coverage of primary entry tear (exclusion of false lumen)
    - Extension of dissection (proximally or distally) with or without complications
    - Continuing or new false lumen (FL) perfusion
        - Primary intimal tear false lumen perfusion (PIT FLP)
        - Proximal aorta false lumen perfusion (PA FLP)
        - Distal aorta false lumen perfusion (DA FLP)
        - Proximal branch false lumen perfusion (PB FLP)
        - Distal branch false lumen perfusion (DB FLP)
    - Aortic remodeling post-procedure as measured by:
        - 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 discharge computerized tomography angiogram (CTA) will be used as baseline to assess aortic changes. If a discharge CTA is not performed, then the one month follow-up CTA will be used for baseline purposes.

7.1.4 Periprocedural and Discharge Clinical Utility Measures

The following periprocedural through discharge clinical utility measures will be summarized using descriptive statistics.

1. Mean duration (min) of procedure.
2. Mean time (min) to implant the LSA Branch device.
3. Proportion of subjects who underwent general anesthesia.
4. Mean volume (cc) of estimated blood loss.
5. Proportion of subjects requiring blood transfusions.
6. Mean time (hours) in intensive care unit.
7. Mean time (days) of overall hospital stay (from hospital admission to discharge).

7.2 Sample Size Calculations

There is no sample size calculation since this is not a hypothesis driven study.

7.3 Analysis of Observations

7.3.1 Data Analysis Set

An analysis set will be constructed from the Valiant Mona LSA Stent Graft subjects. All safety and effectiveness analyses will be performed on all enrolled subjects, according to the intention-to-treat (ITT) principle. The subject will be considered enrolled after arterial access is achieved and the Valiant Mona LSA Thoracic Stent Graft System has been introduced into the vasculature.

7.3.2 Analysis of the Primary Safety Observation

Descriptive statistics (frequency and percentage) will be calculated for the primary safety observation and its component events.

7.3.3 Analysis of the Primary Effectiveness Observation

Descriptive statistics (frequency and percentage) will be calculated for the primary effectiveness observation of Treatment Success within 1-month.

7.3.4 Analysis of the Additional Observations

Descriptive statistics for categorical variables (frequency and percentage) will be calculated for all of the secondary observations.

7.3.5 Analysis of the Periprocedural through Discharge Clinical Utility Measures

Descriptive statistics will be calculated - Categorical variables, including binary variables, will be reported by giving the number and percentage of subjects in each category; Continuous variables will be reported by presenting the mean, Standard Deviation (S.D.), median, minimum, and maximum of each variable.

7.3.6 Analysis of Baseline Variables

All clinically relevant baseline variables will be tabulated. Descriptive statistics will be calculated. Categorical variables, including binary variables, will be reported by giving the number and percentage of patients in each category. Continuous variables will be reported by presenting the mean, S.D., median, minimum, and maximum of each variable. For all baseline variables, only patients with evaluable assessments will be included.

7.3.7 Subset Analyses

Subset analyses of the primary safety and effectiveness observations will be created for each indication - aneurysms, penetrating ulcers, and chronic Type B dissections.

Descriptive statistics will be used for each subset to analyze the primary observations, additional observations, and periprocedural and discharge clinical utility measures as outlined in Sections 7.1.1, 7.1.2, 7.1.3, and 7.1.4 above.

7.3.8 Time Window Conventions Used in Analysis of Observations

Throughout this study, all attempts will be made to collect complete and compliant data. Thus, the majority of data are expected to be within the protocol-specified timeframes for follow-up visits. However, in practice, it may not be possible to achieve this completely. For example, an unscheduled visit may take place and then the patient may miss the next follow-up or withdraw.

For these exceptions, and to take into account all available data, the following rules and time windows will be applied in the statistical analyses for imaging observations (**Table 7-1**).

Table 7-1: Windows and Analysis of Noncompliance or Missing Data

Study Visit	Target Day	Scheduled Follow-Up Window	Analysis Window for Imaging Assessments
Implant	0	Day 0	Day 0
1 Month	30	15-45 Days	1-122 Days
6 Months	183	153-239 Days	123-270 Days
12 Months	365	335-421 Days	271-480 Days
24 Months	730	674-842 Days	481-913 Days
36 Months	1095	1039-1207 Days	914-1278 Days
48 Months	1460	1404-1572 Days	1279-1644 Days
60 Months	1825	1769-1937 Days	1645-2008 Days

If follow-up data are not available for a specific visit, subsequent follow-up data may be used, e.g., when there is evidence of stent graft patency, endoleak, or freedom from migration at 12-months post index procedure. The larger time window around the 12-

month visit takes this into account. If there are 2 or more assessments in the same time window, then the assessment closest to the target day will be used in the analysis.

For an adverse event or death, date of onset will be defined as the time when the event occurred. In cases where the date of onset is incomplete, the 15th day of the known month or July 1st of the known year will be used.

Furthermore, adverse events or death may be observed at any time during the study, so no time windows will be applied. An event that occurs "within 1 month" is an event that takes place between Days 0 to Day 30 inclusive. The same applies to events for the 12-month window, i.e., Day 0 – Day 365 inclusive.

7.3.9 Patient Withdrawal and Missing Data

In general, all analyses will be performed using the ITT analysis set, which constitutes all available (or observed) cases. Imputation of missing data will not be performed. For example, to determine the rate of freedom from MAEs, all subjects with MAEs reported or no MAEs observed during the defined time period will be counted in the analysis.

8. CLINICAL STUDY PREPARATION PROCEDURES

As the Sponsor of this clinical study, Medtronic Vascular has the overall responsibility for the conduct of the study, including assurance that the study will be conducted according to the Investigational Plan and the US Food and Drug Administration (FDA) regulations. During this study, Medtronic Vascular will have certain direct responsibilities and may delegate other responsibilities to, for example, a CRO. Medtronic Vascular and/or its designees will conform to the US Code of Federal Regulations (CFR) including but not limited to: Investigational Device Exemptions (21 CFR 812), Electronic Records/Electronic Signatures (21 CFR 11), Protection of Human Subjects (21 CFR Part 50), Financial Disclosure by Clinical Investigators (21 CFR Part 54), and Institutional Review Boards (21 CFR 56).

8.1 SELECTION OF CLINICAL INVESTIGATORS

Investigators who are qualified by training and experience will be selected to participate in this study. All investigators will sign the appropriate study-related agreements (Investigator/Sub-Investigator Agreement and Clinical Research Agreement) before they are added to the clinical study.

8.2 INSTITUTIONAL REVIEW BOARD REQUIREMENTS

Investigators are required to submit all required study documents to the Institutional Review Board (IRB) with oversight responsibility for the study center. The investigator must notify Medtronic Vascular when IRB approval is granted and provide a copy of the approval letter and approved informed consent form.

8.3 INFORMED CONSENT

All subjects must provide written informed consent in accordance with 21 CFR Part 50, Part 812 and local law. Informed Consent must be obtained from all study subjects prior to initiation of any study required activity that is not standard of care/routine medical care administered by the investigator for this patient population. The informed consent form must be signed by the subject or the subject's legally authorized representative. A sample Informed Consent is included in Appendix E. Each Investigational Site must provide Medtronic with a copy of the Informed Consent approved for use by the site's Institutional

Review Board (IRB). The original signed Informed Consent should be retained in the study subject's study records.

It is recommended that the informed consent document have an IRB approval stamp and be version controlled. The informed consent process should be documented in the patient's medical record. The original informed consent document should be filed at the investigational site and a copy of the signed informed consent should be given to the subject.

8.4 Study Training

Prior to the start of the study, the investigator and study staff at each site will undergo training to provide in-depth information about the use of the device, the clinical investigational plan, and study requirements. Medtronic Vascular personnel (or designees) will conduct the training. Training of study personnel will be documented on the appropriate training record form and maintained at the site and in the Medtronic Vascular study files.

Physician proctoring will be provided to the Investigators as directed by Medtronic Vascular. Medtronic personnel may be present for the investigational implants at sites.

8.5 Required Investigational Equipment

The following devices packaged will be provided for this clinical investigation. Devices will be labeled with the required investigational caution language. The Valiant Mona LSA Stent Graft IFU is provided in Appendix A and labeling is found in Appendix F.

The Valiant Mona LSA Thoracic Stent Graft Systems are composed of the following components.

- Main Stent Graft
- Branch Stent Graft
- Main Delivery System
- Branch Delivery System

Each stent graft component (e.g., main stent graft or branch stent graft) is individually contained within a delivery system. The delivery systems are sterilized using E-beam and are supplied sterile for single use only. The system should be stored at room temperature in a secure, dark, dry place. Ancillary required and recommended equipment associated with implantation of the Valiant Mona LSA Thoracic Stent Graft System are listed in the

Valiant Mona LSA Thoracic Stent Graft System Instructions for Use—Section 9: Clinician Use Information (Appendix A and as packaged with the investigational device).

After proper measurements and a therapeutic plan are established for a subject, the appropriate components of the Valiant Mona LSA Thoracic Stent Graft System will be shipped to the site (refer to the IFU in Appendix A and the packaged device for sizes available). Only the investigator and the clinical study staff should have access to the investigational system components.

8.6 Site Activation and Supply of Study Materials

Investigators will receive written approval to commence study enrollment from Medtronic Vascular after all required regulatory documents are received and training has occurred.

The Investigator is responsible for supervising the use of all investigational devices. Medtronic Vascular will control the supply of study devices, case report form materials, return shipment containers for explanted devices, and other items required to conduct the clinical study.

8.7 Protocol Amendments

The investigator can propose any appropriate modification(s) of the clinical investigation plan or investigational device or investigational device use. Medtronic will review this proposal and decide whether the modification(s) will be implemented.

Medtronic will submit any significant amendment to the clinical investigation plan, including a justification for this amendment, to the appropriate regulatory authorities and to the investigators to obtain approval from their IRB/EC. The investigator will only implement the amendment after approval of the IRB/EC, regulatory authority and sponsor. Administrative amendments to the clinical investigation plan will be submitted to the IRB/EC for notification. Furthermore, investigators shall sign any approved amendment of the clinical investigation plan, if required per local regulation.

9. CLINICAL STUDY PROCEDURES

Clinical data will be collected preoperatively to establish eligibility, at baseline, during implantation of the Valiant Mona LSA Stent Graft, throughout the hospital stay, and postoperatively. Each subject will continue to be followed after the 30-day, 6-month, and 12-month evaluation on an annual basis to collect a total of 5 years' experience. When all enrolled subjects have been followed for 5 years post index procedure or have previously exited from the study, the study will be closed and the final report generated.

Study data will be collected using electronic case report forms (eCRFs). eCRFs should be electronically reviewed and approved by the clinical investigators. Medtronic Vascular monitors (or designees) will review all case report forms.

The data collection schedule is summarized in **Table 9-1**.

Table 9-1: Overview of the Study Procedures and Data Collection Requirements

Data	Screening/ Baseline	Procedure	Hospital Discharge	1-Month FU ±15 days	6-Month FU -30 /+56 days	12-Month FU -30 days/ +56 days	2 - 5 Year FU -8 /+16 weeks
GENERAL							
Informed Consent	✓						
Physical Examination (Left arm assessment; pulses, BP in both arms)	✓	✓	✓	✓	✓	✓	✓
Medical History	✓						
Current Health Status and Risk Factors	✓						
Pregnancy Test (for female of child-bearing potential)	✓						
Laboratory Tests: CBC, creatinine, and INR (if subject taking Coumadin)	✓[77]		✓[78]	✓[78]	✓[78]	✓[78]	✓[78]
Device and Procedure Information		✓					
Neurological Evaluation[79]	✓						
Hospital Discharge Information			✓				
Pre-Implant Adjunctive Procedures		✓					
Adverse Event Assessment		✓	✓	✓	✓	✓	✓
IMAGING							
3D CTA with contrast (aorta and thoracic branch vessels)	✓		✓	✓	✓	✓	✓
3D CTA of head/neck/abdomen/pelvis	✓						
DUS of the LSA/Carotid vessels	✓						
DUS of the LSA/thoracic branch vessels			✓	✓	✓	✓	✓
Angiogram of Thoracic aorta		✓					
Chest X-Ray			✓	✓	✓	✓	✓

Table 9-1: Overview of the Study Procedures and Data Collection Requirements

Data	Screening/ Baseline	Procedure	Hospital Discharge	1-Month FU ±15 days	6-Month FU -30 /+56 days	12-Month FU -30 days/ +56 days	2 - 5 Year FU -8 /+16 weeks
ADDITIONAL PROCEDURES REQUIRED IF A POST-OPERATIVE NEUROLOGICAL CHANGE OCCURS							
Neurological Evaluation[80]			✓	✓	✓	✓	✓
Diffusion-weighted MRI of head/neck			✓	✓	✓	✓	✓

[77] CBC, serum creatinine, and INR (if subject is taking Coumadin pre-operatively) are required at baseline only.
[78] Serum creatinine is required post-operatively at each visit, from discharge through 5 years.
[79] Refer to section 9.2 for neurological evaluation testing requirements at baseline.
[80] Refer to section 9.4 for neurological evaluation testing requirements for discharge, 1 month, 6 months, 12 months, and annually through 5 years.

9.1 Eligibility Criteria

The study population will include those patients diagnosed with an aneurysmal thoracic aorta, penetrating ulcer, or chronic type B dissection who are candidates for revascularization of the left subclavian artery (LSA) and who meet the inclusion and exclusion criteria. Data will be recorded on the Inclusion and Exclusion Criteria Form.

Following review of the preliminary safety data of the first 18 enrolled patients, 5 additional subjects with TAA or PAU will be enrolled to further evaluate the device's safety.

The safety data for these 5 subjects will be reviewed by the investigator(s) in coordination with MDT and the DSMB to determine whether to start enrollment of the CTBD arm.

9.1.1 Inclusion Criteria for Thoracic Aortic Aneurysms and Penetrating Ulcers

- Subject is at least 18 years of age.
- Subject understands and has signed an Informed Consent approved by the Sponsor and by the IRB for this study.
- Subject must be considered a candidate for revascularization of the Left Subclavian Artery). Subject must be able to tolerate a surgical revascularization of the LSA.
- Subject has a TAA/PAU which will require coverage of the LSA and is:
    - a fusiform aneurysm with a diameter of ≥ 5.5 cm OR is > 2 times the diameter of the non-aneurysmal thoracic aorta;
      AND/OR
    - a saccular aneurysm or penetrating atherosclerotic ulcer (ulcer defined as ≥ 10 mm in depth and 20 mm in diameter, or symptomatic)
- Subject has a healthy, non-diseased aortic proximal seal zone of at least 20 mm from the distal end of the LCC ostium to the beginning of the disease, including at least 10 mm between the LSA and the LCC.
- Subject has a non -diseased aortic proximal neck length of >0mm distal to the LSA
- Subject has a non-diseased aortic diameter between 25 mm and 42 mm
- Subject has a non-diseased LSA with a diameter between 8 mm and 13 mm.
- Subject has sufficient landing zone within the LSA to accommodate the BSG without occlusion of any significant vessels
- Brachial, iliac or femoral artery access vessel morphology (diameter, calcification, tortuosity) that is compatible with vascular access techniques, the device, or accessories.

- Introducer sheath is required for all procedures.
- An iliac conduit is required for access if the above requirements are not met.

9.1.2 Exclusion Criteria for Thoracic Aortic Aneurysms and Penetrating Ulcers

- Subjects will be excluded if they have conditions requiring prospective revascularization of the LSA including:
  - Dominant left vertebral artery requiring revascularization
  - Prior coronary artery bypass graft utilizing the left mammary artery requiring revascularization
  - Incomplete circle of Willis or other neurological vasculature requiring revascularization
- Subject has an aneurysmal, tortuous, or atherosclerotic LSA.
- Subject has an acute dissection of the descending thoracic aorta.
- Subject has an intramural hematoma of the descending thoracic aorta.
- Subject has prohibitive calcification, occlusive disease, or tortuosity of intended fixation sites.
- Subject has circumferential calcification in the external iliac artery or in the common iliac artery with an intraluminal diameter (ID) less than 10mm at any point proximal to or at the access vessel site unless a surgical adjunctive procedure is planned.
- Subject requiring an aortic conduit or direct aortic access.
- Subject has an aortic atheroma classified as grade IV or grade V.
- Subject has had previous endovascular repair of the ascending and/or descending thoracic aorta <30 days of implantation of investigational device or previous repair was a non-Medtronic device.
- Treatment with the Valiant Mona LSA Thoracic Stent Graft system would require intentional coverage of the left common carotid artery with the stent graft fabric.
- Subject has significant and/or circumferential aortic mural thrombus at either the proximal or distal attachment sites that would compromise fixation and seal of the device.
- Subject is a pregnant female.

- Subject has a known allergy or intolerance to the device components.
- Subject is in acute renal failure or has renal insufficiency with a serum creatinine ≥ 2.0 mg/dL or is on dialysis.
- Subject has a body habitus which prevents adequate visualization of the aorta.
- Subject has coronary artery disease with unstable angina and who has not received treatment.
- Subject has a connective tissue disease (e.g. Marfan's syndrome, medial degeneration).
- Subject has active systemic infection and/or a mycotic aneurysm.
- Subject is currently participating in an investigational drug or device clinical trial that would interfere with the observations of this study.
- Subject has other medical, social, or psychological problems that, in the opinion of the investigator, will interfere with treatment and follow-up procedures.
- Subject has a life expectancy of less than 1 year.
- Subject requires treatment of an infrarenal aneurysm at the time of the implantation.
- Subject has had previous surgical or endovascular treatment of an infra-renal aortic aneurysm <30 days of implantation of investigational device.
- Subject has a history of bleeding diathesis, coagulopathy, or refuses blood transfusion.
- Subject has had a cerebral vascular accident (CVA) within 3 months prior to the procedure.
- Subject has had a myocardial infarction (MI) within 3 months prior to the procedure.
- Subject has a known hypersensitivity or contraindication to anticoagulants or contrast media, which is not amenable to pre-treatment.

9.1.3 Inclusion Criteria for Chronic Type B Dissections

- Subject is at least 18 years of age.
- Subject understands and has signed an Informed Consent approved by the Sponsor and by the IRB for this study.

- Subject must be considered a candidate for revascularization of the Left Subclavian Artery (LSA). Subject must be able to tolerate a surgical revascularization of the LSA.
- Subject has a chronic type B dissection which will require coverage of the LSA. A chronic type B dissection is defined as > 30 days from symptom onset and is complicated with an aortic diameter ≥ 5.5 cm or has progressive aortic enlargement (> 5 mm/year).
- Subject has a healthy, non-diseased aortic proximal seal zone of at least 20 mm from the distal end of the LCC ostium to the beginning of the disease, including at least 10 mm between the LSA and the LCC
- Subject has a non-diseased aortic diameter between 28 mm to 44 mm.
- Subject has a non-diseased LSA with a diameter between 8 mm and 13 mm.
- Subject has sufficient landing zone within the LSA to accommodate the BSG without occlusion of any significant vessels
- Brachial, iliac or femoral artery access vessel morphology (diameter, calcification, tortuosity) that is compatible with vascular access techniques, the device, or accessories.
    - Introducer sheath is required for all procedures.
    - An iliac conduit is required for access if these requirements are not met.

9.1.4 Exclusion Criteria for Chronic Type B Dissections

- Subjects will be excluded if they have conditions requiring prospective revascularization of the LSA including:
    - Dominant left vertebral artery requiring revascularization
    - Prior coronary artery bypass graft utilizing the left mammary artery requiring revascularization
    - Incomplete circle of Willis or other neurological vasculature requiring revascularization
- Subject has an aneurysmal, tortuous, or atherosclerotic LSA.
- Subject has an acute dissection of the descending thoracic aorta.
- Subject has an intramural hematoma of the descending thoracic aorta.

- Subject has prohibitive calcification, occlusive disease, or tortuosity of intended fixation sites.
- Subject has circumferential calcification in the external iliac artery or in the common iliac artery with an intraluminal diameter (ID) less than 10mm at any point proximal to or at the access vessel site unless a surgical adjunctive procedure is planned.
- Subject requiring an aortic conduit or direct aortic access.
- Subject has an aortic atheroma classified as grade IV or grade V.
- Subject has had previous endovascular repair of the ascending and/or descending thoracic aorta <30 days of implantation of investigational device or previous repair was a non-Medtronic device.
- Treatment with the Valiant Mona LSA Thoracic Stent Graft system would require intentional coverage of the left common carotid artery with the stent graft fabric.
- Subject has significant and/or circumferential aortic mural thrombus at either the proximal or distal attachment sites that would compromise fixation and seal of the device.
- Subject is a pregnant female.
- Subject has a known allergy or intolerance to the device components.
- Subject is in acute renal failure or has renal insufficiency with a serum creatinine ≥ 2.0 mg/dL or is on dialysis.
- Subject has a body habitus which prevents adequate visualization of the aorta.
- Subject has coronary artery disease with unstable angina and who has not received treatment.
- Subject has a connective tissue disease (e.g. Marfan's syndrome, medial degeneration).
- Subject has active systemic infection and/or a mycotic aneurysm.
- Subject is currently participating in an investigational drug or device clinical trial that would interfere with the observations of this study.
- Subject has other medical, social, or psychological problems that, in the opinion of the investigator, will interfere with treatment and follow-up procedures.
- Subject has a life expectancy of less than 1 year.

- Subject requires treatment of an infrarenal aneurysm at the time of the implantation.
- Subject has had previous surgical or endovascular treatment of an infra-renal aortic aneurysm <30 days of implantation of investigational device.
- Subject has a history of bleeding diathesis, coagulopathy, or refuses blood transfusion.
- Subject has had a cerebral vascular accident (CVA) within 3 months prior to the procedure.
- Subject has had a myocardial infarction (MI) within 3 months prior to the procedure.
- Subject has a known hypersensitivity or contraindication to anticoagulants or contrast media, which is not amenable to pre-treatment.

9.2 Patient Screening, Enrollment, and Pre-implant Procedures

Investigators will assess potential patients diagnosed with fusiform/saccular aneurysm of the descending thoracic aorta, penetrating ulcer, or chronic type B dissection who are candidates for revascularization of the LSA and anatomically appropriate for the device for suitability for enrollment. Following review of the preliminary safety data of the first 18 enrolled patients, 5 additional subjects with TAA or PAU will be enrolled to further evaluate the device's safety.

The safety data for these 5 subjects will be reviewed by the investigator(s) in coordination with MDT and the DSMB to determine whether to start enrollment of the CTBD arm.

Initially, patient eligibility will be determined by the investigator based on the diagnosis of DTA, penetrating ulcer, or chronic type B dissection as evidenced on screening contrast-enhanced CT/MRA. If the patient appears to meet the eligibility criteria, then the investigator will discuss the study with the patient and provide information relating to the potential risks and benefits, and required follow-up procedures per the informed consent process (Section 8.3 – Informed Consent). After the patient has voluntarily signed and dated the informed consent document, the patient will be considered screened. If a patient does not sign the informed consent document, then no further procedures for the clinical study will occur. Subjects who were screened but do not qualify for enrollment will be documented as ineligible on the **Subject Screening Log**. Patients who do not pass the eligibility evaluations will neither be enrolled in the study nor followed. Subjects enrolled, but with no device implant, will be followed through the one month follow-up only.

Those subjects who sign and date the informed consent document, and meet all of the study eligibility criteria will be eligible for enrollment into the clinical study.

For those subjects who are enrolled, baseline information will include the following and be recorded on the appropriate eCRFs

- Patient Demographics
- Preoperative Assessments/Medical History
- Stent Graft Sizing
- Device Selection

The following should take place prior to the implant procedure:

- Informed consent.
- Demographic data.
- Medical history.
- Physical examination including left arm assessment and bilateral upper extremity blood pressures and pulses (within 1 month of index procedure).
- Neurological exam to establish neurological baseline, conducted by a neurologist and including:
    - NIH Stroke Scale Assessment
    - Modified Rankin Score
    - Mini Mental Status Exam
    - Additional Neurological Testing that may include Visual Fields Testing and Gait Assessment
- Pregnancy test (for female patients of childbearing potential). Test must be completed at the time of screening, prior to the index procedure. Results must be negative.
- Laboratory tests (completed within 14 days prior to the index procedure) to include: WBC (not differential), serum creatinine, and INR for patients taking Coumadin preoperatively.
- CT or MRA with contrast of the chest, abdomen and pelvis (celiac to external iliac arteries) completed within 4 months prior to the index procedure.
    - A copy of this CTA imaging (electronic or otherwise) should be submitted to the Medtronic Vascular Clinical Study Team. Pre-operational CT scan will be reviewed by an independent physician reviewer in order to check that aortic anatomy fulfills anatomical inclusion/exclusion criteria
- Contrast-enhanced computerized tomography angiography (CTA) scan (head/neck) with 3-D reconstruction for evaluation of intracranial circulation to

determine patient anatomic suitability for the Valiant Mona LSA Thoracic Stent Graft System implantation.
- Ultrasound of the LSA and carotid vessels.

The subject will be considered enrolled after arterial access is achieved and the Valiant Mona LSA Thoracic Stent Graft System has been introduced into the vasculature.

9.3 STENT GRAFT IMPLANT PROCEDURES

All investigators will read, understand and be trained to The Valiant Mona LSA Thoracic Stent Graft System IFU prior to initiation of the procedure. The IFU which is packaged with the device must be followed for implantation of the stent graft system.

The following events will be performed and documented in the medical records and in the Index Procedure eCRFs as applicable:

- Information pertaining to any preoperative adjunctive procedures and data collected during the procedure will be recorded on the eCRF
- The anesthesia and general surgical protocol (e.g., administration of prophylactic antibiotic therapy, technique for access and closure of the arterial site, use of systemic heparin) will be left to the discretion of the implanting physician and the standard medical practice at the hospital.
- Verification of the dimensions and characterization of the DTA and pertinent arteries will be documented using angiography at the time of the procedure and prior to the insertion of the Valiant Mona LSA Thoracic Stent Graft System. Use of an angiographic catheter with calibrated radiopaque marking is preferred. The investigator will verify dimensions and characterizations of the subject's anatomy in relation to the Valiant Mona LSA Thoracic Stent Graft System. Subjects who are found not to be candidates for the Valiant Mona LSA device, because of findings detected during the treatment angiogram, will be documented as such on the appropriate eCRFs.
- Arterial site will be accessed per Investigator's standard method.
- All Mona LSA Stent Grafts used for implantation and any issues related to the device will be documented in the medical chart and on the eCRFs.
- Fluoroscopic guidance will be used for placement of the stent graft throughout the endovascular procedure. Total fluoroscopic time and volume of contrast used will be documented.

- All devices should be deployed following the steps outlined in the IFU, which is provided with the packaged device (also Appendix A).
- Additional procedures performed during the treatment will be documented on the appropriate eCRFs.
- Upon completion of the index procedure, a final run-off angiography should be performed to document the status of the Valiant Mona LSA Stent Graft device(s), the thoracic aorta, and the surrounding vasculature.
    - A copy of the implant procedural angiographic imaging (electronic or otherwise) may be requested and should be submitted to the Medtronic Vascular Clinical Study Team in a timely manner.
- The estimated blood loss, number of blood units replaced, and any adverse events experienced during the treatment will be documented.
- The access site will be closed as per the Investigator's standard of care.

Additional information to be recorded on the **Index Procedure eCRF** includes the following.

- Date of hospital admission prior to the index procedure
- Date of the index procedure
- General procedural information
- Success of device implantation
- Occurrence of adverse events or technical observation

Identification and/or serial numbers for all investigational components of the Valiant Mona LSA Thoracic Stent Graft System used or opened during the index procedure will be recorded on the **Device Disposition log**. Product that was opened and not used or damaged during the procedure must be returned to Medtronic Vascular. Refer to Appendix H for return instructions.

Adverse events should be reported on the **Adverse Event eCRF** as specified in Section 9.9 – Adverse Events.

Inability to implant the Valiant Mona LSA Stent Graft following arterial access due to deployment issues or entrapment of the delivery system will be considered a treatment failure. These subjects will be followed through the 1-month follow-up time point and then exited from the study.

The **Adverse Event eCRF** should be completed for any conversion, as appropriate. If a primary conversion to open repair is required during the index procedure, then the subject will be followed for 1 month, at which time the subject will be exited from the study.

9.4 Hospital Discharge Procedures

Information pertaining to the subject's hospital experience and discharge will be recorded on the **Hospital Discharge eCRF**. Data will include the following.

- Date of hospital discharge
- Duration of stay in the ICU, if applicable
- Physical examination including left arm assessment and bilateral upper extremity blood pressures and pulses
- For postoperative subjects who are clinically symptomatic or have a changed neurological deficit, a diffusion-weighted MRI (head/neck) will be required, in conjunction with:
    - Neurological exam conducted by a neurologist and will include:
        - NIH Stroke Scale Assessment
        - Modified Rankin Score
        - Mini Mental Status Exam
        - Additional Neurological Testing that may include Visual Fields Testing and Gait Assessment
- Duplex ultrasound (DUS) of LSA/thoracic branch vessel
- Chest X-Ray (performed per Investigator's standard of care)
- CTA w/ 3D reconstruction capabilities
- Any other aorta-related imaging
- Serum creatinine
- Occurrence of adverse events

Copies of aorta-related films (electronic or otherwise) should be submitted to the Medtronic Vascular Clinical Study Team in a timely manner. Images will be collected by the Clinical Study Team for all subjects enrolled at screening/baseline, discharge, 1-month, 6-months, 12-months, and annually through 5 years.

9.5 Required Follow-Up Evaluations

Follow-up evaluations will be scheduled for 1 month (± 15 days), 6 months (-30/+56 days), 12 months (-30 days/+56 days) and annually thereafter to 5 years post implant (-8/+16weeks).

It is expected that the Investigator enrolling the subject at the participating site where the implantation occurred will follow the subject during the course of the study. It is the responsibility of the Investigator to make sure that the subject is followed and that integrity and accuracy of the data is maintained.

The following tests and procedures will be included at each of these visits:

- Physical exam including left arm assessment and bilateral upper extremity blood pressures and pulses
- Adverse event assessment
- Serum creatinine value
- Technical observations, evaluations, and additional treatment in relation to the Valiant Mona LSA Stent Graft
- For postoperative subjects who are clinically symptomatic or have a changed neurological deficit, a diffusion-weighted MRI (head/neck) will be required as well as:
    - A neurological exam conducted by a neurologist which will include:
        - NIH Stroke Scale Assessment
        - Modified Rankin Score
        - Mini Mental Status Exam
        - Additional Neurological Testing that may include Visual Fields Testing and Gait Assessment
- All related stent graft imaging (completed with date of imaging recorded) including:
    - CTA w/ 3D reconstruction capabilities at: 1 month, 6 months, 12 months, 2, 3, 4 and 5 years. Doppler ultrasound of the LSA and carotid arteries will be required at each follow-up timepoint.
    - Chest X-Ray (performed per Investigator's standard of care)
    - Any additional images requested by the physician.

Copies of aorta-related films (electronic or otherwise) should be submitted to the Medtronic Vascular Clinical Study Team in a timely manner. Images will be collected by the Clinical Study Team for all subjects enrolled at screening/baseline, discharge, 1-month, 6-months, 12-months, and annually through 5 years.

Follow-up visits are scheduled for appointed times from the date of the implant procedure. It is important that this schedule is followed as closely as possible for all subjects. The Sponsor recognizes that subjects may not be able to return for follow-up visits at exactly the required date; therefore, a window has been created in which each visit is allowed (time period). Follow-up visits should be scheduled as closely as possible to the earlier part of the time period to allow for possible re-scheduling, preventing the visit from occurring outside

of the allowed window. Follow-up window timeframes are summarized in **Table 9-2**. All data required for the follow-up must be collected within the window for that scheduled visit, though not necessarily on the same day.

Table 9-2: Required Post Operative Follow-Up Schedule and Windows

Follow-Up Visit	Window Start Day	Target Day	Window Close Day
1 Month (± 15 days)	15	30	45
6 Months (-30 /+56 days)	153	183	239
12 Months (-30/+ 56 days)	335	365	421
24 Months (-8/+16 weeks)	674	730	842
36 Months (-8/+16 weeks)	1039	1095	1207
48 Months (-8/+16 weeks)	1404	1460	1572
60 Months (-8/+16 weeks)	1769	1825	1937

9.6 UNSCHEDULED VISITS

If a subject has a visit specifically associated with the treated disease and/or Valiant Mona LSA Stent Graft and this visit is not within any of the protocol specified study-related visit windows, data should be recorded as appropriate on the **Unscheduled Follow-Up Forms and/or Adverse Event Case Report Form.**

9.7 PROTOCOL DEVIATIONS

A protocol deviation occurs when a clinical Investigator and/or study site personnel do not conduct the study according to the CIP. All deviations are recorded on a **Protocol Deviation eCRF.** United States regulations (21 CFR 812.140) require that investigators maintain accurate, complete, and current records relating to the clinical study. This includes documents showing the dates and reasons for each deviation from the CIP. Depending upon the nature of the protocol deviation, expedited reporting and prior approval from Medtronic Vascular may be required. Protocol deviations should be reported

to your Institutional Review Board (IRB) in accordance with IRB policies and/or local laws. All deviations will be summarized and submitted in scheduled progress reports.

If Medtronic Vascular finds that an investigator is not complying with the executed study agreements, the CIP, FDA regulations, or the requirements of the reviewing IRB, prompt action will be taken to secure compliance. In addition, shipment of the device may be stopped or the participation of the investigator may be terminated (21 CFR 812.46). Additional information is provided in Section 9.15 – Study Termination.

9.7.1 Deviations with Expedited Reporting Requirements

For the following types of protocol deviations (per 21 CRF 812.150), an investigator is required to notify Medtronic Vascular and the IRB within 5 business days of the deviation.

- Emergency Deviation from the CIP (a deviation to protect the life or physical well-being of a subject in an emergency).
- Failure to obtain Informed Consent.

Notification to Medtronic Vascular and/or the IRB should be documented and maintained in the clinical study file at the site and at Medtronic Vascular.

9.7.2 Deviations Requiring Prior Approval

An investigator is required to obtain prior approval from clinical study management at Medtronic Vascular and the IRB before initiating deviations from the CIP that affect the scientific soundness of the plan, or the rights, safety, and welfare of the subjects (non-emergent situation). However, prior approval is not required in situations where unforeseen circumstances are beyond the investigator's control, e.g., subject did not attend scheduled follow-up visit, laboratory test was performed incorrectly, and test equipment did not operate properly.

9.7.3 Non-Urgent Deviations

Protocol deviations which do not have the urgency associated with expedited notification or prior Medtronic Vascular/ IRB approval (as discussed in Sections 9.7.1 and 9.7.2) will be reported upon discovery, such as during completion of eCRFs or a monitoring visit.

9.8 TECHNICAL OBSERVATIONS

A technical observation is a defect, malfunction, or failure of the Valiant Mona LSA Thoracic Stent Graft System to function according to its design intent. This includes, but is not limited to, migrations and device access difficulties. Technical observations may or may not be related to an adverse event. Technical observations that are not associated with an adverse event will be reported on the appropriate eCRF (e.g. Follow-Up Imaging Form, Procedure Form). If an adverse event occurred as a result of the technical observation, then the appropriate adverse events forms must be completed as well. Refer to Appendix D for definitions for technical observations.

9.9 ADVERSE EVENTS

An adverse event is defined as any untoward medical occurrence or worsening of an existing condition in a subject that occurs following enrollment. All adverse events that meet the study definition noted above will be reported to the Sponsor and documented on the **Adverse Event Form** and in the subject's medical records. Refer to Appendix C for adverse event definitions.

Potential (anticipated) adverse events that may be associated with thoracic aortic stent graft procedures are listed in Section 15 - Risk Analysis. Adverse events will be reported to Medtronic Vascular on the **Adverse Event eCRF**.

Clinical events that are inherent to a surgical procedure and expected to occur in most subjects for a projected duration are considered unavoidable. Such events include, but are not limited to, those listed in **Table 9-3**. These events are not required to be reported as adverse events during this study.

Table 9-3: Expected and Unavoidable Adverse Events Related to the Surgical Procedure

Description of the Event	Time Frame from the Index Procedure
Endoleaks observed and resolved during the index procedure	Resolved by the time the subject leaves the OR
Anesthesia-related nausea and/or vomiting	Within 24 hours
Low-grade fever (< 100° F or < 37.8° C)	Within 48 hours
Back pain related to laying on OR table	Within 72 hours
Incisional pain (pain at access site)	Within 72 hours
Sleep problems or insomnia	Within 72 hours
Mild to moderate bruising or ecchymosis	Within 168 hours

9.10 Patient Death

The investigator is responsible for reporting the death of a subject to Medtronic Vascular and the IRB. The procedures and reporting timeframes detailed in Section 10 – Adverse Event Definitions and Expedited Reporting must be followed. All deaths will be reviewed and adjudicated by the Clinical Events Committee (CEC).

Patient deaths must be documented on the **Study Exit Form**. A copy of the dictated death summary report death certificate, and autopsy report (if performed) should be sent to Medtronic Vascular. If a death occurs at a non-investigational site, it is the investigative center's responsibility to attempt to retrieve information about the death. If the death does not occur in an institution, then the investigator must submit a summary of the known events surrounding the death.

All subject deaths will be classified according to the following definitions of mortality.

Aorta-Related Mortality

Any death occurring within 30 days from either the index procedure or any secondary endovascular procedure intended to treat the disease will be considered Aorta-Related Mortality (ARM) unless there is evidence to the contrary. Additionally, deaths occurring as a consequence of any procedure intended to treat

the targeted disease, aneurysm rupture, or a conversion to open repair will also be considered as ARM.

Ultimate adjudication of relatedness of death will be made by the CEC. Excluded from ARM designation are deaths related to disease in anatomic areas other than the targeted segment treated by the Valiant Mona LSA Thoracic Stent Graft System.

Perioperative Mortality

Any death that occurs intraoperatively or within 30 days of the index procedure will be considered perioperative mortality. In addition, any death that occurs beyond 30 days while the patient is still hospitalized following the index procedure will be considered a perioperative death.

In the event of a patient death, the Valiant Mona LSA Stent Graft should be explanted (when feasible) and returned to Medtronic Vascular for analysis. Refer to Section 9.11 - Explanted Devices.

9.11 Explanted Devices

All explanted devices should be returned to Medtronic Vascular for analysis. Information pertaining to the explant procedure should be recorded on the **Explant Form**. If a product is explanted and not returned to Medtronic Vascular, an explanation should be provided. The final disposition of the device must be recorded on the device accountability log. Relevant information should also be recorded on associated case report forms, e.g., **Adverse Event and Study Exit Form**.

Detailed instructions are provided in Appendix H for explant of the device and its return.

An overview of the explant procedure follows.

- Notify Medtronic Vascular when an explant has occurred. Medtronic Vascular will provide a shipping container for the explanted product, which includes instructions and a return shipping label.
- Before the device is explanted, if possible, obtain an *in situ* photograph of the stent graft. At the time of removal, care should be taken to avoid excessive manipulation with metallic instruments at the proximal and distal fixation sites. Leave the stent graft as intact as possible and avoid deforming the device. All

efforts should be taken to preserve the connection between the MSG and the BSG during explant

- When the explant is performed as part of an autopsy or a postmortem procedure, the device should be carefully excised with at least 1 cm of host tissue adjacent to the proximal and distal fixation sites. Do not disturb the inside surface of the stent graft.
- Record the location of the site of the tissue removal relative to the position of the stent graft.
- If possible, immediately after its removal, make photographic records of the explanted device and the explant site.
- Clearly identify all components relative to surgical placement and orientation. Identify the proximal and distal ends. The anterior portion of the stent graft should also be labeled. Surgical clips and sutures can be used to label the explanted device. A complete record of labeling methodology should be made at the time of the explant procedure and be included with the explanted product and any relevant reports.
- Complete the **Explant Form**. Labels are provided in the explant kit.
- The subject undergoing explant as a secondary procedure will be followed for 1 month subsequent to removal of the device.
- A summary of the explant findings will be provided to the investigator.

9.12 Study Exit

The **Study Exit Form** should be completed at the time a subject is exited from the study. A subject will be considered to have exited from the study for any of the following reasons.

- Subject completes follow-ups required by the investigational plan.
- Subject dies.
- Subject requests to be withdrawn.
- Physician requests that patient be withdrawn to protect the welfare of the patient.
- Subject is lost to follow-up.
- Other (specify).

A subject may elect to withdraw from the study at any time. The subject should notify the investigator. The investigator and research staff should encourage all subjects to return for required follow-up visits. Every attempt must be made to ensure all subjects complete the follow-up visit schedule. For subjects who fail to appear for a scheduled study visit, the site must contact the subject in a timely manner to reschedule the visit and associated required evaluations within the subject's window, if possible.

The efforts to obtain follow-up information must include, at a minimum, three (3) attempts to make contact via telephone. If contact via phone is not successful, a certified letter from the Principal Investigator must be sent to the subject's last known address. When possible, public records should be searched to identify vital status. All contact efforts to obtain follow-up must be documented in both the subject's medical records and on the eCRFs.

9.13 Subject Confidentiality

Subject confidentiality will be maintained throughout the clinical study to the extent permitted by law. That is, every attempt will be made to remove subject identifiers from clinical study documents. For this purpose, a unique subject identification code (site number, subject number and subject initials) will be assigned and used to allow identification of all data reported for each subject. This will also ensure that the information can be tracked back to the source data.

Study data may be made available to third parties, e.g., in the case of an audit performed by regulatory authorities, provided the data are treated confidentially and that the subject's privacy is guaranteed. The identity of a subject will never be disclosed in the event that study data are published.

Medtronic Vascular recommends that the study sites comply with the subject confidentiality provisions of the Health Insurance Portability and Accountability Act (HIPAA) issued by the U.S. Department of Health and Human Services (HHS). Sites should maintain patient privacy in accordance to federal regulations (45 CFR Parts 160 and 164), local regulations, and institutional requirements.

9.14 Device Accountability

Medtronic Vascular is responsible for the availability and traceability of all investigational products. Documentation is required at each step of the process via a device disposition log. Investigational product will be reconciled on a regular basis.

The investigator also is required to maintain adequate records of the receipt and disposition of all investigational devices. A device disposition log will be provided for this purpose.

Explanted or abandoned product should be returned to Medtronic Vascular (see Appendix H). All unused product must be returned to Medtronic Vascular at the close of the study.

9.15 Study Termination

Medtronic Vascular and/or the US FDA have the right to terminate this study at any time and remove all study materials from the site. A study may be terminated for any of the following reasons.

- Unsatisfactory rate of patient enrollment or compliance to eligibility criteria.
- Repeated noncompliance with the investigational plan.
- Inaccurate, incomplete, and/or untimely submission of data.
- The rate or severity of adverse events in this study or other similar studies indicates a potential health hazard to the subjects caused by the device.
- Inadequate accountability of the investigational device.

9.16 Study Closure

Upon completion (when all subjects enrolled have completed the 5-year follow-up visit or previously exited the study, and the eCRFs and queries have been completed) or termination (closure that occurs prior to meeting defined endpoints) of the study, Medtronic Vascular and/or its designees will notify the site. Study closeout visits will be performed. All unused study devices and any unused study materials and equipment will be collected and returned to Medtronic Vascular and/or its designees. The monitors will ensure that the investigator's regulatory files are up to date and complete and that any outstanding issues from previous visits have been resolved. Other issues that will be reviewed at this visit include: discussing record retention requirements, device accountability, possibility of site audits, publication policy, and notifying the IRB of study closure, etc.

10. ADVERSE EVENT DEFINITIONS AND EXPEDITED REPORTING

A list of potential adverse events is provided in Section 15 - Risk Analysis. Adverse event definitions and reporting schedules are defined in the following sections.

10.1 DEFINITIONS

Adverse Event

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, whether or not related to the investigational medical device after the patient was enrolled in the study.

The events identified as expected clinical procedure events (**Table 9-3**) will not be considered adverse events. Specific adverse event definitions are provided in Appendices B – C.

Major Adverse Event

Major adverse events include the occurrence of any of the following and are defined in Appendix B.

- All-Cause Mortality
- Myocardial Infarction
- Paraplegia
- Renal Failure
- Stroke
- Left Arm/Hand Ischemia

Serious Adverse Event

A serious adverse event is an adverse event that:

- Led to a death.
- Led to a serious deterioration in the health of the subject that resulted in:
  a. a life threatening illness or injury, or
  b. a permanent impairment of a body structure or a body function, or
  c. in-patient hospitalization or prolongation of existing hospitalization
  d. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function. *

- Led to fetal distress, fetal death, or a congenital abnormality or birth defect.

* Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered a serious adverse event.
* An observational, overnight hospital admission < 24 hours in duration does not qualify an adverse event as a serious adverse event.

Unanticipated Adverse Device Effect

An unanticipated adverse event is defined as any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

10.2 Expedited Adverse Event Reporting

Investigators are responsible for reporting all adverse events to Medtronic Vascular as described in Section 9.9 – Adverse Events. The investigator should follow the reporting requirements of the reviewing IRB for all adverse events (including serious events). In addition, Medtronic requires that the following timeframes be used for the reporting of adverse events.

Adverse Events

The investigator must report to Medtronic Vascular any adverse event as soon as possible. In addition, the investigator must report the adverse event to the reviewing IRB according to its policies and procedures.

Information should be submitted on the **Adverse Event eCRF**.

Documentation of the IRB and Medtronic notification should be maintained in the site's clinical study files. It is recommended that acknowledgement of receipt from the IRB be maintained in the study file as well.

Serious Adverse Events

The investigator must report to Medtronic Vascular any serious adverse event as soon as possible, but in no case later than **3 working days** after the investigator first learns of the

event. In addition, the investigator must report the serious adverse event to the reviewing IRB according to its policies and procedures.

Information should be submitted on the **Adverse Event eCRF**. All relevant source documentation should be faxed to Medtronic.

Documentation of the IRB and Medtronic notification should be maintained in the site's clinical study files. It is recommended that acknowledgement of receipt from the IRB be maintained in the study file as well.

Unanticipated Adverse Device Effect

The investigator must report to Medtronic Vascular any unanticipated adverse device effect as soon as possible, but in no case later than **10 working days** after the investigator first learns of the event. The investigator's report to the reviewing IRB must be completed within 10 working days of the investigator's knowledge of the event (per 21 CFR 812.150).

Information should be submitted on the **Adverse Event eCRF**. All relevant source documentation should be faxed to Medtronic Vascular Clinical Trial Safety Department at (651) 367-0278.

Documentation of the IRB and Medtronic notification should be maintained in the site's clinical study files. It is recommended that acknowledgement of receipt from the IRB be maintained in the study file as well.

Questions about reporting of adverse events may be directed to the Valiant Mona LSA Thoracic Stent Graft System clinical study team.

11. DATA MANAGEMENT PROCEDURES

Medtronic Vascular will oversee all data management functions. Medtronic Vascular will be responsible for database development, system maintenance, user training, data queries, and report generation.

11.1 Case Report Forms

Medtronic Vascular will use an electronic data capture (EDC) system to collect patient data. The eCRFs are the primary component of EDC. Training on use of the system will be provided to the study site personnel. Instructions for completion of the eCRFs also will be provided.

The eCRFs must be completed, saved, and approved via electronic signature by the Investigator using a unique ID and password. This ID and password are for the use of the investigator only and may not be used by any other person. Because of the potential for errors or inaccuracies in transcribing data into eCRFs, source documentation must be maintained in each subject's hospital chart and/or electronic medical record. The eCRFs and source documentation must be available at all times for inspection by the study monitors or regulatory inspectors.

Changes made to eCRFs will be electronically recorded in a complete audit trail that cannot be changed, but can be accessed by authorized personnel at any time. All data are transmitted via the Internet in an encrypted fashion. When received at the server site, the data are decrypted and stored. Data can be extracted for Medtronic Vascular review and analysis at any time.

11.2 Source Documentation

IDE regulations require Investigators to maintain records of each subject's case history and exposure to the device. Investigators should maintain source documents to support the data recorded on the study case report forms. Source documents should be made available as required by Medtronic Vascular and/or its designees and/or regulatory inspectors during monitoring visits and/or audits or inspections.

11.3 Transmission of Data

Required data will be recorded on the appropriate eCRF at the time of or as soon as possible after the patient visit. The eCRFs and any requested supporting source documents must be de-identified and sent to Medtronic Vascular and/or retrieved from the investigator during monitoring visits. Questions about completion of the eCRFs may be directed to the Valiant Mona LSA Thoracic Stent Graft System clinical study team.

11.4 Data Queries

Any discrepancies in data observed during a monitoring visit or during a review of the data will be queried by Medtronic Vascular or its designee and should be resolved by the investigational site staff and investigator in a timely manner.

12. MONITORING AND AUDITING PROCEDURES

12.1 Clinical Study Sponsor and Monitors

Study monitoring and auditing will be performed by appropriately trained personnel appointed by the study Sponsor to ensure that the investigation is conducted in accordance with Medtronic requirements and applicable laws and regulations, i.e., US FDA IDE regulations.

A monitor is an individual designated by a sponsor or contract research organization to oversee the progress of an investigation. The monitor may be an employee of a sponsor or a consultant to the sponsor, or an employee of or consultant to a contract research organization.

12.2 Monitoring Methods

Monitoring of the clinical study will be a continuous, interactive process to ensure that high-quality data are obtained in compliance with the CIP and regulatory requirements. Monitoring functions will be conducted by Medtronic Vascular or designee. Specific monitoring requirements are detailed in the Valiant Mona LSA Thoracic Stent Graft System Monitoring Plan (maintained in the Medtronic Vascular clinical study project files). Frequent communication will be maintained with each investigational site to keep both the clinical center and Medtronic Vascular up-to-date and aware of the study progress. Electronic case report forms will be reviewed for completeness and accuracy.

On-site monitoring of all study centers will be frequent enough (at a minimum annually) to assure continued integrity and acceptability of the data. Accuracy of data reported on case report forms will be verified by comparison to source documents. Follow-up correspondence will be provided to the clinical study personnel at each site. Corrective action will be taken to resolve any issues of noncompliance. If Medtronic Vascular finds that an investigator is not complying with the executed study agreements, the CIP, FDA regulations, or the requirements of the reviewing IRB, then prompt action will be taken to secure compliance. In addition, shipment of the device may be stopped or the participation of the investigator may be terminated (21 CFR 812.46). Additional information is provided in Section 9.15 – Study Termination.

12.3 Monitoring Visits

Scheduled visits to the clinical investigational site will occur at the following intervals: prior to the start of the clinical trial (pre-study qualification visit, if applicable), at initiation of the study (at first implant or shortly thereafter), interim visits throughout the clinical study as needed, annually, and upon completion of the clinical study.

An on-site audit may be completed periodically throughout the study at each clinical site by Medtronic Vascular or an independent third party group. The purpose of the audit will be to ensure compliance to the investigational plan and regulatory requirements.

13. RECORDS AND REPORTS

Throughout the course of this clinical study, Medtronic Vascular, the investigators, and reviewing IRBs are responsible for the records and reports detailed in the following sections. Additional information is provided in the US FDA IDE regulations (21 CFR 812.140 and 21 CFR 812.150).

13.1 Investigator Records

Records must be maintained by the investigator in compliance with national regulations. Investigator records are subject to regulatory inspection (and Medtronic Vascular) and copying, and must be retained for a period of 2 years after the investigation is completed or terminated, or, 2 years after the records are no longer required to support the application to market the device (whichever date is later).

The investigator is responsible for the preparation (review and signature) and retention of the records cited below.

- All correspondence with another investigator, IRB, Medtronic Vascular, a monitor, or FDA, including required reports and study documents which pertain to the investigation.
- Records of receipt, use, and final disposition of a device.
- Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting source data (signed and dated informed consent forms, medical records, e.g., progress notes of the physician, patient's hospital chart, nursing notes).
- The clinical investigational plan, with documents showing the dates of and reasons for each deviation from the protocol.
- Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

13.2 Investigator Reports

The investigator is responsible for the preparation and submission of the reports cited in **Table 13-1**. Reports must be prepared in complete, accurate and timely manner. These reports may be subject to regulatory inspection (and inspection by Medtronic Vascular) and copying, and the retention requirements described above for Investigator Records. In

addition to the reports listed in the following table, FDA or the reviewing IRB may request reports pertaining to any aspect of the clinical study.

Table 13-1: Investigator Reporting Responsibilities

REPORT	SUBMIT TO	DESCRIPTION/CONSTRAINTS
Unanticipated Adverse Device Effects	Sponsor and IRB	The report must be submitted to Medtronic Vascular within 3 working days after the investigator first learns of the effect. Notification to the IRB should be made according to the reporting requirements of the reviewing IRB, but no later than 10 working days after the investigator first learns of the effect.
Serious Adverse Events	Sponsor and IRB	The report must be submitted to Medtronic Vascular within 3 working days after the investigator first learns of the event. Notification to the IRB should be made according to the reporting requirements of the reviewing IRB.
Adverse Events	Sponsor and IRB	The report must be submitted to Medtronic Vascular as soon as possible after the investigator first learns of the event. Notification to the IRB should be made according to the reporting requirements of the reviewing IRB.
Withdrawal of IRB Approval	Sponsor	The investigator must report a withdrawal of the reviewing authority within 5 working days.
Progress Report	Sponsor, IRB, and Monitor	The investigator must submit this report at least annually for the duration of the study.
Deviation from Investigation Plan (Emergency)	Sponsor and IRB	Notification must be made within 5 working days if the deviation was made to protect the life or physical well-being of a subject.
Deviation from Investigation Plan (Other – Non-Emergent)	Sponsor and IRB	If the deviation may affect the scientific soundness of the plan or the rights, safety and welfare of the subjects (and is not an emergency), then the deviation must be approved by Medtronic Vascular and the reviewing authority prior to its implementation. If the deviation does not affect these issues (study soundness, rights, safety, etc.) then only Medtronic Vascular must approve it, (except in cases which are beyond the control of the investigator—see Section 9.7 – Protocol Deviations).

Table 13-1: Investigator Reporting Responsibilities

REPORT	SUBMIT TO	DESCRIPTION/CONSTRAINTS
Failure to Obtain Informed Consent	Sponsor and IRB	The Investigator must notify Medtronic Vascular and the reviewing authority within 5 working days after device use. The report must include a brief description of the circumstances justifying the failure to obtain informed consent.
Final Report	Sponsor and IRB	This report must be submitted within 3 months after termination or completion of the investigation.

13.3 Sponsor Records

Medtronic Vascular will maintain the following study-related records.

- All correspondence with another sponsor, a monitor, an investigator, an IRB, or FDA, including required reports.
- Records of shipment and disposition of the investigational device.
- Signed investigator agreements including the financial disclosure information required to be collected under 21 CFR 812.43 in accordance with 21 CFR 54.
- Records concerning adverse events related to the device (whether anticipated or unanticipated) and complaints.
- Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigation or a particular investigation.

13.4 Sponsor Reports

Medtronic Vascular is responsible for the reports cited in **Table 13-2**. These reports are subject to regulatory retention and inspection requirements. In addition to the reports listed in the following table, FDA or the reviewing IRB may request reports pertaining to any aspect of the clinical study.

Table 13-2: Medtronic Vascular Reporting Responsibilities

REPORT	SUBMIT TO	DESCRIPTION
Unanticipated Adverse Device Effects	Regulatory authorities and all participating IRBs and investigators	Medtronic Vascular will report on unanticipated adverse event within 10 working days after receiving notice of the effect.
Informed Consent	Regulatory authorities	Medtronic Vascular will submit a copy of any report from an investigator of use of the device without obtaining informed consent within 5 working days of receipt of notice of such use.
Withdrawal of IRB Approval	IRBs, investigators, and regulatory authorities, as appropriate	Notification will be made within 5 working days after receipt of the withdrawal of approval.
Withdrawal of Regulatory Approval	All IRBs and investigators	Notification will be made within 5 working days of receipt of notice of the withdrawal of approval.
Current Investigator List	Regulatory authorities	Medtronic Vascular will submit at 6-month intervals (starting 6 months after FDA approval of the IDE).
Progress Report	Regulatory authorities and IRBs	A progress report will be submitted at least annually.
Recall and Device Disposition	Regulatory authorities, IRBs, and investigators	Notification will be made within 30 working days and will include the reasons for any request that an investigator return, repair or otherwise dispose of any devices.
Final Report	Regulatory authorities, IRBs, and investigators	Medtronic Vascular will notify reviewing authorities within 30 working days of the completion or termination of the investigation. A final report will be submitted within 6 months of completion or termination.

14. STUDY COMMITTEES

14.1 Clinical Events Committee

A Clinical Events Committee (CEC) is a group of physicians independent of the clinical study with expertise and experience in the area of DTA stent grafts. The members may be interventional cardiologists, vascular surgeons, cardiothoracic surgeons, interventional radiologists, or neurologists. The CEC will review and adjudicate all major adverse events (MAEs) as defined in the clinical investigational plan. Any unanticipated adverse device events (UADEs) will be reviewed and adjudicated by the Clinical Events Committee (CEC). In addition, the CEC will review and adjudicate specific adverse events identified by the Sponsor or an independent Data Safety Monitoring Board (DSMB) that occur during the course of the trial. The CEC will review events when Medtronic Vascular personnel forward the relevant documentation to the members.

A charter will be developed that will detail the operations of the committee. Results of the adjudication process will be recorded by the CEC members on the appropriate **CEC Event Adjudication Forms.**

14.2 Data Safety Monitoring Board

The DSMB is composed of at least 5 members, consisting of 4 physicians from the fields of vascular, cardiovascular surgery, interventional radiology, interventional cardiology, or neurology and 1 biostatistician, who are not directly involved in the conduct of the study. The DSMB will be convened when four (4) subjects have completed follow-up through the 30-day visit and this data is fully monitored. Based on the available subject safety data, the DSMB may recommend that Medtronic Vascular continue enrollment in the study as per the approved investigational plan, modify the clinical study, or stop study enrollment in accordance with parameters previously agreed upon between the DSMB and Medtronic Vascular. All final decisions, however, regarding study modifications, rest with Medtronic Vascular.

After the first DSMB meeting, subsequent meetings of the DSMB will be based on the DSMB's guidance, and this will be outlined in the DSMB charter.

14.3 Independent Physician Reviewer

The Independent Physician Reviewer will review imaging prior to subject enrollment into the study in order to determine that each subject meets the anatomical requirements set forth in this investigational plan.

Further details will be outlined in the Independent Physician Reviewer Manual of Operations.

14.4 Imaging Core Lab

An imaging core lab will be established to independently analyze images based on the imaging protocol/core lab guidelines. Imaging guidelines will be provided in the investigational site file.

15. RISK ANALYSIS

15.1 POTENTIAL RISKS

Following is a list of potential (expected) risks that may be associated with use of the Valiant Mona LSA Thoracic Stent Graft System. The occurrence of the listed complications may lead to a repeat endovascular intervention and/or open surgical repair. Since the Valiant Mona LSA Thoracic Stent Graft System is an investigational device, the risks are not entirely known, but are believed to be similar to those that are associated with the existing endovascular devices in clinical use or commercially available as well as the standard surgical repair of DTAs. The long-term effectiveness of endovascular repair has not been established. The potential adverse events/complications are listed in Table 15-1.

Table 15-1: Potential Adverse Events/Complications Associated with Use of the Valiant Mona LSA Thoracic Stent Graft System

Access failure	Endoleaks	Procedural bleeding
Access site complications (e.g., spasm, trauma, bleeding, rupture, dissection)	Excessive or inappropriate radiation exposure	Prosthesis dilatation
Adynamic ileus	Extrusion/erosion	Prosthesis infection
Allergic reaction (to contrast, anti-platelet therapy, stent graft material)	Failure to deliver the stent graft	Prosthesis rupture
Amputation	False lumen perfusion	Prosthesis thrombosis
Anesthetic complications	Femoral neuropathy	Pseudoaneurysm
Aneurysm or false lumen expansion	Fistula (aortobronchia, aortoenteric, aortoesophogeal, arteriovenous, lymph)	Pulmonary edema
Aneurysm rupture	Gastrointestinal bleeding/complications	Pulmonary embolism
Angina	Genitourinary complications	Reaction to anesthesia

Arrhythmia	Hematoma	Renal failure
Arterial stenosis	Hemorrhage/bleeding	Renal insufficiency
Atelectasis	Hypotension/hypertension	Re-operation
Blindness	Infection or fever	Respiratory depression or failure
Bowel ischemia/infarction	Insertion or removal difficulty	Sepsis
Bowel necrosis	Intercostal pain	Seroma
Bowel obstruction	Intramural hematoma	Shock
Branch vessel occlusion	Leg edema/foot edema	Spinal neurological deficit
Buttock claudication	Lymphocele	Stent graft material failure (including breakage of the metal portion of the device)
Cardiac tamponade	Myocardial infarction	Stent graft migration
Catheter breakage	Neuropathy	Stent graft misplacement
Cerebrovascular accident (CVA)/Stroke	Occlusion – Venous or Arterial	Stent graft occlusion
Change in mental status	Pain/reaction at catheter insertion site	Stent graft twisting or kinking
Coagulopathy	Paralysis	Transient ischemic attack (TIA)
Congestive heart failure	Paraparesis	Thrombosis
Contrast toxicity	Paraplegia	Tissue necrosis
Conversion to surgical repair	Paresthesia	Vascular ischemia
Death	Peripheral ischemia	Vascular trauma
Deployment difficulties/failures	Peripheral nerve injury	Wound dehiscence

Dissection, perforation, or rupture of the aortic vessel & surrounding vasculature	Pneumonia	Wound healing complications
Embolism	Post-implant syndrome	Wound infection
	Post-procedural bleeding	

All efforts will be made to minimize these risks by selecting investigators who are experienced and skilled in using endoluminal aortic devices and who have been adequately trained. Also, risk minimization activities were performed during development and design verification testing of the device. Activities intended to minimize risks include the following:

- Investigator and study personnel training will be conducted to share information regarding the design of the Valiant Mona LSA Thoracic Stent Graft System, its application, and pre-clinical results.
- The Investigator will adhere to eligibility criteria and screening procedures to ensure that appropriate patients are enrolled.
- An Independent Physician Reviewer will review the Screening images of each patient to ensure that the appropriate patients are enrolled.
- The Investigator will adhere to the Valiant Mona LSA Thoracic Stent Graft System Instructions for Use packaged with the device.
- The subjects will be carefully monitored throughout the study period.
- The Investigator will evaluate the subject adverse events during the course of the study.
- Data submitted from the investigative centers will be monitored during the course of the study.
- An imaging core lab will review the study related images on an ongoing basis.
- Monitoring visits will be conducted to evaluate protocol compliance and data quality.
- Safety and effectiveness data obtained during the course of the study will be shared with Investigators in periodic reports to increase understanding of the device and potential adverse events.
- Any subject death or any device related issue will be reported to the FDA.
- A DSMB will monitor safety outcomes and provide guidance on whether or not the study should continue.

Detailed study procedures are provided in **Section 9 - Clinical Study Procedures**.

15.2 Clinical Risk Benefit

In current clinical practice, the LSA is commonly covered during endovascular treatment for pathologies of the thoracic arch occurring close to the LSA. In some cases, prior revascularization either as a bypass or transposition of the LSA may be required. This usually requires a separate hospitalization two to three days prior to the endovascular procedure. Additionally, a proximal subclavian ligation or embolization to prevent type II endoleak may also be undertaken. As with any surgical procedure, this revascularization procedure carries some risk. Current literature places the risk of phrenic nerve damage at approximately 4% and a low associated risk of mortality.

As an off-the-shelf system, the Valiant Mona LSA Thoracic Stent Graft System serves an unmet clinical need by providing a complete endovascular solution for perfusion of the LSA as a part of TEVAR, thereby reducing one endovascular and one surgical procedure to a single endovascular procedure. The implication of this for the Valiant Mona LSA Thoracic Stent Graft System is that if perfusion of the LSA fails with the proposed device, the outcome would then resemble the current clinical standard of care of covering the LSA. As in current cases in which the LSA is covered, revascularization would still be an option if the patient presented with issues associated with the occlusion.

15.3 Potential Benefits

The potential benefits of the Valiant Mona LSA Thoracic Stent Graft Systems have not been documented; nevertheless, they are expected to be similar to those associated with endovascular stent graft systems currently in clinical trials or commercially available.

Endovascular treatment of DTA has been shown to be an effective, less invasive procedure that may result in a reduced rate of early mortality and comorbidities associated with open surgical repair.[22-26] Stent graft repair also provides a treatment option for patients who would not otherwise be eligible for surgical repair. Additional potential benefits include the following.

- Reduced operating room and anesthesia time
- Reduced requirement for blood transfusions
- Shorter time in intensive care
- Shorter length of hospital stay
- Shorter recovery time and return to activities of daily living

- Preservation of the LSA without the need for a surgical revascularization

16. PUBLICATION POLICY

Publications based on the results of the Evaluation of the Valiant Mona LSA Thoracic Stent Graft System in Descending Thoracic Aortic Aneurysms and Chronic Dissections study will follow the process outlined in the Clinical Research Agreement. A publication committee may be formed to oversee the preparation of manuscripts and identify first authors and writers for primary and ancillary publications of the study results.

At the conclusion of the study, a multicenter manuscript may be prepared for publication in a peer-reviewed, scientific journal. The manuscript will be made available for review by all co-authors, including Medtronic Vascular personnel, prior to submission.

Publication of the primary results from any single site experience within the study will not be allowed until the multicenter results are published. Exceptions to this rule will require the prior approval of Medtronic Vascular.

Secondary or ancillary manuscripts also are anticipated. For the purposes of timely abstract presentation and publication, such publications will be delegated to the appropriate principal author(s). Final analysis and review of the manuscript for all multicenter publications will require the approval of Medtronic Vascular.

As owners of the Evaluation of the Valiant Mona LSA Thoracic Stent Graft System in Descending Thoracic Aortic Aneurysms and Chronic Dissections study database, Medtronic Vascular has the discretion to determine who will have access to the data. This includes raw as well as summary data. Complete study data, which may contain health information that could be identified with a subject, will be made available only for study-related/business-related activities, or to regulatory authorities and other government bodies.

17. INSURANCE

Medtronic Vascular has umbrella insurance in an amount common in the medical device industry to cover significant exposures. Medtronic Vascular will comply with local regulatory requirements concerning insurance coverage.