Medtronic

Clinical Investigation Plan

Clinical investigation plan/Study Title	Evaluation of the Valiant Mona LSA Thoracic Stent Graft System in Descending Thoracic Aortic Aneurysms and Chronic Dissections
Clinical Investigation Plan Identifier	10151194DOC
Study Product Name	Valiant Mona LSA Thoracic Stent Graft System
Sponsor/Local Sponsor	Medtronic Vascular, Inc. 3576 Unocal Place Santa Rosa, CA 95403
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Lead Principal Investigator(s)	Eric Roselli, MD Cleveland Clinic Cleveland, OH

VERSION HISTORY

Version	Summary of Changes	Author(s)/Title
1A	Not Applicable, New Document	[redacted]
1B	See Appendix J	[redacted]
1C	See Appendix K	[redacted]
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1E	See Appendix M	[redacted]
1F	See Appendix N	[redacted]

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Clinical Study Synopsis

Protocol Number:	10151194DOC
Investigational Device:	Valiant Mona LSA Thoracic Stent Graft System (Comprised of the Main Stent Graft and Branch Stent Graft Systems)
Study Title:	Evaluation of the Valiant Mona LSA Thoracic Stent Graft System in Descending Thoracic Aortic Aneurysms and Chronic Dissections
Clinical Study Type:	Feasibility
Sponsor:	Medtronic Vascular 3576 Unocal Place Santa Rosa, CA 95403
Indications for Use:	The Valiant Mona LSA Thoracic Stent Graft System is for the endovascular repair of fusiform/saccular aneurysms , type B chronic dissections (CTBD), and penetrating ulcers (PAU) of the descending thoracic aorta (DTA) in patients who require coverage of the left subclavian artery (LSA) presenting with the appropriate anatomy, including: Aortic diameter ≥ 5.5 cm or in whom the aneurysmal thoracic aorta is > 2 times the diameter of the non-aneurysmal thoracic aorta and which will require coverage of the LSA. Iliac or femoral artery access vessel morphology that is compatible with vascular access techniques, devices, or accessories Non-diseased aortic diameter in the range of 25 mm to 42 mm for fusiform/saccular aneurysms and penetrating ulcers Non-diseased aortic diameter in the range of 28 mm to 44 mm for chronic dissections Non-diseased LSA diameter in the range of 8 mm to 13 mm

	Total effective non-diseased aortic proximal neck length of > 0 mm between the distal end of the LSA ostium to the beginning of the disease Total effective non-diseased aortic proximal neck length of ≥ 20 mm between the distal end of left common carotid (LCC) ostium to the beginning of the disease, including ≥ 10 mm between the LSA and LCC Non-aneurysmal aortic distal neck length ≥ 20 mm
Study Purpose:	The purpose of the clinical investigation is to assess the feasibility of the Valiant Mona LSA Thoracic Stent Graft System to repair fusiform/saccular aneurysms, penetrating ulcers and chronic type B dissections of the DTA in patients who require coverage of the LSA, including an assessment of the safety and effectiveness of the device acutely and at the 30 day visit in the identified subject population. Procedural information will be collected in order to enhance the current instructions for use and delivery and deployment steps. The chronic Type B Dissection expansion subjects will be prospectively enrolled in support of a future premarket approval analysis for the Valiant Mona LSA device.
Product Status:	The Valiant Mona LSA Thoracic Stent Graft System is a modular system intended to maintain perfusion of the LSA when the device is implanted in Zone 2 of the aortic arch for the exclusion of a Thoracic Aortic Aneurysm (TAA), PAU, and CTBD. The Valiant Mona LSA Thoracic Stent Graft System is comprised of two key components: • The Main Stent Graft (MSG) which is delivered using the Main Delivery System (MDS) • The Branch Stent Graft (BSG) which is delivered using the Branch Delivery System (BDS) This device is considered investigational in the United States (US).
Study Objective:	The primary safety and effectiveness objectives will be measured acutely and at the 30 day visit after implantation of the Valiant

	Mona LSA Thoracic Stent Graft System. The safety parameters will be assessed through a composite at the 30 day visit post implantation, consisting of aorta-related mortality, stroke, paraplegia and left arm/hand ischemia. The primary effectiveness objective for the Valiant Mona LSA Thoracic Stent Graft System is defined as successful delivery and deployment of the Main Stent Graft (MSG) and Branch Stent Graft (BSG) at implant and successful exclusion of the aneurysm/penetrating ulcer or primary entry tear while maintaining patency of the BSG at the 30 day visit. In addition, analyses of periprocedural through discharge clinical utility measures will be conducted.
Primary Observations:	**Primary Safety Observation:** Within 1 month (Day 0 – Day 30) from the index procedure, composite endpoint consisting of: • Aorta-Related Mortality • Stroke • Paraplegia • Left Arm/Hand Ischemia **Primary Effectiveness Observation:** The primary effectiveness observation is treatment success (defined below) and will be captured within the initial reporting period of 1 month from the index procedure. **Treatment success** is defined as technical success, which is the successful delivery and deployment of the stent graft (deployment of the Valiant Mona LSA Thoracic Stent Graft System in the planned location with no unintentional coverage of other vessels, assessed intra-operatively, and the removal of the delivery system) and successful exclusion of the aneurysm/penetrating ulcer or primary entry tear while maintaining patency of the MSG and BSG at the 30 day visit.
Additional Observations:	Periprocedural through Discharge Clinical Utility Measures

	• Mean duration (min) of procedure.
	• Mean time (min) to implant the LSA Branch device.
	• Proportion of subjects who underwent general anesthesia.
	• Mean volume (cc) of estimated blood loss.
	• Proportion of subjects requiring blood transfusions.
	• Mean length of time (hours) in intensive care unit.
	• Mean length of time (days) of overall hospital stay (from hospital admission to discharge).
	
	The following additional observations will be evaluated through 30 days and at each follow-up visit:
	
	• Major adverse event (MAE) rates within 30 days of the initial or secondary procedures, including:
	  ○ All-Cause Mortality
	  ○ Myocardial Infarction
	  ○ Paraplegia
	  ○ Renal Failure
	  ○ Stroke
	  ○ Left Arm/Hand Ischemia
	• Secondary endovascular procedures
	• 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 surgical repair
	• 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.
Study Design:	Prospective, single-arm, non-randomized, multicenter, pre-market clinical study evaluating subjects implanted with the Valiant Mona LSA Thoracic Stent Graft System for the treatment of aneurysms/penetrating ulcers and chronic dissections of the descending thoracic aorta who are candidates for revascularization of the left subclavian artery.
Patient Population:	Subjects diagnosed with an aneurysmal thoracic aorta, penetrating ulcer, or chronic Type B dissection who are

	candidates for elective revascularization of the LSA and who meet the inclusion and exclusion criteria.
Type of Control:	No control is expected for this study. All subjects enrolled into this study will be followed for 5 years and information collected will be reported to the FDA on an annual basis, or as otherwise required by the agency.
Number of Subjects:	44 subjects 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. To ensure adequate disease state representation in the overall study dataset, a minimum of approximately 25% of the subjects will be enrolled for the treatment of TAA/PAU and a minimum of approximately 25% of the subjects will be enrolled for the treatment of CTBD.
Inclusion/Exclusion Criteria **(Thoracic Aortic Aneurysms and Penetrating Ulcers, TAA/PAU)**	**Inclusion Criteria:** • 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 LSA. 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 PAU (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. **Exclusion Criteria** • 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. • Subject has had a myocardial infarction (MI) within 3 months. • Subject has a known hypersensitivity or contraindication to anticoagulants or contrast media, which is not amenable to pre-treatment.
Inclusion/Exclusion Criteria **(Chronic Type B Dissections, CTBD)**	**Inclusion Criteria** • 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 LSA. Subject must be able to tolerate a surgical revascularization of the LSA. • Subject has a CTBD which will require coverage of the LSA. A CTBD 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 as well as the diameter of the LSA ostium. • 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 the above requirements are not met. **Exclusion Criteria** • 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. • Subject has had a myocardial infarction (MI) within 3 months.

	• Subject has a known hypersensitivity or contraindication to anticoagulants or contrast media, which is not amenable to pre-treatment.
Number of Sites:	Up to 10 investigational sites in the United States
Sample Size Calculation:	There is no sample size calculation since this is not a hypothesis driven study; however, the number of enrolled subjects is pre-specified. This study will enroll up to 44 subjects.
Study Hypothesis:	N/A
Analytical Sets:	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. The chronic Type B Dissection expansion subjects will be prospectively enrolled in support of a future premarket approval analysis for the Valiant Mona LSA device. Descriptive statistics will be used for each subset (TAA, PAU and CTBD) to analyze the primary observations, additional observations, and periprocedural and discharge clinical utility measures.
Pre-Enrollment Testing:	Physical exams, vital signs, medical history, 3D CTA with visualization of geometry of aorta and branch vessel, CTA/MRA of head and neck vessels, Doppler Ultra Sound (DUS) of the LSA/carotid vessels, Neurological baseline exam

Follow-Up Schedule:	Subjects will have required follow-up evaluations at these time points: 1. Discharge 2. 1 month post index procedure 3. 6 months post index procedure 4. 12 months post index procedure 5. Annually thereafter, for a total of 5 years post index procedure
Follow-Up Data Collection:	• Vital signs, Physical Exam, collection of Adverse Events at: 1 month, 6 months, 12 months, 2, 3, 4 and 5 years. • CTA w/ 3D reconstruction at: discharge, 1 month, 6 months, 12 months, 2, 3, 4 and 5 years. • Ultrasound of the LSA/thoracic branch vessels at: discharge, 1 month, 6 months, 12 months, 2, 3, 4 and 5 years. • Chest X-Ray at: discharge, 1 month, 6 months, 12 months, 2, 3, 4 and 5 years. • Additional imaging as required per physician
Clinical Events Committee (CEC):	All MAEs as defined by the clinical investigational plan will be reviewed and adjudicated by the Clinical Events Committee (CEC). Any unanticipated adverse device events (UADEs) will be reviewed and adjudicated by the 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. Syntactx, LLC 7 World Trade Center 250 Greenwich Street 46th Floor New York, NY 10007

Data Safety Monitoring Board (DSMB):	Syntactx, LLC 7 World Trade Center 250 Greenwich Street 46th Floor New York, NY 10007
Independent Physician Reviewer	An 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.
Principal Investigator:	Eric E. Roselli, MD Cleveland Clinic 9500 Euclid Avenue Cleveland, OH 44195
Sponsor:	[redacted] Medtronic Vascular 3576 Unocal Place Santa Rosa, CA 95403 [redacted]
Safety Monitoring:	Medtronic Core Clinical Solutions 710 Medtronic Parkway NE Minneapolis, MN 55432
Monitoring:	Medtronic Clinical Operations 710 Medtronic Parkway NE Minneapolis, MN 55432

1. INTRODUCTION

An Early Feasibility study was conducted in order to provide important information regarding the Valiant Mona LSA Thoracic Stent Graft System. This included:

- Validation of the procedure in humans, including the procedural steps, physician technique, and patient characteristics.
- Assessment of the safety and performance of the device acutely and at the 30 day visit, specifically in regards to delivery and deployment and exclusion of the aneurysm and patency of the LSA.
- Collection of thoracic arch movement parameters in humans, both before and after placement of the device.
- Collection of imaging data to augment the current use conditions data set.

The device was successfully implanted into nine (9) subjects and continues to function as intended. Data collected from the Early Feasibility study allowed Medtronic to identify implantation procedural steps that required further clarification, in particular that manipulations of the stent graft devices and accessory devices should be performed distal to the LSA. In order to further characterize the study device, additional subjects will be enrolled into a Feasibility study for the Valiant Mona LSA Thoracic Stent Graft System.

The purpose of the Feasibility Study is to characterize the Valiant Mona LSA Thoracic Stent Graft System, in particular to assess the safety and effectiveness of the device acutely and at the 30 day visit in the identified subject population. This study will also evaluate the current instructions for use (IFU) and may direct changes to the delivery and deployment steps.

The purpose of the expansion to the Feasibility Study is to characterize the Valiant Mona LSA Thoracic Stent Graft System, in particular to assess the safety and effectiveness of the device acutely and at the 30 day visit, in subjects enrolled with chronic, Type B dissections. The chronic Type B Dissection expansion subjects will be prospectively enrolled in support of a future premarket approval analysis for the Valiant Mona LSA device. This Clinical Investigational Plan (CIP) describes the study requirements for the Valiant Mona LSA Thoracic Stent Graft System.

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 performed 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 Physician Screening Committee, and/or

CROs. Medtronic Vascular and/or its designees will conform to the US Code of Federal Regulations (CFR) including: 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).

2. BACKGROUND

There has been a remarkable evolution in the treatment of thoracic aortic diseases, from open surgery to endovascular therapy, which has significantly decreased morbidity and mortality in these patients.[1]

The early success of endovascular stent graft repair of abdominal aortic aneurysms (AAA) has fostered the application of these devices for the management of descending thoracic aortic diseases, including thoracic aortic aneurysms (TAA), acute and chronic Type B dissection, intramural hematoma, penetrating ulcer, traumatic injury, mycotic aneurysms

[1] Narayan P, Wong A, Davies I, Anegelini GD, Bryan AJ, Wilde P, Murphy GJ. Thoracic endovascular repair versus open surgical repair – which is the more cost-effective intervention for descending thoracic aortic pathologies? Eur J Cardiothorac Surg. 2011:40(4):869-74.

and anastomotic aneurysms.[2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17] This procedure offers an alternative method of treatment that is potentially less invasive, less expensive, and less risky than standard operative repair.[18] Endovascular repair of thoracic aortic pathology consists of trans-femoral or iliac introduction of a metallic stent coupled with a vascular graft. When the stent graft device is deployed and expanded within the diseased blood vessel, the stent graft creates a new aortic lumen for blood flow, excluding the lesion from blood flow while maintaining perfusion to the lower body. Essential design features of

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[2] Doroghazi RM, Slater EE, DeSanctis RW, Buckley MJ, Austen WG, Rosenthal S. Long-term survival of patients with treated aortic dissection. J Am Coll Cardiol. 1984;3:1026-1034.
[3] Appelbaum A, Karp RB, Kirklin JW. Ascending vs descending aortic dissections. Ann Surg. 1976;183:296-300.
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[6] Kato N, Hirano T, Shimono T et al. Treatment of chronic type B aortic dissection with endovascular stent-graft placement. Cardio-vasc Interv Radiol 2000;23:60-2.
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[11] Dake MD, miller DC, Mitchell RS et al. The "first generation" of endovascular stent-grafts for patients with aneurysms of the descending thoracic aorta. J Thorac Cardiovasc Surg 1998;116:689-703.
[12] Kato N, Dake MD, Miller DC et al. Traumatic thoracic aortic aneurysm: treatment with endovascular stent-grafts. Radiology 1997;205:657-62.
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[14] Sakai T, Dake MD, Semba CP et al. Descending thoracic aortic aneurysm: thoracic CT findings after endovascular stent-graft placement. Radiology 1999;212:169-74.
[15] Nienaber CA, Fattori R, Lund G et al. Nonsurgical reconstruction of thoracic aortic dissection by stent-graft placement. N Engl J Med 1999;340:1539-45.
[16] Dake MD, Miller DC, Semba CP et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. N Engl Med 1994;331:1729-34.
[17] Criado FJ, Clark NS, BArnatan MF. Stent graft repair in the aortic arch and descending thoracic aorta: a 4 year experience. J Vasc Surg 2002; 36 (6): 1121-8.
[18] Semba CP, Dake MD. Endoluminal Stent-Grafting in the Thoracic Aorta. In Chuter TAM, Donayre CE, White RA (eds). Endoluminal Vascular Prostheses. Boston: Little, Brown and Company; 1995:153-171.

conventional surgical vascular grafts, such as low blood permeability, resistance to radial dilatation, and long-term patency, are also important for a covered endoluminal stent graft. In addition, stent grafts must firmly anchor to the artery wall, without the use of sutures. The following sections discuss treatment of descending thoracic aortic aneurysm and dissection in greater detail.

Descending Thoracic Aortic Aneurysm

An aortic aneurysm is defined as a dilatation of the aortic vessel greater than 50% of its normal diameter for a given segment of the adhering normal vessel.[19] A descending thoracic aneurysm (DTA) is defined as involving any portion of the thoracic aorta distal to the left subclavian artery and extending to above the diaphragm.[20] In adults, the diameter of the normal aorta is approximately 30 mm at the aortic root and approximately 25 mm at the level of the diaphragm. Age is the major influential factor in aortic diameter enlargement and all aortic diameters increase with age.[21] It has been reported that aortic diameters increase about 1 mm per decade during adulthood.[22] Generally, a diameter in the thoracic aorta greater than 4.5 cm is considered aneurysmal.[19,20,21,22,23]

A DTA is a life-threatening condition. Annually, the incidence of thoracic aortic aneurysms (TAA) in a population-based study is 10.4 per 100,000 person-years, and the descending thoracic aorta is involved in about 40% of those cases.[24] The number of people diagnosed with DTA is thought to be increasing. Factors that contribute to this rise include increased

[19] Faries PL, Dayal R, Lin S, Trociolla S, Rhee J, Craig Kent K. Endovascular stent graft selection for the treatment of abdominal aortic aneurysms. J Cardiovasc Surg 2005;46:9-17.
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[21] Brewster DC, Geller SC, Kaufman JA, et al. Initial experience with endovascular aneurysm repair: comparison of early results with outcome of conventional open repair. J Vasc Surg 1998;27:992-1005.
[22] Matsumura JS, Brewster DC, Makaroun MS, Naftel DC. A multicenter controlled clinical trial of open versus endovascular treatment of abdominal aortic aneurysm. J Vasc Surg 2003;37:262-271.
[23] Salartash K, Sternbergh III WC, York JW, Money SR. A comparison of open transabdominal AAA repair with endovascular AAA repair in reduction of postoperative stress response. Ann Vasc Surg 2001;15:53-59.
[24] Cuypers WM, Gardien M, Buth J, et al. Randomized study comparing cardiac response in endovascular and open abdominal aortic aneurysm repair. Br J Surg 2001;88:1059-1065.

longevity of the population and improved diagnostic capability.[24,25,26] The natural history of TAA, including DTA, is one of progressive enlargement and rupture, and rupture is almost invariably fatal. Current available treatment options include medical treatment, open surgical repair, and endovascular stent graft repair.

Standard surgical treatment involves a thoracotomy, aortic clamping, re-section of the aneurysmal segment, and replacement using a Dacron graft. Thoracic endovascular aortic repair (TEVAR) consists of transfemoral or iliac introduction of the device. When the stent graft device is deployed and expanded within the aneurysmal blood vessel, it creates a new aortic lumen for blood flow, excluding the aneurysm sac, while maintaining perfusion to the lower body. Studies comparing open surgical repair to endovascular repair concluded that the latter offers a less invasive, less expensive alternative, a decrease in mortality and morbidity in high-risk patients, and is associated with a shorter hospital stay and a quicker return to normal activities after surgery.[27,28] Because of the invasive nature of the open surgical repair, physicians consider multiple endovascular options for high-risk patients.

Dissection

Improved diagnostic imaging modalities combined with longer life expectancy and exposure to high blood pressure has enhanced awareness of the spectrum of acute and chronic aortic syndromes.[29] One such condition is aortic dissection, which involves a progressive tear in the aorta. The inner lining (intima) of the aorta tears resulting in propagation of blood within the middle layer (media), usually distally, but sometimes retrograde with multiple reentry sites. An aortic dissection is classified as Stanford Type A or B depending on involvement of the ascending or descending thoracic aorta. Type A dissection begins in the ascending part of the aorta and typically moves to another part of the chest. Type B dissection begins in the descending part of the aorta and typically moves

[25] EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomized controlled trial. Lancet 2005;365:2179-2186.
[26] Greenhalgh RM, Brown LC, Kwong GP, et al. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomized controlled trial. Lancet. 2004;364:843-848.
[27] Sicard GA, Zwolak RM, Sidawy AN, White RA, Siami FS. Endovascular abdominal aortic aneurysm repair: long-term outcome measures in patients at high risk for open surgery. J Vasc Surg 2006;44:229-236.
[28] Du Toit DF, Saaiman JA, Carpenter JP, Geldenhuys KM. Endovascular aortic aneurysm repair by a multidisciplinary team: lessons learned and six-year clinical update. Cardiovasc J South Africa
[29] Nienaber CA, Eagle KA. Aortic dissection: new frontiers in diagnosis and management: Part I: from etiology to diagnostic strategies. Circulation. 2003 Aug 5;108(5):628-35.

towards the abdomen, but in certain circumstances can also propagate towards the heart.[30]

Conventional treatment of thoracic aortic dissection has either been medical management or an open surgical procedure, depending upon the patient's clinical presentation. For Type B aortic dissections a complication specific treatment approach with surgery is usually followed with medical management applied as the primary treatment for uncomplicated cases. Medical management primarily focuses on reducing blood pressure to reduce the stresses on the diseased vessel, but does not treat the dissection or underlying disease. This has been the preferred treatment for acute Type B dissections in many institutions.[2,3,4,31,32,33,34,35] Outcomes prior to hospital discharge for uncomplicated, acute Type B dissections are considered acceptable with 90% survival reported;[36] however, 20% to 40% of patients who have passed their acute phase with medical anti-hypertensive therapy will likely need surgery during the chronic phase due to aneurysmal enlargement of the aortic dissection.[2,31,32,35,37]

Complicated dissection is associated with at least one of the following: malperfusion syndrome (visceral, renal or lower limb), rupture, uncontrollable hypertension or refractory pain. Patients with acute, complicated Type B aortic dissections are reported to have a greater than 50%[38] likelihood of dying from this disease and as such require emergent surgical treatment.

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[30] Daily PO, Trueblood HW, Stinson EB, Wuerflein RD, Shumway NE: Management of acute aortic dissections. Ann Thorac Surg 1970;10:237-247.
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[37] Neya K, Omoto R, Kyo S, Kimura S, Yokote Y, Takamoto S, Adachi H. Outcome of Stanford Type B acute aortic dissection. Circulation. 1992;86(suppl II):II-1-II-7.
[38] Trimarchi S, Nienaber CA, Rampoldi V, Myrmel T, Suzuki T, Bossone E, Tolva V, Deeb MG, Upchurch GR Jr, Cooper JV, Fang J, Isselbacher EM, Sundt TM 3rd, EagleKA; IRAD Investigators. Role and results of surgery in

Open surgical repair of type B aortic dissection has been reserved for patients presenting with complications such as imminent rupture, expansion of the aorta, extension of dissection, organ or limb malperfusion syndromes.[39,40] Standard surgical technique requires resection of the severely damaged segments of the aorta and replacement with a Dacron graft. This procedure involves a thoracotomy, significant blood loss, aortic clamping, and possibly aortic bypass. The surgical mortality rate has been reported to be as high as 35% and even higher (50%) in patients with acute disease and end organ ischemia or rupture.[38,39,40] Neinaber[29] reported a 20% mortality rate by day 2 and 25% by day 30 for patients with type B dissections who have ischemic leg symptoms, renal failure, visceral ischemia or contained rupture. Suzuki et al[41] reported a 32% in hospital mortality rate for acute, complicated type B dissection patients who required surgery. Trimarchi et al[38] reported a 29.3% hospital mortality rate for patients who required surgical treatment of acute, complicated Type B dissections. Fann et al[42] reported a 39 ± 8% hospital mortality rate for acute, complicated Type B dissection patients. Open thoracic surgeries are ranked among the most complex, invasive and extensive surgical procedures.

Chronic type B dissection is defined as an aortic dissection that is treated greater than 30 days after symptom onset. The natural history for chronic type B dissection is different based on which part of the thoracic aorta is involved, the ascending aorta or the descending aorta. Having a history of Marfan's syndrome, age, greater size of aorta at baseline, persistent hypertension that is not well controlled, and having a patent false lumen are risk factors that predispose these patients to development of aorta-related complications during the chronic phase. Aortic growth rate may be from 10mm to 74mm

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acute type B aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD).Circulation. 2006 Jul 4;114(1 Suppl):I357-64.

[39] Song TK, Donayre CE, Walot I, Kopchok GE, Litwinski RA, Lippmann M, SarkisyanGE, Omari B, White RA. Endograft exclusion of acute and chronic descending thoracic aortic dissections. J Vasc Surg. 2006 Feb;43(2):247-58.

[40] Dake MD, Kato N, Mitchell RS et al. Endovascular stent-graft placement for the treatment of acute aortic dissection. N Engl J Med 1999;340:1546-52.

[41] Suzuki T, Mehta RH, Ince H, Nagai R, Sakomura Y, Weber F, Sumiyoshi T, Bossone E, Trimarchi S, Cooper JV, Smith DE, Isselbacher EM, Eagle KA, Nienaber CA; International Registry of Aortic Dissection. Clinical profiles and outcomes of acute type B aortic dissection in the current era: lessons from the International Registry of Aortic Dissection (IRAD). Circulation. 2003 Sep 9;108 Suppl 1:II312-7.

[42] Fann JI, Smith JA, Miller DC, Mitchell RS, Moore KA, Grunkemeier G, Stinson EB, Oyer PE, Reitz BA, Shumway NE. Surgical management of aortic dissection during a 30-year period. Circulation. 1995 Nov 1;92(9 Suppl):II113-21.

per year,[43] dependent on if the false lumen is patent, if hypertension is controlled, and what the baseline aortic diameter was at diagnosis. The most common causes of morbidity and mortality for patients with chronic type B dissection are aortic rupture, aneurysmal degeneration of the aorta, and malperfusion leading to ischemia.[43]

Treatment of type B aortic dissections includes optimal medical therapy (OMT) for those patients who are stable, open surgical repair for those patients who are symptomatic and have lower surgical risks based on their medical history and presentation, and endovascular repair for symptomatic patients at higher risk for open surgery. Hypertensive and beta-blocker medications are considered foundations of OMT for patients who make the transition from acute to chronic aortic dissection.[44] OMT plays an important role in patients who have chronic distal aortic dissection, yet some patients' aortas continue to enlarge and become aneurysmal.[45,46,47,48] A high incidence of enlargement, with women having a higher risk of enlargement, during the follow-up period has been reported, with a growth rate in the thoracic aorta as great as 4 mm/year.[49] One-third of patients with OMT for uncomplicated acute type B aortic dissection will require surgery for aortic-related complications within 5 years of their dissection event, most often for aneurysmal enlargement of the chronic thoracic aortic dissection.[50] Once the aortic diameter exceeds 55 to 60 mm, the risk of aortic rupture is estimated at 30% per year.[51] Other sequelae, such as the onset of unrelievable pain or progression of the initial dissection including organ malperfusion may necessitate urgent or emergent repair of the

[43] Giugliano G, Spadera L, De Laurentis M, Brevetti G. Acta Cardiol. 2009 Oct;64(5):653-663.
[44] Genoni M, Paul M, Jenni R, Graves K, Seifert B, Turina M. Chronic beta-blocker therapy improves outcome and reduces treatment costs in chronic type B aortic dissection. Eur J Cardiothorac Surg 2001;19:606 –10.
[45] Halstead JC, Meier M, Etz C, et al. The fate of the distal aorta after repair of acute type A aortic dissection. J Thorac Cardiovasc Surg 2007;133:127–35.
[46] Haverich A, Miller DC, Scott WC, et al. Acute and chronic aortic dissections–determinants of long-term outcome for operative survivors. Circulation 1985;72 (3 pt 2):II22–34.
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[48] Glower DD, Fann JI, Speier RH, et al. Comparison of medical and surgical therapy for uncomplicated descending aortic dissection. Circulation 1990;82(5 suppl):IV39–46.
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[51] Fattori R, Cao P, De Rango P, et al. Interdisciplinary expert consensus document on management of type B aortic dissection. J Am Coll Cardiol 2013;61:1661–78.

chronic thoracic aortic dissection.[52,53,54] Surgical options for these patients include open surgical repair (OSR) or thoracic endovascular aortic repair (TEVAR).

Pertaining to OSR for the treatment of patients with chronic type B aortic dissections, the early mortality rate from literature with contemporary data with available endograft technology was 8.0%, with rate of other complications such as early stroke and spinal cord ischemia at 5.5% and 5.7%, respectively.[51] These rates indicate that surgical repair of chronic dissection is usually followed by a non-negligible rate of short-term morbidity and mortality. In the longer-term, patients who are treated by OSR have mortality rates that are in line with TEVAR.[55,56] Reintervention after OSR is uncommon and the false lumen is at a lower risk of rupture due to the aortic resection as shown in a propensity adjusted analysis of OSR and TEVAR as reported by treatment efficacy 3-year freedom rupture or reintervention at rates of 96.7% for OSR vs TEVAR at 87.5%.[56] More detail pertaining to complication rates associated with TEVAR are reported in the sections below.

TEVAR has a documented lower rate of perioperative mortality, shorter hospital stays, and post-operative morbidity and mortality in comparison to open surgical repair for patients treated for chronic type B dissection.[57] In addition, TEVAR is associated with improved long-term aortic mortality and slowing of disease progression.[58] However, patients treated with TEVAR for chronic type B dissection have a higher rate of post-operative

[52] Hata M, Shiono M, Inoue T, et al. Optimal treatment of type B acute aortic dissection: long-term medical follow-up results. Ann Thorac Surg 2003;75:1781– 4.
[53] Gysi J, Schaffner T, Mohacsi P, Aeschbacher B, Althaus U, Carrel T. Early and late outcome of operated and nonoperated acute dissection of the descending aorta. Eur J Cardiothorac Surg 1997;11:1163–70.
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[58] Nienaber CA, Kische S, Rousseau, H, Eggebrecht H, Rehders TC, Kundt G, Glass A, Scheiner D, Czerny M, Kleinfeldt T, Zipfel B, Labrousse L, Fattori R, Ince H. Long-term results of the randomized investigation of the stent grafts in aortic dissection trial. Circ Cardiovasc Interv. 2013 Aug;6(4):407-416.

secondary interventions for aortic dissection pathology than in open repair,[59] with rates for aortic dissection as high as 38-72% at 3 years[60,61,62] and as high as 13-41% for chronic type B dissection.[63,64] The lack of TEVAR durability in treatment of aortic dissection may be attributable to the fragility of the aortic tissues involved in the repair. The necessity for secondary interventions to address continued false lumen perfusion and aneurysm expansion post-TEVAR for aortic dissection may be an expected part of the treatment standard for these patients, yet these secondary interventions are not impacting long-term survival for these patients.[65]

Penetrating Atherosclerotic Ulcer

Penetrating atherosclerotic ulcer (PAU) occurs most often in patients with extensive atherosclerotic disease. PAU is defined by an ulceration of an aortic atherosclerotic plaque penetrating through the internal elastic lamina into the aortic media. PAUs can progress to a localized aneurysm, IMH, or free wall rupture.[66] PAU is associated with an elderly patient population having a history of moderate to severe hypertension, tobacco use, and a heavily lined atherosclerotic aorta. The patients typically are symptomatic on

[59] Nozdrzykowski M, Etz CD, Luehr M, Garbade J, Misfeld M, Borger MA, Mohr FW. Optimal treatment for patients with chronic Stanford type B aortic dissection: endovascularly, surgically or both? Eur J Cardiothorac Surg. 2013 Sep:44(3):e165-174.
[60] Eggebrecht H, Nienaber CA, Neuhauser M, Baumgart D, Kische S, Schmermund A, et al. Endovascular stent-graft placement in aortic dissection: A meta-analysis. Eur Heart J. 2006; 27:489–498.
[61] Schoder M, Czerny M, Cejna M, Rand T, Stadler A, Sodeck GH, et al. Endovascular repair of acute type b aortic dissection: Long-term follow-up of true and false lumen diameter changes. Ann Thorac Surg. 2007; 83:1059–1066.
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[66] Brinster DR. Endovascular repair of the descending thoracic for penetrating atherosclerotic ulcer disease. J Cardiovasc Surg. 2009;24:203-8.

presentation.[67,68] Aggressive management is recommended for PAUs as there is a higher rate of rupture (as high as 38%) associated with this pathology acutely, yet asymptomatic PAUs have lower rates of rupture and disease progression.[69] **Figure 2-1** below shows the management pathway for PAU. As shown, TEVAR is the preferred treatment course in both acute and chronic settings, unless contraindicated.[70]

[67] Cho KR, Stanson AW, Potter DD, Cherry KJ, Schaff HV, Sundt TM. Penetrating atherosclerotic ulcer of the descending thoracic aorta and arch. J Thorac Cardiovasc Surg. 2004;127:1393-1401.
[68] Coady MA, Rizzo JA, Hammond GL, Pierce JG, Kopf GS, Elefteriades JA. Penetrating ulcer of the thoracic aorta. What is it? How do we recognize it? How do we manage it? J Vasc Surg. 1998;27:1006 –16.
[69] Nathan DP, Boonn W, Lai E, et al. Presentation, complications and natural history of penetrating atherosclerotic ulcer disease. J Vasc Surg. 2012;55:10 –5.
[70] Evangelista A, Czerny M, Nienaber C, Schepens M, Rousseau H, Cao P, Moral S, Fattori R. Interdisciplinary expert consensus on management of type B intramural hematoma and penetrating aortic ulcer. Eur J Cardiothorac Surg. 2015;47(2):209-217.

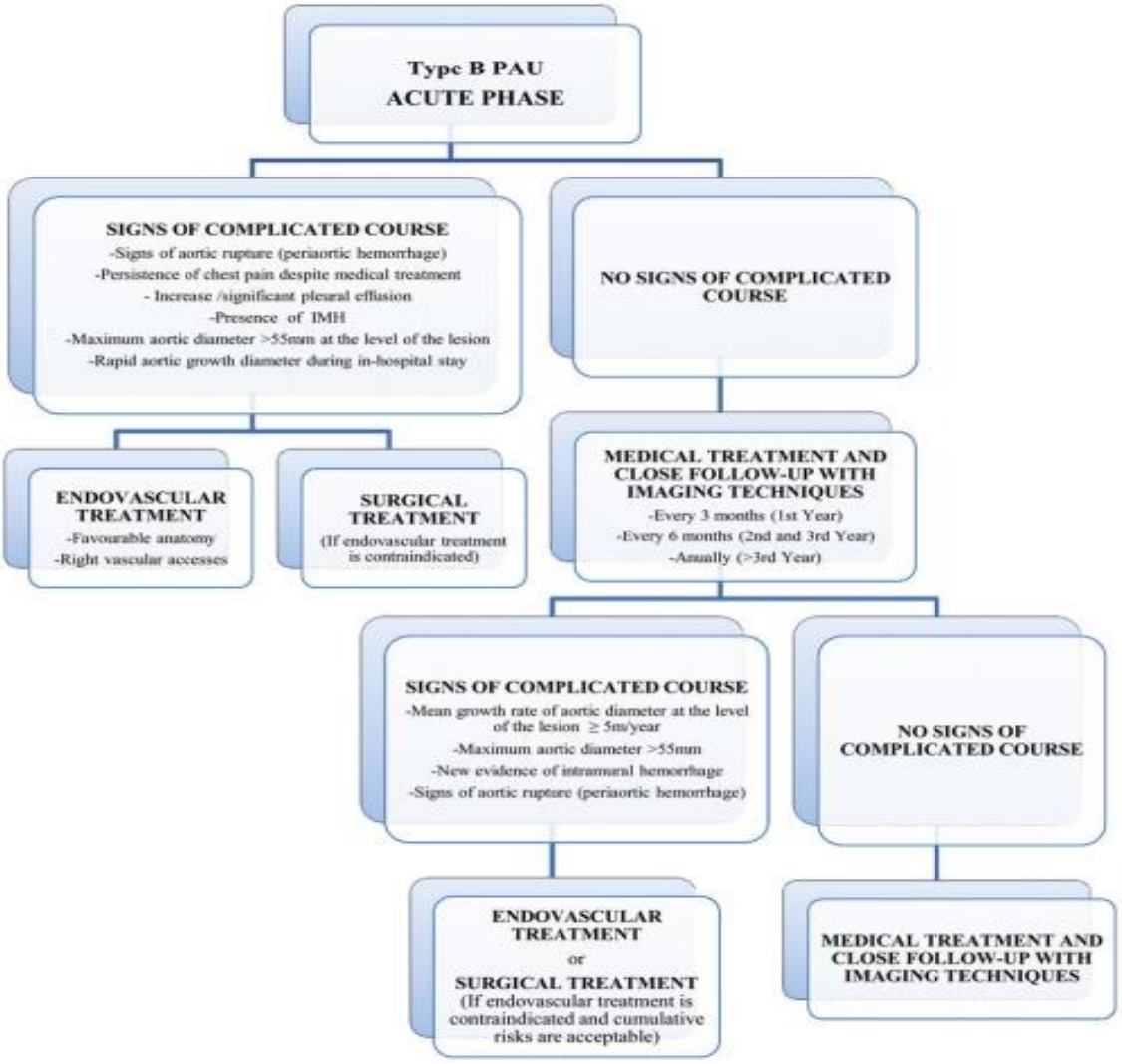

Figure 2-1: Acute and Chronic Management Pathway for PAU[70]

Open surgical repair in an elderly population with comorbidities such as coronary artery disease and chronic obstructive pulmonary disease, carries a high risk of mortality (15%) for patients with PAUs.[67] TEVAR is an acceptable alternative to open surgical repair for PAU, having a lower acute mortality rate than open surgery (7.2% vs 15.9%, respectively)

and a reported CVA rate of 4%.[71] Secondary interventions related to endoleaks or other post-operative aorta-related changes may occur in patients treated for PAU. One article[71] cites a rate as high as 21% of secondary interventions for PAU patients.

While endovascular stent graft treatment has significantly improved outcomes in patients with DTA disease, further evolution and innovation of these devices is necessary as many patients have disease that involves the aortic arch. The stent grafts currently available in the United States for treatment of disease of the DTA require a minimum proximal neck length (the distance from the proximal edge of the aneurysm to the distal origin of the LSA) in order to ensure an adequate seal of the graft to healthy aorta. Approximately 40% of TEVAR patients do not meet this criteria.[72,73] In these cases, consideration needs to be given to whether the patient's left subclavian artery (LSA) provides additional treatment options, whereby covering the origin of the LSA with the fabric portion of a stent graft lengthens the proximal landing zone. When blood flow is excluded from the LSA, patients are at a higher risk of left arm ischemia, spinal cord ischemia, vertebrobasilar ischemia, anterior circulation stroke, and death.[74]

To manage the treatment of these patients, consideration is given whether or not to revascularize the LSA. Revascularization can be performed before TEVAR or after, if symptoms present. The Society for Vascular Surgery's (SVS) published practice guidelines recommend preoperative revascularization in all patients unless an emergent situation prevents the option or local surgical expertise is unavailable.[75] Patients for which preoperative revascularization is strongly recommended include those with:

- Coronary artery bypass graft involving a patent left internal mammary artery

[71] Czerny M, Funovics M, Sodeck G, Dumfarth J, Schoder M, Juraszek A, Dziodzio T, Loewe C, Reineke D, Krahenbuhl E, Grimm M, Ehrlich M. Results after thoracic endovascular aortic repair in penetrating atherosclerotic ulcers. Ann Thorac Surg. 2011;92:562-567.
[72] Cooper DG, Walsh SR, Sadat U, Noorani A, Hayes PD, Boyle JR. Neurological complications after left subclavian artery coverage during thoracic endovascular aortic repair: a systematic review and meta-analysis. J Vasc Surg. 2009 Jun;49(6):1594-601.
[73] Peterson BG, Eskandari MK, Gleason TG, Morasch MD. Utility of left subclavian artery revascularization in association with endoluminal repair of acute and chronic thoracic aortic pathology. J Vasc Surg. 2006; 43:433–439.
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[75] Matsumura JS, Rizvi AZ; Society for Vascular Surgery. Left subclavian artery revascularization: Society for Vascular Surgery Practice Guidelines. J Vasc Surg. 2010 Oct;52(4 Suppl):65S-70S.

- Occlusion or absence of the right vertebral artery
- Left arm arteriovenous shunt
- Prior infrarenal aortic repair with ligation of the lumbar and middle sacral arteries
- Long segment coverage of the descending thoracic aorta affecting critical intercostal arteries
- Hypogastric occlusion
- Discontinuity in the vertebrobasilar collaterals namely the termination of the left vertebral artery at the posterior inferior cerebellar artery

Preoperative revascularization consists of either bypassing or transposing the LSA to the carotid artery. Additionally, the LSA is occluded or ligated in order to prevent potential Type II endoleaks post-TEVAR. However, subclavian revascularization is not without serious risks. Complications of LSA revascularization have been reported to occur in 2.4 to 12.2% of patients. These include stroke, bleeding, injury to the thoracic duct, and left cervical nerves including the phrenic nerve and brachial plexus. Although most nerve damage is temporary, permanent defects can persist in approximately 3% of patients.[74]

Because of the potential complications and the additional surgical procedure, and despite the Society for Vascular Surgery practice guidelines, some physicians decide not to perform LSA revascularization. Often, LSA revascularization is performed when the patient has a dominant left vertebral artery, a previous left internal mammary coronary artery bypass graft (CABG), or an absent distal right vertebral segment. Alternatively, advances in stent graft design provide additional options for preserving patency of the LSA with fenestrated, multi-branched, or the use of chimney grafts.

A well-established procedure and materials for TEVAR provides a foundation for these treatment option advances. All three options require modifications to currently available stent graft systems. The fenestrated device requires the operator to create fenestrations (i.e., holes) in the stent graft (pre-implant) in order to facilitate blood flow to the great vessels within the covered region. These fenestrations are secured with bare-metal or covered stents used as bridging stents. The multi-branch option incorporates axially oriented, covered stent graft cuffs to accommodate the great vessels. These stent graft configurations are custom-made, adding at least six to eight weeks[76] between evaluation and treatment. A hybrid approach combines stent graft cuffs positioned in the

[76] Resch TA, Dias NV, Sobocinski J, Sonesson B, Roeder B, Haulon S. Development of off-the-shelf stent grafts for juxtarenal abdominal aortic aneurysms. Eur J Vasc Endovasc Surg. 2012 Jun;43(6):655-60.

fenestrations to allow for a seal to be established within the branched artery, rather than at the origin, providing more flexibility for patient-specific variations in arch morphology. The primary limitation to the advancement of this option has been in the lack of covered stent graft cuffs sized appropriately for the great vessels.

A modular, off-the-shelf option needs to incorporate elements of all three techniques in order to preserve patency of the LSA and provide a more established treatment option. Valiant Mona LSA provides that unmet need of a singular endovascular procedure for disease encroaching the LSA. The Valiant Mona LSA device provides off-the-shelf, branched, endograft technology to the patient, with the benefits of endovascular technology – namely decreased procedure time, decreased blood loss, and decreased mortality rates.

An Early Feasibility study was conducted in order to provide important information regarding the Valiant Mona LSA Thoracic Stent Graft System in descending thoracic aortic aneurysms and penetrating ulcers including validation of the procedural steps and patient selection, an acute assessment of the safety and performance of the device at 1 month, and collection of imaging from the subjects in order to understand device movements in humans to augment the current use conditions data set.

The device was successfully implanted into nine (9) subjects and continues to function as intended. Data collected from the Early Feasibility study allowed Medtronic to identify patient selection and implantation procedural steps that required further clarification, in particular to exclude grade IV and grade V aortic atheroma anatomies and that manipulations of the stent graft devices and accessory devices should be performed distal to the LSA. In order to further characterize the study device, a traditional Feasibility study for the Valiant Mona LSA Thoracic Stent Graft System is necessary. The Valiant Mona LSA Thoracic Stent Graft System design used during the Early Feasibility study will be used for the Feasibility Study.

The purpose of the Feasibility Study is to characterize the Valiant Mona LSA Thoracic Stent Graft System, in particular to assess the safety and effectiveness of the device acutely and at the 30 day visit in the identified subject population. This study will also evaluate the current instructions for use and may direct changes to the delivery and deployment steps.

Initial clinical data from the Feasibility Study suggest the measures taken to reduce post-procedural neurological events have had a positive impact on the clinical outcomes seen in the subjects enrolled to date. The performance data obtained from the Early Feasibility and

the Feasibility Study to date demonstrates that the Valiant Mona LSA device design is performing as intended.

The positive combined safety and performance indicators reported for subjects enrolled under protocol version 1A led Medtronic to pursue an expansion to the Feasibility Study to gain clinical experience with chronic Type B dissection and to allow for broader investigator experience with the Valiant Mona LSA device. The design elements, procedural implant techniques, and patient selection measures in place were deemed appropriate to expand assessment of the safety and performance outcomes in subjects with chronic Type B dissections. The purpose of the expansion to the Feasibility Study is to characterize the Valiant Mona LSA Thoracic Stent Graft System, in particular to assess the safety and effectiveness of the device acutely and at the 30 day visit, in subjects enrolled with chronic, Type B dissections. The chronic Type B Dissection expansion subjects will be prospectively enrolled in support of a future premarket approval analysis for the Valiant Mona LSA device.

3. INTENDED USE OF THE DEVICE

The Valiant Mona LSA Thoracic Stent Graft System is for the endovascular repair of fusiform/saccular aneurysms, type B chronic dissections, and penetrating ulcers of the descending thoracic aorta (DTA) in patients who require coverage of the left subclavian artery (LSA) presenting with the appropriate anatomy, including:

- Iliac or femoral artery access vessel morphology that is compatible with vascular access techniques, devices, or accessories
- Non-diseased aortic diameter in the range of 25 mm to 42 mm (fusiform/saccular aneurysms and penetrating ulcers) or 28 mm to 44 mm (dissections)
- Non-diseased LSA diameter in the range of 8 mm to 13 mm
- Total effective non-diseased aortic proximal neck length of ≥ 20 mm between the distal end of LCC ostium to the beginning of the disease, including the LSA ostium diameter and non-diseased aortic neck length ≥ 10 mm between the LSA and LCC
- Non-aneursymal aortic distal neck length ≥ 20 mm
- Total effective non-diseased aortic proximal neck length of >0 mm between the distal end of the LSA ostium to the beginning of the disease

4. DESCRIPTION OF THE DEVICE

The Valiant Mona LSA Thoracic Stent Graft System is a modular system intended to maintain perfusion of the LSA when the device is implanted in Zone 2 of the aortic arch for the exclusion of a TAA, PAU, and CTBD. Details regarding the device design are presented in the following sections.

4.1. DEVICE COMPONENTS

The Valiant Mona LSA Thoracic Stent Graft System is comprised of two key components (See **Figure 4-1**):

- The Main Stent Graft (MSG) which is delivered using the Main Stent Graft Delivery System
- The Branch Stent Graft (BSG) which is delivered using the Branch Stent Graft Delivery System

Figure 4-1: Valiant Mona LSA Thoracic Stent Graft System

Note: Graphical representation not to scale.

4.2. MAIN STENT GRAFT SYSTEM

The Main Stent Graft System is comprised of the Main Stent Graft and the Main Delivery System. An overview of the Main Stent Graft System is provided below.

Main Stent Graft

The Main Stent Graft (MSG) is based on the commercial Valiant Stent Graft platform (P100040 approved on April 1, 2011). As shown in **Table 4-2** below, the MSG includes a "cuff" at the proximal section of the stent graft. This cuff is used for mating of the MSG with the Branch Stent Graft (BSG).

The MSG (with the exception of the cuff) is manufactured using monofilament polyester fabric and nitinol stents. The stent graft material, stent material and surface finish are identical to those used on the Valiant Stent Graft. The designs of all stents are also identical to Valiant with the exception of the two most proximal body stents and the stent on the cuff (Mobile External Connector [MEC] stent).[redacted].

The cuff is intended to seal with the BSG which provides for perfusion of the LSA. This cuff is made using HDM polyester fabric which is identical to that used on the commercially available Endurant II stent graft (P100021, approved on April 27, 2012). The design of the cuff[redacted] is the same across all sizes of the MSG. The cuff contains two Platinum Iridium (Pt-Ir) radiopaque marker coils at the top and bottom of the cuff to assist with visualization during deployment and guide placement. These coils are located within a fold of fabric and as such do not directly come in contact with either the BSG or the vessel. An additional Pt-Ir marker is placed immediately distal to the cuff, again to assist with visualization and deployment accuracy. The cuff features a stent at the top, called the MEC Stent.[redacted]

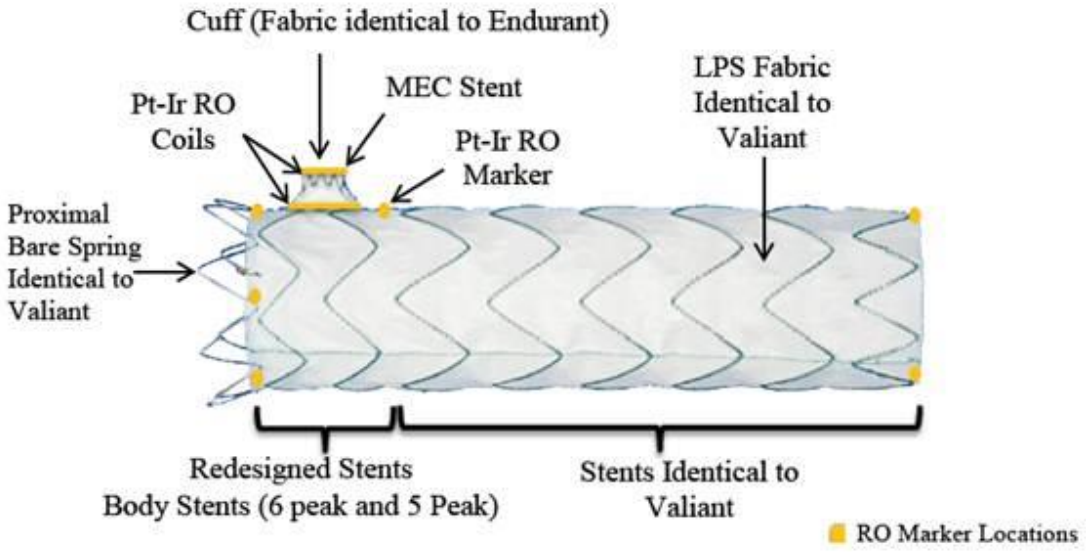

Figure 4-2: The Main Stent Graft

The MSG is available in diameters ranging from 30mm to 46mm with 2mm increments. An overview of the MSG sizes and configurations is provided in **Table 4-3**: Sizes and Configuration of the MSG and BSG**3**.

Table 4-1: MSG Materials

below lists the materials used on the MSG including the cuff.

Table 4-1: MSG Materials

Component	Material	Comments
Stents	Nitinol	Same as Valiant
Fabric, Main Body	Monofilament Polyester	Same as Valiant
Fabric, cuff	Multifilament (HDM) Polyester	Same as Endurant II
Suture	Polyester	Same as Valiant
Radiopaque markers (Figure 8 and Button)	Platinum-Iridium	Same as Valiant
Radiopaque markers (coil)	Platinum-Iridium	Same as Endurant II

Main Delivery System

The Main Delivery System (MDS) will be used to deploy the MSG. The MDS design is based on the commercially available Valiant Captivia Delivery System. The modifications made to the Valiant Captivia Delivery System include the addition of proximal and distal end components and features to provide pre-cannulation of the MSG cuff with the LSA guidewire.

This delivery system platform provides a mechanical advantage during deployment coupled with a tip capture mechanism for deployment accuracy. The modifications to the current Valiant Captivia Delivery System include the following:

- a modified 4-groove Tapered Tip assembly
- [redacted]
- a modified End Seal Y-adapter assembly
- a modified External Slider assembly
- a modified Screw Gear half
- a new Second Lumen assembly

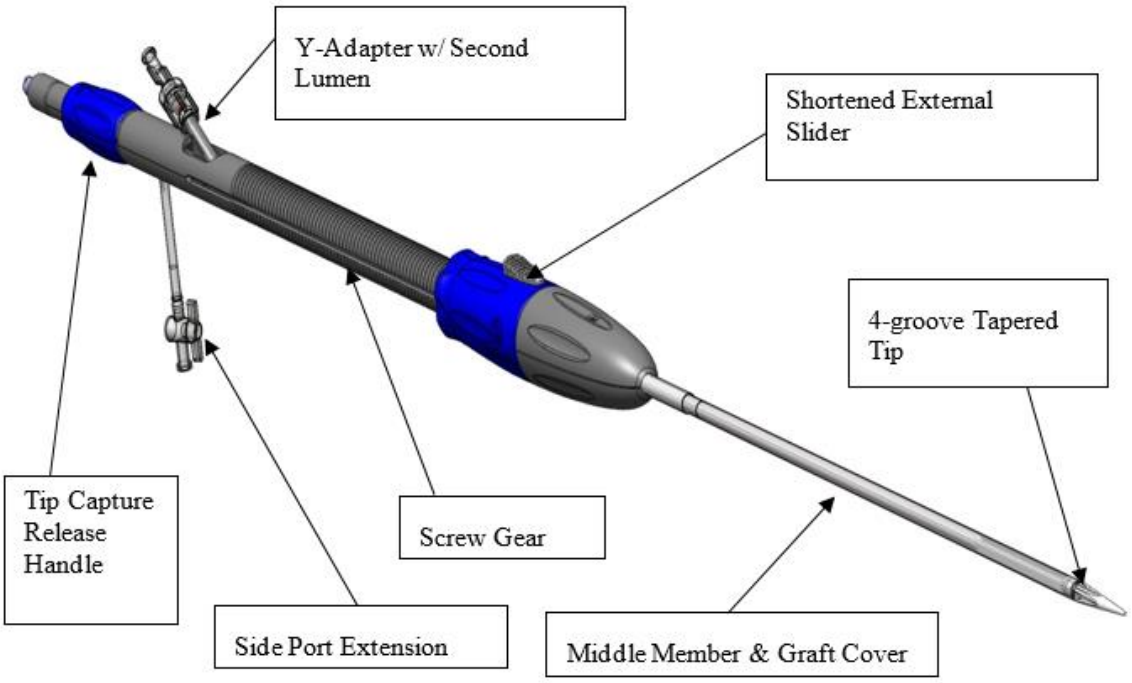

Figure 4-3: Main Delivery System (Figure not to Scale)

4.3. BRANCH STENT GRAFT SYSTEM

Branch Stent Graft

The primary function of the Branch Stent Graft (BSG) is to mate with the MSG cuff and perfuse the Left Subclavian Artery (LSA). The BSG is offered in 10mm, 12mm and 14mm diameters. All three size offerings have a 40mm length and mate with the single 10mm diameter cuff opening on the MSG. To maximize the separation resistance of the junction between the MSG and the BSG, a flared section was added to the proximal end of the 10mm and 12mm BSG designs. This flared section is not required on the 14mm design, since the larger diameter forms a natural flare on either side of the cuff opening.

The BSG is composed of a multifilament polyester graft fabric and nitinol stents. The stent material and surface finish are identical to those used on the commercial Valiant Stent Graft. The multifilament polyester material is similar to that used on the commercially available Endurant Stent Graft, [redacted]

[redacted] The sutures on the BSG are composed of Ultra High Molecular Weight Polyethylene (UHMWPE) which is the same base material used on commercial Endurant II Stent Grafts for attaching the suprarenal stents to the proximal edge of the graft. The BSG suture has a smaller diameter than the Endurant II suture.

The body stent of the BSG is a helical design connected to end stents with nitinol crimps. The flared stent on the 10mm and 12mm is a standalone stent and is not connected to the helical or end stent. [redacted]

Spherical Platinum Iridium radiopaque markers are located on both the proximal and distal ends of the BSG.

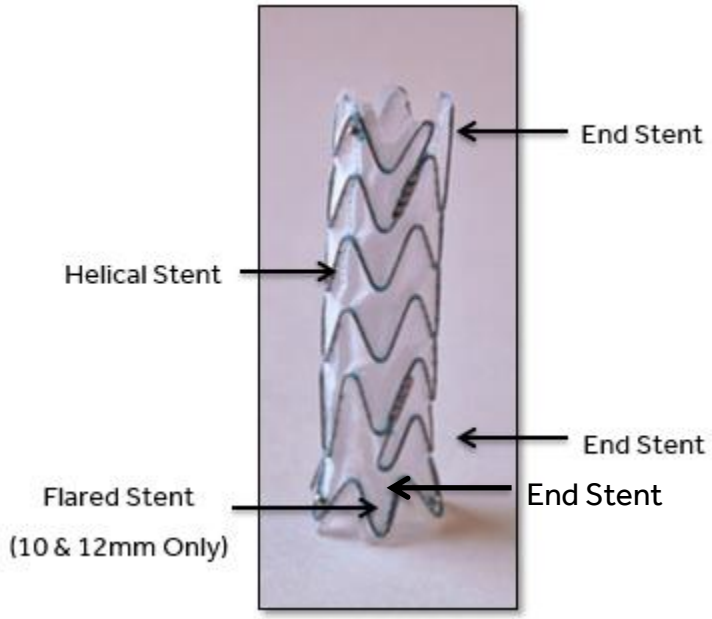

Figure 4-4: Branch Stent Graft

Table 4-2 below lists the materials used on the BSG.

Table 4-2: BSG Materials

Component	Material	Comments
Stents	Nitinol	Same as Valiant
Fabric	Polyester	Similar to Endurant II
Radiopaque Markers	Platinum Iridium	Same as Valiant
Suture	UHMWPE	Similar to Endurant II

Branch Delivery System

The Branch Delivery System (BDS) will be used for the deployment of the BSG. The BDS design is based on both the commercially available Endurant II Limb and Valiant Captivia Delivery Systems. The distal end of the BDS is a modification of the 14Fr Endurant II Limb Delivery System while the proximal end of the delivery system is leveraged from Valiant Captivia Closed Web Delivery System. Additionally, the Graft Cover, Tapered Tip assembly and Middle Member have been modified for improved kink resistance in the new use conditions associated with navigating into the LSA. **Figure 4-5** below presents the Branch Delivery System.

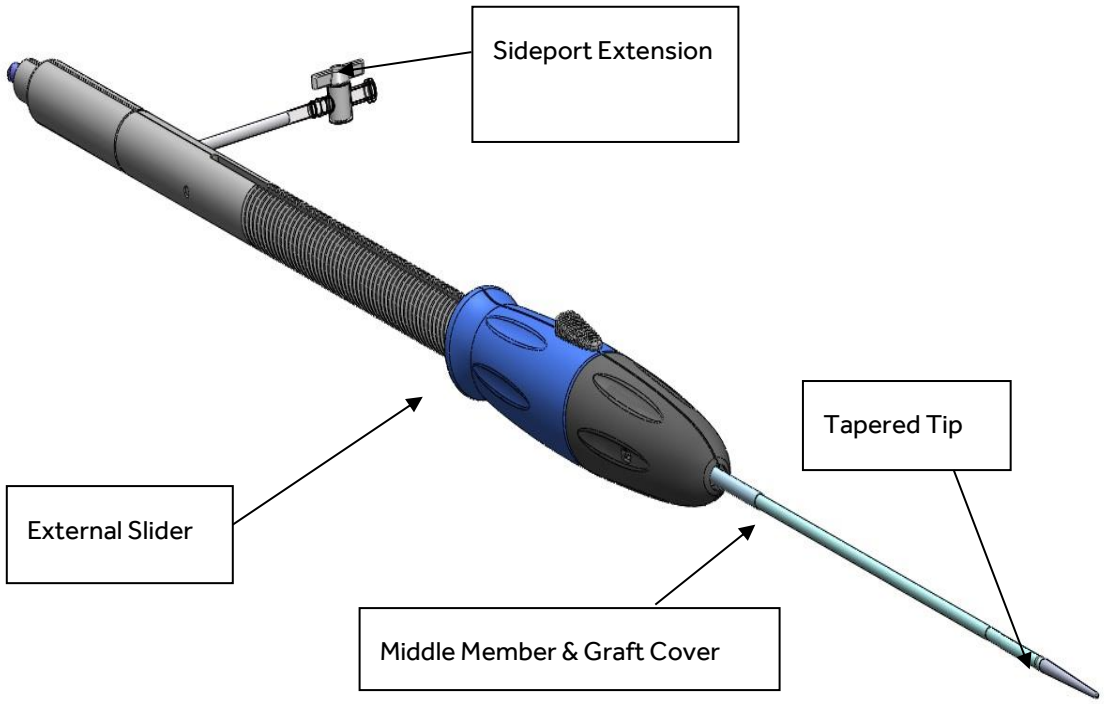

Figure 4-5: Branch Delivery System (Figure not to Scale)

4.4. DEVICE SIZES AND CONFIGURATIONS

Table 4-3 presents the sizes and configurations of the MSG and the BSG Systems. No tapered configurations will be offered for the MSG or the main body portion of the BSG. All MSG sizes have the same MSG cuff diameter opening of 10mm.

Table 4-3: Sizes and Configuration of the MSG and BSG

Component	Delivery System (Fr)	Proximal x Distal Diameter (mm)	Covered Length (mm)	Native Vessel Inner Diameter (mm)	
				Aneurysm/ Penetrating Ulcer	Dissection
Main Stent Graft	24	30x30	150	25,26,27	28
	24	32x32	150	27,28,29	29, 30
	24	34x34	157	29,30,31	31, 32
	24	36x36	158	31,32	33, 34
	24	38x38	159	33,34	35, 36
	24	40x40	161	35,36	37, 38
	25	42x42	168	37,38	39, 40
	25	44x44	170	39,40	40, 41, 42
	25	46x46	172	41,42	42, 43, 44
Branch Stent Graft	15	10x10	40	8,9	
	15	12x12	40	10,11	
	15	14x14	40	12,13	

5. STUDY OBJECTIVES

5.1 STUDY PURPOSE

The purpose of the clinical investigation is to assess the feasibility of the Valiant Mona LSA Thoracic Stent Graft System to repair fusiform/saccular aneurysms, penetrating ulcers and chronic type B dissections of the DTA in patients who require coverage of the LSA, including an assessment of the safety and effectiveness of the device acutely and at the 30 day visit in the identified subject population. Procedural information will be collected in order to enhance the current instructions for use and delivery and deployment steps.

The chronic Type B Dissection expansion subjects will be prospectively enrolled in support of a future premarket approval analysis for the Valiant Mona LSA device.

Patients diagnosed with an aneurysmal descending thoracic aorta, penetrating ulcer, or chronic type B dissection who meet the eligibility criteria for the study may be enrolled (see Section 9.1 - Eligibility Criteria). Additionally, these patients must be candidates for revascularization of the LSA and anatomically appropriate for the device.

5.2 SCOPE AND DURATION OF THE CLINICAL STUDY

Study enrollment started in the United States in 2015. Up to ten (10) investigational sites may participate. The enrollment period is estimated to be 20 months. To ensure adequate disease state representation in the overall study dataset, a minimum of approximately 25% of the subjects will be enrolled for the treatment of aneurysms or penetrating ulcers and a minimum of approximately 25% of the subjects will be enrolled for the treatment of chronic Type B dissections.

Data from the 44 subjects who undergo treatment with the Valiant Mona LSA Thoracic Stent Graft System in this study will be analyzed and summarized in the Annual Progress Reports (APR) for FDA. Data collected in this study may be used to submit original marketing applications for approval to commercially distribute the device system.

To permit collection of long-term safety and effectiveness data on the stent graft system, subjects will be followed for a total of 5 years under this same clinical protocol. After the scheduled 12-month study visit, patients will continue to be evaluated on an annual basis for up to 5 years post implantation. When all enrolled subjects have been followed for 5 years post index procedure, or have exited, the study will be closed.

6. CLINICAL STUDY DESIGN

This study is a prospective, single-arm, non-randomized, multicenter, pre-market clinical study evaluating subjects implanted with the Valiant Mona LSA Thoracic Stent Graft System for the treatment of aneurysms, type B chronic dissections, and penetrating ulcers of the descending thoracic aorta who are candidates for revascularization of the left subclavian artery. All analyses will be descriptive in nature and no statistical comparisons are planned. This study is not a hypothesis driven study; no hypotheses testing will be carried out.

There is no sample size calculation since this study is not a hypothesis driven study; however, the number of enrolled subjects is pre-specified. This study will enroll up to 44 subjects.

7. METHODS AND ANALYSES

7.1 DESCRIPTION OF STUDY OBSERVATIONS

7.1.1 Primary Safety Observation

The following data points will be collected for reporting. The initial reporting period will be all occurrences within 1 month (Day 0 – Day 30) from the index procedure. The data will consist of:

- Aorta-Related Mortality
- Stroke
- Paraplegia
- Left Arm/Hand Ischemia

7.1.2 Primary Effectiveness Observation

The primary effectiveness observation is treatment success (defined below) and will be captured within the initial reporting period of 1 month from the index procedure.

Treatment success is defined as:

Technical success, which is the successful delivery and deployment of the stent graft (deployment of the Valiant Mona LSA Thoracic Stent Graft System in the planned location with no unintentional coverage of other vessels, assessed intra-operatively, and the removal of the delivery system) and successful exclusion of the aneurysm/penetrating ulcer or primary entry tear while maintaining patency of the MSG and BSG at 30 day visit.

7.1.3 Additional Observations

The following additional observations will be evaluated through the 30 day visit and at each follow up visit.

- Major adverse events (MAEs) rates within 30 days of the initial or secondary procedures, including:
  - All-Cause Mortality
  - Myocardial Infarction
  - Paraplegia
  - Renal Failure
  - Stroke
  - Left Arm/Hand Ischemia
- Secondary endovascular procedures