CLINICAL PROTOCOL
CP-0015 Rev 01

The COMPLEX AAA Study

Prospective, multicenter, non-randomized study with consecutive, eligible subject enrollment at each site, for the evaluation of the ChEVAS System for Endovascular Repair of Paravisceral, Juxtarenal, and Pararenal Abdominal Aortic Aneurysms.

THE COMPLEX AAA STUDY

Prospective, multicenter, non-randomized study with consecutive, eligible subject enrollment at each site, for the evaluation of the ChEVAS System for Endovascular Repair of Paravisceral, Juxtarenal, and Pararenal Abdominal Aortic Aneurysms.

Protocol Number: CP-0015

National Clinical Trial (NCT) Identified Number: NCT04252573

National Principal Investigator: TBD

Prospective, multicenter, non-randomized study with consecutive, eligible subject enrollment at each site, for the evaluation of the ChEVAS System for Endovascular Repair of Paravisceral, Juxtarenal, and Pararenal Abdominal Aortic Aneurysms.

Revision Number: 01
19August 2019

Sponsor: Endologix, Inc.
2 Musick
Irvine, CA 92618
USA

Sponsor Signature/Date:

[redacted]

Summary of Changes from Previous Revision: *N/A for revision 01*

Revision	Date	Affected Section(s)	Summary of Revisions Made	Rationale

TABLE OF CONTENTS

1 STATEMENT OF COMPLIANCE 9
1 PROTOCOL SUMMARY 9
1.1 Synopsis 9
1.2 Schema 11
1.3 Schedule of Activities (SoA) 12
2 INTRODUCTION 13
2.1 Study Rationale 13
2.2 Background 13
2.2.1 Abdominal Aortic Aneurysms 13
2.2.2 Complex AAA 14
2.3 Current Treatment Options for Complex AAA Repair 15
2.3.1 Aneurysm Surveillance 15
2.3.2 Open Surgical Repair for Complex AAA 15
2.3.3 Endovascular Treatment Options for Complex AAA 16
2.3.3.1 Chimney Endovascular Aneurysm Repair 17
2.3.3.1.1 ChEVAR Limitations 18
2.3.3.2 Fenestrated Endovascular Aneurysm Repair 19
2.3.3.2.1 Custom fEVAR 19
2.3.3.2.2 Off the Shelf fEVAR 20
2.3.3.3 Physician Modified Endovascular Stent Grafts (PMESG) 23
2.3.3.4 Off-Label Use of EVAR Devices 24
2.3.3.5 EndoAnchors 24
2.3.4 ChEVAS Overview 25
2.3.4.1 Current Clinical Experience
27
2.4 Risk/Benefit Assessment 31
2.4.1 Risks 31
2.4.2 Benefits 31
3 OBJECTIVES AND ENDPOINTS 33
3.1 1-Month Primary Endpoint 33
3.2 1-Year Primary Endpoint 34
3.3 Additional Measurements 36
3.3.1 Demographics 36
3.3.2 Medical History 36
3.3.3 Procedural and In-Hospital Evaluations 37
3.3.4 Outcomes 37
4 STUDY DESIGN 38
4.1 Overall Design 38
4.2 End of Study Definition 40
5 STUDY POPULATION 40
5.1 Inclusion Criteria 40
5.2 Exclusion Criteria 41

5.3 Screen Failures 41
6 STUDY INTERVENTION 42
6.1 ChEVAS System Overview 42
6.1.1 ChEVAS System Description 42
6.2 Nellix System 43
6.2.1 Nellix 3.5 Delivery System 44
6.2.2 Nellix Polymer (Formulation 5.5) 46
6.2.3 Nellix 3.5 Accessory Kit 47
6.2.4 Nellix Polymer Dispenser 48
6.3 Ovation iX Iliac Stent Grafts 48
6.4 Verta Self-Expanding Stent Graft System 49
6.5 Adjunctive Stents 51
6.6 Preparation/Handling/Storage/Accountability 51
6.6.1 Acquisition and accountability 51
6.6.2 Product Storage and Stability 51
7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL 52
7.1 Discontinuation of Study Intervention 52
7.2 Participant Discontinuation/Withdrawal from the Study 52
7.3 Lost to Follow-Up 52
8 STUDY ASSESSMENTS AND PROCEDURES 53
8.1 Screening 53
8.2 Case Review Board (CRB) 53
8.3 Schedule of Activities 53
8.4 Safety and Other Assessments 54
8.5 Adverse Events and Serious Adverse Events 55
8.5.1 Definition of Adverse Events (AE) 55
8.5.2 Definition of Serious Adverse Events (SAE) 56
8.5.3 Severity of Event 56
8.5.4 Classification of an Adverse Event 57
8.5.5 Relationship to Study INTERVENTION 57
8.5.6 Expectedness 58
8.5.7 Time Period and Frequency for Event Assessment and Follow-Up 59
8.5.8 Adverse Event Reporting 59
8.5.9 Serious Adverse Event Reporting 59
8.5.10 Major Adverse events 60
8.5.11 Additional Adverse Event Definitions 60
8.6 Unanticipated Adverse Device Effects 61
8.6.1 Definition of Unanticipated Adverse Device Effects (UADEs) 61
8.6.2 Unanticipated Adverse Device Effect Reporting 62
8.6.3 Reporting Unanticipated Problems to Participants 62
9 STATISTICAL CONSIDERATIONS 62
9.1 Statistical Hypotheses 62
9.2 Sample Size Determination 63
9.3 Populations for Analyses 63

9.4 Statistical Analyses 63
9.4.1 General Approach 63
9.4.2 Analysis of the Primary Endpoint(s) 64
9.4.3 Analysis of the Secondary Endpoint(s) 64
9.4.4 Safety Analyses 64
9.4.5 Baseline Descriptive Statistics 64
9.4.6 Planned Interim Analyses 64
9.4.7 Sub-Group Analyses 64
9.4.8 Tabulation of Individual participant Data 65
9.4.9 Exploratory Analyses 65
10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS 65
10.1 Regulatory, Ethical, and Study Oversight Considerations 65
10.1.1 Informed Consent Process 65
10.1.1.1 Consent/assent and Other Informational Documents Provided to participants 65
10.1.1.2 Consent Procedures and Documentation 65
10.1.2 Study Discontinuation and Closure 66
10.1.3 Confidentiality and Privacy 67
10.1.4 Key Roles and Study Governance 68
10.1.5 Safety Oversight 68
10.1.6 Clinical Monitoring 69
10.1.7 Quality Assurance and Quality Control 70
10.1.8 Data Handling and Record Keeping 70
10.1.8.1 Data Collection and Management Responsibilities 70
10.1.8.2 Study Records Retention 72
10.1.9 Protocol Deviations 72
10.1.10 Conflict of Interest Policy 72
10.2 Abbreviations 72
11 REFERENCES 74
12 BIBLIOGRAPHY 74

LIST OF TABLES

TABLE 1 : SCHEDULE OF ACTIVITIES (SOA) 12
TABLE 2: STUDY CHARACTERISTICS OF ARTICLES REPORTING ON CHEVAS FOR THE TREATMENT OF COMPLEX AAA 28
TABLE 3: PERFORMANCE AND SAFETY OUTCOMES FOR CHEVAS IN THE TREATMENT OF COMPLEX AAA FROM THE LITERATURE 29
TABLE 4 : VISIT WINDOW SCHEDULE 54

LIST OF FIGURES

FIGURE 1: CLASSIFICATION OF COMPLEX ABDOMINAL AORTIC ANEURYSMS BASED ON RELATIONSHIP TO RENAL AND SUPERIOR MESENTERIC ARTERIES. 15
FIGURE 2: CHIMNEY ENDOVASCULAR AORTIC REPAIR FOR COMPLEX AAA....17
FIGURE 3: COOK ZENITH FENESTRATED AAA ENDOVASCULAR GRAFT 19
FIGURE 4: VENTANA FENESTRATED SYSTEM....21
FIGURE 5: COOK ZENITH P-BRANCH....22
FIGURE 6: PHYSICIAN MODIFIED ENDOVASCULAR STENT GRAFT FOR TREATMENT OF COMPLEX AAA....24
FIGURE 7: NELLIX SYSTEM WITH BRANCH STENTS IN A 3-VESSEL REPAIR 26
FIGURE 8: NELLIX SYSTEM....42
FIGURE 9: CHEVAS SYSTEM WITH BRANCH STENTS IN A 3-VESSEL REPAIR....43
FIGURE 10: NELLIX 3.5 DELIVERY CATHETER....45
FIGURE 11: NELLIX STENT SHOWN AFTER EXPANSION 46
FIGURE 12: ENDOBAG 46
FIGURE 13: POLYMER CARTRIDGE....46
FIGURE 14: CONSOLE 47
FIGURE 15: ACCESSORIES 48
FIGURE 16: REUSABLE DISPENSER (LEFT) AND DISPOSABLE DISPENSER (RIGHT) 48
FIGURE 17: OVATION IX ILIAC LIMB (LEFT) AND EXTENSION (RIGHT) 49
FIGURE 18: OVATION IX ILIAC STENT GRAFT DELIVERY CATHETER....49
FIGURE 19: VERTA SELF-EXPANDING BRANCH STENT GRAFT....50
FIGURE 20: VERTA SELF-EXPANDING BRANCH STENT GRAFT DELIVERY SYSTEM 50

1 STATEMENT OF COMPLIANCE

This trial will be carried out in accordance with International Conference on Harmonization Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (21 CFR Part 50, 54, 56, and 812)
- ISO 14155:2011 Clinical investigation of medical devices for human subjects – Good clinical practice
- Additional national and local Regulations as required for study compliance

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) or Ethics Committee (EC) for review and approval. At a minimum, IRB or EC Approval of the protocol and the informed consent form must be obtained before any participant is enrolled. All amendments to the protocol will require review and approval by the IRB or EC. In addition, all changes to the informed consent form will be IRB or EC approved. The IRB and/or EC will determine whether existing participants will require re-consenting of the revised informed consent form, unless specified by Sponsor.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	The COMPLEX AAA Study
Study Description:	Prospective, multicenter, non-randomized study with consecutive, eligible subject enrollment at each site, for the evaluation of the ChEVAS System for Endovascular Repair of Paravisceral, Juxtarenal, and Pararenal Abdominal Aortic Aneurysms. The total enrollment will be 120 subjects, and the total number of sites will be up to 50.
Objectives:	To study the safety and effectiveness of the ChEVAS System for Endovascular Repair of Paravisceral, Juxtarenal, and Pararenal Abdominal Aortic Aneurysms.
Endpoints:	Primary 1-month Endpoint: Technical success and the absence of severe bowel ischemia, permanent paraplegia/paraparesis, renal failure, disabling stroke, abdominal aortic aneurysm rupture, and aneurysm-related mortality within 30 days of the index procedure. Primary 1-year Endpoint: Freedom from abdominal aortic aneurysm rupture and aneurysm-related mortality up until 1 year (day 365), freedom from imaging-related findings in the 1-year window (Type I or III endoleak, migration > 10 mm, AAA sac expansion > 5 mm, and occlusion within the ChEVAS System not seen at the index procedure), and open conversions and other major device-related interventions through day 365.
Study Population:	Patients diagnosed with an abdominal aortic or aortoiliac aneurysm and an infra-renal neck <10mm (including 0mm), with at least one, and a maximum of three, required chimney stent graft deployment(s) who are considered candidates for endovascular repair using the ChEVAS System and who meet the study eligibility criteria for the ChEVAS study may be screened for enrollment in the study.

Description of Sites/Facilities Enrolling Participants:	Physicians (vascular surgeons or interventional cardiologists/radiologists as part of a multi-specialty team with vascular surgeons) with well-established experience in complex endovascular aneurysm repair techniques using upper extremity access (e.g. ≥5 cases in the prior year) may participate. In those cases where the investigator is an interventionalist, a vascular surgeon must be immediately available during the procedure to perform any necessary surgical intervention. Up to 50 sites will be activated for participation in the trial, with data from up to 15 of the 50 sites being outside the USA, in geographies such at Europe and Asia.
Description of Study Intervention:	The ChEVAS System consists of the Nellix® System (to treat juxtarenal, pararenal, and/or paravisceral aneurysms) used in conjunction with the Verta™ Self-Expanding Branch Stent Graft System (to maintain renal/visceral blood flow) and Ovation® iX iliac limbs/extensions, if needed (to ensure adequate distal seal zone). The ChEVAS System is intended to provide a sealing zone from the proximal extent of the device (healthy aortic neck) throughout the aneurysm and to the distal aspect of the device implanted into the iliac arteries. The proximal end of target landing zone is below the celiac for SMA and bilateral renal artery chimneys, below the SMA for bilateral renal artery chimneys, and below the proximal renal artery for distal renal artery chimney.
Study Duration:	The study enrollment is projected to last from 18 to 24 months, with a primary endpoint at 1 year of follow-up. The total follow-up requirement will be 5 years. Therefore, the primary endpoint will be ready for analysis roughly 30 to 36 months after trial initiation, with the final subject exiting the trial 96 months after enrollment began.
Participant Duration:	Subjects will be followed procedurally to discharge, at 30 days, six months, one year and annually thereafter to five years (total follow-up commitment).

1.2 SCHEMA

A schema is provided below, with further detail provided in Section 8.

Screening (Site)	•Obtain informed consent. •Site screens potential participants by inclusion and exclusion criteria. •Qualified CTA submitted to the Core Lab.
Screening (Core Lab)	•Core Lab reviews the CTA for anatomical inclusion/exclusion criteria conformity. If the subject does not pass this step the subject is dropped from further consideration. •If the subject passes Core Lab, the subject is referred to the Case Review Board (CRB) for further evaluation.
Screening (CRB)	•The Case Review Board (CRB) reviews case for overall study suitability. The CRB may also make procedural recomendations to the Site. •If the CRB recommends the subject for the study, the subject is approved for implantation. Baseline and Medical History data are entered by the site.
Enrollment	•The subject is enrolled into the study upon the first attempt to insert one of the ChEVAS System catheters into the patient. •The subject is treated with the ChEVAS System. •Procedural data are collected.
Discharge	•Ward stay information collected. •Vitals and creatinine lab results collected. •Medications and Adverse Event records.
1 Month, 6 Months, Annually	•CTA and X-rays are submitted to Core Lab. •Vitals and creatinine lab results collected. •Medications and Adverse Event records.

1.3 SCHEDULE OF ACTIVITIES (SOA)

A schedule of activities is provided in Table 1 below, with further detail provided in Section 8.

TABLE 1 : SCHEDULE OF ACTIVITIES (SOA)

Procedures	Screening	Enrollment Day 0	Discharge Day 0 till discharge	30-Day Visit Day 30 +/- 14 days	6-Month Visit Day 180 +/-30 days	1-Year Visit Day 365 +/-60 days	2-Year Visit Day 730 +/-90 days	3-Year Visit Day 1095 +/-90 days	4-Year Visit Day 1460 +/-90 days	5-Year Visit Day 1825 +/-90 days
Informed consent	X									
Demographics	X									
Medical history	X									
Device Implantation		X								
Vitals (including height and weight)	X	X		X	X	X	X	X	X	X
Serum creatinine	X			X	X	X	X	X	X	X
Serum Pregnancy Test [a]	X									
CTA[b]	X			X	X	X	X	X	X	X
X-ray[c]				X		X		X		X
Complete Case Report Forms (CRFs)/Data collection	X	X	X	X	X	X	X	X	X	X
Adverse event review and evaluation		X	X	X	X	X	X	X	X	X

a: Only for women of childbearing potential
b: For follow-up (not screening), a non-contrast CT and duplex ultrasound may be done in place of the CTA, if the subject has renal insufficiency.
c: 2-view abdominal (left and right oblique)

2 INTRODUCTION

2.1 STUDY RATIONALE

There is a major therapeutic gap in the contemporary treatment of complex abdominal aortic aneurysm (AAA), in which the aneurysm is located in proximity to the renal or superior mesenteric artery. Current surgical and endovascular treatment options for complex AAA are associated with patient applicability limitations and adverse outcomes. In order to bridge this therapeutic gap, it is proposed that Chimney Endovascular Aneurysm Sealing (ChEVAS) using the Nellix endoprosthesis with covered branch stent grafts may offer a potential treatment solution in this challenging patient population. Clinical experience with ChEVAS for complex AAA to date is limited and involved heterogenous study designs and patient populations. Therefore, there is a distinct need for clinical trial data with ChEVAS for complex AAA that are derived from a prospective clinical trial in which patient characteristics and study methodology are well defined. The purpose of this study will be to assess the safety and effectiveness of ChEVAS in patients with complex AAA.

2.2 BACKGROUND

2.2.1 ABDOMINAL AORTIC ANEURYSMS

Abdominal Aortic Aneurysms (AAA) are defined as focal dilatations of the abdominal aorta causing a diameter increase to more than 1.5x the normal aortic diameter.[1] The incidence of Abdominal Aortic Aneurysms in individuals older than 65 years of age are observed more in men than in women, with an estimate range between 1.7% to 4.5% in men[2] vs. 0.5% to 1.3% in women[3]. Alternative studies reported 2.4:1 male-to-female ratio in one Norwegian study[4] and 4:1 in a population-based study of 3 million individuals in the United States.[5] The prevalence of AAA also varies by ethnicity. A study of approximately 19,000 men screened for AAA found an incidence of 4.69% in Caucasians, 3.9% in those of Afro-Caribbean descent, and 0.45% in Asians.[6] The lower prevalence in Asian vs. Caucasian men was statistically significant (P<.0001).

Abdominal Aortic Aneurysms are treated to prevent rupture and death. Rarely, the thrombus or atheromatous debris within the aneurysm sac may dislodge and embolize to the lower extremity or pelvis and in these cases even small aneurysms should be repaired. Ruptured AAA account for approximately 6,000 deaths annually in England and Wales and were responsible for 1 in 50 deaths in males over 65 years of age.[7] The most recent reported mortality data from the U.S. Department of Health and Human Services lists 9,758 deaths from aortic aneurysms in 2016, equating to a rate of 3.0/100,000 population (all ages).[8] While aortic aneurysms are not segregated as an independent disease class in the National Vital Statistics Report and are grouped with aortic dissection, they accounted for 7.1 deaths per 100,000 population in individuals aged 65-74 years, rising to 18.3/100,000 in those between the ages of 75 and 84 and 40.1/100,000 for those aged 85 and above. These figures may underestimate the actual mortality rates since many deaths resulting from ruptured aneurysms remain undiagnosed and undocumented, with deaths occurring outside the hospital. Some researchers have reported that the overall lethality associated with rupture of AAA may approach 80% or greater, including those deaths that occur before a definitive diagnosis has been made.[9]

Prior to the mid-20th century, however, no definitive treatment was available for AAA.[10] Attempts to treat aneurysms with cellophane wrapping and other modalities short of complete exclusion of the diseased aorta from the circulation were often followed by delayed rupture and death.[11] Open surgical AAA repair awaited

the development of fabric grafts in the early 1950s[12], but perioperative morbidity and mortality remained high due to the markedly invasive nature of the operations and the often medically-compromised nature of the patient population.[13] It was not until the final decade of the last century that minimally invasive AAA treatment became available. Volodos and Parodi separately demonstrated the feasibility of trans-femoral endograft repair.[14,15,16] The first aortic endografts were commercialized shortly thereafter, first in Europe and subsequently in the United States.[17,18,19] Within a decade of commercialization, endovascular aneurysm repair (EVAR) supplanted open surgical repair as the most common method to treat patients with AAA and, by 2010, almost three-quarters of AAA were treated with EVAR.[20]

While EVAR has resulted in a significant reduction in perioperative morbidity and mortality,[21] long-term durability has remained problematic.[22,23] Failure to reliably seal the aneurysm sac from pressurized arterial circulation has resulted in high rate of complications including continued aneurysm expansion, sac rupture and death.[24,25,26,27] Close follow-up with regular imaging studies such as duplex ultrasonography, plain x-rays, and computed tomography are recommended to monitor the adequacy of the repair and guide secondary interventions to treat graft migration and endoleaks before complications arose. Still, late complications, at least in part, nullify the early benefit of EVAR over open repair such that the overall mortality rate of the two techniques is not significantly different.[28]

2.2.2 COMPLEX AAA

Hostile aneurysm anatomy remains a major obstacle in the endovascular treatment of AAA. Up to 50% of patients that are considered for EVAR are deemed unsuitable due to challenging aortoiliac anatomy such as short and complex proximal aortic neck seal zones and narrow access vessels.[29,30,31,32,33,34,35] In order to successfully exclude an AAA from the circulation, the endograft must seal at the aortic neck and iliac arteries to prevent blood from entering and repressurizing the sac. Aortic morphology is a major determinant not only in EVAR eligibility, but also in long-term outcomes following treatment.[36,37]

The complexity of AAA is commonly characterized based on location and involvement with visceral vessels (**Figure 1**). Infrarenal AAA generally involves the infrarenal aorta and may involve the aortoiliac vasculature. For the purposes of this document, the term “complex AAA” includes aneurysms that extend up to the level of but does not involve the renal arteries (juxtarenal aortic aneurysm, JAA), aneurysms that involve the renal arteries (pararenal aortic aneurysm, PAA), and aneurysms that involve the superior mesenteric artery (paravisceral aortic aneurysm).

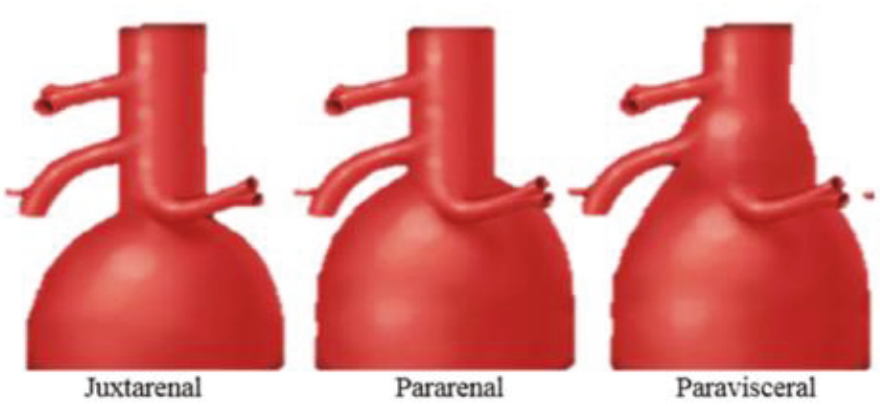

FIGURE 1: CLASSIFICATION OF COMPLEX ABDOMINAL AORTIC ANEURYSMS BASED ON RELATIONSHIP TO RENAL AND SUPERIOR MESENTERIC ARTERIES[38].

2.3 CURRENT TREATMENT OPTIONS FOR COMPLEX AAA REPAIR

2.3.1 ANEURYSM SURVEILLANCE

One option for patients diagnosed with an aneurysm is watchful waiting, where the patient is followed at regular intervals with serial imaging to assess the stability of aneurysm size. This option is generally reserved for smaller aneurysms, as aneurysm size is associated with risk of rupture, and for patients who are very elderly and/or considered very high risk for surgical intervention[39]. However, the annual rupture risk of untreated AAAs increases to ~3-15% for aneurysms between 5-6 cm and ~30-50% for those larger than 8 cm.[40] This is further supported in a review of patients deemed unsuitable for open repair in which 47% of the deaths that occurred during follow-up were due to ruptured aneurysms.[41]

2.3.2 OPEN SURGICAL REPAIR FOR COMPLEX AAA

Conventional surgical treatment of AAA requires a major operation. The repair of the aneurysm involves opening the aneurysmal sac, removing any thrombus and then suturing a graft, generally made of a polyester material, to healthy aortic/iliac tissue that borders the proximal and distal ends of the aneurysm. Upon completion of the graft attachment, the aneurysm sac is closed around the graft. The benefits of open surgical repair include its excellent durability and low rates of aneurysm-related reinterventions as compared to EVAR.[42,43]

Although open surgery offers the potential for durable repair and relatively low risk for secondary intervention, approximately 1 in 4 patients may be ineligible for open surgery owing to significant comorbidities and associated high surgical risk.[44] Of patients who undergo surgery, operative mortality is 3-5% with respiratory complications in 19% and renal complications in 19-21%.[45,46] Due to the fact that suprarenal or supraceliac aortic cross-clamping is required for aortic control/exposure in these cases, with a concomitant period of renal/visceral ischemia, open repair in these patients is necessarily more complicated and carries higher risks of serious morbidity than patients in whom infrarenal cross clamping is performed.

An early report of JAA repair by Crawford and associates identified dialysis dependence in 8% of patients and perioperative mortality in 7.9%.[47] In a single center series of 1,020 open AAA repairs, Chong and associates reported no difference in mortality, but did identify a significantly increased incidence of renal dysfunction and major adverse events post-operatively when suprarenal cross clamping was performed instead of infrarenal cross clamping.[48]

Discussion continues whether further proximal cross clamping should be applied in the open repair of JAA/PAA patients. Some suggest that supraceliac clamping may be considered as an alternative to the more widely used suprarenal cross clamping to reduce postoperative morbidity if calcification or intraluminal thrombus are present in the suprarenal segment.[49] Researchers at the Cleveland Clinic, however, found significantly increased operative mortality following supraceliac cross clamping compared to suprarenal cross clamping in such patients (12% vs. 2.1%, P=.02).[50] In some cases, the choice of open surgical clamping approach is limited by anatomical factors, and must be considered in weighing the decision to proceed with an open repair.

Significantly increased perioperative mortality following open repair of JAA compared to open repair of less complex infrarenal AAA was reported in observational series by Faggioli and coworkers (12% vs. 3.5%; P<.02)[51] and by Ayari and associates (11% vs. 3.0%; P<.01).[52] Later observational experiences with open JAA or PAA repair report lower perioperative mortality rates of 3% to 6%.[53,54,55,56,57] In one of the largest series reported to date, researchers at the University of California at San Francisco identified perioperative mortality and renal morbidity rates of 5.8% and 41%, respectively, in 257 patients undergoing JAA or PAA open repair, with 4.3% of the cohort requiring permanent dialysis.[50] In a subsequent report, researchers at the Cleveland Clinic found a significantly increased perioperative mortality rate in patients undergoing open JAA repair versus infrarenal AAA repair (5.1% vs. 2.8%, P=.03), with 28% of JAA patients experiencing transient renal insufficiency, but with only 5.8% of patients requiring dialysis.[51] In a more recent review, researchers at the Mayo Clinic identified low perioperative mortality (0.8%) following elective open repair of 126 patients with JAA, with renal insufficiency or dysfunction occurring in 18% of patients.[58] The most current, comprehensive US population-based analysis indicates significantly increased operative mortality following open repair of JAA/PAA compared to infrarenal AAA (5.8% vs. 4.4%, P<.001); predicted significantly by a history of renal failure, female gender, and cardiac morbidity.[59]

In any case, limitation of ischemic time is essential to reduce the risks of cardiac morbidity and renal insufficiency, which are reported to occur in 15% and 5 to 12%, respectively, of patients undergoing open surgical infrarenal AAA repair. Owing to its more complicated repair, mortality, renal complication rates and other major morbidity are increased following JAA or PAA repair. In a recent meta-analysis of peer-reviewed, published outcomes following open repair of JAA with suprarenal cross-clamping, Jongkind and associates determined a median post-operative incidence of renal dysfunction of 18%, with a median dialysis rate of 5.7% in patients who received intraoperative renal perfusion.[60] The pooled estimate of perioperative mortality was 2.9%; due to poor reporting among the reviewed literature, no estimates for other major morbidity could be made.

2.3.3 ENDOVASCULAR TREATMENT OPTIONS FOR COMPLEX AAA

Due to the limitations with open surgical repair, less invasive endovascular techniques for complex AAA have been developed and continue to evolve with increased experience.

Endovascular Aneurysm Repair is considered relatively safe and effective for treating standard infrarenal AAA with demonstrated advantages of lower perioperative rates of mortality and major complications,

shorter hospital stays, and quicker return to functional status. However, current infrarenal device indications are lacking for aneurysms with complex anatomies, such as unfavorable neck or iliac anatomy. An evaluation of 10,228 patients treated with EVAR 1999 to 2008 showed only 42-69% of patients had anatomy that met the IFU.[61] Current treatment options to treat complex aneurysms include chimney EVAR (ChEVAR), fenestrated EVAR (fEVAR), physician modified endovascular stent grafts (PMESG), and utilization of off-label infrarenal devices.

2.3.3.1 CHIMNEY ENDOVASCULAR ANEURYSM REPAIR

Chimney Endovascular Aneurysm Repair (ChEVAR) is a parallel graft chimney technique which uses commercially available covered stents combined with a standard aortic stent graft. With ChEVAR, covered grafts are placed parallel to the aortic stent graft to maintain perfusion through the visceral branches. As with fEVAR, this endovascular technique is suitable in nonsurgical candidates. However, in contrast to custom fEVAR, the components required for ChEVAR are available off-the-shelf. Although Medtronic received CE approval for the Medtronic Endurant graft in conjunction with commercially available renal stent grafts, the ChEVAR technique remains off-label in the US.

The ChEVAR technique typically involves a minimum of 2 access points: femoral and an upper extremity. Femoral access can be completed in a percutaneous fashion. One or both upper extremities are accessed dependent on the number of chimney grafts planned. Once the selected branches have wires and sheaths in place, the aortic endograft is deployed and subsequently, each chimney graft is deployed with a planned 15 mm to 20 mm overlap with the aortic endograft and extending 10 mm to 15 mm beyond the proximal extent of fabric of the aortic endograft. An effort is made to place the chimney graft below the "suprarenal" or active fixation of the device (**Figure 2**). If utilizing the ChEVAR technique using devices designed with suprarenal fixation, the chimney stents are placed above the fabric of the device, but below the fixation, so that fixation is not compromised.

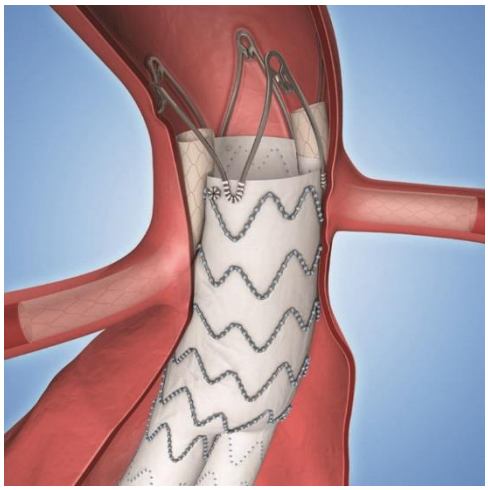

FIGURE 2: CHIMNEY ENDOVASCULAR AORTIC REPAIR FOR COMPLEX AAA

Two of the largest studies of the ChEVAR technique include the PERICLES Registry and the PROTAGORAS study.

The PERICLES Registry treated 517 high-risk patients with paravisceral AAAs between 2008 and 2014.[62] There were 119 patients treated at 2 U.S. centers and 398 patients treated at 3 European centers. A total of 898 chimney grafts were implanted in conjunction with a variety of commercially available endografts. Of the total 898 chimney grafts, 692 were renal chimneys, 156 were SMA chimneys, and 50 were celiac chimneys. Of these, 49.2% (442 stents) were balloon-expandable covered stents (Advanta V12/iCAST) and 39.6% (355 stents) were self-expanding covered stents (Viabahn). Balloon-expandable bare-metal stents were used as the primary chimney stent in 11.2% of the cases. Bare-metal Nitinol stents were used to reline the inside of a covered chimney stent in 25.4% (220/898) of the cases. Twenty-five post-operative deaths (4.9%) occurred within 30 days for the entire cohort, but 18 (3.7%) post-operative deaths occurred within 30 days in elective patients. Nine (9) patients (1.7%) had an embolic stroke. At a mean follow-up of 17 months, primary patency was 94%, secondary patency of 95%, 7.9% presented with Type Ia endoleak, and 6.6% required a secondary intervention. Survival was 85% at 1-year follow-up and 77% at 2 years.

The PROTAGORAS study treated 128 high-risk patients with pararenal AAAs at 2 European centers.[63] A total of 187 chimney grafts were implanted in conjunction with the Endurant endograft. All procedures were completed successfully. One post-operative death occurred within 30 days (0.8%) due to cardiac decompensation. Two patients (1.6%) presented with new onset of Type Ia endoleak. Primary chimney graft patency was 95.7%. Eight (8) chimney grafts were occluded during follow-up. Six (6) patients required intervention to resolve renal artery stenosis. Freedom from chimney graft-related reinterventions was 93.1%. Over 17 months mean follow-up, survival was 83%.

2.3.3.1.1 CHEVAR LIMITATIONS

The ChEVAR technique is an off-label technique in the US but is gaining popularity as early feasibility studies demonstrate promising results. Due to the lack of long-term data and this unapproved technique being performed in a non-standardized manner with varying combinations of endografts and branch stents, there are concerns regarding durability and component interaction.

Despite favorable outcomes of ChEVAR at experienced centers, systematic reviews have reported Type Ia endoleak rates of 10-14%, which may be even higher when more than two chimney grafts are used.[46,64,65] Left untreated, Type Ia endoleak in the setting of complex AAA poses the same problems as with standard EVAR, namely repressurization of the aneurysm sac with potential for sac growth and rupture.

Additionally, loss of long-term efficacy through aortic neck dilatation remains a concern since neck dilatation has been associated with oversizing, leading to increased rates of Type I endoleaks, migration and re-interventions. [66] The aortic and chimney grafts need to accommodate each other in the aorta, therefore adequate sizing is essential to prevent Type I endoleaks. Currently, there is a lack of consensus on how to size the aortic graft parallel to the chimney graft. A size selection model has been proposed, but it currently lacks supporting data.[67] Oversizing (by >30%) in relation to the suprarenal aorta or inadequate apposition to the aortic wall can lead to infolding of the endograft and a Type Ia endoleak.[68] Whereas, inadequate stent-graft oversizing can lead to a Type Ia gutter endoleak, involving blood flow through small channels between the main body of the aortic endograft and the chimney grafts that perfuse the aneurysm sac.[68] A retrospective analysis of the results from the PERICLES Registry on the degree of oversizing of the Endurant stent-graft showed that oversizing of 30% was associated with a significantly lower incidence of reintervention for Type Ia endoleaks in patients treated with ChEVAR.[69]

Additional risks that are specific to ChEVAR techniques relate to the necessity for upper extremity access to place the chimney grafts in the target vessels. [70] The need to cross the vertebral arteries and aortic arch

may increase risk of stroke. Further, management of hemostasis is a consideration with ChEVAR since a higher number of chimney grafts is associated with greater procedural blood loss.

2.3.3.2 FENESTRATED ENDOVASCULAR ANEURYSM REPAIR

The goal of extending an endovascular option for aneurysms with short infrarenal necks or the involvement of visceral arteries led to the development of the Fenestrated Endovascular Aneurysm Repair (fEVAR) method for treating complex AAA. The fEVAR technique extends the seal zone proximally above the renal arteries by use of a fenestrated endograft with branch stent grafts that pass through the fenestrations and into the target vessel providing perfusion to the abdominal viscera. Two categories of fEVAR designs have been developed; custom fEVAR and off-the-shelf fEVAR as discussed in further detail in Sections **2.3.3.2.1** and **2.3.3.2.2** below.

2.3.3.2.1 CUSTOM FEVAR

ZENITH FENESTRATED AAA ENDOVASCULAR GRAFT (ZFEN):

Currently, the only branched/fenestrated stent graft approved and marketed in the US is a custom fEVAR device called the Zenith Fenestrated AAA Endovascular Graft (Cook Medical, **Figure 3**).[71] This device is indicated to treat short-neck (≥4mm) infrarenal aneurysms and features fenestrations and scallops that accommodate a variety of patient anatomies. In order to account for anatomical variation, each stent graft is custom-made with up to three fenestrations for a specific patient.

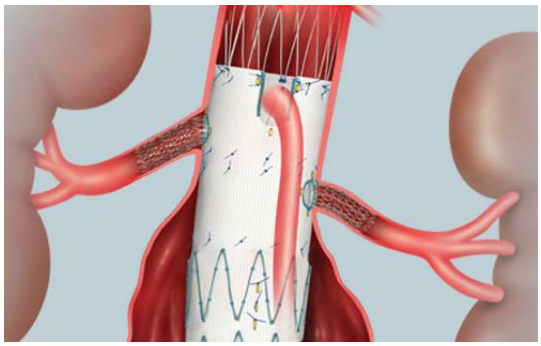

FIGURE 3: COOK ZENITH FENESTRATED AAA ENDOVASCULAR GRAFT

During the procedure, the proximal body is advanced to align the fenestrations and/or scallops with the visceral vessels and deployed within the suprarenal abdominal aorta by means of a catheter delivery system. Multisheath access is achieved in the femoral artery using a 20- or 22-F sheath for two or three fenestrations, respectively. After alignment of the fenestrations and the stents, the proximal end of the aortic stent is deployed and dilated. The stents are then deployed across small fenestrations to assist in maintaining the patency of the renal arteries and to complete the endovascular repair. A short segment of the stents within the visceral arteries protrudes into the aorta and may be subsequently flared to essentially rivet the stent graft to the aortic wall. The universal bifurcated component is then deployed, followed by iliac extensions.

In the prospective trial[71], sixty-seven (67) patients with juxtarenal AAAs were treated. A total of 178 visceral arteries were incorporated (129 renal arteries and 49 SMAs). One post-operative death occurred within 30 days (1.5%) due to bowel ischemia. No aneurysm ruptures or conversions were

noted during a mean follow-up of 37 ± 17 months (range, 3-65 months). Two patients (3%) had migration ≥10 mm with no endoleak, both due to cranial progression of aortic disease. Of a total of 129 renal arteries targeted by a fenestration, there were four (3%) renal artery occlusions and 12 (9%) stenoses. Placement of two stents was required in seven renal arteries and one SMA due to the presence of a kink or inadequate overlap between the fenestration and the first stent. Fifteen patients (22%) required secondary interventions for renal artery stenosis/occlusion in 11 patients, Type II endoleak in three patients, and Type I endoleak in one patient.

CUSTOM FEVAR LIMITATIONS

While fenestrated endografts are custom made, specifically for the patient's anatomy, this also limits the application of fEVAR as the technique cannot be used in urgent situations, compared to ChEVAR which is available for "off the shelf" use. For instance, the customized Zenith device requires a minimum of 3-4 weeks for manufacture and delivery[72].

Although the Zenith Fenestrated device has been proven to be effective in treating complex aortic disease, anatomical restrictions remain a primary limitation in treatment. The design of the Zenith device requires the distance and orientation of the vessels to fit within a handful of engineering rules, resulting in limited patient applicability in those with close proximity of the SMA and the most cranial renal artery.[72] Additionally, the larger delivery sheath profile limits the applicability for subjects with hostile iliofemoral access. In a study conducted between July 2012 and September 2013, 85 subjects with complex AAA were treated, of which 37 (44%) did not meet the criteria for the Zenith Fenestrated device. [73] In contrast, ChEVAR is not as limited by the patient's anatomy as commercially available covered stents are used in combination with a standard aortic stent graft. In addition, the costs are lower compared to a customized endograft.

A study using the National Surgical Quality Initiative, compared fEVAR and ChEVAR to open surgery and found lower mortality and morbidity following endovascular repair. [74] Procedure time was longer with fEVAR than ChEVAR or open repair, which increases the fluoroscopy time, radiation, dose and the risk of renal failure. [74] Overall, there were no significant differences in outcomes between fEVAR and ChEVAR.[74] Larger prospective studies are required to confirm these results.

2.3.3.2.2 OFF THE SHELF FEVAR

Due to the constraints that limit the proportion of patients who have access to fenestrated graft technology, manufacturers have attempted to develop an off-the-shelf fenestrated solution. These devices incorporate fenestrations and/or scallops in a variety of designs to accommodate a range of visceral artery positions. Two off-the-shelf devices have been investigated to date: the Ventana Fenestrated System and the Zenith P-Branch.

VENTANA FENESTRATED SYSTEM

The Ventana Fenestrated System (Ventana System, Endologix, Inc., **Figure 4**) was designed as an off-the-shelf system for the treatment of JAA or PAA. The Ventana System consisted of an integrated endovascular stent graft system deployed as a proximal extension to the AFX infrarenal stent graft (Endologix, Inc.).

A scalloped section with length 4 cm from the most proximal edge was present to align below the SMA and celiac artery. The mid-section contained oversized graft having circular 3 mm diameter fenestrations that could be expanded up to 10 mm for cannulation of the renal arteries and introduction of renal stent grafts. Balloon expandable renal stent grafts were preloaded into the sheath to maintain renal artery patency.

During the endovascular aneurysm repair procedure, the Ventana self-expanding stent graft was deployed within the suprarenal abdominal aorta by means of a catheter delivery system and the distal end was deployed within the proximal end of an AFX stent graft. Balloon-expandable renal stent grafts were delivered through the Ventana System and across the fenestrations to assist in maintaining the patency of the renal arteries and to complete the endovascular repair. The renal stent grafts could be moved *in-situ* to accommodate the renal artery spacing for each patient. A scallop was designed in the proximal segment for placement below the superior mesenteric artery (SMA) and the celiac artery.

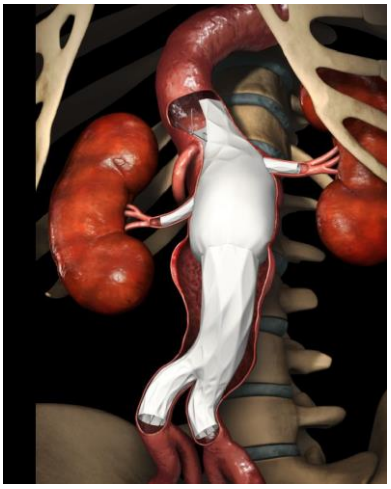

FIGURE 4: VENTANA FENESTRATED SYSTEM

The Ventana System clinical program was initiated in 2010 and enrolled 125 patients (49 patients in the feasibility study, 76 patients in the US IDE study), with an additional 7 patients treated outside of the US under individual compassionate use requests, resulting in a total of 132 patients treated globally. Two hundred forty-nine (249) renal stents were implanted (129 left and 120 right). In addition, 26 patients (20.8%) had received more than one device in one or both renal arteries mainly due to the patient's anatomy and/or to obtain adequate apposition. All procedures were successfully completed. No post-operative deaths occurred within 30 days. In April 2013, it was noted that the rates associated with renal occlusions and reinterventions increased. In addition, one patient treated under a compassionate use request had undergone device explant due to renal failure, implant lateral movement, and device integrity failure, including stent strut fracture in the Ventana 'W' mid-section, separation of the renal stent from the Ventana stent graft and renal stent fracture. As a result, Endologix placed all enrollment (US and OUS) on hold in May 2013 (G110067/S013) and subsequently terminated enrollment in March 2015 (G110067/S019).
As of the October 22, 2018 data cut, a total of 76 secondary interventions were performed in 46 patients (36.8%) that were endovascular in nature (G110067/R028). Of these secondary interventions, 47 secondary interventions were performed for renal stenosis or occlusion. Thirty-one

(31) patients were observed with 75 fractures of the Ventana device. Twenty-one (21) patients were observed with 68 renal stent fractures.

ZENITH P-BRANCH

The Zenith pivot-branch (p-branch) device (Cook Medical, **Figure 5**) is an investigational off-the-shelf fenestrated graft. The device is indicated to treat juxtarenal and pararenal aneurysms with at least 4mm healthy neck available below the superior mesenteric artery (SMA) to ensure a circumferential seal.[75] The device consists of a tubular proximal stent graft with a scallop for the celiac artery, a fenestration for the SMA, and 2 pivot fenestrations for the renal arteries (p-branches).[76] The stent graft is available in two designs with either pivot fenestrations at the same level or offset with the right renal fenestration located more cranially.

FIGURE 5: COOK ZENITH P-BRANCH[77]

During the procedure, the proximal body is advanced to align the SMA fenestration with the SMA orifice and deployed within the suprarenal abdominal aorta by means of a catheter delivery system. Multisheath access is achieved in the femoral artery using a 20-F sheath. After the delivery sheath is withdrawn, the preloaded renal sheaths are advanced to the pivot fenestrations, the SMA sheath is advanced and placed within the SMA, and the renal sheaths are advanced. The mating renal stent grafts are deployed and flared, followed by the SMA stent graft. The universal bifurcated component is then deployed, followed by iliac extensions.

A review of four single-center studies evaluated the safety and effectiveness of the Zenith p-Branch device in 76 patients between August 2011 and September 2015 in the United States and Europe.[78] The device was deployed successfully in all patients, and stents were placed in all target vessels except in three cases. There was no 30-day mortality, but 10 late deaths occurred unrelated to the device or procedure. No aneurysm ruptures or conversions were noted during a mean follow-up of 25 ± 13 months. Two patients experienced bowel ischemia. Renal artery occlusion occurred in eight patients (11%) and was deemed procedure related in 63% (5/8) of these patients. Renal artery stenosis requiring intervention occurred in 6 patients (8%). Two patients required adjunctive stenting of the renal arteries during the procedure due to occlusion caused by stent deformation.

Patient applicability remains the top unmet need in off-the-shelf fEVAR devices. In a study conducted between July 2012 and September 2013, 85 subjects with complex AAA were treated, of which only

23 (27%) were eligible for off-the-shelf devices based on their anatomy, whereas ChEVAR has fewer anatomical restrictions.[73] Patients were excluded from the Ventana device mainly because of either an insufficient proximal sealing region below the SMA or renal anatomic criteria. The major exclusion criteria for the p-Branch device was renal axial or circumferential position.

From a technical standpoint, implantation of these devices can be more difficult compared with custom-made stent grafts because of the mismatch between aortic anatomy and the intended off-the-shelf configuration. Bailout maneuvers for errors of design or deployment may be needed if the fenestration is not properly aligned with the target.[38] One advantage of ChEVAR compared to fEVAR is that procedure time is lower than for fEVAR, and this is likely to be true for off-the-shelf fEVAR also.[74] However, ChEVAR requires more extensive upper extremity access.[70]

Durability is a concern in the setting of misaligned bridging stents that can be prone to kinks, fracture, or migration. These concerns proved correct in Ventana, which had a high renal artery occlusion rate and fractures, resulting in termination of the IDE study and halting commercialization of the device in other regions.

2.3.3.3 PHYSICIAN MODIFIED ENDOVASCULAR STENT GRAFTS (PMESG)

A Physician Modified Endovascular Stent Graft (PMESG) is an off-label technique that modifies an off-the-shelf stent (**Figure 6**) while the patient is prepared for surgery.[79] This option was developed to offer a solution for patients with complex AAA deemed unsuitable for traditional open surgical repair or who, while presenting in an urgent fashion, cannot wait for entry into a clinical trial or wait for a custom-made fEVAR device.

There are limited data to support the long-term safety and effectiveness of this technique. Nevertheless, a few recent studies present short-term data supporting the applicability of PMESGs.[70,80,81] There is some evidence to show equivalence of PMESGs to other techniques for complex endovascular repair.[70,80] Due to availability, PMESGs may be used more frequently for urgent repairs, which is important to consider when reviewing the outcomes for these procedures.[80] Also, it is recommended that oversizing of devices should not exceed 10-15%. [81] Results from the Vascular Quality Initiative (VQI) show that PMESGs were used more often for extensive aneurysms, that were more likely to include the celiac and superior mesenteric vessels.[70] Perioperative mortality, acute kidney injury (AKI), and overall complications were similar between the PMESG, fEVAR and ChEVAR groups in the VQI study.[70] A study by Dossabhoy et al. showed no statistical advantage between PMESGs and custom-fEVAR, however, procedure time and reinterventions at 1-year were higher in the PMESGs group.[80] The results of a single-arm study on the use of PMESGs in juxtarenal aneurysm repair support the use of PMESGs, as there was a significant decrease in aneurysm size up to 3 years post-procedure and there were no Type Ia endoleaks reported in 4 years of follow-up.[81]

Overall, more studies and longer follow-up are required to confirm the suitability of PMESGs. The limitations of this technique are that once a commercially available device has been modified the long-term data associated with the approved device is no longer applicable. Longer-term follow-up is needed to determine the durability of this approach and the potential for device-related complications. For now, PMSEG should be considered a solution to be employed in an individual patient where the anatomy precludes the use of currently-marketed devices and where the patient's medical comorbidities preclude an

open surgical approach.[82] In all cases, the risk of repair with a PMSEG must be balanced against the risks of observation alone.

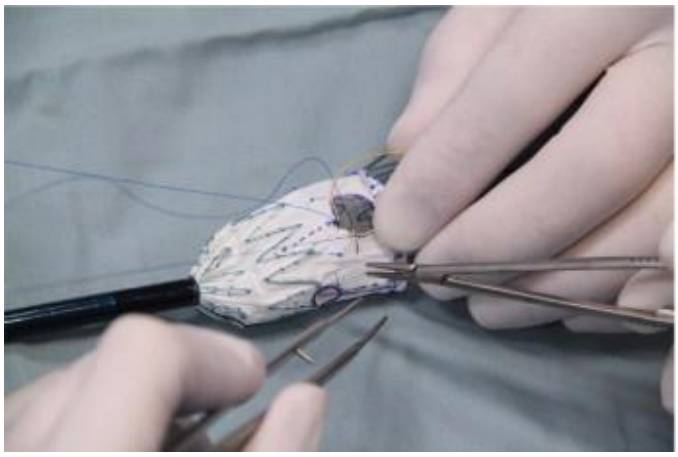

FIGURE 6: PHYSICIAN MODIFIED ENDOVASCULAR STENT GRAFT FOR TREATMENT OF COMPLEX AAA

2.3.3.4 OFF-LABEL USE OF EVAR DEVICES

Short and complex infrarenal aortic neck seal zones result in a restricted patient applicability and remain a primary limitation for commercially approved EVAR devices. Complex neck anatomy is the primary reason that patients with infrarenal aortic aneurysm must undergo open repair. [83] As a result, a large population of patients who are high-risk for open repair and undergo EVAR are considered off-label.[61,84]

Off-label treatment can result in more endoleaks, however spontaneous sealing is still possible in these cases.[84] Several studies have compared different aspects of aortic neck morphology as a predictor of outcomes after EVAR, including neck length and angle.[85] As patients are treated off-label, patient outcomes decline, including Type I endoleak and aneurysm enlargement.

2.3.3.5 ENDOANCHORS

One common treatment option to improve the performance of endograft fixation and seal to the aorta in short and/or complex necks includes the use of EndoAnchors. EndoAnchors, such as the Heli-FX EndoAnchor System, were developed to provide active fixation of existing endografts, thereby reducing migration and Type Ia endoleaks due to inadequate sealing and fixation to the aortic wall. EndoAnchors may be implanted at the time of the initial endograft placement or during a secondary procedure. Although Medtronic received approval for the Medtronic Endurant graft in conjunction with the Heli-FX EndoAnchor System in patients with proximal neck lengths ≥ 4mm and < 10 mm, the use with other endografts remains off-label for complex anatomy.

The ANCHOR study treated 319 patients with the Heli-FX EndoAnchor at the time of an initial EVAR procedure (primary arm, 242 patients) or with an existing endograft and proximal aortic neck complications (revision arm, 77 patients).[86] Technical success was achieved in 303 patients (95.0%) and procedural success in 279 patients (87.5%), 217 of 240 (89.7%) and 62 of 77 (80.5%) in the primary and revision arms, respectively. There were 29 residual Type Ia endoleaks (9.1%) at the end of the procedure. During mean

follow-up of 9.3 ± 4.7 months, 301 patients (94.4%) were free from secondary procedures. Among the 18 secondary procedures, eight were performed for residual Type Ia endoleaks and the others were unrelated to EndoAnchors. There were no open surgical conversions, there were no aneurysm-related deaths, and no aneurysm ruptured during follow-up.

Several situations have been identified where the use of EndoAnchors is not advisable. EndoAnchors should not be used to treat Type Ia endoleaks that are associated with >2mm gaps.[87] In a sub-group of patients from the ANCHOR study, who were treated for Type Ia endoleaks, it was found that 30% of EndoAnchors were maldeployed.[88] Maldeployment can lead to inadequate EndoAnchor penetration and to free floating EndoAnchors which have to be retrieved or trapped in place using a cuff. Maldeployed EndoAnchors were also associated with Type Ia endoleaks.[87] Calcification of the aorta and large aortic neck were associated with poor EndoAnchor penetration.[89] In addition, dense vessel calcification can result in EndoAnchor fracturing.

There have only been a few reports of EndoAnchors used in conjunction with ChEVAR.[90,91,92] In a studies where patients were treated with ChEVAR and utilizing EndoAnchors, none of the patients developed a Type Ia endoleak.[87,91] EndoAnchors have also been used to repair Type Ia endoleaks in 2 patients, 5-15 years following ChEVAR.[92] The use of EndoAnchors in conjunction with ChEVAR could aid in preventing compression of the chimney grafts and gutter formation, however the technique is technically challenging.[87] Using an *in-vitro* model of a juxtarenal aneurysm, EndoAnchors have been shown to reduce gutter size.[93] Whether this will be true in a real-world clinical setting remains unproven.

Overall, patients need to be carefully selected for the use of EndoAnchors. In patients who are high risk for open repair and not suited to the use of EndoAnchors, other therapeutic options such as ChEVAR and fEVAR should be considered.[87]

2.3.4 CHEVAS OVERVIEW

In order to address the limitations seen in complex AAA repair, Endologix has identified an opportunity to leverage the aneurysm sealing technology in the Nellix System to provide a better treatment option for patients with complex AAA. Utilizing the chimney technique used with ChEVAR, the Nellix System may be used with parallel stent grafts in the renal arteries and superior mesenteric artery (SMA) as a new treatment option referred to as Chimney Endovascular Aneurysm Sealing (ChEVAS). ChEVAS may offer an advantage over ChEVAR, as the intraoperative filling of the EndoBags also results in the filling of the spaces between the parallel grafts which may help to reduce the occurrence of gutters or Type Ia endoleaks.[94,95] Also, there may be a reduced risk of compression of the chimney stents with ChEVAS, and therefore thrombosis compared to ChEVAR, as the sealing polymer used to fill the EndoBags also conforms around the chimney stent grafts.[94]

Careful planning is essential prior to the ChEVAS procedure, including imaging to delineate the aortic morphology.[96] The centerline length from the proximal sealing zone to the iliac bifurcation is used to determine device length and to estimate the polymer fill volume. A proximal sealing zone of ≥15mm is required, with a 20-30 mm diameter, to reduce the risk of chimney compression.[97,98] The ChEVAS procedure involves the use of the Nellix System in conjunction with parallel branch chimney stents for the treatment of juxtarenal, pararenal, or paravisceral abdominal aortic aneurysms.
The procedure requires bi-lateral placement of the Nellix stent grafts in conjunction with deployment of branch stents in the renal arteries and/or Superior Mesenteric Artery (SMA) through upper extremity access. One, two, or three arteries may need to be stented during the treatment to provide adequate aneurysm

exclusion while maintaining patency of the visceral arteries. The chimney stents are positioned first. Once the chimney stents are in position, the Nellix System EndoBags are introduced. The Nellix System is positioned so as the Nellix stents align with the top of the parallel stents and are aligned proximally to the planned sealing zone.[96,97] Intraoperative angiography is used to confirm stent position. The chimney stents are deployed, and the chimney delivery systems are exchanged for PTA balloons. Some investigators prefer to use balloon expandable stents, as the balloons can be left in place during polymer curing, thereby protecting the chimney stents.[94,96] The Nellix EndoBags are then filled with saline solution and intraoperative angiography is performed to confirm the absence of endoleaks. The saline is then removed from the EndoBags and they are filled with a polymer up under pressure monitoring. The polymer conforms around the branch stents and aortic vessel wall, thereby creating a seal to exclude blood flow to the aneurysm sac. The Nellix stents form lumens through which blood flows to the distal limbs and vasculature and the branch stents maintain blood flow to the visceral arteries. The EndoBags with cured polymer exclude the aneurysm from blood flow, preventing aneurysm pressurization and rupture. This seals the entire anatomy from the proximal end of target landing zone to the iliac arteries with a distal seal zone (**Figure 7**). To assess the technical success of the procedure, intraoperative angiography is performed to confirm exclusion of the aneurysm and to assess for endoleaks.

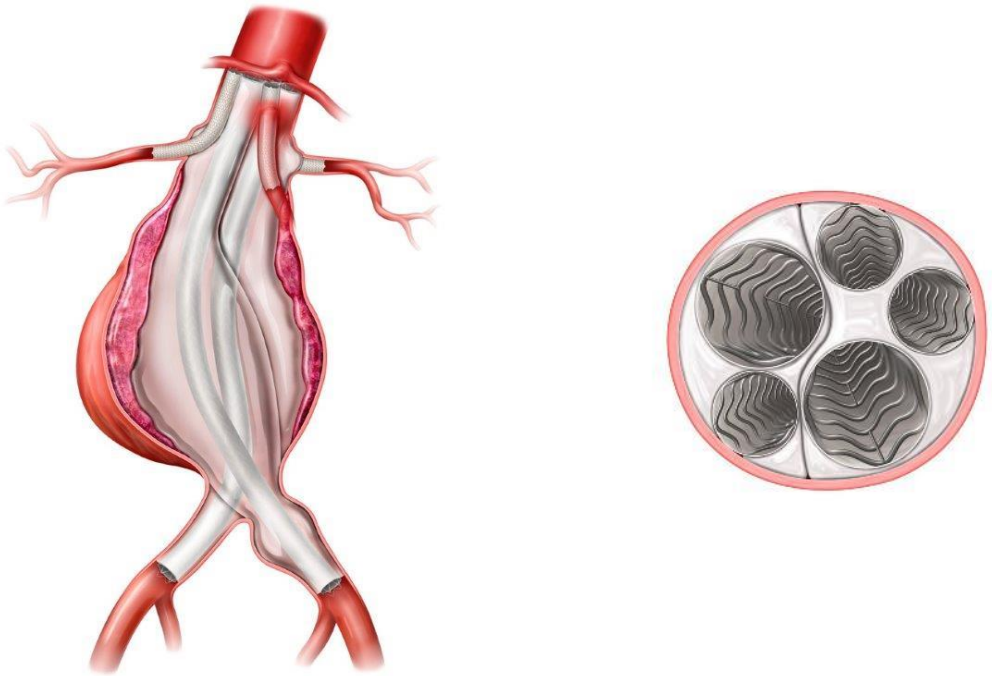

FIGURE 7: NELLIX SYSTEM WITH BRANCH STENTS IN A 3-VESSEL REPAIR

2.3.4.1 CURRENT CLINICAL EXPERIENCE

The ChEVAS procedure has been described in benchtop studies, [99] , [100] case reports[94,98,101,102,103,104,105,106,107,108,109] and in small series involving mainly emergent cases.[110,111,112] It was apparent from the early experience that standardization of the therapy with regard to technique and components was desirable.

To date there have been five articles reporting on the feasibility and safety of ChEVAS in retrospective and prospective studies of > 10 patients. The characteristics of these studies are presented in **Table 2**. The majority of patients included in these studies were male and in the eighth decade of life. A summary of the performance and safety outcomes from these studies is presented in **Table 3**.

These studies reported on primary repair or repair of a previous EVAR or aortic graft using ChEVAS. There have been other reports where ChEVAS was used, however the outcomes were not stratified by type of EVAS repair and were therefore not included in the analysis below.[113,114] These studies, Paraskevas et al. (2018) and Youssef et al. (2017) are discussed qualitatively below.

Paraskevas et al. conducted a retrospective analysis of a prospectively maintained aneurysm database to investigate late complications following EVAR.[113] There were 10 patients included in the analysis who underwent interventions for complications of the EVAR procedure. All interventions were performed using EVAS with or without chimney grafts. Technical success for Type Ia endoleaks was 100%, with no perioperative deaths. One Type Ia endoleak re-occurred during follow-up, and 2 undetermined endoleaks were explored with laparotomy were found to be Type II endoleaks.

Youssef et al. also conducted a retrospective study of patients who required reintervention following EVAR.[114] Fifteen patients were included in the study and all patient were treated with EVAS. There were 10 patients treated with ChEVAS. Technical success was 100%, with sealing of all endoleaks. There was 1 aneurysm related death 2 months post-procedure and there was 1 renal artery injury. No other complications were observed during a mean of 8 months follow-up.

Both studies show that EVAS/ChEVAS is a beneficial treatment for failed EVAR. With good short-term results. More studies with longer follow-up are required to fully evaluate long-term outcomes.

TABLE 2: STUDY CHARACTERISTICS OF ARTICLES REPORTING ON CHEVAS FOR THE TREATMENT OF COMPLEX AAA

Publication	Subjects	Treatment Period	Mean/Median Follow-Up (months)	Mean/Median Age (years)	Male (%)	Study Design*	Country/Countries
De Bruin, J. L., J. R. Brownrigg, B. O. Patterson, A. Karthikesalingam, P. J. Holt, R. J. Hinchliffe, I. M. Loftus and M. M. Thompson. "The Endovascular Sealing Device in Combination with Parallel Grafts for Treatment of Juxta/Suprarenal Abdominal Aortic Aneurysms: Short-term Results of a Novel Alternative." *Eur J Vasc Endovasc Surg* 52(2016): 458-465[115]	28	March 2013-April 2015	4	75	79	P1SN	1 site in the U.K.
Dinkelman, M. K., S. P. Overeem, D. Bockler, D. E. V. JP and J. M. Heyligers. "Chimney technique in combination with a sac-anchoring endograft for juxtarenal aortic aneurysms: technical aspects and early results." *J Cardiovasc Surg (Torino)* 57(2016): 730-736[116]	16	November 2014-March 2016	1	73	87.5	P1MN	2 sites in Europe
Harrison SC, Winterbottom AJ, Coughlin PA, Hayes PD, Boyle JR. Editor's Choice - Mid-term Migration and Device Failure Following Endovascular Aneurysm Sealing with the Nellix Stent Graft System - A Single Centre Experience. *Eur J Vasc Endovasc Surg* 2018;56(3):342-348.[117]	18	February 2013-August 2017	53	NS	NS	R1SN	1 site in the U.K.
Stenson K, Patterson B, Grima MJ, de Bruin J, Holt P, Loftus I. Endovascular Aneurysm Sealing with Chimney Grafts to Treat Juxtarenal and Suprarenal Abdominal Aortic Aneurysms: Early Results from 62 Cases. *J Vasc Surg.* 2018. (E-publication ahead of print). †[96]	62	July 2013-June-2016	13	73.9	77.4	P1SN	1 site in the U.K.
Thompson M, Youssef M, Jacob R, et al. Early Experience with Endovascular Aneurysm Sealing in Combination with Parallel Grafts for the Treatment of Complex Abdominal Aneurysms: The ASCEND Registry. *J Endovasc Ther.*2017;24(6):764-772. ‡[97]	154	July 2013-March 2016	5.6	72.3	80.5%	R1MN	7 sites in European and 1 site in New Zealand

NS, Not specified
**P, Prospective: R, Retrospective; 1, Single-Arm Study; S, Single-Center Study; M, Multi-Center Study; N, Non-Randomized Study*
†Stenson et al. reports on the first 50 patients from the ASCEND Registry, which are included in the study by Thompson et al.
‡Note: the first author of this study is now the chief medical officer of Endologix.

TABLE 3: PERFORMANCE AND SAFETY OUTCOMES FOR CHEVAS IN THE TREATMENT OF COMPLEX AAA FROM THE LITERATURE

Outcome	Study				
	De Bruin et al[115]	Dinkelman et al[116]	Harrison et al[117]	Stenson et al*[96]	Thompson et al[97]
Performance Outcomes					
Technical success (%)	100	100	100	100	100
Median number of chimney grafts (range)	1 (1-2)	2 (1-3)	NS	1 (1-3)	2 (1-4)
Mean procedure time (min)	185	165	NS	205	216
Mean blood loss (ml)	300	175	NS	390	339
Graft failure (%)	NS	NS	16.7	NS	NS
Migration (%)	NS	NS	NS	4.8	NS
Safety Outcomes					
30-day all-cause mortality (%)	3.6	0	11.1	3.2	2.8
All-cause mortality (%)	14.33	0	16.7	16.1	7.4
AAA-related mortality (%)	3.6	0	5.5	3.2	2.8
Stroke (%)	7.1	6.25	NS	6.5	2.6
Transient ischemic attack (%)	3.6	NS	NS	NS	NS
Type I endoleak (%)	3.6	6.25	11.1	12.9	5.8
Type II endoleak (%)	3.6	NS	NS	1.6	0
Secondary intervention (%)	14.3	18.75	NS	17.7	17.1
Limb occlusion (%)	NS	6.25	NS	3.2	NS
Graft occlusion (%)	NS	6.25	NS	3.0	NS
Chimney graft patency (%)	100	NS	NS	97	99
Dialysis (%)	NS	6.25	NS	1.6	1.3

NS, Not specified
**Stenson et al. reports on the first 50 patients from the ASCEND Registry, which are included in the study by Thompson et al.*

The results presented in **Table 3** on the use of ChEVAS for the treatment of complex AAAs in general are promising. These data support a proof of concept for the use of polymer technology and EVAS with parallel grafts in managing patients with complex aortic disease. Technical success was achieved in all cases and AAA-related mortality was low (≤5.5%). The rate of stroke was similar across studies (2.6% – 7.1%). The rate of Type I endoleaks varied from 3.6%-12.9%. A systematic review showed Type I endoleaks and chimney graft thrombosis following ChEVAR were higher than with ChEVAS, however the difference was not statistically different.[94] As to be expected, given the nature of the EVAS technique, Type II endoleaks were low across all studies. There were no Type III endoleaks reported in any of the study reviewed above.

Chimney graft patency was high across ChEVAS studies presented in **Table 3**. The majority of patients included in the studies listed in **Table 2** we treated with 1-2 chimney grafts (see **Table 3**). Stenson et al. found that with ChEVAS there were more complications where there was only a single chimney graft. They speculate that the shorter sealing zone and asymmetry of the single chimney configuration may have an effect on the columnar strength of the endograft, however the exact reasons for these complications is unknown.[96]

There was one study, Thompson et al., where up to 4 chimney grafts were used.[97] They reported increased procedural blood loss in procedures with 3 or 4 chimneys, compared to procedures where there were 1 or 2 chimney grafts implanted.[97] There is evidence from ChEVAR studies that complications increase with the number of chimney grafts, which is logical, since there is a greater chance of endoleaks developing with more chimney grafts.[118] In general, there is a lack of Nellix experience with ChEVAS with 4 chimney grafts, as only a small number of patients in the ASCEND registry were treated with 4 chimney grafts (2.6%), and there were no patients in the other studies included in **Table 3** treated with 4 chimney grafts. Due to the fact that the majority of patients can be treated with 1-3 chimney grafts and the number of complications increase with the number of chimney grafts, only 3 branches will be allowed in the IDE. In addition, ChEVAS with 4 chimney grafts is technically challenging with an increased risk of complications due to managing 4 self-expanding stents and the auxiliary vessels with increased procedure time and blood loss. At this stage, ChEVAS is not designed for complex, thoracoabdominal vessels, it is designed for the juxtrarenal/pararenal aneurysm (1-3 vessels).

There were several limitations associated with EVAS that were identified in these studies. Harrison et al. was the only EVAS study identified with longer term follow-up (4.4 years). In this study the long-term durability of EVAS was questioned, due to a high rate of graft failure > 2 years post-procedure.[117] Therefore, frequent monitoring and imaging of patients is warranted.

Another limitation of the chimney technique is that an additional upper extremity access site is required in order to cannulate target vessels. The use of an additional upper extremity access site increases the risk of cerebral embolization when compared to fEVAR. Stroke rates of up to 10% have been reported with ChEVAR, and the incidence of stoke was higher with ChEVAR compared to open repair and fEVAR.[115] [119] [120] Therefore, methods to minimize embolizations prior, during and following the procedure are required, such as pre-operative clopidogrel and antiplatelet drugs post-operatively.[96]

Despite the limitations outlined above, the results from these early experiences with ChEVAS are encouraging and show the feasibility of the technique. However, apart from the ASCEND registry, all of these studies were small and with the exception of the Harrison et al. study, lacked longer term follow-up. Therefore, larger controlled studies, with longer follow-up are required, as well as studies with comparisons to other techniques for the treatment of complex AAAs. When interpreting the results of these EVAS studies it should be noted that the majority of patients in these studies were treated prior the modifications to the

Nellix IFU in 2016. In addition, these studies report on the early experiences with the Nellix System. It is important to consider that with any new technology there is a learning curve, not only concerning the technical attributes of the device, but also concerning patient selection, and these factors may affect the long-term outcomes associated with the device. The impact of the EVAS learning curve became apparent when Endologix initiated its investigation in order to understand the mechanisms around migration, Type Ia endoleak, and aneurysm enlargement beyond the 1-year timepoint. During the development of the ChEVAS System, Endologix reviewed the ChEVAS indications based on the revised indications developed for EVAS. Specifically, an internal assessment was conducted on a subset of patients that had undergone a *de novo* ChEVAS procedure from the Global Registry and ASCEND study to confirm applicability and incorporate relevant revised anatomical criteria to the ChEVAS indications. In addition to the revised anatomical criteria captured in the narrowed indications, additional procedural techniques (e.g., proper positioning of the Nellix stents, always performing pre-fill, balloon inflation during polymer fill, confirmation of adequate seal) that were established for EVAS were also incorporated into the ChEVAS procedure. Overall, encompassing the lessons learned from these early studies, along with more careful patient selection, and standardization of the procedure should lead to improved outcomes in the future.

2.4 RISK/BENEFIT ASSESSMENT

2.4.1 RISKS

There are several risks that are specific to both the ChEVAR and ChEVAS techniques. As outlined above in **Section 2.3.4.1**, there is a risk of cerebral embolization associated with the necessity for upper extremity access to place the chimney grafts in the target vessels.[70,119,120] The need to cross the vertebral arteries and aortic arch may also increase risk of stroke. Therefore, in order to mitigate this risk patients should be assessed for the risk of stroke and pre- and post-operative medical therapy should be considered to reduce emoblizations.[96]

Management of hemostasis is also a consideration with ChEVAR/ChEVAS since a higher number of chimney grafts is associated with greater procedural blood loss.[97] Furthermore, the Nellix System had higher than anticipated rates of migration and aneurysm enlargement at 2 years; however, ChEVAS is not expected to experience these events due to the revised indications for use and procedural best practices that have been incorporated to ensure optimal outcomes moving forward.[117] Additionally, the mechanism of migration is thought to be further mitigated due to the lower force from pulsatile flow exerted on the EndoBag shelf due to the increased number of stents. When patients were treated with EVAS in accordance with the current IFU no incidences of migration were observed.[121]

Overall, while risks exist for the ChEVAS technique, many of these risks are comparable to those of currently available standard techniques for complex AAA. In addition, the risks associated with ChEVAS may be mitigated with careful patient selection and adherence to the current IFU for the Nellix System.

2.4.2 BENEFITS

The use of ChEVAS may offer a potential solution to the subset of patients that currently have unmet clinical needs due to being unsuitable for open surgery or need urgent treatment and cannot risk waiting for a custom fenestrated endografts. ChEVAS maintains the widespread applicability and the ability to perform this technique using off-the-shelf components in urgent and emergent cases that fEVAR lacks.

The conformability of the Nellix EndoBag filled with polymer offers a unique solution capable of sealing around the branch stent grafts to create a more durable seal with a potential reduction in risk of gutter or Type I endoleak.[94] A systematic review of ChEVAS versus ChEVAR showed a trend towards a lower rate of Type I endoleaks in patients treated with ChEVAS.[94] Additionally, chimney graft thrombosis trended lower with ChEVAS.[94] The results of the ChEVAS studies presented in **Table 3** show excellent chimney graft patency due to the improved seal of the chimney graft patency, and a low level of chimney graft occlusion.[96,97,115,116] Better sealing and incorporation of the chimney grafts, without impacting the radial strength of the device may reduce the risk of chimney graft occlusion with ChEVAS.

The ability to completely fill the aneurysm combined with the material properties of polymer may also help stabilize the visceral segment of the aorta and reduce the occurrence rates of branch stent graft fractures. Furthermore, the polymer based ChEVAS technique may be associated with less aortic neck dilatation, since a self-expanding aortic stent is not used at the proximal seal zone. This speculation, however, must await long term anatomic outcomes.[122]

As with EVAS, ChEVAS should offer the same unique advantages associated with the aneurysm sealing technique. Firstly, there may be a reduction in the Type II endoleak rate through active sac management. Type II endoleaks were only reported in 2 patients out of > 200 patients treated with ChEVAS in the 5 studies that were reviewed above (**Table 3)**. Only 1 of these Type II endoleaks required interevention.[96,115] A recent systematic review of EVAS studies showed the rate of Type II endoleaks was 1.8%, a 30-days.[123] This compares well to a rate of 10.2% for Type II endoleaks at 30-days, that has been reported for EVAR, in a systematic review of 32 studies.[124]

Another advantage of EVAS, which may also apply to ChEVAS is a reduction of radiation dose and procedural time compared to EVAR.[125] Also, systematic review of EVAS showed a 30-day mortality rate of 1.0% for elective patients and 2.6% including emergency cases.[123] These rates are comparable to EVAR, but lower than for open repair.[126]

Finally, as Nellix utilizes active sac management in both EVAS and ChEVAS, it is expected that the potential mortality benefit may also be applicable to the ChEVAS procedure. Although many factors impact the long-term survival, underlying cardiovascular disease explains much of the risk associated with the high rate of adverse cardiovascular events. The relationship between inflammation and atherothrombosis has been established in the last decade. After an endograft excludes the aneurysm sac using EVAR, the aneurysm remains biologically active. The aneurysm sac undergoes a biological response related to a change in pressure and produces an inflammatory response in order to induce fibrosis and regression. If the aneurysm sac is not successfully excluded due to endoleaks, intraluminal thrombus, and pressure transmitted from a porous endograft, the inflammation does not subside and may accelerate. Consequently, the risk of cardiovascular events may increase due to the ongoing inflammatory response. However, EVAS utilizes active sac management to completely seal with the EndoBags and exclude the aneurysm sac. As a result, this seal may reduce the wall stress on the aneurysm sac and blunt the inflammatory response and cardiovascular risk.

Despite the potential risk associated with ChEVAS, it also offers distinct potential benefits over currently available standard treatments for complex AAA, including open surgical repair, fEVAR, and ChEVAR. As such, there is adequate justification to initiate a study to further evaluate the risks and benefits of ChEVAS.

3 OBJECTIVES AND ENDPOINTS

3.1 1-MONTH PRIMARY ENDPOINT

The primary 1-month endpoint is defined in terms of an event rate, and includes technical failure and any of the following:

- *Severe Bowel Ischemia* – lack of adequate blood flow to the intestines leading to surgical/endovascular intervention or death and reported within 30 days of the index procedure
- *Permanent Paraplegia/Paraparesis*- event reported within 30 days of the index procedure without resolution at 30 days post-procedure
- *Renal Failure* – new onset renal failure requiring dialysis that remains on-going at 30 days post-procedure
- *Disabling Stroke* – new neurological deficit resulting from vascular insult reported within 30 days of the index procedure without resolution at 6 months post-procedure. Disabling is considered a value of 2 (slight disability) or above on the modified Rankin Scale (mRS) at both the 1-month and 6-month visits.
- *Abdominal Aortic Aneurysm Rupture* - Intraoperative and Post-procedural rupture through the aneurysm wall within the stented segment of the aorta reported within 30 days of the index procedure.
- *Aneurysm-related mortality* - death reported within 30 days of the index endovascular procedure

The technical success component of the endpoint (counterpart to technical failure) is defined as:

a. Successful access and delivery of all ChEVAS components (i.e., ability to deliver each component to the intended location, without the need for unanticipated corrective intervention related to delivery);
b. Successful and accurate deployment, defined as:
    i. Deployment of the Nellix stent-grafts, Ovation limbs, and chimney(s) in the planned location;
    ii. Patency of the Nellix stent-grafts, Ovation limbs, and chimney(s) with absence of device deformations (e.g., kinks[1], mal-deployment[2], misaligned deployment[3]) requiring unplanned placement of an additional device within the endovascular stent-grafts or chimney(s);
    iii. Adequate seal without the need for unanticipated corrective interventions[4]. No use of components outside the defined ChEVAS System for the purpose of achieving seal. The use of adjunctive stenting for purposes outside of achieving seal or use

[1] Defined as a focal narrowing of the stent lumen of >50%, with concurrent stent wall deformation at that location.

[2] Defined as concluding the procedure without having all components of the ChEVAS System successfully deployed.

[3] Defined as, at the conclusion of the procedure, a > 10mm difference between the top of the Nellix stents, or the top of a visceral stent being > 14mm below the Nellix stent (the bag shelf is 4mm below the top of the Nellix stents).

[4] Concomitant procedures, including those for infrequently encountered circumstances, may be anticipated and prepared for as part of a comprehensive endovascular approach

of adjunctive stents that are part of the defined system, does not result in technical failure.[5]

c. Successful withdrawal (i.e., successful withdrawal of the delivery systems without the need for unanticipated corrective intervention related to withdrawal).

Multiple events occurring to a subject are considered a single subject failure for the purposes of calculating the composite one-month rate, as the rate is based on the total number of subjects. Since none of these variables are restricted by imaging requirements for detection, the cutoff date for the endpoint is exactly 30 days from the index procedure.

3.2 1-YEAR PRIMARY ENDPOINT

The primary 1-year endpoint is a blend of safety and effectiveness indicators. The endpoint is defined as the absence of:

- Abdominal aortic aneurysm rupture (0 - 365 days);
- Aneurysm-related mortality (0 – 365 days)
- Imaging-determined events at the 12-month imaging window. These do not require an intervention within 12 months to count as events:
  - Type I or Type III endoleak
  - Migration[6] > 10mm
  - Sac Expansion[7] > 5mm
  - Loss of Patency (100% occlusion) in Branches[8], Nellix, or iliac limbs not seen at the index procedure
- Open conversion through day 365

[5] Examples of acceptable procedures include:

- Placing an additional stent (Verta or Lifestent) to correct kink in visceral vessel (or a kink in the stent resulting from the vessel anatomy) or to smooth transition from Verta to visceral vessel (transition stenting)
- Placing an additional stent (Verta or Lifestent to treat pre-existing visceral artery stenosis (spot stenting)
- Placing Verta stent within initial Verta stent due to length discrepancy, need to achieve a Verta length not covered by available lengths, or inadequate initial seal
- Placing Ovation limb to extend Nellix in order to obtain an adequate distal seal;
- Coiling of non-treated branch vessels
- Ballooning of any vessel or stent

[6] As measured by the proximal end of the Nellix stents relative to the reference artery
[7] As measured across the maximum transverse sac diameter relative to the 1-month scan
[8] Branches refer to stents in the left renal artery, right renal artery, and superior mesenteric artery

- Other major device-related[9] surgical or endovascular re-interventions through day 365 for:
    - Type I or III endoleak, or gutters
    - Migration
    - Thrombotic events/Occlusions - complete loss of patency in any of the components of the ChEVAS System due to thrombotic events and/or device deformation
    - Device deformation resulting from fracture, that leads to clinical sequelae of vessel stenosis progressing to decreased perfusion, or puncturing of graft material leading to endoleak
    - Relining of the Nellix Stents to correct stenosis or kink
    - Mal-deployed device that leads to clinical sequelae of migration, endoleak, or thrombosis
    - Device infection

Non-major interventions are not included in the endpoint:

- Endovascular intervention for branch stenosis (within the stent or distal to the stent) for a reason other than stent fracture
- Interventions for Type II endoleaks
- Non endovascular treatments for procedural complications that are non-device specific, e.g., seroma, surgical site infection etc.

The 1-year endpoint is a collection of variables that may be detected at any time or require imaging to be detected. As such, variables are evaluated differently for the "1-year" timeframe. Variables lacking imaging restrictions (rupture, mortality, interventions) are evaluated until day 365 for the 1-year endpoint as the exact day of the event will be known. Onset dates for imaging-driven variables are unknown (they have may occurred at any time prior to the imaging scan that detected them) and thus are evaluated at the one-year imaging window as determined by the scan date. Presence of positive imaging-related findings within the 1-month or 6-month imaging windows does not factor into the endpoint analysis. Rather, the endpoint analysis restricts positive findings to only those within the 1-year imaging window. Imaging results used in the endpoint analysis will be sourced from core lab assessments.

In contrast to classic EVAR studies that analyze safety at 1 month and effectiveness at 1 year, the ChEVAS study is designed to evaluate both safety and effectiveness across dual endpoints (thus, passing both endpoints will indicate the trial has demonstrated safety and effectiveness).

[9] Device refers to main Nellix EndoVascular Aneurysm Sealing System (Nellix System), Verta Self-Expanding Stent Graft and Ovation iX iliac Limbs/Extensions

3.3 ADDITIONAL MEASUREMENTS

3.3.1 DEMOGRAPHICS

- Age (years) at time of implant
- Gender
- Race (% Caucasian)
- Height (cm)
- Weight (kg)
- Calculated body mass index (BMI)
- ASA class
- Serum Creatinine (mg/dL)
- Calculated eGFR (mL/min/m^2)
- Aneurysm and vascular characteristics (Assessed by Core Lab)

3.3.2 MEDICAL HISTORY

- Medication types
- Arrhythmia
- Angina
- CHF
- Hypertension
- Coronary artery disease
- Heart valve disease
- Peripheral arterial occlusive disease
- Cerebrovascular accident
- Myocardial infarction (MI)
- Thoracic aortic aneurysm
- Prior abdominal surgery
- Prior aortic valve repair or replacement
- Prior coronary artery bypass grafting (CABG)
- Pacemaker or implantable cardioverter-defibrillator (ICD)
- Percutaneous coronary intervention
- Family history of Abdominal Aortic Aneurysm (AAA)
- Cancer
- Chronic obstructive pulmonary disease
- Coagulopathy or bleeding disorder
- Diabetes
- Hyperlipidemia
- Hypercholesterolemia
- Liver disease
- Paraplegia
- Renal insufficiency

- Smoking

Pertinent current medication categories are recorded and will be summarized:

- Aspirin
- Antiplatelet meds not including aspirin
- Anticoagulants (with Vitamin K antagonists noted)
- Anti-hypertensives (with calcium channel blockers and ACE-I noted)
- Statins
- Analgesics

3.3.3 PROCEDURAL AND IN-HOSPITAL EVALUATIONS

- Blood Pressure at index hospitalization (mmHg)
- Anesthesia type (n, %: general, regional, or local)
- Vascular access type (n, %: i.e. bilateral percutaneous, bilateral femoral exposure, or unilateral percutaneous), vascular access for branch stents.
- Volume of contrast media used (mL)
- Visceral vessels implanted
- Access arteries utilized
- Estimated blood loss (mL)
- Fluoroscopy time (min)
- Catheter time (min)
- Polymer fill volume (mL)
- Polymer fill pressure (mmHg)
- Adjunctive device placement (n, %: proximal or distal, and by type of device)
- Subjects requiring blood transfusion (n, %)
- Total procedure time (min)
- Anesthesia time (min)
- Concomitant procedures (n, %: iliac conduit placement, iliac endarterectomy, fem-fem bypass, vascular patch repair, etc.)
- Time in ICU (days)
- Time to hospital discharge (days)

3.3.4 OUTCOMES

Additional outcomes will be collected for each follow-up time point through 5 years post procedure.
All outcomes will be differentiated, where appropriate, by the stents involved (Nellix vs. Verta stents)

- Mortality (all-cause and aneurysm-related)
- MAE Individual Components
- Aneurysm Rupture
- Conversion to Open Repair
- Adverse Events
- Renal Function (assessed via creatinine and eGFR)
- All Types of Endoleak (Ia, Ib, Ic, II, III, IV, or unknown)

- Gutters
- Device Patency and Integrity
  - Stenosis
  - Occlusion
  - Kinking
  - Fracture
- Aneurysm Sac Diameter
- Migration (e.g., migration > 5 mm, migration > 10 mm, clinically significant migration)
- Secondary Procedures
  - All Types of Endoleaks
  - Device stenosis/occlusion
  - Device kink
  - Device fracture
  - Luminal thrombus
  - Rupture
  - Migration
  - Aneurysm sac expansion
  - Device defect
  - Gutters

4 STUDY DESIGN

4.1 OVERALL DESIGN

This is a prospective multicenter study with consecutive eligible subject enrollment at each site. Enrollment will include up to 150 subjects (120 ChEVAS subjects and up to 30 infrarenal roll-in subjects) at a maximum of 50 sites. A maximum of 15 sites among those 50 may be outside of the United States (OUS). A maximum of 50% of the subjects in the analysis cohort may be from OUS sites. These OUS sites will leverage a harmonized protocol and will be pooled with the data from the sites in the United States to reach the required sample size of 120 ChEVAS subjects.

The trial will consist of three (3) cohorts. The infrarenal Roll-In cohort consists of the first one (1) infrarenal subject enrolled at sites where the investigator has no prior EVAS treatment experience. The ChEVAS Roll-In cohort consists of one (1) subject and will be enrolled at sites where the investigator has no prior ChEVAS treatment experience. The ChEVAS Pivotal cohort consists of all ChEVAS cases subsequently implanted. Among the ChEVAS Pivotal and Roll-In cohorts, a single site may not enroll more than 20% of the total enrollment.
Thus, three distinct cohorts are included in this study:

- Infrarenal Roll-In Cohort: This is comprised of the first one (1) infrarenal EVAS subject enrolled at a site if EVAS cases have not been performed prior. These cases are intended to be reported with the EVAS2 study (CP-0008) and will not be analyzed as part of the endpoint for the ChEVAS study. Sites will follow the EVAS infrarenal Roll-In protocol (**Appendix 1**) for inclusion/exclusion purposes.

- ChEVAS Roll-In Cohort: This consists of the first one (1) ChEVAS subject enrolled at a site when the investigator has no prior ChEVAS[10] treatment experience. Please note only certain OUS sites will have prior ChEVAS experience.
- ChEVAS Pivotal Cohort: If a site has previously performed a ChEVAS case (whether as part of the study or not) then subsequent cases are considered Pivotal subjects.

The Pivotal and Roll-In ChEVAS cohorts will be combined to reach the sample size of 120 subjects for analysis of the primary endpoints.

A subject is enrolled into the trial at the point where one of the ChEVAS System catheters is inserted into the subject. All enrolled ChEVAS subjects will undergo the endovascular aneurysm repair procedure with the Nellix System, Verta stent grafts, and Ovation iX iliac limb extensions when needed. Subjects will be followed procedurally to discharge, at 30 days (primary 30-day endpoint), six months, one year (primary 1-year endpoint), and annually thereafter to five years (total follow-up commitment). These are the required follow-up imaging and visits of the study, though all subjects should be monitored and evaluated per instructions for use, standardized protocols, and institutional standards of care for patients who receive an endovascular stent graft, as long as the required follow-up (imaging and visits) within this protocol are followed.

The Primary analysis will be conducted on the implanted population within the ChEVAS Roll-In and Pivotal cohorts. A subpopulation is the per-protocol population, consisting of subjects that have an implanted device, and have not violated the anatomical or procedural IFU criteria. Standardized training and baseline imaging review should prevent the enrollment of subjects who would be considered off protocol. The primary 1-year (i.e. late) endpoint requires evaluable subjects, so completed cases (subjects who have enough information to be evaluated at 1 year) comprise an additional way to stratify the population. ChEVAS Roll-In subjects may be evaluated as a separate group for investigational purposes. The analysis is only meant to provide information as to the presence and extent of a learning curve and makes no impact to the method that will be utilized to evaluate the primary study endpoints. Subjects who initially consent but then withdraw prior to the procedure will not be included in any analysis.

An external Core Lab will be used for this study. The Core Lab will be responsible for reading both screening and follow-up scans provided by the sites. Their findings and measurements will be recorded into the Electronic Data Capture (EDC) system. The results from the Core Lab will be used in the assessment for device-related findings, including endoleaks, aneurysm enlargement, gutters, kinking, and stent fractures. Occlusion will be primarily reported by the site due to a clinical finding (e.g., claudication) and confirmed via angiogram with the subject in the operating theater (i.e., utilizing CT scan results would under-report this event).

[10] Secondary ChEVAS does not count as prior ChEVAS experience

4.2 END OF STUDY DEFINITION

A clinical trial is considered completed when the last participant's last study visit has occurred or the final subjects have reached the end of the 5-year window with no follow-up (which would count as a missed visit). Any subject who passes the end of the 5-year follow-up window may be exited from the trial with appropriate documentation shows diligence on the part of the site to bring the subject in for their visit within window.

A subject has completed the trial after the Year 5 visit has been completed and all protocol required data has been collected.

A subject may withdraw consent at any time. At the discretion of the Investigator, the subject may be exited from the trial at any time with required documentation.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. Adults at least 18 years old;
2. Subject provided informed consent;
3. Subject agrees to all follow-up visits;
4. Abdominal aortic aneurysm (AAA) with maximum sac diameter ≥5.0cm, or ≥ 4.5 cm which has increased by ≥0.5cm within the last 6-months, or which exceeds 1.5 times the transverse dimension of an adjacent non-aneurysmal aortic segment. No AAA <4 cm will be included;
5. Adequate iliac/femoral access compatible with the required delivery systems
6. Aneurysm blood lumen diameter ≤60mm;
7. Proximal non-aneurysmal aortic neck: length[11] ≥15mm; diameter[12] 19 to 29mm for one visceral vessel repair, 19-30mm for two visceral vessels repair, 22-31mm for three visceral vessels repair; angle (β) ≤60° to the aneurysm sac;
8. Absence of significant cranial angulation of the visceral vessels that would preclude vessel cannulation and stenting
9. Proximal end of target landing zone to each hypogastric artery length ≥100mm;
10. Proximal end of target landing zone to the bifurcation length ≤185mm;
11. Renal artery diameter 5-9mm (if targeted to be stented);
12. Superior mesenteric artery diameter 5-9mm (if targeted to be stented);
13. Common iliac artery lumen diameter between 9 and 35mm outside the distal seal zone;
14. Distal iliac artery seal zone with length of ≥10mm and diameter[13] range of 9 to 25mm;
15. Ability to preserve at least one hypogastric artery;

[11] The length from the proximal end of target landing zone to a point distally where the inner vessel wall to wall diameter increase is 10% and within the proximal neck diameter range. The proximal end of target landing zone is below the celiac for SMA and bilateral renal arteries repair, below the SMA for bilateral renal arteries repair, and below the proximal renal artery for distal renal artery repair.

[12] The proximal non-aneurysmal aortic neck diameter is determined by inner vessel wall to wall measurement.

[13] The inner vessel wall to wall diameter of the iliac artery at the intended sealing zone.

16. Ratio of maximum aortic aneurysm diameter to maximum aortic blood lumen diameter <1.40.
17. Suitable anatomy of the thoracic aorta and great vessels allowing for upper extremity access to the visceral vessels;
18. Suitable anatomy of the paravisceral segment of the abdominal aorta allowing for visceral vessel cannulation and stent implantation.

5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Life expectancy <2 years as judged by the Investigator;
2. Requirement of home oxygen;
3. Psychiatric or other condition that may interfere with the study;
4. Participating in another clinical drug and/or device study, which could confound the results of this study (patient must have completed the primary endpoint of any previous study at least 30 days prior to enrollment in this study);
5. Known allergy or contraindication to any device material, contrast, or anticoagulants;
6. Body habitus or other medical condition which prevents adequate fluoroscopic and CT visualization of the aorta;
7. Systemic infection which may increase risk of endovascular graft infection;
8. Coagulopathy or uncontrolled bleeding disorder;
9. Ruptured, leaking or mycotic aneurysm;
10. Serum creatinine level >1.8mg/dL;
11. CVA or MI within three months of enrollment/treatment;
12. Aneurysmal disease of the descending thoracic aorta;
13. Prior renal transplant;
14. Prior stent in any target visceral vessel, the aorta or iliac artery that may interfere with delivery system introduction or stent placement;
15. Significant occlusive disease (stenosis >75%), calcification, or tortuosity of visceral vessels (if stented);
16. Significant mural thrombus and/or calcification within the proximal landing zone of the non-aneurysmal neck that can compromise the seal;
17. Landing zone in any visceral vessel[14] < 10mm (if stented)
18. Connective tissue diseases (e.g., Marfan Syndrome);
19. Unsuitable vascular anatomy that may interfere with device introduction or deployment;
20. Pregnant, planning to become pregnant within 60 months, or breastfeeding.

5.3 SCREEN FAILURES

Candidates who are consented to the trial, meet inclusion criteria, and do not meet any exclusion criteria will be considered a potential study subject. Subjects may be screen failed from the trial for any reason during the screening process. A subject is not considered enrolled until a ChEVAS System catheter is inserted in the subject. Once enrolled, subjects will be followed according to this protocol. The reasons for screen failures and all study exits must be reported on the case report form.

[14] Landing zone is defined as the segment of a visceral vessel to be stented that does not include a significant branch artery

6 STUDY INTERVENTION

6.1 CHEVAS SYSTEM OVERVIEW

6.1.1 CHEVAS SYSTEM DESCRIPTION

The Nellix EndoVascular Aneurysm Sealing System (Nellix System) is intended to be an alternative to open repair and endovascular aneurysm repair (EVAR) for suitable patients with an abdominal aortic aneurysm (AAA). The concept is based on providing an implant that seals the aneurysm sac, spanning from the infrarenal segment to the distal iliac segment and filling the blood lumen space (**Figure 8**). This concept is translated into dual balloon-expandable covered stents with surrounding EndoBags that are filled with a biostable polymer solution that cures *in-situ* in <10 minutes. The stent lumens form the new blood lumens to the distal limbs. Because the polymer is a fluid having the viscosity similar to water upon mixing, the polymer-filled EndoBags conform to the aneurysmal blood lumen. Upon curing, the solidified polymer within the EndoBags exclude the aneurysm from blood flow, preventing aneurysm pressurization and rupture.

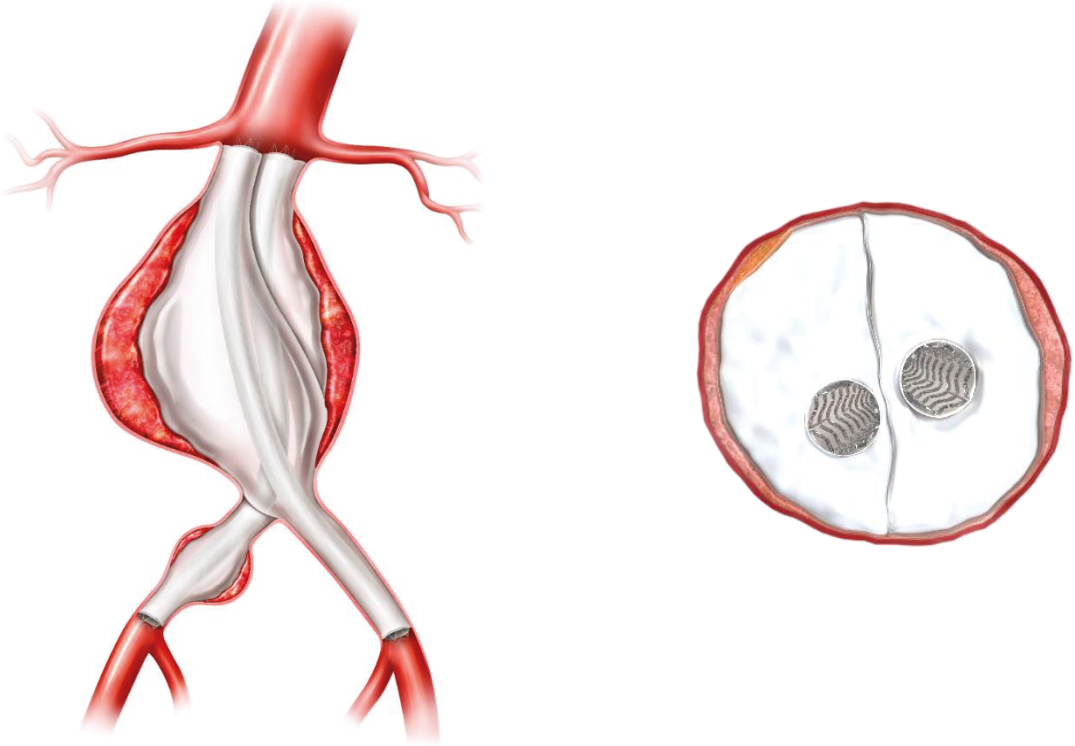

FIGURE 8: NELLIX SYSTEM

The Chimney EndoVascular Aneurysm Sealing (ChEVAS) procedure expands on the mode of action of the Nellix System in conjunction with parallel branch stents for the treatment of juxtarenal, pararenal, or paravisceral abdominal aortic aneurysms. The procedure requires bi-lateral placement of the Nellix stent grafts in conjunction with deployment of branch stents in the renal arteries and potentially the Superior Mesenteric Artery (SMA) through upper extremity access. One, two, or three arteries may need to be stented during the treatment to provide adequate aneurysm exclusion while maintaining patency of the visceral

arteries. The Nellix EndoBags are then filled with polymer, which conforms around the branch stents and aortic vessel wall, thereby creating a seal to exclude blood flow to the aneurysm sac. The Nellix stents form lumens through which blood flows to the distal limbs and vasculature and the branch stents maintain blood flow to the visceral arteries. The EndoBags with cured polymer exclude the aneurysm from blood flow, preventing aneurysm pressurization and rupture. This seals the entire anatomy from the proximal end of target landing zone to the iliac arteries with a distal seal zone (**Figure 9**).

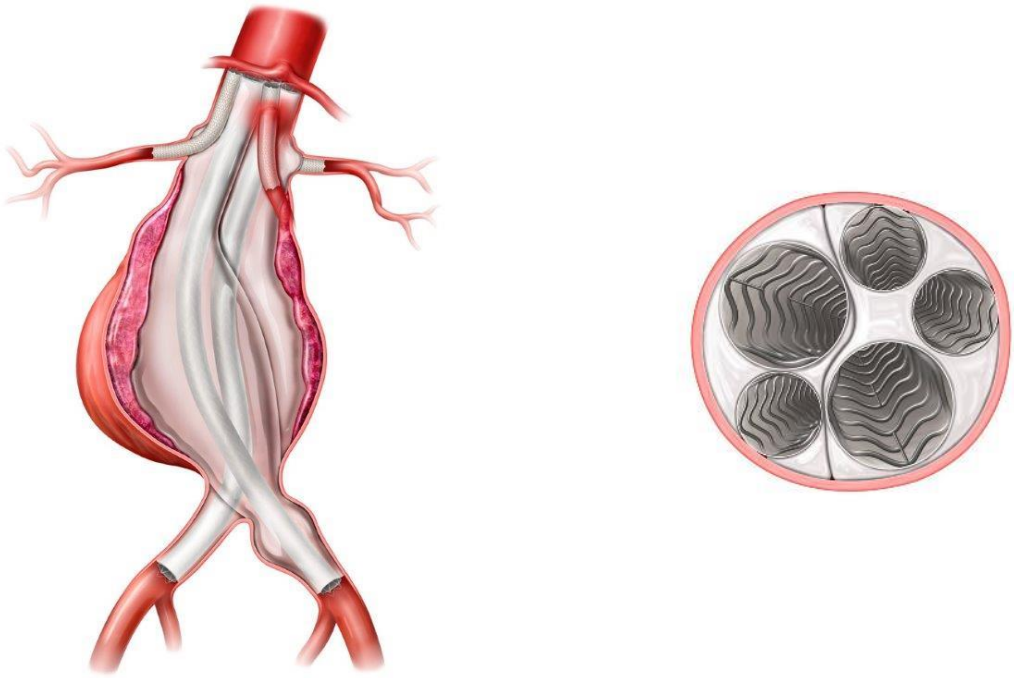

FIGURE 9: CHEVAS SYSTEM[15] WITH BRANCH STENTS IN A 3-VESSEL REPAIR

The Nellix System is identical to the Nellix System currently approved in the EVAS2 study via G130005/S020 and G130005/S030. There are no changes required to the design or components of the Nellix System for use as part of the ChEVAS System.

The ChEVAS System consists of the following components:

- Nellix EndoVascular Aneurysm Sealing System (Nellix System)
- Ovation iX Iliac Limb and Iliac Extension Stent Grafts (as needed)
- Verta Self-Expanding Branch Stent Graft System (Verta System)

Each of these are discussed in further detail in the subsequent sections.
Additionally, optional adjunctive stents may be used, as described in Section 6.5 below.

6.2 NELLIX SYSTEM

[15] Note: Ovation iX Iliac Limb and Iliac Extension Stent Grafts are not pictured in Figure 9.

The Nellix System is identical to the Nellix System currently approved in the EVAS2 study via G130005/S020 and G130005/S030. There are no changes required to the design or components of the Nellix System for use as part of the ChEVAS System.
The Nellix System includes the following components:

1. Nellix 3.5 Delivery System (including the Nellix Implant)
2. Nellix Polymer (Formulation 5.5)
3. Nellix 3.5 Accessory Kit
4. Nellix Polymer Dispenser

The ChEVAS System can be used in patients who have a juxtarenal, pararenal, or paravisceral abdominal aortic or aortoiliac aneurysm (AAA) with suitable anatomy as indicated below:

- Iliac and femoral artery access that allows for atraumatic device introduction.
- Suitable anatomy of the thoracic aorta and great vessels allowing for upper extremity access to the visceral vessels
- Suitable anatomy of the paravisceral segment of the abdominal aorta allowing for visceral vessel cannulation and stent implantation. Absence of significant cranial angulation of the visceral vessels that would preclude vessel cannulation and stenting.
- Proximal non-aneurysm aortic neck diameter range of 19 to 29 mm for one vessel repair, 19 to 30 mm for two vessels repair, and 22-31mm for three vessels repair.
- Proximal non-aneurysmal neck length ≥15 mm
- Proximal neck angulation of ≤60°
- Aortic aneurysm with a blood lumen diameter ≤60 mm
- Ratio of maximum aortic aneurysm diameter to maximum aortic blood lumen diameter <1.40.
- Iliac artery blood lumen diameter range of 9 to 35 mm outside the distal seal zone.
- Distal seal zone with:
  - Length of ≥10 mm and
  - Diameter range of 9 to 25 mm
- Nellix stent length ≥ 15mm into the common iliac artery
- Renal artery diameter range of 5 to 9mm
- Superior mesenteric artery diameter range of 5 to 9mm

6.2.1 NELLIX 3.5 DELIVERY SYSTEM

The Nellix Delivery System (**Figure 10**) consists of a 17Fr nylon balloon catheter with a central guidewire lumen, distal radiopaque angiographic tip (AngioTip), outer sheath with a radiopaque marker, sheath handle, catheter handle with ports and color-coded connectors for attachment to the console (packaged separately in the Accessory kit). Each catheter contains an injection port in the sheath handle for flushing and contrast injection and is compatible with 0.035-inch guidewires.

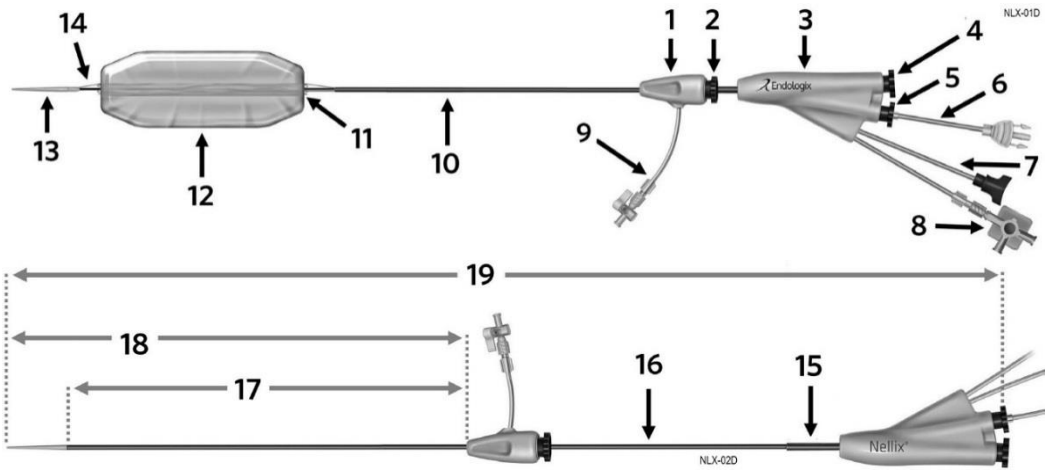

FIGURE 10: NELLIX 3.5 DELIVERY CATHETER

Figure Legend

1. Sheath handle
2. Sheath-handle locking knob
3. Catheter handle
4. Hemostasis valve and guidewire lumen
5. EndoBag fill-line knob
6. EndoBag fill line
7. Stent balloon inflation line
8. Angiographic line with stopcock
9. Sheath-handle angiographic line and flush port
10. Outer sheath, 17 Fr outside diameter (OD)
11. Balloon (shown expanded inside EndoBag)
12. EndoBag (shown expanded)
13. AngioTip
14. Lockwire
15. Sheath stopper
16. Inner core
17. Outer sheath length: 45 cm (nominal)
18. Working length: 50 cm (nominal)
19. Overall length: 99 cm (nominal)

The delivery system is comprised of the following features/sub-assemblies:

- Outer Sheath: The outer sheath has a 17 Fr OD profile and is made from stainless steel braid reinforced PEBAX® with a hydrophilic coating. It is mated with the AngioTip to provide atraumatic delivery through the vasculature. The sheath handle is used to retract the sheath exposing the implant and includes a knob to secure the sheath handle to the delivery system to provide device stability. The sheath injection port allows for device preparation as well as retrograde angiography if desired.
- Angiographic Line: The angiographic central lumen, through which the guidewire passes, and the tip of the catheter are designed to allow contrast medium to be injected through the catheter, proximal of the implant without the need of a separate angiographic catheter to image the aorta near the renal arteries and provide an image of the anatomy.
- Fill Line: The polymer filling system is a coaxial tubing system that is comprised of an outer and inner fill tube. The outer fill tube attaches to the iliac end of the implant and terminates at the handle. The inner fill tube is positioned inside of the outer fill tube with the tip ending inside of the EndoBag and terminating at the handle. The inner lumen is used for the primary filling procedure. The inner fill tube is removed from the device at the end of the procedure before device removal. The outer fill tube provides added support for the inner fill tube and

can be used as a backup line in the event additional polymer filling is desired after the initial bolus of polymer is already cured. This lumen can be accessed once the inner fill tube is removed.

- Lockwire: The lockwire is a stainless-steel wire that tethers the implant to the catheter during deployment. The lockwire tethers the implant to the catheter on the proximal and distal end of the implant and terminates proximally at the Angio Tip and distally at the handle. The lockwire releases the implant from the catheter when the physician completes primary filling and removes the inner fill tube.

The Nellix Implant consists of a stent and EndoBag. The stent (**Figure 11**) is a cobalt chromium (CoCr) alloy balloon-expandable stent with a high density expanded polytetrafluoroethylene (ePTFE) graft cover attached at both ends of the stent with polypropylene sutures.

FIGURE 11: NELLIX STENT SHOWN AFTER EXPANSION

The EndoBag (**Figure 12**) is formed with polyurethane film with a contained inner polyester sleeve and is attached to the stent proximally and distally using polyethylene sutures. The Nellix implant is pre-mounted onto the balloon catheter and is tethered to the Nellix Delivery System. Nellix implants are available in stent lengths of 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, or 200 mm having a nominal deployed lumen diameter of 10 mm.

FIGURE 12: ENDOBAG

6.2.2 NELLIX POLYMER (FORMULATION 5.5)

The Nellix Polymer (Formulation 5.5) is contained in a 40mL (NP-002) or 70mL (NP-004) dual chamber polypropylene cartridge (**Figure 13**) filled with aqueous polyethylene glycol-based solutions that are designed to be mixed (using the mixer) at the time of the procedure and cure *in-situ* in approximately 3 to 5 minutes after injection into the EndoBags to form a solid, biostable polymer. The polymer cartridge must be stored frozen (-40 °C to -20 °C) until ready for use. Prior to use, the cartridge must be thawed at room temperature. The thawed cartridge is loaded onto the dispenser and the mixer is attached to permit injection of polymer through the pressure transducer and console.

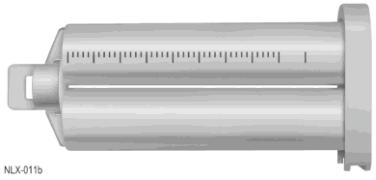

FIGURE 13: POLYMER CARTRIDGE

6.2.3 NELLIX 3.5 ACCESSORY KIT

The Nellix Accessory Kit contains a console, two reciprocal connectors with caps, four mixers, two rotating male-to-male connectors and a pressure transducer. The console (**Figure 14**) contains two identical sets of color-coded snap and luer connectors for attachment to the mating connectors on the two selected Nellix® Delivery Systems at the time of use. The white console snap connectors denote the polymer fill lines and are to be attached to each mating white connector on the two Nellix Delivery Systems. The polymer fill line white snap connectors are reversed for safety to ensure that they can only be connected to the white polymer connectors on the Nellix Delivery System. The black console snap connectors denote the balloon inflation lines and are to be attached to each mating black connector on the two Nellix Delivery Systems. The luer connectors denote the console angiographic contrast medium injection lines and are to be attached to each mating luer connector on the two Nellix Delivery Systems.

The console packaging includes reciprocal connectors with caps to close the lines on one side of the console in the event that only one side of the console is used. The console contains labeled ports that aid in the procedural steps:

- STENT port: To balloon-expand the two stents
- ENDOBAG port: To evacuate the two EndoBags, inject saline for the saline pre-fill step under pressure monitoring, and inject polymer solution to fill both EndoBags under pressure monitoring
- ANGIO port: To inject contrast agent to facilitate angiographic imaging using a Power Injector (the line is rated to 1050 psi)

The mixer attaches to the polymer dual chamber cartridge and mixes the two-part polymer solution in-line while transferring it through the pressure transducer to the console (**Figure 15**).
The Pressure Transducer is a disposable device that displays pressure in units of mmHg. The pressure transducer is intended for attachment between the console and the mixer/polymer cartridge to enable monitoring of pressure during injection of pre-fill non-heparinized saline and subsequently of polymer into the EndoBags (**Figure 15**). Refer to the manufacturer's instructions for use for further information on proper use.

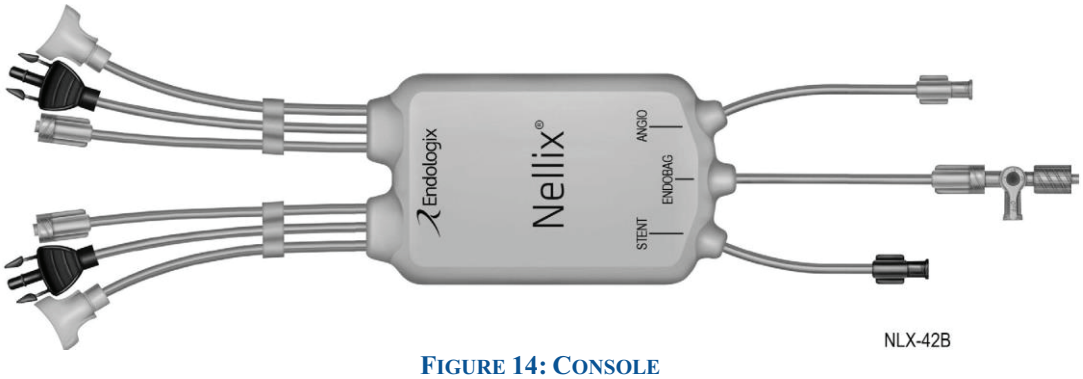

FIGURE 14: CONSOLE

MIXER | MALE TO MALE ADAPTOR | RECIPROCAL CONNECTORS | PRESSURE TRANSDUCER

FIGURE 15: ACCESSORIES

6.2.4 NELLIX POLYMER DISPENSER

The Nellix Polymer Dispenser is a hand-held, re-useable (NP-001 or NP-003) or disposable (NP-005) device intended to actuate delivery of the mixed polymer solution at the time of use (**Figure 16**).

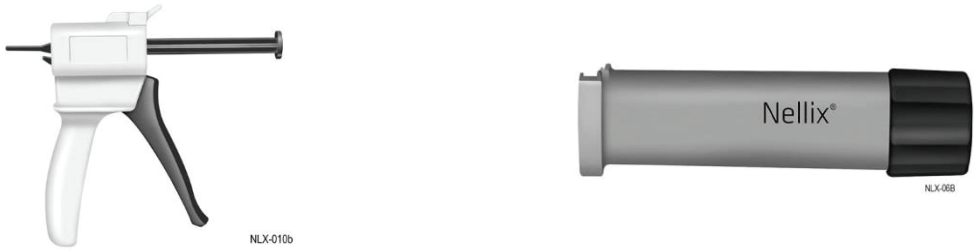

FIGURE 16: REUSABLE DISPENSER (LEFT) AND DISPOSABLE DISPENSER (RIGHT)

6.3 OVATION IX ILIAC STENT GRAFTS

The Endologix Ovation iX Iliac Limb and Iliac Extension Stent Grafts (Ovation iX Iliac Stent Grafts) used in the ChEVAS System are identical to the commercially available Ovation iX Iliac Stent Grafts currently approved via P120006/S015. No changes were required to the Ovation iX Iliac Limb and Extender Stent Grafts or delivery system for use as part of the ChEVAS System. The Ovation iX Iliac Stent Grafts are used to establish or re-establish the distal seal zone by being deployed into the leg sections of the Nellix Implant. Similarly, the iliac extensions are deployed into the iliac limbs.

The Ovation iX Iliac Limb Stent Grafts (**Figure 17**) are available in straight, flared, and tapered configurations and the Ovation iX Iliac Extension Stent Grafts are available only in a straight configuration. The Ovation iX Iliac Stent Grafts are comprised of a Nitinol stent encapsulated in low-permeability PTFE. The Ovation iX Iliac Stent Grafts are manufactured from polished Nitinol wire and shape set into a sinusoidal pattern superimposed on a helix. The PTFE covering is laminated on both sides of the Nitinol stent. Furthermore, the stent grafts contain radiopaque markers, which enable the physician to visualize both the proximal and the distal ends of the stent grafts.

FIGURE 17: OVATION IX ILIAC LIMB (LEFT) AND EXTENSION (RIGHT)

The Ovation iX Iliac Stent Graft Delivery Catheter (**Figure 18**) is used to position and deploy the Ovation iX Iliac Limb Stent Graft within the Nellix implant and the Iliac Extension within the Iliac Limb, if needed. The Ovation iX Iliac Stent Grafts are constrained over a central guidewire lumen by an integral introducer sheath. The sheath is retracted to deploy the stent graft. After deployment, the delivery system chassis is retracted through the integral introducer sheath.

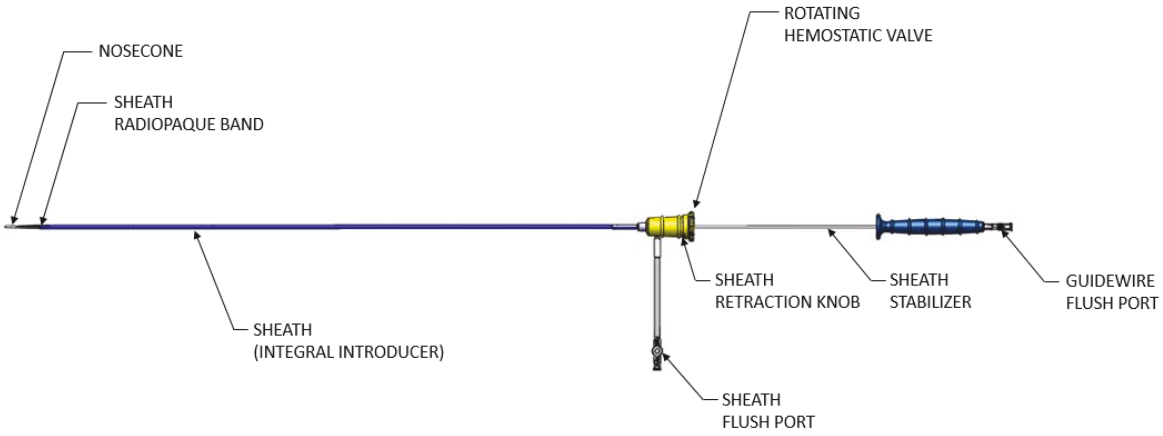

FIGURE 18: OVATION IX ILIAC STENT GRAFT DELIVERY CATHETER

6.4 VERTA SELF-EXPANDING STENT GRAFT SYSTEM

The Verta Self-Expanding Branch Stent Graft System is manufactured for Endologix by Bard Peripheral Vascular, Inc. (Tempe, Arizona; establishment registration number 2020394) and is intended for use solely with the Nellix System in a ChEVAS procedure. Bard Peripheral Vascular, Inc. (BPV) will be the contract manufacturer for the device and is responsible for manufacture, sterilization, labels, and shipping of the device to Endologix. Endologix will receive a finished device from BPV and will not subject the device to any additional processing prior to shipping the device to the investigational sites.

As described in §**6.1.1** above, the ChEVAS procedure utilizes the chimney parallel graft technique in order to treat juxtarenal, pararenal, or paravisceral aneurysms. The Verta Self-Expanding Branch Stent Grafts (Verta Stent Graft) are implanted in renal arteries and potentially the SMA, such that the proximal end of

the Verta Stent Graft is parallel to the two Nellix stents in the aorta and the distal end is at least 10mm into the intended visceral artery. The polymer-filled EndoBags conform around the Nellix and Verta stents to seal the aneurysm while maintaining blood flow to the visceral and iliac arteries.
The Verta Stent Graft is a flexible, self-expanding Nitinol stent encapsulated within two layers of ePTFE, the inner (i.e., blood contacting) of which is carbon impregnated. Stent graft diameters range from 6mm to 10mm and the stent graft lengths range from 30mm to 100mm. Each end of the stent graft (**Figure 19**) has six radiopaque tantalum markers.

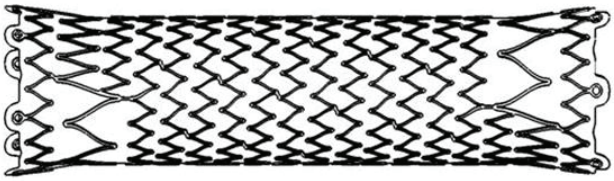

FIGURE 19: VERTA SELF-EXPANDING BRANCH STENT GRAFT

The Verta stent graft is compressed between the inner catheter and the stent graft sheath at the distal end of the delivery system (**Figure 20**). The delivery system is an over-the-wire delivery system compatible with 8Fr and 9Fr introducer sheaths, depending on stent graft size, and compatible with 0.035-inch guide wires. The delivery system handle has a deployment mechanism offering two deployment options. The Big Thumbwheel allows for slower deployment of the stent graft for better placement control at the beginning of deployment and the Small Thumbwheel allows for faster deployment of the stent graft once the distal end engages the vasculature. Furthermore, a Safe Lock Slider is included to prevent premature release of the stent graft; the Safe Lock Slider must be unlocked before device deployment.

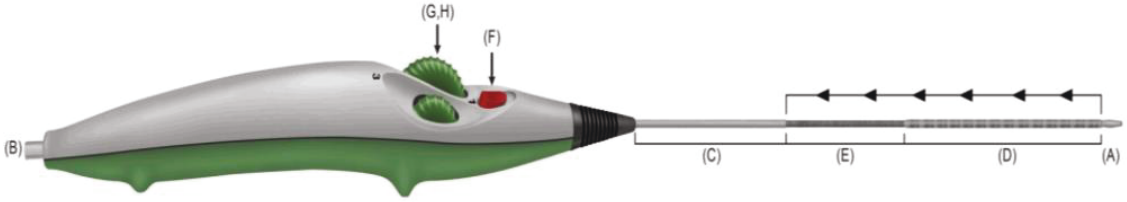

FIGURE 20: VERTA SELF-EXPANDING BRANCH STENT GRAFT DELIVERY SYSTEM

Legend:

A: Atraumatic Tip
B: Guidewire Lumen with Luer Connector
C: Stability Sheath
D: Stent Delivery Sheath
E: Catheter Shaft
F: Safe Lock Slider
G: Big Thumbwheel
H: Small Thumbwheel

The Verta Self-Expanding Branch Stent Graft System is identical to the Covera Vascular Covered Stents (Covera) which has been approved for treatment of stenoses at the venous anastomosis of ePTFE or other synthetic arterio-venous (AV) access grafts under P170042. The only difference between the Verta and the Covera devices are the final labeling of the device and that the Verta device is shipped to Endologix for inclusion as part of the ChEVAS System.

6.5 ADJUNCTIVE STENTS

During treatment of complex aneurysms, the primary clinical objective of the ChEVAS procedure is to seal the aneurysm from blood flow and prevent subsequent rupture; however, the use of additional stents in the visceral arteries may be required to treat common clinical situations that arise within the visceral arteries unrelated to aneurysm exclusion. In the event an additional stent is required, the Verta Stent Graft or the LifeStent Vascular Stent may be used at the physician's discretion based upon positive clinical experience, standard clinical use, and reported benefit to customize patient's treatment.

6.6 PREPARATION/HANDLING/STORAGE/ACCOUNTABILITY

6.6.1 ACQUISITION AND ACCOUNTABILITY

Investigators, or designated personnel, will be responsible for maintaining accurate, complete and current records pertaining to device accountability for any investigational product sent to the site. Device accountability will be tracked for reporting purposes by the sponsor.

The investigational components that will require accountability are the following:

- The Nellix body stents
- The Verta stents
- The Nellix polymer cartridges
- The Nellix polymer dispenser
- The Nellix console
- The Ovation iX iliac limb/extension stents

6.6.2 PRODUCT STORAGE AND STABILITY

The Nellix and Verta stents will be shipped on a case-by-case basis. These must be stored in a secure location. Any unused product must be returned to Endologix. Shipped and returned catheters must be recorded by the site.

The polymer will be shipped to the site on a case by case basis. The polymer will be required to be kept between -40°C and -20°C. This will be delivered in a special packaging that will include a regulator/indicator to ensure adequate temperature during transport and handling. The Case Specialist that will be at the site will have the key and/or combination to the lock on this case. It is important that you remember to log the polymer on the device accountability log (DAL). Unused or remaining polymer may be disposed of per normal hospital protocol (the polymer is non-toxic).

The site will want to inspect the device packaging to verify that no damage has occurred as a result of shipping. If any damage has occurred to the device or the polymer is yellowing, or discolored, do not use the product and contact Endologix immediately.

If needed, the Ovation iX Iliac Stent Graft may be shipped. As with the ChEVAS device system and the polymer, these supplies will arrive STERILE. The site will want to inspect the packaging to verify that there has been no damage as a result of shipping. If there is any damage to the device or the sterility packaging is damaged, contact Endologix immediately.

Any unused investigational devices must be returned to Endologix after completion of the procedure. Waybills for return are included in all packages.

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION

If an attempt is made to insert one of the ChEVAS System catheters into the subject, the subject is considered enrolled. If the procedure is aborted subsequent to the attempted insertion, the case will be considered a technical failure. The subject will be exited from the study after having completed 30 days of follow-up and recording of all adverse events up until 30 days. A 30-day CT on such a subject is not required.

If a subject in Converted to Open Repair at any time during the study, the subject will be exited from the study after 30 days of follow-up post-surgery.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request. The investigator should make it clear to participants that regular follow-up visits are strongly recommended, regardless of study participation, as the subject will still have an implanted investigational device.

An investigator may discontinue or withdraw a participant from the study for the following reasons:

- Significant study intervention non-compliance
- If any clinical adverse event (AE), laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant.

The reason for participant discontinuation or withdrawal from the study will be recorded on the Exit CRFs. Subjects who sign the informed consent form, and receive the study intervention, and subsequently withdraw, or are withdrawn or discontinued from the study, will not be replaced.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to return for 2 scheduled visits and is unable to be contacted by the study site staff.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site will attempt to contact the participant and reschedule the missed visit and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified

letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record or study file.

- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 SCREENING

The site begins the screening process by obtaining informed consent from the patient. The site must ensure they are using the correct IRB approved version of the informed consent and are following their informed consent process. After obtaining informed consent for the patient, the site records the informed consent date in the Electronic Data Capture System (EDC), and then completes the inclusion/exclusion CRF page (this might also involve a serum pregnancy test if the subject is a female of childbearing potential). The site then submits the patient's CTA to the Core Lab, which can be done either electronically, or via mail. The site may now enter the Demographics & Vascular Characteristics (including vitals and serum creatinine) and Medical History information into the EDC.

The Core Lab reviews the CTA for anatomical inclusion/exclusion criteria conformity. If the subject does not pass this step the subject is dropped from further consideration. If the subject passes Core Lab, the subject is referred to the Case Review Board (CRB) for further evaluation.

The CRB reviews the case for overall trial suitability. The CRB may also make procedural recommendations to the Site. If the CRB recommends the subject for the study, the subject is approved for implantation.

Reasons for subject exclusions (Core Lab or CRB), along with any CRB procedural recommendations, will be captured and reported.

8.2 CASE REVIEW BOARD (CRB)

The Case Review Board consists of clinicians in the fields of vascular disease or radiology that have experience in the treatment of subjects with abdominal aortic aneurysm (AAA) and experience with the Nellix device. The CRB will evaluate clinical and anatomical criteria of each subject, as appropriate, and give advice regarding technical aspects of the procedure. The CRB may also recommend/require procedural steps.

8.3 SCHEDULE OF ACTIVITIES

Implantation

The subject is enrolled into the study upon the first attempt to insert the Nellix catheter into the patient. The subject is treated with the ChEVAS System, following the IFU. Procedural data is collected, including concomitant procedures, and device accountability information.

Discharge

Upon discharge of the subject from the hospital, ward stay information is collected, along with creatinine levels, blood pressure, and medications.

Follow-up visits (30 days, 6 months, 1 year, 2 years, 3 years, 4 years, and 5 years)

The site will schedule and conduct a clinical visit with each subject within the required follow-up visit windows (**Table 4**), where vitals will be collected. Required imaging and labs must also be conducted during the required visit window. The required imaging and labs include:

- CT with contrast (CTA), 3mm slice thickness maximum
  - Note: In cases of renal insufficiency, CT without contrast (3mm slice thickness maximum) and a duplex ultrasound may be conducted instead of the CTA
- X-ray (30-day, 1 year, 3 year and 5 year): 2-view abdominal (left and right oblique)
- Serum Creatinine

In addition to imaging, at each follow-up visit, medication categories will be collected, along with Adverse Event collection and assessment

The following table (**Table 4**) shows the required visit schedule. Subjects must have their required scans, visits, and labs completed within the given time frames.

TABLE 4 : VISIT WINDOW SCHEDULE

Visit	Beginning of visit window	Target Day	End of Visit Window
1 Month	16	30	44
6 Month	150	180	210
1 Year	305	365	425
2 Years	640	730	820
3 Years	1005	1095	1185
4 Years	1370	1460	1550
5 Years	1735	1825	1915

8.4 SAFETY AND OTHER ASSESSMENTS

Information collected at the following procedures/evaluations, as applicable:

- **Physical examination** Including weight, blood pressure, medication assessment. If patient exhibits potential neurological change, the patient will undergo an mRS exam for endpoint analysis
- **Blood Laboratory Analysis** Including Serum Creatinine, eGFR (calculated)
- **Contrast-enhanced CT scan:** imaging requirements include slice thickness of ≤3mm; axial, coronary, sagittal views. To ensure consistency, below are the requirements for CT acquisition:
  - Only high resolution, contrast-enhanced spiral CT scans are acceptable. Sites are required to use radiation reduction techniques
  - Data must be uncompressed
  - **Preferred maximum slice spacing is 2mm.** In no case should it exceed 3mm
  - The preferred protocol, shown below, is easier to attain with a multi-row scanner. If the preferred protocol cannot be used, an alternate protocol is provided.
  - Instruct patient not to move during scan. Do not move table height, position, or field of view during scan. If such movement occurs, repeat scan in its entirety.

Parameter	Preferred	Alternate
Scan Mode	Helical/Spiral	
Scan Parameters	140kVp, Auto mA, 0.5sec	140kVp, 280mA (min), 1.0sec
Collimation	0.625 to 2mm	3mm
Slice Spacing	0.625 to 2mm	3mm
Superior Extent	Cervical Spine – C2 or base of ears	
Inferior Extent	Lesser trochanter of femur	
Patient Instruction	Single breath hold	1st hold: above celiac to bifurcation 2nd hold: bifurcation to lesser trochanter
Contrast*	Standard non-ionic	
Volume and Rate	150mL at 3 to 4 mL/sec or as per institutional standards	
Scan Delay	ROI - threshold 90Hu in aorta	
Field of View	Large body	
Window Level	400/40	

*For those subjects with renal insufficiency, a non-contrast CT and duplex ultrasound will be acceptable.

- **Procedural Information:** The Index Procedure CRF will capture all relevant procedural data including access times and types, anesthesia type, all devices implanted, any adjunctive devices used, timing of procedural events, post-procedural findings, complications and concomitant procedures performed, blood loss, contrast volume, fluoroscopy time and any observations on the procedure
- **Adverse Events:** these will be captured at any point after enrollment until study exit. This is determined by the time the patient enters the operating room or catheter lab.
- **Assessment of adverse events.** All reported adverse events will be reviewed and assessed by the Endologix Safety team.

8.5 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

Adverse events will be entered on the applicable eCRF and in the patient's corresponding binder. The date of onset, classification, coding, outcome, severity, device and procedure relationship, and action taken are requested to be identified by the PI, as well as a brief narrative to provide further details regarding the event presentation, diagnostics, course and resolution.

8.5.1 DEFINITION OF ADVERSE EVENTS (AE)

An adverse event (AE) is any undesirable clinical occurrence in a patient enrolled in the trial that does not necessarily have a causal relationship with the treatment. An AE can therefore be any unintended sign, symptom or disease temporally associated with the use of an investigational product, whether or not related to the use of the product (ISO 14155)

For purposes of this study, the following events are not considered adverse events, because they are expected to occur in conjunction with the index procedure or are associated with subjects undergoing customary, standard of care endovascular AAA repair procedures:

- Early post-operative pain (within 24 hours of index procedure) at the access site and/or related to position on procedure table
- Post-anesthesia/conscious sedation emesis, nausea, or headache (within 24 hours of index procedure)
- Electrolyte imbalance without clinical sequelae following index procedure, even if requiring brief correction
- Low grade temperature increase (<101.0°F)
- Hematocrit decrease from baseline of less than 6 points (2 grams of hemoglobin) that remains above 30% and is not associated with hemodynamic changes and does not require transfusion
- Blood loss not requiring transfusion and not resulting in decreased hematocrit
- Minor, localized tenderness, swelling, induration, bruising, erythema, hematoma etc. at vascular access site that does not require surgical intervention, evacuation, transfusion or antibiotics
- Prophylactic administration of atropine
- Prophylactic pacing
- Isolated, non-sustained PVCs/PACs
- Non-sustained arrhythmia not requiring treatment or intervention
- Hypotension or hypertension not requiring treatment or intervention
- Atelectasis not requiring treatment
- Prolonged hospitalization due to logistical delays relating to discharge to a skilled nursing facility, care facility, rehabilitation center, etc.

The Investigator and/or IRB/EC may require that these events are reported as adverse events. In this case, the Investigator should report these observations based on their medical judgment and requirements of the IRB/EC.

8.5.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

A serious adverse event (SAE) is an adverse event that:

- Led to death
- Led to a serious deterioration in the health of the subject that:
  - Resulted in life threatening illness or injury
  - Resulted in a permanent impairment of a body structure or a body function
  - Required in-patient hospitalization or a prolongation or existing hospitalization
- Resulted in medical or surgical endovascular procedure to prevent permanent impairment to a body structure or a body function
- Led to fetal distress, fetal death, or a congenital abnormality or birth defect

8.5.3 SEVERITY OF EVENT

The Severity of an AE is a clinical determination of the event intensity. The severity assessment for a clinical AE should be completed using the following guidelines:

- **Mild (+1)** – Awareness of sign or symptom, but easily tolerated.
- **Moderate (+2)** – Discomfort enough to cause interference with usual activity
- **Severe (+3)**– Incapacitating with inability to work or do usual activity.

8.5.4 CLASSIFICATION OF AN ADVERSE EVENT

All AEs will have a classification determined by the PI. The following options will be available for classification:

- Bleeding/Anemia
- Bowel
- Cardiac
- Chimney Device
- Endoleak
- Malignancies
- Miscellaneous
- Nellix Device
- Neurological
- Pulmonary
- Renal
- Surgical Site Wound
- Urogenital
- Vascular

8.5.5 RELATIONSHIP TO STUDY INTERVENTION

All AEs will have their relationship to the study device and the index procedure assessed by the investigator and the Sponsor. All aspects of past medical history, current comorbidities, other reported adverse events, and protocol defined criteria will be reviewed to provide a determination of device or procedure relationships. The Clinical Events Committee (CEC) will review events as prescribed in the Study CEC Charter. The following definitions will be used to guide investigator, sponsor and CEC assessments:

- **Device Related** – Complication associated with the device design as it relates to placement, efficacy or durability, which many involve the delivery system
- **Procedure Related** – Complication associated with the initial placement of the device or any necessary secondary intervention. This includes morbidity associated with either anesthesia or surgical procedure. This also includes inappropriate patient selection and errors attributed to inappropriate operator techniques, measurements or judgment

The degree of certainty about causality will be graded using the categories below:

- **Definitely Related** – There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out. The clinical event, including an abnormal laboratory test result, occurs in a plausible time relationship to study intervention administration.

- **Probably Related** – There is evidence to suggest a causal relationship, and the influence of other factors is unlikely. The clinical event, including an abnormal laboratory test result, occurs within a reasonable time after administration of the study intervention.
- **Possibly Related** – There is some evidence to suggest a causal relationship However, other factors may have contributed to the event (e.g., the participant's clinical condition, other concomitant events). Although an AE may rate only as "possibly related" soon after discovery, it can be flagged as requiring more information and later be upgraded to "probably related" or "definitely related", as appropriate.
- **Unlikely to be related** – A clinical event, including an abnormal laboratory test result, whose temporal relationship to study intervention administration makes a causal relationship improbable and in which other drugs or chemicals or underlying disease provides plausible explanations (e.g., the participant's clinical condition, other concomitant treatments).
- **Unrelated** – The AE is completely independent of study intervention administration, and/or evidence exists that the event is definitely related to another etiology. There must be an alternative, definitive etiology documented by the clinician.

In any instance of uncertainty, the more conservative assessment will be used.

8.5.6 EXPECTEDNESS

Expected adverse events that could potentially occur during the course of the investigation and follow-up are called anticipated adverse events. These events must be reported if clinically significant. Anticipated AEs are listed below:

- Access site complications and sequelae (e.g., dehiscence, infection, pain, hematoma, pseudoaneurysm)
- Allergic reaction to contrast agent (e.g., pruritus, urticaria, bronchospasm, angioedema, hypotension or anaphylaxis that occurs during or post-procedure)
- Amputation
- Anesthetic complications and sequelae (e.g., aspiration)
- Aneurysm enlargement
- Aneurysm rupture
- Arterial damage or trauma (e.g., bleeding, perforation, dissection, rupture)
- Arterial or venous thrombosis and/or pseudoaneurysm
- Arteriovenous fistula
- Bleeding requiring transfusion and/or surgical intervention
- Bowel complications (e.g., ileus, ischemia, infarction, necrosis)
- Cardiac complications and sequelae (e.g., arrhythmia, myocardial infarction, congestive heart failure, hypotension, hypertension)
- Catheter or implant component fragmentation and sequelae (e.g., embolization, vessel trauma)
- Claudication
- Coagulopathy
- Death (due to any cause)
- Edema
- Embolization (micro and macro) with transient or permanent ischemia or infarction
- Endoleak (Type Ia, Type Ib, Type Ic, Type II, Type IIIa, Type IIIb, Type IV)
- Fever and localized inflammation

- Genitourinary complications and sequelae (e.g., ischemia, fistula, incontinence, hematuria, impotence, infection)
- Gutter leaks
- Hepatic failure
- Infection of the aneurysm, device(s), device access site, including abscess formation, transient fever and pain.
- Local or systemic neurologic complications and sequelae, transient or permanent (e.g., stroke, transient ischemic attack, paraplegia, paraparesis, paralysis, numbness and/or tingling in legs)
- Lymphatic complications and sequelae (e.g., lymph fistula)
- ChEVAS System: improper component placement; incomplete component deployment; component migration; component stenosis/compression; occlusion/thrombosis; infection; stent fracture; EndoBag damage or separation; dilatation; erosion; loss of integrity; polymer leak, puncture and perigraft flow
- Thrombosis or occlusion of stent graft or arterial vessel of the lower extremities
- Pulmonary/respiratory complications and sequelae (e.g., pneumonia, respiratory failure, prolonged intubation, pulmonary embolism)
- Post-implant syndrome
- Renal complications and sequelae (e.g., artery occlusion, infarction, insufficiency, failure)
- Secondary Intervention
- Surgical conversion to open repair

Updates to the IFU, Investigator Brochure, or updated reporting guidelines may affect the anticipated adverse events.

8.5.7 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

Adverse events will be assessed at each follow-up visit at a minimum. Should the investigator become aware of an adverse event outside of protocol-defined intervals, these will be reported to the Sponsor within the applicable time frame.

8.5.8 ADVERSE EVENT REPORTING

For all adverse events occurring during the study period, data must be entered in the Adverse Event eCRF in the EDC system. For serious adverse events (SAEs), the section of the eCRF describing the serious nature of the AE must also be completed. The PI should supply to Endologix and the responsible EC/IRB any redacted source documentation and information (e.g., other diagnostic testing, discharge reports, autopsy reports, etc.) as it is available. All adverse events reported in the database or discovered in source documentation will be investigated by Endologix.

8.5.9 SERIOUS ADVERSE EVENT REPORTING

Serious Adverse Events (SAE) with a procedure or device relationship will be reported to the Sponsor within 2 working days of site awareness. SAEs with no device or procedure relationship will be reported to the Sponsor within 5 business days of site awareness.
Death – for any death, regardless of cause or timing, it is recommended that the site notify the Endologix Clinical Department via the EDC system within 1 working day of awareness. The PI should supply to Endologix and the responsible EC/IRB with any redacted source documentation and information (e.g.,

death summary, autopsy report). In all cases, every attempt should be made to obtain as much detailed information on the events or conditions leading up to the death as possible.

8.5.10 MAJOR ADVERSE EVENTS

Major Adverse Events (MAE) are defined as below and will be adjudicated by the Clinical Events Committee.

Major Adverse Event: An event occurring during the study that meets one of the following criteria:

- *All-Cause Death:* Any death occurring during the study period, regardless of cause. Death will be further categorized as one of the following:
  - *Aneurysm-related death* – any death occurring within 30 days from the date of the procedure, regardless of cause, and death due to aneurysm rupture of following any procedure intended to treat the aneurysm
  - *Cardiac-related death* – death due to arrhythmia, heart failure (including cardiogenic shock), or myocardial infarction
  - *Pulmonary-related death* – death due to pulmonary edema, respiratory failure, or pulmonary embolism
  - *Vascular-related death* – death due to stroke, cerebral hemorrhage, or other clear vascular event that is not categorized as cardiac-related, pulmonary-related or aneurysm-related
  - *Other* – a death that cannot be clearly categorized as above, but where information on the circumstances of death is available
  - *Unknown* – a death where no information is available
- *Bowel Ischemia:* The lack of adequate blood flow to the intestines that requires intensification of medical therapy or surgical/endovascular intervention
- *Paraplegia:* Paralysis of the lower extremities inclusive of the lower trunk, with deficits present at the subsequent scheduled follow-up visit
- *Renal Failure:* renal injury resulting in the need for temporary or permanent dialysis
- *Disabling Stroke:* new neurological deficit resulting from vascular insult confirmed by imaging. Disabling is considered a value of 2 (slight disability) or above on the modified Rankin Scale (mRS)

8.5.11 ADDITIONAL ADVERSE EVENT DEFINITIONS

Additional events or occurrences of interest that have relevance to the study device, therapy, disease, re-intervention or evaluations to be captured for endpoint analysis are as follows:

- *Abdominal Aortic Aneurysm Rupture* – intra-operative or post-procedural rupture through the aneurysm wall within the stented segment of the aorta
- *All-Cause Mortality* – Death from any cause
- *Aneurysm Related Mortality* – death reported within 30 days of the index endovascular procedure, due to aneurysm rupture, within 30 days of re-intervention or conversion to open repair, or as otherwise determined by the Clinical Events Committee
- *Aneurysm Sac Enlargement* – aneurysm sac diameter increase of >5mm in late follow-up as compared to the initial post-operative measurement (30 day follow-up)
- *Conversion to Open Repair* – open surgical repair of the abdominal aortic aneurysm due to unsuccessful delivery or deployment of the stent graft and/or renal stents, due to complications or other clinical situations that precluded successful endovascular treatment, or at any time

following initial successful endovascular treatment for any reason. Conversion to Open Repair shall always be captured as a re-intervention

- *Distal Ischemia* – New onset of compromised peripheral blood flow resulting in femoral or peripheral arteria occlusion or stenosis (attributable to the index procedure and not related to natural progression of atherosclerotic disease) causing a threat to the viability of the limb and requiring surgical or percutaneous intervention
- *Endoleak* – Clear evidence of contrast outside of one or both EndoBags, which communicates with the aneurysm sac
    - *Type Ia* – originating proximally at the infrarenal segment
    - *Type Ib* – originating distally
    - *Type Ic* – originating at a chimney stent (visceral vessel)
    - *Type II* – originating from a patent lumbar artery, inferior mesenteric artery, or other collateral visceral vessel
    - *Type III* – between components, if an extender is used
    - *Type IV* – trans-device
- *Gutters* – – Clear evidence of contrast outside of one or both EndoBags, which does not communicate with the aneurysm sac
- *Implant Occlusion* – Radiological finding indicating 100% blockage of device lumen
- *Luminal Thrombus* – endograft thrombosis resulting in any endovascular or surgical intervention after completion of the Nellix system implantation
- *Migration* – CoreLab reported individual stent distal movement >5mm from the original implant location relative to the center of the distal renal artery
    - *Clinically Significant Migration* – CoreLab reported distal movement >10mm from the original implant location relative to the center of the distal renal artery resulting in an intervention or serious complication
- *Secondary Procedure* – any non-diagnostic surgical intervention after the index procedure intended to correct or repair any site reported endoleak, gutters, device occlusion, migration, aneurysm sac expansion and/or a device defect, including infection
- *Stent Thrombosis* – Blood clot that results in stenosis or occlusion of a stent
- *Thromboembolic Event* – Blood clot that has broken loose and is carried distally

8.6 UNANTICIPATED ADVERSE DEVICE EFFECTS

8.6.1 DEFINITION OF UNANTICIPATED ADVERSE DEVICE EFFECTS (UADES)

A UADE is 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 (21 CFR 812.3(s)).

The reporting of UADEs applies to non-exempt human subjects' research conducted or supported by HHS. Provide the definition of an UADE being used for this clinical trial. An incident, experience, or outcome that meets the definition of an UADE generally will warrant consideration of changes to the protocol or consent in order to protect the safety, welfare, or rights of participants or others. Other UADEs may warrant corrective actions at a specific study site. Examples of corrective actions or changes that might need to be considered in response to an UADE may include:

- Modification of inclusion or exclusion criteria to mitigate the newly identified risks
- Implementation of additional safety monitoring procedures
- Suspension of enrollment of new participants or halting of study procedures for enrolled participants
- Modification of informed consent documents to include a description of newly recognized risks
- Provision of additional information about newly recognized risks to previously enrolled participants.

8.6.2 UNANTICIPATED ADVERSE DEVICE EFFECT REPORTING

An investigator shall submit to the sponsor and to the reviewing Institutional Review Board (IRB) a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 days after the investigator first learns of the effect (21 CFR 812.150(a)(1)), a sponsor who conducts an evaluation of an unanticipated adverse device effect under 812.46(b) shall report the results of such evaluation to the Food and Drug Administration (FDA) and to all reviewing IRB's and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests (21 CFR 812.150(b)(1)).

8.6.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

Notification of unanticipated adverse device effects (UADE) to study subjects will be managed and communicated by the PI.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

A formal Statistical Analysis Plan (SAP) has been created, thus these sections will present summaries. Please refer to the SAP for additional detail. The study evaluates two primary endpoints: a 1-month endpoint and a 1-year endpoint. Both these endpoints blend safety and effectiveness measures so they are not termed “Safety Endpoint” or “Effectiveness Endpoint.”

Primary 1-Month Endpoint

The primary 1-month endpoint for the ChEVAS Cohort is defined as an event rate, including technical failure, and the occurrence of severe bowel ischemia, permanent paraplegia/paraparesis, renal failure, disabling stroke, abdominal aortic aneurysm rupture, and aneurysm-related mortality within 30 days of the index procedure. The null and alternative hypotheses are defined below.

$$H0: \pi \geq 25\% \text{ vs. } H1: \pi < 25\%$$

where π is the event rate at 30 days for the study test group, and 25% is the 30-day goal. A univariate test utilizing the exact binomial distribution will be performed to determine if the frequency of the 30-day

composite endpoint is statistically significantly less than the performance goal of 0.25. This is discussed further in the SAP.

Primary 1-Year Endpoint

The primary 1-year endpoint is defined as freedom from abdominal aortic aneurysm rupture and aneurysm-related mortality through 1 year (day 365), freedom from imaging-related findings in the 1-year window (Type or III endoleak, migration > 10 mm, AAA sac expansion > 5 mm, and occlusion within the ChEVAS System not seen at the index procedure), and open conversions and other major device-related interventions through day 365. The primary 1-year analysis will compare the treatment success composite to a target performance goal of 75%. The null and alternative hypotheses are defined below.

$$H0: \pi \leq 0.75 \quad \text{vs. } H1: \pi > 0.75$$

where π = the proportion of treated patients who meet the Treatment Success definition. A univariate test will be performed to determine if the frequency of subjects who meet the treatment success definition is statistically significantly higher than the performance goal of 0.75. This is discussed further in the SAP.

9.2 SAMPLE SIZE DETERMINATION

The number of patients enrolled into this study is driven by the performance goals, expected device performance, and requirements for the alpha error and power. Due to the decrease in number of evaluable subjects at 1 year, the size of the study is determined entirely by the 1-year primary endpoint. Given a minimum power requirement of 80%, alpha=0.05, target goal=75%, estimated 1-year performance of 85.7%, and the univariate binomial test plan, a minimum evaluable sample size of 103 is needed. Accounting for an approximate drop-out rate of 14%, 120 subjects would be needed to achieve the minimum power and alpha requirements. The 1-month endpoint assumes a target goal of 25%, estimated performance of 14.5%, and a similar univariate binomial test structure. Given that all 120 subjects will be analyzed for the primary 1-month endpoint, the 1-month endpoint has power of 85.6%. This is described further in the SAP.

9.3 POPULATIONS FOR ANALYSES

The Primary analysis will be conducted on the implanted population within the ChEVAS Roll-In and Pivotal cohorts. The Intention-to-Treat paradigm is not applied here as this is conventionally applied to two-armed randomized studies. Rather, all subjects receiving an implant are analyzed for the endpoint. The primary 1-year endpoint requires evaluable subjects, so completed cases (subjects who have enough information to be evaluated at 1 year) comprise an additional way to stratify the population. A subpopulation is the per-protocol population, consisting of subjects that have an implanted device, and have not violated the anatomical or procedural IFU criteria. Details of populations are explained further in the SAP.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

Analysis depends on the variable type. For nominal variables, summary statistics will include counts and proportions. Exact confidence limits for binomial variables will be given when they aid in understanding the results. Comparisons will be made with Fisher's Exact Test for 2x2 tables, and the extension of the test (Fisher-Freeman-Halton) when more than 2 categories exist. For continuous variables, summary statistics will be presented including means (or medians for non-normal distributions), standard deviations (or quartile estimates for non-normal distributions), and range. Quantitative comparisons of demographics and vascular variables between sites will be performed by 2-sided F-tests. Unless otherwise specified, the exact form of each algorithm will be the default of SAS version 9.4 or later (SAS Institute, Cary, NC).

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

The components that go into the endpoints and the methodology of their analysis are detailed thoroughly in the SAP.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

There will be no formal statistical testing of secondary endpoints. However, the imaging-driven outcomes (migration and sac enlargement) will be evaluated at the 2nd year using a one-sided 95% exact confidence interval. Please refer to the SAP for additional details.

9.4.4 SAFETY ANALYSES

As mentioned, prior, there is no specific endpoint dedicated solely to safety. Both primary endpoints will be evaluated, and each contains information regarding safety. Additional analyses regarding major adverse events will be presented in a descriptive fashion. Adverse events will be tabulated per their system organ class and presented descriptively. Please refer to the SAP for additional details.

9.4.5 BASELINE DESCRIPTIVE STATISTICS

Demographic and baseline characteristics such as medical history and vascular characteristics will be descriptively summarized. A set of important demographic or prognostic variables will be compared across study sites to determine homogeneity of sites in terms of baseline subject characteristics. Nominal variables will be tested via Fisher-Freeman-Halton test, and continuous variables will be tested via the F-test. Please refer to the SAP for detailed descriptions of these variables.

9.4.6 PLANNED INTERIM ANALYSES

No interim analyses are planned. The Data Safety Monitoring Board (DSMB) analyses that will be conducted are considered routine and descriptive in nature, and do not include any hypothesis testing.

9.4.7 SUB-GROUP ANALYSES

The primary endpoints will be stratified by juxtarenal, pararenal, and paravisceral aneurysm subtype and tabulated. These analyses will be descriptive in nature and no statistical tests will be performed on the groups.

The primary endpoints will be stratified by gender and tabulated. These analyses will be descriptive in nature and no statistical tests will be performed on the gender groups. In addition, the primary endpoints will also be stratified on geography (US vs OUS). Again, these will be descriptive in nature.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Subject-level listings will be presented to support the information presented in tables. This includes the analyses covered in the SAP.

9.4.9 EXPLORATORY ANALYSES

If site-to-site differences are noted, baseline risk factors will be explored to evaluate for the presence of possible contributors. No other exploratory analyses are planned.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

In obtaining and documenting informed consent, the investigator must comply with applicable regulatory requirements (e.g., 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56) and should adhere to ISO 14155 and ICH GCP. Prior to the beginning of the trial, the investigator should have the IRB's written approval for the protocol and the written informed consent form(s) and any other written information to be provided to the participants.

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

The consent form will describe in detail the study intervention, study procedures, risks given to the participant. Written documentation of informed consent is required prior to enrollment in the study.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

The informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be Institutional Review Board (IRB)/ Ethics Committee (EC)-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to enrollment in the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document

will be given to the participants for their records. The informed consent process will be conducted and documented in each participant's record, and the form signed, prior to the study procedure. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

For this study, two informed consent templates will be provided to the sites. The first one is an optional screening informed consent. This ICF will inform the subject that their CT and relevant clinical information will be provided anonymously to the sponsor, in order to screen them for the study. Note that the screening CT is standard-of-care in the treatment and management of complex AAA, and the subject is only consenting to the anonymous data transfer.

The second informed consent, which is required, covers the both the screening process on the full device and trial description, as described in the previous paragraph.
A site may either use the second informed consent prior to screening, or the site may use BOTH the 1st and 2nd consent; the 2nd consent form will be required prior to implantation with the investigational device.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

List possible reasons for termination or temporary suspension of the study (e.g., study closure based on PI decision, sponsor/funder decision, regulatory or other oversight bodies; review of serious, unexpected, and related AEs; noncompliance; futility). For any study that is prematurely terminated or temporarily suspended, the PI will promptly inform study participants, the IRB, and sponsor and provide the reason(s) for the termination or temporary suspension.

When a study is prematurely terminated, refer to **Section 7, Study Intervention Discontinuation and Participant Discontinuation/Withdrawal**, for handling of enrolled study participants.

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the study participants, investigators, the Investigational Device Exemption (IDE) sponsor and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor, IRB and/or Food and Drug Administration (FDA).

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. This confidentiality is extended to cover testing of biological samples in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study, or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), regulatory agencies or pharmaceutical company supplying study product may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

Study participant de-identified research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored in the IBM eClinicalOS database system. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by Endologix research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived. Sites are responsible for ensuring that source medical data, when required for Adverse Event analysis by the sponsor, is de-identified prior to uploading to the database.

This study makes use of an independent core lab, for the purpose of reviewing Computerized Tomography (CT) scans. If the scans are uploaded by the sites through the AgMedNet system, that system will automatically de-identify the films prior to the core lab receiving the data. If the scans are sent via mail, without the site de-identifying the film, the independent core lab may also have visibility to personal identifying information. In this case, the core lab, prior to making the film available to the sponsor, will de-identify the scans. The sponsor will therefore, regardless of the method of transmission, not have access to identifying information from CT or other scanning medical data.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

10.1.4 KEY ROLES AND STUDY GOVERNANCE

Function	**DSMB & CEC**	**Core Lab**
Company Name	[redacted]	[redacted]
Contact Name	[redacted]	[redacted]
Address	[redacted]	[redacted]
Phone Number	[redacted]	[redacted]
Email	[redacted]	[redacted]

Function	**EDC**	**Monitoring**
Company Name	[redacted]	[redacted]
Contact Name	[redacted]	[redacted]
Address	[redacted]	[redacted]
Phone Number	[redacted]	[redacted]
Email	[redacted]	[redacted]

10.1.5 SAFETY OVERSIGHT

All adverse events (AEs) will be reviewed by the Endologix Safety Representative or qualified personnel. Assessments on device and procedure relationships, event classification, potential for adjudication and any additionally required assessments will be made each business day by a qualified Safety representative.

Information to be collected will include classifications and coding as appropriate, dates of onset, assessment of severity and serious adverse event (SAE) potential, action taken, outcome, as well as further details on the clinical presentation or management of the event. If required, queries to the sites will be placed to clarify or confirm information, and if required, source documents will be requested for review.

In the instance of endpoint events or events of special interest, independent review will be performed by the Clinical Events Committee (CEC), comprised of 3 independent physicians who have significant experience in the disease space and therapy. The CEC will provide an independent review and adjudication of adverse events identified by the study team. CEC adjudicable events will be identified in the CEC Charter including, but not limited to:

- All Serious Adverse Events with a potentially positive (possible, probable, or definite) device relationship.
- All events resulting in a secondary intervention
- All aneurysm ruptures
- All deaths, regardless of cause
- All events that may potentially be considered a Major Adverse Event (MAE)

The CEC will convene a minimum of once a quarter. CEC activities will be managed by Syntactx, Inc. and results will be provided to the Data Safety and Monitoring Board (DSMB).

The DSMB, comprised of 4 independent physicians and a biostatistician (none of them may be members of the CEC), will review aggregate study data at regular intervals to ensure patient safety across all sites in the study. The DSMB will convene at a minimum after 30-day follow-up data are collected on the 30th, 60th, 90th, and final patient enrollment. All available clinical data on the study subjects (out to all time points) will be provided to the DSMB. Ad-hoc meetings and analyses may be called by the Sponsor or the DSMB at any point.

The DSMB will provide their recommendations on study conduct as per their review of the study data at Meetings. The recommendations will include but not be limited to, modifications to the protocol, suspension or termination of enrollment, modification of inclusion/exclusion criteria, modification of follow-up scheduling or assessments, or no recommendations on modification. The decision to implement any DSMB recommendations lies solely with the Sponsor.

Events will be followed for outcome information until resolution or stabilization.

For additional training and risk mitigation, all roll-in subjects will have a proctor (physician with prior relevant experience) present during the procedure.

10.1.6 CLINICAL MONITORING

Clinical site monitoring is conducted to ensure that the rights and well-being of trial participants are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with International Conference on Harmonization Good Clinical Practice (ICH GCP), any local IRB/EC conditions imposed, the signed Clinical Trial and Investigator Agreements, and with applicable national and local regulatory requirements.

Endologix staff and designees will monitor the study in accordance with Standard Operating Procedures (SOP) and a study specific clinical monitoring plan (CMP). The CMP uses a risk-based approach. It includes who will conduct the monitoring, at what frequency monitoring will be done, at what level of detail monitoring will be performed, and the review and distribution of monitoring reports. The CMP focuses on preventing or mitigating important and likely risks to data integrity and compliance. The types of monitoring visit (e.g., on-site, centralized), frequency, and extent of source document verification (SDV). Considerations during the risk assessment, including the complexity of the study design, types of study endpoints, clinical complexity of the study population, geography, relative experience of the PI and of the sponsor with the PI, electronic data capture, relative safety of the study intervention, stage of the study, quantity of data, and related study processes.

The CMP for ChEVAS will include 100% SDV for primary endpoints. The frequency of onsite visits will be determined by study enrollment, adverse event rates, and other compliance considerations such as protocol deviations and study record keeping.

10.1.7 QUALITY ASSURANCE AND QUALITY CONTROL

Endologix will send a Case Specialist out for each implant case during enrollment. The Case Specialist will verify that all expiration dates are correct and check the device while being opened. If the device is unable to be used for some reason, the Case Specialist will return the device to the Sponsor.

Each participating site is expected to maintain appropriate medical and research records for this trial, in compliance with ICH GCP and regulatory and institutional requirements for the protection of confidentiality of participants. A monitor will be on site four to six weeks after initial implant for each site to verify all subject source and regulatory documents (e.g. Device Accountability Log, training logs, Delegation of Authority log, etc). A quality verification of the data entered into the Electronic Data Capture system will be part of this process.

Investigators are responsible for maintaining accurate, complete and current records pertaining to correspondence, device accountability, individual subject case history including informed consent. Reports of any IRB/EC withdrawal, unanticipated adverse device effects, deviations from the protocol, use of a device without obtaining subject consent, as well as progress reports to the IRB/EC (annually at minimum) are also the responsibility of the investigator.

Endologix retains the right to terminate the study and remove all study materials from the investigational site at any time. Specific instances, which may precipitate study termination are:

- Unsatisfactory subject enrollment
- Deviations from protocol, without prior approval from Endologix
- Inaccurate, incomplete and/or untimely data recording on a recurrent basis.
- The incidence and/or severity of adverse experiences in this or other studies indicating a potential health hazard caused by the device.
- Submission of fraudulent data

10.1.8 DATA HANDLING AND RECORD KEEPING

10.1.8.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Each participating site will maintain appropriate medical and research records for this trial, in compliance with ICH GCP and regulatory and institutional requirements for the protection of confidentiality of participants. As part of participating in IDE Pivotal study, each site will permit authorized representatives of the sponsor, and regulatory agencies to examine (and when permitted by applicable law, to copy) clinical records for the purposes of quality assurance reviews, audits, and evaluation of the study safety, progress, and data validity. All documents that are copied, sent, or uploaded into electronic data capture (EDC) system must be redacted of any study subject identifiable personal information except the study assigned subject identification. All study documents must be archived per their institutional procedures during conduct and after closure of the study.

The data management or their designee is responsible for design of case report forms to collect study data, electronic data capture database development, validation, control and management of input from study sites/monitored data, maintenance, and reporting for statistical analysis. The EDC system will be developed on IBM Clinical Development “eClinicalOS” system, an FDA part 11 compliant platform. A detailed clinical data management plan (DMP) will be developed for this study per Endologix procedures CWI-096,

CWI-097 and CWI-099. The DMP will define roles that will have access to the clinical study data in the EDC, responsibilities, the EDC system design, study update, and validation process, data query / edit check types and the handling of them, data entry/correction, source data verification, quality control, data cleaning, ad hoc and final EDC closure processes. The DMP will be kept in the Sponsor Trial Master File.

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data.

Hardcopies of the study visit worksheets will be provided for use as source document worksheets for recording data for each participant enrolled in the study. Data recorded in the electronic case report form (eCRF) derived from source documents should be consistent with the data recorded on the source documents.

Clinical data (including adverse events (AEs), concomitant medications, and expected adverse reactions data) and clinical laboratory / Corelab data will be entered into EDC by the sites. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data will be entered directly from the source documents.

Source data are all information, original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Electronic source data are data initially recorded in electronic form. Examples of source data include, but are not limited to, hospital records, clinical and office charts, laboratory notes, memoranda, participants' memory aids or evaluation checklists, pharmacy dispensing records, audio recordings of counseling sessions, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiches, photographic negatives, microfilm or magnetic media, x-rays, and participant files and records kept at the pharmacy, at the laboratories, and medico-technical departments involved in the clinical trial. In the event that device-specific information is not regularly recorded within the hospital medical record, study worksheets may be used to record the information. Any such worksheet must be kept within the study files. In all cases, the primary source document is considered the medical record.

It is not acceptable for the CRF to be the only record of a participant's inclusion in the study. Study participation should be captured in a participant's medical record. This is to ensure that anyone who would access the patient medical record has adequate knowledge that the patient is participating in a clinical trial.

10.1.8.2 STUDY RECORDS RETENTION

Study documents should be retained for a minimum of 2 years after the last approval of a marketing application in an International Conference on Harmonization (ICH) region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the study intervention. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

10.1.9 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol, International Conference on Harmonization Good Clinical Practice (ICH GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

These practices are consistent with ICH GCP:

- 4.5 Compliance with Protocol, Sections 4.5.1, 4.5.2, and 4.5.3
- 5.1 Quality Assurance and Quality Control, Section 5.1.1
- 5.20 Noncompliance, Sections 5.20.1, and 5.20.2.

It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 5 working days of identification of the protocol deviation, or within 5 working days of the scheduled protocol-required activity. All deviations must be addressed in study source documents. Protocol deviations must be sent to the reviewing Institutional Review Board (IRB) per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements.

10.1.10 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence, such as by the pharmaceutical industry, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. Financial Disclosures will be collected from all investigators in the trial.

The cost of the device in the study does not constitute commercialization as defined in 21 CFR 812.7(b).

10.2 ABBREVIATIONS

The list below includes abbreviations utilized in this template. However, this list should be customized for each protocol (i.e., abbreviations not used should be removed and new abbreviations used should be added to this list).

AAA	Abdominal Aortic Aneurysm
AE	Adverse Event
ANCOVA	Analysis of Covariance
ASA	American Society of Anesthesiologists
CFR	Code of Federal Regulations
CLIA	Clinical Laboratory Improvement Amendments
CMP	Clinical Monitoring Plan
COC	Certificate of Confidentiality
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
CTA	Coronary Computed Tomography Angiography
DCC	Data Coordinating Center
DHHS	Department of Health and Human Services
DSMB	Data Safety Monitoring Board
DRE	Disease-Related Event
EC	Ethics Committee
eCRF	Electronic Case Report Forms
eGFR	Estimated Glomerular Filtration Rate
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FFR	Federal Financial Report
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
GWAS	Genome-Wide Association Studies
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IDE	Investigational Device Exemption
IFU	Instructions for Use
IRB	Institutional Review Board
ISM	Independent Safety Monitor
ISO	International Organization for Standardization
ITT	Intention-To-Treat
LSMEANS	Least-squares Means
MAE	Major Adverse Event
MI	Myocardial Infarction
MOP	Manual of Procedures
MSDS	Material Safety Data Sheet
NCT	National Clinical Trial
NIH	National Institutes of Health
NIH IC	NIH Institute or Center
OHRP	Office for Human Research Protections
PI	Principal Investigator
QA	Quality Assurance

QC	Quality Control
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SDV	Source Document Verification
SMA	Superior Mesenteric Artery
SMC	Safety Monitoring Committee
SOA	Schedule of Activities
SOC	System Organ Class
SOP	Standard Operating Procedure
UP	Unanticipated Problem
US	United States

11 REFERENCES

CP-0008 – Nellix US IDE for Infra-renal indication (ongoing)

12 BIBLIOGRAPHY

1 Johnston KW, Rutherford RB, Tilson MD, Shah DM, Hollier L, Stanley JC. "Suggested standards for reporting on arterial aneurysms. Subcommittee on Reporting Standards for Arterial Aneurysms, Ad Hoc Committee on Reporting Standards, Society for Vascular Surgery and North American Chapter, International Society for Cardiovascular." *J Vasc Surg* 1991 (1991): 452-8.

2 A comparative study of the prevalence of abdominal aortic aneurysms in the United Kingdom, Denmark, and Australia. J Med Screen 2001;8: 46-50

[3] Svensjo S, Bjorck M, Gurtelschmid M, Djavani Gidlund K, Hellberg A, Wanhainen A. Low prevalence of abdominal aortic aneurysm among 65-year-old Swedish men indicates a change in the epidemiology of the disease. Circulation 2011;124:1118-23.

4 Forsdahl SH, Singh K, Solberg S, Jacobsen BK. "Risk factors for abdominal aortic aneurysms: a 7-year prospective study: the Tromso Study, 1994-2001." *Circulation* 119 (2009): 2202-8.

5 Kent KC, Zwolak RM, Egorova NN, et al. "Analysis of risk factors for abdominal aortic aneurysm in a cohort of more than 3 million individuals." *J Vasc Surg* 52 (2010): 539-48.

[6] Salem MK, Rayt HS, Hussey G, et al. "Should Asian men be included in abdominal aortic aneurysm screening programmes?" *Eur J Vasc Endovasc Surg* 38 (2009): 748-9.

[7] *Abdominal Aortic Aneurysm*. n.d. 2 February 2017. <http://www.nhs.uk/Conditions/repairofabdominalaneurysm/Pages/Introduction.aspx>.

[8] Xu J, Murphy S, Kochanek K, Bastian B, Arias E. "Deaths: Final Data for 2016." *Natl Vital Stat Rep* 67 (2018)

[9] Assar AN, Zarins CK. "Ruptured abdominal aortic aneurysm: a surgical emergency with many clinical presentations." *Postgrad Med J* 85 (2009): 268-73.

[10] Bhogal RH, Downing R. "The Evolution of Aortic Aneurysm Repair: Past Lessons and Future Directions." *Aneurysmal Disease of the Thoracic and Abdominal Aorta*. 2011. 21-54.

[11] Poppe JK. "Cellophane treatment of syphilitic aneurysms with report of results in six cases." *Am Heart J* 36 (1948): 252-6.

[12] Voorhees ABJ, Jaretzki A III, Blakemore AH. "The use of tubes constructed from vinyon "N" cloth in bridging arterial defects." *Ann Surg* 135 (1952): 332-6.
[13] Crawford ES, Saleh SA, Babb JW 3rd, Glaeser DH, Vaccaro PS, Silvers A. "Infrarenal abdominal aortic aneurysm: factors influencing survival after operation performed over a 25-year period." *Ann Surg* 193 (1981): 699-709.
[14] Volodos NL, Shekhanin VE, Karpovich IP, Troian VI, Gur'ev IA. "A self-fixing synthetic blood vessel endoprosthesis." *Vest Khir Im I Grek* 137 (1986): 123-5.
[15] Parodi JC, Palmaz JC, Barone HD. "Transfemoral intraluminal graft implantation for abdominal aortic aneurysms." *Ann Vasc Surg* 5 (1991): 491-9.
[16] Volodos NL. "Clinical experience of the use of self-fixing synthetic prostheses for remote endoprosthetics of the thoracic and the abdominal aorta and iliac arteries through the femoral artery and as intraoperative endoprosthesis for aorta reconstruction." *Vasa* 33 (1991): 290-5.
[17] Mialhe C, Amicabile C. "Endovascular treatment of aneurysms of the subrenal aorta using the Stentor endoprosthesis." *J Mal Vasc* 20 (1995): 290-5.
[18] Zarins CK, White RA, Schwarten D. "AneuRx stent graft versus open surgical repair of abdominal aortic aneurysms: multicenter prospective clinical trial." *J Vasc Surg* 29 (1999): 292-305.
[19] Sarkar R, Moore Ws, Quinones-Baldrich WJ, Gomes AS. "Endovascular repair of abdominal aortic aneurysm using the EVT device: limited increased utilization with availability of a bifurcated graft." *J Endovasc Surg* 6 (1999): 131-5.
[20] Dua A, Kuy S, Lee CJ, Upchurch GR, Jr, Desai SS. "Epidemiology of aortic aneurysm repair in the United States from 2000 to 2010." *J Vasc Surg* 59 (2014): 1512-7.
[21] Bush RL, Johnson ML, Collins TC. "Open versus endovascular abdominal aortic aneurysm repair in VA hospitals." *J Am Coll Surg* 202 (2006): 577-87.
[22] Chuter TA. "Durability of endovascular infrarenal aneurysm repair: when does late failure occur and why?" *Semin Vasc Surg* 22 (2009): 102-10.
[23] Participants ET. "Endovascular aneurysm repair versus open repair in patients iwth abdominal aortic aneurysm (EVAR 1): randomised controlled trial." *Lancet* 365 (2005): 2179-86.
[24] Hobo R, Buth J. "Secondary interventions following endovascular abdominal aortic aneurysm repair using current endografts." *J Vasc Surg* 43 (2006): 896-902.
[25] Jacobs TS, Won J, Gravereaux EC. "Mechanical failure of prosthetic human implants: a 10-year experience with aortic stent graft devices." *J Vasc Surg* 37 (2003): 16-26.
[26] Schermerhorn ML, Buck DB, O'Malley AJ. "Long-Term Outcomes of Abdominal Aortic Aneurysm in the Medicare Population." *N Engl J Med* 373 (2015): 328-38.
[27] Chang DC, Parina RP, Wilson SE. "Survival After Endovascular vs Open Aortic Aneurysm Repairs." *JAMA Surg* 150 (2015): 1160-6.
[28] Paravastu SC, Jayarajasingam R, Cottam R, Palfreyman SJ, Michaels JA, Thomas SM. Endovascular repair of abdominal aortic aneurysm. *Cochrane Database Syst Rev* 2014;1:CD004178.
[29] Arko FR, Filis KA, Seidel SA, Gonzalez J, Lengle SJ, Webb R, et al. "How many patients with infrarenal aneurysms are candidates for endovascular repair? The Northern California experience." *J Endovasc Ther* 11 (2004): 33-40.
[30] Armon MP, Yusuf SW, Latief K, Whitaker SC, Gregson RH, Wenham PW, et al. "Anatomical suitability of abdominal aortic aneurysms for endovascular repair." *Br J Surg* 84 (1997): 178-180.
[31] Carpenter JP, Baum RA, Barker CF, Golden MA, Mitchell ME, Velazquez OC, et al. "Impact of exclusion criteria on patient selection for endovascular abdominal aortic aneurysm repair." *J Vasc Surg* 34 (2001): 1050-1054.

[32] Elkouri S, Martelli E, Gloviczki P, McKusick MA, Panneton JM, Andrews JC, et al. "Most patients with abdominal aortic aneurysm are not suitable for endovascular repair using currently approved bifurcated stent-grafts." *Vasc Endovascular Surg* 38 (2004): 401-412.
[33] Moise MA, Woo EY, Velazquez OC, Fairman RM, Golden MA, Mitchell ME, et al. "Barriers to endovascular aortic aneurysm repair: past experience and implications for future device development." *Vasc Endovascular Surg* 40 (2006): 197-203.
[34] Schumacher H, Eckstein HH, Kallinowski F, Allenberg JR. "Morphometry and classification in abdominal aortic aneurysms: patient selection for endovascular and open surgery." *J Endovasc Surg* 4 (1997): 39-44.
[35] Velazquez OC, Larson RA, Baum RA, Carpenter JP, Golden MA, Mitchell ME, et al. "Gender-related differences in infrarenal aortic aneurysm morphologic features: issues relevant to Ancure and Talent endografts." *J Vasc Surg* 33 (2001): S77-84.
[36] Aburahma AF, Campbell JE, Mousa AY, Hass SM, Stone PA, Jain A, et al. "Clinical outcomes for hostile versus favorable aortic neck anatomy in endovascular aortic aneurysm repair using modular devices." *J Vasc Surg* 54 (2011): 13-21.
[37] Aburahma AF, Yacoub M, Mousa AY, Abu-Halimah S, Hass SM, Kazil J, et al. "Aortic Neck Anatomic Features and Predictors of Outcomes in Endovascular Repair of Abdominal Aortic Aneurysms Following vs Not Following Instructions for Use." *Am Coll Surg* 222 (2016): 579-589.
[38] Oderich, GS. *Endovascular Aortic Repair: Current Techniques with Fenestrated, Branched and Parallel Stent-Grafts*. Springer, 2017.
[39] Valentine RJ, Decaprio JD, Castillo JM, Modrall JG, Jackson MR, Clagett GP. "Watchful waiting in cases of small abdominal aortic aneurysms - appropriate for all patients?" *J Vasc Surg* 32 (2003): 441-8.
[40] Brewster DC, Cronenwett JL, Hallett JW, Jr., Johnston KW, Krupski WC, Matsumura JS, et al. "Guidelines for the treatment of abdominal aortic aneurysms. Report of a subcommittee of the Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery." *J Vasc Surg* 37 (2003): 1106-17.
[41] Hansen PA, Richards JMJ, Tambryaja AL, Khan LR, Chalmers RTA. "Natural History of Thoraco-abdominal Aneurysm in High-Risk Patients." *Eur J Vasc Endovasc Surg* 39 (2010): 255-270.
[42] Schermerhorn ML, O'Malley AJ, Jhaveri A, Cotterill P, Pomposelli F, Landon BE. "Endovascular vs. open repair of abdominal aortic aneurysms in the Medicare population." *N Engl J Med* 358 (2008): 464-474.
[43] Lederle FA, Kane RL, MacDonald R, Wilt TJ. "Systematic review: repair of unruptured abdominal aortic aneurysm." *Ann Intern Med* 146 (2007): 735-741.
[44] Richards JM, Nimmo AF, Moores CR, Hansen PA, Murie JA, Chalmers RT. "Contemporary results for open repair of suprarenal and type IV thoracoabdominal aortic aneurysms." *Br J Surg* 97 (2010): 45-49.
[45] Deery SE, Lancaster RT, Baril DT, Indes JE, Bertges DJ, Conrad MF, et al. "Contemporary outcomes of open complex abdominal aortic aneurysm repair." *J Vasc Surg* 63 (2016): 1195-1200.
[46] Katsargyris A, Oikonomou K, Klonaris C, Topel I, Verhoeven EL. "Comparison of outcomes with open, fenestrated, and chimney graft repair of juxtarenal aneurysms: are we ready for a paradigm shift?" *J Endovasc Ther* 20 (2013): 159-169.
[47] Crawford ES, Beckett WC, Greer MS. "Juxtarenal infrarenal abdominal aortic aneurysm. Special diagnostic and therapeutic considerations." *Ann Surg* 203 (1986): 661-670.
[48] Chong T, Nguyen L, Owens CD, Conte MS, Belkin M. "Suprarenal aortic cross-clamp position: a reappraisal of its effects on outcomes for open abdominal aortic aneurysm repair." *J Vasc Surg* 49 (2009): 873-880.

[49] Jean-Claude JM, Reilly LM, Stoney RJ, Messina LM. "Pararenal aortic aneurysms: the future of open aortic aneurysm repair." *J Vasc Surg* 29 (1999): 902-912.
[50] Sarac TP, Clair DG, Hertzer NR, Greenberg RK, Krajewski LP, O'Hara PJ, et al. "Contemporary results of juxtarenal aneurysm repair." *J Vasc Surg* 36 (2002): 1104-1111.
[51] Faggioli G, Stella A, Freyrie A, Gargiulo M, Tarantini S, Rodio M, et al. "Early and long-term results in the surgical treatment of juxtarenal and pararenal aortic aneurysms." *Eur J Vasc Endovasc Surg* 15 (1998): 205-211.
[52] Ayari R, Paraskevas N, Rosset E, Ede B, Branchereau A. "Juxtarenal aneurysm. Comparative study with infrarenal abdominal aortic aneurysm and proposition of a new classification." *Eur J Vasc Endovasc Surg* 22 (2001): 169-174.
[53] Shortell CK, Johansson M, Green RM, Illig KA. "Optimal operative strategies in repair of juxtarenal abdominal aortic aneurysms." *Ann Vasc Surg* 17 (2003): 60-65.
[54] Chiesa R, Marone EM, Brioschi C, Frigerio S, Tshomba Y, Melissano G. "Open repair of pararenal aortic aneurysms: operative management, early results, and risk factor analysis." *Ann Vasc Surg* 20 (2006): 739-746.
[55] West CA, Noel AA, Bower TC, Cherry KJ, Jr., Gloviczki P, Sullivan TM, et al. "Factors affecting outcomes of open surgical repair of pararenal aortic aneurysms: a 10-year experience." *J Vasc Surg* 43 (2006): 921-928.
[56] Ockert S, Schumacher H, Bockler D, Malcherek K, Hansmann J, Allenberg J. "Comparative early and midterm results of open juxtarenal and infrarenal aneurysm repair." *Langenbecks Arch Surg* 392 (2007): 725-730.
[57] Pearce JD, Edwards MS, Stafford JM, Deonanan JK, Davis RP, Corriere MA, et al. "Open repair of aortic aneurysms involving the renal vessels." *Ann Vasc Surg* 21 (2007): 676-686.
[58] Knott AW, Kalra M, Duncan AA, Reed NR, Bower TC, Hoskin TL, et al. "Open repair of juxtarenal aortic aneurysms (JAA) remains a safe option in the era of fenestrated endografts." *J Vasc Surg* 47 (2008): 695-701.
[59] Martin MC, Giles KA, Pomposelli FB, Hamdan AD, Wyers MC, Schermerhorn ML. "National outcomes after open repair of abdominal aortic aneurysms with visceral or renal bypass." *Ann Vasc Surg* 24 (2010): 106-112.
[60] Jongkind V, Yeung KK, Akkersdijk GJ, Heidsieck D, Reitsma JB, Tangelder GJ, et al. "Juxtarenal aortic aneurysm repair." *J Vasc Surg* 52 (2010): 760-767.
[61] Schanzer A, Greenberg RK, Hevelone N, Robinson WP, Eslami MH, Golberg RJ, Messina L. "Predictors of Abdominal Aortic Aneurysm Sac Enlargement After Endovascular Repair." *Circulation* 24 (2011): 2848-55.
[62] Donas KP, Lee JT, Lachat M, Torsello G, Veith FJ, investigators P. "Collected world experience about the performance of the snorkel/chimney endovascular technique in the treatment of complex aortic pathologies: the PERICLES registry." *Ann Surg* 262 (2015): 546-553.
[63] Donas KP, Torsello GB, Piccoli G, Pitoulias GA, Torsello GF, Bisdas T, et al. "The PROTAGORAS study to evaluate the performance of the Endurant stent graft for patients with pararenal pathologic processes treated by the chimney/snorkel endovascular technique." *J Vasc Surg* 63 (2016): 1-7.
[64] Wilson A, Zhou S, Bachoo P, Tambyraja AL. "Systematic review of chimney and periscope grafts for endovascular aneurysm repair." *Br J Surg* 100 (2013): 1557-1564.
[65] Moulakakis KG, Papapetrou A, Giannakopoulos TG, Avgerinos ED, Kakisis J, Brountzos EN, et al. "The chimney graft technique for preserving renal arteries in stent-graft sealing zones." *Vasa* 4 (2012): 295-300.

[66] Kouvelos GN, Oikonomou K, Antoniou GA, Verhoeven ELG, Katsargyris A. "A Systematic Review of Proximal Neck Dilatation After Endovascular Aneurysm Repair for Abdominal Aortic Aneurysm." *J Endovasc Ther* 24 (2017): 59-67.
[67] Chou, H. W., C. Y. Chan, S. S. Wang and I. H. Wu. "How to size the main aortic endograft in a chimney procedure." *J Thorac Cardiovasc Surg* 147(2014): 1099-1101
[68] Donas, K. P., F. J. Criado, G. Torsello, F. J. Veith and D. J. Minion. "Classification of Chimney EVAR-Related Endoleaks: Insights From the PERICLES Registry." *J Endovasc Ther* 24(2017): 72-74
[69] Donas, K. P., M. V. Usai, G. T. Taneva, F. J. Criado, G. B. Torsello, P. Kunilis, S. Scali and F. J. Veith. "Impact of aortic stent-graft oversizing on outcomes of the chimney endovascular technique based on a new analysis of the PERICLES Registry." *Vascular* (2018): 1708538118811212
[70] O'Donnell, T. F. X., V. I. Patel, S. E. Deery, C. Li, N. J. Swerdlow, P. Liang, A. W. Beck and M. L. Schermerhorn. "The state of complex endovascular abdominal aortic aneurysm repairs in the Vascular Quality Initiative." *J Vasc Surg*(2019)
[71] Oderich GS, Greenberg RK, Farber M, Lyden S, Sanchez L, Fairman R, Jia F, Bharadwaj P. "Results of the United States multicenter prospective study evaluating the Zenith fenestrated endovascular graft for treatment of juxtarenal abdominal aortic aneurysms." *J Vasc Surg* 60 (2014): 1420-8.
[72] Ullery BW. "Snorkel/Chimney Versus Fenestrated Endovascular Aneurysm Repair: What Works and When?" *Endovascular Today* 15.3 (2016): 76-81.
[73] Farber MA, Vallabhaneni R, Marston WA. ""Off-the-shelf" devices for complex aortic aneurysm repair." *J Vasc Surg* 60 (2014): 579-584.
[74] Locham, S., H. Dakour-Aridi, J. Bhela, B. Nejim, A. Bhavana Challa and M. Malas. "Thirty-Day Outcomes of Fenestrated and Chimney Endovascular Repair and Open Repair of Juxtarenal, Pararenal, and Suprarenal Abdominal Aortic Aneurysms Using National Surgical Quality Initiative Program Database (2012-2016)." *Vasc Endovascular Surg* (2018): 1538574418819284
[75] Kitagawa A, Greenberg RK, Eagleton MJ, Mastracci TM. "Zenith p-branch standard fenestrated endovascular graft for juxtarenal abdominal aortic aneurysms." *J Vasc Surg* 58.2 (2013): 291-300.
[76] Kristmundsson T, Sveinsson M, Bjorses K, Tornqvist P, Dias N. "Suitability of the Zenith p-Branch Standard Fenestrated Endovascular Graft for Treatment of Ruptured Abdominal Aortic Aneurysms." *J Endovasc Ther* 22.5 (2015): 760-764.
[77] Bargay-Juan P, Gomez-Palones FJ, Pepen-Moquete LA, Plaza-Martinez A, Zaragoza-Garcia JM, Morales-Gisbert SM. "Applicability of Zenith p-branch Standard Fenestrated Endograft in our Series." *Ann Vasc Surg* 33 (2016): 187-93.
[78] Farber MA, Eagleton MJ, Mastracci TM, McKinsey JF, Vallabhaneni R, Sonesson B, Dias N, Resch T. "Results from multiple prospective single-center clinical trials of the off-the-shelf p-Branch fenestrated stent graft." *J Vasc Surg* 66.4 (2017): 982-990.
[79] Starnes BW. "Physician-modified endovascular grafts for the treatment of elective, symptomatic, or ruptured juxtarenal aortic aneurysms." *J Vasc Surg* 56 (2012): 601-607.
[80] Dossabhoy, S. S., J. P. Simons, J. M. Flahive, F. A. Aiello, P. Sheth, E. J. Arous, L. M. Messina and A. Schanzer. "Fenestrated endovascular aortic aneurysm repair using physician-modified endovascular grafts versus company-manufactured devices." *J Vasc Surg* 67(2018): 1673-1683
[81] Qaderi, S. M., N. T. Tran, B. Tatum, J. D. Blankensteijn, N. Singh and B. W. Starnes. "Aortic neck dilation is not associated with adverse outcomes after fenestrated endovascular aneurysm repair: Midterm results from an investigational device exemption clinical trial." *J Vasc Surg*(2018)
[82] Georgiadis, G. S., J. A. van Herwaarden, G. A. Antoniou, C. E. Hazenberg, A. D. Giannoukas, M. K. Lazarides and F. L. Moll. "Systematic Review of Off-the-Shelf or Physician-Modified Fenestrated and Branched Endografts." *J Endovasc Ther* 23(2016): 98-109

[83] AbuRahma AF, Campbell J, Stone PA, Nanjundappa A, Jain A, Dean LC, Habib J, Keiffer T, Emmett M. "The Correlation of Aortic Neck Length to Early and Late Outcome sin Endovascular Aneurysm Repair Patients." *J Vasc Surg* 50 (2009): 738-747.
[84] Kontopodis, N., E. Tavlas, N. Galanakis, C. Chronis, A. Kafetzakis, D. Tsetis and C. V. Ioannou. "Spontaneous Type Ia Endoleak Sealing in Patients Undergoing Endovascular Aneurysm Repair With the Ovation Stent Graft." *Ann Vasc Surg* 54(2019): 240-247
[85] AbuRahma AF, Campbell JE, Mousa AY, Hass SM, Stone PA, Jain A, Nanjundappa A, Dean LS, Keiffer T, Habib J. "Clinical outcomes for hostile versus favorable aortic neck anatomy in endovascular aortic aneurysm repair using modular devices." *J Vasc Surg* 54 (2011): 13-21.
[86] Jordan WD, Mehta M, Varnagy D, Moore WM, Arko FR, Joye J, Ouriel K, de Vries JP. "Results of the ANCHOR prospective, multicenter registry of EndoAnchros for type Ia endoleaks and endograft migration in patients with challenging anatomy." *J Vasc Surg* 60 (2014): 885-92.
[87] Goudeketting, S. R., J. Wille, D. A. F. van den Heuvel, J. A. Vos and J. P. M. de Vries. "Midterm Single-Center Results of Endovascular Aneurysm Repair With Additional EndoAnchors." *J Endovasc Ther* 26(2019): 90-100
[88] Goudeketting, S. R., K. van Noort, J. J. M. Vermeulen, K. Ouriel, W. D. Jordan, Jr., J. M. Panneton, C. H. Slump and J. P. M. de Vries. "Analysis of the position of EndoAnchor implants in therapeutic use during endovascular aneurysm repair." *J Vasc Surg* (2018)
[89] Goudeketting, S. R., K. van Noort, K. Ouriel, W. D. Jordan, Jr., J. M. Panneton, C. H. Slump and J. P. M. de Vries. "Influence of aortic neck characteristics on successful aortic wall penetration of EndoAnchors in therapeutic use during endovascular aneurysm repair." *J Vasc Surg* 68(2018): 1007-1016
[90] Goudeketting, S. R., J. Wille, D. A. F. van den Heuvel, J. A. Vos and J. P. M. de Vries. "Midterm Single-Center Results of Endovascular Aneurysm Repair With Additional EndoAnchors." *J Endovasc Ther* 26(2019): 90-100
[91] Galinanes, E. L., E. Hernandez and Z. Krajcer. "Preliminary results of adjunctive use of endoanchors in the treatment of short neck and pararenal abdominal aortic aneurysms." *Catheter Cardiovasc Interv* 87(2016): E154-159
[92] Donselaar, E. J., R. J. van der Vijver-Coppen, L. H. van den Ham, J. W. Lardenoye and M. M. Reijnen. "EndoAnchors to Resolve Persistent Type Ia Endoleak Secondary to Proximal Cuff With Parallel Graft Placement." *J Endovasc Ther* 23(2016): 225-228
[93] Niepoth, W. W., J. L. de Bruin, K. K. Yeung, R. J. Lely, A. N. Devrome, W. Wisselink and J. D. Blankensteijn. "A proof-of-concept in vitro study to determine if EndoAnchors can reduce gutter size in chimney graft configurations." *J Endovasc Ther* 20(2013): 498-505
[94] Stella, N., R. Ficarelli, R. Dito, D. Brancadoro, M. Rossi and M. Taurino. "A Double Nellix and Chimney Covered Stents: Challenging Treatment of Pararenal Aortic Aneurysm." *Vasc Endovascular Surg* 51(2017): 209-214
[95] Mazzaccaro, D., A. M. Settembrini, L. Muzzarelli, F. Ambrogi, V. Milani and G. Nano. "Sealing Devices in Chimney Aortic Repair (CH EVAS) Versus Chimney Aortic Repair with Conventional Devices (CH EVAR): A Systematic Review." *Cardiovasc Intervent Radiol* (2019)
[96] Stenson, K., B. Patterson, M. J. Grima, J. de Bruin, P. Holt and I. Loftus. "Endovascular aneurysm sealing with chimney grafts to treat juxtarenal and suprarenal abdominal aortic aneurysms: Early results from 62 cases." *J Vasc Surg* (2018)
[97] Thompson M, Youssef M, Jacob R, Zerwes S, Reijnen M, Szopinski P, et al. "Early Experience With Endovascular Aneurysm Sealing in Combination With Parallel Grafts for the Treatment of Complex Abdominal Aneurysms: The ASCEND Registry." *J Endovasc Ther* 24 (2017): 764-772.
[98] Truijers M, van Sterkenburg SM, Lardenoije JW, Reijnen MM. "Endovascular repair of a ruptured pararenal aortic aneurysm using the Nellix endovascular aneurysm sealing system and chimney grafts." *J Endovasc Ther* 22 (2015): 291-294.

[99] Boersen JT, Donselaar EJ, Groot Jebbink E, Starreveld R, Overeem SP, Slump CH, et al. "Benchtop quantification of gutter formation and compression of chimney stent grafts in relation to renal flow in chimney endovascular aneurysm repair and endovascular aneurysm sealing configurations." *J Vasc Surg* 66 (2017): 1565-1573 e1561.
[100] Niepoth WW, de Bruin JL, Lely RL, Wisselink W, de Vries JP, Yeung KK, et al. "In vitro feasibility of a sac-sealing endoprosthesis in a double chimney graft configuration for juxtarenal aneurysm." *Endovasc Ther* 21 (2014): 529-537.
[101] Dijkstra ML, Lardenoye JW, van Oostayen JA, Zeebregts CJ, Reijnen MM. "Endovascular aneurysm sealing for juxtarenal aneurysm using the Nellix device and chimney covered stents." *J Endovasc Ther* 21 (2014): 541-547.
[102] Kisis K, Savlovskis J, Gedins M, Ezite N, Zellans E, Krievins D. "Chimney Technique with Nellix EndoVascular Aneurysm Sealing System in a Patient with Single Kidney and Juxtarenal Abdominal Aortic Aneurysm." *Aorta (Stamford)* 4 (2016): 134-137.
[103] Malkawi AH, de Bruin JL, Loftus IM, Thompson MM. "Treatment of a juxtarenal aneurysm with the Nellix endovascular aneurysm sealing system and chimney stent." *J Endovasc Ther* 21 (2014): 538-540.
[104] Quintas A, Alves G. "Three-vessel Chimney Technique Combined with Endovascular Aortic Sealing Device for the Treatment of a Type Ia Endoleak." *Eur J Vasc Endovasc Surg* 53 (2017): 379.
[105] Rouer M, El Batti S, Julia P, de Blic R, Fabiani JN, Alsac JM. "Chimney stent graft for endovascular sealing of a pararenal aortic aneurysm." *Ann Vasc Surg* 28 (2014): 1936 e1915-1938.
[106] Varetto G, Castagno C, Quaglino S, Garneri P, Trevisan A, Destro M, et al. "Bailout Chimney Technique during Endovascular Aneurysm Sealing for Accidental Renal Artery Coverage." *J Vasc Interv Radiol* 27 (2016): 1710-1712.
[107] Garriboli, L. and A. M. Jannello. "Uncovered Chimney Stent Graft for Renal Arteries With the Nellix Endovascular Aneurysm Sealing Technique." *Vasc Endovascular Surg* 52(2018): 148-153
[108] Klonaris, C., A. Katsargyris, D. Athanasiadis and T. Liakakos. "Use of the Nellix Endovascular Aneurysm Sealing System in Combination With Parallel Grafts for the Treatment of a Symptomatic Type V Thoracoabdominal Aortic Aneurysm." *J Endovasc Ther* 24(2017): 779-782
[109] Malaj, A., O. Martinelli, M. Fresilli, V. Picone, A. Giglio, C. Belli, J. Ben Hamida and B. Gossetti. "Treatment of a Juxtarenal Aneurysm with a Parallel Graft in the Left Renal Artery and Polymer-Based Technology to Seal the Entire Aneurysmal Sac." *Ann Vasc Surg* 29(2015): 1662.e1619-1622
[110] Youssef M, Dunschede F, El Beyrouti H, Salem O, Vahl CF, Dorweiler B. "Endovascular Repair of Paravisceral Aortic Aneurysms Combining Chimney Grafts and the Nellix Endovascular Aneurysm Sealing Technology (Four-Vessel ChEVAS)." *Thorac Cardiovasc Surg* 65 (2017): 112-119.
[111] Youssef M, Zerwes S, Jakob R, Salem O, Dunschede F, Vahl CF, et al. "Endovascular Aneurysm Sealing (EVAS) and Chimney EVAS in the Treatment of Failed Endovascular Aneurysm Repairs." *J Endovasc Ther* 24 (2017): 115-120.
[112] Joseph, S. Z., C. H. R. Kwok, J. A. Hockley, M. W. Garbowski, J. Ferguson, S. Samuelson and S. J. Jansen. "A Technique of "Chimney Nellix" for the Management of Type 1a Endoleak After EVAR." *J Vasc Interv Radiol* 29(2018): 623-627
[113] Paraskevas, K. I., M. Karouki, A. Rehman, F. Torella, R. G. McWilliams, A. England and R. K. Fisher. "Endovascular Aneurysm Sealing (EVAS) Alone or in Combination with Chimney Grafts (chEVAS) for Treating Complications of Previous Endovascular Aneurysm Repair (EVAR) Procedures." *Cardiovasc Intervent Radiol* 41(2018): 1015-1020
[114] Youssef, M., S. Zerwes, R. Jakob, O. Salem, F. Dunschede, C. F. Vahl and B. Dorweiler. "Endovascular Aneurysm Sealing (EVAS) and Chimney EVAS in the Treatment of Failed Endovascular Aneurysm Repairs." *J Endovasc Ther* 24(2017): 115-120

[115] De Bruin, J. L., J. R. Brownrigg, B. O. Patterson, A. Karthikesalingam, P. J. Holt, R. J. Hinchliffe, I. M. Loftus and M. M. Thompson. "The Endovascular Sealing Device in Combination with Parallel Grafts for Treatment of Juxta/Suprarenal Abdominal Aortic Aneurysms: Short-term Results of a Novel Alternative." *Eur J Vasc Endovasc Surg* 52(2016): 458-465
[116] Dinkelman, M. K., S. P. Overeem, D. Bockler, D. E. V. JP and J. M. Heyligers. "Chimney technique in combination with a sac-anchoring endograft for juxtarenal aortic aneurysms: technical aspects and early results." *J Cardiovasc Surg (Torino)* 57(2016): 730-736
[117] Harrison SC, Winterbottom AJ, Coughlin PA, Hayes PD, Boyle JR. "Editor's Choice - Mid-term Migration and Device Failure Following Endovascular Aneurysm Sealing with the Nellix Stent Graft System - a Single Centre Experience." *Eur J Vasc Endovasc Surg*. 56 (2018): 342-8.
[118] Scali, S. T., A. W. Beck, G. Torsello, M. Lachat, P. Kubilis, F. J. Veith, J. T. Lee and K. P. Donas. "Identification of optimal device combinations for the chimney endovascular aneurysm repair technique within the PERICLES registry." *J Vasc Surg* 68(2018): 24-35
[119] Katsargyris, A., K. Oikonomou, C. Klonaris, I. Töpel and E. L. G. Verhoeven. "Comparison of Outcomes With Open, Fenestrated, and Chimney Graft Repair of Juxtarenal Aneurysms: Are We Ready for a Paradigm Shift?" *J Endovasc Ther* 20(2013): 159-169
[120] Bruen, K. J., R. J. Feezor, M. J. Daniels, A. W. Beck and W. A. Lee. "Endovascular chimney technique versus open repair of juxtarenal and suprarenal aneurysms." *J Vasc Surg* 53(2011): 895-904; discussion 904-895
[121] Zoethout, A. C., J. T. Boersen, J. M. M. Heyligers, J. P. M. de Vries, C. Zeebregts and M. Reijnen. "Two-Year Outcomes of the Nellix EndoVascular Aneurysm Sealing System for Treatment of Abdominal Aortic Aneurysms." *J Endovasc Ther* 25(2018): 270-281
[122] Savlovskis, J., D. Krievins, J. P. de Vries, A. Holden, K. Kisis, M. Gedins, N. Ezite and C. K. Zarins. "Aortic neck enlargement after endovascular aneurysm repair using balloon-expandable versus self-expanding endografts." *J Vasc Surg* 62(2015): 541-549
[123] Brown, S. L., A. Awopetu, M. S. Delbridge and P. W. Stather. "Endovascular abdominal aortic aneurysm sealing: A systematic review of early outcomes." *Vascular* 25(2017): 423-429
[124] Sidloff, D. A., P. W. Stather, E. Choke, M. J. Bown and R. D. Sayers. "Type II endoleak after endovascular aneurysm repair." *Br J Surg* 100(2013): 1262-1270
[125] Ockert, S., M. Heinrich, T. Kaufmann, T. Syburra, R. Lopez and R. Seelos. "Endovascular aortic sealing with Nellix reduces intraoperative radiation dose when compared to endovascular aortic repair." *J Vasc Surg* 67(2018): 1068-1073
[126] Stather, P. W., D. Sidloff, N. Dattani, E. Choke, M. J. Bown and R. D. Sayers. "Systematic review and meta-analysis of the early and late outcomes of open and endovascular repair of abdominal aortic aneurysm." *Br J Surg* 100(2013): 863-872

APPENDICES

APPENDIX 1- EVAS Infrarenal Roll-In Protocol

APPENDIX 1 - EVAS Infrarenal Roll-In Protocol