Medtronic

Clinical Investigation Plan

Clinical Investigation Plan/Study Title	A prospective, multi-center, single-arm study of the Medtronic Hugo™ Robotic Assisted Surgery (RAS) System in Inguinal and Ventral Hernia Repair Surgery
Clinical Investigation Plan Identifier	MDT21022
Study Product Name	Medtronic Hugo™ Robotic Assisted Surgery (RAS) System
Sponsor/Local Sponsor	Covidien LP, Medtronic Medical Surgical Surgical Robotics 60 Middletown Ave North Haven, CT 06473 USA
Document Version	5.0
Version Date	02 Sep 2025
Lead Principal Investigator	Jacob Greenberg, MD, EdM Chief of Minimally Invasive Surgery Associate Professor of Surgery Duke University Medical Center

1 Investigator Agreement and Signature Page

Study product Name	Medtronic Hugo™ RAS system
Sponsor	Covidien LP, Medtronic Medical Surgical Surgical Robotics 60 Middletown Ave. North Haven, CT 06473 USA
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Version Number/Date	Version 5.0 / 02 Sep 2025
I have read the protocol, including all appendices, and I agree that it contains all necessary details for me and my staff to conduct this study as described. I will conduct this study as outlined herein and will make a reasonable effort to complete the study within the time designated. I agree to comply with the Declaration of Helsinki, the Clinical Investigation Plan, and Good Clinical Practice, as well as local laws, regulations, and standards. I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation and conduct of the clinical investigation without the prior written consent of Medtronic. I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Medtronic. I will discuss this material with them to ensure that they are fully informed about the products and the study.	
Investigator's Signature:	
Investigator's Name:	
Institution:	
Date:	

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2 Glossary

Term	Definition
ACHQC	Abdominal Core Health Quality Collaborative
ADE	Adverse Device Effect
AE	Adverse Event
ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CA	Competent Authority
CDC	Centers for Disease Control and Prevention
CEC	Clinical Event Committee
CFR	Code of Federal Regulation
CIP	Clinical Investigation Plan
Clavien-Dindo Classification of Surgical Complications	Grade I: Any deviation from the normal post-operative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside. Grade II: Requiring pharmacological treatment with drugs other than such allowed for grade I complications Blood transfusions and total parenteral nutrition are also included. Grade III: Requiring surgical, endoscopic, or radiological intervention Grade IIIa: Intervention not under general anesthesia Grade IIIb: Intervention under general anesthesia

Term	Definition
	Grade IV: Life-threatening complication (including CNS complications) * requiring IC/ICU management Grade IVa: Single organ dysfunction (including dialysis) Grade IVb: Multiorgan dysfunction Grade V: Death of a patient NOTE 1: *Brain hemorrhage, ischemic stroke, subarachnoid bleeding, but excluding transient ischemic attacks. CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.
Conversion	Conversion is defined as the switch from the robotic-assisted approach using the Hugo™ RAS system to laparoscopic, open surgery, or use of an alternative robotic-assisted system.
CDISC	Clinical Data Interchange Standards Consortium
CRF	Case Report Form
CSR	Clinical Study Report
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DD	Device Deficiency
DMC	Data Monitoring Committee
DoH	Declaration of Helsinki
DTL	Delegated Task List
eCRF	Electronic Case Report Form
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act

Term	Definition
FAL	Foreseeable Adverse Event List
FAS	Full Analysis Set
FD	Financial Disclosure
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator Brochure
IC	Informed Consent
ICH	International Conference of Harmonization
IDE	Investigational Device Exemption
IFU	Instructions For Use
Interoperative Bleeding	Bleeding that occurs during the course of the surgical operation.
IRB	Institutional Review Board
LOS	Length of Stay
MAOI	Monoamine Oxidase Inhibitors
MedDRA	Medical Dictionary for Regulatory Activities
NSAID	Non-steroidal Anti-inflammatory Drug
NSR	Non-Significant Risk

Term	Definition
OR	Operating Room
PG	Performance Goal
PHI	Protected Health Information
PPAS	Per Protocol Analysis Set
QoL	Quality of Life
RA	Regulatory Authority
Readmission	Admission for a direct consequence or complication associated with the treated hernia or with the surgical procedure to treat the hernia
Recurrence	Clinical hernia recurrence is defined as a palpable fascial defect and/or a clinically manifested bulge within 7 cm of the original hernia repair, exacerbated by a Valsalva maneuver during physical examination by a study investigator.
Reoperation	Operation for a direct consequence or complication associated with the treated hernia or with the surgical procedure to treat the hernia
RPI	Report of Prior Investigations
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SC	Steering Committee
SR	Surgical Robotics
SID	Subject Identification
SoC	Standard of Care
SOP	Standard Operating Procedure
SSE	Surgical-Site Event
SSI	Surgical-Site Infection

Term	Definition
SSO	Surgical-Site Occurrence
UAE	Unavoidable Adverse Event
UADE	Unanticipated Adverse Device Effect
US	United States

3 Synopsis

Title	A prospective, multi-center, single-arm study of the Medtronic Hugo™ Robotic Assisted Surgery (RAS) System in Inguinal and Ventral Hernia Repair Surgery (Enable Hernia Repair)
Clinical Study Type	Pivotal
Product Name	Medtronic Hugo™ Robotic Assisted Surgery (RAS) System
Sponsor	Covidien LP, Medtronic Medical Surgical Surgical Robotics 60 Middletown Ave. North Haven, CT 06473 USA
Indication under investigation	Inguinal and Ventral Robotic Hernia Repair
Investigation Purpose	This study will evaluate the safety and performance of the Medtronic Hugo™ RAS system when used for inguinal and ventral robotic hernia repair procedures
Product Status	Pre-market
Primary Objectives	The primary objectives of this study are to demonstrate that the Medtronic Hugo™ RAS system is safe and effective when used for inguinal and ventral robotic hernia repair.
Primary Endpoints	The primary effectiveness endpoint is the surgical success rate defined as the procedure not going into conversion. Conversion is defined as the switch from the robotic-assisted approach using the Hugo™ RAS system to laparoscopic, open surgery, or use of an alternative robotic-assisted system. Procedural steps that are usually performed without robotic assistance per standard of care, including but not limited to mesh insertion, suture needle removal, or tacking, are not considered a conversion and will not contribute to the primary effectiveness endpoint. A subgroup analysis

	will be performed on the device-related conversions.
	
	The primary safety endpoint is the overall rate of subjects with one or more procedure- and/or device-related surgical site events (SSEs), from the first incision through 30 days post-procedure. SSE is defined as the following complications:
	
	• Surgical-site occurrence (SSO):
	  ○ Bleeding, Hemorrhage: Requiring transfusion
	  ○ Bowel Injury
	  ○ Mechanical Bowel Obstruction
	  ○ Cellulitis
	  ○ Epigastric Vessel Injury
	  ○ Symptomatic Hematoma: Requiring procedural intervention
	  ○ Symptomatic Seroma: Requiring procedural intervention
	  ○ Symptomatic Edema: Requiring procedural intervention
	• Surgical-site infection (SSI): Infection occurring where the surgery took place, including superficial, deep, and organ space infections (standardized definition developed by the CDC)
	
	Refer to **Section 5** for the full definitions of the endpoints.

Secondary Objectives	The secondary objective of this study is to demonstrate that the Medtronic Hugo™ RAS system performs as intended when used in inguinal and ventral hernia repair robotic assisted surgery. The secondary endpoints of this study will assess the overall performance of the Medtronic Hugo™ RAS system when used for hernia repair robotic assisted surgery.
Secondary Endpoints	Secondary objectives include descriptive analyses of secondary endpoints. The following safety and performance data shall be collected through 30 days post-procedure to assess the overall safety and performance of the Medtronic Hugo™ RAS system when used for hernia repair robotic assisted surgery: • Complication rate: Overall rate of subjects with one or more procedure- and/or device-related complications (Clavien-Dindo Grade I or higher), from the first incision through 30 days post-procedure • Major complication rate: overall rate of subjects with one or more major procedure- and/or device-related complications (Clavien-Dindo Grade III or higher), from the first incision through 30 days post-procedure • Operative time

	• Readmission rate through 30 days post-procedure • Reoperation rate through 30 days post-procedure • Recurrence rate through 30 days post-procedure The following long-term secondary endpoints will be assessed through 2 years post-procedure in all treated subjects: • Recurrence rate through 2 years post-procedure Refer to **section 5** for the full definitions of the endpoints.
Ancillary Endpoints	Descriptive analyses of other pre-specified outcome measures beyond the primary and secondary objectives will be exploratory in nature and are not intended as a focus of the study for the evaluation of the study device. • Estimated intraoperative blood loss • Transfusion rate through 30 days • Mortality through 30 days • Device- and/or procedure-related AEs through 2 years • Hospital length of stay • Readmission rate through 2 years • Reoperation rate through 2 years • Surgeon experience • Pain scores at baseline, 30-days, and 3-months (Abdominal Core Health Quality Collaborative [ACHQC] questionnaire)
Study Design	A prospective, multicenter, single-arm pivotal study will be performed with 192 subjects enrolled to have an inguinal or ventral robotic hernia repair procedure using the Medtronic Hugo™ RAS system. Subjects will be followed through two years. This study will be conducted using up to ten investigative sites in the United States (US).
Sample Size	Up to 192 subjects (with 96 each in inguinal and ventral respectively) will be enrolled to have a robotic-assisted hernia repair procedure for this study at up to ten different sites, to ensure a sample size of at least 86 patients with primary safety endpoint assessed for analysis in inguinal and ventral respectively, with 10% attrition considered.
Inclusion/Exclusion Criteria	Inclusion Criteria: 1. Adult subjects (age ≥ 22 years) as required by local law 2. Subject has been indicated for one of the following hernia repairs: a. primary or incisional ventral hernia(s). Multiple small hernia defects are allowed with total distance of

	combined defects being < 10cm b. inguinal (unilateral or bilateral) hernia(s) 3. Subject is an acceptable candidate for a fully robotic assisted surgical procedure, a laparoscopic surgical procedure, or an open surgical procedure 4. The subject is willing to participate and consents to participate, as documented by a signed and dated informed consent form Exclusion Criteria: 1. Subjects for which minimally invasive surgery is contraindicated as determined by the Investigator 2. Subjects with a recurrent hernia 3. Subjects with femoral hernia defects 4. Subjects with ventral hernia defect(s) located in M1, M5, or L4[(1)] 5. Subjects with emergent hernia repair 6. Ventral hernia is CDC grade 2 or higher 7. Use of component separation techniques to close the hernia defect 8. Inability to close the defect in ventral hernia subjects 9. Hernia defect is ≥ 10 cm 10. Subject has BMI > 40 11. Subjects with comorbidities or medical characteristics, which would preclude the surgical procedure in the opinion of the Investigator 12. Subjects diagnosed with a bleeding disorder and/or cannot be removed from their anticoagulants prior to surgery based on surgeon discretion and standard-of-care 13. Subjects pregnant at the time of the surgical procedure. 14. Subjects who are considered to be part of a vulnerable population (e.g., prisoners or those without sufficient mental capacity) 15. Subjects who have participated in an investigational drug or device research study within 30 days of enrollment that would interfere with this study 16. Subjects with active infections including but not limited to pneumonia, urinary tract infection, cellulitis, or bacteremia

Study Procedures and Assessments	Screening, Surgical Procedure, Hospital Discharge, and Post-Discharge Follow-Up at 30 days (±7 days), 3 months (±14 days), 1 year (±30 days) and 2 years (±30 days): **Screening:** To determine study eligibility and collect baseline information (i.e., demographics, medications, medical history, surgical history) **Surgical Procedure:** To re-confirm eligibility criteria, procedure set-up and take-down, medication changes, interoperative complication evaluation, disease state evaluation, procedure success, conversion, adverse event evaluation, device deficiency evaluation **Up to Hospital Discharge:** Adverse event evaluation, subject complication rate, disease state evaluation, protocol deviation and medications. **Post-Discharge Follow-Up:** Adverse event evaluation, subject complication rate, disease state evaluation, length of hospital stay, readmission (if applicable), reoperation (if applicable), recurrence (if applicable), chronic pain, protocol deviation, medications, and study exit.
Safety Assessments	Data on the presence of adverse events (AEs) will be collected from the time of consent. Safety assessments will be based on the full analysis set (FAS). Data including AE term, incidence, severity, and procedure/device relatedness will be reported. AEs for all FAS subjects will be collected from time of consent through the study exit. AEs will be assessed by the Investigator and the sponsor. All Serious Adverse Events (SAE), deaths, and Surgical Site Events (SSEs) will be adjudicated by an external, independent Clinical Events Committee (CEC). AEs occurring in subjects excluded from the full analysis set will be followed post-consent through study exit and will be reported in a listing in the clinical study report (CSR). These AEs will not be included in the FAS summary for either AE reporting or the analysis of the primary and secondary endpoints. AEs and Device Deficiencies will be summarized in tables displaying the

	number of events, and the number and percentage of subjects with events.
Statistics	**Sample Size** Up to a total of 192 subjects are planned to enroll into the study. Sample size for primary effectiveness is based on combined cohorts of inguinal and ventral. A performance goal of 85% is pre-defined to test the statistical hypothesis. The sample size of 172 in the combined inguinal and ventral hernia cohort will provide 90% power to evaluate the primary effectiveness endpoint at one-sided alpha of 0.025, assuming the expected surgery success rate of 93%. If we account for 10% attrition, the target enrollment is 192 subjects, which combines number of subjects from inguinal and ventral. Additionally, performance goal of 30% are pre-defined to assess the primary safety endpoint (rate of procedure- and/or device-related SSE) of the two surgery types respectively through 30-days. Assuming a PG of 30% and expected effect size of 15%, a sample size of 86 in each of the inguinal and hernia cohort will provide 86% power with one-sided alpha of 0.0125 (Bonferroni Correction for hernia type). Accounting for 10% attrition rate, the treatment target is 96 subjects for each cohort (up to a total of 192 for two cohorts combined). **Primary Hypothesis** The primary effectiveness hypothesis is to test if the surgical success rate is above the performance goal. The hypothesis will be tested using an exact binomial test at one-sided alpha of 0.025. The analysis set for the primary effectiveness will be FAS (Full Analysis set, which includes all enrolled subjects in whom the Hugo™ RAS procedure is begun, defined as the first skin incision) for the combined inguinal and hernia cohort. If 5% of the data or fewer are missing for the primary analysis, no imputation will be used. Otherwise, missing data will be imputed for the FAS using multiple imputation. Sensitivity analysis will be performed for the primary effective endpoint using available data with no imputation in FAS, PPAS as well as tipping-point analysis in FAS to fully understand the missing data impact on the study results. The primary safety hypothesis is to test if the 30-day procedure- and/or device-related SSE is below the performance goal of 30% for each of the inguinal and ventral hernia cohort. The hypothesis will be tested using an

	exact binomial test with multiplicity adjustment considered. The analysis for primary safety objectives will be performed with available data in FAS. **Other Information** All secondary endpoints and other prespecified outcome measures will be evaluated using descriptive statistics with all available data. Statistical analyses will be performed using SAS version 9.4 or higher or other widely accepted statistical or graphical software.

4 Introduction

4.1 Background

4.1.1 Hernia Repair

A hernia is a protrusion of tissue or part of an organ through bone, muscular tissue, or membrane. Hernias may be classified as primary or incisional and may occur spontaneously as a result of weak muscles, congenital defects or trauma, while incisional hernias occur at the site of previous surgical incisions and are believed to occur as a consequence of the fascia failing to heal fully after surgery. Inguinal hernias occur in or near the inguinal canal and are the most commonly occurring type of hernia. Lifetime risk for inguinal hernia occurrence is 3% for women and 27% for men. Incidence increases with age for men[(2)]. About 800,000 inguinal hernia repair procedures are performed annually in the US [(3)].

Ventral hernias occur in the abdomen wall and are sometimes referred to as abdominal hernias; sub-types of ventral hernias include incisional hernias, umbilical hernias, and epigastric hernias. Incisional hernias are the second most common type of hernia. About 350,000 ventral hernia repair procedures were performed in the US in 2006[(4)]. By 2016, US procedure volume nearly doubled to 611,000 procedures per year[(5)]. With an aging population exposed to a higher cumulative risk of developing incisional hernias after both minimally invasive surgery (MIS) and open surgery, the management of ventral hernias will continue to be a central focus of surgical disease[(4)].

Choices relating to the surgical repair of hernias are guided by the size and location of the hernia.

4.1.2 Robotic Assisted Surgery

Over the course of history, surgery has generally evolved towards less invasive methods for performing the same procedures.

A major paradigm shift in the realm of surgical technique came with the introduction of MIS, a technique in which operations are performed through small incisions (usually 0.5–1.5 cm) in the body. Trocars — hollow tubes that prevent air from escaping — are inserted into the abdomen or chest. Carbon dioxide is used to insufflate the abdomen and create a working space (although this step is not needed in thoracoscopic surgery). Instruments are inserted through the trocars to gain access to internal anatomical

structures. The phases of tissue dissection and resection can then be performed without the need for large incisions. Resected tissue is put into a retrieval bag and removed through one of the trocars or a slightly extended trocar incision. MIS includes laparoscopic surgery and robotic-assisted surgery (RAS). RAS is based on the accurate translation of user input to a robotically assisted output. Similar to laparoscopic surgery, RAS involves the use of endoscopic instrumentation for manipulation of tissues and vessels in the insufflated body cavity. However, RAS offers advantages including improved optics (3D stabilized view), better dexterity (articulated instruments, tremor reduction) and superior ergonomics[6].

4.1.3 Robotic Assisted Procedures in Hernia Repair

Robotic surgery was initially applied to hernia repair in the 2010s and has been adopted rapidly. A United States multi-hospital database analysis found 27% of surgical hernia repairs were performed via RAS in 2021[7]. Published research on robotic surgery has also surged in the last two decades, particularly in the field of hernia repair.

RAS offers advantages in the repair of both inguinal and ventral hernias. In ventral hernia repair, fewer procedures needed to be converted to open surgery with RAS compared to laparoscopic surgery. On average, the use of RAS reduces the risk of conversion by nearly 80%[8]. RAS ventral hernia repair reduced the risk of wound infection by 70% compared to an open approach, and RAS had a similar surgical site infection risk as laparoscopic surgery[9]. Although a smaller meta-analysis found no difference in hernia recurrence following RAS and laparoscopic ventral hernia repair[8], a larger meta-analysis found that RAS reduced the risk of ventral hernia recurrence by more than 65% compared to both laparoscopic and open surgical approaches[9].

4.1.4 Medtronic Hugo™ RAS system

The Medtronic Hugo™ RAS system is a modular robotic platform for performing robotic assisted minimally invasive surgery. It enables the surgeon, sitting at an ergonomically adjustable console, to view the surgical field in 3D and control movements of the endoscope and instruments with individual arms at the surgical table. It also allows surgeons and operating room (OR) teams to manually control arms at the bedside.

The Hugo RAS system has been commercially available in select geographies outside the United States since 2021. As of April 2024, Hugo has been installed in 25 countries and over 7,000 procedures have been performed. Approximately 10% of procedures have been hernia repairs.

As of February 2024, more than 50 publications reported on the use of the Hugo™ RAS system in human studies. Five publications included cohorts of greater than 100 patients[10-14]. In a study of gynecological procedures (n=138), intraoperative complications (any Clavien-Dindo grade) were reported in 2 patients (1%), and post-operative complications were reported in 9 patients (7%)[13]. A comparative study of radical prostatectomies performed with the DaVinci® (Intuitive Surgical) robot (n=378) or the Hugo™ RAS system (n=164) reported that the rate of post-operative complications (Clavien-Dindo ≥2) did not differ between groups (4% DaVinci®, 6% Hugo™ RAS; p = 0.3)[10].

To date, three publications have reported on hernia repair procedures utilizing the Hugo™ RAS system. The authors reported that the post-operative outcomes were comparable to their previous experiences with similar approaches[15-17].

All necessary design verification and validation activities have been conducted on the Medtronic Hugo™ RAS system in compliance with FDA 21 CFR Part 820. Details of all testing can be found within the Medtronic Hugo™ RAS system Report of Prior Investigations (ROPI) (**Appendix 18.2**).

4.2 Purpose

The purpose of the Medtronic Hugo™ RAS system in Inguinal and Ventral Hernia Repair Surgery (Enable Hernia Repair) study, a prospective, multi-center, single-arm, pivotal study is to specifically and directly assess the safety and performance of the Hugo™ RAS system for inguinal and ventral hernia repair surgery based on evidence-based endpoints and performance goals.

5 Objectives and/or Endpoints

5.1 Objectives

5.1.1 Primary Objective(s)

The primary objectives of this study are to demonstrate that the Medtronic Hugo™ RAS system is safe and effective when used for inguinal and ventral robotic hernia repair.

5.1.2 Secondary Objective(s)

The secondary objective of this study is to demonstrate that the Medtronic Hugo™ RAS system performs as intended when used in inguinal and ventral hernia repair robotic assisted surgery. The secondary endpoints of this study will assess the overall performance of the Medtronic Hugo™ RAS system when used for hernia repair robotic assisted surgery.

5.2 Endpoints

5.2.1 Primary Endpoints

The primary effectiveness endpoint is the surgical success rate defined as the procedure not going into conversion. Conversion is defined as the switch from the robotic-assisted approach using the Hugo™ RAS system to laparoscopic, open surgery, or use of an alternative robotic-assisted system.

Procedural steps that are usually performed without robotic assistance per standard of care, including but not limited to mesh insertion, suture needle removal, or tacking, are not considered a conversion and will not contribute to the primary effectiveness endpoint.

The primary safety endpoint is the overall rate of subjects with one or more study procedure- and/or device-related surgical-site events (SSEs), from the first incision through 30 days post-procedure. SSE is defined as the following complications:

- Surgical-site occurrence (SSO):
  - Bleeding, Hemorrhage: Requiring transfusion
  - Bowel Injury
  - Bowel Obstruction
    - Note: Functional obstruction associated with general anesthesia and/or pain killer drugs (opioids) is excluded for this endpoint
  - Cellulitis
  - Epigastric Vessel Injury
  - Symptomatic Hematoma: Requiring procedural intervention
  - Symptomatic Seroma: Requiring procedural intervention
  - Symptomatic Edema: Requiring procedural intervention
    - Note: Procedural intervention is defined as percutaneous drainage, wound opening or debridement, suture excision, or mesh removal (partial or total)
- Surgical-site infection (SSI): Infection occurring where the surgery took place, including superficial, deep, and organ space infections (standardized definition developed by the CDC)

The relatedness of the SSEs being classified as "procedure- and/or device-related" may include three scenarios: (1) only procedure-related SSEs, (2) only device-related SSEs, and (3) SSEs that are both procedure- and device-related. In this study procedure-relatedness refers to an AE that occurs due to the hernia repair procedure with the Hugo™ RAS system, and device-relatedness refers to an AE that results from the presence or performance (intended or otherwise) of the Hugo™ RAS system.

5.2.2 Secondary Endpoints

Secondary objectives include descriptive analyses of secondary endpoints.

The following safety and performance data shall be collected through 30 days post-procedure to assess the overall safety and performance of the Medtronic Hugo™ RAS system when used for hernia repair robotic assisted surgery:

- Complication rate: Overall rate of subjects with one or more procedure- and/or device-related complications (Clavien-Dindo Grade I or higher), from the first incision through 30 days post-procedure
- Major complication rate: Overall rate of subjects with one or more major procedure- and/or device-related complications (Clavien-Dindo Grade III or higher), from the first incision through 30-days post-procedure
- Operative time: time from skin incision to skin closure
- Readmission rate through 30 days post-procedure: Admission for a direct consequence or complication associated with the treated hernia or with the surgical procedure to treat the hernia
- Reoperation rate through 30 days post-procedure: Operation for a direct consequence or complication associated with the treated hernia or with the surgical procedure to treat the hernia
- Recurrence rate through 30 days post-procedure: Clinical hernia recurrence is defined as a

palpable fascial defect and/or a clinically manifested bulge within 7 cm of the original repair, exacerbated by a Valsalva maneuver during physical examination by a study investigator.

The following long-term secondary endpoints will be assessed through 2 years post-procedure in all treated subjects:

- Recurrence rate through 2 years post-procedure
    - Note: Suspected hernia recurrence(s) reported by a subject, but not confirmed by an investigator, will not be considered as a clinical hernia recurrence for this endpoint, but will be reported separately as a subject-reported recurrence.

Clinical hernia recurrence is defined as a palpable fascial defect and/or a clinically manifested bulge within 7 cm of the original hernia repair, exacerbated by a Valsalva maneuver during physical examination by a study investigator.

- Hernia recurrence will be evaluated by physical examination and confirmed, if deemed necessary, by a study investigator following site standard of care for medical imaging of hernia evaluation.
- If standard of care imaging (Computerized Tomography Scan (CT scan), ultrasound, or Magnetic Resonance Imaging (MRI)) is done for hernia recurrence confirmation, at the discretion of the study investigator, the final decision to report a clinical hernia recurrence will be based on the study investigator's assessment. Standard of care imaging may be done by a non-study, standard of care assessor, such as a radiologist.
- Secondary hernias will need to be differentiated from primary hernia recurrences by a study investigator. Secondary hernias are defined as a hernia located >7 cm of the original hernia repair. Secondary hernias will be excluded from hernia recurrence reporting for all hernia recurrence endpoints, but will be captured on an adverse event electronic case report form (eCRF).

5.3 Ancillary Objectives

Descriptive analyses of other pre-specified outcome measures beyond the primary and secondary objectives are as follows, and are not intended as a focus of the study for the evaluation of the study device:

- Estimated intraoperative blood loss
- Transfusion rate through 30 days
- Mortality through 30 days
- Device- and/or procedure-related AEs through 2 years
- Hospital length of stay
- Readmission rate through 2 years: Admission for a direct consequence or complication associated with the treated hernia or with the surgical procedure to treat the hernia
- Reoperation rate through 2 years: Operation for a direct consequence or complication associated with the treated hernia or with the surgical procedure to treat the hernia

- Surgeon experience
- Pain scores at baseline, 30-days, and 3-months (Abdominal Core Health Quality Collaborative [ACHQC] questionnaire)

A surgeon experience survey (**Appendix 18.9**) will be conducted after the first procedure and after the tenth procedure. If the surgeon conducts fewer than ten procedures in the study, the second survey will be conducted after the final procedure. The ACHQC questionnaire is available in **Appendix 18.10.**

6 Study Design

A prospective, multicenter, single-arm pivotal study will be performed with up to 192 enrolled subjects undergoing inguinal or ventral hernia repair RAS procedure using the Medtronic Hugo™ RAS system. Subjects will be followed for two years post procedure. This study will be conducted using up to ten investigative sites in the US.

6.1 Duration

The expected total study duration is approximately three years, representing 15 months of enrollment and 2 years of subject follow-up.

The duration of individual subject participation will be at least two years.

6.2 Rationale

6.2.1 Justification for the Clinical Evaluation

The Hugo RAS system has been commercially available in select geographies outside the United States since 2021. As of April 2024, Hugo has been installed in 25 countries and over 7,000 procedures have been performed. Approximately 10% of procedures have been hernia repairs.

As of February 2024, more than 50 publications reported on the use of the Hugo™ RAS system in human studies. Five publications included cohorts of greater than 100 patients[10-14]. In a study of gynecological procedures (n=138), intraoperative complications (any Clavien-Dindo grade) were reported in 2 patient (1%), and post-operative complications were reported in 9 patients (7%)[13]. A comparative study of radical prostatectomies performed with the DaVinci® (Intuitive Surgical) robot (n=378) or the Hugo™ RAS system (n=164) reported that the rate of post-operative complications (Clavien-Dindo ≥2) did not differ between groups (4% DaVinci®, 6% Hugo™ RAS; p = 0.3)[10].

To date, three publications have reported on hernia repair procedures utilizing the Hugo™ RAS system. The authors reported that the post-operative outcomes were comparable to their previous experiences with similar approaches[15-17].

The safety and performance of available RAS systems have been evaluated in the literature, as summarized in **Table 1**. Robotic assisted surgery was comparable or superior to open or traditional laparoscopic surgery in all but two comparisons. This section provides a general overview of the literature comparing RAS hernia repair procedures to laparoscopic and open surgical procedures. For the literature

data assessed to determine the primary and secondary objectives and performance goals, please refer to **Section 6.2.2** with references presented in **Section 17.1**.

Table 1. Analyses of Available RAS systems

	RAS vs. Open Surgery		RAS vs. Laparoscopic	
RAS Safety and Performance Metrics	**Statistical Significance in Favor of RAS**	**RAS Comparable to Open Surgery**	**Statistical Significance**	**RAS Comparable to Laparoscopic**
Overall Complication Rate	**8/17 studies**[18-25]	**9/17 studies**[26-34]	**In Favor of RAS (2/8 studies):**[35, 36] **In Favor of Lap (1/8 studies):**[24]	**5/8 studies** (25, 26, 37-39)
Length of Hospital Stay	**11/16 studies** (18-20, 22-24, 26-28, 34, 40)	**5/16 studies**[29-33]	**In Favor of RAS (3/8 studies):** (24, 36, 37)	**5/8 studies** (18, 26, 35, 38, 39)
Blood Loss	**14/15 studies** [18-24, 26, 29, 30, 32-34, 41]	**1/15 studies**[40]	**In Favor of RAS (1/8 studies):**[24] **In Favor of Lap (1/8 studies):**[36]	**6/8 studies** (18, 26, 35, 37-39)
Conversion to Open Surgery	**N/A**	**N/A**	**In Favor of RAS (3/3 studies):** (18, 35, 37)	**0/3 studies**

Lap: Laparoscopic surgery; RAS: Robot-assisted surgery.

This study seeks to specifically and directly assesses the safety and performance of the Hugo™ RAS system for inguinal and ventral hernia repair surgery by collecting data on evidence-based endpoints as defined in **Section 5.25**.

6.2.2 Clinical Study Design Justification

A systematic literature search was conducted on 11-Oct-2023 for the search period of 01-Jan-2018 and 10-Oct-2023 to identify published clinical data on the use of RAS and laparoscopy/minimally invasive surgery (MIS) for hernia repair. The databases searched were MEDLINE, Embase and Journals@Ovid Full Text. The population was adult (non-pediatric) subjects.

MIS, including traditional laparoscopy and RAS, is recommended by different international guidelines for

ventral[1] and inguinal[2] repair in most cases. Given the ubiquity of laparoscopic procedures, and in comparison, the relatively smaller proportion of reported RAS procedures, the datasets used to justify the clinical study design combine both laparoscopy and RAS to present a more holistic view of the current state of clinical practice. For the primary effectiveness endpoint, surgical success rate, only RAS hernia repair data were assessed, and laparoscopic datasets were excluded.

The literature search returned 803 articles, and subsequent screening to include procedures that were closely aligned with those that will be conducted in this study yielded a total of 31 articles, which were used to establish the study design (safety and effectiveness endpoints, performance goals, sample size, and follow-up timeframes). The full bibliography of all 31 publications supporting the primary and secondary endpoints and performance goals is included in **Section 17.1**. Confidence intervals and prediction intervals obtained from the literature data meta-analyses were used to support the primary endpoint performance goals, as described in **Section 14.4**.

The primary effectiveness endpoint is surgical success rate, which has been widely used in RAS studies. Upon review of the applicable literature, there were four cohorts of patients who underwent ventral hernia repair in three publications and six cohorts of patients who underwent inguinal hernia repair reported in four publications with data on conversions from RAS to open or laparoscopic surgery. The inguinal and ventral literature data were analyzed together for the primary effectiveness endpoint. Surgical success rate is determined by subtracting the conversion rate from 100%. The rate of conversions during RAS hernia repair ranged from 0.0% (Saito 2020; Saito 2022; El Dahdah 2023) to 9.4% (Dixon 2023) for inguinal hernia repair and from 0.0% (Orthopoulos 2018; Kennedy 2018) to 11.1% (Dixon 2023) for ventral hernia repair.

For the primary safety endpoint, the literature review showed that most publications report on more minor and specific complications following the procedures, such as SSIs and SSOs. Literature definitions of complications vary widely across published literature on hernia repairs[3]. In our study, SSEs represent a composite endpoint that aims to capture the more commonly reported complications resulting from hernia repair procedures.

SSE is defined as the following complications:

- Surgical-site occurrence (SSO):
  - Bleeding, Hemorrhage: Requiring transfusion
  - Bowel Injury

[1] Bittner, R., Bain, K., Bansal, V.K. et al. Update of Guidelines for laparoscopic treatment of ventral and incisional abdominal wall hernias (International Endohernia Society (IEHS)): Part B. Surg Endosc 33, 3511–3549 (2019). https://doi.org/10.1007/s00464-019-06908-6

[2] The HerniaSurge Group. International guidelines for groin hernia management. Hernia 22, 1–165 (2018). https://doi.org/10.1007/s10029-017-1668-x

[3] DeBord, J., Novitsky, Y., Fitzgibbons, R. *et al.* SSI, SSO, SSE, SSOPI: the elusive language of complications in hernia surgery. *Hernia* 22, 737–738 (2018).

- Bowel Obstruction
- Cellulitis
- Epigastric Vessel Injury
- Symptomatic Hematoma: Requiring intervention
- Symptomatic Seroma: Requiring intervention
- Symptomatic Edema: Requiring intervention

- Surgical-site infection (SSI): Infection occurring where the surgery took place, including superficial, deep, and organ space infections (standardized definition developed by the CDC[4]).

Upon review of the applicable literature, there were 22 cohorts of patients who underwent inguinal hernia repair with data on SSEs in 16 publications and 10 cohorts of patients who underwent ventral hernia repair with data on SSEs reported in 8 publications. The rate of SSEs following RAS or laparoscopic inguinal hernia repair ranged from 0.0% (Jan 2021; Saito 2020; Gundogdu 2021; Charles 2018; Dixon 2023) to 30.0%

Section 5 describes the study objectives in detail. The details on primary endpoints and their associated performance goals (PGs) based on the systematic literature review and meta-analyses are provided in **Section 14.4**. Secondary endpoints are detailed in **Section 14.5**., which are descriptive in nature, and their PGs are provided for benchmark only.

6.3 Study Oversight

The study will utilize a Steering Committee. The Steering Committee advises on the scientific content of the study and provides input for the execution. Members may be study site investigators. The purpose of the Steering Committee is to provide unbiased opinions and expertise to the clinical study design and process. The Steering Committee will support the execution of the Enable Hernia Repair study and provide guidance, feedback, and direction to the study. Detailed information, such as the member selection, composition, duties, procedures, and deliberation rules are documented in the Steering Committee Charter.

7 Product Description

7.1 General

The Medtronic Hugo™ RAS system is a modular robotic platform for performing robotically assisted minimally invasive surgery. It enables the surgeon, sitting at an ergonomically adjustable console, to view the surgical field in three dimensions (3D) and control movements of the endoscope and instruments with individual robotic arms at the operating table. It also allows surgeons and OR teams to manually control arms at the bedside, including using one arm as an endoscope holder. The Medtronic Hugo™ RAS system platform supports a portfolio of wristed instruments.

[4] As defined in the CDC National Healthcare Safety Network document "Surgical Site Infection Event (SSI)" https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf

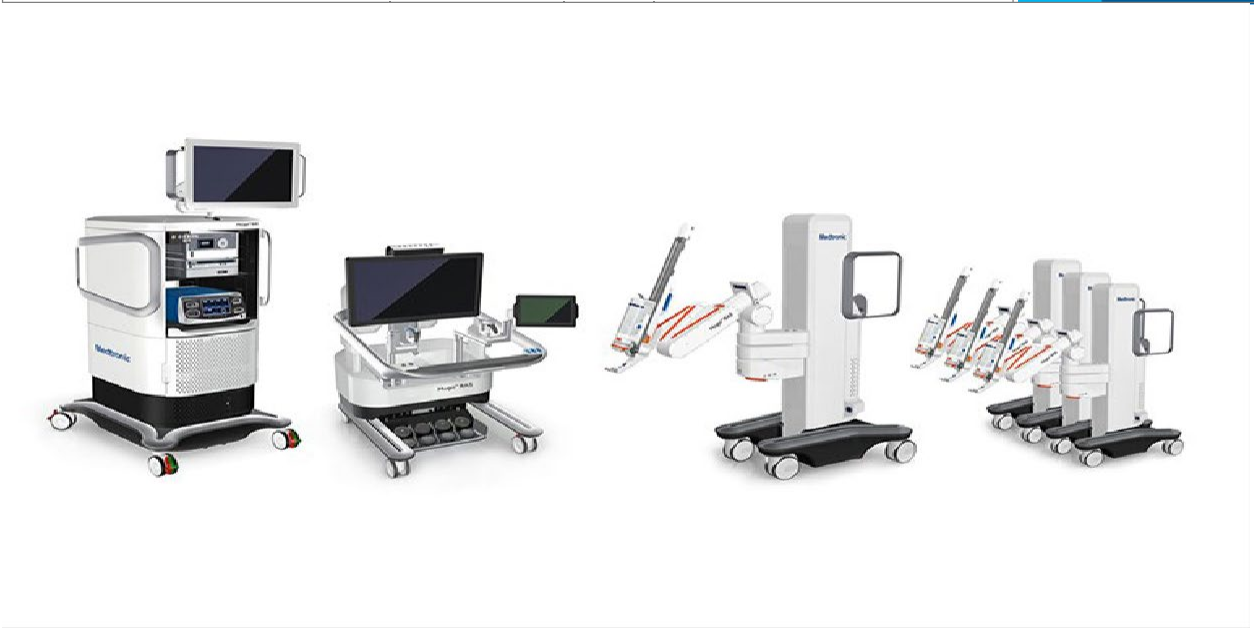

Figure 1: Medtronic RAS Overview- Left to Right: System Tower, Surgeon Console, Arm Carts (4)

The main components of the Medtronic Hugo™ RAS system are described in the following subsections.

7.1.1 Hugo™ RAS Tower, 120v

The system tower houses computers, the endoscope system, the electrosurgical generator, the power management system with a backup battery, and the high-definition OR team touchscreen interactive display. The system tower allows the surgeon console to control the movements of up to four arms. It may also be used without the surgeon console to power up to four arms for standalone manual control at the bedside, or by itself for standard laparoscopic visualization and electrosurgery.

7.1.2 Hugo™ RAS Surgeon Console

The surgeon console is an open console that consists of a large flat screen with a high-definition 3D passive display, a small touchscreen interactive display, adjustable ergonomic controls, an armrest, two surgeon hand controllers, a set of foot pedals, and 3D surgeon and observer glasses. Sensors in the surgeon console track the movement of the 3D glasses worn by the surgeon and can clutch movement of the instruments if the surgeon looks away from the 3D display. The surgeon hand controllers are easy to move and respond to wrist movement.

7.1.3 Hugo™ RAS Arm Cart Assembly

The arm carts consist of movable platforms with casters, each supporting a modular and extendable arm. Up to four arm carts can be connected to the system tower for simultaneous use during RAS. The arm carts are portable and easily movable within the operating room and the hospital. Prior to surgery, the OR team positions the arm carts around the surgical table according to the surgical procedure. The team can adjust the arm carts and arms to accommodate subject positioning and optimize bedside access to the

subject.

7.1.4 Hugo™ RAS Endoscope Adapter

The Hugo™ RAS endoscope adapter is intended to hold the compatible Karl Storz TIPCAM ®1 S 3D endoscope used with the Medtronic Hugo™ RAS system. The endoscope adapter will be attached to the robotic arm for the Medtronic Hugo™ RAS system during the representative surgical procedures set forth in the Medtronic Hugo™ RAS system User Guide.

7.1.5 Hugo™ RAS Sterile Interface Module

The Hugo™ RAS sterile interface module device is intended to be used with the Hugo™ RAS system as a universal connection on the robotic arm for the Hugo™ RAS sterile instruments and endoscope adapter during the representative surgical procedures set forth in the Hugo™ RAS system User Guide.

7.1.6 Hugo™ RAS Arm Cart Sterile Drapes

The Hugo™ RAS Arm Cart Sterile Drape is a single use, sterile drape that is designed as part of the Hugo™ RAS system. There are three types of sterile drapes, and each is designed to cover a different non-sterile section of the Hugo™ RAS Arm Cart. The Arm Cart Sterile Drape covers the non-sterile robotic arm, or upper part of the arm cart, or lower part of the arm cart of the Hugo™ RAS system to allow the system to be used within the sterile field.

For Hugo™ RAS system configuration information, Instructions for Use, indications, contraindications, warnings, and precautions, refer to the Hugo™ RAS system User Guide.

The product is to be used by medical professionals qualified in the transportation, preparation, and use of surgical devices. The Hugo™ RAS system is intended for use in a sterile operating room environment.

7.1.7 Wristed Instruments

The Hugo™ RAS system's wristed instruments are minimally invasive instruments that provide two degrees of freedom (pitch, yaw) at the distal end of the instrument in addition to the opening and closing of the instrument jaws. These degrees of freedom, when commanded from the surgeon console, allow for precise and dexterous control of the instrument by the surgeon. For Hugo™ RAS system configuration information, Instructions for Use, indications, contraindications, warnings, and precautions, refer to the Hugo™ RAS system User Guide.

These products are to be used by medical professionals qualified in the transportation, preparation, and use of surgical devices. The Hugo™ RAS system is intended for use in a sterile operating room environment.

7.1.7.1 Hugo™ RAS Monopolar Curved Shears

The Hugo™ RAS Monopolar Curved Shears is a Hugo™ RAS wristed instrument with a sharp curved cutting-blade end effector for tissue manipulation including blunt dissection, sharp dissection, electrocautery and cutting. The Hugo™ RAS monopolar tip cover is required when using the Hugo™ RAS monopolar curved shears.

7.1.7.2 Hugo™ RAS Monopolar Tip Cover

Monopolar shears are used to cut and cauterize tissue, however only the jaws should be energized. A tip cover is installed over the distal end of the instrument to prevent other metallic parts of the distal end from conducting electricity. This cover should be checked for structural integrity after every instrument extraction to prevent unintended burns to the subject as outlined in the Instructions for Use.

7.1.7.3 Hugo™ RAS Bipolar Fenestrated Grasper

The Hugo™ RAS Bipolar Fenestrated Grasper is a Hugo™ RAS wristed instrument with a fenestrated jaw end effector for tissue manipulation including grasping, blunt dissection, approximation, electrocautery, and suturing.

7.1.7.4 Hugo™ RAS Bipolar Maryland Forceps

The Hugo™ RAS Bipolar Maryland Forceps is a Hugo™ RAS wristed instrument with a curved tapered jaw end effector with fenestration at the base of the jaw for tissue manipulation including grasping, blunt dissection, approximation, electrocautery, and suturing.

7.1.7.5 Hugo™ RAS Large Needle Driver

The Hugo™ RAS Large Needle Driver is a Hugo™ RAS wristed instrument with an end effector designed to hold and drive large needles.

7.1.7.6 Hugo™ RAS Extra Large Needle Driver

The Hugo™ RAS Extra Large Needle Driver is a Hugo™ RAS wristed instrument with an end effector designed to hold and drive large needles.

7.1.7.7 Hugo™ RAS Cadiere Forceps

The Hugo™ RAS Cadiere Forceps is a Hugo™ RAS wristed instrument with a rounded, wide fenestrated jaw end effector for tissue manipulation including grasping, blunt dissection, approximation, and suturing.

7.1.7.8 Hugo™ RAS Double Fenestrated Grasper

The Hugo™ RAS Double Fenestrated Grasper is a Hugo™ RAS wristed instrument with a long fenestrated jaw end effector for tissue manipulation including grasping, blunt dissection, approximation, and suturing.

7.1.7.9 Hugo™ RAS Toothed Grasper

The Hugo™ RAS Toothed Grasper is a Hugo™ RAS wristed instrument with a toothed claw grasper end effector for tissue manipulation including grasping and approximation.

7.1.8 Software

Software versions will be captured in shipment records, including the clinical shipment/return form.

7.2 Manufacturer

The manufacturer of record for the Hugo™ Robotically RAS system is located at the following address:

Covidien LLC
15 Hampshire Street
Mansfield, MA 02048
USA

Establishment Registration: 1282497

7.2.1 Design & Development:

The Hugo™ RAS system is, and has been, designed and developed at three different locations, as outlined in **Table 2**. The North Haven, CT facility has been responsible for general oversight of the design and development activities related to the Hugo™ RAS system.

Table 2: Design and Development Sites for Hugo™ RAS system

Site Location	Activities and Responsibilities
Medtronic 60 Middletown Avenue North Haven, CT 06473	Full quality management system, including management review, complaint handling, supplier controls, change control, design, and development of the Hugo™ RAS system. The North Haven, CT site is the principal location that directs the design and development activities of the other two sites in accordance with Medtronic's Quality Management System (QMS).
Medtronic 266 Summer Street Boston, MA 02210	Design and development of the RAS Console and software. Provision of Subject Matter Experts and competencies in technical areas pursuant to designing and developing the RAS system according to the design and development plan.
Medtronic Argelsrieder Feld 10 82234 Wessling Germany	Design and development of the RAS Arm and RAS Setup Arm. Provision of Subject Matter Experts and competencies in technical areas pursuant to designing and developing the RAS system according to the design and development plan.

7.2.2 Contract Manufacturing Sites:

Manufacturing activity is conducted at various contract manufacturing sites, with the contract manufacturing of the three main components of the Hugo™ RAS system being conducted by Plexus Corporation, as identified in **Table 3**.

Table 3: Contract Manufacturers

Product Description	Catalog Number/SKU	Contract Manufacturer
Surgeon Console	MRASC0001	[redacted]
Arm Cart Assembly	MRASC0002	
Tower, 120V	MRASC0003	
Task Simulator	MRASC0004	
Robotic Arm Assembly	MRASC0007	
3D Glasses, Surgeon Only	MRASA0004	
3D Glasses, Observer	MRASA0005	
Robotic Arm Sterile Drape	MRASA0006	
Upper Arm Cart Sterile Drape	MRASA0007	
Lower Arm Cart Sterile Drape	MRASA0008	
Sterile Monopolar Cover	MRASA0009	
Endoscope Adapter	MRASA0002	
Sterile Interface Module	MRASA0003	
Monopolar Curved Shears	MRASI0001	
Bipolar Fenestrated Grasper	MRASI0004	
Bipolar Maryland Forceps	MRASI0005	
Large Needle Driver	MRASI0006	
Extra Large Needle Driver	MRASI0007	
Cadiere Forceps	MRASI0011	
Double Fenestrated Grasper	MRASI0012	
Toothed Grasper	MRASI0016	

7.3 Packaging

The Medtronic Hugo™ RAS system components and instruments will be labelled as investigational according to regulations, such as: “CAUTION – Investigational device. Limited by Federal (or United States)

law to investigational use".

7.4 Intended Population

The target population will consist of subjects 22 years of age or older indicated for an inguinal or ventral hernia repair robotic assisted surgery with the Hugo™ RAS system.

7.5 Equipment

The necessary equipment to complete the study procedure, includes but is not limited to, the lists below.

Medtronic Hugo™ RAS system (Investigational Device):

The investigational device will be provided by the study sponsor (**Table 4**).

Table 4. Investigational Devices

SKU	Description (Branding Company)	Investigational or Commercially Available
MRASC0001	Surgeon Console (Medtronic)	Investigational
MRASC0002	Arm Cart Assembly (Medtronic)	Investigational
MRASC0003	Tower, 120v (Medtronic)	Investigational
MRASA0002	Endoscope Adapter (Covidien)	Investigational
MRASA0003	Sterile Interface Module (Covidien)	Investigational
MRASA0004	3D Glasses, Surgeon Only (Medtronic)	Investigational
MRASA0005	3D Glasses, Observer (Medtronic)	Investigational
MRASA0006	Assy, Sterile Pouch, Robotic Arm Drape (Covidien)	Investigational
MRASA0007	Assy, Sterile Pouch, Robotic Upper Cart Drape (Covidien)	Investigational
MRASA0008	Assy, Sterile Pouch, Robotic Lower Cart Drape (Covidien)	Investigational
MRASA0009	Sterile Monopolar Cover (Covidien)	Investigational
MRASI0001	Monopolar Curved Shears (Covidien)	Investigational
MRASI0004	Bipolar Fenestrated Grasper (Covidien)	Investigational
MRASI0005	Bipolar Maryland Forceps (Covidien)	Investigational
MRASI0006	Large Needle Driver (Covidien)	Investigational
MRASI0007	Extra Large Needle Driver (Covidien)	Investigational
MRASI0011	Cadiere Forceps (Covidien)	Investigational
MRASI0012	Double Fenestrated Grasper (Covidien)	Investigational
MRASI0016	Toothed Grasper (Covidien)	Investigational

NOTE: All Hugo™ RAS SKU's regardless of branding are manufactured by Covidien LP, 15 Hampshire Street,

Mansfield, MA 02048 USA.

Medtronic Hugo™ RAS system-Compatible Components:

The following components are required, if applicable, for study procedures and will be provided by the study sponsor (**Table 5**).

Table 5. Medtronic Hugo™ RAS system-Compatible Components

SKU	Product Description (Manufacturer)	Investigational or Commercially Available
TC200EN	Storz 3D Camera Control / System (Karl Storz)	Commercially Available
TC302EN	Storz 3D SCB Interface & Spies System (Karl Storz)	Commercially Available
TL 300	Storz Cold Light Fountain Power LED 300 (Karl Storz)	Commercially Available
26605BA	Storz 30 Degree 3D Endoscope (Karl Storz)	Commercially Available
26605AA	Storz 0 Degree 3D Endoscope (Karl Storz)	Commercially Available
495VIT	Storz Fiber Optic Light 5.5m Cable (Karl Storz)	Commercially Available
TC015	Storz Video Extension Cable (Karl Storz)	Commercially Available
VLFT10GEN	FT-10 Generator (Covidien)	Commercially Available
FT0510	Reusable Monopolar Electrosurgery Cord (Covidien)	Commercially Available
E0020V	Reusable Bipolar Electrosurgery Cord (Covidien)	Commercially Available
RUNVCA8STF	VersaOne™ Universal Cannula Positioning Trocar System – 8mm standard Universal Fixation Cannula (Covidien)	Commercially Available
RNONB8STF	VersaOne™ Bladeless Positioning Trocar System – 8mm standard fixation trocar (Covidien)	Commercially Available
RONB11STF	VersaOne™ Optical Positioning Trocar System – 11mm standard fixation trocar (Covidien)	Commercially Available
RSEAL	VersaOne™ Reusable Positioning Trocar System – 5mm - 12mm Seal (Covidien)	Commercially Available
OBTNONB8ST	VersaOne™ Reusable Positioning Trocar System – 8mm standard Bladeless Obturator (Covidien)	Commercially Available

OBTONB11ST	VersaOne™ Reusable Positioning Trocar System – 11mm standard Optical Obturator (Covidien)	Commercially Available
RC8STS	VersaOne™ Reusable Positioning Trocar System – 8mm standard Reusable Positioning Cannula (Covidien)	Commercially Available
RC11STS	VersaOne™ Reusable Positioning Trocar System – 11 mm standard Reusable Positioning Cannula (Covidien)	Commercially Available
KSZ-39301TS	Endoscope Sterilization Tray	Commercially Available

Mesh:

- The choice of the mesh is at the surgeons' discretion depending on their local standard of care for this indication. The mesh will not be provided by the study sponsor and should be used in accordance with the instructions for use.

Other Equipment:

The following components may be required for the study procedures and will not be provided by the study sponsor.

- Energy Sealing Device
- Linear Stapler
- Reticulating Stapler
- Surgical Clips

7.6 Product Use

This information is contained in the Hugo RAS system User Guide and accompanying labeling (**Appendix 18.3**). The User Guide and additional labeling should always be consulted.

The device will be in contact with the abdominal region including tissues and body fluids. All device components and materials are biocompatible. Device biocompatibility testing and results are summarized in the RPI (**Appendix 18.2**).

For instructions on study product scope of use and handling, please refer to the IFU (**Appendix 18.3**).

7.7 Product Training Materials

The Medtronic Hugo™ RAS system should only be used by surgeons and OR staff who have received specific product training provided by Medtronic in the use of this device (**Table 6**). The training provided by Medtronic does not replace the necessary medical training and experience required to perform

surgery.

Surgeons and hospital staff performing study procedures will be required to demonstrate a minimum level of professional competency and product training outlined below prior to performing study procedures.

Technical Training focus areas include:

- Hugo™ System Operation
- Hugo™ System Surgical Field Set-up
- Hugo™ System Console Skills
- Hugo™ System Clinical Application
- RAS Fundamental Surgical Task Skills

Table 6. Professional Competency and Product Training

	Professional Competency	Product Training
Principal Investigator(s)	• At least 2 years of surgical training and/or experience conducting laparoscopic surgery • At least 2 years robotic experience with the specific study procedure(s) they will be performing for the study • On average, completing 10-12 procedures annually (specifically the study procedure (s) they will be performing for the study)	• Completed simulator exercises on the Medtronic Hugo™ RAS system • Didactic training on the capability and features of the Medtronic Hugo™ RAS system • Completed hands-on training course
OR Staff	• At least 2 years of surgical training and/or experience in robotic surgery	• Didactic training on the capability and features of the Medtronic Hugo™ RAS system • Completed hands-on training course

All study site personnel will be trained on relevant information prior to their participation in the study.

Surgeon proctoring will be provided to the Investigators as directed by Medtronic Robotic Surgical Technologies. Medtronic personnel may be present for the investigational implants at the sites.

7.8 Product Receipt and Tracking

The Medtronic Hugo™ RAS system and necessary equipment will be shipped to each site and tracked. In the case that model, lot, and/or serial numbers are not available on the packaging, the sponsor will assign lot, batch, or serial numbers to the study product to maintain traceability. Each site will review the content

of the shipping form and investigational product upon receipt. The use of the device for a procedure or disposition of the devices (e.g., if returned due to damage upon arrival) will be recorded on a site device accountability log to be maintained at the site and reconciled by the end of the study.

The Medtronic Hugo™ RAS system and necessary instruments will be provided to each site upon sponsor collection and approval of all required regulatory documents.

The date when the site receives the Hugo™ RAS system, will be recorded and maintained during the clinical investigation. Each Medtronic Device and Device Instrument will be traced with the serial or lot number.

7.9 Product Storage

Access to the study should be limited to designated study staff only. Study device components should be covered with sponsor provided device covers when not in use for study procedures.

Study devices should be kept in or otherwise contained where only qualified study personnel can access the device (i.e., locked or secured). This area/container should be kept at ambient temperatures without exposure to water with adequate provisions for maintaining ambient temperatures if a loss of power is experienced. If the devices are exposed to water or a drastic change in temperature, sites should contact the study team for possible replacement devices.

7.10 Product Return

It is the responsibility of the site to return the Medtronic Hugo™ RAS system to Medtronic at the end of the study, along with any unused or expired Medtronic Hugo™ RAS wristed instruments or other components. Sites should follow instructions and complete all appropriate forms provided by the study team for product return.

7.11 Product Accountability

Access should be limited to designated study staff only. A device accountability log will be maintained at the site and reconciled by the end of the study. It is the site's responsibility to document the receipt (which includes shipping/dispersal date, the quantity, model, lot, and serial numbers, and expiration date), disposition of the product (per subject use, including amount used, amount remaining, etc.), transfer (if applicable), and return of all unopened investigational medical devices at the end of the study. The sponsor shall also keep records to document the physical location of all investigational devices from shipment of investigational devices to the investigation sites until return or disposal. Medtronic will perform periodic reconciliation of the investigational product to ensure traceability through monitoring.

8 Study Site Requirements

8.1 Investigator/Investigation Site Selection

All Investigators managing the subject's hernia repair must be qualified practitioners and experienced in the diagnosis and treatment of subjects with inguinal or ventral hernias. All physicians must be experienced and/or trained in the handling of the Medtronic Hugo™ RAS system.

The role of the Principal Investigator is to implement and manage the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical investigation.

The Principal Investigator shall:

- Be qualified by education, training, and experience to assume responsibility for the proper conduct of the clinical investigation
- Be experienced in the field of application and training in the use of the Medtronic Hugo™ RAS system
- Disclose potential conflicts of interest, including financial, that interfere with the conduct of the clinical investigation or interpretation of results
- Be able to demonstrate that the proposed investigational study site:
  - Has the required number of eligible subjects needed within the recruitment period
  - Has one or more qualified Investigators, a qualified investigational study site team and adequate facilities for the foreseen duration of the clinical investigation

Study site personnel training will be completed and documented prior to participation in this study.

8.2 Study Site Activation

During the activation process (prior to subject enrollment), Medtronic will train study site personnel on the clinical investigation plan (CIP), on relevant standards and regulations, informed consent, and on data collection and reporting tools. If new members join the study site team, they will receive training on the applicable study requirements relevant to their role before contributing to the study.

Prior to performing study related activities, all regulatory requirements shall be fulfilled, including, but not limited to the following:

- Institutional Review Board (IRB) approval (and voting list, as required by local law) of the current version of the CIP and informed consent (IC).
- Regulatory Authority (RA) approval or notification (as required per local law)
- Fully executed Clinical Trial Agreement (CTA)
- Financial disclosure (if applicable)
- Curriculum vitae (CV) of Investigators and key members of the investigation study site team (as required). The signature on the CV must be dated within 3 years prior to the date of activation of the study site.
- Documentation of delegated tasks

- Documentation of study training
- Additional requirements imposed by local regulations, the IRB and RA shall be followed, if appropriate

In addition, all participating study site staff must be trained on the current version of the CIP as well as on the applicable study requirements depending on their role and must be delegated by the Principal Investigator to perform study related activities.

Medtronic will provide each study site with documentation of study site/investigator readiness; this letter must be received prior to performing study related activities.

8.3 Role of the Sponsor Representatives

In addition to performing monitoring and auditing activities, sponsor representatives may provide support at the study site as required for the study under supervision of the Principal Investigator, including:

- Provide study training relevant and pertinent to the involvement of personnel conducting study activities and Investigator responsibilities.
- Technical support will be provided during the procedure under the supervision of a study Investigator, but no data entry, shall be performed by Medtronic personnel or their representatives at study sites.

In addition, for this study, sponsor representatives may be authorized by the Principal Investigator to perform the following significant trial related duties:

- Support study Investigators in performing the study implant procedure.
- Support data collection during the implant procedure and device testing.
- Support data collection during the study follow-up visits.

Any data collection completed by Medtronic personnel will be clearly identified as such.

9 Selection of Subjects

9.1 Study Population

Up to 192 subjects will be enrolled at up to ten sites in the US.

The Medtronic Hugo™ RAS system is intended to be used in this study for robotic assisted hernia repair procedures, including procedures to be performed in subjects that meet the inclusion criteria listed in **Section 9.3**.

Subject conditions and/or diagnoses may include, but are not limited to, inguinal and ventral hernia repair.

The subjects must be acceptable candidates for a fully robotic assisted procedure with the Medtronic Hugo™ RAS system, as determined by the investigating surgeon.

9.2 Subject Enrollment

A subject is considered enrolled in the study when the informed consent form is signed and dated. As soon as the surgical procedure has begun with the Medtronic Hugo™ RAS system, the subject must be followed regardless of whether the subject completed the surgical procedure with the Medtronic Hugo™ RAS system. Subject enrollment will be consecutive at the institution according to required procedure types and eligibility criteria. See **Section 14** for additional details.

9.3 Inclusion Criteria

1. Adult subjects (age ≥ 22 years) as required by local law
2. Subject has been indicated for one of the following hernia repairs:
    a. primary or incisional ventral hernia(s). Multiple small hernia defects are allowed with total distance of combined defects being < 10cm (**Figure 2: A and B**)
    b. inguinal (unilateral or bilateral) hernia(s)
3. Subject is an acceptable candidate for a fully robotic assisted surgical procedure, a laparoscopic surgical procedure, or an open surgical procedure
4. The subject is willing to participate and consents to participate, as documented by a signed and dated informed consent form

9.4 Exclusion Criteria

1. Subjects for which minimally invasive surgery is contraindicated as determined by the Investigator
2. Subjects with a recurrent hernia
3. Subjects with femoral hernia defects
4. Subjects with ventral hernia defect(s) located in M1, M5, or L4[(1)] (**Figure 2: C and D**)
5. Subjects with emergent hernia repair
6. Ventral hernia is CDC grade 2 or higher
7. Use of component separation techniques to close the hernia defect
8. Inability to close the defect in ventral hernia subjects
9. Hernia defect is ≥ 10 cm
10. Subject has BMI > 40
11. Subjects with comorbidities or medical characteristics, which would preclude the surgical procedure in the opinion of the Investigator
12. Subjects diagnosed with a bleeding disorder and/or cannot be removed from their anticoagulants prior to surgery based on surgeon discretion and standard-of-care
13. Subjects pregnant at the time of the surgical procedure
14. Subjects who are considered to be part of a vulnerable population (e.g., prisoners or those without sufficient mental capacity)
15. Subjects who have participated in an investigational drug or device research study within 30 days

of enrollment that would interfere with this study

16. Subjects with active infections including but not limited to pneumonia, urinary tract, cellulitis, or bacteremia

Classification of Abdominal Wall Hernias

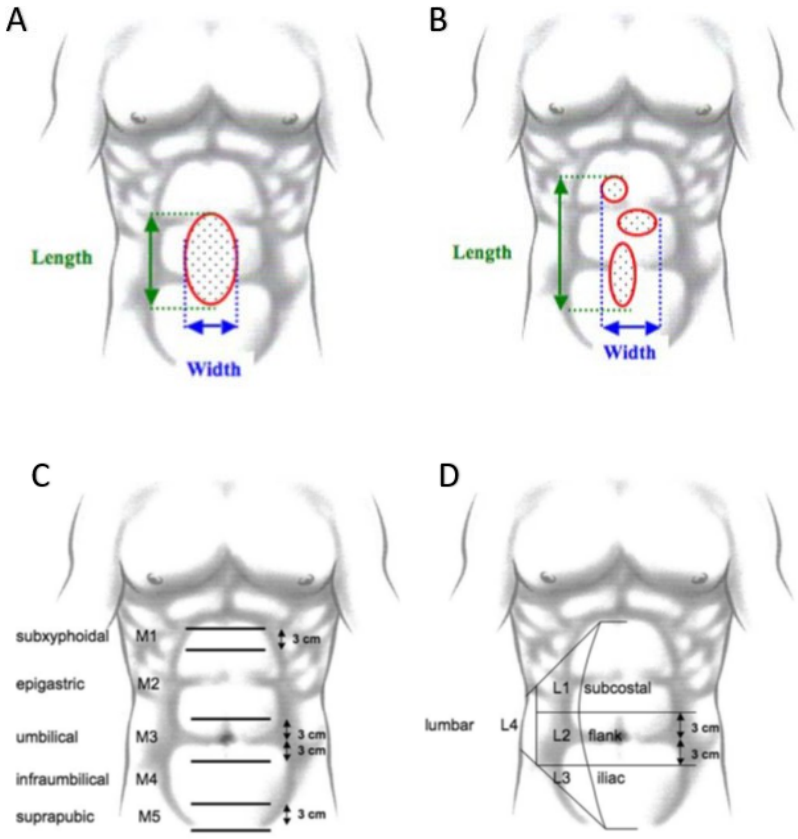

Figure 2: A and B – Definition of the width and length for single hernia defects and multiple hernia defects, respectively. C – To classify midline hernias, five zones were defined. D – To classify lateral hernias, four zones were defined (1)

10 Study Procedures

10.1 Schedule of Events

10.1.1 Screening Visit (Visit 1)

A screening visit will be performed within 30 days prior to the scheduled procedure and may be combined with the surgical procedure visit. Subjects will be consented before any procedures specific to the study are undertaken. The purpose and all aspects of the study will be explained to the subject. Subjects who agree to study participation must sign and personally date an IRB-approved informed consent form prior to participating in any study activities.

Once informed consent has been obtained according to IRB requirements and eligibility is confirmed, the subject's demographics and medical history will be assessed. Relevant medical and surgical history will be assessed and included in the electronic case report form (eCRF). All efforts to screen a diverse subject population should be made.

10.1.2 Surgical Procedure Visit (Visit 2)

The subject will arrive for admission to the hospital, will be checked in, placed in pre-op, and prepped for surgery according to local standard of care. Upon arrival to the operating room the subject will be placed on the plinth, the anesthesia and surgical teams will place the subject in position and the operation will begin at the time of the first incision. The study Investigator should perform the surgical procedure according to the appropriate standard procedures, practices, and set-up guidelines. See **Table 7** for the data that will be collected during this procedure.

10.1.3 Up to Hospital Discharge (Visit 2.1)

Visit 2.1 will begin when the subject arrives in recovery after the operation is over and will last through the subject being discharged from the hospital. All standard-of-care practices will be followed for this visit. See **Table 7** for the data that will be collected during this procedure.

10.1.4 Post-Operative Follow-Up Visit (Visit 3)

The 30 (±7) days post-operative visit should be made by an in-person follow-up visit to the site.

Only in extreme circumstances (e.g., COVID-related in person restrictions at the site, etc.), the 30 (±7) day follow-up visit may be conducted via phone call and/or video conference for the collection of adverse event and medical follow-up information.

10.1.5 Post-Operative Follow-Up Visit (Visit 4)

The 3-Month (±14 days) post-operative visit should be made by an in-person follow-up visit to the site.

Only in extreme circumstances (e.g., COVID-related in person restrictions at the site, etc.), the 3-Month

(±14 days) day follow-up visit may be conducted via phone call and/or video conference for the collection of adverse event and medical follow-up information.

10.1.6 Post-Operative Follow-Up Visit (Visit 5 and 6)

Post-operative visits 5 at 1 year (±30 days) and 6 at 2 years (±30 days) will be made via phone call. It is permissible for the visits to be conducted in person if it coincides with a standard of care office visit.

Subjects who report a hernia recurrence or an AE that requires investigator assessment must then complete an in-person office visit. If this occurs, the rest of the visit data in this section may be collected either over the phone or in person. If collected in person, the visit should still be entered in the eCRF as a standard follow-up visit. Importantly, data listed below should be collected only once per annual visit whether collected via phone, in person, or combination of both. If any data is collected out of window, a protocol deviation should be reported.

Every attempt must be to have all subjects complete the follow-up visit schedule. For subjects who do not show up for a scheduled study visit, the site must contact the subject in a timely manner to reschedule the visit and associated required evaluations within the subject's window, if possible.

In cases where the required attempts to make contact have been unsuccessful but there is no evidence that the subject has expired, sites will complete a Protocol Deviation for Visit Not Done and attempts to contact subjects will be made again the following year. Also refer to **Section 10.10.3 - Lost to Follow-up**.

10.2 Data Collection

Data collection requirements are summarized in **Table 7**. In addition, a surgeon experience survey (**Appendix18.9**) will be conducted after the first procedure and after the tenth procedure. If the surgeon conducts fewer than ten procedures in the study, the second survey will be conducted after the final procedure. The ACHQC questionnaire is available in **Appendix 18.10.**

Table 7. Data Collection and Study Procedure Requirements at Subject Visits

Procedure/Assessment	Screening (Day -30 to 0) Visit 1	Surgical Procedure (Day 0) Visit 2	Hospital Discharge Visit 2.1	Follow-Up (30±7 Days) Visit 3	Follow-Up (3-Months ±14 Days) Visit 4	Follow-Up (Years 1-2 ±30 Days) Visit 5-6 (Phone)
	May be Combined					
Informed Consent Form[1]	X					
Eligibility Criteria	X	X				
Demographic Data	X					
Medical/Surgical History	X					
Concomitant Medication(s)	X	X	X	X	X	X
Robot Setup Time		X				
Total Operative Time (skin to skin)		X				
Surgeon Console Time		X				
Instruments Used		X				
Estimated Blood Loss		X				
Transfusion[3]		X	X	X	X	
Conversion to a laparoscopic, open surgery, or use of an alternative robotic-assisted system		X				
Robot Take Down Time		X				
Mortality			X	X	X	X
Length of Hospital Stay			X			
Reoperation			X	X	X	X
Pain Medication[4]			X	X	X	X
Adverse Events and Device Deficiencies[2]	X	X	X	X	X	X

Readmission				X	X	X
Recurrence				X	X	X
Device Accountability		X				
ACHQC Questionnaire	X			X	X	
Protocol Deviation Collection (if applicable)	X	X	X	X	X	X
Study Exit						X

[1]Study specific procedures may only be performed after subject has agreed to participate and signed the informed consent form. Screening and informed consent are considered as a process that may occur over multiple days within 30 days prior to procedure. Any new information about the subject's eligibility and willingness to participate must be considered prior to the procedure with the investigational device.

[2]AEs must be followed until resolution or study exit, whichever comes first. Adverse Events will be collected from the moment of consent. If any events are ongoing at study exit, they will be monitored by the physician per their institutional standard-of-care. Refer to section 12 for AEs and DDs collected in scope of this study.

[3]Transfusion will only be collected when associated with an adverse event.

[4] Pain medication(s) must be reported if given when pain is reported as an AE.

Note: The target number of days for the 3-month, 1-year, and 2-year visits is 90 days, 365 days, and 730 days post-procedure, respectively.

10.3 Subject Screening

Consented subjects will be considered for the study if they meet specified inclusion criteria and none of the exclusion criteria. The criteria for enrollment must be followed explicitly.

10.4 Prior and Concomitant Medications/Therapies

Institutional standard of care (SoC) pre-operative protocols and guidelines are typically in place to manage medications and are not reportable for the purposes of this study. Follow the guidelines below to report medications relevant to this study:

- Report applicable pre-procedure medications if taken within 30 days of the study procedure as listed in **Section 10.4.1 and 10.4.2**.
- Pain medication(s) must be reported if given when pain (Clavien-Dindo Grade I or higher – pain exceeds that which is considered within normal limits) is reported as an AE.
- Medications given during the procedure and/or post-procedure as treatment or preventative that result in a reportable AE should be captured.

For study purposes, reporting of the following drugs are required to evaluate potential AEs and endpoints.

10.4.1 Anticoagulants Taken within 30 Days Prior to Surgery

Prescription anticoagulants may include:

- Warfarin (Coumadin)
- Enoxaparin (Lovenox)
- Clopidogrel (Plavix)
- Ticlopidine (Ticlid)
- Aspirin (in many versions)
- Non-steroidal anti-inflammatory (NSAIDs) (in many versions)
- Dipyridamole (Persantine)

Non-prescription (over-the counter or herbal) anticoagulants may include:

- Non-steroidal anti-inflammatory (NSAIDs) (in many versions)
- Vitamin E
- Garlic
- Ginger
- Ginkgo biloba

10.4.2 Monoamine Oxidase Inhibitors (MAOIs) Taken within 30 days Prior to Surgery

MAOIs may include:

- Tranylcypromine (Parnate, Sicoton)
- Phenelzine (Nardil, Nardelzine)
- Isocarbonazid (Marplan)
- Rasagiline (Azilect)
- Selegiline (Eldepryl, Deprenyl)
- Linezolid (Zuvox) (an antibiotic)
- St. John's Wort

In addition to the above, any medication given because of a study reported adverse event will be reported. Exclude the reporting of antiemetics, antipyretics, analgesics, diuretics and electrolytes and physiotherapy when given per standard of care procedures and/or within normal limits (dosage and frequency).

10.5 Subject Consent

Informed consent is defined as a legally effective documented confirmation of a subject's voluntary agreement to participate in a particular study after information has been given and explained to the subject on all aspects of the study that are relevant to the subject's decision to participate. This process includes obtaining an IC form that has been approved by the study site's IRB and signed and dated by the subject or their legally authorized/designated representative or guardian. A subject may only consent after information has been given and explained to the subject on all aspects of the clinical investigation that are relevant to the subject's decision to participate.

Prior to enrolling subjects, the site's consent form must be approved by the IRB. The IC document(s) must be controlled (i.e., versioned and dated) to ensure it is clear which version(s) were approved by the IRB. Any adaptation of the sample IC form must be reviewed and approved by Medtronic and the IRB reviewing the application prior to enrolling subjects.

The Investigator must notify the subject (or their legally authorized/designated representative or guardian) of any significant new findings about the study that become available during the course of the study which are pertinent to the safety and well-being of the subject, as this could impact a subject's willingness to participate in the study. If relevant, consent may be requested from subjects to confirm their continued participation.

Subjects will be informed that despite signing the informed consent form, the screening assessment may demonstrate the subject is not a suitable candidate for the study or the procedure and may be withdrawn. Subjects will also be informed that after the investigation visits are completed, the subjects will receive the standard medical care, just as they would have had they not participated in the study.

The template IC form will be provided under separate cover. Prior to initiation of any study-specific procedures, IC must be obtained from the subject (or their legally authorized/designated representative or guardian). Likewise, privacy or health information protection regulation may require subjects to sign additional forms to authorize study sites to submit subject information to the study sponsor. The IC process must be conducted by the Principal Investigator or an authorized designee, and the IC form must be given to the subject (or their legally authorized/designated representative or guardian) in a language he/she is able to read and understand. The process of IC must be conducted without using coercion or undue improper influence on or inducement of the subject to participate by the Investigator or other study site personnel. The IC process shall not waive or appear to waive subject's legal right. The language used shall be as non-technical as possible and must be understandable to the subject and the impartial witness, where applicable.

The subject must have ample time and opportunity to read and understand the IC form, to inquire about details of the study, and to decide whether or not to participate in the study. All questions about the study should be answered to the satisfaction of the subject.

When the subject decides to participate in the study, the IC form must be signed and personally dated by the subject and Investigator or authorized designee, as required by the IC form, and ensured by the Principal Investigator or his/her authorized designee.

A copy of the IC form, signed and dated as required by law, must be provided to the subject and his/her authorized designee.

If the IC form is obtained the same day the subject begins participating in study-related procedures, it must be documented in the subject's case history that consent was obtained prior to participation in any study-related procedures. It is best practice for the IC process to be documented in the subject's case history, regardless of circumstance.

The original of the signed IC form must be filed in the hospital/clinical chart and/or with the subject's study documents.

The IC form must be available for monitoring and auditing. Any Medtronic Field personnel who support the Enable Hernia Repair Study must be able to review the subject's signed and dated IC form and verify its completeness prior to proceeding with the procedure. In the event the Medtronic Field personnel identify the IC from as being incomplete, the study procedure will not be allowed to occur until the consent of the subject can be adequately and appropriately obtained.

Consistent with the DoH, vulnerable adults (i.e., those subjects mentally incapable of giving consent) are excluded from this protocol. Any subjects with mental incompetence (e.g., Alzheimer's, dementia, psychiatric disorders, developmental disorders) should be assessed for vulnerable status. If the IC is signed by an individual other than the subject, the monitor may discuss whether the Investigator believes the subject meets the definition of a vulnerable adult. This protocol defines vulnerable adult as those subjects mentally incapable of giving consent, in the Investigator's opinion. The Investigator should consider the definition of vulnerable adult per ISO 14155, which defines vulnerable adults as: "individuals who are unable to fully understand all aspects of the investigation that are relevant to the decision to participate, or who could be manipulated or unduly influenced as a result of a compromised position, expectation of benefits or fear of a retaliatory response. For example, this could include Individuals with loss of autonomy due to immaturity or through mental disability, persons in nursing homes, children, impoverished persons, subjects in emergency situations, ethnic minority groups, homeless persons, nomads, refugees, and those incapable of giving IC. Other vulnerable subjects could include, for example, members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the sponsor, members of the armed forces, and persons kept in detention.

10.6 Assessment of Performance

The secondary endpoints of this study (**Section 5.2.2**) will assess the overall performance of the Medtronic Hugo™ RAS system when used for inguinal and ventral hernia repair robotic assisted surgery.

10.7 Assessment of Safety

Safety will be evaluated through the study primary safety endpoint (one or more procedure- and/or device- related SSEs) and several secondary endpoints (**Section 5.2.2**).

Safety will also be assessed by monitoring the occurrence of AEs, serious adverse events (SAEs), deaths, adverse device effects (ADE), serious adverse device effects (SADE), unanticipated adverse device effects (UADE) or device deficiencies (DD). Adverse event assessments will take place starting with the point of

informed consent, through the end of study exit, or until resolution, whichever comes first and will be recorded in the eCRF.

10.8 Recording Data

Data entered must be traceable to source documents. Source documentation is defined as all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical investigation necessary for the reconstruction and evaluation of the clinical investigation (e.g., hospital records, clinical and office charts, procedure reports, laboratory notes, memoranda, subjects' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, X-rays, subject files, device data and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the study).

In general, eCRFs (or paper copies) may not serve as source documents. Source documentation for data elements not routinely captured in medical records may vary from study site to study site; the study site may use source document worksheets if identified as source documents.

The Investigator must ensure the availability of source documents from which the information on the eCRFs was derived. The type and location of source documents should be documented. Where printouts of electronic medical records, are provided as source documents, or where copies of source documents are retained as source documents, those should be certified. Certification must contain (1) the signature of the individual making the copy, (2) the date the copy was made and (3) a statement attesting to the accuracy and completeness of the copy.

The source documents must be made available for monitoring or auditing by Medtronic's representative or representatives of the competent authorities and other applicable regulatory agencies.

The CRF may be considered source for the following data collection elements:

- Enrollment Notification
  - Study site assigned subject reference
- Baseline
  - Administrative information
- AE eCRF
  - Date study site became aware of event
  - Relatedness of adverse event
- DD eCRF
  - Date study site became aware of event
- Subject Death
  - Date study site became aware of death
  - Relatedness of death
- Deviations

- Reason for deviation

10.9 Deviation Handling

A study deviation is defined as an event within a study that did not occur according to the CIP or the CTA.

The investigator may not deviate from the CIP, unless the deviation is necessary in an emergency situation to protect the rights, safety and wellbeing of the subject. Prior approval by Medtronic is expected in situations where the Investigator anticipates, contemplates, or makes a conscious decision to deviate from the CIP or CTA. Prior approval is not required when a deviation is necessary to protect the safety, rights, or well-being of a subject in an emergency or in unforeseen situations beyond the Investigator's control (e.g., subject failure to attend scheduled follow-up visits, inadvertent loss of data due to computer malfunction, inability to perform required procedures due to subject illness).

For medically justifiable conditions which preempt a subject's ability to complete a study-required procedure, it may be permitted to report only one deviation which will apply to all visits going forward. This may also apply for other unforeseen situations (e.g., the subject permanently refuses to complete a study required procedure and the data will not contribute to the primary end point analysis). However, prior approval from Medtronic is required for such situations.

All study deviations must be reported on the CRF regardless of whether medically justifiable, pre-approved by Medtronic, an inadvertent occurrence, or taken to protect the subject in an emergency. Multiple deviations of the same type at the same visit may be reported on one case report form.

In the event the deviation involves a failure to obtain a subject's consent or is made to protect the life or physical well-being of a subject in an emergency, the deviation must be reported to the IRB as well as Medtronic within five (5) working days. Reporting of all other study deviations should comply with IRB policies and/or local laws and must be reported to Medtronic as soon as possible upon the study site becoming aware of the deviation. Reporting of deviations must comply with IRB policies, local laws, and/or RA requirements.

Medtronic is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g., amend the CIP, conduct additional training, terminate the investigation). Repetitive or serious investigator compliance issues may result in initiation of a corrective action plan with the Investigator and study site, and in some cases, may necessitate suspending enrollment until the problem is resolved or ultimately terminating the Investigator's participation in the study. Medtronic will provide study site-specific reports to Investigators summarizing information on deviations that occurred at the investigational study site on a periodic basis.

Examples of study deviations include but are not limited to:

- Failure to obtain proper IC
- Failure to collect required study data (e.g., required echocardiograms)
- Inclusion/exclusion criteria not met

10.10 Subject Exit, Withdrawal or Discontinuation

Subjects may voluntarily withdraw from the study at any time. Additionally, the Principal Investigators may withdraw or choose not to enroll subjects if they feel they do not meet the CIP defined inclusion and exclusion criteria or if it is in the best medical interest of the subject in question. If the study Investigator voluntarily removes a subject from further study participation, supporting documentation must be in place for the rationale and date of removal.

In cases of early study exits, all data collected from the time of informed consent to the time of study exit may be used. Subjects who exited early will not be replaced. Enrollment will continue as per CIP definitions up to the predefined maximum number of subjects.

The reason and date for study exit of all enrolled subjects will be documented on the applicable eCRF.

All subjects will be followed per institutional standard of care after any withdrawal, discontinuation, or completion of the study follow-ups.

10.10.1 Study Exit

A Study Exit eCRF is required for all subjects. Prior to exiting a subject from the study, it is recommended to follow the subject until all ongoing system and/or procedure related AEs are resolved or unresolved with no further actions planned. Following exit, subjects will continue to receive standard medical care. Upon exiting from the study, no further study data will be collected, or study visits will occur for the subject. All data available through the time of the subject's exit will be used for analysis.

Subjects are urged to remain in the study as long as possible but may be exited from the study for any of the following situations:

- Study completed
- Subject lost to follow-up
- Subject death
- Subject did not meet inclusion/exclusion criteria
- Subject did not provide consent or data use protection authorization
- Subject chooses to withdraw (e.g., consent withdrawal, relocation to another geographic location)
- Investigator deems withdrawal necessary (e.g., medically justified, inclusion/exclusion criteria not met, failure of subject to maintain adequate study compliance)

The following information is required to be collected at study exit:

- Reason for exit

If discontinuation is because of safety or lack of effectiveness, the subject shall be asked to be followed for collecting safety data outside the clinical investigation.

10.10.2 Study Completed

At the completion of the 2-year follow-up visit subjects will be exited from the study. The 2-year Follow-Up visit and Exit visit should be combined, and both the 2-year Follow-up eCRF and the Study Exit eCRF need to be completed.

10.10.3 Lost to Follow-up

Every attempt will be made to contact subjects whose status is unknown, including at a minimum:

- Three phone calls with each attempt clearly documented in the source documents including response or lack thereof.
- If there is no response to the phone calls, then a certified/registered letter should be written to the subject. A copy of the letter should be retained in the subject's source document.

To ensure all efforts have been made, the site should check public health records to identify vital status.

A subject will not be considered lost to follow-up prior to the 1-year visit window closure. A subject would not be considered lost to follow-up until all efforts to obtain current status have been exhausted per the attempts noted above (including review of medical charts and public health records).

In addition, regulation set forth by the governing IRB must be followed.

10.10.4 Subject Chooses to Exit (i.e., Revokes Consent)

A subject can withdraw from the study at any time. If the subject wishes to exit from the study (i.e., the subject revokes consent), the study site is required to document the reason for exit on the Study Exit CRF. In addition, study sites shall follow the regulations set forth by the governing IRB. If possible, the following data should be collected prior to subject withdrawal:

- Reason for exit

10.10.5 Investigator Withdraws Subject

No subjects should be withdrawn by Investigators unless compelling medical justification is present. It is recommended Investigators discuss any withdrawals with the study team prior to withdrawing subjects. If an Investigator Withdrawal is necessary, the following data should be collected prior to subject withdrawal if possible:

- Reason for subject withdrawal

10.10.6 Conditional Disengagement

After a subject is enrolled every effort should be made to keep the subject in the study. However, it is recognized that there are circumstances where limited data may be collected, or study exit will need to occur. In these cases, we will consider either modified data collection requirements where subjects may conditionally disengage in study procedures but data from the subject can still be collected because the subject has not revoked consent or exit when study participation is completely ended.

Subjects may be conditionally disengaged from study procedures for any of the following reasons:

- Subject chooses to disengage (e.g., follow-up schedule cannot be adhered to, study burden too large, relocation to another geographic location but telephone follow-up still acceptable)
- Investigator deems conditional disengagement necessary (e.g., medically justified)

If the subject wishes to disengage from the study, or the Investigator deems it necessary, the study site is required to document the reason. Data collection requirements no longer apply, but study sites are encouraged to collect as much data as possible on the eCRFs.

11 Risks and Benefits

11.1 Potential Risks

Medtronic follows rigorous Quality Assurance and Control procedures throughout the life of a product, from the business analysis phase through development, market release, and post-market surveillance. The Medtronic risk management process follows ISO 14971:2012, Medical Devices – Application of Risk Management to Medical Devices and applicable requirements of YY/T 0316-2008 Medical devices—Application of risk management to medical devices (ISO 14971: 2007, IDT).

The Risk Management Report (RE00308824) summarizes the risk management activities for the Hugo™ RAS system as stated in the Risk Management Plan (R0057077), as well as the overall acceptability of risk. The Risk Management Report addresses risks resulting from the interaction between the user, the subject, and the device. It does not focus on risks inherent to medical treatment enabled by the Hugo™ RAS system. This risk analysis assumes that the product shall only be operated by qualified, properly trained medical personnel. While every attempt has been made to reduce subject and user risks, all surgeries using the Hugo™ RAS system carry some residual risk, even when used by trained physicians.

Specific details of hazardous situations, causes, and risk control measures are identified in the Risk Analysis Chart (RE00027518). Hazardous situations as described in the Risk Management Plan, their associated harms, and specific device benefits to mitigate these hazardous situations are identified below.

- Arrhythmia
- Bleeding
- Blunt Trauma
- Bowel Perforation
- Burn (varying degrees)
- Burn, Bowel
- Burn, Thermal
- Crushing Injury
- Damage to equipment/facility

- Delay of Treatment (prolonged procedure)
- Electrical Shock
- Foreign Body in Subject
- Implant, Failure of
- Infection
- Inflammation
- Tissue Damage/Tissue Trauma
- Toxicity
- Vessel Perforation

The incidence of these risks may be different than anticipated due to unknown circumstances or medical conditions.

There may be other discomforts and risks related to the Hugo™ RAS system and/or this study that are not foreseen at this time. In addition, the Hugo™ RAS system for inguinal and ventral hernia repair indications is investigational in the United States and may be no more or less safe or effective than other commercially available robotic surgery systems.

The study sponsor may decide to stop the study before obtaining approval of the investigational product but will continue to guarantee subjects safety.

11.2 Risk Minimization

The potential risks associated with the Medtronic Hugo™ RAS system were identified and have been successfully mitigated. Medtronic has further minimized the possibility of risks by performing required laboratory and preclinical testing prior to this clinical study and implementing quality control measures into production processes.

Any potential risks associated with participation in this study are further minimized by providing guidelines for subject selection and evaluation, providing adequate instructions and labeling, selecting qualified investigators, and training study personnel on the safe use of the device and on the CIP procedures.

Medtronic has also attempted to minimize risk to subjects by using an external, independent CEC to review safety issues identified as part of the study.

The potential risks associated with the Medtronic Hugo™ RAS system have been identified above and will be constantly monitored, assessed, and documented by the Investigators and sponsor.

11.3 Potential Benefits

The Hugo™ RAS system may offer no benefit. As with commercially available robotic surgery systems, the potential benefits of undergoing inguinal and ventral hernia repair surgery using the Hugo™ RAS system may include lower complication rates compared to traditional laparoscopic and open surgical procedures

(**Section 6.2.1**).

As described in **Section 6.2.1**, the safety and performance of commercially available RAS systems have been evaluated in the literature search showing that robotic assisted surgery was comparable or superior to open or traditional laparoscopic surgery in most comparisons.

Other benefits listed below may more directly impact surgeon performance, although ultimately, they affect the end result of subject outcomes and thus are important safety and performance factors.

- Better ergonomics and less strain or fatigue for the user. The torque forces are delegated to the robotic arms, which decreases the strain on surgeon's muscles in the neck, shoulders, and back.
- Mitigation of hand tremors, which results in fewer surgeon errors.
- Better 3D visualization of surgical field for the console surgeon. The camera is controlled by the surgeon and not the assistant. The trainees see what the surgeon is seeing at the console, albeit in 2D rather than 3D.
- Lack of fulcrum effect. This factor helps to shorten the learning curve for RAS use.
- Shorter learning curve compared to traditional laparoscopic surgery.

The data collected from this study will also help characterize the safety and performance of the Hugo™ RAS system. If the results of this study support additional clinical research, further studies may be justified to evaluate the potential for improved standard-of-care using robotic assisted inguinal and ventral hernia repair surgery.

This study does not exclude any adults based on age; therefore, this risk-benefit rationale should be generalizable to Medicare beneficiaries who qualify for a robotic assisted inguinal and ventral hernia repair surgery.

11.4 Risk-Benefit Rationale

As described in the Risk Management Report (RE00308824), use of the Hugo™ RAS system involves residual risk. The established controls provide adequate assurance that the identified potential risks described above have been eliminated, reduced to an acceptable level, or deemed acceptable. These controls will ensure that a consistently safe and effective product is produced for the intended user.

In addition, cadaver studies, human factors/usability testing and product validation labs demonstrate that the Hugo™ RAS Platform performs as intended. Verification testing shows that the Hugo™ RAS Platform meets all product and system design input requirements. The clinical literature (**Section 6.2.1**) provides relevant patient experience for RAS. The safety and performance of commercially available RAS systems are supported by the observation that length of hospital stay, complication rate, level of intra-operative blood loss, complications, and conversion rates were comparable or superior to conventional laparoscopic or open technologies (**Section 6.2.1**).

In conclusion, the contributions of the Hugo™ RAS system to subject outcomes substantially outweigh the minimal reported risks and side effects associated with the use of this device. The overall residual risks associated with the Hugo™ RAS system have been determined to be acceptable. Therefore, these assessments present a favorable benefit/risk profile and justify the use of the product in humans and an

evaluation of clinical data relevant to the proposed investigation.

11.5 Risk Determination

The Hugo™ RAS system and instruments are considered significant risk.

12 Adverse Events and Device Deficiencies

12.1 Adverse Events

All AEs, including non-subject AEs, will be collected throughout a subject's participation, starting from the time the informed consent form is signed, through 30 days after the day of the procedure, regardless of their severity, relationship to the Hugo™ RAS system or study procedures.

After 30 days, all AEs will be assessed by the surgeon and those AEs deemed attributable to the procedure and / or study device will be reported. All deaths will be collected throughout a subject's participation, regardless of relatedness.

Reporting of these events to Medtronic will occur on an AE Form, including event description, date of AE, treatment, resolution, assessment of both the seriousness of the AE and the relatedness to the study device, procedure. Each AE must be recorded on a separate AE eCRF.

AE definitions used in this study (**Table 8**) are based on ISO 14155:2020 (Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice). Documented pre-existing conditions are not considered AEs unless the nature or severity of the condition has worsened. See **Section 14** for details regarding AE analyses in each study analysis set. In addition, AEs impacting users or other persons (non-subject AEs) will be collected on a non-subject AE CRF.

Any unresolved procedural or device-related events that are still ongoing past study exit will be monitored by the Investigator per their institutional standard-of-care.

Unavoidable adverse events (UAE) (those that are inherent to the procedure and are expected to occur in all subjects for an expected duration) listed in **Table 11** will not be captured or reported unless the adverse event worsens or persists outside the stated timeframe post procedure. **Section 11.1** includes a list of several but not all-encompassing anticipated adverse events.

All Serious Adverse Events (SAE), deaths, and Surgical Site Events (SSEs) will be adjudicated by an independent CEC through 30 days post-procedure as of revision 5.0 of the protocol.

12.2 Device Deficiency

The DD definition is provided in **Table 8**. DD information will be collected throughout the study and reported to Medtronic. Note that DD that result in an AE to the subject should be captured as an AE only.

12.3 Processing Updates and Resolution

For any changes in status of a previously reported adverse event or DD (i.e., change in actions taken, change in outcome, change in relatedness), information needs to be updated on, or added to the original

AE or DD form. All AEs must be followed until the AE has been resolved, is unresolved with no further actions planned, the subject dies or exits the study, or until study closure, whichever occurs first.

In the event that a subject is exited from the study prior to study completion, all efforts should be made to continue following the subject until all unresolved system or procedure related AEs, as classified by the Investigator, are resolved, or unresolved with no further actions planned.

At the time of study exit, all collected adverse events that are unresolved must be reviewed by the investigator and an update to the original AE must be reported.

12.4 Definitions/Classifications

This study is not within the scope of ISO 14155:2020 but will use AE definitions according to ISO 14155:2020 for consistency in reporting.

This study will collect the following:

- All adverse events, including non-subject AEs, from the time the informed consent is signed through the first 30 days after the day of the procedure, regardless of their severity, relationship to the Hugo™ RAS system or study procedures. After 30 days, all AEs will be assessed by the surgeon and those AEs deemed attributable to the procedure and/or study device will be reported. All deaths will be collected throughout a subject's participation, regardless of relatedness.
- All device deficiencies (all components of the Hugo™ RAS system)

Table 8. Adverse Event and Device Deficiency Definitions

General	
Adverse Event (AE) (ISO 14155:2020, 3.2)	Untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated. NOTE 1: This definition includes events related to the investigational medical device or the comparator. NOTE 2: This definition includes events related to the procedures involved. NOTE 3: For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.
Adverse Device Effect (ADE) (ISO 14155:2020, 3.1)	AE related to the use of an investigational medical device. NOTE 1: This definition includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device. NOTE 3: this includes 'comparator' if the comparator is a medical device.

Device Deficiency (DD) (ISO 14155:2020, 3.19)	Inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance. NOTE 1: DD include malfunctions, use s and inadequacy in the information supplied by the manufacturer including labeling. NOTE 2: This definition includes device deficiencies related to the investigational medical device or the comparator.
Relatedness	
Device Relatedness	An AE that results from the presence or performance (intended or otherwise) of any component of the device. This includes all components of the Hugo™ RAS system, associated introduction tools, operational and installed software and programmers.
Procedure Relatedness	An AE that occurs due to the hernia repair procedure with the Hugo™ RAS system.

Relatedness Classification (Procedure, Device)	Not related: The relationship can be excluded when: • the event has no temporal relationship with the use of the device or procedure; • the event does not follow a known response pattern to the device (if the response pattern is previously known) and is biologically implausible; • the discontinuation of device application or the reduction of the level of activation/exposure – when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the event; • the event involves a body-site, or an organ not expected to be affected by the device or procedure; • the event can be attributed to another cause (e.g., an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors); • the event does not depend on a false result given by the device used for diagnosis, when applicable; To establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the event. Possible: The relationship is weak but cannot be ruled out completely. Alternative causes are also possible (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug, or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible. Probable: The relationship seems relevant and/or the event cannot reasonably be explained by another cause.

	Causal: The event is associated beyond reasonable doubt when:
	• the event is a known side effect of the product category the device belongs to or of similar devices and procedures;
	• the event has a temporal relationship with device use/application or procedures;
	• the event involves a body-site or organ that
	  ○ the device or procedures are applied to;
	  ○ the device or procedures have an effect on;
	• the event follows a known response pattern to the device (if the response pattern is previously known);
	• the discontinuation of device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible);
	• other possible causes (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
	• harm to the subject is due to error in use;
	• the event depends on a false result given by the device used for diagnosis, when applicable.
	To establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the event. For purposes of analysis categories considered “related” will include Possible, Probably, and Causal.

Seriousness	
Serious Adverse Event (SAE) (ISO 14155:2020, 3.45)	AE that led to any of the following a) death, b) serious deterioration in the health of the subject, users or other persons as defined by one or more of the following: 1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function, including chronic diseases, or 3) in-patient or prolonged hospitalization, or 4) medical or surgical intervention to prevent life- threatening illness or injury, or permanent impairment to a body structure or a body function, c) foetal distress, foetal death, a congenital abnormality, or birth defect including physical or mental impairment NOTE 1: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered an SAE.
Serious Adverse Device Effect (SADE) (ISO 14155:2020, 3.44)	Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.
Unanticipated Adverse Device Effect (UADE) (21 CFR 812.3(s))	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.

Complication	Complications will be defined according to the Clavien- Dindo classification system. **Grade I:** Any deviation from the normal post-operative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside. **Grade II:** Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included. **Grade III:** Requiring surgical, endoscopic, or radiological intervention. **Grade IIIa**: Intervention not under general anesthesia **Grade IIIb:** Intervention under general anesthesia **Grade IV:** Life-threatening complication (including CNS complications)* requiring IC/ICU management **Grade Iva:** Single organ dysfunction (including dialysis) **Grade Ivb:** Multiorgan dysfunction **Grade V:** Death of a patient NOTE 1: *Brain hemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks. CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

Other	
Severity	**Mild** A type of adverse event that is usually transient and may require only minimal treatment or therapeutic intervention. The event does not generally interfere with usual activities of daily living. Clinical Data Interchange Standards Consortium (CDISC) **Moderate** A type of adverse event that is usually alleviated with additional specific therapeutic intervention. The event interferes with usual activities of daily living, causing discomfort but poses no significant or permanent risk of harm to the research participant. (CDISC) **Severe** A type of adverse event that interrupts usual activities of daily living, or significantly affects clinical status, or may require intensive therapeutic intervention. (CDISC)
Unavoidable Adverse Event (UAE)	An AE inherent to a surgical procedure that is expected to occur in all subjects for a projected duration according to the Investigator's opinion. See **Table 11**.

12.5 Reporting of Adverse Events

12.5.1 Adverse Event and Device Deficiency Classification

All AEs and DDs will be reviewed by a Medtronic representative. AEs will be classified according to the definitions provided.

Upon receipt of an AE at Medtronic, a Medtronic representative will review the AE/DD for completeness and accuracy and when necessary, will request clarification and/or additional information from the Investigator. Medtronic will utilize MedDRA for Regulatory Activities, to assign a MedDRA term for each AE/DD based on the information provided by the Investigator.

AEs will be classified according to the standard definitions as outlined in **Table 9**.

Table 9. Adverse Event Classification Responsibilities

What is classified?	Who classifies?	Classification Parameters
Relatedness	Investigator	Device, Procedure[1]
	Sponsor	Device, Procedure
Seriousness	Investigator	SAE, Complication[1], Severity
	Sponsor	SAE, UADE
Diagnosis	Investigator	Based on presenting signs and symptoms and other supporting data
	Sponsor	MedDRA term assigned based on the data provided by Investigator

Note 1: This assessment is not applicable for non-subject Adverse Events

12.5.2 Adverse Event and Device Deficiency Reporting Requirements

Investigator and sponsor timeframes for reporting requirements of AEs and DDs are outlined in Table 10. Regulatory reporting of AEs and DDs will be recorded and reported according to local regulatory requirements. It is the responsibility of the Investigator and the sponsor to abide by the AE reporting requirements stipulated by local law and the study site's IRB. For AEs that require immediate reporting, initial reporting may be done by phone to Medtronic or on the AE CRF completing as much information as possible. The completed AE CRF must be submitted to Medtronic. Please refer to **Table 10** for more information.

Unavoidable adverse events (UAE) (those that are inherent to the procedure and are expected to occur in all subjects for an expected duration) listed in **Table 11** will not be captured or reported unless the adverse event worsens or persists outside the stated timeframe post procedure.

Table 10. Reporting Requirements

SAEs	
Investigator Shall Submit to:	
Medtronic	Report to sponsor immediately (but no later than 10 working days) after the investigator / Study Staff first learns of the event or of new information in relation with an already reported event, all serious adverse events.
RA	Submit to RA per local reporting requirement.
IRB	Submit to IRB per local reporting requirement.
Sponsor shall submit to:	
RA	Submit to RA per local reporting requirement.
IRB	Submit to IRB per local reporting requirement.
ADEs	

Investigator Shall Submit to:	
Medtronic	Submit as soon as possible (but no later than 30 calendar days) after investigator/ Study Staff first learns of the effect.
RA	Submit to RA per local reporting requirement.
IRB	Submit to IRB per local reporting requirement.
Sponsor shall submit to:	
RA	Submit to RA per local reporting requirement.
IRB	Submit to IRB per local reporting requirement.
SADEs	
Investigator Shall Submit to:	
Medtronic	Report to sponsor immediately (but no later than 10 working days) after the investigator/ Study Staff first learns of the event or of new information in relation with an already reported event, all serious adverse events.
RA	Submit to RA per local reporting requirement.
IRB	Submit to IRB per local reporting requirement.
Sponsor shall submit to:	
RA	Submit to RA per local reporting requirement.
IRB	Submit to IRB per local reporting requirement.
Investigators	Submit per local reporting requirement.
UADEs	
Investigator Shall Submit to:	
Medtronic	Submit to sponsor immediately, but in no event later than 10 working days after the investigator/ Study Staff first learns of the effect. (21 CFR 812.150(a)).
RA	Submit to RA per local reporting requirement.
IRB	Submit immediately, but in no event later than 10 working days after the investigator/ Study Staff first learns of the effect. (21 CFR 812.150(a)).
Sponsor shall submit to:	
RA	Submit to RA per local reporting requirement.
IRB	Submit to IRB per local reporting requirement.
Investigators	Submit per local reporting requirement.
All other reportable AEs	
Investigator Shall Submit to:	
Medtronic	Submit to sponsor as soon as possible (but no later than 30 calendar days) after investigator/ Study Staff first learns of the effect.
RA	Submit to RA per local reporting requirement.
IRB	Submit to IRB per local reporting requirement.
All other Device Deficiencies	
Investigator Shall Submit to:	
Medtronic	Submit to sponsor as soon as possible (but no later than 30 calendar days) after investigator/ Study Staff first learns of the effect.
RA	Submit to RA per local reporting requirement.
IRB	Submit to IRB per local reporting requirement.

Table 11. Unavoidable Adverse Events (UAE)

Unavoidable Event Description	Timeframe (hours) from the Procedure
Anesthesia-related nausea / vomiting	24
Low-grade fever (<100°F or 37.8°C)	48
Incisional pain	72
Constipation	72
Sleep problems (insomnia)	72
Mild to moderate bruising / ecchymosis	168
Asymptomatic hematoma	30 days
Asymptomatic seroma	30 days
Asymptomatic edema	30 days

12.6 Subject Death

All subject deaths must be reported by the Investigator to Medtronic on an AE form (AE with a fatal outcome) upon site's first awareness of the death and in accordance with the reporting timeframe in **Table 10**. In case of death, there should be one AE with the outcome of fatal.

If a subject's death is assessed as related to study procedure and/or study device, it is recommended that the Hugo™ RAS system or components are returned to Medtronic for analysis whenever possible per local process. Local laws and procedures must be followed where applicable. If any system component is returned to Medtronic, internal return product reporting systems may be used to gather additional information about the returned device/component.

A copy of the death certificate, if available and allowed by state/local law, should be sent to the Medtronic clinical study team. When a death occurs in a hospital, a copy of the death summary report and all relevant hospital records, if available should be sent to the Medtronic clinical study team. If an autopsy is conducted, a copy of the autopsy report should also be sent to the Medtronic clinical study team if available and allowed by state/local law. When the death occurs at a remote study site, it is the investigative study site's responsibility to attempt retrieval of information about the death. Additionally, device disposition information should be updated.

In summary, the following data will be collected:

- Date of death
- Detailed description of death
- Cause of death
- Relatedness to system and/or procedure
- Device disposition information
- Death summary/hospital records (if available and allowed by state/local law)

- Autopsy report (if available and allowed by state/local law)
- Death certificate (if available and allowed by state/local law)

12.7 Product Complaint Reporting

Product complaint reporting and vigilance reporting are applicable, and AEs related to any market-released device during the study must be reported. The reporting of product complaints is not part of the study and should be done in addition to the AE reporting requirements. Refer to local regulations for reporting requirements.

Product Complaint: Any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a medical device that has been placed on the market.

It is the responsibility of the Investigator to report all product complaint(s) associated with a medical device distributed by Medtronic, regardless of whether the complaints are related to intended use, misuse, or abuse of the product. Reporting must be done immediately and via the regular channels for market-released products. The reporting of product complaints by the Clinical team must be done according to the local Standard Operating Procedures (SOP). Medtronic will notify the RAs (e.g., Competent Authority (CA)) as applicable for the following incidents immediately upon learning of them and is not limited to AEs and DDs only:

- Any malfunction or deterioration in the characteristics and/or performance of a device, as well as any inadequacy in the labeling or instructions for use which led or might have led to the death or serious deterioration in the state of health of a subject, user, or other person.
- Any technical or medical reason resulting in withdrawal of a device from the market by the manufacturer.
- Any serious deterioration in the state of health, including:
    - Life-threatening illness or injury
    - Permanent impairment of a body function or permanent damage to a body structure
    - A condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure

13 Data Review Committees

13.1 Clinical Events Committee Review

An external, independent CEC will be utilized to adjudicate all Serious Adverse Events (SAE), deaths, and Surgical Site Events (SSEs) through 30 days post-procedure, as of revision 5.0 of the protocol. The CEC will consist of a minimum of three (3) non-Medtronic employed physicians that are not participating

Investigators for the study, including a CEC chairperson. Medtronic personnel may facilitate and participate in a CEC meeting but will be non-voting members.

The CEC will be external to Medtronic and independent of the study Investigators. The members will have specialties appropriate to the therapeutic areas and meet requirements established in the CEC Charter. The CEC Charter will define the CEC processes for member selection, meeting frequency, roles and responsibilities, procedures and record keeping. Prior to making a final adjudication decision, the CEC may request clarification and/or additional information from the Principal Investigator who reported the event.

The site Investigator may agree or disagree with the CEC's adjudication, and the eCRF documenting the AE may be updated accordingly. If the investigator does not agree with the CEC's adjudication assessment, both determinations will be provided within the final report; Ultimately, the CEC's adjudication will be used for data analysis.

13.2 CRO/Core Lab(s)

This information may be subject to change during the study. Periodic updates to study contact information will be sent to study sites as needed (**Table 12**).

Table 12. CRO and Core Laboratory Information

Contact Information	Role
[redacted]	Independent clinical events adjudication committee

13.3 Data Monitoring Committee

DMC is not needed for this study. This decision was made based on the following criteria: fast enrollment in this trial makes a DMC impractical, and there are no additional benefits of a DMC reviewing the data in addition to the CEC.

14 Statistical Design and Methods

This section presents statistical considerations for the study design and provides a high-level description of planned analyses and reporting. More technical details will be provided in a separate statistical analysis plan (SAP) that will be finalized and approved prior to database snapshot used for the primary objective analyses. Any deviations to the pre-specified statistical analyses will be noted in the final CSR.

14.1 General Aspects of Analysis

Data analysis will be performed by Medtronic or its designee. Descriptive statistics will be used to summarize study outcomes. Continuous variables will be summarized using number of subjects (n), mean, standard deviation, median, interquartile range (IQR) and ranges. Categorical variables will be summarized using frequencies and percentages.

Subject disposition will be illustrated in a CONSORT diagram. Subject visits will be tabulated and compliance to visit schedules and visit windows will be summarized.

All statistical analyses will be performed using Statistical Analysis System (SAS) for Windows (version 9.4 or higher, SAS Institute Inc. Cary, NC) or other widely accepted statistical or graphical software.

This study includes 3 primary hypothesis tests (alpha controlled tests for the 2 primary objectives, which are all one-sided tests with maximum alpha of 0.025). Multiple testing considerations are described in section 14.12. A P-value less than the stated alpha is considered statistically significant. Confidence intervals will be presented at the 95% level unless otherwise stated.

The study will be considered successful when the primary effectiveness and safety endpoints are met.

14.2 Analysis Execution

The primary safety and effectiveness analyses will occur after all subjects complete the 30-day follow-up or study exit visit. The analyses will include both primary and secondary 30-day objectives. A CSR will be prepared once all data collection has ended and all subjects have completed the 30-day follow-up or have been exited. A final report will be completed at the end of the study that will include 2-year study endpoints.

All available data will be included in the analysis. Sensitivity analysis may be performed for missing data to assess the robustness of study results as described in **Section 14.1**.

14.3 Interim Analysis

No interim analysis is planned for the primary objectives in this study.

14.4 Primary Objective(s)

14.4.1 Primary Objective #1 (Effectiveness)

The primary objectives of this study are to demonstrate that the Medtronic Hugo™ RAS system is safe and effective when used for inguinal and ventral robotic hernia repair. The primary effectiveness endpoint is the surgical success rate, which is defined as the procedure not going into conversion.

The primary effectiveness hypothesis is to test if the surgical success rate is above the performance goal. A performance goal (PG) of 85% (100%-conversion rate) is pre-defined to evaluate the surgical success rate. Let *P* be the surgical success rate in this study. The statistical hypothesis is formulated as follows:

$$H_0: P \leq 85\% \text{ vs. } H_a: P > 85\%$$

The hypothesis will be tested using an exact binomial test at one-sided alpha of 0.025. The 95% two-sided confidence interval will also be reported; the confidence interval will be calculated using the Clopper-Pearson exact binomial method.

The analysis set for the primary effectiveness will be the full analysis set (FAS) for the combined inguinal and ventral hernia cohort, which will be further elaborated in **section 14.9**. If 5% of the data or fewer are missing for the primary analysis, no imputation will be used[42]. Otherwise, missing data will be imputed for the FAS using multiple imputation. Sensitivity analysis will be performed for the primary effective

endpoint using available data with no imputation in FAS, PPAS as well as tipping-point analysis in FAS to evaluate the robustness of the study results. A summary of device-related conversions will be provided as well.

See **Table 13** below for the rationale supporting the 85% performance goal for the primary effectiveness endpoint. For details on the sample size calculation based on the primary effectiveness endpoint, see details in **Section 14.7**.

Table 13: Primary Effectiveness Endpoint – Performance Goal Determination

Primary Effectiveness Endpoint: Surgical Success Rate		
Surgery Type	**Performance goal (PG)**	**Rationale**
Inguinal and Ventral Hernia Repair	85%	The literature-based mean effect size for conversions is 1.5% with a 95% CI of 0.2% to 9.4%. The 95% prediction interval is 0.1% to 29.3%. A PG of 85% for the surgical success rate, equivalent to a 15% conversion rate, is set, which is aligned with the upper 95% CI with an added 5.6% margin and falls within the 95% prediction interval.

14.4.2 Primary Objective #2 (Safety)

The primary safety objective of this study is to demonstrate that the Medtronic Hugo™ RAS system is safe when used in inguinal and ventral hernia repair. The primary safety endpoint is the rate of subjects with one or more procedure- and/or device-related SSEs from the first incision through 30 days post-procedure.

The primary safety hypothesis is to test the overall 30-day procedure- and/or device-related SSEs rate (i.e., rate of subjects with one of more procedure- and/or device-related SSEs) against a performance goal. The performance goals are determined based on meta-analyses of published literature data.

Let *R* be the 30-day procedure- and/or device-related SSEs rate, and PG be the performance goal for a specific surgery group. The statistical hypothesis is formulated as follows:

$$H_0: R \geq PG \quad vs. \quad H_a: R < PG$$

The hypothesis will be tested using an exact binomial test at the significance level and the null hypothesis will be rejected if the p-value is significant comparing to alpha determined after multiplicity adjustment as described in **Section 14.12**. The 95% two-sided confidence interval will also be reported; the confidence interval will be calculated using the Clopper-Pearson exact binomial method.

The analysis set for the primary safety objective will be FAS with available data at 30 days, i.e., those subjects whose status (event, no event) at 30 days can be determined. The inguinal hernia cohort and ventral hernia cohort will be analyzed separately.

Performance Goal Rationale

A literature search was performed to include each of the surgery types (inguinal hernia repair and ventral hernia repair) and both RAS and laparoscopic MIS procedure types. Point estimates along with 95% confidence intervals (CIs) and prediction intervals were calculated based on the reported literature data. Clinically meaningful margins and statistical precisions have been considered to determine the appropriate performance goals. The calculation details and rationales for the primary safety endpoint are summarized in **Table 14**.

Table 14: Primary Safety Endpoint – Performance Goal Determination

Primary Safety Endpoint: Rate of Subjects with One or More Procedure-/Device-Related Surgical Site Events (SSEs) through 30 Days Post-Procedure			
Surgery Type	**Performance Goal (PG)**	**Sample Size**	**Rationale**
Inguinal Hernia	30%	96	The literature-based maximum possible SSE rate is 3.8% with a 95% CI of 2.1% to 6.9%. The 95% prediction interval is 0.3% to 36.0%. A PG of 30% falls within the 95% literature-based prediction interval and is clinically relevant.
Ventral Hernia	30%	96	The literature-based maximum possible SSE rate is 4.5% with a 95% CI of 1.8% to 10.8%. The 95% prediction interval is 0.3% to 45.5%. A PG of 30% falls within the 95% literature-based prediction interval and is clinically relevant. Additionally, Medtronic-sponsored clinical study data show a 14.5% procedure- and/or device-related SSI+ SSO pooled rate, with a 95% CI of 8.8% to 22.0%. With an approximate 8% clinical margin added to the upper 95% confidence bound, these data support the PG of 30%.

14.5 Secondary Objective(s)

The secondary objective of this study is to demonstrate the Medtronic Hugo™ RAS system performs as intended when used in inguinal and ventral hernia repair. The secondary endpoints of this study will assess the overall performance of the Medtronic Hugo™ RAS system when used for the robotic surgery.

The following short-term secondary endpoints will be assessed through 30 days in all treated subjects:

- Complication rate: Overall rate of subjects with one or more procedure- and/or device-related complications (Clavien-Dindo Grade I or higher), from the first incision through 30 days post-procedure
- Major complication rate: Overall rate of subjects with one or more major procedure- and/or device-related complications (Clavien-Dindo Grade III or higher), from the first incision through

30-days post-procedure

- Operative time
- Readmission rate (through 30 days post-procedure): the proportion of subjects with any hospital readmissions through 30-days post-procedure
- Reoperation rate (through 30 days post-procedure): the proportion of subjects with any reoperation on the same target hernia through 30-days post-procedure
- Recurrence rate (through 30 days post-procedure): the proportion of subjects with any recurrences of hernia on the same anatomical region as the target hernia through 30-days post-procedure

The following long-term secondary endpoints will be assessed through 2 years in all treated subjects:

- Recurrence rate (through 2 years post-procedure): the proportion of subjects with any recurrences of hernia on the same anatomical region as the target lesion through 2 years post-procedure

The analysis set for the secondary objectives will be the FAS with available data. The secondary endpoints will be analyzed for the inguinal and ventral hernia cohort respectively.

Descriptive statistics will be used to summarize secondary endpoints. In addition, performance goals are pre-specified based on meta-analyses of published study data as well as considerations of clinically meaningful margins and statistical estimates (see details below and references in **Section 17.1**). Two-sided 95% confidence intervals will be provided as appropriate. The secondary objectives are not powered in this study. Instead, the secondary endpoints will be analyzed using descriptive statistics, which broadly negate the need for multiplicity adjustments. The role of the secondary endpoints is to explore additional effects and outcomes associated with either the procedure or the disease state. The pre-specified performance goals serve as benchmarks for interpretation rather than thresholds for statistical significance of clinical trial success in this study.

The performance goal details and rationales are summarized in **Tables 15 and 16** for short- and long-term secondary endpoints, respectively.

Performance Goals for Short-term Secondary Endpoints (through 30 days post-procedure)

Table 15: Short-term Secondary Endpoints – Performance Goal Determination

Short-term Secondary Endpoints: through 30 Days Post-Procedure			
Endpoint	**Surgery Type**	**PG**	**Rationale**
Rate of subjects with any complications (through 30 days)	Inguinal Hernia Repair	40%	Only three cohorts of patients who underwent inguinal hernia repair and had data reporting on any complications CD grade I or higher were identified in the literature review. Thus, there were insufficient data to perform a statistical analysis. The upper 95% CI range for these three cohorts was 13.1 to 36.4%. A PG of 40%, which is approximately 4% above the range of upper limits of the individual cohorts and captures the complication rate for all three individual cohorts, would be clinically relevant for a descriptive comparison.
	Ventral Hernia Repair	40%	Only three cohorts of patients who underwent ventral hernia repair and had data reporting on any complications CD grade I or higher were identified in the literature review. Thus, there were insufficient data to perform a statistical analysis. The upper 95% CI range for these three cohorts was 9.2 to 78.8%. A PG of 40%, which falls within the range of upper limits of the individual cohorts and captures the complication rate for two of the three individual cohorts, would be clinically relevant for a descriptive comparison.
Rate of subjects with major complications (through 30 days)	Inguinal Hernia Repair	10%	Only one cohort of patients who underwent inguinal hernia repair and had data reporting on major complications CD grade III or higher was identified in the literature review. Thus, there were insufficient data to perform a statistical analysis. The upper 95% CI range for this cohort was 10.9%. A PG of 10%, which falls within the range of the upper limit of this individual cohort, would be clinically relevant for a descriptive comparison.

	Ventral Hernia Repair	15%	Only three cohorts of patients who underwent ventral hernia repair and had data reporting on major complications CD grade III or higher were identified in the literature review. Thus, there were insufficient data to perform a statistical analysis. The upper 95% CI range for these three cohorts was 5.1 to 60.0%. A PG of 15%, which falls within the range of upper limits of the individual cohorts and captures the complication rate for two of the three individual cohorts, would be clinically relevant for a descriptive comparison.
Operative time (min)	Inguinal Hernia Repair	Unilateral Hernia Repair: 125 (min)	This analysis is based on 15 cohorts. The effect size index is the mean time. The random-effects model was employed for the analysis. The mean effect size is 80.9 min with a 95% CI of 70.7 to 91.0 min. If we assume that the true effects are normally distributed (in raw units), we estimate that the 95% prediction interval is 37.3 to 124.4 min. A PG of 125 minutes would be clinically relevant for a descriptive comparison.
		Bilateral Hernia Repair: 180 (min)	This analysis is based on 12 cohorts. The effect size index is the mean time. The random-effects model was employed for the analysis. The mean effect size is 109.6 min with a 95% CI of 91.8 to 127.4 min. If we assume that the true effects are normally distributed (in raw units), we estimate that the 95% prediction interval is 39.3 to 180.0 min. A PG of 180 minutes would be clinically relevant for a descriptive comparison.
	Ventral Hernia Repair	200 (min)	The analysis is based on nine cohorts. The effect size index is the mean time. The random-effects model was employed for the analysis. The mean effect size is 81.5 min with a 95% CI of 51.0 to 112.0 min. If we assume that the true effects are normally distributed (in raw units), we estimate that the 95% prediction interval is 0 to 196.8 min. A PG of 200 minutes would be clinically relevant for a descriptive comparison.
Readmission	Inguinal Hernia Repair	15%	The analysis is based on ten cohorts. The effect size index is the mean readmission rate. The mean effect size is 1.6% with a 95% CI of 1.0 to 2.7%. If we assume that the true effects are normally distributed (in raw units), we estimate that the 95% prediction interval is 0.9 to 3.0%. With a 12% clinical margin added, a PG of 15% would be clinically relevant for a descriptive comparison.

rate (through 30 days post-procedure)	Ventral Hernia Repair	20%	This analysis was based on five cohorts. The effect size index is the mean readmission rate. The mean effect size is 11.0% with a 95% CI of 9.1 to 13.3%. If we assume that the true effects are normally distributed (in logit units), we estimate that the 95% prediction interval is 8.0 to 14.9%. With a 5% clinical margin added, a PG of 20% would be clinically relevant for a descriptive comparison
Re-operation rate (through 30 days post-procedure)	Inguinal Hernia Repair	10%	Only two cohorts of patients who underwent inguinal hernia repair and had data reporting on reoperation rate through 30 days were identified in the literature review. Thus, there were insufficient data to perform a statistical analysis. The upper 95% CI range for these two cohorts was 10.9 to 16.8%. A PG of 10%, which falls below the upper limits of the individual cohorts, would be clinically relevant for a descriptive comparison.
	Ventral Hernia Repair	15%	Only two cohorts of patients who underwent ventral hernia repair and had data reporting on reoperation rate (one through 30 days, one through 90 days) were identified in the literature review. Thus, there were insufficient data to perform a statistical analysis. The upper 95% CI range for these two cohorts was 3.1 to 33.6%. A PG of 15%, which falls within the range of upper limits of the individual cohorts and captures the mean transfusion rate for both individual cohorts, would be clinically relevant for a descriptive comparison.
Recurrence rate (through	Inguinal Hernia Repair	8%	This analysis was based on five cohorts. The effect size index is the mean recurrence rate. The mean effect size is 0% with a 95% CI of 0.0 to 1.0%. Adding an approximate
30 days post-procedure)			7% clinical margin to the upper 95% CI bound, a PG of 8% would be clinically relevant for a descriptive comparison.
	Ventral Hernia Repair	10%	Only one cohort of patients who underwent ventral hernia repair and had data reporting on recurrence rate through 30 days was identified in the literature review. Thus, there were insufficient data to perform a statistical analysis. The upper 95% CI range for this cohort was 7.7%. Adding an approximate 2% clinical margin, we set the PG at 10% for recurrence rate through 30 days following ventral hernia repair, which will be clinically relevant for a descriptive comparison.

Performance Goals for Long-term Secondary Endpoints (through 2 years)

Table 16: Recurrence Rate through 2 Years – Performance Goal Determination

Long-term Secondary Endpoint: Hernia Recurrence Rate			
Endpoint	**Surgery Type (Inguinal, Ventral Hernia)**	**PG**	**Rationale**
Recurrence rate (through 2 years)	Inguinal Hernia Repair	15%	This analysis was based on eight cohorts. The effect size index is the mean recurrence rate. The mean effect size is 0.6% with a 95% CI of 0.2 to 1.3%. If we assume that the true effects are normally distributed (in logit units), we estimate that the 95% prediction interval is 0.2 to 1.7%. The PG for recurrence through 30 days is set at 8%. Adding a 7% clinical margin to the 30-day PG, we set the 2-year PG at 15% for reoperation rate through 2 years following inguinal hernia repair.
	Ventral Hernia Repair	37%	This analysis was based on seven cohorts. The effect size index is the mean recurrence rate. The mean effect size is 10.9% with a 95% CI of 4.7 to 23.1%. If we assume that
			the true effects are normally distributed (in logit units), we estimate that the 95% prediction interval is 1.3 to 53.6%. We set a PG of 37% recurrence rate through 2 years following ventral hernia repair, which falls between the upper bounds for the 95% CI and 95% prediction interval and is clinically relevant.

14.6 Ancillary Objective(s)

Descriptive analyses of other pre-specified outcome measures beyond the primary and secondary objectives will be exploratory in nature and are not intended as a focus of the study for the evaluation of the study device.

The following data will be collected as applicable:

- Estimated intraoperative blood loss
- Transfusion rate
- Hospital length of stay
- Mortality through 30 days
- Device- and procedure-related AEs through 2 years
- Readmission rate through 2 years

- Reoperation rate through 2 years
- Surgeon experience
- Pain scores at baseline, 30 days, and 3 months (ACHQC questionnaire)

The analysis set for these ancillary objectives will be the FAS with available data. The ancillary endpoints will be analyzed for the inguinal and ventral hernia cohort respectively.

14.7 Sample Size Determination

The sample size for the study was estimated based on the primary safety and effectiveness hypotheses.

The effectiveness hypothesis is to test if the surgical success rate is above the performance goal. Based on published data and clinical practice presented in **section 14.4.1**, the performance goal of the conversion rate is set to be 85% (100%-conversion rate). Assuming a success rate of 93%, a sample size of 172 subjects for the combined inguinal and ventral hernia cohort will provide 90% of power with one-sided alpha of 0.025. Calculation was performed using the PASS 2023. Account for 10% attrition rate, the enrollment is 192 subjects.

The primary safety objective is also part of the consideration for the sample size determination. The primary safety endpoint is the rate of subjects with any procedure- and/or device-related SSEs from the first incision through 30 days post-procedure. A statistical hypothesis with a performance goal is specified for each of the two surgery types (inguinal hernia repair and ventral hernia repair). The sample size for each surgery type is 96 with up to 192 subjects in total, after accounting for an estimate 10% attrition rate. For details, refer to **section 14.4.2**.

With the consideration of both the effectiveness and safety primary objectives, up to a total of 192 subjects are planned to be enrolled in this study. Up to ten study sites will be used. To keep enrollment balanced, a single study site will be allowed to treat no more than 30% of the total population.

14.8 Demographics and Baseline Characteristics

The number of subjects screened, treated, discontinued during the study, as well as the reasons for discontinuations will be summarized for all centers combined and each center separately. Disposition and reason for study discontinuation will also be provided as a by-subject listing. All demographics and baseline characteristics will be summarized using descriptive statistics.

14.9 Analysis Populations

The following populations will be considered for the analysis of data for this study:

Enrolled Analysis Set

All subjects who signed the informed consent.

Full Analysis Set

The full analysis set (FAS) is defined as all enrolled subjects in whom the Hugo™ RAS procedure is begun, defined as the first skin incision. This is also known as a modified intent-to-treat population. If a subject is

consented, but the first incision does not occur (e.g., if the subject becomes ineligible during the timeframe between consent and the procedure day), that subject will not be considered part of the FAS. The FAS will be the primary analysis set for the evaluation of the primary and secondary endpoints as appropriate. The analysis sets for various study endpoints are detailed in **Section 14.4** through **Section 14.5**.

AEs will be collected from the time of consent. AEs occurring in subjects excluded from the FAS will be followed post-consent through study exit and will be reported in a listing in the clinical study report. These AEs will not be included in the primary FAS analysis for either AE reporting or the analysis of the primary and secondary endpoints. The number and proportion of subjects experiencing each type of adverse event will be summarized by site and overall, for the FAS.

Per Protocol Analysis Set

The per protocol analysis set (PPAS) is a subset of the FAS including only those subjects without any major protocol deviations and completed 30-day visit. Details on PPAS definitions will be provided in the SAP. Reasons for exclusion of subjects from PPAS will be documented and reported.

All enrolled subjects will be included in a subject disposition table indicating reasons for exclusion from the FAS and PPAS analysis sets.

14.10 Data Poolability

An assessment of data poolability of the sites will be performed using the logistic regression for the primary effectiveness endpoint. A significance level of 0.15 will be considered (per FDA recommendation). Sites with fewer than five subjects will be combined into large sites to ensure statistical robustness. If the sites are found to be significantly heterogeneous with respect to the primary endpoint, additional analyses will be conducted to further assess variations across sites in baseline and procedural variables that might contribute to the variations.

14.11 Missing Data Handling

The primary effectiveness analysis will be based on the FAS. If 5% of the data or fewer are missing for the analysis, no imputation will be used[42]. Otherwise, missing data will be imputed for the FAS using multiple imputation (MI). The model variables used for the MI analysis may include baseline variables such as age, gender, and BMI. Ten imputations will be conducted and combined using the Rubin's rule[43]. Sensitivity analysis will be performed using available data in both FAS and PPAS as well as tipping-point analysis in FAS to fully understand the missing data impact on the study results.

The primary safety analysis will be based on the FAS subjects with available data at 30-days, i.e. whose status (event, no event) at 30-days can be determined. No imputation will be conducted.

For the secondary and ancillary endpoints, analysis will be conducted with available data in FAS. No imputation will be conducted.

14.12 Multiplicity Adjustment

For the primary effectiveness endpoint, only one hypothesis will be tested at alpha of 0.025 one-sided. If

the one-sided primary objective p-value is <0.025, then the null hypothesis will be rejected, and the test will be declared statistically significant. After the primary effectiveness objective is met, the primary safety objective for each surgery type will be tested. For the primary safety endpoint (procedure- and/or device-related SSEs rate), the closed test procedure (Holm's Bonferroni method) will be used to protect the overall study-wise error rate for surgery types (inguinal hernia, ventral hernia), thereby maintaining an overall type I error of one-sided of 0.025 for these objectives. No multiplicity adjustment will be performed for supporting, sensitivity, or subgroup analyses. Secondary objectives and ancillary objectives are intended to be descriptive only. No multiplicity adjustment will be applied.

14.13 Subgroup Analysis

Subgroup analysis for the primary effectiveness objective will be performed by cohort (inguinal, ventral), gender, age group, race, and ethnicity. Additional subgroup analysis may be specified in the SAP prior to data analysis. Sub-group analysis will be performed using FAS with available data. No imputation will be applied. Any subgroup with less than 10 subjects may not be reported.

14.14 Minimization of Bias

Selection of subjects, treatment of subjects, and evaluation of study data are potential sources of bias. Methods incorporated in the study design to minimize potential bias include (but are not limited to):

- Potential for bias during this clinical investigation has been minimized by a well-controlled design, expected conduct under the terms of an approved clinical investigational plan and prospectively defined methods of data collection and analysis.
- All subjects meeting the study criteria will have all available data relevant to the study objectives collected per the investigational plan.
- Any known or foreseeable factors that comprise the outcomes of the clinical investigation or interpretation of results have been accounted for by the design the clinical investigation.

In summary, potential sources of bias that may be encountered in this study have been considered and minimized by careful study design.

14.15 Safety Summaries

AEs and DDs will be collected as outlined in **Section 12.1** and **Section 12.2**. AEs occurring in subjects excluded from the FAS will be followed post-consent through study exit and will be reported in a listing in the CSR. These AEs will not be included in the FAS summary analysis for either AE reporting or the analysis of the primary and secondary endpoints. Besides the primary and secondary objectives related to safety, AEs and DDs will be coded and summarized using the most recent version of Medical Dictionary for Regulatory Affairs (MedDRA). All Serious Adverse Events (SAE), deaths, and Surgical Site Events (SSEs) will be adjudicated by an independent CEC. Cases where the investigator's classification does not match CEC's adjudication classification, both determinations will be provided within the final report; however, the CEC's adjudication will be used for data analysis.

For the FAS, the type, incidence, seriousness, and procedure/device relatedness of AEs will be reported. AEs for all FAS subjects will be collected from first incision through the study exit as outlined in **Section 12.1** and **Section 12.2**.

AEs and DDs will be summarized with number of events, number of subjects who experienced the event, and percentage of subjects who experienced one or more events.

15 Ethics

15.1 Statement(s) of Compliance

This study will be conducted in compliance with international ethical and scientific quality standards, known as Good Clinical Practice (GCP). GCP includes review and approval by an independent IRB before initiating a study, continuing review of an ongoing study by an IRB, and obtaining and documenting the freely given informed consent of a subject before initiating the study.

The Enable Hernia study was designed to reflect GCP. These include the protection of the rights, safety and well-being of human subjects, controls to ensure the scientific conduct and credibility of the clinical investigation and the definition of responsibilities of the sponsor and Investigators. The sponsor shall avoid improper influence on, or inducement of, the subject, monitor, any Investigator(s) or other parties participating in, or contributing to, the clinical investigation. All Investigators shall avoid improper influence on or inducement of the subject, sponsor, monitor, other Investigator(s) or other parties participating in or contributing to the clinical investigation.

The principles of the DoH have been implemented through the IC process, IRB approval, study training, clinical trial registration, pre-clinical testing, risk-benefit assessment, and publication policy.

Ultimately, all study sites in all geographies will follow and comply with:

- Principles of DoH
- 21 CFR Part 11 (Electronic Records, Electronic Signatures)
- 21 CFR Part 54 (Financial Disclosure by Clinical Investigators)
- The CTA
- The procedures described within this CIP
- Local IRB Requirements

In addition to the regulatory requirements outlined above, the study will be conducted according to federal, national, and local laws, regulations, standards, and requirements of the countries/geographies where the study is being conducted. These include but are not limited to:

- In the United States, the study will be conducted under an FDA IDE in compliance with 21 CFR Parts:
  - 50: Protection of Human Subjects

- 54: Financial Disclosure by Clinical Investigators
- 56: IRBs
- 812: IDEs

The study will be publicly registered prior to subject enrollment in accordance with the 2007 FDAAA and DoH on http://clinicaltrials.gov (PL 110-85, section 801(a)). In addition, the study may be registered in local regulatory databases where required by local law.

Approval of the CIP and CIP amendments is required from the following groups prior to any study procedures at a study site:

- Medtronic
- Principal Investigators (where required by local law/regulations)
- Geography-specific regulatory authorities (if regulatory approval is required)
- An independent medical IRB.

Similarly, approval of subsequent revisions to the CIP is required at each study site from the above-mentioned groups prior to implementation of the revised CIP at the study site.

16 Study Administration

16.1 Monitoring

It is the responsibility of Medtronic to ensure proper monitoring of this study. Trained Medtronic personnel or delegates appointed by Medtronic may perform study monitoring at the study site to ensure that the study is conducted in accordance with the CIP, the CTA, and the applicable regulatory and local requirements. Medtronic, or delegates, must therefore be allowed direct access to the subjects' case histories (clinic and hospital records, and other source data/documentation) upon request as per the IC form, Research Authorization (where applicable) and CTA. The Principal Investigator should also be available during monitoring visits.

16.1.1 Monitoring Visits

Frequency of monitoring visits may be based upon subject enrollment, study compliance, number of adverse events, number of deviations, observations from previous monitoring visits and any suspected inconsistency in data that requires investigation. Regulatory documents will be reviewed at each study site. Monitoring for the study, including site initiation visits, interim monitoring visits, and closeout visits, will be done in accordance with the study-specific monitoring plan. Monitoring visits may be conducted onsite or remotely.

Monitoring visits may be conducted periodically to assess study site progress, the Investigator's adherence to the CIP, regulatory compliance including but not limited to IRB approval and review of the study, maintenance of records and reports, and review of source documents against subject eCRFs in accordance with the study-specific monitoring plan. Monitors review study site regulatory and study compliance by identifying observations of non-compliance and communicating those observations along

with recommendations for preventative/corrective actions to study site personnel. Monitors may work with study personnel to determine appropriate corrective action recommendations and to identify trends within the study or at a particular study site.

16.2 Data Management

Data will be collected using an electronic data management system for studies. CRF data will be stored in a secure, password-protected database hosted in a cloud service which is owned and validated by a third party. Data will be reviewed using programmed and manual data checks. Data queries will be made available to study sites for resolution. Study management reports may be generated to monitor data quality and study progress. At the end of the study, the data will be frozen and will be retained by Medtronic in accordance with applicable regulations.

All records and other information about subjects participating in this study will be treated as confidential. Data will be transferred and processed by Medtronic, or a third party designated by Medtronic in a key coded form, unless it is impossible to pseudonymize for instance, where the subject's name cannot be removed from the data carrier.

Procedures in the CIP require source documentation. Source documentation will be maintained at the study site. Source documents, which may include worksheets, subject medical records, programmer printouts, and interrogation files, must be created and maintained by the investigational study site team.

The Principal Investigator must ensure the accuracy, completeness, and timeliness of the recorded data and then provide his/her electronic signature on the appropriate eCRFs.

The Investigator's signature for specific eCRFs will be documented in compliance with local regulations. Changes to data previously submitted to the sponsor will require a new electronic signature by the Investigator to acknowledge/approve the changes.

16.3 Direct Access to Source Data/Documents

Medtronic may conduct audits at participating study sites. The purpose of an audit is to verify the performance of the monitoring process and the study conduct, independently of the personnel directly involved in the study. Regulatory Authorities, such as the FDA, may also perform inspections at participating study sites. The Investigator and/or institution shall permit Medtronic, IRBs and the FDA direct access to source data and documents during monitoring, audits and regulatory inspections.

16.4 Confidentiality

All information and data sent to parties involved in study conduct concerning subjects or their participation in this study will be considered confidential. Study sites will assign a unique subject identification (SID) to each subject. Records of the subject/SID relationship will be maintained by the study site. The SID number is to be recorded on all study documents to link them to the subject's medical records at the study site. Confidentiality of data will be observed by all parties involved at all times throughout the clinical investigation. All data shall be secured against unauthorized access. The privacy of each subject and confidentiality of his/her information shall be preserved in reports and when publishing any data. In

the US, "Protected Health Information" (PHI) will be maintained in compliance with the Health Insurance Portability and Accountability Act (HIPAA) of 1996. To maintain confidentiality, the subject's name or any other PHI should not be recorded on any study document other than the IC form. This scenario will be covered in the IC form. In the event a subject's name/PHI is included for any reason, it will be blinded as applicable. In the event of the inability to blind the identification (e.g., digital media), it will be handled in a confidential manner by the authorized personnel. Data relating to the study might be made available to third parties (for example in case of an audit performed by RA), provided the data are treated as confidential and that the subject's privacy is guaranteed. No identifiable subject information will be published.

16.5 Liability/Warranty/Insurance Information

Medtronic maintains appropriate clinical study liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a clinical study insurance statement/certificate will be provided to the IRB.

16.6 CIP Amendments

Any revisions or amendments to the CIP or IC document, along with a statement of justification for the changes, will be submitted to the FDA and governing IRBs, according to applicable regulations. All amendments to the CIP shall be agreed upon between Medtronic and the Principal Investigator(s), or the coordinating Investigator. Approval by the FDA and the site's IRB must be obtained prior to implementing a CIP revision at the study site.

16.7 Record Retention

All study-related documents must be retained for a period of at least 2 years after market-release in the region in which the product is marketed and after study closure (or longer if required by local law). Medtronic will inform the Investigator/study site when these documents are no longer required to be retained.

No study document or image will be destroyed without prior written agreement between Medtronic and the Investigator. The Investigator should take measures to prevent accidental or premature destruction of documents. Should the Investigator wish to assign the study records to another party or move them to another location, advance written notice must be given to Medtronic.

Medtronic will retain the study records according to Medtronic corporate policy and record retention schedule.

16.7.1 Investigator Records

The Investigator is responsible for the preparation and retention of the records cited below. All the below records, except for case history records and case report forms, should be kept in the Investigator Site File (i.e., the study binder provided to the investigator) or Subject Study Binder. eCRFs must be maintained and signed electronically within the electronic data capture system during the study. The following records are subject to inspection and must be retained for a period of two years (or longer as local law or hospital

administration requires) after product approval or the date on which the investigation is terminated, or the date that the records are no longer required for purposes of supporting a pre-market approval application.

- All correspondence between the IRB, sponsor, monitor, FDA, RA, and the Investigator that pertains to the investigation, including required reports.
- Subject's case history records, including:
  - Signed and dated by the subject IC form
  - Observations of AEs/ADEs/DDs
  - Medical history
  - Procedure and follow-up data (if applicable)
  - Documentation of the dates and rationale for any deviation from the protocol
- List of investigation study sites
- Financial Disclosure (FD)
- Subject screening log & ID log (if applicable)
- Normal value(s)/range(s) for clinical laboratory test (if applicable)
- Lab certificate (if applicable)
- Device Disposition Logs containing model and serial numbers of devices delivered to the study site, returned-to-sponsor dates and reasons, initials of all persons who received, used, or disposed each device, and method of disposal/destruction.
- All approved versions of the CIP, IC, and Report of Prior Investigation Summary
- Signed and dated CTA.
- CV of Principal Investigators and key members of investigation study site team as required by applicable regulations.
- Documentation of delegated tasks.
- IRB approval documentation. Written information that the Investigator or other study staff, when member of the IRB, did not participate in the approval process. Approval documentation must include the IRBs composition, where required per local law.
- RA notification, correspondence, and approval, where required per local law.
- Study training records for study site staff.
- Any other records that FDA and local regulatory agencies require to be maintained.
- Final Study Report including the statistical analysis.

16.7.2 Sponsor Records

Medtronic shall maintain the following accurate, complete, and current records:

- All correspondence which pertains to the investigation
- Investigational device traceability record containing model and serial numbers of devices, shipping date and name and address of person that received shipped device,

location (if different than person shipped to), transfer and receipt by Medtronic dates.

- Sample of label attached to investigational device
- Signed Investigator Trial Agreements, FD (if applicable) and current signed and dated CV of Principal Investigator and key members of the investigation study site team (as required by local law), delegated task list
- All signed and dated case report forms submitted by investigator, including reports of AEs, ADEs and DDs
- All approved IC templates, and other information provided to the subjects and advertisements, including translations
- Copies of all IRB approval letters and relevant IRB correspondence and IRB voting list/roster/letter of assurance
- Names, addresses, and professional positions of the clinical investigators, of the principal investigator and coordinating clinical investigator if appointed
- Names of the institutions in which the study will be conducted
- RA correspondence, notification and approval as required by national legislation
- Names/contact addresses of monitors
- Monitoring visit reports
- Statistical analyses and underlying supporting data
- Final report of the study
- The CIP, Report of Prior Investigations summary and study related reports, and revisions
- Study training records for study site personnel and Medtronic personnel involved in the study
- Any other records that local regulatory agencies require to be maintained.

Medtronic records and reports will be maintained in a password-protected document management system.

After closure of the study Medtronic will archive records and reports indefinitely.

16.8 Reporting Requirements

16.8.1 Investigator Reports

The Investigator is responsible for the preparation (review and signature) and submission to the sponsor of all case report forms, adverse events, and adverse device effects (reported per the country-specific collection requirements), device deficiencies, deaths, and any deviations from the CIP. If any action is taken by an IRB with respect to this study, copies of all pertinent documentation must be forwarded to Medtronic in a timely manner. Safety data Investigator reporting requirements are listed in **Table 17 and Table 18**. The Investigator shall prepare and submit these reports in a complete, accurate and timely manner.

Reports are subject to inspection and to the retention requirements as described above for Investigator

records.

Table 17. Investigator Reports Applicable for All Geographies per Medtronic Requirements

Report	Submit to	Description/Constraints
Withdrawal of IRB/EC approval	Sponsor and Relevant Authorities	The Investigator must report a withdrawal of approval by the reviewing IRB of the Investigator's part of the investigation within 5 working days.
Study Deviations	Sponsor and IRB	Any deviation from the clinical investigational plan shall be recorded together with the explanation of the deviation. Notice of deviations from the CIP to protect the life or physical well-being of a subject in an emergency shall be given as soon as possible, but no later than 5 working days after the emergency occurred. Except in such emergency, prior approval is required for changes in the plan or deviations.
Final Report	Sponsor and IRBs and Relevant Authorities	This report must be submitted within 3 months of study completion or termination.

Table 18. Additional Investigator Reports Applicable to the United States per FDA Regulations

Report	Submit to	Description/Constraints
Progress Report	Sponsor and IRB	The Investigator must submit this report to the sponsor and IRB at regular intervals, but in no event less than yearly intervals. (21 CFR 812.150 (a)(3)).
Study Deviations	Sponsor and IRB	Notice of deviations from the CIP to protect the life or physical well-being of a subject in an emergency shall be given as soon as possible, but no later than 5 working days after the emergency occurred. Except in such emergency, prior approval is required for changes in the plan or deviations. If the deviation may affect the scientific soundness of the plan or the rights, safety and welfare of the subjects, the deviation must be approved by Medtronic, the IRB, and the FDA/applicable RA. If the deviation does not affect these issues, then only Medtronic must approve it. (21 CFR 812.150(a)(4))

Report	Submit to	Description/Constraints
Failure to Obtain IC Prior to Investigational Device Use	Sponsor and IRBs	If an Investigator uses a device without obtaining IC, the Investigator shall report such use within 5 working days after device use. (21 CFR 812.150(a)(5))
Final Report	Sponsor IRBs Relevant Authorities	This report must be submitted within 3 months of study completion or termination of the investigation or completion or termination of the Investigator's part of the investigation. (21 CFR 812.150(a)(6))
Other	IRB and FDA	An Investigator shall, upon request by a reviewing IRB, FDA, or any other RA, provide accurate, complete, and current information about any aspect of the investigation. (21 CFR 812.150(a)(7))

16.8.2 Sponsor Reports

Medtronic shall prepare and submit the following complete, accurate, and timely reports listed in **Table 19**. In addition to the reports listed below, Medtronic shall, upon request of the reviewing IRB, RA, or FDA, provide accurate, complete, and current information about any aspect of the investigation.

Table 19. Sponsor Reports for the United States

Report	Submit to	Description/Constraints
Withdrawal of IRB Approval	Investigators, IRB, FDA, and Relevant authorities	Notification within five working days. (21 CFR 812.150(b)(2))
Withdrawal of FDA Approval	Investigators, IRB, and Relevant authorities	Notification within five working days. (21 CFR 812.150(b)(3))
Investigator List	FDA	Submit at 6-month intervals, a current list of the names and addresses of all Investigators participating in the investigation. (21 CFR 812.150(b)(4))
Progress Reports	IRB and FDA	Progress reports will be submitted at least annually. (21 CFR 812.150(b)(5), 812.36(f)

Report	Submit to	Description/Constraints
Recall and Device Disposition	Investigators, Head of Institution, IRB, Relevant authorities, and FDA	Notification within 30 working days and will include the reasons for any request that an Investigator return, repair, or otherwise dispose of any devices. (21 CFR 812.150(b)(6))
Final Report	Investigators, IRB, RAs upon request, and FDA	Medtronic will notify FDA within 30 working days of the completion or termination of the investigation. A final report will be submitted to the FDA, Investigators, and IRBs within six months after completion or termination of this clinical study. (21 CFR 812.150(b)(7))
Failure to Obtain Informed Consent	FDA	Investigator's report will be submitted to FDA within five working days of notification. (21 CFR 812.150(b)(8))
Study Deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate clinical Investigator(s), are reported on the CRFs and the final report of the clinical investigation. Study site specific study deviations will be submitted to Investigators periodically.
Other	IRB, FDA	Accurate, complete, and current information about any aspect of the investigation. (21 CFR 812.150(b)(10))
Premature Termination or Suspension of Clinical Study	IRB, Investigators, and Regulatory authorities, where applicable	Medtronic will provide prompt notification of termination or suspension and reason(s) to Investigator and where required to IRB and RAs.

16.9 Publication and Use of Information

Publications from the Enable Hernia study will be handled according to Standard Operating Procedures and as indicated in the CTA.

16.9.1 Publication Committee

Medtronic may form the Enable Hernia Study Publication Committee from study investigators. Medtronic personnel may serve as members of the committee. This committee will manage study publications with the goal of publishing findings from the data. The Publication Committee will develop the final Publication Plan as a separate document.

The Publication Committee's role is to: 1) manage elements addressed in the publication plan as outlined in this appendix, 2) develop the final Publication Plan under separate cover, 3) execute the Publication

Plan, 4) oversee the publication of primary, secondary, and ancillary study results, 5) review and prioritize publication proposals, 6) provide input on publication content, and 7) determine authorship. In addition, the committee will apply and reinforce the authorship guidelines set forth in the Publication Plan.

Membership in the Publication Committee does not guarantee authorship. The committee will meet at regular intervals, at least yearly, as needed.

16.9.2 Management of Primary, Secondary, and Ancillary Publications The Publication Committee reviews, prioritizes, and manages all publications including primary, secondary and ancillary publications. Primary and secondary publications are those that address analyses of any or all primary objectives or secondary objectives, respectively, as specified in the CIP.

An ancillary publication is any publication that does not address the study objectives identified in the CIP. They include publications proposed and developed by other Medtronic departments or entities, clinicians participating in this study, and clinicians not participating in this study. The committee will work with Medtronic to ensure that requests do not present conflicts with other proposals, are not duplicative, and to determine which ancillary publication proposals, if any, will be supported.

The committee may decide that no publications, including abstracts, will be published prior to the end of the study or with individual study site data. Requests for publications on study objectives utilizing subset data (e.g., regional) will be evaluated for scientific validity and the ability of Medtronic to provide resources.

16.9.3 Criteria for Determining Authorship

Publications will adhere to authorship criteria defined by the International Committee of Medical Journal Editors (ICMJE, Uniform requirements for manuscripts submitted to biomedical journals, www.icmje.org). Individual authorship criteria defined by the target journal or conference will be followed when it differs from ICMJE criteria.

Authors, including Medtronic personnel, must at a minimum meet all the conditions below:

- Substantial contributions to conception and design of the work, or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Decisions regarding authorship and contributor-ship will be made by the committee. The selected authors will be responsible for drafting the publication. All selected authors must fulfill the authorship conditions stated above to be listed as authors, and all contributors who fulfill the conditions must be listed as authors.

All Investigators not listed as co-authors will be acknowledged as the “Medtronic Enable Hernia Study

Investigators" and will be individually listed according to the guidelines of the applicable scientific journal when possible and affiliation. Any other contributors will be acknowledged by name with their specific contribution indicated.

16.9.4 Transparency

Transparency of clinical study results will be maintained by the following means:

- A final report, describing the results of all objectives and analysis, will be distributed to all Investigators, IRBs and RAs of participating countries when required by local law
- Registering and posting the study results on ClinicalTrials.gov based on the posting rules stipulated
- Submitting for publication the primary study results after the study ends
- Disclosing conflicts of interest (e.g., financial) of the co-authors of publications according to the policies set forth by the corresponding journals and conferences
- Making an individual study sites study data accessible to the corresponding investigator after the completion of the study, if requested

16.10 Suspension or Early Termination

16.10.1 Planned Study Closure

Study Closure is a process initiated by distribution of a study closure letter. Study closure is defined as closure of a study that occurs when Medtronic and/or regulatory requirements have been satisfied per the CIP and/or by a decision by Medtronic or RA, whichever occurs first. The study closure process is complete upon distribution of the Final Report or after final payments, whichever occurs last. Ongoing IRB oversight is required until the overall study closure process is complete. Refer to **Section 10.10.1** for additional information regarding study exit procedures.

16.10.2 Early Termination or Suspension

Early Termination is the closure of a study that occurs prior to meeting defined endpoints. This is possible for the whole study or a single study site. Suspension is a temporary postponement of study activities related to enrollment and distribution of the product. This is possible for the whole study or a single study site.

16.10.2.1 Study-wide Termination or Suspension

Medtronic reserves the right to suspend or terminate the study at any time. Reasons may include, but are not limited to, the following:

- Insufficient enrollment to complete the study within the expected timeframe
- Identification of unacceptable safety profile; suspicion of an unacceptable risk will result in a suspension, confirmation of an unacceptable risk will result in termination
- Inadequate subject adherence to follow-up requirements
- Product performance/product supply issues

Medtronic reserves the right to suspend or terminate the study at an individual site. Reasons may include, but are not limited to, the following:

- Noncompliance with the protocol, including inadequate subject adherence to follow-up requirements
- Serious or repeated deviations at the site
- Failure to implement required corrective and preventive actions
- Insufficient enrollment to complete the study within the expected timeframe
- Loss of appropriately trained site personnel

Investigators are required to notify the IRB and FDA (as applicable) of study suspension/termination. In addition, Investigators should assess whether or not to continue the study based on reasons above. Subjects will be notified by the investigator of suspension/termination due to unacceptable risk or of termination due to any other cause.

16.10.2.2 Investigator/Study Site Termination or Suspension

Possible reasons for Investigator or study site termination or suspension include but are not limited to:

- Failure to obtain initial IRB approval or annual renewal of the study
- Persistent non-compliance to the clinical investigation (e.g., failure to adhere to inclusion/exclusion criteria, failure to follow subjects per scheduled follow-ups)
- Lack of enrollment
- Noncompliance to regulations and the terms of the CTA (e.g., failure to submit data in a timely manner, failure to follow-up on data queries and monitoring observations in a timely manner, etc.)
- IRB suspension of the study site
- Fraud or fraudulent misconduct is discovered (as defined by local law and regulations)
- Investigator request (e.g., no longer able to support the study)

16.10.3 Procedures for Termination or Suspension

16.10.3.1 Medtronic-initiated and Regulatory Authority-initiated

- Medtronic will promptly inform the clinical investigators of the termination or suspension and the reasons and inform the RAs where required
- In the case of study termination or suspension for reasons other than a temporary IRB approval lapse, the Investigator will promptly inform the IRB
- In the case of study termination, the Investigator must inform the subjects and may inform the personal physician of the subjects to ensure appropriate care and follow-up is provided
- In the case of a study suspension, subject enrollment must stop until the suspension is lifted by Medtronic

- In the case of a study suspension, enrolled subjects should continue to be followed out of consideration of their safety, rights and welfare

16.10.3.2 Investigator-initiated

- The Investigator will inform Medtronic and provide a detailed written explanation of the termination or suspension
- The Investigator will promptly inform the institution (where required per regulatory requirements)
- The Investigator will promptly inform the IRB
- The Investigator will promptly inform the subjects and/or the personal physician of the subjects to ensure appropriate care and follow-up is provided
- In the case of a study suspension, subjects enrolled should continue to be followed out of consideration of their safety, rights and welfare

16.10.3.3 Institutional Review Board-initiated

- The Investigator will inform Medtronic and provide a detailed written explanation of the termination or suspension within 5 business days
- Subject enrollment must stop until the suspension is lifted
- Subjects already enrolled should continue to be followed in accordance with IRB policy or its determination that an overriding safety concern or ethical issue is involved
- The Investigator will inform his/her institution (where required per local requirements)
- The Investigator will promptly inform the subjects, or legally-authorized designees or guardians and/or the personal physician of the subjects, with the rationale for the study termination or suspension

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18 Appendices

18.1 Clavien-Dindo Grades and Examples

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Grade	Definition
Grade I	Any deviation from the normal post-operative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade III	Requiring surgical, endoscopic or radiological intervention
Grade IIIa	Intervention not under general anesthesia
Grade IIIb	Intervention under general anesthesia

Grade IV	Life-threatening complication (including CNS complications) * requiring IC/ICU management
Grade iVa	Single organ dysfunction (including dialysis)
Grade iVb	Multiorgan dysfunction
Grade V	Death of a patient
Suffix "d"	If the patient suffers from a complication at the time of discharge (see examples on next page), the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication.
*Brain hemorrhage, ischemic stroke, subarachnoid bleeding, but excluding transient ischemic attacks. CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.	

Grades	**Organ System**	**Examples**
Grade I	Cardiac	Atrial fibrillation converting after correction of K^+-level
	Respiratory	Atelectasis requiring physiotherapy
	Neurological	Transient confusion not requiring therapy
	Gastrointestinal	Noninfectious diarrhea
	Renal	Transient elevation of serum creatinine
	Other	Wound infection treated by opening of the wound at the bedside
Grade II	Cardiac	Tachyarrhythmia requiring 13-receptor antagonists for heart rate control
	Respiratory	Pneumonia treated with antibiotics on the ward
	Neurological	TIA requiring treatment with anticoagulants
	Gastrointestinal	Infectious diarrhea requiring antibiotics
	Renal	Urinary tract infection requiring antibiotics

	Other	Same as for I but followed by treatment with antibiotics because of additional phlegmonous infection
Grade IIIa	Cardiac	Bradyarrhythmia requiring pacemaker implantation in local anesthesia
	Neurological	See grade IV
	Gastrointestinal	Biloma after liver resection requiring percutaneous drainage
	Renal	Stenosis of the ureter after kidney transplantation treated by stenting
	Other	Closure of dehiscent noninfected wound in the OR under local anesthesia
Grade IIIb	Cardiac	Cardiac tamponade after thoracic surgery requiring fenestration
	Respiratory	Bronchopleural fistulas after thoracic surgery requiring surgical closure
	Neurological	See grade IV
	Gastrointestinal	Anastomotic leakage after descendorectostomy requiring relaparotomy
	Renal	Stenosis of the ureter after kidney transplantation treated by surgery
	Other	Wound infection leading to eventration of small bowel
Grade iVa	Cardiac	Heart failure leading to low-output syndrome
	Respiratory	Lung failure requiring intubation
	Neurological	Ischemic stroke/brain hemorrhage
	Gastrointestinal	Necrotizing pancreatitis
	Renal	Renal insufficiency requiring dialysis
Grade iVb	Cardiac	Same as for iVa but in combination with renal failure
	Respiratory	Same as for iVa but in combination with renal failure

Grades	Organ System	Examples
	Gastrointestinal	Same as for iVa but in combination with hemodynamic instability
	Neurological	Ischemic stroke/brain hemorrhage with respiratory failure
	Renal	Same as for iVa but in combination with hemodynamic instability
Suffix “d”	Cardiac	Cardiac insufficiency after myocardial infarction (iVa–d)
	Respiratory	Dyspnea after pneumonectomy for severe bleeding after chest tube placement (IIIb– d)
	Gastrointestinal	Residual fecal incontinence after abscess following descendorectostomy with surgical evacuation. (IIIb–d)
	Neurological	Stroke with sensorimotor hemisyndrome (iVa–d)
	Renal	Residual renal insufficiency after sepsis with multiorgan dysfunction (iVb–d)
	Other	Hoarseness after thyroid surgery (I–d)
TIA, transient ischemic attack; OR, operating room.		

18.2 Report of Prior Investigations

Provided under separate cover.

18.3 Instructions for Use/Labeling

Provided under separate cover.

18.4 Sample Informed Consent Form

Provided under separate cover.

18.5 Training Plan

Provided under separate cover.

18.6 List of Monitors

Provided under separate cover.

18.7 List of Institutions/IRBs

Provided under separate cover.

18.8 Statement of Generalizability to Medicare Beneficiaries

As described in the background section of this protocol, epidemiological data on abdominal and inguinal hernia shows relevance to the Medicare population. Lifetime risk for inguinal hernia is 3% for women and 27% for men. Incidence increases with age for men[2]. With an aging population exposed to a higher cumulative risk of developing incisional hernia after both minimally invasive and open surgery, the management of ventral hernia will continue to be a central focus of surgical disease[4].

An analysis of a US hospital claims/chargemaster database (Premier Inc. PINC AI™ Healthcare Database) containing US hospital-reported, service-level, all-payer information identified over 124,831 inguinal and abdominal surgical hernia repair cases in 2021. Medicare patients represented 37% (45,417/124,831) of cases. RAS was performed for 27% of total cases (33,178/124,831). Medicare patients represented 34% of RAS cases (11,17/33,178)[7]. This representation of surgical hernia repairs in the Medicare population is further validated by an analysis of the CMS 2021 CMS Inpatient & Outpatient Standard Analytic Files (SAF) Limited Dataset (LDS) in which over 56,000 ventral hernia repair cases and over 76,000 inguinal hernia repair cases were identified[44]. Since coding for the outpatient setting does not specify surgical approach, the proportion of RAS cases is not presented in the SAF analysis.

Based on the high incidence of hernia in the older adult population and the historical proportion of Medicare beneficiaries comprising patients relevant to this study cohort, it is likely the study results will be generalizable to the Medicare beneficiary population.

18.9 Surgeon Experience Survey

Enable - Hernia	Surgeon Experience
Date of completion	dd MMM yyyy
What are the initials of the surgeon who completed the Surgeon Experience form	
What was the type of hernia	LOV (2)
Communication	
Communication needs to be repeated (i.e. requests, questions, responses)	LOV (1)
Specify	
Communication is misunderstood (i.e. tasks to be done are different than asked)	LOV (1)
Specify	
Unacknowledged communication (i.e. request is not completed when asked)	LOV (1)
Specify	
External distraction (i.e. unable to hear due to others talking)	LOV (1)
Specify	
Accommodation for noise (i.e. surgeon needs to leave console to communicate to team)	LOV (1)
Specify	
Coordination	
Equipment needs adjustment or repositioning (i.e. after initial set-up to improve operation)	LOV (1)
Specify	
Coordination around robot (i.e. reposition other equipment to accommodate robot)	LOV (1)
Specify	
Equipment needs to be moved to access patient (i.e. conversion)	LOV (1)
Specify	
Accommodation for patient (i.e. reposition patient to accommodate robot)	LOV (1)
Specify	
Troubleshooting (i.e. stop procedure to address something)	LOV (1)
Specify	
Equipment	
Visual problems (i.e. camera blurry/foggy/distorted)	LOV (1)
Specify	
Awareness of robot arm (i.e. hit each other, hit bedside assist)	LOV (1)
Specify	
Robot is inoperative (i.e. error message noted, unresponsive)	LOV (1)
Specify	
Equipment or instrument inoperative (i.e. pedal not working, grip not working)	LOV (1)
Specify	

Inadequate equipment or instruments (I.e. grasper not closing completely, scissors are dull)	LOV (1)
Specify	
Human slip (I.e. surgical team accidently unplugs console)	LOV (1)
Specify	

Training

Instrument verbal instruction (I.e. explain how to best use an instrument, position a patient)	LOV (1)
Specify	
General verbal instruction (I.e. describing how to approach something)	LOV (1)
Specify	
Equipment placement (I.e. explains how to place the cannula, position the arm cart assembly)	LOV (1)
Specify	
Position of anatomy (I.e. instructs how to position anatomy)	LOV (1)
Specify	
Operating room arrangement (I.e. instructs how to position console, tower, and arm cart)	LOV (1)
Specify	
Halt action (I.e. stops procedure to prevent harm to the patient)	LOV (1)
Specify	

Ergonomic Assessment

Do you have chronic neck or back pain	o NO o YES
If yes, do you feel the pain is exacerbated due to performing RAS	o NO o YES
Do you experience neck/back pain after performing RAS	o NO o YES
Do you experience arm/hand/foot pain after performing RAS	o NO o YES
Is your operative approach when performing RAS influenced by musculoskeletal pain considerations	o NO o YES
When wearing the surgeon glasses, do you experience eye fatigue	o NO o YES
Do the surgeon glasses induce dizziness or nausea	o NO o YES

LOV (1)
I HAVE NO PROBLEMS
I HAVE MODERATE PROBLEMS
I HAVE CONSTANT PROBLEMS

LOV (2)	User Data String
C05	COMBINED
F05	FEMORAL
L05	LATERAL (INDIRECT)
M05	MEDIAL (DIRECT)
M10	M1: SUBXIPHOIDAL
M15	M2: EPIGASTRIC
M20	M3: UMBILICAL
M25	M4: INFRAUMBILICAL
M30	M5: SUPRAPUBIC
L10	L1: SUBCOSTAL
L15	L2: FLANK
L20	L3: ILIAC
O05	OTHER

LOV (100)	User Data String
N	NO
Y	YES

18.10 ACHQC Questionnaire

Abdominal Core Health Quality Collaborative	
What would your doctor need to know regarding your experience of your hernia (or hernia surgery) to take good care of you?	
Please respond to each item by marking one box per row	
How intense was your pain at its worst?	✓ Had no pain ✓ Mild ✓ Moderate ✓ Severe ✓ Very Severe
How intense was your average pain?	✓ Had no pain ✓ Mild ✓ Moderate ✓ Severe ✓ Very Severe
What is your level of pain right now?	✓ Had no pain ✓ Mild ✓ Moderate ✓ Severe ✓ Very Severe
For the following statements, please circle the number that is most appropriate for you	
1. My abdominal wall has a huge impact on my health	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree

2. My abdominal wall causes me physical pain	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree
3. My abdominal wall interferes when I perform strenuous activities (e.g. heavy lifting)	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree
4. My abdominal wall interferes when I perform moderate activities (e.g. bowling, bending over)	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree
5. My abdominal wall interferes when I walk or climb stairs	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree

6. My abdominal wall interferes when I dress myself, take showers and cook	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree
7. My abdominal wall interferes with my sexual activity	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree
8. I often stay home because of my abdominal wall	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree
9. I accomplish less at home because of my abdominal wall	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree

10. I accomplish less at work because of my abdominal wall	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree
11. My abdominal wall affects how I feel everyday	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree
12. I often feel blue because of my abdominal wall	1. Strongly Disagree 2. Moderately disagree 3. Slightly disagree 4. Slightly agree 5. Moderately agree 6. Strongly agree

19 Version History

Version	Summary of changes	Author(s)/Title
1.0	• Not Applicable, New Document	[redacted]
2.0	• Added 3-Month, 1-Year and 2-Year Follow-up visits throughout the protocol. Added secondary endpoints for long term follow-up timepoints. • Added clarification for mesh selection.	[redacted]
3.0	• Redefined Primary Safety Endpoint • Redefined Secondary Endpoints • Updated Ancillary Endpoints • Increased sample size from 120 to 192 and number of sites from 6 to up to 10 • Added definitions for Readmission, Recurrence, Reoperation, SSE, SSI, and SSO • Updated Inclusion Criteria to specify type of hernia repair • Updated Exclusion Criteria to restrict hernia defect location • Removed AE relatedness assessment for underlying condition or disease • Added Figure 2 for clarity on classification of hernias • Increased window of visit schedule for all study visits • Updated Statical Design and Performance Goals • Added Clinical Study Design Justification Section 6.2.2 • Added clarity on mesh usage and assessing hernia recurrence • Added Section 17.8 – Statement of Generalizability to Medicare Beneficiaries • Checked for applicability of CIP Template Version F • Terms aligned within document	[redacted]
4.0	• Added Appendix 18.11 for the Touch Surgery™ Ecosystem (TSE Sub-Study)	[redacted]
5.0	• Added “IRB” and “OR” to glossary list • Added the word “clinical” as clarification and consistency when referring to hernia recurrence in section 5.2.2, Secondary Endpoints • Removed duplicative wording in section 10.1.6, Post-Operative Follow-Up Visit • Added clarification on the target number of days for each follow-up assessment for Table 7 in section 10.2, Data Collection	[redacted]

	• Added “safety” as reference to endpoint for clarification in section 10.7, Assessment of Safety
	• Updated Lost to Follow Up Section 10.10.3 to allow for patient lost to follow-up designation for 1-year visit and onward.
	• Updated Sections 12.1 (Adverse Events) and 13.1 (Clinical Events Committee Review) to specify CEC adjudication of SAEs, deaths and SSEs through primary endpoint analysis (30 days post-procedure) instead of through study participation.
	• Updated section 12.5.2 for adverse event and device deficiency reporting timeframes and updated section 12.6 (Subject Death) to cross reference
	• Updated Section 14 to follow clarifications made in the pre-specified Statistical Analysis Plan (SAP). The SAP was completed prior to any analyses of the study objectives.
	  ○ Clopper Pearson method vs exact binomial test.
	  ○ Use of 30 calendar days for assessments “through 30 days”.
	  ○ Corrections of previously incorrect information (alignment with Medtronic Standard Operating Procedures, use of 0.05 two-side alpha was never used in the study, etc.).
	• Corrected section number for clinicaltrials.gov reference in section 15.1
	• Removed Optional Touch Surgery Ecosystem (TSE Sub Study) section 18.11. This sub-study was not incorporated at the investigational centers and removed in this version of the CIP.	