EXPAND URO

A prospective, multi-center, single-arm study of the Medtronic Hugo™ Robotic Assisted Surgery (RAS) System in Urologic Surgery

Clinical Investigation Plan v9.0
21/AUG/2024

NCT05696444

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 Urologic Surgery (Expand URO)
Clinical Investigation Plan Identifier	MDT19051EINURO
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	9.0
Version Date	21-Aug-2024

Confidentiality Statement

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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
Clinical Investigation Plan Identifier	MDT19051EINURO
Version Number/Date	9.0, 21-Aug-2024
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
ADE	Adverse Device Effect
ADL	Activities of Daily Living
AE	Adverse Event
ASA	American Society of Anesthesiologists
CA	Competent Authority
CEC	Clinical Event Committee
CFR	Code of Federal Regulation
CIP	Clinical Investigation Plan
Clavien-Dindo Classification of Surgical Complications[1]	Grade I: Any deviation from the normal postoperative 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

Term	Definition
	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: If the patient suffers from a complication at the time of discharge (see examples in Appendix 18.1), 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. NOTE 2: *Brain hemorrhage, ischemic stroke, subarrachnoidal 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 system to laparoscopic, open surgery, or utilizing an FDA cleared robotic-assisted system
CRF	Case Report Form
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DD	Device Deficiency

Term	Definition
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
IRB	Institutional Review Board
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
MedDRA	Medical Dictionary for Regulatory Activities
OR	Operating Room
NSR	Non-Significant Risk
PHI	Protected Health Information
RAS System	Robotic Assisted Surgery System
RA	Regulatory Authority
SADE	Serious Adverse Device Effect

Term	Definition
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SC	Steering Committee
SCD	Sudden Cardiac Death
SID	Subject Identification
SR	Surgical Robotics
SOC	Standard of Care
USA	United States of America
UAE	Unavoidable Adverse Event
UADE	Unanticipated Adverse Device Effect

3. Synopsis

Title	A prospective, multi-center, single-arm study of the Medtronic Hugo™ Robotic Assisted Surgery (RAS) System in Urologic Surgery (Expand URO)
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	Urologic Robotic Assisted Surgery
Investigation Purpose	This study will evaluate the safety and performance of the Medtronic Hugo™ RAS System when used for urologic RAS procedures

Product Status	Pre-Market
Primary Objectives	The primary objectives of this study are to confirm that the Medtronic Hugo™ RAS System is safe and effective when used for urologic robotic assisted surgery.
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 a robotic-assisted approach using the Hugo system to a robotic-assisted approach utilizing an FDA cleared robotic-assisted device, laparoscopic or open surgery. The primary safety endpoint is the rate of subjects with complications meeting Grade III criteria or higher per the Clavien-Dindo Classification system,[1] from the first incision through 30 days post-procedure.
Secondary Objective	The secondary objective of this study is to demonstrate that the Medtronic Hugo™ RAS System performs as intended when used in urologic robotic assisted surgery. The secondary endpoints of this study will assess the overall performance of the Medtronic Hugo™ RAS System when used for urologic robotic 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 urologic RAS: • Complication rate: Overall rate of subjects with one or more complication(s) (Clavien-Dindo Grade I or higher), from the first incision through 30 days post-procedure • Operative time • Intraoperative estimated blood loss (mL) • Transfusion rate • Rate of device-related conversion • Hospital length of stay • Readmission rate (through 30 days) • Reoperation rate (through 30 days)

	• Mortality rate (through 30 days) • Rate of device deficiencies The following long-term secondary endpoints will be assessed through 5 years in oncologic subjects: • Overall survival • Progression-free survival • Disease-free survival
Other Prespecified Outcomes Measures	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. • Rate of positive surgical margins • Lymph node yield • Warm ischemia time • Surgeon experience
Study Design	A prospective, multicenter, single-arm pivotal study will be performed in up to 141 subjects undergoing a urologic RAS procedure using the Medtronic Hugo™ RAS System. Subjects without an oncologic indication will be followed for 30 days (+7 days) post-procedure. Oncologic subjects will be followed through 5 years. This study will be conducted using up to six investigative sites in the United States of America (USA).
Sample Size **(Roll-in + Open Enrollment)**	A total of up to 141 subjects (up to 31 for Cystectomy; up to 55 for Nephrectomy; and up to 55 for Prostatectomy) undergoing a urologic robotic assisted procedure will be treated for this study at up to six different sites (including 15 roll-in subjects).
Inclusion/Exclusion Criteria	Inclusion Criteria: 1. Adult subjects (age ≥ 22 years) as required by local law 2. Subject has been indicated for a radical prostatectomy, radical cystectomy, or nephrectomy (partial or radical) surgical procedure

	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 comorbidities or medical characteristics, which would preclude the surgical procedure in the opinion of the Investigator 3. 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 4. Non-oncology subjects with an estimated life expectancy of less than 6 months; oncology subjects considered for cystectomy with a life expectancy less than 24 months; oncology subjects considered for nephrectomy with a life expectancy less than 60 months; oncology subjects considered for prostatectomy with less than a 10-year life expectancy. 5. Female subjects pregnant at the time of the surgical procedure. 6. Subjects who are considered to be part of a vulnerable population (e.g., prisoners or those without sufficient mental capacity) 7. Subjects who have participated in an investigational drug or device research study within thirty (30) days of enrollment that would interfere with this study 8. Subjects with active infections including but not limited to pneumonia, urinary tract, cellulitis, or bacteremia

Study Procedures and Assessments	Screening, Surgical Procedure, Hospital Discharge, and Post-Discharge Follow-Up (see full protocol for data collection/assessment windows): **Screening:** To determine study eligibility and collect baseline information (demographics, medications, medical history, surgical history, kidney function). **Surgical Procedure:** To re-confirm eligibility criteria, procedure set-up and take-down, medications associated with adverse events, interoperative complication evaluation, disease state evaluation, procedure success, conversion rates, protocol deviation, device deficiency and adverse event evaluation. **Up to Hospital Discharge:** Adverse event evaluation, subject complication rate, disease state evaluation, protocol deviation and medications associated with adverse events. **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), protocol deviation, medications associated with adverse events and study exit.
Safety Assessments	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 event type, incidence, severity, duration, and procedure/device relatedness will be reported. AEs for all FAS subjects will be analyzed from first incision through the study exit. AEs will be assessed by the Investigator and the sponsor as well as an external independent CEC for events requiring adjudication. 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.
Statistics	**Primary Analysis Set**

	The full analysis set (FAS) includes all enrolled subjects in whom the Hugo™ RAS procedure is begun, defined as the first skin incision. The FAS will be the primary analysis set for the evaluation of the primary and secondary endpoints. **Sample Size** A total of up to 141 subjects are planned to be treated in the study. The sample size will provide more than 80% power to evaluate the primary effectiveness endpoint at one-sided alpha of 0.025. A performance goal of 85% is pre-defined to test the statistical hypothesis. Additionally, separate performance goals are pre-defined to assess the primary safety endpoint (rate of subjects with one or more major complications) for the three surgery types, and technical details are provided in **Section 14.** **Primary Hypothesis** The primary effectiveness hypothesis is to test if the surgical success rate is above the performance goal. The primary safety hypothesis is to test if the 30-day major complication rate is below the performance goal for each of the three surgery types. The major complication rate is defined as the rate of subjects with one or more adverse event meeting Grade ≥ III per the Clavien-Dindo Classification system. **Other Information** All secondary endpoints and other prespecified outcome measures will be evaluated using descriptive statistics. Statistical analyses will be performed using SAS version 9.4 or higher.

4. Introduction

4.1 Background

4.4.1 Robotic Surgery

Over the course of history, surgery has generally evolved towards less invasive methods for performing the same procedures. As surgical diseases are better understood, and adjunct tools such as imaging techniques continue to improve, the operative management of these diseases has also become safer, more effective, and more elegant. Better outcomes are driven by refinement of surgical procedures, such as shorter recovery and less pain while reducing costs in efforts to increase access to robotic procedures around the world.

The first major paradigm shift in the realm of surgical technique came with the introduction of laparoscopic surgery. Around the beginning of the 20th century, surgeons in the United States and Europe began using rudimentary tools to inspect abdominal cavities of subjects, typically during gynecologic procedures, for diagnostic purposes only. The popularity of laparoscopy increased substantially with the introduction of the rod-lens optical system and cold light fiber-glass illumination. In the late 1980s French and German surgeons performed the first known laparoscopic cholecystectomies, which started a boom in the development of laparoscopic surgery.[2] Many procedures that were once executed in open fashion are now performed entirely laparoscopically as the standard of care.

Presently, surgical technique is undergoing another revolution – the growth of robotic assisted surgery (RAS). Much as the laparoscope changed how surgery was practiced in the 20th century, RAS will similarly propel forward surgical specialties in the 21st century. 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, robotic systems allow for a three-dimensional stabilized view, articulated instruments, and superior ergonomics and dexterity.[3]

4.4.2 Robotic Procedures in Urology

Robotic surgery was initially applied to urology in the early 2000s. RAS has now almost entirely replaced laparoscopy in the United States.[4] RAS adoption for radical prostatectomy increased from 0.7% in 2003 to 42% in 2010. Published research on robotic surgery has also surged in the last two decades, particularly in the field of urology.[5]

Systematic reviews and meta-analyses comparing RAS to open and laparoscopic approaches for urological procedures have demonstrated similar oncologic outcomes with lower complication rates for minimally invasive approaches.[6]

The benefits of RAS compared to open or traditional laparoscopic surgery have been demonstrated in meta-analyses for all of the highest-volume[4] urology oncologic surgeries: radical prostatectomy,[7-11] radical cystectomy,[12-24] and nephrectomy.[25-32]

Currently, most of this research describes the da Vinci™ robotic surgical platform (Intuitive Surgical, Sunnyvale, CA). Development of that system started in the early 1990s and it was approved for the management of urological procedures in the United States in 2000.[33] More recently, Asensus Surgical US, Inc. (formerly known as TransEnterix Inc, Morrisville, NC) has entered the market with the Senhance™ robotic assisted platform.[34-38]

The Medtronic Hugo™ RAS System is a modular robotic platform for performing robotically assisted minimally invasive surgery. This study will evaluate the safety and effectiveness of the Medtronic Hugo™ RAS System when used for urologic RAS.

4.1.3 Medtronic Hugo™ RAS System

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 clinical, animal, and laboratory testing can be found within the Medtronic Hugo™ RAS System Report of Prior Investigations (Appendix 18.2).

4.2 Purpose

This study will evaluate the safety and performance of the Medtronic Hugo™ RAS System when used for urologic RAS procedures.

5. Objectives and/or Endpoints

5.1 Objectives

5.1.1 Primary Objectives

The primary objectives of this study are to confirm that the Medtronic Hugo™ RAS System is safe and effective when used for urologic robotic assisted surgery.

5.1.2 Secondary Objective

The secondary objective of this study is to demonstrate that the Medtronic Hugo™ RAS System performs as intended when used in urologic robotic assisted surgery. The secondary endpoints of this study will assess the overall performance of the Medtronic Hugo™ RAS System when used for urologic robotic surgery.

5.1.3 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 a robotic-assisted approach using the Hugo system to a robotic-assisted approach utilizing an FDA cleared robotic-assisted device, laparoscopic or open surgery.

The primary safety endpoint is the rate of subjects with complications meeting Grade III criteria or higher per the Clavien-Dindo Classification system[1] from the first incision through 30 days post-procedure.

5.1.4 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 urologic RAS:

- Complication rate: Overall rate of subjects with one or more complications (Clavien-Dindo Grade I or higher), from the first incision through 30 days post-procedure
- Operative time
- Intraoperative estimated blood loss (mL)
- Transfusion rate
- Rate of device-related conversion
- Hospital length of stay
- Readmission rate (through 30 days)
- Reoperation rate (through 30 days)
- Mortality rate (through 30 days)
- Rate of device deficiencies

The following long-term secondary endpoints will be assessed through 5 years in oncologic subjects:

- Overall survival
- Progression-free survival
- Disease-free survival

Performance Goals for Secondary Endpoints

The details are summarized in the table found in **Section 14.5.**

5.1.5 Other Prespecified Outcomes Measures

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 will be collected as applicable:

- Rate of positive surgical margins
- Lymph node yield
- Warm ischemia time
- Surgeon experience

6. Study Design

A prospective, multicenter, single-arm pivotal study will be performed in up to 141 subjects undergoing a urologic RAS procedure using the Medtronic Hugo™ RAS System. Subjects without an oncologic indication will be followed for 30 days (+7 days) post procedure. Oncologic subjects will be followed through 5 years. This study will be conducted using up to six investigative sites in the United States of America (USA).

This study will have two phases, a roll-in phase and an open enrollment phase.

6.1 Roll-in Phase

Two (2) sites will consecutively enroll a total of 15 subjects who will be treated with the Hugo™ RAS System as “roll-in cases”. These subjects will undergo the same preoperative and postoperative assessments (with the same schedule) as subjects who are enrolled in the open enrollment phase. Outcomes through 30 days for the first 15 roll-in cases will be provided in a summarized fashion and provided to the FDA for initial review without statistical inferences. The roll-in subjects will be included in the primary analysis with the open enrollment subjects and for all required reports.

6.2 Open Enrollment Phase

Following completion of the roll-in phase and sponsor approval, all sites will be allowed to enroll subjects in the study. During the open enrollment phase, all subjects enrolled will follow the Clinical Investigation Plan.

6.3 Duration

The expected study duration is approximately 5 years. The duration of individual subject participation will be approximately 67 days (30 to 30+7) for non-oncologic subjects and 5 years for oncological subjects.

6.4 Rationale

6.4.1 Justification for the Clinical Evaluation

Extensive pre-clinical testing has been performed to justify the use of the Hugo™ RAS System in humans.

Verification testing demonstrates the Hugo™ RAS System meets all product and system design requirements. Validation activities including cadaver procedural studies, pre-clinical (animal) studies, product validation labs testing, and usability studies show the Hugo™ RAS System can be used safely by the intended users in the intended use environment. In addition, an analysis of the risk-benefit profile (**Section 11.4**) demonstrates that the Hugo™ RAS System has a favorable benefit-risk profile based on criteria that consider the medical conditions of the target population, level of device performance and safety, risks to the patient, availability of alternatives, and level of clinical data available.

An evaluation of published clinical data relevant to the proposed investigation was also performed. The safety and performance of commercially available RAS systems have been evaluated in the literature review, as summarized in **Table 1**. Robotic-assisted surgery was comparable or superior to open or traditional laparoscopic surgery in all but two comparisons.

Table 1. Analyses of Commercially 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** [8,11,12,19,22,25-27]	**9/17 studies** [13,15-18,20,21,24,39]	**In Favor of RAS (2/8 studies):** [14,30] **In Favor of Lap (1/8 studies):** [8]	**5/8 studies** [11,13,23,29,32]
Length of Hospital Stay	**11/16 studies** [8,9,13,19,20,22,24-27,39]	**5/16 studies** [15-18,21]	**In Favor of RAS (3/8 studies):** [8,14,29]	**5/8 studies** [13,23,25,30,32]
Blood Loss	**14/15 studies** [8,12,13,15-19,22,25-27,31,39]	**1/15 studies** 9	**In Favor of RAS (1/8 studies):** [8] **In Favor of Lap (1/8 studies):** [14]	**6/8 studies** [13,23,25,29,30,32]
Conversion to Open Surgery	**N/A**	**N/A**	**In Favor of RAS (3/3 studies):** [25,29,30]	**0/3 studies**

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

6.4.2 Clinical Study Design Justifications

The Hugo™ RAS System will be evaluated through a prospective, multi-center, single-arm, non-

randomized study in a total of up to 141 subjects indicated for radical prostatectomy, radical cystectomy, or nephrectomy (partial or radical) surgical procedures.

For version 8.0 of this protocol, an updated systematic literature search was conducted between June 1, 2018 – 4 Jun 13, 2023 to identify published clinical data on the use of RAS for urologic surgery (nephrectomy, prostatectomy, and cystectomy). The databases searched were Medline, Embase and Journals@Ovid Full Text. The population was adult (non-pediatric) subjects. Version 9.0 was updated based on the qualitative review of the literature.

A total of 130 articles were used to establish the study design (safety and effectiveness endpoints, performance goals, sample size, and follow-up timeframes). The full bibliography of all 130 publications supporting the updated primary and secondary endpoint performance goals is included in **Section 17.1**.

The safety endpoint (30-day major complication rate) and effectiveness endpoint (surgical success rate) are described below:

Safety:

Critical appraisal of the information collected in the literature review established a 30-day major complication rate (Clavien-Dindo Grade III or higher) in order to assess the safety of the Hugo™ RAS System.

Major Complication Primary Endpoint: The rate of subjects with major complications (usually defined as Clavien-Dindo Grade ≥ III) is a more commonly reported and clinically relevant measure than overall complications. The Expand URO study is designed to evaluate the three most complex and highest volume urology procedures.[4] However, the procedural complexity, patient profile, and overall complication rates vary across the three procedure types. In the literature review, the overall complication rates varied from 0.2% (Hennessey 2018) to 53.3% (Abdul-Muhsin 2020) for radical nephrectomy and 0.5% (Covas Moschovas 2022) to 50% (Gaboardi 2019) for radical prostatectomy versus 1.4% (Tamhankar 2020) to 76% (Jeglinschi 2020) for radical cystectomy. Cystectomy procedures carry a particularly high risk of anticipated low-grade complications due to patient age and comorbidity. Therefore, the rate of overall complications may not be a clinically meaningful evaluation of device safety for radical cystectomy. Major complication rates range from 0.7% (Boga Long-term 2021) to 13.3% (Abdul- Muhsin 2020) for nephrectomy, 0.4% (Bahouth 2022) to 11.7% (Wilson 2020), versus 0.3% (Piazza 2022) to 19.7% (Arora 2020) for radical cystectomy in the literature review.

The primary endpoint for the Expand URO study is the 30-day rate of subjects with major complications (Clavien-Dindo Grade ≥III). The overall rate of subjects with any complications (Clavien-Dindo Grade ≥I) will be captured and reported as a secondary endpoint.

Other commonly reported safety measures (e.g., blood loss, transfusions, conversions, length of stay, reoperation, and readmission rates) will be also captured and reported to provide a comprehensive assessment of device safety.

- **Sample Size and Enrollment Proportions:** The sample size and performance goal estimates were derived from the literature search. The statistical design is therefore based on review of published data. A performance goal is specified for each of the three procedures. Additional details are provided in **Section 14.**
- **Follow-up Timeframe:** Based on the preponderance of data in the literature search, a 30-day primary endpoint was chosen for safety reporting. Oncologic subjects will be followed for 5 years.

Effectiveness:

Critical appraisal of the information collected in the literature review established the surgical success rate in order to assess the effectiveness of the Hugo™ RAS System.

- **Surgical Success Primary Endpoint:** The primary effectiveness endpoint is the surgical success rate, defined as the procedure not going into conversion. Conversion is defined as the switch from a robotic-assisted approach using the Hugo system to a robotic-assisted approach utilizing an FDA cleared robotic-assisted device, laparoscopic or open surgery.
- **Sample size and enrollment proportions:** The effectiveness endpoint sample size of up to 141, is based on the rationale of an acceptable surgical success rate of 90% or higher, a power of 80% or higher, and a performance goal of 85%.

The hypothesis will be tested using the Clopper-Pearson exact method at one-sided alpha of 0.025.

- **Follow-up timeframe:** Surgical success will be assessed at the index procedure.

Additional specific design justifications were also considered while developing this clinical investigation of the intended use.

- **Subject Selection:** Excluding subjects with high-risk comorbidities affecting their surgical eligibility will minimize the risk to subjects. Restricting enrollment to subjects with a life expectancy of 6 months or more is intended to provide a greater follow-up rate on the primary endpoint.
- **Study Procedures:** The study procedures chosen (partial or radical nephrectomy, radical prostatectomy, and radical cystectomy) are representative, in terms of technical difficulty, of

most surgical procedures in urology. They are also the highest-volume urology oncologic surgeries.[4] Since the safety profiles or major complication rates are very different among the three surgeries, a separate performance goal is pre-specified for each of the three surgery types (as per FDA recommendation). The performance goals are determined based on published data from the literature search.

- **Number of Study Sites:** Up to 6 study sites with up to 15 surgeons are planned in order to ensure generalizability of the data and account for the expected low volume of subjects undergoing radical cystectomy. The sponsor reserves the right to halt enrollment at any individual site for any individual procedure type to ensure a balanced enrollment and avoid the introduction of bias.

6.5 Study Oversight

The study will utilize a Steering Committee. The Steering Committee will advise on the scientific content of the study and provide 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 is comprised of the individuals in **Table 2**. As membership may change, the current list of members can be made available upon request.

Table 2. Steering Committee Members

Committee Member	Contact information
James Porter, MD Steering Committee Chair	Director, Robotic Surgery Swedish Medical Center-Swedish Urology Group 1101 Madison, Suite 1400 Seattle, WA 98104 United States of America [redacted] [redacted]

Committee Member	Contact information
Peter Wiklund, MD, PhD	Medical Director Mount Sinai 625 Madison Ave, 2nd Floor New York, NY 10022 United States of America [redacted]
Alvin Goh, MD	Medical Director Memorial Sloan Kettering 1275 York Ave New York, NY 10065 United States of America [redacted]
Michael Abern, MD	Medical Director Associate Professor of Urologic Oncology Urologic Oncology Fellowship Director Duke University Department of Surgery and Duke Cancer Institute 20 Trent Drive, Durham, NC 27710 United States of America [redacted]

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 operating room (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.

There are no anticipated changes to the Medtronic Hugo™ RAS System during the course of the investigation.

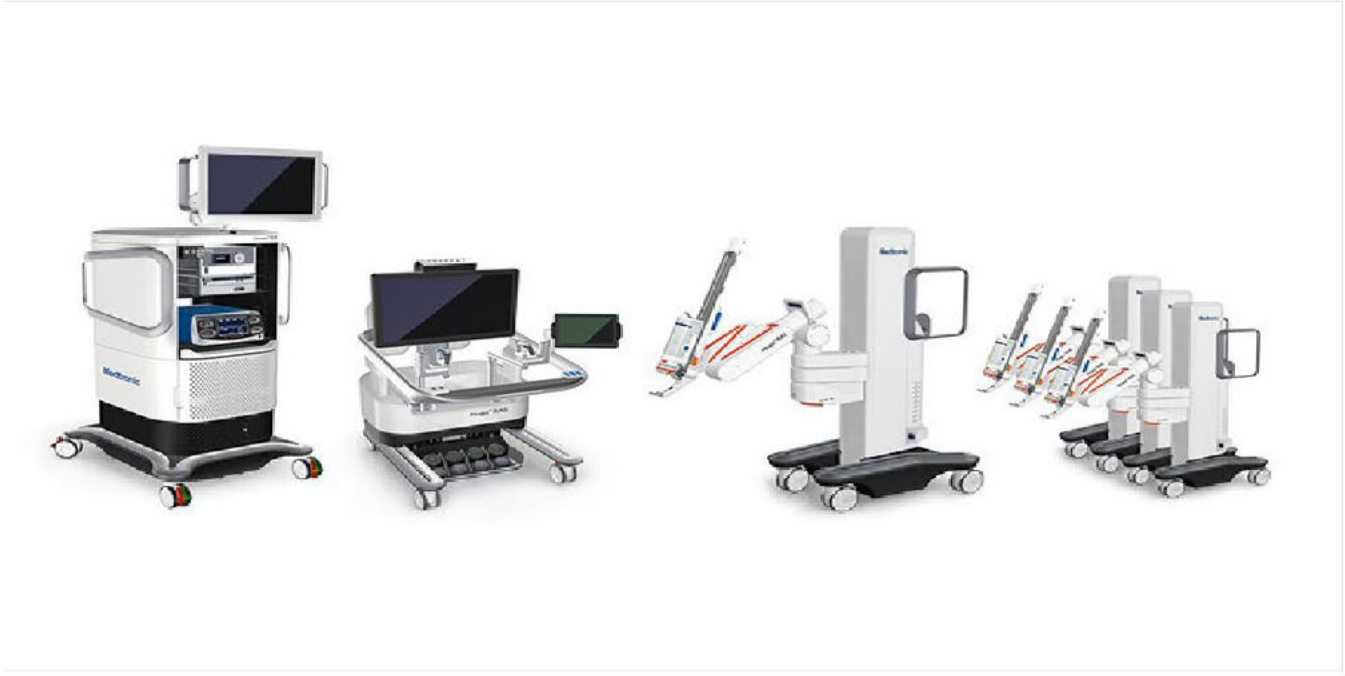

Figure 1: Medtronic RAS Overview -- Left to Right: System Tower, Surgeon Console, Arm Carts (4)

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

7.1.1 Hugo™ RAS 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.

7.1.2 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.

7.1.3 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.

7.1.4 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 in order 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 User Guide for the Hugo™ RAS System.

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. 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

Please see **Table 3** and **Table 4**.

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 a urological robotic assisted surgery with Hugo™ RAS.

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 3**).

Table 3. Investigational Device

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

SKU	Description (Branding Company)	Investigational or Commercially Available
MRASI0011	Cadiere Forceps (Covidien)	Investigational
MRASI0012	Double Fenestrated Grasper (Covidien)	Investigational
MRASI0016	Toothed Grasper (Covidien)	Investigational

NOTE: All Hugo™ RAS SKUs 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 4. Medtronic Hugo™ RAS System-Compatible Components

SKU	Product Description (Manufacturer)	Investigational or Commercially Available
TC200US	Storz 3D Camera Control / System (Karl Storz)	Commercially Available
TC302US	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

SKU	Product Description (Manufacturer)	Investigational or Commercially Available
E0020V	Reusable Bipolar Electrosurgery Cord (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
ONB5STF	5MM Auxiliary Port, Versaone OPT 5 MM STD Trocar	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
ONB12STF	12MM Auxiliary Port, Versaone OPT 12 MM STD Trocar	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

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 IFU (**Appendix 18.3**). The IFU accompanying the device should always be consulted.

The device will be in contact with the urologic region including tissues and body fluids. All device components and materials are biocompatible. Device biocompatibility testing and results are summarized in the Report of Prior Investigations (**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

See **Table 5**. 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. 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 5. 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.

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 in order 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 urologic condition must be qualified practitioners and experienced in the diagnosis and treatment of subjects with study specific urologic conditions. 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 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, 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 clinical investigation plan (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

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
- Monitoring and auditing activities

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 procedure
- Support data collection during the 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

A minimum of 141 subjects will be enrolled at up to 6 sites in the USA.

The Medtronic Hugo™ RAS System is intended to be used in this study for urologic surgical procedures including radical prostatectomy, radical cystectomy, nephrectomy (partial or radical) 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, prostate cancer, pelvic tumors, interstitial cystitis, congenital abnormalities, end-stage kidney disease (kidney failure), renal tumor, kidney injury.

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 consent process is signed and dated. Screening data will not be collected for the study until the subject has been determined to be eligible for the study and signed consent (see **Section 10.2** for details). If the subject is consented prior to the day of surgery, a re-verification of eligibility will be signed off by the PI or Sub-I on the day of surgery. As soon as the surgical procedure has begun with the Medtronic Hugo™ RAS System, the subject must be followed

regardless of whether or not 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 9.3** for additional details.

9.3 Inclusion Criteria

1. Adult subjects (age ≥ 22 years) as required by local law
2. Subject has been indicated for a radical prostatectomy, radical cystectomy, or nephrectomy (partial or radical) surgical procedure
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 signed informed consent form

9.4 Exclusion Criteria

1. Subjects for which minimally invasive surgery is contraindicated as determined by the Investigator
2. Subjects with comorbidities or medical characteristics, which would preclude the surgical procedure in the opinion of the Investigator
3. The patient has been diagnosed with a bleeding disorder and/or cannot be removed from their anticoagulants prior to surgery based on surgeon discretion and standard-of-care
4. Non-oncology subjects with an estimated life expectancy of less than 6 months; oncology subjects considered for cystectomy with a life expectancy less than 24 months; oncology subjects considered for nephrectomy with a life expectancy less than 60 months; oncology subjects considered for prostatectomy with less than a 10-year life expectancy.
5. Female subjects pregnant at the time of the surgical procedure
6. Subjects who are considered to be part of a vulnerable population (e.g., prisoners or those without sufficient mental capacity)
7. Subjects who have participated in an investigational drug or device research study within thirty (30) days of enrollment that would interfere with this study
8. Subjects with active infections including but not limited to pneumonia, urinary tract, cellulitis, or bacteremia

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. If the subject is consented prior to the day of surgery, a re-verification of eligibility will be signed off by the PI or Sub-I on the day of surgery. 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).

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 practices. 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 of procedures, practices, and set-up guidelines. See **Table 6** 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 6** 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 (i.e., COVID-related in person restrictions at the site, difficulties of the subject travelling to the site), 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 Visits (Visit 4-8)

Post-operative visits 4-8 for oncologic subjects will be made via a phone call to assess overall survival, progression-free survival, and disease-free survival.

Table 6. 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 (Years 1 - 5) (+/- 3 mo. window) Visits 4-8
	May be Combined				
Informed Consent Form[1]	X	X			
Eligibility Criteria	X	X			
Demographic Data	X				
Medical/Surgical History	X				
Concomitant Medication(s)	X	X	X	X	
Lab Values (if applicable)	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	
Conversion to a robotic-assisted approach utilizing an FDA cleared robotic-assisted device, open or manual laparoscopy		X			
Robot Take Down Time		X			
Warm Ischemia Time (if applicable)		X			
Anastomotic Leak Test performed (if applicable)		X			
Anastomotic Stricture (if applicable)		X			
Rate of Positive Circumferential Margins on Final Pathology (if applicable)		X			
Margin (mm) (if applicable)			X		

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 (Years 1 - 5) (+/- 3 mo. window) Visits 4-8
Tumor Size (if applicable)			X		
Tumor Stage (if applicable)			X		
Total number of lymph nodes retrieved			X		
Catheterization Time			X	X	
Mortality			X	X	X
Length of Hospital Stay			X		
Reoperation			X	X	X
Pain Medication			X	X	
Medications if associated with an AE	X	X	X	X	X
Adverse Events [2]	X	X	X	X	X
Readmission				X	X
Device Accountability		X			
Device Deficiency		X			
Protocol Deviation Collection (if applicable)	X	X	X	X	X
Study Exit				X	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/SAEs 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.

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

10.2 Subject Screening

Consented subjects will be considered for the study if they meet specified inclusion criteria and none of the exclusion criteria. If the subject is consented prior to the day of surgery, a re-verification of eligibility will be signed off by the PI or sub-I on the day of surgery. The criteria for enrollment must be followed explicitly.

10.3 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 below
- 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 adverse event (AE)
- Medications given during the procedure and/or post-procedure as treatment or preventative that result in reportable AE should be captured
- Please reference # 3 of the I/E for clarification

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

10.3.1 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

10.3.2 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 as a result 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).

10.4 Subject Consent

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

The Investigator must notify the subject 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 informed consent, 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.

Prior to initiation of any study-specific procedures, IC must be obtained from the subject. The informed consent form must be personally signed and dated by the subject themselves and Investigator or the Investigators designee at the time of consent. 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 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.

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 must be signed and personally dated by the subject and Investigator or authorized designee, as required by the IC, and ensured by the Principal Investigator or his/her authorized designee.

A copy of the IC signed and dated as required by law, must be provided to the subject.

If the IC 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.

10.5 Assessment of Performance

The secondary endpoints of this study (operative time, device-related conversions, device deficiencies) will assess the overall performance of the Medtronic Hugo™ RAS System when used for urologic robotic surgery. Secondary endpoints will evaluate the safety and performance of the study device and will not evaluate specific label claims.

10.6 Assessment of Safety

Safety will be evaluated through the study primary endpoint (major complications) and several secondary endpoints (**Section 5.1.4**).

Safety will also be assessed by monitoring the occurrence of adverse events (AEs), serious adverse events (SAEs), deaths, adverse device effects (ADE), serious adverse device effects (SADE), unanticipated adverse device effects (UADE) or device deficiencies. Adverse event assessments will take place starting with the point of consent, through the end of study exit through 5-year follow-up, or until resolution whichever comes first and will be recorded in the eCRF.

AEs will be collected from the time of consent. AEs occurring in subjects excluded from the full analysis set (FAS) (**Section 14.1**) 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 analysis for either AE reporting or the analysis of the primary and secondary endpoints.

For the FAS, the type, incidence, severity, duration, and procedure/device relatedness of AEs will be reported. AEs for all FAS subjects will be analyzed from first incision through the study exit.

10.7 Recording Data

Data entered must be traceable to source documents. Source documentation is defined as the first-time data appear, and may include original documents, data, and records (e.g., hospital records, clinical and office charts, procedure reports, laboratory notes).

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 and (2) the date the copy was made.

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

10.8 Deviation Handling

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

Prior approval by Medtronic is expected in situations where the Investigator anticipates, contemplates, or makes a conscious decision to deviate. 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.

If during the procedure, the Investigator changes from HUGO™ to another RAS system (even if it is in conjunction with HUGO™), it will no longer be a protocol deviation, but it will be captured as a device deficiency as needed/applicable. If the Investigator converts to laparoscopic or open surgery, it will not be considered a protocol deviation.

Examples of study deviations include but are not limited to:

- Failure to obtain proper IC
- Failure to collect required study data
- Inclusion/exclusion criteria not met

10.9 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.

Every attempt will be made to contact subjects who are noncompliant. Subjects will be considered lost to follow-up once the following steps have been taken:

- Three phone calls should be made to the subject. Each attempt should be clearly documented in the source documents and the response or lack thereof should be captured.
- 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.
- After a period of two weeks following completion of the above actions, the subject will be considered lost to follow-up. The sponsor should be notified and the Study Exit form should be completed.

In cases of early study exits, all data collected from the time of informed consent to the time of 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 electronic case report form (eCRF).

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

10.9.1 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.

10.9.2 Study Completed

At the completion of the 30 (+7) day follow-up visit, non-oncologic subjects will be exited from the study. At the completion of the 5-year follow-up visit, oncologic subjects will be exited from the study. The 30 (+7) day or the 5-year follow-up visit and exit visit should be combined, and either the 30 (+7) or the 5-year follow-up eCRF and the Study Exit eCRF need to be completed.

10.9.3 Lost to Follow-up

A subject is considered to be lost to follow-up if the conditions in **section 10.9** are met. The method of attempt must be documented in the subject's medical record. In addition, regulation set forth by the governing IRB must be followed.

When subjects are lost to follow-up the Investigator will make efforts to confirm the vital status of the subject, as described in the informed consent.

10.9.4 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 eCRF. 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

10.9.5 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

10.9.6 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. Modified data collection is always preferred over exit.

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 regular 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 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)
- Electric Shock
- Foreign Body in Patient
- 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 urological 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 in the risk management process described above. 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 independent Clinical Events Committee 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 urologic surgery using the Hugo™ RAS System may include lower complication rates compared to traditional laparoscopic and open surgical procedures (**Section 6.4.1**).

As described in **Section 6.4.1**, 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 urologic 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 urologic surgery. In literature, typical age ranges for the three included procedures are 52 to 70 years for partial nephrectomy,[31] 57 to 67 years for radical prostatectomy,[7] and 59 to 79 years for radical cystectomy.[19]

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, preclinical, animal, and cadaver studies 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 6.4.1**) provides relevant subject 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 6.4.1**).

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 and instruments are considered significant risk.

12. Adverse Events and Device Deficiencies

12.1 Adverse Events

All Adverse Events (AEs) will be collected, starting from the time the informed consent form is signed through 30 days (+7) after the day of the procedure regardless of their severity or relationship to the Hugo™ RAS or study procedures. After 30 days, AEs will be assessed by the surgeon and those AEs deemed attributable to the underlying surgical indication, procedure or surgical device will be reported. All deaths will be collected via AE 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 system components. Each AE must be recorded on a separate AE eCRF.

AE definitions used in this study 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 14.1** 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 physician 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 9** 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 an all-encompassing anticipated adverse events.

All deaths, serious adverse events related to the Hugo™ RAS System and/or study procedures and Clavien-Dindo Grade III and IV complications will be adjudicated by an independent CEC.

12.2 Device Deficiency

The device deficiency (DD) definition is provided in **Table 7**. DD information will be collected throughout the study and reported to Medtronic on a DD eCRF. Note that DDs 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, 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 and an update to the original AE must be reported.

12.4 Definitions/Classifications

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

This study will collect the following:

- All adverse events from the time the informed consent is signed through the first 30 days (+7) after the day of the procedure regardless of their severity or relationship to the Hugo RAS or study procedures. After 30 days, AEs will be assessed by the surgeon and those AEs deemed attributable to the underlying surgical indication, procedure or surgical device will be reported. All unrelated deaths will be collected even after 30 days.
- All device deficiencies

Table 7. 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.

General	
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 errors 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	
System Related (Includes all components of the Hugo™ RAS System, associated introduction tools, operational and installed software and programmers as defined in the CIP)	An AE that results from the presence or performance of any component of the system. Device-related: An AE that results from the presence or performance (intended or otherwise) of the device. Refer to **Section 7.1.** Investigational Feature: An AE that results from the presence or performance (intended or otherwise) of the Hugo™ RAS System.
Procedure Relatedness	An AE that occurs due to any procedure related to the Hugo™ RAS System.
Underlying Condition or Disease Relatedness	Underlying condition refers to a chronic disease or condition that a subject has prior to any acute treatment/surgery (like diabetes, heart disease, obesity, cancer, etc.).
Relatedness Classification (Procedure, underlying condition, or device)	Not related: 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; In order 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. In order 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.
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) fetal distress, fetal 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 a 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.[1] **Grade I:** Any deviation from the normal postoperative 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: If the patient suffers from a complication at the time of discharge (see examples in Appendix 18.1), 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. NOTE 2: *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 9.**

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 in **Table 7**.

Upon receipt of an AE/DD 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. Adverse Event Classification Responsibilities listed in **Table 8**.

Table 8. Adverse Event Classification Responsibilities

What is classified?	Who classifies?	Classification Parameters
Relatedness	Investigator	Procedure, Underlying Condition[1], Device
	Sponsor	Procedure, Underlying Condition[1], Device
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
Death Classification[1]	Investigator	Sudden Cardiac, Non-sudden Cardiac, Non-Cardiac, Unknown
[1]This assessment is not applicable for non-subject Adverse Events		

12.5.2 Adverse Event and Device Deficiency Reporting Requirements

Regulatory reporting of AEs and DDs will be recorded and reported according to local regulatory requirements. Refer to **Table 10** for a list of required Investigator and Medtronic reporting requirements and timeframes. 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.

Table 9. 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
Mild to moderate bruising / ecchymosis	168
Sleep problems (insomnia)	72
Constipation	72

Table 10. Reporting Requirements

SAEs	
Investigator shall submit to:	
Medtronic	Report to the sponsor, without unjustified delay, 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.
Investigator	Submit to other investigators per local reporting requirement.
ADEs	
Investigator shall submit to:	
Medtronic	Submit in a timely manner after the investigator first learns of the effect.
RA	Submit to RA per local reporting requirement.
IRB	Submit to IRB per local reporting requirement.

Table 10. Reporting Requirements

Sponsor shall submit to:	
RA	US: Submit to RA per local reporting requirement.
IRB	US: Submit to IRB per local reporting requirement.
SADEs, UADEs	
Investigator shall submit to:	
Medtronic	All geographies: Immediately after the investigator learns of the event or of new information in relation to an already reported event.
RA	All geographies: Submit to RA per local reporting requirement
IRB	All geographies: Submit to IRB per local reporting requirement.
Sponsor shall submit to:	
RA	All geographies: Submit to RA per local reporting requirement.
IRB	All geographies: Submit to IRB per local reporting requirement.
Investigators	All geographies: Submit per local reporting requirement.
FDA	All geographies: Submitted in accordance to the 812.150 regulation.
All other reportable AEs	
Investigator shall submit to:	
Medtronic	All geographies: Submit in a timely manner (but no later than 30 calendar days) after investigator first learns of the event
RA	All geographies: Submit to RA per local reporting requirement.
IRB	All geographies: Submit to IRB per local reporting requirement.

Table 10. Reporting Requirements

All other Device Deficiencies	
Investigator shall submit to:	
Medtronic	All geographies: Submit in a timely manner after the investigator first learns of the deficiency.
RA	All geographies: Submit to RA per local reporting requirement.
IRB	All geographies: Submit to IRB per local reporting requirement.

12.6 Subject Death

All subject deaths must be reported by the Investigator to Medtronic on an AE form (AE with a fatal outcome) as soon as possible after the Investigator first learns of the death. In case of death, there should be only one AE with the outcome of the event that led to death regardless of whether the death is related to the device system or procedure.

In the event that 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
- Classification of death
- Relatedness to device and procedure
- Death 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)

12.6.1 Death Classification and Reporting

Sufficient information will be required in order to properly classify the subject's death. The Investigator shall classify each subject death per the following definitions:

- Cardiac Death: A death directly related to the electrical or mechanical dysfunction of the heart.
  - Sudden Cardiac Death: Natural death due to cardiac causes, indicated by abrupt loss of consciousness within one hour of the onset of acute symptoms; preexisting heart disease may have been known to be present, but the time and mode of death are unexpected. If time of onset cannot be determined, SCD will alternatively be defined as any unexpected cardiac death occurring out of the hospital or in the emergency room as dead on arrival.
  - Non-sudden Cardiac Death: All cardiac deaths that are not classified as sudden deaths, including all cardiac deaths of hospitalized subjects on inotropic support.
- Non-cardiac Death: A death not classified as a cardiac death.
- Unknown Cardiac Classification: Unknown death classification is intended for use only when there is insufficient or inadequate information to classify the death

The CEC will review all deaths and provide a final adjudication of the relatedness of death.

Regulatory reporting of Subject Deaths will be completed according to local regulatory requirements.

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.

Abuse: Abnormal use (definition acc. #4.1 of Meddev 2.12-1)

Misuse: Use error (definition acc. #4.20 of Meddev 2.12-1). It is the responsibility of the Investigator to report all product complaint(s) associated with a medical device distributed by Medtronic, regardless of whether they 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. Medtronic will notify the RAs (e.g., 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 AEs during the study. 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 attend 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. Ultimately, the CEC's adjudication will be captured in the eCRF used for data analysis.

13.2 CRO/Core Lab(s)

This information may be subject to change during the course of the study. Periodic updates to study contact information will be sent to study sites as needed.

Table 11. CRO and Core Laboratory Information

Contact Information	Role
[redacted]	Review of electronic case report forms and management of discrepancies
[redacted]	Independent clinical events adjudication committee

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. If necessary, real-world evidence (RWE) may be supplemented to the data collected in this prospective trial and included in the study analyses. More technical details will be provided in a separate statistical analysis plan (SAP) that will be finalized and approved prior to database lock. Any deviations to the pre- specified statistical analyses will be noted in the final clinical study report.

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, 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.

All tests of treatment effects will be conducted at a two-sided alpha level of 0.05 unless otherwise stated. A P-value less than 0.05 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 study safety and performance analyses will occur after all subjects complete the 30-day follow-up. The analyses will include both primary and secondary 30-day objectives. A clinical study report will be prepared once all data collection has ended and all subjects have completed the 30-day follow-up or have been exited. Annual progress reports will be prepared for oncologic subjects through 5 years. A final report will be completed at the end of the 5-year follow-up that will include the 5-year secondary analyses.

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 14.11.**

14.3 Interim Analysis

No interim analysis is planned for this study. Outcomes through 30 days for the first 15 roll-in cases will be summarized descriptively and provided to the FDA for initial review without statistical inferences. The roll-in subjects will be included in the final data analysis for the study.

14.4 Primary Objectives

A systematic literature search was conducted for Jan 1, 2018 – Jun 13, 2023 to identify published clinical data on the use of RAS devices in nephrectomy, prostatectomy, and cystectomy procedures. Literature data reporting on the study objectives were used to determine the appropriate sample sizes and performance goals for each endpoint and surgery cohort. The full bibliography of all 130 publications supporting the updated performance goals is included in **Section 17.1**.

14.4.1 Primary Objective #1 (Effectiveness)

The primary effectiveness objective of this study is to confirm that the Medtronic Hugo™ RAS System is effective when used for urologic robotic assisted surgery. The primary effectiveness endpoint is the surgical success rate, as defined in **Section 6.4.2**.

The primary effectiveness hypothesis is to test if the surgical success rate is above the performance goal. Based on published data and clinical practice, a surgical success rate of 90% or higher is expected. A performance goal of 85% (based on the literature) 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 the Clopper-Pearson exact method at one-sided alpha of 0.025.

Performance Goal Rationale and Sample Size

Analyses were performed based on available literature. Point estimates along with 95% and 99% predicted intervals were calculated to provide plausible range of potential effect size. Clinically meaningful margins and statistical precisions have been taken into account to determine the appropriate performance goals. The calculation details and rationales are summarized in the following table.

Surgery Type	PG	Sample Size	Rationale
Nephrectomy Prostatectomy Cystectomy	85%	141	The mean effect size for conversions is 0.022 with a 95% confidence interval of 0.017 to 0.029. The 95% prediction interval is 0.005 to 0.098. The 99% prediction interval is 0.003 to 0.153. A performance goal of 85% for surgical success rate was set, which is equivalent to 0.15 as the conversion rate (1-success rate), aligned with the 95% to 99% of predictive intervals upper limit of 0.098 to 0.153. A single-group design will be used to test whether the proportion is greater than 0.85 (H0: P ≤ 0.85 versus H1: P > 0.85). The comparison will be made using a one-sided, one-sample exact test, with a target Type I error rate (α) of 0.025. To detect a difference (P1 - P0) of 0.102 with a sample size of 126, which accounts for 10% attrition from the overall study sample size of up to 141, the power is 0.96.

14.4.2 Primary Objective #2 (Safety)

The primary safety objective of this study is to confirm that the Medtronic Hugo™ RAS System is safe when used for urologic robotic assisted surgery. The primary safety endpoint is the rate of subjects with major complications (meeting Grade III criteria or higher per the Clavien-Dindo Classification system) from the first incision through 30 days post-procedure. Further details can be found in **Section 6.4.2.**

The primary safety hypothesis is to test the overall 30-day major complication rate (i.e., rate of subjects with one or more major complications) against a performance goal. Since the safety profiles or major complication rates are very different among the three surgeries, a separate performance goal is pre-specified for each of the three surgery types (as per FDA recommendation). The performance goals are determined based on published literature data.

Let *R* be the 30-day major complication rate, and *PG* be performance goal for a specific surgery group. The statistical hypothesis is formulated as follows:

$$H_0: R \geq PG \text{ vs. } H_a: R < PG$$

The hypothesis will be tested using the Clopper-Pearson exact method and the null hypothesis will be rejected if one-sided p-value is significant comparing to alpha determined after multiplicity adjustment as described in **Section 14.12.**

Performance Goal Rationale and Sample Size

The literature search was performed based on available literature for each of the three surgery types (nephrectomy, prostatectomy, cystectomy). Point estimates along with 95% and 99% predicted intervals were calculated to provide plausible range of potential effect sizes. Clinically meaningful margins and statistical precisions have been taken into account to determine the appropriate performance goals. In some situations, considerations were also given to align with the studies from comparable sample sizes. The calculation details and rationales are summarized in the following table.

All sample size calculations are based on exact test. Presuming a one-sample proportion and one-sided test with the least alpha of 0.008 (0.025/3) when performing three hypothesis testing (nephrectomy, prostatectomy, and cystectomy, respectively) and adjusting for multiplicity in primary safety objectives, sample size justification and performance goals are described as below:

Surgery Type	Performance Goal (PG)	Sample Size	Rationale
Nephrectomy	20%	55	The mean effect size is 0.029 with a 95% confidence interval of 0.022 to 0.038. The 95% prediction interval is 0.017 to 0.047. The 99% prediction interval is 0.014 to 0.058. A performance goal of 0.20, while greater than the predicted interval, broadly aligns with the upper limits for each nephrectomy study with a comparable study size (95% upper limits ranging from 0.100 to 0.539) and is clinically appropriate. A performance goal of 0.20, assuming a sample size of up to 55 (with 10% attrition n=49), one-sided alpha of 0.008 (Bonferroni Correction), and mean effect size of 0.029, results in a power of 95%.
Prostatectomy	20%	55	The mean effect size is 0.029 with a 95% confidence interval of 0.016 to 0.051. The 95% prediction interval is 0.004 to 0.173. The 99% prediction interval is 0.002 to 0.316. A performance goal of 0.20 (20%), is clinically appropriate. A performance goal of 0.20, assuming a sample size of up to 55 (with 10% attrition n=49), one-sided alpha of 0.008 (Bonferroni Correction), and mean effect size of 0.029, results in a power of 95%.
Cystectomy	45%	31	The mean effect size is 0.162 with a 95% confidence interval of 0.132 to 0.198. The 95% prediction interval is 0.047 to 0.354. The 99% prediction interval is 0.024 to 0.520. A performance goal of 0.45 (45%), is clinically appropriate. A mean effect size of 14.1% is used in the sample size calculations as it is more aligned with internal assumptions of the performance of Hugo. A performance goal of 0.45, assuming a sample size of up to 31 (with 10% attrition n=27), one-sided alpha of 0.008 (Bonferroni Correction), and mean effect size of 0.141, results in a power of 83%.

14.5 Secondary Objectives

The secondary objective of this study is to demonstrate the Medtronic Hugo™ RAS System performs as intended when used in urologic robotic assisted surgery. The secondary endpoints of this study will assess the overall performance of the Medtronic Hugo™ RAS System when used for urologic robotic surgery.

The following short-term secondary endpoints will be assessed:

- Complication rate: Overall rate of subjects with one or more major complications (Clavien-Dindo Grade I or higher), from the first incision through 30 days post-procedure
- Operative time
- Intraoperative estimated blood loss (mL)
- Transfusion rate
- Rate of device-related conversion
- Hospital length of stay
- Readmission rate (through 30 days)
- Reoperation rate (through 30 days)
- Mortality rate (through 30 days)
- Rate of device deficiencies

The following long-term secondary endpoints will be assessed through 5 years in oncologic subjects:

- Overall survival
- Progression-free survival
- Disease-free survival

Descriptive statistics will be used to summarize secondary endpoints. In addition, performance goals are pre-specified based on meta-analysis of published study data as well as considerations of clinically meaningful margins and statistical confidences for most secondary endpoints (see details below; the full bibliography of 130 publications supporting the updated performance goals is included in **Section 17.1**). 95% confidence intervals might be provided as appropriate. Statistical evaluations for secondary objectives with performances goals are not powered in this study. Additionally, the secondary endpoints are planned to 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.

Performance Goals for Secondary Endpoints

Performance goals are specified for each of the secondary endpoints. The details are summarized in the following table.

Endpoint	Procedure Type	PG	Rationale
Rate of subjects with complications (through 30 days)	Nephrectomy	30.0%	The mean effect size is 0.116 with a 95% confidence interval of 0.087 to 0.152. The 95% prediction interval is 0.048 to 0.252. A performance goal of 0.30 is clinically appropriate for descriptive comparison.
	Prostatectomy	45.0%	The mean effect size is 0.056 with a 95% confidence interval of 0.038 to 0.082. The 95% prediction interval is 0.006 to 0.372. A performance goal of 0.45 is clinically appropriate for descriptive comparison.
	Cystectomy	85.0%	The mean effect size is 0.417 with a 95% confidence interval of 0.272 to 0.577. The 95% prediction interval is 0.080 to 0.854. A performance goal of 0.85 is clinically appropriate for descriptive comparison.
Operative time (min)	Nephrectomy	255 min	The mean effect size is 170.1 with a 95% confidence interval of 155.5 to 184.7. The 95% prediction interval is 81.9 to 304.9. A performance goal of 255 minutes is clinically appropriate for a descriptive comparison.
	Prostatectomy	340 min	The mean effect size is 190.6 with a 95% confidence interval of 169.7 to 211.5. The 95% prediction interval is 96.9 to 324.8. A performance goal of 340 minutes is clinically appropriate for a descriptive comparison.
	Cystectomy	500 min	The mean effect size is 376.2 with a 95% confidence interval of 315.9 to 436.6. The 95% prediction interval is 185.6 to 682.1. A performance goal of 500 minutes is clinically appropriate for a descriptive comparison.
Intraoperative estimated blood loss (mL)	Nephrectomy	490 mL	The mean effect size is 181.0 with a 95% confidence interval of 131.5 to 230.5. The 95% prediction interval is 34.3 to 507.7. A performance goal of 490 mL is clinically appropriate for a descriptive comparison.
	Prostatectomy	500 mL	The mean effect size is 193.3 with a 95% confidence interval of 168.2 to 218.4. The 95% prediction interval is 54.7 to 486.5. A performance goal of 500 mL is clinically appropriate for a descriptive comparison.

Endpoint	Procedure Type	PG	Rationale
	Cystectomy	500 mL	The mean effect size is 133.0 with a 95% confidence interval of 102.6 to 163.4. The 95% prediction interval was not able to be obtained due to a lack of data. As there are few literature cohorts available for this endpoint, the performance goals of the other two surgical cohorts were considered in setting this endpoint's performance goal of 500.
Transfusion rate	Nephrectomy	30%	The mean effect size is 0.079 with a 95% confidence interval of 0.056 to 0.11. The 95% prediction interval is 0.021 to 0.257. A performance goal of 0.30 is clinically appropriate for descriptive comparison.
	Prostatectomy	60%	The mean effect size is 0.020 with a 95% confidence interval of 0.011 to 0.037. The 95% prediction interval is 0 to 0.534. A performance goal of 0.60 is clinically appropriate for descriptive comparison.
	Cystectomy	55%	The mean effect size is 0.133 with a 95% confidence interval of 0.050 to 0.308. The 95% prediction interval is 0.004 to 0.869. While below the 95% prediction interval upper limit, a performance goal of 0.550 is better aligned for a descriptive comparison.
Rate of device-related conversion	Nephrectomy	15%	The literature search failed to identify studies that reported on device-related conversions. Device related conversions are expected to be a fraction of the total conversions. Conversion Rate = 100% - Surgical Success Rate, which has a performance goal of 85%. Thus, a 15% performance goal is assumed for conversions.
	Prostatectomy	15%	The literature search failed to identify studies that reported on device-related conversions. Device related conversions are expected to be a fraction of the total conversions. Conversion Rate = 100% - Surgical Success Rate, which has a performance goal of 85%. Thus, a 15% performance goal is assumed for conversions.
	Cystectomy	15%	The literature search failed to identify studies that reported on device-related conversions. Device related conversions are expected to be a fraction of the total conversions. Conversion Rate = 100% - Surgical Success Rate, which has a performance goal of 85%. Thus, a 15% performance goal is assumed for conversions.

Endpoint	Procedure Type	PG	Rationale
Hospital length of stay [LOS] (days)	Nephrectomy	7 days	The mean effect size is 3.7 with a 95% confidence interval of 3.1 to 4.2. The 95% prediction interval is 1.1 to 8.5. A performance goal of 7 days is clinically appropriate for a descriptive comparison.
	Prostatectomy	11 days	The mean effect size is 4.9 with a 95% confidence interval of 4.0 to 5.8. The 95% prediction interval is 0.6 to 15.0. A performance goal of 11 days is clinically appropriate for a descriptive comparison.
	Cystectomy	7 days	The mean effect size is 5.6 with a 95% confidence interval of 4.9 to 6.2. The 95% prediction interval was not able to be obtained due to lack of data. The longest literature-reported hospital length of stay was 5.9 days, applying a 20% relative margin to this gives 7.08 days. Thus, a performance goal of 7 days was set and deemed to be clinically appropriate.
Readmission rate (through 30 days)	Nephrectomy	16.8%	The mean effect size was 0.063 with a 95% confidence interval of 0.028 to 0.132. The 95% prediction interval was not able to be obtained due to a lack of data. The highest literature-reported readmission rate within 30 days was 0.068, applying a 10% absolute margin to this gives 0.168. Thus, a performance goal of 16.8% was set and deemed to be clinically appropriate.
	Prostatectomy	30.0%	The mean effect size is 0.050 with a 95% confidence interval of 0.025 to 0.097. The 95% prediction interval is 0.010 to 0.224. Thus, a performance goal of 30.0% was clinically appropriate for descriptive comparison.
	Cystectomy	39.4%	The mean effect size was 0.136 with a 95% confidence interval of 0.033 to 0.419. The 95% prediction interval was not able to be obtained due to a lack of data. The highest literature-reported readmission rate within 30 days was 0.229, applying a 10% absolute margin to this gives 0.329. Thus, a performance goal of 39.4% was set and deemed to be clinically appropriate.
Reoperation rate (through	Nephrectomy	25.6%	There was no literature found, therefore the prostatectomy performance goal was leveraged to assign a performance goal of 25.6%.

Endpoint	Procedure Type	PG	Rationale
30 days)	Prostatectomy	25.6%	The mean effect size was 0.062 with a 95% confidence interval of 0.005 to 0.469. The 95% prediction interval was not able to be obtained due to a lack of data, as there were only two cohorts as part of this meta-analysis. The highest literature-reported reoperation rate within 30 days was 0.156, applying a 10% absolute margin to this gives 0.256. Thus, a performance goal of 25.6% was set and deemed to be clinically appropriate.
	Cystectomy	25.6%	There was no literature found, therefore the prostatectomy performance goal was leveraged to assign a performance goal of 25.6%.
Mortality rate (through 30 days)	Nephrectomy	24.3%	Limited to two cohorts from one study, the performance goal is derived based on the individual cohort upper limits of 0.143. A value of 0.243 provides 10% margin on the upper limit, while remaining clinically appropriate.
	Prostatectomy	21%	Limited to one cohort, the performance goal is derived based on the individual cohort upper limit of 0.110. A value of 0.210 provides 10% margin on the upper limit, while remaining clinically appropriate.
	Cystectomy	35.1%	This analysis was based on 6 cohorts. As there was no variance between cohorts, the performance goal is derived based on the individual cohort upper limits of 0.040 to 0.251. A value of 0.351 provides 10% margin on the upper limit, while remaining clinically appropriate.
Rate of device deficiencies	Nephrectomy	20%	Device specific deficiencies were not reported in the literature. Recognizing that device deficiencies include those of preference and not all will impact the safety or performance of the device, a clinically appropriate performance goal of 20% has been selected.
	Prostatectomy	20%	Device specific deficiencies were not reported in the literature. Recognizing that device deficiencies include those of preference and not all will impact the safety or performance of the device, a clinically appropriate performance goal of 20% has been selected.

Endpoint	Procedure Type	PG	Rationale
	Cystectomy	20%	Device specific deficiencies were not reported in the literature. Recognizing that device deficiencies include those of preference and not all will impact the safety or performance of the device, a clinically appropriate performance goal of 20% has been selected.
Overall survival (OS) (5 years)	Nephrectomy	51.6%	The mean effect size is 0.931 with a 95% confidence interval of 0.614 to 0.991. The 95% prediction interval was 0.0 to 1.00. Thus, a performance goal of 0.516 was clinically appropriate.
	Prostatectomy	50%	The mean effect size is 0.954 with a 95% confidence interval of 0.887 to 0.982. The 95% prediction interval is 0.0 to 1.0. A performance goal of 0.50 is clinically appropriate for descriptive comparison.
	Cystectomy	35%	The mean effect size is 0.645 with a 95% confidence interval of 0.571 to 0.714. The 95% prediction interval is 0.426 to 0.817. A performance goal of 0.35 is clinically appropriate for descriptive comparison.
Progression-free survival (PFS) (5 years)	Nephrectomy	15%	Progression-free survival at 5-years is not reported within the literature. Therefore, the performance goals will be based on a function of those for overall survival, roughly 1/3, and are clinically meaningful.
	Prostatectomy	15%	Progression-free survival at 5-years is not reported within the literature. Therefore, the performance goals will be based on a function of those for overall survival, roughly 1/3, and are clinically meaningful.
	Cystectomy	10%	Progression-free survival at 5-years is not reported within the literature. Therefore, the performance goals will be based on a function of those for overall survival, roughly 1/3, and are clinically meaningful.
Disease-free survival (DFS) (5 years)	Nephrectomy	15%	Disease-free survival at 5-years is not reported within the literature. Therefore, the performance goals for progression-free survival will be leveraged and are clinically meaningful.
	Prostatectomy	15%	Disease-free survival at 5-years is not reported within the literature. Therefore, the performance goal for progression-free survival will be leveraged and are clinically meaningful.

Endpoint	Procedure Type	PG	Rationale
	Cystectomy	10%	Disease-free survival at 5-years is not reported within the literature. Therefore, the performance goal for progression-free survival will be leveraged and are clinically meaningful.

14.6 Ancillary Objectives

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:

- Rate of positive surgical margins
- Lymph node yield
- Warm ischemia time
- Surgeon experience

14.7 Sample Size Determination

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

Power calculation was performed using statistical software NCSS PASS 2023.

The effectiveness hypothesis is to test if the surgical success rate is above the performance goal. The surgical success rate is expected to be 90% or higher. A performance goal is set to be 85%. A sample size of 126 subjects will provide more than 80% power at one-sided alpha of 0.025 (with an expected rate of 95.2% or higher in this study).

Safety is also considered for sample size determination. The primary safety endpoint is the major complication rate. A statistical hypothesis with a performance goal is specified for each of the three surgery types. The performance goals are determined based on analyses of published literature by taking into account clinically meaningful margins and statistical precisions. Each individual hypothesis is adequately powered with at least 80% power at a one-sided alpha level of 0.008 with multiplicity adjustment taken into consideration. The sample sizes for the three surgery types are up to 55, up to 55 and up to 31 for Nephrectomy, Prostatectomy and Cystectomy respectively, after taking 10% attrition into account (up to 141 subjects in total).

With the consideration of both effectiveness and safety, a total of up to 141 subjects are planned to be treated in this study. Up to six study sites will be used. To keep enrollment balance, each study site will be allowed to enroll 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:

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 (mITT) population. In the event that 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.

AEs will be collected from the time of consent. AEs occurring in subjects excluded from the FAS will be followed for 30 days 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. Prior to data analysis, a protocol deviation listing will be produced and sent to the clinical manager/team for review in order to verify which subjects will be excluded from the PPAS. 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 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 and Sensitivity Analysis

The primary analysis will be based on the full analysis set with no imputation of missing data. Sensitivity analysis will be performed for both the primary effectiveness and safety endpoints using multiple imputations for missing data if the missing data percentage is greater than 5% (https://pubmed.ncbi.nlm.nih.gov/29207961/), as well as tipping-point analysis for the primary effectiveness endpoint to fully understand the missing data impact on the study results.

14.12 Multiplicity Adjustment

For the primary effectiveness endpoint only one hypothesis will be tested at alpha of 0.025 one-sided. For the primary safety endpoint (major complication rate), the closed test procedure (Holm's method) will be used to protect the overall study-wise error rate for surgery types (Nephrectomy, Prostatectomy and Cystectomy).

14.13 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.

15. Ethics

15.1 Statement(s) of Compliance

This study will be conducted in compliance with international ethical and scientific quality standards, known as 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 Expand URO study was designed to reflect GCP principles. 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. 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 in accordance with the 2007 FDAAA and DoH on http://clinicaltrials.gov (PL 110-85, section 810(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 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. Should an IRB or Regulatory Authority impose any additional requirements, they will be followed. If any action is taken by the IRB with respect to the investigation, that information is to be forwarded to Medtronic.

Pediatric, legally incompetent, or other vulnerable subjects are not eligible for the study. No insurance or compensation will be provided to study subjects.

16. Study Administration

16.1 Monitoring

It is the responsibility of Medtronic to ensure monitoring of this study. Trained Medtronic representatives will perform study monitoring in accordance with Medtronic SOPs and the Monitoring Plan, in order to ensure that the study is conducted in accordance with the CIP, the CTA, and the applicable regulatory and local requirements. These Medtronic representatives must therefore be allowed direct access to the subjects' case histories (clinic and hospital records, and other source data/documentation) upon request. The Principal Investigator should make every attempt to be available during monitoring visit.

Table 12. Monitoring

Member	Contact information
[redacted]	8200 Coral Sea Street, N.E., MVS33 Mounds View, MN 55112, USA

16.1.1 Monitoring Visits

A site qualification visit may be conducted by Medtronic personnel (or designees) to review the clinical investigational plan and, regulatory and study requirements with the Investigator and study personnel.

Site initiation visits will be completed prior to enrollment of the first subject to ensure appropriate site staff are trained and delegated where applicable, and all required study documents are completed and collected.

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 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 the study. eCRF data will be stored in a secure, password-protected database which will be backed up nightly. 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 indefinitely by Medtronic.

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.

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

The Investigator(s)/institution(s) will permit inspection and study-related monitoring, audits, IRB review, and regulatory inspection(s), including direct access to original source data/documents per applicable laws and regulations.

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 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 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. This scenario will be covered in the IC. In the event a subject's name/PHI is included for any reason, it will be blinded as applicable. In the event of 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, will be submitted to the FDA according to applicable regulations. 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

The Principal Investigator will maintain the records of the study including all pertinent correspondence, the CIP with any/all amendments, all correspondence with and approval from the IRB, the clinical investigation agreement, the Investigator Agreement, individual subject records, and signed informed consent forms (ICFs).

The Principal Investigator is responsible for ensuring that all essential study documentation is retained and accessible for a minimum period of two years after the date the investigation is completed or terminated, or the records are no longer required to support a marketing application (or longer in compliance to local requirements). The retention period may be longer if required by Medtronic or local or global regulatory requirements. Medtronic will not store any personal data longer than necessary and always in line with the required storage periods defined by the applicable laws. Medtronic will delete or make any personal data anonymous after the applicable storage period has expired. The Principal Investigator will ensure that essential study documents are not destroyed until written permission has been obtained from Medtronic. Medtronic will be notified in writing prior to the transfer of study documentation.

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 clinical investigation plan according to **Table 13**. 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. Reports are subject to inspection and to the retention requirements as described above for Investigator records.

Safety data investigator reporting requirements are listed in **Section 16.8.1.** The investigator shall prepare and submit in a complete, accurate and timely manner the reports listed in this section.

Table 13. Investigator Reports Applicable to the United States per FDA Regulations

Report	Submit to	Description/Constraints
Withdrawal of IRB approval (either suspension or termination)	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. (21 CFR 812.150(a)(2))
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 wellbeing 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))

16.9 Publication and Use of Information

- The Medtronic Publication and Authorship Policy is aligned with the International Committee of Medical Journal Editors (ICMJE) recommendations (www.icmje.org). The Sponsor will seek to publish, in appropriate peer-reviewed journals and scientific conferences, results of clinical studies where human subjects are involved. Publication will be pursued regardless of outcome, with the intent to communicate ROPI.

- information that will advance scientific and/or medical knowledge.

- While study results are owned by the Sponsor, all data on which a publication is based will be made available to all authors as required for their participation in the publication process. Furthermore, data may be published or used by study Investigators provided that such publication or use is in accordance with this protocol, the Medtronic Publication and Authorship Policy, and the Clinical Trial Agreement. Investigators must submit a copy of all manuscripts and/or abstracts to the Sponsor for review and comment at least 30 days prior to the planned submission. Medtronic acknowledges that its right to review and comment shall relate solely to the proprietary, licensing, and/or confidential rights Medtronic may have in such proposed publication, rather than whether such results and/or opinions are favorable to Medtronic.

- The publication of sub-studies, post-hoc analyses, regional results, or single-center experiences based on multicenter clinical studies should not precede that of the primary multicenter publication, and should cite the primary publication whenever possible, as required by specific journal and scientific meeting guidelines.

- Medtronic prohibits compensation for publication writing or editing activities to consultant health care providers (HCPs) (or to healthcare organizations) who serve as authors. Medtronic involvement in a publication (e.g., funding of the study; sponsor of the study; collection, analysis, and interpretation of data; professional writing assistance) must be disclosed according to journal-specific policies, submission requirements, and prevailing editorial standards, in addition to those specified by the ICMJE. Authors must ensure that an acknowledgement/disclosure statement is included in the body of the manuscript for Medtronic to review for accuracy. All authors must also disclose financial or personal affiliations that could be considered conflicts of interest as per journal/conference requirements.

- In compliance with independent ethical codes across the industry, Medtronic does not reimburse Investigators or healthcare providers for travel or registration to present Medtronic-sponsored clinical study data at third party scientific conferences.

16.9.1 Publication Committee

The study Steering Committee (**Section 6.5**) will also serve as the Publication Committee, in addition to appropriate members of the Medtronic medical and clinical departments (excluding marketing and sales). This committee will manage study publications with the goal of publishing findings from the data. The Publication Committee will develop the Publication Plan as a separate document.

The Publication Committee's role is to: (1) develop the Publication Plan under separate cover; (2) execute the Publication Plan; (3) oversee the publication of primary, secondary, and exploratory study results; (4) review and prioritize publication proposals; (5) provide input on publication content; and (6) apply and reinforce the authorship guidelines set forth in the Publication Plan. The committee will meet at regular intervals as needed.

The Publication Committee may use professional medical writers to assist in writing publications and/or presentations; however, all medical writing support must be appropriately disclosed according to the Medtronic Publication and Authorship Policy and journal/conference policies.

16.9.2 Criteria for Determining Authorship

- Publications will adhere to authorship criteria defined by the ICMJE. Individual authorship criteria defined by the target journal or conference will be followed when it differs from ICMJE criteria.

- All authors, including Medtronic personnel, must meet all four of the conditions below:

1. Substantial contributions to conception and design of the work, or the acquisition, analysis, or interpretation of data for the work; AND
2. Drafting the work or revising it critically for important intellectual content; AND

3. Final approval of the version to be published; AND
4. 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.

– Study enrollment alone and membership in the Publication Committee do not guarantee authorship. Authorship on one publication does not guarantee authorship on any subsequent study publications.

– Author selection strategy (based on ICMJE criteria) and potential authors will be discussed by the Publication Committee and included in the Publication Plan. Authorship will be evaluated on a continuous basis as writing and review progresses. Final authorship will be determined based on ICMJE contributions and must be reviewed by the Steering Committee prior to submission.

16.9.3 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 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 coauthors 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 10.9** 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

Possible reasons for considering study-wide suspension or termination of the study include but are not limited to:

- AEs associated with the system or product under investigation which might endanger the safety or welfare of the subject
- Observed/suspected performance different from the product's design intent
- Decision by Medtronic or RA (where the study is operating under RA)
- Technical issues during the manufacturing process

Clavien-Dindo Grade IV complications will be continuously monitored by the sponsor for the safety and well-being of the subjects. Events reported as Clavien-Dindo Grade IV will be assessed by the Investigator and the sponsor as well as sent for adjudication by the independent CEC upon the sponsor's awareness date for the reported event.

Safety thresholds for Grade IV complication rates for the three study procedures are noted below:

- Cystectomy: 10%
- Nephrectomy: 8%
- Prostatectomy: 5%
- The above safety thresholds will be used by the sponsor to modify or stop the trial. The sponsor will review the Clavien-Dindo Grade IV complications for the first 30 subjects with 30-day data. A second review will be conducted for the second 30 subjects with 30-day data to ensure ongoing monitoring of subject safety.

16.10.2.2 Investigator/Study Site Termination or Suspension

Possible reasons for an 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

16.10.4 Procedures for Termination or Suspension

16.10.4.1 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

16.10.4.2 Ethics Committee-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

17. References

1. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240(2):205-213.
2. Vecchio R, MacFayden B, Palazzo F. History of laparoscopic surgery. *Panminerva medica.* 2000;42(1):87-90.
3. Araujo SEA, Seid VE, Klajner S. Robotic surgery for rectal cancer: current immediate clinical and oncological outcomes. *World Journal of Gastroenterology: WJG.* 2014;20(39):14359.
4. Cacciamani GE, Gill K, Gill IS. Robotic versus open urological oncological surgery: study protocol of a systematic review and meta-analysis. *BMJ Open.* 2020;10(2):e036609.
5. Jackson SR, Patel MI. Robotic Surgery Research in Urology: A Bibliometric Analysis of Field and Top 100 Articles. *Journal of Endourology.* 2019;33(5):389-395.
6. Steffens D, Thanigasalam R, Leslie S, Maneck B, Young JM, Solomon M. Robotic Surgery in Uro-oncology: A Systematic Review and Meta-analysis of Randomized Controlled Trials. *Urology.* 2017;106(1):9-17.
7. Cao L, Yang Z, Qi L, Chen M. Robot-assisted and laparoscopic vs open radical prostatectomy in clinically localized prostate cancer: perioperative, functional, and oncological outcomes: A Systematic review and meta-analysis. *Medicine (Baltimore).* 2019;98(22):e15770.
8. De Carlo F, Celestino F, Verri C, Masedu F, Liberati E, Di Stasi SM. Retropubic, laparoscopic, and robot-assisted radical prostatectomy: surgical, oncological, and functional outcomes: a systematic review. *Urol Int.* 2014;93(4):373-383.
9. Veccia A, Antonelli A, Grob BM, et al. Impact of Robotic Surgery on Sick Leave and Return to Work in Patients Undergoing Radical Prostatectomy: An Evidence-Based Analysis. *Urology*

Practice. 2020;7(1):47-52.

10. Wang L, Wang B, Ai Q, et al. Long-term cancer control outcomes of robot-assisted radical prostatectomy for prostate cancer treatment: a meta-analysis. *International urology and nephrology.* 2017;49(6):995-1005.
11. Alder R, Zetner D, Rosenberg J. Incidence of Inguinal Hernia after Radical Prostatectomy: A Systematic Review and Meta-Analysis. *J Urol.* 2020;203(2):265-274.
12. Clement KD, Pearce E, Gabr AH, Rai BP, Al-Ansari A, Aboumarzouk OM. Perioperative outcomes and safety of robotic vs open cystectomy: a systematic review and meta-analysis of 12,640 cases. *World J Urol.* 2020.
13. Feng D, Li A, Hu X, Lin T, Tang Y, Han P. Comparative effectiveness of open, laparoscopic and robot-assisted radical cystectomy for bladder cancer: a systematic review and network meta-analysis. *Minerva Urol Nefrol.* 2020;72(3):251-264.
14. Feng D, Liu S, Tang Y, Yang Y, Wei W, Han P. Comparison of perioperative and oncologic outcomes between robot-assisted and laparoscopic radical cystectomy for bladder cancer: a systematic review and updated meta-analysis. *International urology and nephrology.* 2020;52(7):1243-1254.
15. Tang JQ, Zhao Z, Liang Y, Liao G. Robotic-assisted versus open radical cystectomy in bladder cancer: A meta-analysis of four randomized controlled trails. *Int J Med Robot.* 2018;14(1).
16. Tan WS, Khetrapal P, Tan WP, Rodney S, Chau M, Kelly JD. Robotic Assisted Radical Cystectomy with Extracorporeal Urinary Diversion Does Not Show a Benefit over Open Radical Cystectomy: A Systematic Review and Meta-Analysis of Randomised Controlled Trials. *PLoS One.* 2016;11(11):e0166221.
17. Shen Z, Sun Z. Systematic review and meta-analysis of randomised trials of perioperative outcomes comparing robot-assisted versus open radical cystectomy. *BMC Urol.* 2016;16(1):59.
18. Satkunasivam R, Tallman CT, Taylor JM, Miles BJ, Klaassen Z, Wallis CJD. Robot-assisted Radical Cystectomy Versus Open Radical Cystectomy: A Meta-analysis of Oncologic, Perioperative, and Complication-related outcomes. *Eur Urol Oncol.* 2019;2(4):443-447.
19. Tzelves L, Skolarikos A, Mourmouris P, et al. Does the Use of a Robot Decrease the Complication Rate Adherent to Radical Cystectomy? A Systematic Review and Meta-Analysis of Studies Comparing Open with Robotic Counterparts. *J Endourol.* 2019;33(12):971-984.
20. Rai BP, Bondad J, Vasdev N, et al. Robotic versus open radical cystectomy for bladder cancer in adults. *Cochrane Database Syst Rev.* 2019;4:CD011903.
21. Lauridsen SV, Tonnesen H, Jensen BT, Neuner B, Thind P, Thomsen T. Complications and health-related quality of life after robot-assisted versus open radical cystectomy: a systematic review and meta-analysis of four RCTs. *Syst Rev.* 2017;6(1):150.
22. Kimura S, Iwata T, Foerster B, et al. Comparison of perioperative complications and health-related quality of life between robot-assisted and open radical cystectomy: A systematic review and meta-analysis. *Int J Urol.* 2019;26(8):760-774.
23. Peng L, Li J, Cao D, et al. Can robotic-assisted radical cystectomy provide patients with a smaller trauma and faster recovery period? A systematic review and meta-analysis of comparative trials. *J Cancer Res Clin Oncol.* 2020;146(6):1591-1601.
24. Albisinni S, Veccia A, Aoun F, et al. A systematic review and meta-analysis comparing the outcomes of open and robotic assisted radical cystectomy. *Minerva Urol Nefrol.* 2019;71(6):553-568.
25. Cacciamani GE, Medina LG, Gill T, et al. Impact of Surgical Factors on Robotic Partial Nephrectomy Outcomes: Comprehensive Systematic Review and Meta-Analysis. *J Urol.*

2018;200(2):258-274.
26. Wu Z, Li M, Liu B, et al. Robotic versus open partial nephrectomy: a systematic review and meta-analysis. *PLoS One.* 2014;9(4):e94878.
27. Xia L, Wang X, Xu T, Guzzo TJ. Systematic Review and Meta-Analysis of Comparative Studies Reporting Perioperative Outcomes of Robot-Assisted Partial Nephrectomy Versus Open Partial Nephrectomy. *J Endourol.* 2017;31(9):893-909.
28. Rai BP, Jones P, Tait C, et al. Is Cryotherapy a Genuine Rival to Robotic-assisted Partial Nephrectomy in the Management of Suspected Renal Malignancy? A Systematic Review and Meta-analysis. *Urology.* 2018;118:6-11.
29. Choi JE, You JH, Kim DK, Rha KH, Lee SH. Comparison of perioperative outcomes between robotic and laparoscopic partial nephrectomy: a systematic review and meta-analysis. *Eur Urol.* 2015;67(5):891-901.
30. Leow JJ, Heah NH, Chang SL, Chong YL, Png KS. Outcomes of Robotic versus Laparoscopic Partial Nephrectomy: an Updated Meta-Analysis of 4,919 Patients. *J Urol.* 2016;196(5):1371-1377.
31. Tsai SH, Tseng PT, Sherer BA, et al. Open versus robotic partial nephrectomy: Systematic review and meta-analysis of contemporary studies. *Int J Med Robot.* 2019;15(1):e1963.
32. Zhang X, Yan J, Ren Y, Shen C, Ying X, Pan S. Robot-assisted versus laparoscopic partial nephrectomy for localized renal tumors: a meta-analysis. *Int J Clin Exp Med.* 2014;7(12):4770-4779.
33. Chang SL, Kibel AS, Brooks JD, Chung BI. The impact of robotic surgery on the surgical management of prostate cancer in the USA. *BJU Int.* 2015;115(6):929-936.
34. Aggarwal R, Winter Beatty J, Kinross J, von Roon A, Darzi A, Purkayastha S. Initial Experience With a New Robotic Surgical System for Cholecystectomy. *Surgical Innovation.* 2019;27(2):136-142.
35. Schmitz R, Willeke F, Barr J, et al. Robotic Inguinal Hernia Repair (TAPP) First Experience with the New Senhance Robotic System. *Surg Technol Int.* 2019;34:243-249.
36. Melling N, Barr J, Schmitz R, et al. Robotic cholecystectomy: first experience with the new Senhance robotic system. *J Robot Surg.* 2019;13(3):495-500.
37. Spinelli A, David G, Gidaro S, et al. First experience in colorectal surgery with a new robotic platform with haptic feedback. *Colorectal Dis.* 2017;20.
38. Fanfani F, Monterossi G, Fagotti A, et al. The new robotic TELELAP ALF-X in gynecological surgery: single-center experience. *Surg Endosc.* 2016;30(1):215-221.
39. Yaxley JW, Coughlin GD, Chambers SK, et al. Robot-assisted laparoscopic prostatectomy versus open radical retropubic prostatectomy: early outcomes from a randomised controlled phase 3 study. *Lancet.* 2016;388(10049):1057-1066.

17.1 Bibliography of Publications Supporting Updated Statistical Design

1. Agarwal VV, Thyavihally BY, Waigankar SS, et al. Perioperative, oncological, and survival outcomes of robotic radical cystectomy with urinary diversion in females: A single-center retrospective observational study. Indian Journal of Urology. 2023;39(1):27-32.
2. Arora A, Pugliesi F, Zugail AS, et al. Comparing perioperative complications between laparoscopic and robotic radical cystectomy for bladder cancer. Journal of Endourology.

2020;34(10):1033-1040.

3. Jeglinschi S, Carlier M, Denimal L, et al. Intracorporeal urinary diversion during robot-assisted radical cystectomy using indocyanine green. The Canadian journal of urology. 2020;27(5):10394-10401.
4. Piazza P, Bravi CA, Puliatti S, et al. Assessing pentafecta achievement after robot-assisted radical cystectomy and its association with surgical experience: Results from a high-volume institution. Urologic oncology. 2022;40(6):272.e211-272.e220.
5. Piazza P, Rosiello G, Chacon VT, et al. Robot-assisted Cystectomy with Intracorporeal Urinary Diversion After Pelvic Irradiation for Prostate Cancer: Technique and Results from a Single High-volume Center. European urology. 2021;80(4):489-496.
6. Tyson MD, Mi L. Preliminary Surgical Outcomes After Single Incision Robotic Cystectomy (SIRC). Urology. 2023;171:127-132.
7. Abdul-Muhsin HM, McAdams SB, Syal A, et al. Robot Assisted Renal Allograft Nephrectomy: Initial Case Series and Description of Technique. Urology. 2020;146:118-124.
8. Audige V, Baghli A, Hubert J, Mazeaud C, Larre S, Branchu B. Clinical and oncological outcomes of open partial nephrectomy versus robot assisted partial nephrectomy over 15 years. Journal of Robotic Surgery. 2023;17(2):519-526.
9. Boga MS, Sonmez MG, Karamik K, et al. Long-term outcomes of minimally invasive surgeries in partial nephrectomy. Robot or laparoscopy? International Journal of Clinical Practice. 2021;75(2):e13757.
10. Boga MS, Ates M. Retroperitoneal robot-assisted laparoscopic partial nephrectomy for posterior located renal tumours: Technique and early term outcomes. International Journal of Clinical Practice. 2021;75(2):e13851.
11. Garden EB, Al-Alao O, Razdan S, Mullen GR, Florman S, Palese MA. Robotic Single-Port Donor Nephrectomy with the da Vinci SP R Surgical System. JSLS : Journal of the Society of Laparoendoscopic Surgeons. 2021;25(4).
12. Harrison R, Ahmed M, Billah M, et al. Single-port versus multiport partial nephrectomy: a propensity-score-matched comparison of perioperative and short-term outcomes. Journal of Robotic Surgery. 2023;17(1):223-231.
13. Razdan S, Okhawere KE, Ucpinar B, et al. The State of Robotic Partial Nephrectomy: Operative, Functional, and Oncological Outcomes From A Robust Multi-Institution Collaborative. Urology. 2023;173:92-97.
14. Spaggiari M, Garcia-Roca R, Tulla KA, et al. Robotic Assisted Living Donor Nephrectomies: A Safe Alternative to Laparoscopic Technique for Kidney Transplant Donation. Annals of Surgery. 2022;275(3):591-595.
15. Uemura T, Kato T, Nagahara A, et al. Therapeutic and clinical outcomes of robot-assisted partial nephrectomy versus cryoablation for T1 renal cell carcinoma. In Vivo. 2021;35(3):1573-

1579.

16. Aldousari S, Yaiesh S, Alkandari O, Hussein S. Pathological features of prostate cancer in men treated with robot-assisted radical prostatectomy in the Middle East. Journal of Robotic Surgery. 2021;15(1):125-133.
17. Bahouth Z, Laniado M, Fowler R, Charlesworth PJS. Positive Surgical Margins Rate of Retzius-Sparing Robot-Assisted Radical Prostatectomy in a Contemporary, Unselected Cohort. Journal of Urology. 2022;207(3):609-616.
18. Benarroche D, Paladini A, Grobet-Jeandin E, et al. Robotic versus open simple prostatectomy for benign prostatic hyperplasia in large glands: single-centre study. World journal of urology. 2022;40(12):3001-3006.
19. Dobbs RW, Halgrimson WR, Madueke I, Vigneswaran HT, Wilson JO, Crivellaro S. Single-port robot-assisted laparoscopic radical prostatectomy: initial experience and technique with the da Vinci R SP platform. BJU international. 2019;124(6):1022-1027.
20. Gaboardi F, Pini G, Suardi N, Montorsi F, Passaretti G, Smelzo S. Robotic laparoendoscopic single-site radical prostatectomy (R-LESS-RP) with daVinci Single-Site platform. Concept and evolution of the technique following an IDEAL phase 1. Journal of Robotic Surgery. 2019;13(2):215-226.
21. Islamoglu E, Aktas Y, Ari O, et al. Robotic-assisted laparoscopic prostatectomy: Initial experience of 267 cases. Bulletin of Urooncology. 2019;18(1):14-17.
22. Kulis T, Hudolin T, Penezic L, et al. Comparison of extraperitoneal laparoscopic and extraperitoneal Senhance radical prostatectomy. The international journal of medical robotics + computer assisted surgery : MRCAS. 2022;18(1):e2344.
23. Lee Z, Lee M, Keehn AY, Asghar AM, Strauss DM, Eun DD. Intermediate-term Urinary Function and Complication Outcomes After Robot-Assisted Simple Prostatectomy. Urology. 2020;141:89-94.
24. Martinez PF, Romeo A, Tobia I, Isola M, Giudice CR, Villamil WA. Comparing open and robotic salvage radical prostatectomy after radiotherapy: predictors and outcomes. Prostate International. 2021;9(1):42-47.
25. Moreno-Sierra J, Galante-Romo MI, Senovilla-Perez JL, et al. Oncologic outcomes in 408 consecutive patient cohort treated with da Vinci robot-assisted radical prostatectomy. Resultados oncologicos de un programa de prostatectomia radical asistida por robot <> en una cohorte de 408 pacientes consecutivos. 2020;44(3):179-186.
26. Siripalangkanont J, Panumatrassamee K. Comparison of Treatment Outcomes between Laparoscopic and Robot-Assisted Laparoscopic Radical Prostatectomy in Clinically Localized Prostate Cancer, A Single-Surgeon Experience. Journal of the Medical Association of Thailand. 2020;103(12):1300-1308.
27. Tamhankar AS, Patil S, Singh S, et al. Selecting lymph node-positive patients for adjuvant therapy after radical prostatectomy and extended pelvic lymphadenectomy: An outcome

analysis of 100 node-positive patients managed without adjuvant therapy. Current Urology. 2022;16(4):232-239.

28. Wilson CA, Aminsharifi A, Sawczyn G, et al. Outpatient Extraperitoneal Single-Port Robotic Radical Prostatectomy. Urology. 2020;144:142-146.
29. Buse S, Alexandrov A, Mazzone E, Mottrie A, Haferkamp A. Surgical benchmarks, mid-term oncological outcomes, and impact of surgical team composition on simultaneous enbloc robot-assisted radical cystectomy and nephroureterectomy. BMC urology. 2021;21(1):73.
30. Jin HJ, Shim JS, Kwon TG, et al. Gender-related outcomes in robot-assisted radical cystectomy: A multi-institutional study. Investigative and Clinical Urology. 2022;63(1):53-62.
31. Maibom SL, Roder MA, Aasvang EK, et al. Open vs robot-assisted radical cystectomy (BORARC): a double-blinded, randomised feasibility study. BJU International. 2022;130(1):102-113.
32. Tamhankar AS, Ahluwalia P, Patil SR, Nambiath S, Gautam G. Implementation of ERAS protocol in robot-assisted radical cystectomy with intracorporeal ileal conduit urinary diversion: An outcome analysis beyond the learning curve. Indian journal of urology: IJU: journal of the Urological Society of India. 2020;36(1):37-43.
33. Alimi Q, Peyronnet B, Sebe P, et al. Comparison of Short-Term Functional, Oncological, and Perioperative Outcomes between Laparoscopic and Robotic Partial Nephrectomy beyond the Learning Curve. Journal of Laparoendoscopic and Advanced Surgical Techniques. 2018;28(9):1047-1052.
34. Brunotte M, Rademacher S, Weber J, et al. Robotic assisted nephrectomy for living kidney donation (RANLD) with use of multiple locking clips or ligatures for renal vascular closure. Annals of translational medicine. 2020;8(6):305.
35. Buffi NM, Saita A, Lughezzani G, et al. Robot-assisted Partial Nephrectomy for Complex (PADUA Score >=10) Tumors: Techniques and Results from a Multicenter Experience at Four High-volume Centers. European urology. 2020;77(1):95-100.
36. Casale P, Lughezzani G, Buffi N, Larcher A, Porter J, Mottrie A. Evolution of Robot-assisted Partial Nephrectomy: Techniques and Outcomes from the Transatlantic Robotic Nephron-sparing Surgery Study Group. European urology. 2019;76(2):222-227.
37. El-Asmar JM, Sebaaly R, Mailhac A, et al. Use of Bariatric Ports in 4-Arm Robotic Partial Nephrectomy: A Comparative Study With the Standard 3-Arm Technique. Cureus. 2021;13(7):e16461.
38. Francavilla S, Abern MR, Dobbs RW, et al. Single-Port robot assisted partial nephrectomy: initial experience and technique with the da Vinci Single-Port platform (IDEAL Phase 1). Minerva urology and nephrology. 2022;74(2):216-224.

39. Furukawa J, Hinata N, Teisima J, et al. Robot-assisted partial nephrectomy with minimum follow-up of 5 years: A multi-center prospective study in Japan. Int J Urol. 2022;29(9):1038-1045.

40. Furukawa J, Kanayama H, Azuma H, et al. 'Trifecta' outcomes of robot-assisted partial nephrectomy: a large Japanese multicenter study. International Journal of Clinical Oncology. 2020;25(2):347-353.

41. Gallo F, Sforza S, Luciani L, et al. Simultaneous robotic partial nephrectomy for bilateral renal masses. World journal of urology. 2022;40(4):1005-1010.

42. Hussein AA, Mohsin R, Qureshi H, et al. Transition from da Vinci to Versius robotic surgical system: initial experience and outcomes of over 100 consecutive procedures. Journal of robotic surgery. 2023;17(2):419-426.

43. Idu MM, Bemelman F, Nurmohamed A, van der Pant K. Robot-assisted donor nephrectomy: Initial results and comparison with the hand-assisted laparoscopic technique. A retrospective study. International Journal of Surgery Open. 2022;43:100481.

44. Kim J, Na JC, Lee JS, Jang WS, Han WK. Clinical Implications for da Vinci SP Partial Nephrectomy in High-Complexity Tumors: Propensity Score-Matching Analysis. Journal of endourology. 2022;36(10):1290-1295.

45. Li X, Xu W, Fan S, et al. Robot-assisted Partial Nephrectomy with the Newly Developed KangDuo Surgical Robot Versus the da Vinci Si Surgical System: A Double-center Prospective Randomized Controlled Noninferiority Trial. European urology focus. 2023;9(1):133-140.

46. Motoyama D, Aki R, Matsushita Y, et al. Early Single-Center Experience with Robotic Partial Nephrectomy Using the da Vinci Xi: Comparative Assessment with Conventional Open Partial Nephrectomy. Current Urology. 2019;13(1):13-18.

47. Motoyama D, Ito T, Sugiyama T, Otsuka A, Miyake H. Comparison of perioperative outcomes among patients with exophytic, mesophytic, and endophytic renal tumors undergoing robot-assisted partial nephrectomy. Int J Urol. 2022;29(9):1026-1030.

48. Pellegrino AA, Chen G, Morgantini L, Calvo RS, Crivellaro S. Simplifying Retroperitoneal Robotic Single-port Surgery: Novel Supine Anterior Retroperitoneal Access. European Urology. 2023.

49. Pradere B, Peyronnet B, Khene ZE, Mathieu R, Verhoest G, Bensalah K. Simplified robot-assisted partial nephrectomy: step-by-step technique and perioperative outcomes. Journal of Robotic Surgery. 2019;13(2):245-251.

50. Seyam RM, Alalawi MM, Alkhudair WK, et al. Operative outcomes of robotic partial nephrectomy: A report of the first 101 cases from a single center in Saudi Arabia. Saudi Medical Journal. 2019;40(1):33-40.

51. Shukla D, Small A, Mehrazin R, Palese M. Single-port robotic-assisted partial nephrectomy: initial clinical experience and lessons learned for successful outcomes. Journal of robotic surgery. 2021;15(2):293-298.

52. Takagi K, Kimenai HJAN, Terkivatan T, Tran KTC, Ijzermans JNM, Minnee RC. Learning curves of minimally invasive donor nephrectomy in a high-volume center: A cohort study of 1895 consecutive living donors. International Journal of Surgery. 2021;86:7-12.

53. Wang J, Fan S, Shen C, et al. Partial nephrectomy through retroperitoneal approach with a new surgical robot system, KD-SR-01. Int j med robot comput assist surg. 2022;18(2):e2352.

54. Xu W, Dong J, Xie Y, et al. Robot-Assisted Partial Nephrectomy with a New Robotic Surgical System: Feasibility and Perioperative Outcomes. Journal of endourology. 2022;36(11):1436-1443.

55. Zhuang J, Yang X, Qian J, et al. Renal Functional and Perioperative Outcomes of Retroperitoneal Robot-Assisted Versus Laparoscopic Partial Nephrectomy with Segmental Renal Artery Clamping. Journal of Laparoendoscopic and Advanced Surgical Techniques. 2022;32(5):545-549.

56. Abou Zeinab M, Kaviani A, Ferguson EL, Beksac AT, Eltemamy M, Kaouk J. A Transition Toward a Faster Recovery in Single-Port Transvesical Simple Prostatectomy. Journal of Endourology. 2022;36(8):1036-1042.

57. Agarwal DK, Sharma V, Toussi A, et al. Initial Experience with da Vinci Single-port Robot-assisted Radical Prostatectomies. European Urology. 2020;77(3):373-379.

58. Alip S, Koukourikis P, Han WK, Rha KH, Na JC. Comparing Revo-i and da Vinci in Retzius-Sparing Robot-Assisted Radical Prostatectomy: A Preliminary Propensity Score Analysis of Outcomes. Journal of Endourology. 2022;36(1):104-110.

59. Anakievski D, Marinov R, Gocheva I, Nikolov V, Abushev P. ROBOT-ASSISTED RADICAL PROSTATECTOMY WITH DA VINCI XI: OUR INITIAL EXPERIENCE. Journal of IMAB - Annual Proceeding (Scientific Papers). 2022;28(1):4310-4315.

60. Balestrazzi E, Paciotti M, Piro A, et al. Comparative analysis of robot-assisted simple prostatectomy: the HUGO™ RAS system versus the DaVinci® Xi system. Prostate Cancer and Prostatic Diseases. 2023.

61. Bassett JC, Salibian S, Crivellaro S. Single-Port Retzius-Sparing Robot-Assisted Radical Prostatectomy: Feasibility and Early Outcomes. Journal of endourology. 2022;36(5):620-625.

62. Cardi A, Palleschi G, Patruno G, et al. Robot-assisted simple prostatectomy for treatment of large prostatic adenomas: surgical technique and outcomes from a high-volume robotic centre. World journal of urology. 2023;41(2):515-520.

63. Chang Y, Xu W, Lu X, et al. Robotic Perineal Radical Prostatectomy: Initial Experience with the da Vinci Si Robotic System. Urologia internationalis. 2020;104(9-10):710-715.

64. Deng W, Chen R, Zhu K, et al. Functional Preservation and Oncologic Control following Robot-Assisted versus Laparoscopic Radical Prostatectomy for Intermediate- and High-Risk Localized Prostate Cancer: A Propensity Score Matched Analysis. Journal of Oncology.

65. Fan S, Hao H, Chen S, et al. Robot-Assisted Laparoscopic Radical Prostatectomy Using the KangDuo Surgical Robot System vs the da Vinci Si Robotic System. Journal of endourology. 2023;37(5):568-574.

66. Fan S, Zhang Z, Wang J, et al. Robot-Assisted Radical Prostatectomy Using the KangDuo Surgical Robot-01 System: A Prospective, Single-Center, Single-Arm Clinical Study. Journal of Urology. 2022;208(1):119-127.

67. Francavilla S, Veccia A, Dobbs RW, et al. Radical prostatectomy technique in the robotic evolution: from da Vinci standard to single port-a single surgeon pathway. Journal of robotic surgery. 2022;16(1):21-27.

68. Fulcoli V, Bianco M, Sartor G, Agostini A, Costa G, Laurini L. Safety of robot-assisted radical prostatectomy in an Italian spoke hospital: Long-term oncologic and functional outcomes with median 11.3 years follow-up. Urologia Journal. 2022;89(2):248-256.

69. Garg H, Seth A, Singh P, Kumar R. Changing trends in robot-assisted radical prostatectomy: Inverse stage migration-A retrospective analysis. Prostate international. 2021;9(3):157-162.

70. Ju GQ, Wang ZJ, Shi JZ, et al. A comparison of perioperative outcomes between extraperitoneal robotic single-port and multiport radical prostatectomy with the da Vinci Si Surgical System. Asian journal of andrology. 2021.

71. Kaouk J, Valero R, Sawczyn G, Garisto J. Extraperitoneal single-port robot-assisted radical prostatectomy: initial experience and description of technique. BJU international. 2020;125(1):182-189.

72. Kaouk JH, Ferguson EL, Beksac AT, et al. Single-port Robotic Transvesical Partial Prostatectomy for Localized Prostate Cancer: Initial Series and Description of Technique. European urology. 2022;82(5):551-558.

73. Kim KH, Song W, Yoon H, Lee DH. Single-port robot-assisted radical prostatectomy with the da Vinci SP system: A single surgeon's experience. Investigative and clinical urology. 2020;61(2):173-179.

74. Lei K-Y, Xie W-J, Fu S-Q, Ma M, Sun T. A comparison of the da Vinci Xi vs. da Vinci Si surgical systems for radical prostatectomy. BMC surgery. 2021;21(1):409.

75. Luciani LG, Mattevi D, Puglisi M, et al. Robotic-assisted radical prostatectomy following colo-rectal surgery: a user's guide. Journal of Robotic Surgery. 2022;16(1):189-192.

76. Ng C-F, Teoh JY-C, Chiu PK-F, et al. Robot-assisted single-port radical prostatectomy: A phase 1 clinical study. International journal of urology: official journal of the Japanese Urological Association. 2019;26(9):878-883.

77. Ragavan N, Bharathkumar S, Chirravur P, Sankaran S. Robot-Assisted Laparoscopic Radical Prostatectomy Utilizing Hugo RAS Platform: Initial Experience. J Endourol. 2023;37(2):147-150.

78. Ramos-Carpinteyro R, Ferguson EL, Chavali JS, Geskin A, Kaouk J. First 100 cases of

transvesical single-port robotic radical prostatectomy. Asian Journal of Urology. 2023.

79. Saidian A, Fang AM, Hakim O, Magi-Galluzzi C, Nix JW, Rais-Bahrami S. Perioperative Outcomes of Single vs Multi-Port Robotic Assisted Radical Prostatectomy: A Single Institutional Experience. The Journal of urology. 2020;204(3):490-495.

80. Thillou D, Robin H, Ricolleau C, et al. Robot-assisted Radical Prostatectomy with the Dexter Robotic System: Initial Experience and Insights into On-demand Robotics. European urology. 2023.

81. Tillu ND, Kulkarni JN. Long-term comparative outcome analysis of a robot-assisted laparoscopic prostatectomy with retropubic radical prostatectomy by a single surgeon. Journal of Robotic Surgery. 2023;17(2):677-685.

82. Waigankar SS, Yuvaraja TB, Dev P, Agarwal V, Pednekar AP, Kulkarni B. Robotic Freyer's prostatectomy: Operative technique and single-center experience. Indian Journal of Urology. 2021;37(3):247-253.

83. Yilmazel FK, Sam E, Cinislioglu AE, et al. Comparison of Perioperative, Oncological, and Functional Outcomes of Three-Dimensional Versus Robot-Assisted Laparoscopic Radical Prostatectomy: A Preliminary Study. Journal of laparoendoscopic & advanced surgical techniques Part A. 2022;32(3):304-309.

84. Fang AM, Saidian A, Magi-Galluzzi C, Nix JW, Rais-Bahrami S. Single-port robotic partial and radical nephrectomies for renal cortical tumors: initial clinical experience. Journal of Robotic Surgery. 2020;14(5):773-780.

85. Gandi C, Totaro A, Bientinesi R, et al. Purely Off-Clamp Partial Nephrectomy: Robotic Approach Better than Open Using a Pentafecta Outcome with Propensity Score Matching. Journal of Clinical Medicine. 2022;11(21):6241.

86. Hennessey DB, Wei G, Moon D, et al. Strategies for success: a multi-institutional study on robot-assisted partial nephrectomy for complex renal lesions. BJU International. 2018;121(Supplement 3):40-47.

87. Lin T, Liu G, Zhang S, Guo H. Comparisons of the safety and effectiveness of robot-assisted versus laparoscopic partial nephrectomy for large angiomyolipomas: a propensity score-matched analysis. International Urology and Nephrology. 2020;52(9):1675-1682.

88. Abou Zeinab M, Beksac AT, Corse T, et al. The Multi-Institutional Experience in Single-Port Robotic Transvesical Simple Prostatectomy for Benign Prostatic Hyperplasia Management. The Journal of urology. 2022;208(2):369-378.

89. Abou Zeinab M, Beksac AT, Ferguson E, et al. Single-port Extraperitoneal and Transperitoneal Radical Prostatectomy: A Multi-Institutional Propensity-Score Matched Study. Urology. 2023;171:140-145.

90. Carbonara U, Minafra P, Papapicco G, et al. Xi Nerve-sparing Robotic Radical Perineal Prostatectomy: European Single-center Technique and Outcomes. European Urology Open Science. 2022;41:55-62.

91. Chen SH, Wu CH, Wu R, et al. Surgical and functional outcomes of robotic-assisted radical prostatectomy in patients with previous transurethral resection of the prostate. Urological Science. 2020;31(6):267-272.

92. Covas Moschovas M, Bhat S, Onol F, Rogers T, Patel V. Early outcomes of single-port robot-assisted radical prostatectomy: lessons learned from the learning-curve experience. BJU International. 2021;127(1):114-121.

93. Covas Moschovas M, Kind S, Bhat S, et al. Implementing the da Vinci SP Without Increasing Positive Surgical Margins: Experience and Pathologic Outcomes of a Prostate Cancer Referral Center. Journal of endourology. 2022;36(4):493-498.

94. Khalil MI, Chase A, Joseph JV, Ghazi A. Standard Multiport vs Single-Port Robot-Assisted Simple Prostatectomy: A Single-Center Initial Experience. Journal of endourology. 2022;36(8):1057-1062.

95. Levy A, Wilder S, Butaney M, et al. Solving clinical challenges in prostate cancer using the single-port robot system. Urology Video Journal. 2023;18:100222.

96. Moschovas MC, Bhat S, Sandri M, et al. Comparing the Approach to Radical Prostatectomy Using the Multiport da Vinci Xi and da Vinci SP Robots: A Propensity Score Analysis of Perioperative Outcomes. European urology. 2021;79(3):393-404.

97. Ni K, Xue D, Li G. Transperineal single-port robot-assisted radical prostatectomy with Si da Vinci surgical system: Initial experience and description of technique. Translational Cancer Research. 2021;10(11):4694-4701.

98. Noh TI, Tae JH, Shim JS, et al. Initial experience of single-port robot-assisted radical prostatectomy: A single surgeon's experience with technique description. Prostate international. 2022;10(2):85-91.

99. Noh TI, Kang YJ, Shim JS, et al. Single-Port vs Multiport Robot-Assisted Radical Prostatectomy: A Propensity Score Matching Comparative Study. Journal of endourology. 2022;36(5):661-667.

100. Steinberg RL, Passoni N, Garbens A, Johnson BA, Gahan JC. Initial experience with extraperitoneal robotic-assisted simple prostatectomy using the da Vinci SP surgical system. Journal of robotic surgery. 2020;14(4):601-607.

101. Talamini S, Halgrimson WR, Dobbs RW, Morana C, Crivellaro S. Single port robotic radical prostatectomy versus multi-port robotic radical prostatectomy: A human factor analysis

during the initial learning curve. International Journal of Medical Robotics and Computer Assisted Surgery. 2021;17(2):e2209.

102. Gross JT, Vetter JM, Sands KG, et al. Initial Experience with Single-Port Robot-Assisted Radical Cystectomy: Comparison of Perioperative Outcomes between Single-Port and Conventional Multiport Approaches. Journal of Endourology. 2021;35(8):1177-1183.

103. Bang S, Shin D, Moon HW, et al. Comparison of Transperitoneal and Retroperitoneal Partial Nephrectomy with Single-Port Robot. Journal of endourology. 2023;37(5):551-556.

104. Glaser ZA, Burns ZR, Fang AM, et al. Single- versus multi-port robotic partial nephrectomy: a comparative analysis of perioperative outcomes and analgesic requirements. Journal of Robotic Surgery. 2022;16(3):695-703.

105. Kishore TA, Pathrose G, Raveendran V, et al. Robot-assisted laparoscopic radical nephrectomy and inferior vena cava thrombectomy: A multicentre Indian experience. Arab Journal of Urology. 2020;18(2):124-128.

106. Krishnan NK, Zappia J, Calaway AC, Nagle RT, Sundaram CP, Boris RS. Identifying Preoperative Predictors of Operative Time and Their Impact on Outcomes in Robot-Assisted Partial Nephrectomy. Journal of Endourology. 2022;36(1):71-76.

107. Lin C-Y, Yang C-K, Ou Y-C, et al. Long-term outcome of robotic partial nephrectomy for renal angiomyolipoma. Asian journal of surgery. 2018;41(2):187-191.

108. Park BK, Gong IH, Kang MY, et al. RFA versus robotic partial nephrectomy for T1a renal cell carcinoma: a propensity score-matched comparison of mid-term outcome. European Radiology. 2018;28(7):2979-2985.

109. Watanabe H, Motoyama D, Sato R, et al. Health-Related Quality of Life in Patients with Small Renal Mass Who Underwent Robot-Assisted Partial Nephrectomy: A Prospective Evaluation. Journal of endourology. 2021;35(11):1644-1649.

110. Cho JM, Moon KT, Lee JH, Choi JD, Kang JY, Yoo TK. Open simple prostatectomy and robotic simple prostatectomy for large benign prostatic hyperplasia: Comparison of safety and efficacy. Prostate International. 2021;9(2):101-106.

111. Hou W, Wang B, Zhou L, et al. Single-site multiport vs. conventional multiport robot-assisted radical prostatectomy: A propensity score matching comparative study. Frontiers in surgery. 2022;9:960605.

112. Hwang BY, Lee D, Kwon JY, Kim O, Hong JM, Kim HJ. A Study of 57 Patients with Prostate Cancer to Compare Outcomes of Estimated Blood Loss and Postoperative Pain between Robot-Assisted Laparoscopic Radical Prostatectomy and Standard Laparoscopic Radical Prostatectomy. Medical Science Monitor. 2023;29:e939584.

113. Kaouk J, Aminsharifi A, Wilson CA, et al. Extraperitoneal versus Transperitoneal Single Port Robotic Radical Prostatectomy: A Comparative Analysis of Perioperative Outcomes. The Journal of urology. 2020;203(6):1135-1140.

114. Kim BH, Byun HJ. Robotic-assisted simple prostatectomy versus holmium laser enucleation of the prostate for large benign prostatic hyperplasia: A single-center preliminary study in Korea. Prostate International. 2022;10(3):123-128.

115. Luo C, Yang B, Ou Y, et al. Experience with an innovative surgical approach: 321 cases modified extraperitoneal single-incision robot-assisted laparoscopic radical prostatectomy without dedicated PORT based on Da Vinci SI system. Journal of Robotic Surgery. 2023.

116. Oshima M, Washino S, Nakamura Y, et al. Risks and complications of robot-assisted radical prostatectomy (RARP) in patients receiving antiplatelet and/or anticoagulant therapy: a retrospective cohort study in a single institute. Journal of Robotic Surgery. 2021;15(4):661-670.

117. Tanhaeivash R, Grimm MO. Factors Affecting Transperitoneal Robot-Assisted Laparoscopic Radical Prostatectomy. Journal of Laparoendoscopic and Advanced Surgical Techniques. 2022;32(7):781-786.

118. Carbin DD, Tamhankar AS, Ahluwalia P, Gautam G. Robot-assisted radical prostatectomy in indian men of age 75 years and above: a propensity score-matched analysis. Journal of Robotic Surgery. 2022;16(4):799-806.

119. Iguchi K, Tanaka T, Minami A, Kuratsukuri K, Uchida J, Nakatani T. Characteristics of urodynamic study parameters associated with intermediate-term continence after robot-assisted radical prostatectomy in elderly patients. Aging Male. 2021;23(5):1039-1045.

120. Bray G, Bahadori A, Mao D, Ranasinghe S, Tracey C. Benefits of Robotic Assisted vs. Traditional Laparoscopic Partial Nephrectomy: A Single Surgeon Comparative Study. Journal of clinical medicine. 2022;11(23).

121. Ferriero M, Brassetti A, Mastroianni R, et al. Off-clamp robot-assisted partial nephrectomy for purely hilar tumors: Technique, perioperative, oncologic and functional outcomes from a single center series. European Journal of Surgical Oncology. 2022;48(8):1848-1853.

122. Amornratananont N, Sirisopana K, Worawichawong S, et al. Perioperative outcomes of robot-assisted laparoscopic radical prostatectomy (RALRP) and LRP in patients with prostate cancer based on risk groups. Arab Journal of Urology. 2020;18(3):187-193.

123. De Groote R, Nathan A, De Bleser E, et al. Techniques and Outcomes of Salvage Robot-Assisted Radical Prostatectomy (sRARP). European Urology. 2020;78(6):885-892.

124. Kadhim H, Ang KM, Tan WS, et al. Retzius-sparing technique independently predicts early recovery of urinary continence after robot-assisted radical prostatectomy. Journal of Robotic Surgery. 2022;16(6):1419-1426.

125. Moschovas MC, Bhat S, Fikret O, Travis R, Vipul P. Modified simple prostatectomy: an approach to address large volume BPH and associated prostate cancers. Journal of Robotic Surgery. 2020;14(4):543-548.

126. Simsir A, Kizilay F, Aliyev B, Kalemci S. Comparison of robotic and open radical prostatectomy: Initial experience of a single surgeon. Pakistan Journal of Medical Sciences. 2020;37(1):1-8.

127. Venckus R, Jasenas M, Telksnys T, et al. Robotic-assisted radical prostatectomy with the Senhance R robotic platform: single center experience. World journal of urology. 2021;39(12):4305-4310.
128. Yu J, Park JY, Lee J, Ha S, Hong JH, Kim YK. Preoperative bullae and subsequent pneumothorax in 6605 patients who underwent robotic prostatectomy. Journal of Anesthesia. 2022;36(6):740-746.
129. Yu C, Xu L, Ye L, et al. Single-port robot-assisted perineal radical prostatectomy with the da Vinci XI system: initial experience and learning curve using the cumulative sum method. World journal of surgical oncology. 2023;21(1):46.
130. Koukourikis P, Alqahtani AA, Almujalhem A, Lee J, Han WK, Rha KH. Robot-assisted partial nephrectomy for high-complexity tumors (PADUA score >=10): Perioperative, long-term functional and oncologic outcomes. International Journal of Urology. 2021;28(5):554-559.

18. Appendices

18.1 RAS URO Clavien-Dindo Grades and Examples

Reference: Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 subjects and results of a survey. Ann Surg. 2004;240(2):205-213. https://www.ncbi.nlm.nih.gov/pubmed/15273542

Grade	Definition
Grade I	Any deviation from the normal postoperative 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	Definition
Grade IVa	Single organ dysfunction (including dialysis)
Grade IVb	Multiorgan dysfunction
Grade V	Death of a patient
*Brain hemorrhage, ischemic stroke, subarrachnoidal 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

Grades	Organ System	Examples
	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

Grades	Organ System	Examples
	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 temponade 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
	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)

Grades	Organ System	Examples
	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

Provided under separate cover.

19. Version History

Version	Summary of changes	Author(s)/Title
1.0	Not Applicable, New Document	[redacted]
2.0	• Secondary Endpoints: Added to include 5-year follow-up for oncology subjects • Updated stopping rules to ensure patient safety oversight • Updated exclusion criteria for oncology prostatectomy subjects Added roll-in phase to assess **Hugo™** RAS System performance	[redacted]
3.0	• Added primary effectiveness endpoint • Updated Statistical Design and Methods section	[redacted]
4.0	• Updated definition of Conversion • Updated Clinical Study Design Justifications to include safety and effectiveness	[redacted]

Version	Summary of changes	Author(s)/Title
5.0	• During the review of the investigational plan, the FDA recommended to add performance goals for the secondary endpoints. As per the FDA, pre-specifications of performance goals for the secondary endpoints will help evaluate the benefit-risk profile for the • investigational device to support the marketing approval. Following the recommendation, performance goals are specified for each of the secondary endpoints • Removed Steering Committee Member due to outside of the study conflict of interest not related to the trial • Changed margin, tumor size, tumor stage and total lymph nodes retrieved to follow-up visit. Pathology takes 10-14 days to be returned • Updated causality definitions • Updated template version • Section 16.8.1: Updated requirements due to the combined guidelines	[redacted]
6.0	• Updated template to Rev E • Updated to include a 6th site	[redacted]
7.0	• Added an additional Steering Committee Member • Updated definition of conversion • Updated Risk Section to match the new Risk Management Report. • Added Anastomotic Leak Test (if applicable) to the schedule of events • Added Anastomotic Stricture (if applicable)	[redacted]

Version	Summary of changes	Author(s)/Title
8.0	• Adverse Event reporting guidelines were updated • Administrative changes of commercial materials. We removed TUNVCA8STF and added ONB123TF and ONB5STF • Time to submit events to the CEC for adjudication has been removed to allow for more complete submissions. • Updated the definition of "complication rate" to align with that in published literature data that were used to determine performance goals • Updated sample sizes of the nephrectomy and prostatectomy cohorts • Updated the primary and secondary endpoint performance goals and clinical rationales for all three cohorts • Included the bibliography of publications utilized for the updated statistical design • Time to submit events to the CEC adjudication has been removed to allow for more complete submission	[redacted]
9.0	• Updated the publications supporting the statistical design for the performance goals for all three cohorts • Updated the Secondary performance goals for all three cohorts • Formatting edits • Text edits to provide clarification	[redacted]