

Virtual Incision Corporation IDE Clinical Study Protocol

**Protocol Title: Virtual Incision Robotically Assisted Surgical Device (VI RASD) for Umbrella
 Surgical Procedures: Minimally Invasive Right and Left Colectomy**

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Investigator Acknowledgement and Agreement

I have read the protocol specified below and will abide by the terms of this protocol. In my formal capacity as Investigator, my duties include ensuring the safety of the study subjects enrolled under my supervision, including following all requirements of the informed consent process, and providing Virtual Incision Corporation or its designee with complete and timely information, as outlined in the protocol. It is understood that all information pertaining to the study will be held strictly confidential and that this confidentiality requirement applies to all study staff at this site.

Furthermore, on behalf of the study staff and myself, I agree to maintain the procedures required to carry out the study in accordance with accepted GCP principles, 21 CFR-Part 812, conditions of study approval imposed by the reviewing IRB and/or FDA, sufficient and accurate financial disclosure information that includes relevant updates that may occur during the investigation and for one year following the completion of the study.

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Investigator Signature

Date
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Print Name and Title

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List of Abbreviations

AE	Adverse Event
CEC	Clinical Events Committee
CI	Confidence Interval
CFR	Code of Federal Regulations
CRF	Case Report Form
CRO	Clinical Research Organization
DSMB	Data and Safety Management
EDC	Electronic Data Capture
ESU	Electrosurgical Unit
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Lab Practice
HALS	Hand-Assist Laparoscopic Port
H&P	History and Physical Examination
HIPAA	Health Insurance Portability and Accountability Act of 1996
ICF	Informed Consent Form
IRB	Institutional Review Board
PI	Principal Investigator
RASD	Robotically Assisted Surgical Device
VI RASD	Virtual Incision Robotically Assisted Surgical Device
SAE	Serious Adverse Event
TMF	Trial Master File
TX	Treatment
UADE	Unanticipated Adverse Device Effect/Event
VI or VIC	Virtual Incision Corporation

PROTOCOL SYNOPSIS

TITLE	Virtual Incision Robotically Assisted Surgical Device (VI RASD) for Umbrella Surgical Procedures: Minimally Invasive Right and Left Colectomy
SPONSOR	Virtual Incision Corporation
FUNDING ORGANIZATION	Virtual Incision Corporation
NUMBER OF SITES	Up to 4 US sites
STUDY PURPOSE	The purpose of the clinical study is to evaluate the device's indications for use in the clinical-use environment. The study's data will: 1. Confirm through successful completion of this study that the device functions as intended in the operating room environment; and, 2. Demonstrate safety and efficacy of the device as defined by the primary endpoints 3. Quantify the use of the device relative to the secondary endpoints. This study will not evaluate treatment outcomes or the effect of the treatment on any disease.
STUDY DESIGN	This is a prospective multi-center, multi-operator, non-randomized, consecutively enrolled clinical evaluation study.

PROTOCOL SYNOPSIS (CONTINUED)

PRIMARY OBJECTIVES	Efficacy: Successful completion of the VI RASD steps without conversion to open surgery. VI RASD system will be used to manipulate and dissect the right and left colon for resection using robotic bipolar grasper and robotic mono-polar scissors by dividing the colon attachments and preparing the colon for resection. Laparoscopic ports (trocar sites) may be used for ancillary tasks such as retraction, advanced energy, stapling, and suction. Safety: Determine the safety profile of intraoperative and postoperative clinical data of the VI RASD to current standard of care (robotic, laparoscopic, open) data in right and left colectomies.
SECONDARY OBJECTIVES	Data for twelve (12) key clinical outcomes/clinical assessments measures shall be reported using the following endpoints: ● Length of Stay ● Intraoperative Complications (Including anastomosis adverse events) ● Transfusions ● Conversion Rate ● Operative Time ● Postoperative Complications through 30 days ● Readmission Rates through 30 days ● Re-encounter Rates through 30 days ● Reoperation Rates through 30 days ● Disease Recurrence Rates through 30 days ● Mortality through 30 days ● Number of laparoscopic ports (trocar sites) used and reason for use.
ONCOLOGY RELATED TERTIARY OBJECTIVES	● Incidence of Cancer related death ● Incidence of Cancer status-active, remission, metastasized, reoccurrence

	● Incidence of additional surgery/procedures to treat pre- existing cancer at time of procedure.
NUMBER OF SUBJECTS	Up to 30

PROTOCOL SYNOPSIS (CONTINUED)

SUBJECT SELECTION CRITERIA	<u>Population</u> Patients presenting with the medical and/or surgical indication for right or left colon. <u>Inclusion Criteria</u> a) Subject is able to provide informed consent b) 22-85 years of age c) No history of frozen abdomen due to abdominal adhesions or multiple previous bowel obstructions d) Body mass index (BMI) between 19.5- 45 kg/m² e) A weight of at least 100 lbs. (45.36 kg.). f) Height of at least 60 inches (152 cm) g) ASA grades I through III h) Available for required postoperative follow up visits at 14 days and 30 days <u>Exclusion Criteria</u> a) Subject unable or unwilling to provide informed consent b) Under the age of 22 or greater than the age of 85 years c) Has polyps that can be completely removed with negative surgical margins by colonoscopy. d) Has Stage T4 cancer diagnosis e) History of abdominal adhesions or bowel obstruction f) BMI of < 19.5 and > 45 kg/m² g) Heights < 60 inches h) ASA grades IV-VI i) End stage renal disease j) Liver Cirrhosis k) Women who are pregnant or lactating l) Active infection or has a history of local or systemic infection within 30 days of study screening m) Has had major surgery within 30 days prior to study enrollment or is scheduled to have major surgery within 30 days n) Has participated or is participating in another clinical study which may confound study results o) In the opinion of the Investigator, patient is not likely to comply with the required protocol activities; or, has a medical condition that should exclude the patient from the study p) Hemoglobin < 8.0 q) Not currently coagulopathic
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PROTOCOL SYNOPSIS (CONTINUED)

TEST DEVICE	VI RASD
DEVICE INDICATIONS FOR USE	The VI RASD is a surgical tool intended to assist in the accurate control of Virtual Incision Endoscopic Instruments for endoscopic manipulation of tissue during bowel resection procedures. The system is indicated for use in adults at least 5'0" (1.524 m) tall and having a weight of at least 100 lbs. (45.36 kg.). It is not intended for pediatric use. It is intended to be used by trained physicians in an operating room environment in accordance with the representative specific procedures. The demonstration of safety and effectiveness for the representative specific procedures was based on evaluation of the device as a surgical tool and did not include evaluation of outcomes related to the treatment of cancer (overall survival, disease-free survival, local recurrence) or treatment of the patient's underlying disease/condition. Device usage in all surgical procedures should be guided by the clinical judgment of an adequately trained surgeon.
DURATION OF SUBJECT PARTICIPATION AND DURATION OF STUDY	Subject participation in the study will be for up to 4 months. ● Screening visit: up to 60 days prior to procedure ● Baseline visit: less than 30 days from procedure ● Treatment: 1 day ● Follow-up: 14- and 30-day visits, postoperatively The total duration of the study is expected to be 12 months. Five months for subject recruitment and 3 months for subject treatment and follow up. If the subject has a pre-existing colon cancer diagnosis or newly diagnosed as a result of participating in the study, the subject will be referred to an Oncologist for long term follow up. The Sponsor will follow up with the Oncologist on an annual basis for 5 years to obtain information about living and cancer status.

PROTOCOL SYNOPSIS (CONTINUED)

PRIMARY ENDPOINTS	<u>Efficacy</u> The Primary Efficacy Endpoint is the successful completion of the VI RASD steps without conversion to open surgery. VI RASD steps are defined as manipulating and dissecting the right and left colon for resection using robotic bipolar grasper and robotic mono-polar scissors by dividing the colon attachments and preparing the colon for resection. Laparoscopic ports (trocar sites) may be used for ancillary tasks such as retraction, advanced energy, stapling, and suction. VI RASD steps also include the following steps: 1. Inserting the VI RASD robot through the access port and deploying it to the corresponding abdominal quadrant. 2. Ensuring the colon is adequately and primarily dissected and exposed with the VI RASD end effectors with graspers and scissors for tissue manipulation, cutting, blunt and sharp dissection, tissue hemostasis with electrocautery while maintaining pneumo-peritoneum and visualization. 3. Success transection of the Colon and Small Bowel using assistant port manual surgical stapler (e.g. Edo GIA). 4. Removal of the VI RASD robot from the abdominal cavity <u>Safety</u> Determine the safety profile of intraoperative and postoperative clinical data of the VI RASD in right and left colectomies as demonstrated by: ● Overall intraoperative and post operative (within 30 days) adverse events compared to published literature. ● Incidence of intraoperative serious adverse events, specified as either device-related or procedure-related events. ● Incidence of postoperative serious adverse events, specified as either device-related or procedure-related events within 14 days of surgical procedure. ● Incidence of postoperative serious adverse events, specified as either device-related or procedure-related events within 30 days* of surgical procedure (14 day events are also included in the 30-day analysis). ● Incidence of Serious Adverse Events unrelated to device or procedure. <i>*If the adverse event continues at the 30 day follow up visit, the subject shall continue to be followed until resolution of the event, as determined by the Investigator.</i>
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PROTOCOL SYNOPSIS (CONTINUED)

PLANNED DATA ANALYSIS	Data will be evaluated during throughout the study conduct by the data safety monitoring board (DSMB). These evaluations will occur: • Every three (3) months, for the purpose of monitoring study conduct and assessing patient safety. • After every 10 patients treated and will evaluate primary and safety endpoints. The analysis will be characterized by number of patients, percentages, numbers and rates of occurrence. When the study is complete, VI RASD clinical benefit will be assessed and determined using data collected from the primary and secondary endpoints. As the interim evaluations are intended only to support safety review of the study, there will be no adjustment to confidence interval widths or p-values for any inferential tests provided for the final analysis.
STATISTICS: PRIMARY DATA ANALYSIS PLAN	Study variables will be tabulated and summarized by descriptive analysis (i.e. percentages, rates, number of subjects or total number of subjects). For primary and secondary outcomes, a two-sided 95% CI will be provided based on the exact binomial interval or for the mean value using a T-distribution. Adverse Events and Serious Adverse Events will be summarized by presenting the number and percentage of subjects having any adverse event. Events will be reported using the criteria described in section 5.1- Safety Endpoints.
RATIONALE FOR NUMBER OF SUBJECTS	The sample size was selected to provide at least 80% chance to observe at least one safety event if the event occurs in at least 5.3% of subjects. The upper bound of the event rate if no events are observed or for the rate to conversions to open surgery if no conversions are reported is 11.6% (0/30).

1 Background

1.1 Device Clinical Development and Need

Laparoscopic approaches to general surgical procedures were developed during this same time and have been used for over 30 years, including for the treatment of colorectal surgeries [1]. This minimally invasive surgical approach, compared to open surgical repair, produced similar favorable operative results as robotic medicine. However, manipulation of instrumentation and the accuracy of repetitive tasks remain needs of the surgeon. These needs fostered the development of robotics for surgery.

The application of robotics in surgery were designed to provide surgeons capabilities that enabled the accurate performance of surgical tasks. Robotics have been developed by the ‘master-slave’ concept; that is, to enable the surgeon to perform such tasks from a remote workstation under a magnified field of view [2]. Multiple medical robotic platforms have been developed to address technique shortcomings or enhance surgical procedures in general surgery, cardiothoracic surgery, cardiology, orthopedics, genitourinary surgery and oncology. Clinical studies with the use of these devices have demonstrated reduced operative times, reduced operative and postoperative morbidity, reduced conversion to open repair and reduced operator fatigue with greater patient treatment satisfaction. However, cost of these devices has remained a primary concern for the medical community.

The da Vinci® Surgical System robot (Intuitive Surgical Corporation, Sunnyvale, CA) was the first device to be approved and iterated to meet the needs of multiple surgical specialties. The advancement of this technology has produced smaller instrumentation, more accurate robotic movement, haptic feedback, and enhanced visualization of the operative field. Despite these improvements, the device remains cumbersome to set up and establish the surgical field. These and other shortcomings can lead to procedure conversions, either laparoscopic or open surgical repair.

The Virtual Incision RASD is a medical device used to perform abdominal surgery through one small incision in the abdominal wall. The VI RASD accurately manipulates graspers and scissors for tissue manipulation and approximation, including grasping, cutting, blunt and sharp dissection, ligation, and electrocautery, while maintaining pneumo-peritoneum, visualization and triangulation of the mini-robot’s arms and camera. The system affords the surgeon with situational awareness and precision positioning of the instrumentation to traverse the anatomy, access the surgical target, and excise it for evaluation. As a result, the aforementioned advantages of medical robotics will be sustained while affording the surgeon the technical ease to reach complex anatomical targets.

1.2 Disease Overview

Adenomatous colorectal polyps are fleshy growths that occur in the lumen of the colon or rectum. If untreated, these lesions can progress to colorectal cancer. An estimated 5% of people over 60 will have at least one polyp of 1 cm or greater [3]. Adenomatous polyps should be removed by colonoscopy, if possible, and examined to determine if the tissue removed is cancerous. In many cases the polyp is too large to remove by endoscopy or the base of the polyp has a cancer positive margin and the affected segment of colon should be removed [4].

1.3 Standard of Care and Treatment Options

Colectomy consists of the surgical resection of any extent of the large intestine (colon). It is also an occasional term used to describe removing the entire large intestine along with the rectum. The indications for colectomy include, but are not limited to, colon cancer, diverticulitis and diverticular disease, trauma, inflammatory bowel disease, bowel infarction, typhlitis and prophylactic colectomy in

cases of polyposis, Lynch syndrome, and certain cases of inflammatory bowel disease due to the high risk of cancer development.

Relative to cancer and other pre-existing marketed devices (e.g. Da Vinci), oncological outcomes were not reported. Rather, it was premeditated that the device was evaluated only as a surgical tool used by the adequately trained surgeon applying clinical judgement.

As a result, a precaution statement is used by the device manufacturer for the device's labeling:

"Precaution for Representative Uses (USA) The demonstration of safety and effectiveness for the representative specific procedures was based on evaluation of the device as a surgical tool and did not include evaluation of outcomes related to the treatment of cancer (overall survival, disease-free survival, local recurrence) or treatment of the patient's underlying disease/condition. Device usage in all surgical procedures should be guided by the clinical judgment of an adequately trained surgeon."

Surgical removal of the colon is not without risk [5]. The most common complications are bleeding, infection and anastomotic dehiscence. Anastomotic dehiscence is a breakdown of the stiches used in the surgical procedure to re-attach the intestine, which can lead to a contamination of the peritoneal cavity, peritonitis and death. Incisional hernias are a complication that can occur in all abdominal surgical procedures, both open and laparoscopic. Today, more than 40% of colon resections are performed laparoscopically [6]. Mortality is uncommon from this procedure and is usually attributed to unrelated events [7].

Laparoscopic colectomy has reduced the time needed for patient recovery and return to work. However, current minimally invasive colorectal surgery has numerous constraints on the surgeon's ability to manipulate the bowel and perform an operation. These include: (a) instruments that are positioned through multiple laparoscopic ports and these laparoscopic ports are not movable with respect to target, (b) poor triangulation of the camera and instrumentation, (c) poor ability to access multiple quadrants in the abdomen, and (d) difficult ergonomic considerations for the surgeons, who often have to stand with arms and shoulders raised for long periods of time to perform laparoscopic procedures with long laparoscopic instruments [8].

The VI RASD is designed to perform surgery through mitigation of these issues with improved ergonomics, flexible surgical robot positioning, triangulation built into the instrumentation and camera setup, and the ability of the surgeon to visualize the target surgical area from multiple angles in the body. The VI RASD is designed to be placed completely inside the abdominal cavity.

2 Study Purpose

The purpose of the clinical study is to evaluate the device's indications for use in the clinical-use environment. The study's data will:

1. Confirm through successful completion of this study that the device functions as intended in the operating room environment; and,
2. Demonstrate safety and efficacy of the device as defined by the primary endpoints
3. Quantify the use of the device relative to the secondary endpoints.

This study will not evaluate treatment outcomes or the effect of the treatment on any disease.

3 Risk Benefit Assessment

3.1 Identification of Risk and Mitigation

The major risks relate to:

- The minimally invasive procedure; and
- Anesthesia complications; and
- The use of the VI RASD in right or left colectomy.

Mitigation of these risks include:

- Trained and experienced surgeons in open surgical and laparoscopic approaches to colectomy.
- Surgical operating procedures per surgeon's institutional guidelines, including conversion indications and use.
- The study population is limited to adult patients and a predetermined cohort of subjects to show safety and feasibility of the VI-RASD in colectomy procedures.
- Successful completion of the VI Training Program prior to using the VI RASD in the first procedure.
- Exclusion of patients with a ASA greater than 3.
- Use of the VI RASD per Instruction for Use.

3.2 Risk of a Minimally Invasive Procedure

All surgical procedures carry potential risks. The risks associated with the RASD minimally invasive colectomy procedure are expected to be similar to those associated with a laparoscopic or other RASD colectomy. Potential complications include the following: incision site pain, procedure pain, contact dermatitis, hemorrhage, anastomotic dehiscence, peritonitis, wound infections, incisional hernias, gas embolism, vagal reaction, ventricular arrhythmias, hypercarbia with acidosis, injuries to the abdominal wall, intra-abdominal organs or major blood vessels. These complications may result in the need for medication, the need for additional surgery, or death.

3.3 Risk of Anesthesia

General anesthesia is overall very safe; most people, even those with significant health conditions, are able to undergo general anesthesia itself without serious problems. In fact, risk of complications is more closely related to the procedure and the subject's general physical health, rather than to the type of anesthesia. Older adults, or those with serious medical problems, particularly those undergoing more extensive procedures, may be at increased risk of nausea, vomiting, postoperative confusion, pneumonia, or even stroke and heart attack.

3.4 Risk of the Use of the VI RASD

The risks associated with the use of the VI RASD system are to be quantified in this study. The VI RASD will report its clinical outcomes as compared to current surgical techniques (laparoscopic, open, and robot assisted) in the following twelve (12) clinical outcome/clinical assessment measures:

- Length of Stay
- Intraoperative Complications (Including anastomosis adverse events)

- Transfusions
- Conversion Rate
- Postoperative Complications through 30 days
- Readmission Rates through 30 days
- Re-encounter Rates through 30 days
- Reoperation Rates through 30 days
- Recurrence Rates through 30 days
- Mortality through 30 days
- Operative Time
- Number of laparoscopic ports (trocar sites) used and reason for use.

As an example of comparison data, in a 2017 publication by Dolejs et al analyzing clinical outcomes from the ACS-NSQIP database comparing elective laparoscopic (Lap) approach (N=25,998) to robotic (Robot) approach (N=1484) from 2012-2014 for left and right colectomies, the following data from page 2392 of the publication were reported in Figure 1 below [10].

OABP only	3.0	2.9		3.4	4.1		5.2	6.3	
MBP + OABP	32.3	39.9	0.02	36.5	32.9	0.02	29.9	24.4	0.35

LAR low anterior resection; *Lap* laparoscopic; *IBD* inflammatory bowel disease; *MBP* mechanical bowel preparation; *OABP* oral antibiotic bowel preparation

Table 3 Unadjusted outcomes of laparoscopic and robotic colectomy stratified by colectomy site

	LAR			Left colectomy			Right colectomy		
	Lap	Robot	p	Lap	Robot	p	Lap	Robot	p
Mortality (%)	0.3	0.3	1	0.5	0.2	0.49	0.4	1.2	0.12
Overall morbidity (%)	21.8	20.5	0.36	19.0	15.6	0.08	22.1	22.0	0.99
Serious morbidity (%)	10.8	10.5	0.81	9.0	7.2	0.19	10.4	11.2	0.66
Convert to open (%)	12.8	6.8	<0.01	8.8	7.2	0.25	10.5	6.2	0.03
Anastomotic leak (%)	3.6	3.9	0.75	2.4	1.7	0.32	2.2	2.3	0.90
Post-op sepsis (%)	3.1	1.6	0.02	2.4	1.4	0.20	2.6	2.7	0.94
Ileus (%)	9.2	9.8	0.55	7.8	6.0	0.18	9.6	10.8	0.53
Superficial SSI (%)	4.4	3.0	0.05	4.2	4.8	0.73	4.9	3.1	0.19
Deep SSI (%)	0.7	0.6	0.76	0.6	0.7	0.74	0.5	0.4	1
Organ SSI (%)	3.9	4.7	0.23	2.6	1.7	0.26	2.7	3.5	0.47
Wound dehisc (%)	0.7	0.1	0.05	0.6	0.5	1	0.3	0.0	1
Respiratory compromise (%)	1.7	1.9	0.66	1.8	1.4	0.60	2.0	1.2	0.49
Renal failure (%)	0.9	1.2	0.27	0.5	0.5	1	0.5	1.5	0.04
UTI (%)	2.4	1.6	0.14	1.5	1.7	0.72	1.2	0.4	0.37
Cardiac event (%)	0.6	0.5	1	0.7	0.2	0.53	0.5	0.8	0.39
Bleeding requiring transfusion (%)	4.4	3.1	0.07	4.1	3.8	0.79	5.6	5.8	0.89
Any VTE (%)	0.6	0.7	0.65	0.7	0.2	0.53	0.9	1.5	0.31
Readmission (%)	8.8	10.5	0.09	6.8	6.2	0.63	7.5	8.1	0.73
Operative time (min, median ± IQR)	195 ± 112	240 ± 134	<0.01	153 ± 87	202.5 ± 106	<0.01	133 ± 73	173 ± 91	<0.01
Length of stay (days, median ± IQR)	4 ± 3	4 ± 2	<0.01	4 ± 2	4 ± 2	<0.01	4 ± 3	3 ± 2	<0.01

LAR low anterior resection; *Lap* laparoscopic; *SSI* surgical site infection; *Dehisc* Dehiscence; *UTI* urinary tract infection; *VTE* venous thromboembolism; *IQR* interquartile range; *Post-op* postoperative

Figure 1: Unadjusted Outcomes of Laparoscopic and Robotic Colectomy Stratified by Colectomy Site

In respective morbidities and mortality, the different approaches to left and right colectomy were similar. The robotic approach was associated with longer operative times, however lower conversion rates and length of stay.

3.5 Conclusions from Treatment Risk Analysis & Mitigations

The following summarize the risk analysis:

- Overall intraoperative and post operative (within 30 days) adverse event rates are projected to be similar and lower using the VI RASD in conventional laparoscopic right and left colectomy by a trained surgeon.
- Occurrence of postoperative morbidity and mortality with the use of the RASD are projected to be similar and low when used in conventional laparoscopic right and left colectomy by a trained surgeon.
- The study design (investigator eligibility, use of DSMB, interim analyses, IRB approved informed consent) and study eligibility criteria protects vulnerable populations (pediatric population, childbearing/lactating females, excessively ill, learning disabled) from participating while enabling a meaningful study cohort to be enrolled to evaluate the VI RASD.

4 The Virtual Incision Robotically Assisted Surgical Device

The Virtual Incision Robotically Assisted Surgical System consists of three major components: (1) a surgical robot, (2) a robotically articulated camera, and (3) a surgeon console user interface. It has been designed for general surgical applications. The robot and camera are shown in Figure 2 mounted to the operating table using a robot support arm. The robot and camera are inserted into the patient's abdominal cavity and are remotely controlled via the surgeon console located outside the sterile field. The surgeon console includes a main display showing the real-time video feed from the camera, hand input devices, pedal inputs, and an interactive touchscreen. The System is designed to be operated by a minimum of one surgeon and one surgical assistant.

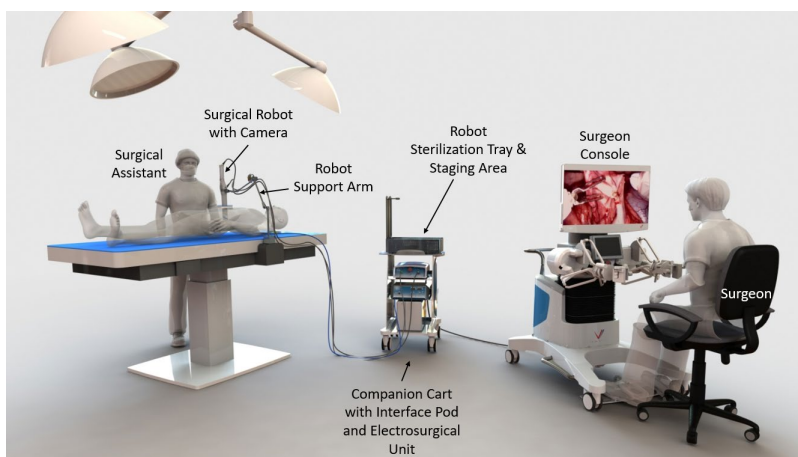


Figure 2: Virtual Incision Robotically Assisted Surgical Device

The Virtual Incision Robotically Assisted Surgical Device (VI RASD) consists of the robot, camera and tools. The robot portion has two miniaturized arms attached to a base link, Figure 3. Two different tools can be attached to complete different surgical tasks. Some robot tools can deliver electrosurgical cautery energy when the robot is connected to an external electro-surgical unit (ESU).

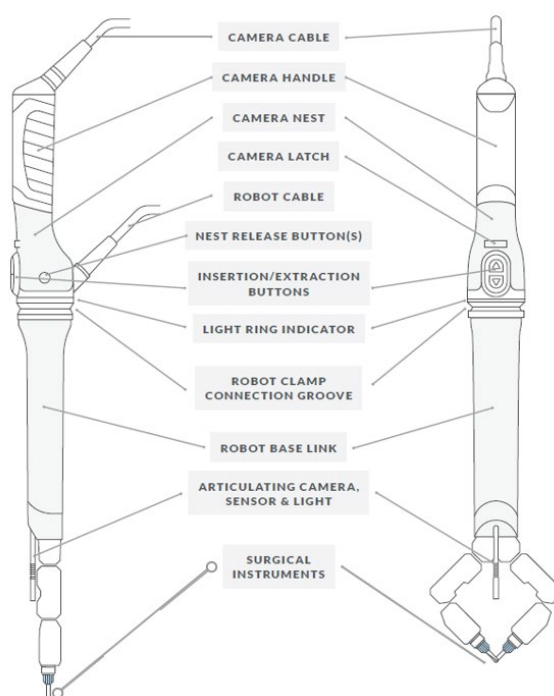


Figure 3: The VI RASD Robot and Camera

5 Study Objectives

This study is a clinical evaluation to assess device performance and safety in the operating room environment using a clinically relevant subset of user (surgeon) needs. The following objectives will be used to demonstrate a pattern of performance in humans and, to adequately describe the clinical variables of the VI RASD.

5.1 VI RASD Steps

VI RASD steps are defined as manipulating and dissecting the right and left colon for resection using robotic bipolar grasper and robotic monopolar scissors by dividing the colon attachments and preparing the colon for resection. The VI RASD steps also include the following steps:

1. Inserting the VI RASD robot through the access port and deploying it to the corresponding abdominal quadrant.
2. Ensuring the colon is adequately and primarily dissected and exposed with the VI RASD end effectors with graspers and scissors for tissue manipulation, cutting, blunt and sharp dissection, tissue hemostasis with electrocautery while maintaining pneumo-peritoneum and visualization.
3. Successful transection of the Colon and Small Bowel using assistant port manual surgical stapler (e.g. Edo GIA).
4. Removal of the VI RASD robot from the abdominal cavity

5.2 Primary Objectives

Efficacy of VI RASD

The Primary Efficacy Endpoint is the successful completion of the VI RASD steps listed in Section 5.1 without conversion to open surgery.

Definition of Conversion to Open

The VI RASD steps are not successful, and any portion of the case is performed open. Conversion to open surgery, defined as the use of a laparotomy wound for any part of the mesentery dissection. The use of a small abdominal wound to facilitate a low, stapled anastomosis and/or specimen extraction is permissible and will not be defined as an open conversion. The use of additional laparoscopic ports (trocar sites) will not be defined as an open conversion.

Safety of VI RASD

Determine the safety profile of intraoperative and postoperative clinical data of the VI RASD in right and left colectomies as demonstrated by the following endpoints:

- Overall intraoperative and post operative (within 30 days) adverse events compared to published literature
- Incidence of intraoperative serious adverse events, specified as either device-related or procedure-related events.
- Incidence of postoperative serious adverse events, specified as either device-related or procedure-related events within 14 days of surgical procedure.
- Incidence of postoperative serious adverse events, specified as either device-related or procedure-related events within 30 days* of surgical procedure (14 day events are also included in the 30-day analysis).
- Incidence of Serious Adverse Events unrelated to device or procedure.

**If the adverse event continues at the 30 day follow up visit, the subject shall continue to be followed until resolution of the event, as determined by the Investigator.*

5.3 Secondary Objectives

Data for twelve (12) clinical outcomes/clinical assessments measures shall be reported using the following endpoints. These measures will be characterized using published literature (refer to References 9 and 10 as examples) that compares conventional laparoscopic technique to robotically assisted laparoscopic technique.

1. Length of Stay – Day of procedure to date of discharge
2. Intraoperative Adverse Events – Report any peri-procedural event
3. Transfusions – Total number of transfusions from beginning of procedure to end of study
4. Conversion Rate – Conversion to open
5. Operative Time – Incision to Closure. Time elapsed between procedure start and stop time
6. Postoperative Complications through 30 days – To be reported as adverse events
7. Readmission Rates through 30 days – Readmission to the hospital for any reason
8. Re-encounter Rates through 30 days – Any medical visit or call related to the procedure
9. Reoperation Rates through 30 days – Any operation related to the underlying medical condition
10. Recurrence Rates through 30 days – recurrence of disease
11. Mortality through 30 days
12. Number of laparoscopic ports (trocar sites) used and reason for use

5.4 Tertiary Objectives

Descriptive analysis for oncological endpoints related to living and cancer status will be performed and reported in final Clinical Study Report.

1. Incidence of Cancer status
2. Incidence of Cancer status-active, remission, metastasized, reoccurrence
3. Incidence of additional surgery/procedures to treat pre-existing cancer at time of procedure.

6 Study Design

6.1 Study Overview

The proposed clinical evaluation study is to assess the technical efficacy and the intraoperative and postoperative safety of the VI RASD.

The study will enroll up to 30 subjects from up to 4 sites using a prospective multi-center, multi-operator, non-randomized, consecutively enrolled approach. No one site may enroll more than fifteen subjects into the study.

6.2 Study Population

Patients presenting with the medical and/or surgical indication for colon resection. Patients will be recruited for the study either through physician referral to the trained surgeon or the trained surgeon's practice.

6.3 Inclusion Criteria

Patients shall be enrolled into the clinical evaluation study if they meet the following inclusion criteria:

- a) Subject is able to provide informed consent
- b) 22-85 years of age
- c) No history of frozen abdomen due to abdominal adhesions or multiple previous bowel obstructions
- d) Body mass index (BMI) between 19.5- 45 kg/m²
- e) A weight of at least 100 lbs. (45.36 kg.).
- f) Height of at least 60 inches (152 cm)
- g) ASA grades I through III
- h) Available for required postoperative follow up visits at 14 days and 30 days

6.4 Exclusion Criteria

Patients shall be excluded from this clinical evaluation study if they meet at least one of the exclusion criteria:

- a) Subject unable or unwilling to provide informed consent
- b) Under the age of 22 or greater than the age of 85 years
- c) Has polyps that can be completely removed with negative surgical margins by colonoscopy.
- d) Has Stage T4 cancer diagnosis
- e) History of abdominal adhesions or bowel obstruction
- f) BMI of < 19.5 and > 45 kg/m²

- g) Heights < 60 inches
- h) ASA grades IV-VI
- i) End stage renal disease
- j) Liver Cirrhosis
- k) Women who are pregnant or lactating
- l) Active infection or has a history of local or systemic infection within 30 days of study screening
- m) Has had major surgery within 30 days prior to study enrollment or is scheduled to have major surgery within 30 days
- n) Has participated or is participating in another clinical study which may confound study results
- o) In the opinion of the Investigator, patient is not likely to comply with the required protocol activities; or, has a medical condition that should exclude the patient from the study
- p) Hemoglobin < 8.0
- q) Not currently coagulopathic

7 Study Treatment

7.1 Method of Assigning Subjects to Treatment Group

Once a patient has been medically indicated for a surgical resection of the colon, potential subjects for the study are selected and screened based on the study's eligibility criteria. Once the potential subject has been deemed eligible, written informed consent is obtained. All subjects are evaluated for treatment. There is no control group or randomization. Subject is considered enrolled in study when insertion of the VI RASD device is initiated.

7.2 Supply of the Investigational Device to the Investigator

The Sponsor will deliver all components of the investigational device. A device accountability form will be completed to identify the investigational device that will reside at the clinical site under secured access for the duration of the clinical evaluation study.

At the completion of the study, all components of the investigational device will be returned to VIC and accounted for using a device accountability log or form.

8 Training and Preparation for the RASD Procedure

Surgical Training: Investigator shall possess privileges and be credentialed to perform open, laparoscopic and robotic surgery at his/her institution of practice. Credentialing includes having performed 30 of each type (open, laparoscopic, robotic) of colectomy surgery.

VI RASD Training: Investigators and the surgical team will participate in a didactic and experiential training program that is conducted by VI personnel or its trained designee in preparation for the first VI RASD procedure. A task list will be used to evaluate each participants' successful completion of the RASD training program. The task list shall be completed by the trainer, signed by the participant and trainer and kept on file in the clinical site file at VI. Participants may also have a copy for personal needs.

RASD Procedure Support by VI: Virtual Incision shall provide technical and/or clinical support for each study procedure. The support shall be by Specialists that have successfully completed a VI's training program for this purpose. This IDE includes a document that defines the roles and responsibilities of these VI representatives (that can be found in Section 2.6 of this IDE).

9 Study Procedure and Guidelines

The schedule of study visits and activities representing the required testing procedures to be performed for the duration of the study is tabulated in Table 1 below.

Prior to conducting any study-related activities an IRB-approved written Informed Consent and the Health Insurance Portability and Accountability Act (HIPAA) authorization shall be signed and dated by the subject. The informed consent process should be documented in the subject's medical record.

9.1 Study Schedule, Activities, and Follow up

The total duration of the study is expected to be 12 months including up to 9 months for subject recruitment and treatment and up to 3 months for follow up.

Subject participation in the study will be for up to 4 months.

- Screening visit: up to 60 days prior to procedure
- Baseline visit: less than 30 days from procedure
- Treatment: 1 day
- Follow-up: 14- and 30-day visits, postoperatively

If the subject has a pre-existing colon cancer diagnosis or newly diagnosed as a result of participating in the study, the subject will be referred to an Oncologist for long term follow up. The Sponsor will follow up with the Oncologist on an annual basis for 5 years to obtain information about living and cancer status.

9.1.1 Screening

All subjects evaluated for potential Laparoscopic Right/Left Colectomy should be screened for eligibility. Screening will be conducted by Principal Investigator and/or qualified designee. A de-identified screening log will be maintained by the site and reason for exclusion in study should be noted. Subjects who may potentially qualify for the study will be approached for participation and completion of Study Specific Informed Consent Form. Informed consent must be obtained prior to undergoing any study related assessments.

9.1.2 Baseline Assessment Activities (<30 days before procedures)

Physical Examination- including subject demographics and vital signs per institution's medical practice guidelines

Medical History - including pre-existing co-morbidities or chronic diseases and a current medication review and documentation in the patient's medical record/chart should be completed.

Surgical History – to include surgeries over most recent 20 years

Serum Laboratory Evaluation, including:

- Complete Blood Count (CBC) with differential
- Complete Metabolic Profile (CMP)
- Pregnancy, if female of childbearing potential

9.1.3 Procedure

Vital signs and concomitant medications (excluding medications given as part of anesthesia for procedure)

Procedure – right or left colectomy

Adverse Event surveillance and reporting.

9.1.4 Follow-up

Discharge

Physical Exam – to include vital signs per institution’s guidelines, medication review and observation of abdominal wound healing (in discharge summary)

Adverse Event surveillance and reporting

14 Day Follow-up Visit (14 days $\pm$ 2 days post procedure)

Physical Exam – to include vital signs per institution’s guidelines, medication review and observation of abdominal wound healing

Pathology Report Data – as available from Colectomy procedure, to include: Specimen weight, size, length, Status of tissue invasion, cancer grade, mitotic rate, tumor margin, lymph node number and if positive/negative, State TNM staging, tumor markers, type of cancer, tumor grade, lymph node status, margin status, stage.

Adverse Event surveillance and reporting

30 Day Follow-up Visit (30 days $\pm$ 5 days post procedure)

Physical Exam – to include vital signs per institution’s guidelines, medication review and observation of abdominal wound healing

Adverse Event surveillance and reporting

9.2 Summary of Schedule of Study Visit and Activities

A summary of the study visits and activities is shown in Table 1.

Table 1: Schedule of Study Visits and Activities

	Visit						
	Screening	Baseline	Procedure	Discharge	14day (±2 days)	30 day (±5 days)	5 yr. Annual Oncology follow up ⁴
Consent	X	X¹					
Physical Exam		X		X	X	X	
Vital Signs		X	X	X	X	X	
Medical/ Surgical History²		X					
CBC w/ Diff		X					
Complete Metabolic Profile		X					
Pregnancy test³		X					
Right/Left Colectomy			X				
Pathology results⁴					X		
Concomitant Medication Review		X	X⁵	X	X	X	
Adverse Event Review			X	X	X	X	
Oncologist Follow up⁶							X

¹If not performed at separate screening visit

²Past 20 years only

³Females of childbearing age only

⁴Recording of available pathology results from colectomy procedure performed on subjects with known/suspected Cancer.

⁵Excluding Concomitant Medications given for anesthesia

⁶Only for subjects with pre-existing or new diagnosis of cancer post procedure

9.3 Longer Term Follow Up for Subjects with a Pre- Existing Cancer Diagnosis

Long term follow-up of subjects with pre-existing or newly diagnosed colon cancer shall be performed annually and reported in an annual IDE report for up to five (5) years post study procedure. The following data shall be collected via a telephone call to the referred Oncologist to determine the subject's status:

Living or deceased – if deceased, cause of death related to the pre-existing cancer shall try to be determined during the telephone call; and, if living

Cancer status – active therapy, repeated surgical intervention for the pre-existing cancer, remission, re-occurrence, metastases.

Incidence of additional surgery to treat pre-existing Cancer.

9.4 Demographics

Demographic information (date of birth, gender, race or ethnic origin) will be recorded at the baseline visit.

9.5 Medical and Surgical History

Relevant medical history, including history of current disease, other pertinent respiratory history, cardiac history, information regarding underlying diseases, including pre-existing/past cancer or cancer treatments, and current medication review will be recorded at the baseline visit.

Similarly, a surgical history that includes a review of all surgeries over most recent 20 years should be taken and recorded.

9.6 Physical Examination

A physical examination at the baseline visit will be performed by either the investigator or a sub-investigator who is a physician. Qualified staff (MD, NP, RN, and PA) may complete an abbreviated physical exam at subsequent follow up study visits. New abnormal physical exam findings must be documented and will be followed by a physician or other qualified staff to the next scheduled study visit.

9.7 Vital Signs

Vital signs to be collected per institution's standards.

9.8 Procedure

Relevant operative data shall be collected such as procedure start and stop times, Surgeon and Surgical Assistant name and credentials (RN, Technician, MD), number of inserted ports (trocar sites used), robot use time and characteristics, anastomosis characteristics, estimated blood loss, transfusion during procedure and need for conversion.

9.9 Adverse Events

Information regarding occurrence of adverse events will be captured throughout the study. All adverse events shall be reported including non-serious events related to the device or procedure and all serious events. Duration (start and stop dates), causality/relatedness, severity, outcome and treatment will be recorded on the case report form (CRF).

10 Adverse Event Reporting and Documentation

An adverse event (AE) is any untoward medical occurrence in a clinical investigation that does not necessarily have a causal relationship with the investigational device or treatment. An AE is therefore any unfavorable and/or unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the administration of an investigational product or treatment/procedure, whether or not it is related to that investigational product or treatment/procedure. An unexpected or unanticipated AE is one not identified in nature, severity, or frequency in the current investigational plan or of greater severity or frequency than expected based on the information in the investigational plan.

The Principal Investigator will probe, via discussion with the subject and review of medical record, for the occurrence of AEs, non-serious and serious, during each subject visit and record the information in the subject's medical/clinic record or other source document. Adverse events will be recorded in the subject's CRF upon first learning of the event from the subject. Adverse events will be described by duration (start and stop dates and times), severity, outcome, treatment and relation to study device, the procedure or, if unrelated, the possible cause.

10.1 Anticipated Adverse Events

It is anticipated that any adverse events that may occur during this study will be the same as those experienced in standard, minimally invasive robotic and non-robotic surgical colectomy. The following list are known complications similar to those associated with standard, minimally-invasive robotic or non-robotic surgical colectomy [11,12]. These complications may result in the need for medication, the need for additional surgery or hospitalization or death:

- incision site pain
- procedure pain
- anesthesia complications
- contact dermatitis
- postoperative coma
- stroke
- pneumonia
- failure to wean from the ventilator
- pulmonary embolism
- bleeding – excessive or hemorrhage
- cardiac arrest
- cardiac arrhythmia
- delayed hemorrhage
- blood transfusion
- deep vein thrombosis (DVT)
- gas embolism
- urinary tract infection
- urinary retention
- prolonged ileus
- anastomotic leak or dehiscence
- abscess (deep space infection)
- wound infection

- wound dehiscence
- bowel obstruction
- injury to surrounding structures - abdominal wall, intra-abdominal organs or major blood vessels
- incisional hernia
- electrolyte abnormality
- renal failure
- anastomotic stricture
- pelvic sepsis
- peritonitis
- sepsis
- enterocutaneous fistula
- fertility
- sexual dysfunction
- dyspareunia
- high levels of carbon dioxide in your blood
- vagal reaction
- death
- worsening of oncological outcomes

10.2 Adverse Event Severity

The Common Terminology Criteria for Adverse Events (CTCAE), Version 5.0, published in November 2017 by the US Department of HSS, the NIH as well as the National Cancer Institute will be used to ‘grade’ the severity of an adverse event. Both the Investigator and the DSMB shall use this grading scale to report the adverse event. The following table provides the schema.

Table 2: Table for Adverse Event Grading

SEVERITY	DESCRIPTION
GRADE 1	Asymptomatic or mild symptoms; clinical or diagnostic observations only; no intervention indicated
GRADE 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL (Activities of Daily Living)
GRADE 3	Severe; or medically significant but not immediately life threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care of ADL
GRADE 4	Life-threatening ; urgent intervention indicated
GRADE 5	Death related to an adverse event

10.3 Defining Adverse Event Relationship

The relationship of an adverse event to the investigational device as well as to the procedure should be assessed using the following guidelines in the table.

Table 3: Defining AE Relationship to Device or Procedure

RELATIONSHIP	COMMENT
DEFINITELY	An event that follows a reasonable temporal sequence from the use of the device or procedure; that follows a known or expected response pattern to the device; and that is not explained by any other reasonable hypothesis.
PROBABLY	An event that follows a reasonable temporal sequence from the use of the device or procedure; that follows a known or expected response pattern to the suspected device; and that is unlikely to be explained by the known characteristics of the subject's clinical state or by other interventions.
POSSIBLY	An event that follows a reasonable temporal sequence from the use of the device or procedure; that follows a known or expected response pattern to that suspected device; but that could readily have been produced by a number of other factors.
UNRELATED	An event that can be determined with certainty to have no relationship to the study device or procedure.

10.4 Serious Adverse Experiences (SAE)

An SAE is defined as any AE with any of the following outcomes:

- death
- a life-threatening adverse experience
- inpatient hospitalization or prolongation of existing hospitalization
- a persistent or significant disability/incapacity
- a congenital anomaly/birth defect

Other important medical events may also be considered an SAE when, based on appropriate medical judgment, they jeopardize the subject or require intervention to prevent one of the outcomes that are listed.

10.5 Serious Adverse Experience Reporting

Study sites will document all SAEs that occur (whether or not related to the study device or procedure). The collection period for all SAEs will begin after informed consent is obtained and end after activities for the final study visit have been completed.

The Principal Investigator will report SAEs to the IRB as per the IRB's SOP. The PI will also report the SAE to the study Sponsor within 48 hours. The study sponsor will in turn will report the SAE to the Clinical Event Committee and FDA.

10.6 Summary of Adverse Event Reporting

Table 4 below summarizes the reporting of adverse events.

Table 4: Summary of Adverse Event Reporting

	REPORTED	NOT REPORTED
ADVERSE EVENT RELATED TO DEVICE/PROCEDURE	X	
ADVERSE EVENT NOT RELATED TO DEVICE/PROCEDURE		X
SERIOUS ADVERSE EVENT RELATED TO DEVICE/PROCEDURE	X	
SERIOUS ADVERSE EVENT NOT RELATED TO DEVICE/PROCEDURE	X	

10.7 Medical Monitoring

Medical monitoring will take place through:

- An external, independent Clinical Events Committee (CEC) will review and adjudicate, at minimum, all deaths and safety-endpoint related adverse events. Endpoint results will be based on CEC adjudications
- An external, independent Data and Safety Monitoring Board (DSMB) will evaluate safety data and advise the Sponsor regarding continued safety of the study to ensure the well-being of the subjects

11 Mechanical Failures, Malfunctions, or Device Defects

All mechanical failures, malfunctions or defects involving any device component must be recorded on the device recorded as a complaint and reported immediately (within 24 hours) to the Sponsor. Every attempt should be made by the Investigator to save or collect the defective device for return to the sponsor. Prior to returning the device, the site should contact the sponsor for a Return Materials Authorization (RMA) number and the device should be packaged appropriately for shipment.

A device malfunction form must be completed if any of these conditions are met:

- Any situation where the device physically deforms or breaks for any reason

- Any situation where a component of the device fails to move or perform as intended according to the study protocol or the IFUs.
- Device contamination, potential for device contamination, or a break in sterility or sterile barrier.

Devices which were opened in error, prepped incorrectly or inadvertently contaminated in the Operating room (i.e. dropped on floor) are not considered device failures and do not need to be returned to the sponsor. A device failure form does not have to be completed in these cases. Date and disposition of these discarded devices will be documented on the appropriate study device accountability log.

12 Discontinuation and Replacement of Subjects

12.1 Early Discontinuation of Study Treatment

A subject may be discontinued from the study at any time if the subject, the investigator, or the Sponsor feels that it is not in the subject's best interest to participate or continue in the study. The following is a list of possible reasons for study treatment discontinuation:

- Subject withdrawal of consent (or assent)
- Subject is not compliant with study requirements of participation in the study
- Adverse event that in the opinion of the investigator would be in the best interest of the subject to discontinue study treatment; or, requires intervention that precludes the follow-up evaluations required by the study protocol.
- Protocol violation requiring discontinuation of study treatment
- Lost to follow-up - Lost to follow up is defined as the site's study personnel and Principal Investigator's inability to contact the subject to attend the scheduled required follow up visit after 14 days out of the study visit scheduling window. If after 3 tracked attempts over a 30-day period by the site's study personnel to contact the subject or subject's family without success, the subject may be considered lost to follow up. Tracked attempts are defined as certified letters or letters delivered by a delivery service that show either attempt to deliver or received with signature.
- Sponsor request for early termination of study
- Positive pregnancy test of childbearing potential females prior to treatment.

If a subject is withdrawn from treatment due to an adverse event, the subject will be followed and treated by the Principal Investigator until the abnormal parameter or symptom has resolved or stabilized.

12.2 Withdrawal of Subjects from the Study

A subject may be withdrawn from the study at any time if the subject, the investigator, or the study Sponsor feels that it is not in the subject's best interest to continue.

All subjects are free to withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice.

Reasonable attempts will be made by the investigator to provide a reason for subject withdrawals. The reason for the subject's withdrawal from the study will be specified in the subject's source documents. Subjects who withdraw should be encouraged to come in for a final visit.

12.3 Replacement of Subjects

Subjects who withdraw prior to the study procedure will be considered screen failures and replaced. The replacement will receive a new sequential numeric-alpha study identifier (see Section 14.2.7). Subjects

who withdraw from the study and have had the study treatment will not be replaced and will be included in all relevant study reports.

13 Protocol Violations

A protocol violation occurs when the subject, investigator, or study Sponsor fails to adhere to the written investigational plan or protocol requirements that affect the informed consent process, inclusion/exclusion criteria, subject safety and primary endpoint criteria. Protocol violations for this study include, but are not limited to, the following:

- Failure to obtain IRB-approved or current version informed consent for the study;
- Failure to conduct the informed consent process prior to protocol required testing;
- Failure to meet inclusion/exclusion criteria.
- Failure to comply with Good Clinical Practice (GCP) guidelines.

The Sponsor will determine if a protocol violation will result in withdrawal of a subject when a protocol violation occurs, it will be discussed with the Principal Investigator and a Protocol Violation Report Form detailing the violation will be generated. This form will be signed by a Sponsor representative and the Principal Investigator. A copy of the form will be filed in the site's study binder and in the Sponsor's site files.

14 Data and Safety Monitoring Board

The study Sponsor will convene a Data and Safety Monitoring Board (DSMB) to review study data as well as specific data relating to safety and efficacy of the subject population. The DSMB will ensure the continued scientific validity and merit of the study, according to the ratified DSMB Charter established for this protocol.

There will be routine assembly of the Board members, every three (3) months, for the purpose of monitoring study conduct and assessing patient safety. The Board will also meet after every 10 patients are treated. Any recommendations by the Board to the Investigator group will be conveyed by the Sponsor to the group unless otherwise specified by the Board.

The Sponsor's role in the DSMB shall be ex-officio and is one to proffer data and study progress information. Study investigators may also participate in a DSMB meeting at the request of the DSMB or Sponsor to clarify study occurrence or adverse event.

Stopping Rules

The DSMB may stop/hold the clinical trial at any time for the following:

Events continuously monitored (each occurrence reviewed as they occur):

Event	Stopping/Holding Rule
Death	If 1 death is observed during any point in the study, temporary stop will occur pending investigation
Significant systemic device malfunction	Defined as a malfunction resulting in serious adverse event and/or requiring conversion to open surgery

Events with interim monitoring:

Event	Stopping/Holding Rule
Secondary Objectives (clinical outcome measures)	To be evaluated after first four subjects and then every 3 months.
All serious adverse events	Incidence of occurrence exceeding that noted in published literature (reference 9 or 10 as an example)

In addition, further subject enrollment may be temporarily placed on hold (pending DSMB review) per discretion of the study's CMO for any of the above noted reasons. Upon review DSMB will determine if temporary hold remains or can be lifted.

15 Clinical Events Committee

The study Sponsor will convene a Clinical Events Committee (CEC). The Clinical Events Committee (CEC) is an independent committee composed of a minimum of two General Surgeons. The CEC will evaluate and adjudicate potential Serious Adverse Events (SAEs), and all device related adverse events. Although the CEC is charged with adjudication of SAEs, the independent committee may be asked to evaluate other events which are potentially device or procedure related. The CEC will act according to the procedures documented in the CEC Charter.

16 Data Management

16.1 Data Analysis Plan

Data will be evaluated during the study conduct in order to allow review of the results by the data safety monitoring board (DSMB). These evaluations will occur at:

- Every three (3) months, for the purpose of monitoring study conduct and assessing patient safety.
- After every 10 patients treated and will evaluate primary and safety endpoints. The analysis will be characterized by number of patients, percentages, numbers and rates of occurrence.

When the study enrollment and follow-up is completed through 30-day visit, VI RASD clinical benefit will be assessed and determined using data collected from the primary and secondary endpoints. As the interim evaluations are intended only to support safety review of the study, there will be no adjustment to confidence interval widths or p-values for any inferential tests provided for the final analysis. When long term follow-up is completed from subjects with a pre-existing cancer diagnosis or newly diagnosed during procedure, data for these specific subjects shall be tabulated and reported in an annual and final post-market report to the FDA.

16.2 Data Associated with Primary Objectives

Efficacy

The Primary Efficacy Endpoint is the successful completion of the VI RASD steps 1-4 listed in Table 5 without conversion to open surgery.

VI RASD steps are defined as manipulating and resecting the right and left colon for resection using robotic bipolar grasper and robotic mono-polar scissors by dividing the colon attachments and preparing the colon for resection. Laparoscopic ports (trocar sites) may be used for ancillary tasks such as retraction, advanced energy, stapling, and suction. Data collected for the individual steps are shown in Table 5.

Table 1: Data collected for Efficacy Steps

VI RASD STEPS	DATA COLLECTED
1. Inserting the VI RASD robot through the access port and deploying it to the corresponding abdominal quadrant.	Data associated with incision length, single umbilical incision use, and robot insertion attempts into single incision will be collected.
2. Ensuring the colon is adequately and primarily dissected and exposed with the VI RASD end effectors with graspers and scissors for tissue manipulation, cutting, blunt and sharp dissection, tissue hemostasis with electrocautery while maintaining pneumo-peritoneum and visualization.	Data collected from the robot that enumerates grasp and cut events throughout surgery will be collected and depicted in a graphic format. Data associated with sustained pneumo-peritoneum after robot insertion through use and extraction will be collected. Data collected from the robot that enumerates all mono-polar and bipolar cautery uses throughout surgery will be collected and depicted in a graphic format. Data collected from the robot's camera video to visualize the status of electrocautery and relative location inside workspace will be used to evaluate effective and maintained hemostasis during surgery.
3. Success transection of the Colon and Small Bowel using assistant port manual surgical stapler (e.g. Edo GIA).	Data collected about the remote robotic field of view sufficiency and number of robot repositions to view entire workspace for targeted colon removal.
4. Removal of the VI RASD robot from the abdominal cavity	Data associated with time of extraction and robot extraction attempts will be collected.

Safety

Determine the safety profile of intraoperative and postoperative clinical data of the VI RASD in right and left colectomies as demonstrated by:

- Overall intraoperative and post operative (within 30 days) adverse events compared to published literature
- Incidence of intraoperative serious adverse events, specified as either device-related or procedure-related events.
- Incidence of postoperative serious adverse events, specified as either device-related or procedure-related events within 14 days of surgical procedure.
- Incidence of postoperative serious adverse events, specified as either device-related or procedure-related events within 30 days* of surgical procedure (14 day events are also included in the 30-day analysis).
- Incidence of Serious Adverse Events unrelated to device or procedure.

**If the adverse event continues at the 30 day follow up visit, the subject shall continue to be followed until resolution of the event, as determined by the Investigator.*

16.3 Data Associated with Secondary Objectives

Data for twelve (12) clinical outcomes/clinical assessments measures shall be reported using the following categories. These measures will be characterized using published literature (refer to References 9 and 10 as examples) that compares conventional laparoscopic technique to robotically assisted laparoscopic technique.

1. Length of Stay – Day of procedure to date of discharge
2. Intraoperative Adverse Events – Recording of any peri-procedural adverse events
3. Transfusions – Total number of required transfusions from beginning of procedure to end of study
4. Conversion Rate – Conversion to open
5. Operative Time – Incision to Closure. Time elapsed between procedure start and stop time
6. Postoperative Complications through 30 days – Will be recorded as Adverse Events
7. Readmission Rates through 30 days – Readmission to the hospital for any reason
8. Re-encounter Rates through 30 days – Any medical visit or call related to the procedure
9. Reoperation Rates through 30 days – Any operation related to the underlying medical condition
10. Recurrence Rates through 30 days – Recurrence of disease
11. Mortality through 30 days
12. Number of laparoscopic ports (trocar sites) used and reason for use.

16.4 Oncology Tertiary Outcomes

Long Term Data from Subjects with a Pre-Existing Cancer Diagnosis or newly diagnosed during procedure.

Data for these specific subjects shall be tabulated and reported in an annual and final IDE report to the FDA. Data will be simply summarized by enumerating the number of subjects living or deceased along with cause of cancer death (if known). The status and treatment, if applicable, of the cancer shall also be reported in the same fashion. Year over year data changes will be described in a narrative.

1. Incidence of Cancer status
2. Incidence of Cancer status-active, remission, metastasized, reoccurrence
3. Incidence of additional surgery/procedures to treat pre- existing cancer at time of procedure.

16.5 Study Limitations

Due to the initial evaluation of the device, we are confident that despite the small study population we can achieve our primary effectiveness and safety endpoints.

Failure to meet the primary endpoints of safety and effectiveness during this trial will result in a careful analysis of risk, study methodology, and device related technology. Development of an appropriate mitigation strategy will be done based on this analysis. Mitigation strategy may include a change in the device itself, protocol revision and/or a creation of a bridging IDE trial proposal.

16.6 Data Collection, Retention and Monitoring

16.6.1 Data Collection Instruments

The Principal Investigator will prepare and maintain adequate and accurate source documents designed to record observations and other pertinent data for each subject receiving the study treatment.

Study personnel at each site will enter data from source documents corresponding to a subject's visit into the protocol-specific CRF in an electronic data collection system, when the information corresponding to that visit is available. Subjects will not be identified by name in the study database or on any study documents to be collected by the Sponsor (or designee), but will be identified by a site number, subject number and 3 alpha initials that correspond to the subject's name.

The Principal Investigator is responsible for all information collected on subjects enrolled in this study. All data collected during the course of the study shall be reviewed and verified for completeness and accuracy by the Principal Investigator. Access to the CRF and all study data will be available to the Investigator and designated study personnel through the completion of the study and final study report.

16.6.2 Data Management Procedures

The data will be entered into a validated database. A Data Management group will be responsible for data processing, in accordance with procedural documentation. A 'database lock' will occur once quality assurance procedures have been completed to assure as much completed and verified data are included in an analysis.

All procedures for the handling and analysis of data will be conducted using good computing practices meeting FDA guidelines for the handling and analysis of data for clinical trials.

16.6.3 Data Quality Control and Reporting

After data have been entered into the electronic data collection database, a system of computerized data validation checks, data clarification queries or database audits will be implemented and applied to the database on a regular basis. All changes to the study database will be documented.

16.6.4 Archival of Data

The database is safeguarded against unauthorized access by established security procedures; appropriate backup copies of the database and related software files will be maintained. Databases are backed up by the Database Administrator in conjunction with any updates or changes to the database.

At critical intervals during the conduct of the study (e.g., production of interim DSMB report, safety query, regulatory body inquiry, IRB request), data for analysis is locked and cleaned per established procedures by the Data Management group.

16.6.5 Availability and Retention of Investigational Records

The Principal Investigator or designee shall make study data accessible to the study monitor, other authorized representatives of the Sponsor (or designee), IRB, and FDA inspectors upon request. A file for each subject must be maintained that includes a signed IRB-approved Informed Consent/Assent Form, HIPAA Authorization and copies of the source documentation related to that subject. The Investigator must ensure the reliability and availability of source documents from which the information on the CRF was derived.

All study documents (patient files, signed informed consent forms, copies of CRFs, Study File Notebook, etc.) must be kept secured for a period of two years following marketing of the investigational device or for two years after centers have been notified that the study has been discontinued or closed. There may be other circumstances for which the Sponsor is required to maintain study records and, therefore, the Sponsor should be contacted prior to removing study records to a remote location for any reason.

16.6.6 Monitoring

Monitoring visits will be conducted by the Sponsor and/or its designee according to the U.S. CFR Title 21 Parts 50, 56, and 312 and ICH Guidelines for GCP (E6). By signing this protocol, the Principal Investigator grants permission to the Sponsor, and appropriate regulatory authorities to conduct on-site monitoring and/or auditing of all appropriate study documentation on an interim basis.

Monitoring of the investigation site shall occur at routine intervals to assess subject safety and adherence to the investigational plan. Monitoring may begin after the 1st enrolled subject has completed the discharge visit and enters the follow up activity schedule. Monitoring of the investigational site must occur when a minimum of 5 subjects have completed the discharge visit and enter the follow up activity schedule. Study data shall be monitored 100% to source documents and study records.

Monitoring visits shall be pre-planned, confirmed and coordinated with each investigator and site study coordinator to ensure completion of Sponsor's interim monitoring objectives per its operating procedures (WI 8409, FM 8410). Visit confirmation letters, interim monitoring visit reports and follow up letters to the investigator and study coordinator shall be used to document adherence by the Sponsor and the site to the investigational plan, 21 CFR and Good Clinical Practices as well as subject safety. Any site issue or compliance inconsistency identified as a result of the interim monitoring visit shall be addressed at the time of the visit and documented in the follow up letter. Persistent or major non-compliance by the investigator and/or site personnel shall be corrected by the Sponsor using WI 8416.

16.6.7 Subject Confidentiality

In order to maintain subject confidentiality, a two-digit site number, a three-digit subject numeric identifier along with the subject's 3 initials of name will identify all study subjects on CRFs and other study source documentation (i.e. physician progress notes, nurse's clinic notes, study coordinator study visit notes, imaging reports, laboratory reports) submitted to the Sponsor or regulatory agency. An example of this subject identification schema is 01-001-ABC.

If study documents are submitted to an entity outside the study site or medical institution, any subject identifier such as name, date of birth, treatment date, medical record number, insurance information shall be redacted from the document and the subject's unique study identifier shall be written onto every page of submitted documentation. Redaction may occur by using 'White Out' paper tape or 'Black Out' paper tape. Fluids or permanent black markers may be insufficient if the page is held into a light source. However, these methods (fluids, black marker) will suffice if the documents are submitted electronically (scanned, email).

17 Statistical Methods

17.1 General Methods

Study analysis will be completed when all 30 subjects have completed the 30-day follow-up following the initial procedure. The study includes several planned safety reports to be provided to the DSMB but will not stop early for reasons of effectiveness, hence there are not planned adjustments to analyses related to the interim evaluations.

The final study data will be made available in electronic format or listings as requested. The study results will be presented using descriptive summary tables. Categorical summaries will be presented with counts and percentages based on the available data. Numeric summaries will include the n (observations), mean,

standard deviation (SD), median, minimum, and maximum values. Any confidence intervals (CIs) provided will be two-sided 95% intervals.

The study does not include prospectively identified inferential analyses. Should inferential analyses be provided in order to aid in the interpretation of the results, two-sided p-values less than or equal to 0.05 will be considered statistically significant. There will be no adjustments for multiplicity. All analyses will be completed using available data. While missing data is not anticipated for the primary effectiveness endpoint, should missing data occur, the overall success rate will also be calculated assuming a worst case (all missing values are failures) and best-case imputation (all missing are successes). No other data imputations are planned.

17.2 Sample Size Justification

The sample size was selected to provide at least 80% chance to observe at least one safety event if the event occurs in at least 5.3% of subjects. The upper bound of the event rate if no events are observed or for the rate to conversions to open surgery if no conversions are reported is 11.6% (0/30).

17.3 Analysis Populations

The Safety Population and Efficacy Population are the same and will consist of all subjects enrolled in the study. A Per-Protocol population may be identified prior to completion of the study consisting of the Efficacy population excluding subjects who were inclusion or exclusion violations and excluding subjects with protocol violations identified as major. A list of major protocol deviations will be identified prior to closure of the study database if a Per-Protocol analysis is to be completed. If a per-protocol population is identified, the primary analysis will be evaluated in the Per-Protocol population.

17.4 Baseline and Procedure Information

Subject disposition will be presented for all subjects. Descriptive summaries will be used to display the subjects in each study population, the visit completion information, study completion, and reasons for discontinuation. Summaries of baseline patient and procedure information will be provided based on the information collected.

17.5 Effectiveness Analyses

17.5.1 Primary Effectiveness Endpoint:

The overall success is defined as completion of the VI RASD steps 1-4 without conversion to an open procedure as described in Section 5. The number and percentage of subjects with success will be provided along with an exact binomial 95% CI. The success rate will be compared to a device effectiveness threshold established from the conversion to open rates reported from similar peer reviewed prospective controlled studies. The combined conversion to open rate reported in these studies was 14.4% with -2.4% to 2.6% for 95% CI. See Table 6 below.

Table 6: Conversion to Open Incidence for Peer Reviewed Prospective Controlled Studies

Reference	Total Subjects	No Reporting Conversion to Open	Conversion Rate	Lower and Upper Bound, CL, 95%
Jayne 2017 ⁹	230	28	12.2%	0.08 -0.17
Schietroma 2015 ¹³	60	5	8.3%	0.03 - 0.18
Park 2012 ¹⁴	35	0	0%	0.00 - 0.10
Veldkamp 2005 ¹⁵	536	91	17%	0.14 – 0.20
Combined Totals	861	124	14.4%	0.12 -0.17 ¹

¹ 95% CI based on normal approximation.⁰

The study will be considered to have demonstrated the effectiveness of the device if the observed conversion rate is less than the upper bound of the combined conversion rate, 17% or, equivalently, has no more than 5 of the patients converting to open surgery. This ensures the observed rate of conversion is less than 20% difference from the overall combined total rate of 14.4%. Two-sided exact binomial 95% CIs will be provided for the observed event rates. The overall success rate will be summarized by gender, diagnosis, subject age, and study site. No inferential analysis is planned as the study is not powered to detect statistically significant differences for subgroup analyses.

17.5.2 Secondary Endpoints

Secondary endpoints are identified in Section 5.2 and will be summarized descriptively for the Efficacy population. Confidence intervals for the mean will be provided for the length of stay and operative time. Total transfusions will be summarized as a numeric and categorical variable. Exact binomial 95% CIs will be provided for the rate outcomes based on the number and percentage of subjects with an event. Exploratory analysis of secondary endpoints may be conducted to characterize these measures with using published literature (refer to References 9 and 10 as examples) that compares conventional laparoscopic technique to robotically assisted laparoscopic technique.

17.6 Safety Analyses

Safety analyses are based on the adverse events (VI will use the MedDRA coding system) collected intra-operatively and post-operative to 30 days. Adverse events will be summarized using counts and percentages for the Safety Population. Events will be summarized as outlined in the safety endpoints section.

The overall rate of device-related and procedure-related adverse events intra-operatively and post-operatively to 30 days will be contrasted with to the ROLARR Trial ⁹ as part of the overall risk-benefit assessment of the device without statistical comparison. Two-sided exact binomial 95% CIs will be provided for the observed event rates.

Overall safety from the ROLLAR trial reported:

- Overall intraoperative complication incidence of 15% (Note: -6.0% to 7.0% for 95% CI per reference 9, ROLARR trial)
- Overall 30-day postoperative complication incidence of 33% (Note: -9.8% to 7.2% for 95% CI per reference 9, ROLARR trial).

17.7 Study Success

Success of the study is defined by demonstrating that the VI RASD performed effectively with an 83% or greater success rate (equivalently, the observed conversion rate is less than the upper bound of the combined conversion rate, 17%, in Table 6) and is safe with a comparable safety profile of the safety endpoints.

17.8 Tertiary Measures

The Tertiary measures will be summarized descriptively.

18 Administrative, Ethical, Regulatory Considerations

The study will be conducted according to the Declaration of Helsinki, Protection of Human Volunteers (21 CFR 50), Institutional Review Boards (21 CFR 56), and Responsibilities of Investigators (21 CFR 812.100, 110).

To maintain subject confidentiality, all laboratory specimens, evaluation forms, reports and other records will be identified by the unique subject identifier schema in Section 14.2.7 of the protocol. All study records will be kept in a locked file cabinet and a code sheet linking the patient's name to the subject identifier number will be stored separately from the study data files and subject source document files in another locked file cabinet. This sheet is not made available to the Sponsor or its monitor designee. Clinical information will not be released without written permission of the subject, except as necessary for monitoring by the FDA. The Investigator must also comply with all applicable privacy regulations (e.g., Health Insurance Portability and Accountability Act of 1996, EU Data Protection Directive 95/46/EC).

18.1 Protocol Amendment or Investigational Plan Changes

Any amendment to the protocol or changes to the investigational plan (collectively amendments) will be written by the Sponsor. Amendments cannot be implemented without prior FDA approval notification and written IRB approval except as necessary to eliminate immediate safety hazards to study subjects. A protocol amendment intended to eliminate an apparent immediate hazard to subjects may be implemented immediately, provided the IRBs are notified within five working days.

The Sponsor will notify the Principal Investigator or a study site designee in writing of an FDA-approved amendment. The notification will include a summary of the changes to the pre-existing study protocol/plan and a rationale for the change(s), if applicable. This notification may then be used to seek IRB approval to implement the amendment and continue the study.

18.2 Institutional Review Boards and Independent Ethics Committees

The protocol and consent form will be reviewed and approved by the IRB/IEC of each participating site prior to study initiation. Serious adverse events, device and procedure related adverse events, and all device deficiencies will be reported to the IRB/IEC in accordance with the standard operating procedures and policies of that IRB/IEC. The Principal Investigator will keep the IRB/IEC informed as to the progress of the study and any relevant study Sponsor communication. The Principal Investigator will obtain assurance of IRB/IEC compliance with regulations.

Any documents that the IRB/IEC may need to fulfill its responsibilities (such as protocol, protocol amendments, Investigator's Brochure, consent forms, information concerning patient recruitment, payment or compensation procedures, or other pertinent information) will be submitted to the IRB/IEC by the Principal Investigator or designee. The study Sponsor will play a supportive role only. The IRB/IEC's written unconditional approval of the study protocol and the informed consent form will be in the possession of the Principal Investigator before the study is initiated and enrollment commences. The IRB/IEC's unconditional approval statement will be transmitted by the Principal Investigator or designee to the Sponsor prior to enrolling subjects. This approval must identify the study by exact protocol title and version and should specify the documents reviewed, the date of review, duration of approval/study renewal and any interim study reporting requirements to the IRB/IEC (if applicable).

Protocol and/or informed consent modifications or changes may not be initiated without prior written IRB/IEC approval except when necessary to eliminate immediate hazards to the subjects or when the

change(s) involves only logistical or administrative aspects of the study. Such modifications will be submitted to the IRB/IEC and written verification that the modifications were submitted and subsequently approved should be obtained and a copy provided to the study Sponsor.

The IRB/IEC must be informed of revisions to other documents originally submitted for review; serious and/or unexpected adverse experiences occurring during the study in accordance with the standard operating procedures and policies of the IRB/IEC. Additional notification examples include

- new information that may adversely affect the safety of subjects;
- new information that may adversely affect the conduct of the study;
- Sponsor annual study update
- request for re-approval;
- study completion;
- sponsor's final report.

18.3 Informed Consent Form

Informed consent will be obtained in accordance with the Declaration of Helsinki, ICH GCP, US Code of Federal Regulations for Protection of Human Subjects (21 CFR 50.25[a, b], CFR 50.27, and CFR Part 56, Subpart A), the Health Insurance Portability and Accountability Act (HIPAA, if applicable), and local regulations.

The Principal Investigator or designee will prepare the informed consent form per IRB guidance procedures, assent and HIPAA authorization; and, provide the documents to the Sponsor or designee for approval prior to submission to the IRB/IEC. The consent form generated by the Investigator must be acceptable to the Sponsor prior to approval by the IRB/IEC. The written consent document will embody the elements of informed consent as described in the International Conference on Harmonization and will also comply with local regulations. The Principal Investigator will send an IRB/IEC-approved copy of the Informed Consent Form to the Sponsor (or designee) for the study file.

A properly executed, written, informed consent will be obtained from each prospective subject prior to entering the subject into the study and commencing with study required activities. Information should be given in both oral and written form and subjects must be given ample opportunity to inquire about details of the study. If appropriate and required by the local IRB/IEC, assent from the subject will also be obtained. A copy of the signed consent form (and assent) will be given to the subject and the original will be maintained with the subject's medical and study records.

18.4 Publications

The preparation and submittal for publication of manuscripts containing the study results shall be in accordance with a process determined by mutual written agreement among the study Sponsor and participating Principal Investigator(s) and institutions. The publication or presentation of any study results shall comply with applicable privacy laws, including, but not limited to, the Health Insurance Portability and Accountability Act of 1996. The study Sponsor should be made aware of intent to publish or present study results well in advance, preferably 60-90 days, of submittal timelines. In this way, the Sponsor may plan a supportive role in gathering intended study data and device technical information.

19 References

1. Bertani E, Chiappa A, Ubiali P, Cossu ML, Arnone P, Andreoni B. Robotic colectomy: is it necessary? *Minerva Chir.* 2013; 68(5): 445-56.
2. Leaf GT, Campos CQ. 30 Years of Robotic Surgery. *World J Surg.* 2016; 40(10): 2550-7.
3. Shussman N, Wexner SD. Colorectal polyps and polyposis syndromes. *Gastroenterol Rep.* 2014; 2(1): 1-15.
4. Von Renteln D, Bouin M, Barkun AN. Current standards and new developments of colorectal polyp management and resection techniques. *Expert Rev Gastroenterol Hepatol.* 2017; 11(9): 835-42.
5. Nfonsom V, Aziz H, Pandit V, Khalil M, Jandova J, Joseph B. Analyzing clinical outcomes in laparoscopic right vs. left colectomy in colon cancer patients using the NSQIP database. *Cancer Treat Comm.* 2016; 8: 1-4.
6. Di B, Li Y, Wei K et al. Laparoscopic versus open surgery for colon cancer: a meta-analysis of 5-year outcomes. *Surg Oncol.* 2013; 23(3): e39-43.
7. Veldkamp R, Kuhry E, Hop WC et al. Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomized trial. *Lancet Oncol.* 2005; 6(7): 477-84.
8. Lorenzon L, Bini F, Balducci G, Ferr M, Salvi PF, Marinozzi F. Laparoscopic versus robotic-assisted colectomy and rectal resection: a systematic review and meta-analysis. *Int J Colorectal Dis.* 2016; 31(2): 161-73.
9. Jayne D, Pigazzi A, Marshall H et al. Effects of robotic-assisted vs conventional laparoscopic surgery on risk of conversion to open laparotomy among patients undergoing resection for rectal cancer The ROLARR Randomized Clinical Trial. *JAMA.* 2017; 318(16): 1569-80.
10. Dolejs SC, Waters JA, Ceppa EP, Zarzaur BL. Laparoscopic versus robotic colectomy: a national surgical quality improvement project analysis. *Surgical Endoscopy.* 2017; 31: 2387-96.
11. Tevis SE, Kennedy GD. Postoperative complications: looking forward to a safer future. *Clin Colon Rectal Surg.* 2016; 29(3): 246-252.
12. Kirchhoff P, Clavien P-A, Hahnloser D. Complications in colorectal surgery: risk factors and preventative strategies. *Patient Saf Surg.* 2010; 4: 5.
- 13 Schietroma, Mario et al. "Laparoscopic versus open colorectal surgery for colon cancer: the effect of surgical trauma on the bacterial translocation. A prospective randomized study." *American journal of surgery* vol. 210,2 (2015): 263-9. doi:10.1016/j.amjsurg.2014.09.031
- 14 Park, J S et al. "Randomized clinical trial of robot-assisted versus standard laparoscopic right colectomy." *The British journal of surgery* vol. 99,9 (2012): 1219-26. doi:10.1002/bjs.8841
- 15 Veldkamp, Ruben et al. "Laparoscopic surgery versus open surgery for colon cancer: short-term outcomes of a randomised trial." *The Lancet. Oncology* vol. 6,7 (2005): 477-84. doi:10.1016/S1470-2045(05)70221-7

Appendix A: Exemplary Description of Colectomy Procedures

This protocol does not dictate how a colectomy procedure should be performed. However, some details are listed as examples. All information in this appendix is exemplary. Exact steps to be undertaken are medical decisions left to the investigator.

A.1 Exemplary Description of Colectomy Procedures

In all surgical procedures, patients will be prepared for surgery in the standard fashion according to all standards of care for minimally invasive colon resection with robotic assistance. The surgical procedure's exemplary steps for left or right colectomy are described in Appendix B.

The VI RASD is not intended to be used for complete procedures and is intended to be used with other laparoscopic tools and techniques. For example, in right hemicolectomy the VI RASD is used only to mobilize the terminal ileum and the segment of colon to be excised. The procedure is completed using standard laparoscopic techniques, where the right colon is divided externally with a stapler and then closed with either a suture or stapler before being returned to the abdominal cavity and the procedure completed.

Appendix B includes a description of how the two umbrella procedures, right hemicolectomy, left/sigmoid hemicolectomy, may be performed. Each of these example procedures are broken into steps. Each procedure is a combination of standard manual laparoscopy and the use of the VI RASD. What technique (manual laparoscopy or VI RASD) may vary for each step. This is a clinical decision left to the investigator. Also, other manual tools are and can be used in conjunction with the VI RASD as shown in the steps of these procedures. For example, a manual tool might be used for additional retraction or a stapler or vessel sealing device might be used in conjunction with the VI RASD. Further, insertion of additional laparoscopic ports (trocar sites) may be used at the surgeon's discretion related to patient anatomy or operative technique.

The VI RASD allows for variations in how surgeons perform surgeries. Not all surgeons perform a given procedure in the same way. For example, some surgeons perform a colectomy from "medial to lateral" and some perform it "lateral to medial" resulting in different steps. Appendix B describes the steps in each of these approaches.

A.2 Unanticipated VI RASD Extraction Procedure

In the event there is a catastrophic event in the surgical environment or the VI RASD stops functioning during surgery or does not accurately perform tasks that the surgeon desires, including arm inaccuracy, the inability of the end effectors to open or close, or problems with the surgical console or mechanical issues with the robot itself arise the robot will be extracted according to the established and tested procedures, summarized here. Detailed procedures are available in the trouble shooting section of the VI RASD User Manual (Section 10.4 of this IDE).

- At any point the surgeon can utilize the all-stop function, which will halt all robot movements.
- The surgeon can use the "override extraction" function to extract the robot.
- If unsuccessful, the surgeon will press the all stop function and grasp the RASD, unlock it from the docking arm, and under direct visualization of the camera, begin to pull the robot out of the HALS port in a slow but firm backwards motion, allowing each shoulder and elbow to back drive to a straight position. Visualization during this portion is critical and if the robot camera fails, a standard laparoscopic camera can be used.

- In the event that the robot stops functioning while manipulating tissue, the surgeon will use the override tool open function.
- If unsuccessful, the bedside assistant will grasp the robot arm with the tissue and rotate it to open the end effector-robot connection, which will allow the tissue to be released from the robot mechanism. Manual laparoscopic tools may also be used to assist in this process.
- The RASD will then be withdrawn by the bedside assistant as described above and the end-effector will then be picked up by the assistant and removed through the HALS port.
- The surgeon will then proceed either with placement of a second robot or conversion to a standard, laparoscopic HALS technique.
- At the conclusion of the surgery, the surgeon will carefully evaluate all tissues and planes where the RASD was in contact to determine whether an injury occurred.

A.3 Failure Recovery Methods

In the event of undiagnosed dense adhesions or other patient characteristics that make robotic or minimally invasive approaches not safe or possible, the procedure will be converted to a conventional laparoscopic operation.

If the VI RASD is not functioning properly at any time the robot will be removed and surgery may be performed in the standard laparoscopic fashion with possible, hand port assistance. Robot malfunctions will be handled according to VI established and tested failure recovery methods summarized here.

Detailed procedures are available in the trouble shooting section of the VI RASD User Manual (Section 10.4 of this IDE).

Any malfunction of the VI RASD will be monitored to ensure patient safety. Continuous monitoring of several systems functions is part of the VI RASD design including monitoring internal temperatures, redundant position sensors, communication failures, several voltages and currents, and other functions.

If the RASD is not functioning properly on insertion, the robot will be removed and surgery will be performed in the standard laparoscopic fashion with possible hand port assistance.

The system is designed with several re-start functions at varying levels. If the VI RASD can be restarted after malfunction without risk to the patient and surgery can continue with the robot.

If restart after malfunction is unsuccessful or cannot be done without risk to the subject, the VI RASD will be removed (as described above) and the surgeon will proceed in the standard laparoscopic fashion.

In the event that a robotic arm malfunctions at the time of tissue contact, laparoscopic tools will be used to safely un-attach the robotic arm from the tissue and then remove the robot. At the conclusion of the surgery, the surgeon will carefully evaluate all tissues and planes where the RASD was in contact to determine whether an injury occurred.

In the event of study subject hemodynamic instability from anesthesia, bleeding, adhesions, or other factors preventing the surgeon from proceeding with the surgery, the surgeon will remove the VI RASD under direct visualization from its port and convert the procedure to either laparoscopic or open procedure. Unanticipated robotic removal is performed in a similar fashion today with current FDA-approved robotic technology.

Again, detailed procedures are available in the trouble shooting section of the VI RASD User Manual (Section 10.4 of this IDE).

Appendix B: Exemplary Steps for Right and Left Hemicolectomy with the VI RASD

This protocol does not dictate how a colectomy procedure should be performed. However, some details are listed here as examples. All information in this appendix is exemplary. The use of the VI RASD in each step may vary from case to case. Exact steps to be undertaken are medical decisions left to the investigator.

The following description is a high-level step by step approach for the use of the VI RASD in Umbrella Procedures, Right and Left Colectomy. The VI RASD will assist with certain steps of established laparoscopic procedures.

In the following sections each of the full procedures to be performed are broken down into a set of actions performed by the surgical staff (surgeon and surgical assistant). The steps required to perform each of these procedures using the VI RASD are illustrated and described. The remaining steps which are simply listed and numbered without illustrations are left to the surgeon according to standard laparoscopic surgical techniques. For each procedure, the system setup is defined including the needed tools, laparoscopic ports (trocar sites), trocars and auxiliary equipment, as well as suggested placement of trocars and the robot in the patient. This is followed by the procedural steps.

A Hand-Assist Laparoscopic port will be used to insert the robot in all procedures. All procedures will be performed in conjunction with standard operating room and laparoscopic equipment including:

- Suction/Irrigation
- Insufflation
- Trocars
- Laparoscopic instruments
- Electrosurgical Generator
- Laparoscope (optional)

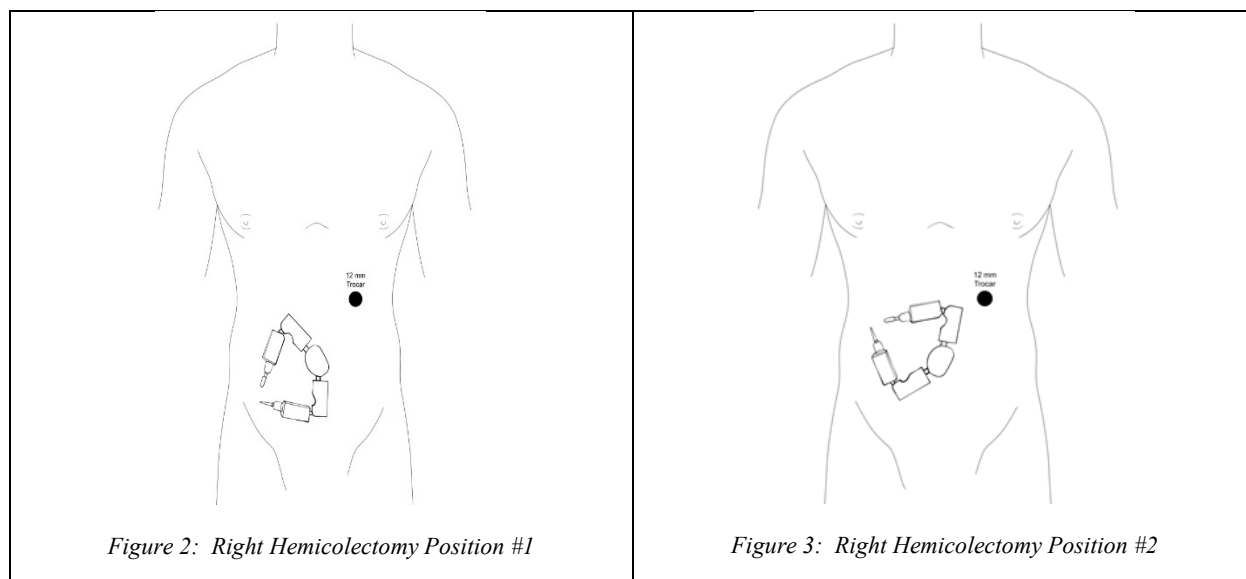
B1. VI RASD Right Hemicolectomy

The suggested procedure for a robotic assisted right hemicolectomy is defined here. A lateral-to-medial approach and a medial-to-lateral approach are both defined.

B1.1 Right Hemicolectomy Setup Procedure

To support this procedure a clip applier, stapler, HALS port (for robot insertion and specimen removal), and one 12 mm trocar will be used. The robot will have a bi-polar fenestrated grasper in the left hand and a scissors in the right.

The robot will be inserted through the umbilicus using the Hand Assist Laparoscopic port. The robot will operate in two general configurations as shown in Figure 4 and Figure 5.

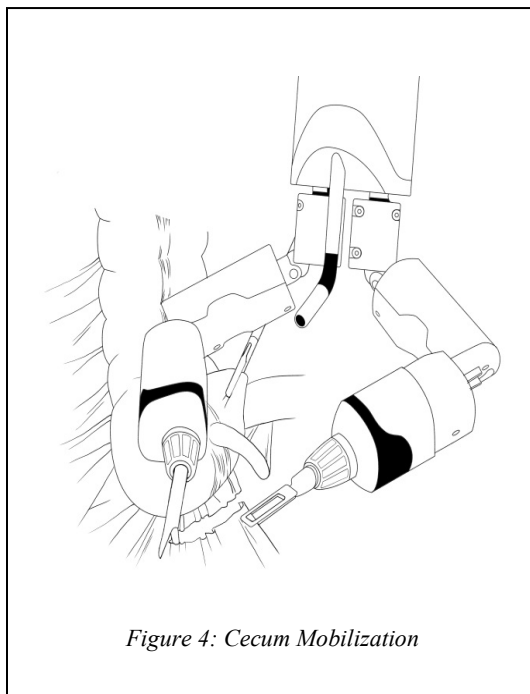


The procedure can be accomplished with the following exemplary steps:

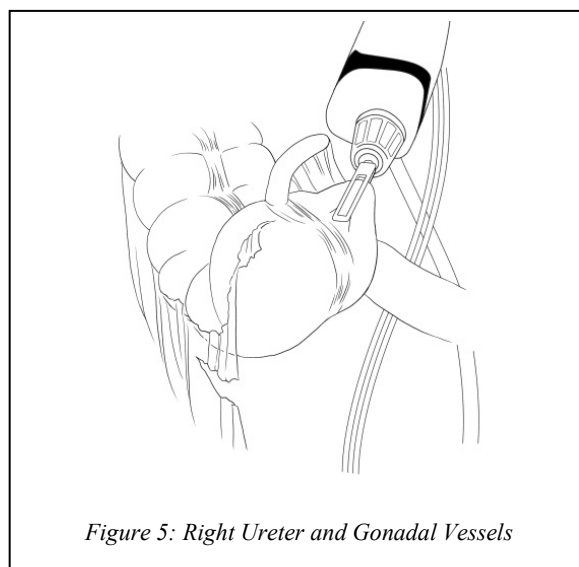
- STEP 1. Peritoneal access via open periumbilical midline Hand Assist Laparoscopic port placement.
- STEP 2. Insufflate to establish pneumo-peritoneum to 15 mm Hg.
- STEP 3. Insert VI RASD camera into Hand Assist Laparoscopic port and perform general preliminary inspection.
- STEP 4. Using camera visualization via the Hand Assist Laparoscopic port insert 12mm trocar suprapubic midway along left coastal margin.
- STEP 5. Use the insertion procedure and position the robot in Position #1 as shown in Figure 4.

B1.2 Lateral-to-Medial Approach

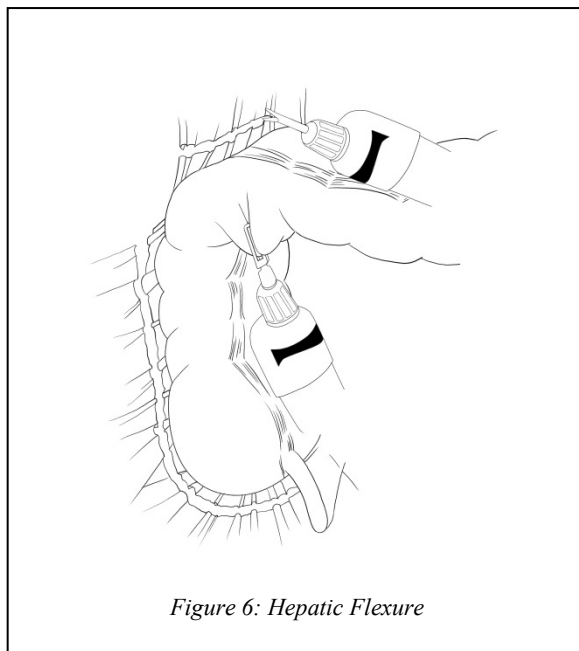
- STEP 6. Place the patient in steep Trendelenburg with the left side of the table down.
- STEP 7. Cecum grasped with robot grasper (left hand) and retracted cephalad. Using scissors (right hand) Cecum is mobilized by dividing the lateral peritoneal attachments starting at the base of the cecum and cephalad along the white line of Toldt, as depicted in Figure 6.



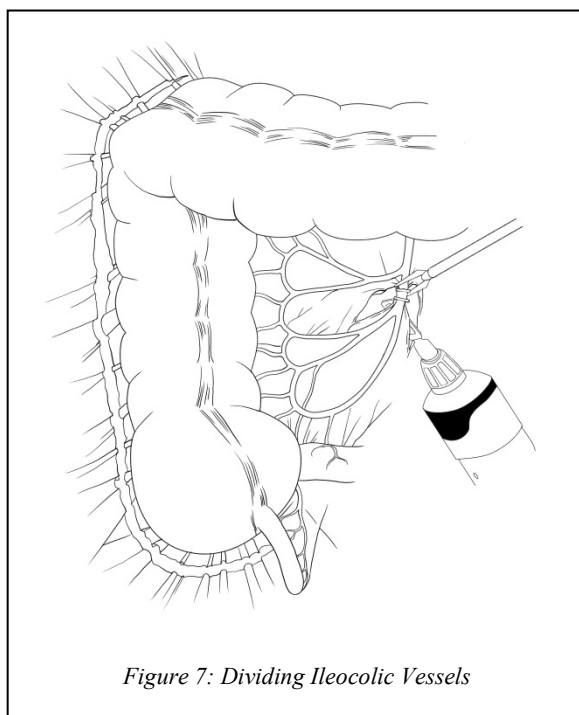
- STEP 8. Division of peritoneal overmesentery of the terminal ileum, and then continue to incise along the white line of Toldt to the hepatic flexure.
- STEP 9. Care should be taken to preserve the right ureter and gonadal vessels, depicted in Figure 7.



- STEP 10. Rotate robot to position #2 as shown in Figure 5. And reposition the patient in reverse Trendelenburg.
- STEP 11. Mobilize hepatic flexure of the colon with scissors and cautery, shown in Figure 8. Divide hepatocolic attachments, applying clips on larger veins. Divide right gastro colic attachments.



STEP 12. Divide ileocolic vessels with laparoscopic linear stapling device, as shown in Figure 9.



- STEP 13. Extract the robot using the Robot Extraction Procedure.
- STEP 14. Remove Hand Assist Laparoscopic port, but leave sleeve inserted.
- STEP 15. Externalize right colon through Hand Assist Laparoscopic port incision.
- STEP 16. Transect distal ileum and distal transection site of right colon with the stapler.
- STEP 17. Side to side (functional end to end) anastomosis is completed with the stapler.

- STEP 18. Closure of common enterotomy with either suture or stapler.
- STEP 19. Return bowel to the mesenteric cavity.
- STEP 20. Replace Hand Assist Laparoscopic port.
- STEP 21. Insufflate to establish pneumoperitoneum to 15mm Hg.
- STEP 22. Insert Visualization Unit into 12mm trocar.
- STEP 23. Inspect abdomen for bleeding.
- STEP 24. Remove Hand Assist Laparoscopic port and 12mm trocar.
- STEP 25. Close incision sites.

B1.3 Medial-to-Lateral Approach

The procedure can be accomplished with the following steps:

- STEP 1. Identify the ileocolic artery by applying right superolateral traction to the mesentery by elevating the cecum at the junction of the bowel and the mesentery.
- STEP 2. Create mesenteric window on each side of the ileocolic artery with robotic scissors and electrocautery.
- STEP 3. Divide the mesentery between ileocolic and middle colic artery.
- STEP 4. Complete lateral mobilization described in steps 6-25 above.

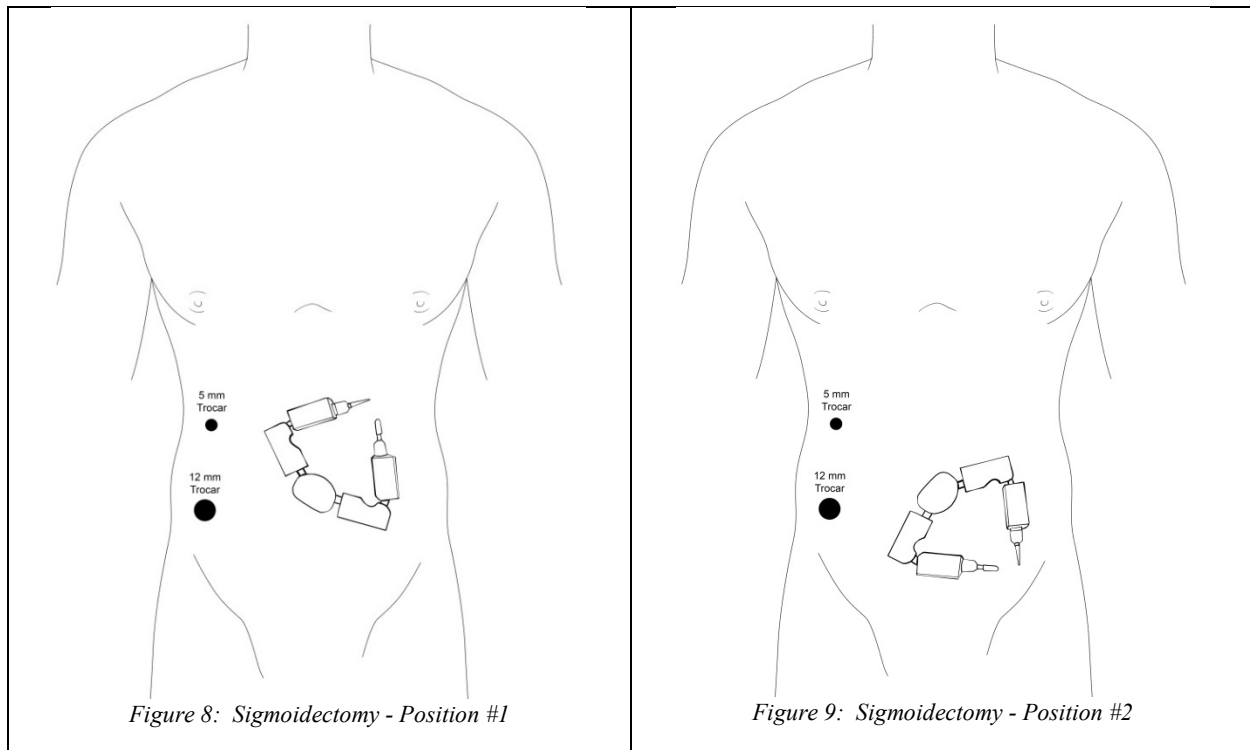
B.2 Robotic Assisted Left Hemicolectomy/Sigmoid Resection

B.2.1 Left Hemicolectomy/Sigmoid Resection Setup Procedure

To support this procedure a babcock grasper, a stapler, HALS port (for robot insertion and specimen removal), one 5 mm trocar, and one 12 mm trocar will be used.

The robot will have one configuration with a grasper in the left hand and a scissors in the right.

The robot will be inserted through the umbilicus using the Hand-Assisted Laparoscopic Port. The robot will operate about two general configurations as shown in the Figure 10 and Figure 11.



B.2.2 Let Hemicolectomy/Sigmoid Resection Procedure

The procedure can be accomplished with the following steps:

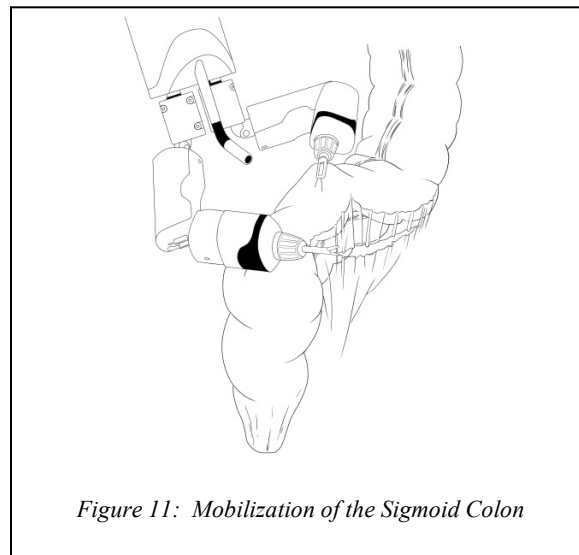
- STEP 1. Peritoneal access via open periumbilical midline Hand Assist Laparoscopic port placement.
- STEP 2. Insufflate to establish pneumoperitoneum to 15 mm Hg.
- STEP 3. Insert VI RASD camera into Hand Assist Laparoscopic port and perform general preliminary inspection.
- STEP 4. Using camera visualization via the Hand Assist Laparoscopic port insert 12mm trocar in right lower quadrant as shown in Figure 10.
- STEP 5. Using camera visualization via the Hand Assist Laparoscopic port insert 5mm trocar in right lower quadrant as shown in Figure 10.
- STEP 6. Remove VI RASD camera from Hand Assist Laparoscopic port and place in 5 mm trocar.
- STEP 7. Use the robot insertion procedure and position the robot in Position #1 as shown in Figure 10.

B.2.3 Lateral-to-Medial Approach

- STEP 8. Place the patient in steep Trendelenburg with the right side of the table down. Gently sweep bowel into right upper quadrant.
- STEP 9. Use the robot grasper (left hand) and scissors (right hand) to mobilize the left colon along the white line of Toldt as depicted in Figure 12.

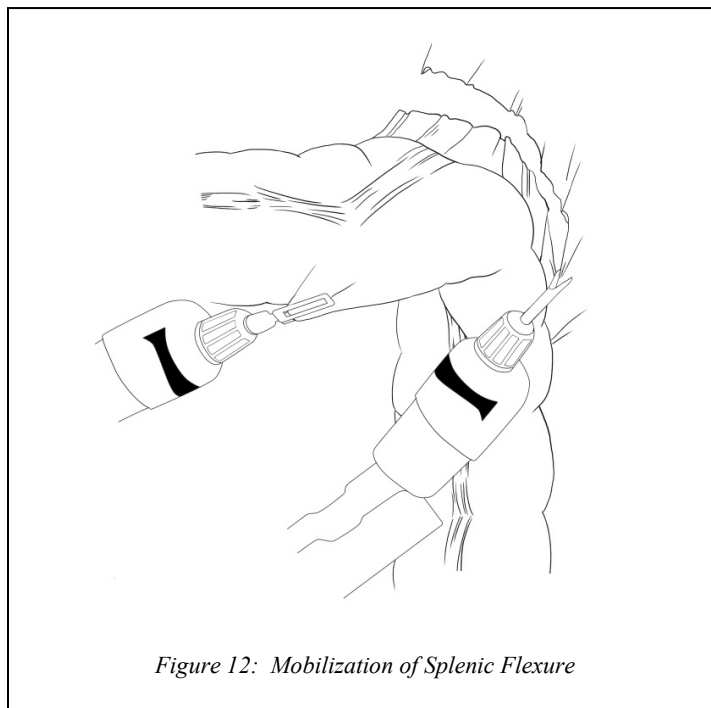


STEP 10. As needed rotate robot to Position #2 (Figure 11) and mobilize the sigmoid colon along the white line of Toldt as shown in Figure 13.

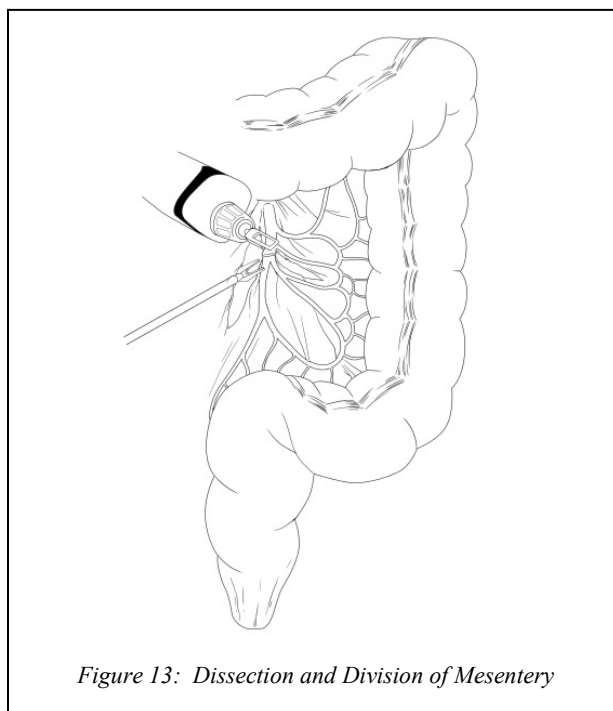


STEP 11. Reposition the patient in reverse Trendelenburg.

STEP 12. Rotate the robot to Position #1 (Figure 10) and mobilize the splenic flexure including the gastrocolic ligament as shown in Figure 14. If the surgeon believes that additional colon length is required, a laparoscopic splenic mobilization may be performed by the surgeon and then the robot will be used for the remainder of the dissection as per protocol.



- STEP 13. Dissect and divide the mesentery (stapler) and transection of either the superior hemorrhoidal and the left colic arteries or the inferior mesenteric artery. To accomplish this task the robot is moved to Position #2 (Figure 11) and used to assist by grasping and retracting while the stapler is used through the auxiliary ports as shown in Figure 15.



- STEP 14. Transect distal sigmoid colon (proximal rectum) with stapler inserted through the 12 mm trocar. The robot is used to assist by grasping and retracting as shown in Figure 16.

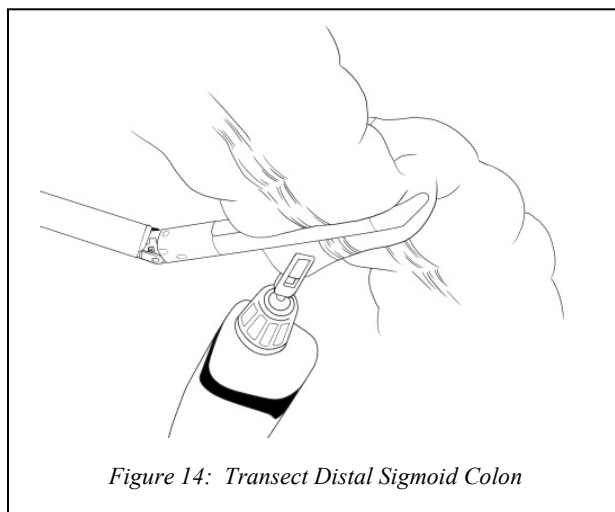


Figure 14: Transect Distal Sigmoid Colon

- STEP 15. Extract the robot using the Robot Extraction Procedure.
STEP 16. Remove the Hand-Assisted Laparoscopic Port leaving the wound retractor in place.
STEP 17. Externalize sigmoid and left colon through the wound retractor.
STEP 18. Divide the proximal left colon with stapler.
STEP 19. Secure the anvil in the proximal colon with purse string.
STEP 20. Re-introduce proximal colon into abdominal cavity.
STEP 21. Replace Hand-Assisted Laparoscopic Port and insufflate to 15 mm Hg. Manual laparoscopic techniques will be used to complete the procedure, but the robot can also be re-inserted to assist with these final steps.
STEP 22. Insert VI RASD camera into 5 mm trocar.
STEP 23. Insert Circular stapler through anus and unite with the anvil. Use stapler to create anastomosis.
STEP 24. Inspect for bleeding.
STEP 25. Remove ports.
STEP 26. Close incision sites.

B.2.4 Medial-to-Lateral Approach

- STEP 1. Identify and ligate the inferior mesenteric artery.
STEP 2. Retract the sigmoid colon superolaterally to identify the inferior mesenteric artery.
STEP 3. Proceed to isolation, ligation and division of superior hemorrhoidal and left colic artery or inferior mesenteric artery as described in step 13.
STEP 4. Complete lateral mobilization as described in steps 8-12.
STEP 5. Then complete the procedure as described in steps 14-26.