Clinical Investigational Plan		
Title: **HYbrid RObotic Surgery in Partial, Radical nephrectomy and Prostatectomy (HYROS-PRnP)**		
Sponsor: Rob Surgical Systems, S.L. Autovia de Castelldefels C-31 km 190.5, 08820 El Prat de Llobregat (Barcelona), Spain		
Standards and applying chapters: **According to IF-PR01-022_A6 Bitrack_Applicable Regulation and IF-PR01-023_B2 Bitrack Aplicable standards, according to IF-PR01-021_A6_Surgical Endoscopic instruments Applicable Regulation and IF-PR01-003_A9 Surgical Endoscopic Instruments Applicable standards, according to IF-PR01-177_A3 Camera Adapter applicable regulation and IF-PR01-178_A3 Camera Adapter applicable standards**		
Protocol Nr: **PL-PR01-076**	Revision Nr: **A2**	Date of issue: **15/05/2024**
Project Code: **PR01**		Author: **Mireia Riera**

REVIEW HISTORY

Reviewed Edition	Date	Section	Rationale	List of Changes
A1	07/07/2023	NA	Initial document release	NA
A2	15/05/2024	[redacted]	[redacted]	[redacted]
		Summary- Electronic Data Capture (EDC)	Type error	The platform name of the Electronic Data Capture was corrected from "Open Clinica" to "Libre Clinica"
		Section 2.1 Device Under Investigation and Table 2-1. "Bitrack System description".	Type error	Serial Number for Bitrack System [redacted]
		Section 2.1 Device Under Investigation	Type error	[redacted]

		Section 3	Type error	[redacted]
		Section 4.1 Overview	[redacted]	[redacted]
		Sections implied: - Summary, - 4.1 Overview - 5.2 Secondary Endpoints - 7.5 Post procedure.	Type error	[redacted]
		Section 4.2 Clinical Investigation Procedures and Follow-up Schedule	Type error	[redacted]
		Section 4.2 Clinical Investigation Procedures and Follow-up Schedule	[redacted]	[redacted]

		Section 5.2 Secondary Endpoints	Type error	[redacted]
		[redacted]	[redacted]	[redacted]
		Section 6.6 Expected Duration of the Participants in the clinical Investigation	Type Error	[redacted]
		Section 7.6 Follow-up Assessments	[redacted]	“[redacted]
		[redacted]	[redacted]	[redacted]

CONTACT INFORMATION

SPONSOR AND LEGAL MANUFACTURER
Rob Surgical Systems, S.L.
Autovia de Castelldefels C-31 km 190.5, 08820 El Prat de Llobregat (Barcelona), Spain
[redacted]

CRO:
ANAGRAM-ESIC S.L
[redacted]

Barcelona Clinical Coordinating Center (BCCC),
represented by Fundació Mon Clínic Barcelona
[redacted]

SITE PRINCIPAL INVESTIGATOR:
Hospital Clinic de Barcelona
C/ Villarroel 170, Esc 12 – 1 Planta, 08036-Barcelona (Spain)
[redacted]

CLINICAL INVESTIGATION PLAN (CIP) SUMMARY

Version Number	A1
Date	7th July 2023
Sponsor	Rob Surgical Systems, S.L. Autovia de Castelldefels C-31, km 190.5 El Prat de Llobregat (Barcelona, Spain), 08820
Clinical Investigation Identification	HYROS-PRnP
Title	**HYbrid RObotic Surgery in Partial, Radical nephrectomy and Prostatectomy (HYROS-PRnP)**
Objectives	The purpose of this clinical investigation is to evaluate the safety and performance of the Bitrack System and its corresponding ESE and NESE instruments and accessories in patients with the indication of a robot assisted laparoscopic Radical/simple nephrectomy (RN), Partial nephrectomy (PN) or Radical Prostatectomy (RP), as applicable and when it applies lysis of adhesions (during RN, PN or P to cut the adherence and reach the organ) and lymphadenectomy (only after a RP with the aim to remove the lymph nodes). HYROS-PRnP is a confirmatory study in which the hypothesis of the primary endpoint is that the ESE/NESE instruments perform as intended when controlled by Bitrack System which operates exclusively under surgeon's orders. The report shall refer to safety and performance of Bitrack System together with its accessories and corresponding ESE/NESE instruments. This report includes the data collected up to 30 days post-surgery and provides the evidence that the tested medical devices fulfill the GSPR. In this clinical study no additional post-study care is required.
Device Under Investigation	Bitrack System, ESE/NESE instruments and the camera adapter which is an accessory of Bitrack System.
Number of Subjects Required for Clinical Investigation	15 subjects shall be included in the clinical investigation.
Planned Number of Sites	1 investigational site located in Spain
Clinical Investigation Design	This is a single-center, confirmatory, clinical investigation with a single arm, open label and non-randomized design.
Primary Endpoints	The primary endpoint of this clinical investigation is:

	Evaluation of Bitrack System to assist in the accurate control of its compatible ESE/NESE instruments, stablishing as hypothesis that they perform as intended by the surgeon (performance score scale ≥ 3) during the intervention without causing any particular SAE related to the use of the medical devices under investigation, when devices are all used according to the respective Instructions for use.
Secondary Endpoints	[redacted]

<table>
<tr><td></td><td>  </td></tr>
<tr><td>Subject Follow-up</td><td>The subjects participating in this clinical investigation will be followed up to 30 days after surgery for safety and performance.

The visit scheduling is planned as follows:

<table>
<tr><th>Visits</th><th>Radical Nephrectomy (RN)</th><th>Partial Nephrectomy (PN)</th><th>Radical Prostatectomy (P)</th></tr>
<tr><td>ICF / Baseline Visit</td><td>√</td><td>√</td><td>√</td></tr>
<tr><td>Surgery Visit</td><td>√</td><td>√</td><td>√</td></tr>
<tr><td>Discharge Visit (exp. 3d post-surgery)</td><td>√</td><td>√</td><td>√</td></tr>
<tr><td>14 days FUP Visit (± 5 days) (onsite)</td><td>√</td><td>√</td><td>√</td></tr>
<tr><td>30 days FUP Visit (± 5 days) (remote)</td><td>√</td><td>√</td><td>√</td></tr>
</table>
m: months
FUP: Follow Up
Exp.: expected

At 14 days Follow Up Visit in case of Radical Prostatectomy, the surgeon removes the catheter of those patients submitted to this procedure.

At 30 days Follow Up visit in case of PN and Radical Prostatectomy, the surgeon explains to patient the results of the histopathology if they have not been explained before and takes the opportunity to evaluate the welfare of the patients. In the specific case of Radical prostatectomy, patient will be asked about urinary continence and erectile function.</td></tr>
<tr><td>Inclusion Criteria</td><td>1. Adult subjects between 18 and 90 years old who have provided written informed consent prior to any clinical investigation related procedures.
2. Subjects who have been scheduled for a laparoscopic Radical/simple Nephrectomy surgery, laparoscopic Partial Nephrectomy or laparoscopic Radical Prostatectomy following the surgeon criteria.</td></tr>
</table>

	3. Ability and willingness to comply with all study requirements to be evaluated for each study visit
Exclusion Criteria	1. Pregnant or breastfeeding women at the time of the surgery 2. Subjects with severe concomitant illness that, at PI´s discretion, increases risk of therapeutic interventions or that have been submitted to multiple prior surgeries. 3. Subjects admitted to the hospital due to an emergency situation. 4. Subjects with untreated active infection 5. Subject with known allergy to some of the device components (i.e., stainless steel, etc.) 6. Subjects not suitable to undergo MIS/MIRS, according to medical criteria. 7. Subjects with life expectancy inferior to 3 months 8. Subjects with a BMI ≥ 40 9. Subjects with any contraindication for the use of the Bitrack System and the ESE/NESE instruments, as specified in the Instructions For Use 10. Subjects with abuses of active substances or with uncontrolled psychiatric disorders 11. Subjects with severe cardiopulmonary or coronary artery disease, bleeding disorders or that have been submitted to multiple prior operations. 12. Subjects scheduled for surgeries intended to be in direct contact with the heart, the central circulatory system or the central nervous system. 13. Inability to adhere to study-related procedures. 14. Subjects who participate in another trial which may affect the outcome data on this study or the ability to complete the follow up requirements.
Electronic Data Capture	Libre Clinica's Electronic Data Capture (EDC platform)
Expected Duration of the Study	The expected duration of the clinical investigation duration will be as follows: Around 7 months, including 6 months of enrollment and the follow up of 30 days after surgery to finalize the assessment of safety and performance of Bitrack and corresponding ESE/NESE instruments. The duration of the study for each individual patient finalizes 30 days after their enrollment.

INVESTIGATOR PROTOCOL SIGNATURE PAGE

I have read the Clinical Investigational Plan and I agree to conduct this clinical investigation as outlined and in accordance with all applicable laws and regulations, including Good Clinical Practice guidelines.

In addition, I agree to provide all the information requested in the case report forms in a timely manner ensuring completeness and accuracy.

[redacted]

Investigator Signature

15-MAY-2024

Date

[redacted]

Investigator Printed Name

PI

Investigator (Study Role)

Hospital Clínic de Barcelona

Investigational Site Name

SPONSOR SIGNATURE PAGE

[redacted]

COMPLIANCE STATEMENT:

This clinical investigation will be conducted in accordance with this Clinical Investigation Plan, the Declaration of Helsinki, ISO 14155:2020 standards, EU Regulation 2017/745 (MDR) and the appropriate local legislation(s) Real Decreto 192/2023. The most stringent requirements, guidelines or regulations must always be followed. The conduct of the clinical investigation will be approved by the appropriate Ethics Committee (EC) of the respective clinical site and as specified by local regulations. Any additional requirement imposed by the EC will be followed.

CONFIDENTIALITY STATEMENT

This document is confidential and is to be distributed for review only to investigators, potential investigators, consultants, study staff, and applicable independent Ethics Committees or Competent Authorities. The contents of this document shall not be disclosed to others without written authorization from the Sponsor unless it is necessary to obtain informed consent from potential study participants.

TABLE OF CONTENTS

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

1. INTRODUCTION

Laparoscopy is defined as a surgical technique that allows surgical procedures to be performed while minimizing trauma to the body. These procedures require a small incision in the body, which permits the introduction of a video-camera system to help the surgeons perform the surgery[1,2].

Bitrack System is a tele-assisted surgical robot intended to assist in the accurate control of the exclusive Bitrack System-compatible range of ESE/NESE (electrosurgical and non-electrosurgical endoscopic) instruments. The Bitrack System is composed by a console, a robotic unit and an embedded software.

This study is designed as an open label, single-center clinical investigation with a single arm, to evaluate the safety and performance of the Bitrack System in patients eligible for robotic assisted laparoscopic Radical/simple Nephrectomy surgery, Partial Nephrectomy and Radical Prostatectomy.

This clinical investigation is sponsored by Rob Surgical Systems (Barcelona, Spain) and will be conducted in accordance with this CIP.

Background

Laparoscopic surgeries have become the gold standard for many surgical procedures as they allow minimally invasive surgery (MIS), while providing benefits over an open procedure, including, among others, reduction in post-operative pain, decrease in the length of hospital stays, faster return to daily activities and improved cosmesis, which increases patients' quality of life[4]. New surgical tools, such as the development of robotic-assisted surgery (RAS), have been designed to improve the effectiveness of the process, minimizing the ergonomic and visualization deficiencies of laparoscopy while preserving the advantages of minimally invasive surgery[3].

During minimally invasive robotic surgery (MIRS) procedures, the robots employed are not considered autonomous

Nevertheless, decades of continued improvement

have significantly increased the potential for these robots to assist during minimally invasive surgeries[6].

One of the main concerns for surgeons is the absence of haptic sensation; however, RAS permits fine and precise movements, as well as the elimination of tremor, which is argued to compensate the forementioned disadvantage. Besides, the robotic platforms used in RAS offer the possibility to reduce ergonomic issues by providing a comfortable seating or neutral posture position, avoiding forced unnatural movements and delegating the torquing forces to the robotic arms, decreasing the burden on surgeon's muscles in the sensitive areas like the neck, shoulders, and upper back[7].

Medical application of laparoscopic procedures includes a wide range of surgical processes, among which the most frequent are gastrointestinal complications, bariatric and metabolic surgeries, and gynecological and urological applications[3,4].

Urology indicates that robotic and laparoscopic procedures, such as radical prostatectomy and partial

nephrectomy (RNP), are equivalent, [redacted] it has been also determined that the use of RAS may improve the precision of movements and reduce the risk of damage to the cavernous nerves to maintain erectile function by mechanical trauma, traction or thermal energy[8,9].

Bitrack System is a surgical robot indicated to be used during urological surgical procedures. This robot is intended to assist in the accurate control of endoscopic instruments and accessories for visualization and endoscopic manipulation. RAS systems and equipment such as Bitrack System, are intended for use in invasive surgical procedures, during which patients are potentially most vulnerable to physical harm. [redacted]

[redacted]

[redacted]

[redacted]

Rationale for Conducting this Clinical Investigation

Traditional laparoscopic surgery has been associated with ergonomic issues due to prolonged operative times, unnatural body postures, and positioning of trocars. Robotic platforms have been introduced as an option to decrease some of these issues. Bitrack System is presented as an open robotic platform designed to improve efficiency with regards to current robotic systems, reducing limitations of conventional laparoscopy and robotic

surgery while maintaining its advantages over the open approach. Additionally, enabling fine and precise movements of the surgical instruments results in accurate control of their corresponding endoscopic surgical instruments in case of urologic laparoscopic surgical procedures carried out by means of an abdominopelvic approach.

The purpose of this clinical investigation is to evaluate the Bitrack System and its ESE/NESE Instruments and confirm the safety and performance of the Bitrack System in patients eligible for robotic assisted laparoscopic Radical/simple nephrectomy surgery, Partial Nephrectomy and Radical Prostatectomy.

[redacted]

2. MEDICAL DEVICE OVERVIEW

[redacted]

Device Under Investigation

Bitrack System is an Open Robotic Platform designed to universalize high precision surgery and improve the efficiency on current robotics solutions.

Hybrid surgery is a new surgical approach that allows for combining minimally invasive surgery (MIS) and minimally invasive robotic surgery (MIRS) in the same procedure and to move quickly from MIS to MIRS.

[redacted]

Finally, in tele-assisted mode, through the console unit, the console user can take control of the system. The system reproduces the user maneuvers (position and orientation) from the console unit manipulators to the instrument end-effectors. [redacted]

[redacted]

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

Characteristic	Description	References
Description of the device	[redacted]	Investigator's Brochure
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Intended purpose

Bitrack System is intended to assist in the accurate control of endoscopic instruments and accessories for visualization and endoscopic manipulation of tissue including grasping, mechanical and monopolar cutting, blunt dissection, approximation, ligation, bipolar coagulation, suturing, and delivery, placement and tracking of its endoscopic assistance instruments.

Bitrack System is indicated for use during urological surgical procedures. The patient target population of Bitrack System is adults.

The intended users are trained physicians in an operating room environment in accordance with the Instructions for Use.

Intended Indication for Use

Bitrack System is a robotic surgical system indicated for urologic surgical procedures. The recommended procedures are listed as follows:

- Urology
  - Partial/Radical nephrectomy
  - Radical prostatectomy
  - Lysis of Adhesions
  - Lymphadenectomy

Summary of Preclinical Studies

[redacted]

[redacted]

The results obtained allow to conclude that Bitrack System safety and performance predefined endpoints have been met. Thus, Bitrack System has the ability to complete successfully these Minimally Invasive Robotic Surgery (MIRS) procedures.

[redacted]

The results of this study allow to affirm that:

The surgeons have safely performed the Radical Prostatectomy (RP) with the aid of Bitrack System. Then performance of the Bitrack System during a RP on a cadaver model has been confirmed.

[redacted]

[redacted]

Description of the Control Device(s) or Historic Control

No Control Devices or Historic Control are applicable to this study since there is no direct comparison to other competitor devices.

[redacted]

Device Handling

[redacted]

ESE/NESE instruments will be handled according to the approved Instructions For Use. Prior to use of the device, there is a non-sterile manipulation of the devices to remove them from third and secondary packages,

[redacted]

Traceability of all components involved will be present in the corresponding device labels.

3. CLINICAL INVESTIGATION OBJECTIVE

The purpose of this clinical investigation is to evaluate the safety and performance of the Bitrack System (and its corresponding ESE and NESE instruments and accessories in patients with the indication of a robot assisted laparoscopic Radical/simple nephrectomy (RN), Partial nephrectomy (PN), Radical Prostatectomy (RP), and when it applies Lysis of Adhesions (during a PN, RN or P to cut the adhesions and reach the organ) and Lymphadenectomy (only after a P with the aim to remove the lymph nodes).

[redacted]

4. CLINICAL INVESTIGATION DESIGN

Overview

The study will be conducted as a confirmatory clinical investigation with a single arm, open-label, and non-randomized design, and will include 15 subjects eligible to a standard of care laparoscopic surgery.

The clinical investigation will be conducted in 1 center in Spain for all 3 procedures.

As already obtained results from previous 3 RN patients during the HYROS, in the HYROS-PRnP the 15-patients will be distributed between the 3 procedures: Radical Nephrectomy, Partial Nephrectomy and Radical Prostatectomy. Patients will be included in the study following the assumption of First patient in.

This clinical investigation will be considered as monocentric. The site investigation details are provided below:

Hospital Clinic de Barcelona
[redacted]

The purpose of this clinical investigation is to evaluate the safety and performance of the Bitrack System and its corresponding ESE and NESE instruments and accessories in patients with the indication of a robot assisted laparoscopic Radical/simple nephrectomy (RN), Partial nephrectomy (PN) or Radical Prostatectomy (RP), and when it applies Lysis of Adhesions (during a PN, RN or P to cut the adhesions and reach the organ) and Lymphadenectomy (only after a P with the aim to remove the lymph nodes).

[redacted] This statistical assessment permits to stablish an hypothesis that the Bitrack System and ESE/NESE instruments perform as intended by the surgeon during the intervention, when devices are all used according to the respective Instructions for use. The primary endpoint, defined to check this hypothesis, is the assessment of the surgeon in a Likert scale with a score range from 1 to 5. The Surgeon Performance Scale Score has been designed to evaluate the performance of Bitrack System in each surgery as a whole procedure and ESE/NESE instruments in all the steps defined for each surgery.

The score ranges of the Surgeon Performance Scale Score have been defined as:

1. Failure: [redacted]
2. Unacceptable: [redacted]
3. Satisfactory: [redacted]
4. Good: [redacted]
5. Excellent: [redacted]

To accomplish with the hypothesis stablished in our primary endpoint, the performance score needs to be ≥ 3 as acceptance criteria.
This acceptance criteria will only be accepted if it has been obtained without causing any particular SAE related to the use of the medical devices under investigation.

The following safety and performance secondary endpoints are planned for the three indications:

The report shall refer to safety and performance of Bitrack System and corresponding ESE/NESE instruments. This report includes the data collected up to 30 days post-surgery and provides the evidence that the tested medical devices fulfill the GSPR.

In this clinical study no additional post-study care is required.

The results of the current study HYROS-PRnP shall confirm safety and performance outcomes found during previous First in Human study with 3 patients, HYROS study, shown in figure 2.

Figure 2.HYbrid RObotic Surgery in Urology - Full Text View - ClinicalTrials.govTitle: HYbrid RObotic Surgery in Urology (HYROS)

Study Design Go to

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	3 participants
Allocation:	N/A
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Device Feasibility
Official Title:	HYROS (HYbrid RObotic Surgery in Urology)
Actual Study Start Date :	April 11, 2023
Estimated Primary Completion Date :	May 26, 2023
Estimated Study Completion Date :	June 20, 2023

Arms and Interventions Go to

The data collected in the FIH study HYROS showed that No Procedure-Related Adverse Events (PRAEs) and Serious Adverse Events (SAEs) occurred and that all surgeries were successfully performed with the Bitrack System and none was converted to laparoscopy/open surgery, indicating that the Bitrack system and its ESE/NESE Instruments performs as intended.

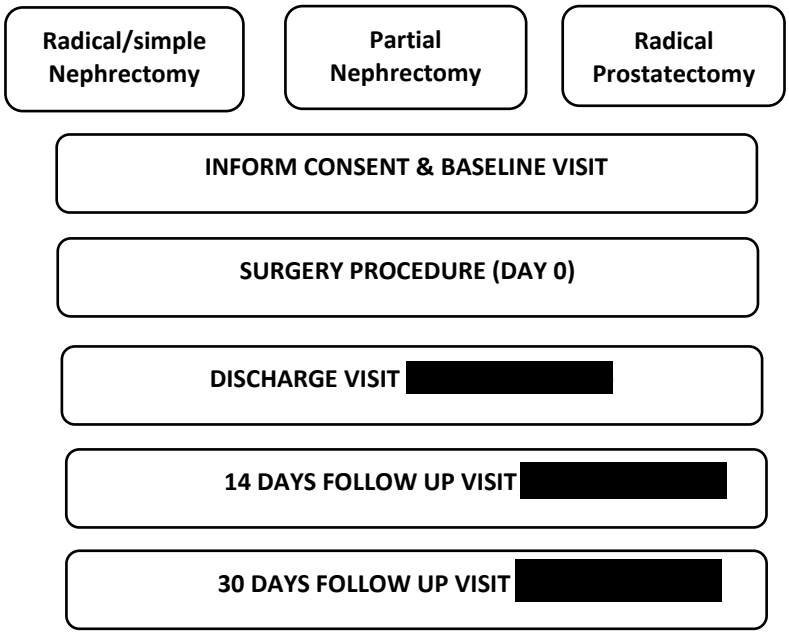
The clinical investigation has been designed to involve as little pain, discomfort, fear, and any other foreseeable risk as possible for subjects participating in the study.

Clinical Investigation Procedures and Follow-up Schedule

The Clinical Investigation visits will occur as in-clinic visits at Baseline, Procedure, Discharge and 14 days. A 30-days follow-up visit will be performed remotely.

The Flow Chart and the Follow-up phases of this clinical investigation are described in Figure 4-1 below.

Figure 3. Flowchart of the Clinical investigation schedule of HYROS-PRnP flow chart.



The scheduling of the clinical investigation visits will include the following:

Baseline visit (Visit 1)

During the baseline visit, the patient will be informed about the clinical study and provide signed informed consent form if surgeon decides that the patient is eligible as applicable. [redacted]. In case of pregnancy, the patient will withdraw of the study, [redacted]

Surgery Procedure – (Visit 2)

The study population consists of subjects that provided signed ICF, met all inclusion criteria and none of the exclusion criteria, and successfully undergo surgery with the Bitrack System and its corresponding ESE/NESE instruments. These patients will be followed up until 30 days post-procedure. On the other hand, those subjects in whom robot assisted laparoscopic radical/simple nephrectomy, Partial Nephrectomy or Radical Prostatectomy is attempted but not achieved, they will be followed-up for 30 days, but not included as population for analysis.

[redacted]

In order to evaluate the Bitrack System and ESE/NESE instruments performance, each surgical procedure has been defined in several steps following the surgeon criteria. Through the Surgeon Performance Scale Score, the surgeon will give its assessment to the Bitrack System for the whole procedure and to the ESE/NESE instruments in each surgical step.

[redacted]

Radical Nephrectomy surgery

1. [redacted]
2. [redacted]

3. [redacted]
4. [redacted]
5. [redacted]
6. [redacted]
7. [redacted]
8. [redacted]
9. [redacted]
10. [redacted]

[redacted]

Partial Nephrectomy surgery

1. [redacted]
2. [redacted]
3. [redacted]
4. [redacted]

5. [redacted]
6. [redacted]
7. [redacted]
8. [redacted]
9. [redacted]
10. [redacted]

[redacted]

Radical Prostatectomy procedure

1. [redacted]
2. [redacted]
3. [redacted]
4. [redacted]
5. [redacted]
6. [redacted]
7. [redacted]
8. [redacted]
9. [redacted]
10. [redacted]

[redacted]

The surgeon ensures hemostasis (control of bleeding) by sealing blood vessels and applying sutures or clips as necessary. [redacted]

A drain may be placed near the surgical site to collect any fluid or blood that may accumulate postoperatively. Additionally, a urinary catheter is inserted into the bladder through the urethra to allow for urine drainage during the initial healing period.

For research purposes, we will consider the start of each procedure at the moment of activating the ESE/NESE instruments in tele assisted mode and console surgeon regain complete control on the ESE/NESE instruments. Therefore, all procedures that passed this point but do not proceed with the use of the Bitrack system or are converted into a conventional laparoscopic/open surgery are included under the Intent-to-treat (ITT) population. Any robot assisted surgery converted to conventional laparoscopic/open surgery due to reasons different than the failure of the Bitrack System and its corresponding sterile endoscopic surgical instruments will be excluded from the endpoint analysis. [redacted]
This event will be considered a procedure failure.

[redacted]

#	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
1	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
2	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
3	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

Discharge (Visit 3)

Subject´s discharge is expected after [redacted] the surgery. This visit will be completed following site´s standard of care practices and always when it is safe for the subject. At the time of discharge, subject´s clinical

information will be collected to assess the post-operative pain, together with the rate of post-procedure complications.

14-Days follow-up visit (Visit 4)

The objective of this visit is to collect data on AEs related to the device and the procedure. During the follow-up [redacted] practice. The information provided by the subject should be appropriately collected in the Case Report Form (CRF).

30-Days follow-up visit (Visit 5)

The 30-Days follow-up visit [redacted] The objective of this follow-up visit will be to collect data about any AE related to the device, the procedure or both. Additionally, information about the patient pain evaluation [redacted]

[redacted]

Measures Taken to Avoid and Minimize Bias

The following steps will be taken to minimize bias in the conduct of the clinical study:

Subject requirement

Patients of both genders will be considered as anatomy does not influence the surgical approach.

[redacted]

Safety monitoring

Measures taken to avoid bias related to safety includes 100% of source data verification related to AEs documented in the Monitoring Plan.

[redacted]

5. ENDPOINTS

Primary Endpoint

The primary endpoint of this clinical investigation is:

Evaluation of Bitrack System to assist in the accurate control of its compatible ESE/NESE instruments, stablishing as [redacted] during the intervention without causing any particular SAE related to the use of the medical devices under investigation, when devices are all used according to the respective Instructions for use.

The primary endpoint, defined to check this hypothesis, is the assessment of the surgeon in a Likert scale with a score range from 1 to 5. The Surgeon Performance Scale Score has been designed to evaluate the performance of Bitrack System in each surgery as a whole procedure and ESE/NESE instruments in all the steps defined for each surgery.

The score ranges of the Surgeon Performance Scale Score have been defined as:

1. Failure: [redacted]
2. Unacceptable: [redacted]
3. Satisfactory: [redacted]
4. Good: [redacted]
5. Excellent: [redacted]

To accomplish with the hypothesis stablished in our primary endpoint, the performance score needs to be ≥ 3 as acceptance criteria.
This acceptance criteria will only be accepted if it has been obtained without causing any particular SAE related to the use of the medical devices under investigation.

Secondary Endpoints

[redacted]

6. SUBJECT SELECTION AND WITHDRAWAL

Subject Population

This clinical investigation will enroll male and female subjects between 18-90 years old candidates to a radical/simple laparoscopic nephrectomy, Partial Nephrectomy or Radical Prostatectomy for benign/malignant pathology.

Subjects must meet all eligibility criteria (described in **section 6.3**) and provide written informed consent prior to conducting any investigation-specific procedures not considered standard of care.

Number of Subjects

A total of 15 subjects will be enrolled in the clinical investigation.

Subject Screening and Informed Consent

Subject Screening

Potential patients presenting at the clinical sites will be fully informed about the clinical investigation, following the established Informed Consent process (described in **section 6.2.2**). The Principal Investigator or designee

previously trained to the CIP will revise patient´s eligibility according to the inclusion/exclusion criteria. Patients meeting general inclusion criteria and no exclusion criteria will be asked to sign an Informed Consent form if they agree to participate in the clinical investigation.

[redacted]

Subject data will be collected following enrollment into the clinical investigation.

Informed Consent

The Investigator or his/her authorized designee (if applicable) will conduct the Informed Consent process, as required by applicable regulations and the center's EC. [redacted]
Withdrawal from the clinical investigation will not jeopardize their future medical care or relationship with the investigator.

During the discussion, the Principal Investigator or his/her authorized designee will avoid any improper influence on the subject and will respect subject's legal rights. Financial incentives will not be given to the subject. [redacted] The subject shall have adequate time to review, ask questions, and consider participation. [redacted] If the subject agrees to participate, the Informed Consent form must be signed and dated by the subject and thereafter by the person obtaining the consent prior to any clinical investigation-specific procedures. [redacted]

[redacted]

- [redacted]
- [redacted]

- [redacted]

Eligibility Criteria

General Eligibility Criteria

Assessment for general eligibility criteria is based on medical records of the site and interview with a candidate patient. If some of the clinical and laboratory tests are not included in site standard tests, they must be done but after written informed consent is obtained. Patients must meet ALL of the inclusion criteria to be considered for the clinical investigation. If ANY of the exclusion criteria are met, the patient is excluded from the clinical investigation and cannot be enrolled.

Inclusion Criteria

1. Adult subjects between 18 and 90 years old who have provided written informed consent prior to any clinical investigation related procedure.
2. Subjects who have been scheduled for a laparoscopic Radical/simple Nephrectomy, Partial Nephrectomy or Radical Prostatectomy.
3. Ability and willingness to comply with all study requirements to be evaluated for each study visit.

Exclusion Criteria

1. Pregnant or breastfeeding women at the time of the surgery
2. Subjects with severe concomitant illness that, at PI´s discretion, increases risk of therapeutic interventions or that have been submitted to multiple prior surgeries.
3. Subjects admitted to the hospital due to an emergency situation
4. Subjects with untreated active infection
5. Subject has known allergy to some of the device components (i.e., stainless steel, etc.)
6. Subjects not suitable to undergo MIS/MIRS, according to medical criteria.
7. Subjects with life expectancy inferior to 3 months
8. Subjects with a BMI ≥ 40.
9. Subjects with any contraindication for the use of the Bitrack System and the ESE/NESE instruments, as specified in the Instructions For Use.
10. Subjects with severe cardiopulmonary or coronary artery disease, bleeding disorders or that have been submitted to multiple prior operations.
11. Subjects with abuses of active substances or with uncontrolled psychiatric disorders.
12. Subjects scheduled for surgeries intended to be in direct contact with the heart, the central circulatory system or the central nervous system.
13. Inability to adhere to study-related procedures.
14. Subjects who participate in another trial which may affect the outcome data on this study or the ability to complete the follow up requirements.

Subject Enrollment

[redacted]. For the HYROS-PRnP study, a patient is considered enrolled in the clinical investigation from the moment they provide written informed consent, has been confirmed to meet all inclusion criteria and none of the exclusion criteria and has been successfully treated with the Bitrack System.

Subject Withdrawal

Each enrolled subject shall remain in the clinical investigation until completion of the required follow-up period; however, a subject's participation in any clinical investigation is voluntary and the subject has the right to withdraw at any time without penalty or loss of benefit. [redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

[redacted]

[redacted]

Expected Duration of the Participants in the Clinical Investigation

[redacted]

6.1.1. Suspension or Early Termination of the Clinical Investigation

While no formal statistical rule for early termination of the clinical investigation for insufficient effectiveness of the device under investigation is defined, the Sponsor reserves the right to discontinue the clinical investigation at any stage or reduce the follow-up period with suitable written notice to the investigator. Possible reason(s) may include, but are not limited to:

- Unanticipated adverse device effect (e.g.,UADE) occurs and it presents an unreasonable risk to the participating subjects.
- An oversight committee (e.g., Steering/Executive Committee, Data Monitoring Committee) makes a recommendation to stop or terminate the clinical investigation (such as higher frequency of anticipated adverse device effects).

- Further product development is cancelled.

Should the clinical investigation be discontinued by the Sponsor, subjects will be followed per routine hospital practice with device-related AEs reported to the Sponsor as per vigilance/commercial reporting requirements.

[redacted]

[redacted]

If the Sponsor suspends or prematurely terminates the clinical investigation at an individual site in the interest of safety, the Sponsor will inform all Principal Investigators.

If suspension or premature termination occurs, the Sponsor will remain responsible for providing resources to fulfill the obligations from the CIP and existing agreements for following the subjects enrolled in the clinical investigation, and the Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her site, if appropriate.

7. TREATMENT AND EVALUATION OF ENDPOINTS

Baseline

Baseline Clinical Assessments

During the baseline visit, in those subjects who have signed the informed consent form and meet all the inclusion and none of the exclusion criteria, the following medical assessments will be performed, as required by the clinical investigation design:

- [redacted]

Randomization

No randomization process will take place in this clinical investigation.

Blinding

This is an open-label clinical investigation. Investigators and subjects will not be blinded to the procedure assignment.

Index Procedure

The robotic assisted laparoscopic Radical/simple Nephrectomy, Partial Nephrectomy or Radical Prostatectomy surgery will be performed a maximum of 4 weeks after Baseline visit and up to the surgeon criteria and patient´s agreement. For the safety and performance, the dates of the following visits are calculated starting from the day that the surgery visit took place [redacted]

Procedures Involved in the Use of the Devices Under Investigation

For further information about the investigational devices, their components and their intended use and applications, refer to the IFU.

[redacted]

- [redacted]

- [redacted]

Post–procedure (In-hospital)

[redacted]f any)

- [redacted]

[redacted]

Schedule of Events

Table 7-1. [redacted]

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]					
[redacted]	[redacted]		[redacted]			
[redacted]		[redacted]				
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]		[redacted]				
[redacted]		[redacted]				
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]				
[redacted]			[redacted]			
[redacted]			[redacted]			
[redacted]			[redacted]			
[redacted]		[redacted]				
[redacted]				[redacted]	[redacted]	[redacted]
[redacted]				[redacted]		
[redacted]				[redacted]	[redacted]	[redacted]
[redacted]						[redacted]
[redacted]						
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]			
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]
[redacted]						X[c]

Notes:

[redacted]

Table 7-2. [redacted]

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]					
[redacted]	[redacted]		[redacted]			
[redacted]		[redacted]				
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]		[redacted]				
[redacted]		[redacted]				
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]				
[redacted]			[redacted]			
[redacted]			[redacted]			
[redacted]			[redacted]			
[redacted]		[redacted]				
[redacted]				[redacted]	[redacted]	[redacted]
[redacted]				[redacted]		
[redacted]				[redacted]	[redacted]	[redacted]
[redacted]			[redacted]			
[redacted]						[redacted]
[redacted]						
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]			
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]
[redacted]						[redacted]

Notes:

- [redacted]

Table 7-3. [redacted]

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]					
[redacted]	[redacted]		[redacted]			
[redacted]		[redacted]				
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	
[redacted]		[redacted]				
[redacted]		[redacted]				
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]				
[redacted]			[redacted]			
[redacted]			[redacted]			
[redacted]			[redacted]			
[redacted]		[redacted]				
[redacted]				[redacted]	[redacted]	[redacted]
[redacted]				[redacted]		
[redacted]				[redacted]	[redacted]	[redacted]
[redacted]		[redacted]				[redacted]
[redacted]		[redacted]				[redacted]
[redacted]		[redacted]				[redacted]
[redacted] • [redacted] • [redacted] • [redacted]						[redacted]
[redacted]						
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]			
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]
[redacted]			[redacted]	[redacted]	[redacted]	[redacted]
[redacted]						[redacted]

Notes:

[redacted]

8. ADVERSE EVENTS

To comply with worldwide standards and guidelines on clinical investigation adverse event reporting, the Sponsor has adopted uniform and worldwide applicable standard definitions and reporting timelines to be used and adhered to by the investigators.

Definition

Adverse Event

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device under investigation.

Note 1: This definition includes events related to the medical device under investigation or the comparator.

Note 2: This definition includes events related to the procedures involved.

Note 3: For users or other persons, this definition is restricted to events related to medical devices under investigation.

Serious Adverse Event

If the AE meets any of the criteria below, it is regarded as a serious adverse event (SAE).

a) Led to a death,

b) Led to a serious deterioration in health of the subject, that either resulted in

   1. a life-threatening illness or injury, or
   2. a permanent impairment of a body structure or a body function, or
   3. in-patient hospitalization or prolongation of existing hospitalization, or
   4. medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function.
   5. chronic disease

c) Led to fetal distress, fetal death or a congenital abnormality or birth defect.

Note: A planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious deterioration in health, is not considered to be an SAE.

Device Deficiency/Device Malfunction

Device deficiency is defined as an inadequacy of a medical device related to its identity, quality, durability, reliability, safety or performance, such as malfunction, misuse or use error and inadequate labeling. This includes the failure of the device to meet its performance specifications or otherwise perform as intended. Note: Performance specifications include all claims made in the labeling of the device.

A device malfunction is the failure of a device to meet its performance specifications or otherwise perform as intended, when used in accordance with the instructions for use or CIP.

Device Relationship

Determination of whether there is a reasonable possibility that an investigational product or device under investigation caused or contributed to an AE is to be **determined by the Investigator** and recorded on the appropriate CRF form. Determination should be based on assessment of temporal relationships, evidence of alternative etiology, medical/biologic plausibility, and patient condition (pre-existing condition).

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

[redacted]	
[redacted]	[redacted]

[redacted]	[redacted]
[redacted]	
[redacted]	[redacted]
	[redacted]

Determination of Adverse Events related to device and/or procedure

As detailed in Section 5.1, the primary endpoint of the study is to measure the safety and performance of Bitrack System. Among the ratios to be measured, the rate of death occurrence (SAE) during the surgery related directly to the use of the Bitrack System and the rate of any adverse event (AE) occurrence during the surgery directly related with the procedure and/or device under investigation will be determined.

Unanticipated Serious Adverse Device Effect Reporting to Sponsor and EC

The Sponsor requires the Investigator to report any USADE to the Sponsor within 24 hours of the investigator's knowledge of the event, unless local requirements are more stringent, and to the EC per EC requirements.

Device Deficiency/Malfunction Reporting

[redacted]

Clinical Sites	Reporting timelines
All Sites	Device deficiencies/malfunctions must be reported to the Sponsor no later than 24 hours from the day the site personnel became aware of the event [redacted]

[redacted]

[redacted]

Note: [redacted]

[redacted]

[redacted]

9. DATA AND DATA ANALYSIS: STATISTICAL CONSIDERATIONS

[redacted]

Analysis Populations

Intent-to-treat Population (ITT)

The intent-to-treat population (ITT) includes all adult humans eligible for a laparoscopic Radical/simple Nephrectomy, Partial Nephrectomy or Radical Prostatectomy surgery using Bitrack System and its sterile endoscopic ESE/NESE instruments medical devices, in whom treatment using the device under investigation is attempted but not achieved.

Per-Protocol Population (PP)

Per-Protocol Population (PP) includes all subjects who fulfill the inclusion criteria, do not meet any exclusion criteria, have signed the informed consent form (ICF), and have undergone to a robotically assisted Radical/simple Nephrectomy, Partial Nephrectomy or Radical Prostatectomy using Bitrack System medical device and corresponding ESE/NESE instruments.

Statistical Analyses

Primary Safety and Feasibility Endpoint Analyses

To evaluate performance of the Bitrack System, more specifically the ESE/NESE instruments, in surgical interventions (partial nephrectomy, radical nephrectomy and prostatectomy) the scores measuring the specific performance (as verification units from 1-failure to 5-excellent as assessed by the surgeon) will be considered. [redacted]

In addition, Mean, median, standard deviation, and interquartile range will be computed for quantitative variables, and absolute frequencies and percentages for categorical variables. To assess the main performance of each ESE/NESE instrument T-tests (and Wilcoxon test as adequate) will be undergone to evaluate whether the performance is higher than 3 in terms of verification units. Chi-square tests (and Binomial exact test as adequate) for one proportion will also be used to assess the remaining performance but also the safety endpoints. In addition, generalized mixed linear models will also be used to adjust for the within-individual variability. All analysis will be made using the statistical program R, setting the threshold for significance at α=0.05.

Sample Size Calculation and Assumptions

The collection and processing of this data will be performed using the PP population. The total PP of this study, HYROS-PRnP, corresponds to a sample size of 15 patients.

Number of subjects participating in the study and repeated measures related to the functionality of ESE/NESE Instruments within each individual allows develop a formal hypothesis for this clinical investigation.

[redacted]

Planned Interim Analysis

Due to the short period of follow-up, no interim analyses are planned for this study.

Statistical Criteria for Termination

There are no statistical criteria for termination of this clinical investigation.

Success Criteria

This clinical investigation will be considered a success when the primary endpoint is met.

Deviations from Statistical Plan

In case of a deviation from the original statistical plan, it will be notified to the sponsor and described in the final study report.

10. QUALITY CONTROL AND QUALITY ASSURANCE

Selection of Clinical Sites and Investigators

The Sponsor will select investigators qualified by training and experience to participate in the clinical investigation. [redacted]

Clinical Investigation Finances and Agreements

The clinical investigation will be financed by Rob Surgical Systems, S.L. [redacted]

Training

Site Training

All Investigators and clinical investigation personnel are required to attend Sponsor training sessions, which may be conducted at an Investigator's meeting, a site initiation visit, or other appropriate training sessions. Over-the-phone or self-training may take place as required. [redacted]

Training Required for the Use of the Device

Bitrack System is to be used by professionals who have been previously trained in MIS procedures. [redacted]

Monitoring

Sponsor and/or designee will monitor the clinical investigation over its duration according to the CIP-specific monitoring plan which will include the planned extent of source data verification. This monitoring plan will be a separate document that can be updated during the curse of the study.

[redacted]

- [redacted]
- [redacted]
- [redacted]

Deviations from CIP

The Investigator should not deviate from the CIP for any reason except in cases of medical emergencies when the deviation is necessary to protect the rights, safety and well-being of the subject or eliminate an apparent immediate hazard to the subject. In that event, the Investigator will notify Sponsor immediately by phone or in writing.

[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

- [redacted]

11. DATA HANDLING AND RECORD KEEPING

Sponsor and/or its affiliates will maintain documentation of the systems and procedures used in data collection at least for the duration of the clinical investigation.

[redacted]

The Sponsor requires the investigational sites to transfer into Sponsor's data management systems only pseudonymous Personal Information (key-coded) necessary to conduct the Clinical Investigation, such as the patient's medical condition, treatment, dates of treatment, etc. [redacted]

The Sponsor maintains a Privacy Incident procedure that complies in all respects with Applicable Law and industry best practices.

Data Management Plan

A Data Management Plan (DMP) will describe procedures used for data entry and collection. Data review and data cleaning, and issuing, resolving data discrepancies and methods for data base lock. [redacted]

[redacted]

Case Report Form Completion

Primary data collection based on source-documented hospital and/or clinic chart reviews will be performed clearly and accurately by site personnel trained on the CIP and CRF completion. [redacted]

Record Retention

The Sponsor and Investigator/Site will archive and retain all documents pertaining to the clinical investigation as per the applicable regulatory record retention requirements, but at least for 10 years. [redacted]

[redacted]

12. RISK ANALYSIS

Anticipated Clinical Benefits

[redacted]

[redacted]

A[redacted]

- [redacted]
- [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]

[redacted]

- [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
- [redacted]
  - [redacted]particular breakdown /missfunction particularly when this affects to movement transmission.

Benefit to Risk Rationale

After the evaluation of the individual benefit risk analysis, it's proven that during design stage proactive measures have been introduced to reduce identified risks as much as possible.

Implementation of already detailed mitigation measures has been applied and verification of part of such measures has been evaluated throughout series of bench testing performed in design stage and verification stage.

In absence of any previous experience gained and based on results coming from such screening tests, it can be considered Risk acceptability has been met.

[redacted]

13. ETHICAL CONSIDERATION

Ethics Committee and AEMPS Review and Approval

Ethics Committee (EC) and Spanish Agency of Medicines and Medical Products (AEMPS) approval for the CIP and ICF/other written information provided to the patient will be obtained at each investigational site prior to consenting and enrolling patients in this clinical investigation. The approval letter must be received prior to the start of this clinical investigation and a copy must be provided to the Sponsor.

[redacted]

14. CLINICAL INVESTIGATION CONCLUSION

The clinical investigation will be concluded when:

- Site is closed AND
- The final report has been provided to investigators or the Sponsor has provided formal documentation of clinical investigation closure.

[redacted]

15. PUBLICATION POLICY

The data and results from the clinical investigation are the sole property of the Sponsor. [redacted]

APPENDIX I: ABBREVIATIONS AND ACRONYMS

Abbreviation/acronym	Words
APS	Acute Procedural Success
CCI	Comprehensive Complication Index
CIP	Clinical Investigation Plan
CRF	Case Report Form
CT	Computed Tomography
DMP	Data Management Plan
DOF	Degree Of Freedom
EC	Ethics Committee
EDC	Electronic Data Capture
EKG	Electrocardiogram
ESE	Electrosurgical Endoscopic Instruments
FIH	First In Human
FU	Follow-up
HYROS	Hybrid Robotic Surgery In Urology
ICF	Informed Consent Form
IFU	Instructions For Use
ITT	Intent-To-Treat Population
MIRS	Minimally Invasive Robotic Surgery
MIS	Minimally Invasive Surgery
MRI	Magnetic Resonance Imaging
NESE	Non-Electrosurgical Endoscopic Instruments
PN	Partial Nephrectomy
PP	Per protocol
PRAEs	Procedure-Related Adverse Events
RAS	Robotic Assisted Surgery
RCC	Renal Cell Carcinoma
RN	Radical Nephrectomy or Radical/simple Nephrectomy
RP	Radical Prostatectomy
SAEs	Serious Adverse Events
UADE	Unanticipated Adverse Device Effect

USADE	Unanticipated Serious Adverse Device Effect
US	Ultrasound
VAS	Visual Analogue Scale

[redacted]