Clinical Trial Protocol

Investigational product	Da Vinci SP Surgical System	
Study Code	TASP-UTUC	
Title	A Pilot Study of Single-Port Robot-Assisted Surgery Using Da Vinci SP Surgical System for Patients with Upper Tract Urothelial Cancer	
Clinical Phase	N.A.	
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Sponsor	National Taiwan University Hospital, Taipei, Taiwan	
Version and Date	**Version:** 1	**Date:** Oct 17, 2024
Status	Final	

Synopsis

Investigational product	Da Vinci SP Surgical System
Study Code	TASP-UTUC
Title:	A Pilot Study of Single-Port Robot-Assisted Surgery Using Da Vinci SP Surgical System for Patients with Upper Tract Urothelial Cancer
Objectives:	• Primary objective To investigate clinical feasibility of radical nephroureterectomy and bladder cuff resection using single-port robotic surgery • Secondary objectives To evaluate safety, surgical outcomes, patient characteristics, and patient-reported outcomes of radical nephroureterectomy using single-port robotic surgery
Eligibility:	Inclusion criteria: 1. Age 20 years or more 2. Histologically or cytologically diagnosed upper tract urothelial cancer 4. Fitting indications of radical nephroureterectomy and ipsilateral bladder cuff resection, and deemed feasible for robotic surgery 5. ASA physical status classification 1-2 and adequate organ function 6. Patients willing and able to comply with study protocol requirements and follow-up 7. With informed consent Exclusion criteria: 1. Synchronous bladder cancer 2. Distant metastasis of cancer 3. BMI ⩾30 or BMI <18.5 4. Unable to tolerate lateral decubitus or Trendelenburg position (relative contra-indication) 5. Severe adhesion due to prior abdominopelvic surgery (relative contra-indication) 6. Previous radiation treatment to the pelvic area 7. Active infectious disease

	8. Severe concomitant illness that drastically shortens life expectancy or increases risk of therapeutic interventions, such as: severe heart disease (NYHA functional class III-IV) or severe lung disease (GOLD Group C-D) 9. Cannot follow trial-required procedures 10. Concomitant systemic or pelvic disease that increases the risk of surgery 11. Long-term use of anti-coagulant(s) 12. Patients with coagulopathy 13. Emergency surgery
Design of trial:	• Prospective • Interventional • Open label • Single arm • Study period: 2 years (From Dec/1/2024 to Nov/30/2026) • Study site: single center study
Study treatment:	Radical nephroureterectomy and ipsilateral bladder cuff resection using da Vinci SP Surgical System (robotic surgery)
Primary endpoint:	Success without conversion to alternative surgery

Statistical analysis and sample size estimation:	• Statistical methods: Descriptive methods will be used.
	• Interim analysis: No
	• Efficacy assessment group: Per Protocol
	• Estimated sample size:
	  ○ Enroll: 25
	  ○ Evaluable: 20

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Abbreviations

AE	Adverse event
ASA	American Society of Anesthesiologists
BMI	Body mass index
CBC D/C	Complete blood count with differential count
CTCAE	Common Terminology Criteria for Adverse Events
EAU	European Association of Urology
GCP	Good Clinical Practice
GOLD	The Global Initiative for Chronic Obstructive Lung Disease
ICH	The International Council for Harmonisation
IRB	Institutional Review Board
MIS	Minimally invasive surgery
NCI	National Cancer Institute
NTUH	National Taiwan University Hospital
NYHA	New York Heart Association
POD	Post-operation day
REC	Research Ethics Committee
RNU+BCR	Radical nephroureterectomy and bladder cuff resection
SAE	Serious adverse event
SARA	Supine anterior retroperitoneal access
SD	Standard deviation
TFDA	Taiwan Food and Drug Administration
UTUC	Upper tract urothelial cancers
VAS	Visual analogue scale

1. Introduction

1.1 Background and rationale

1.1.1 Medical background

Upper tract urothelial cancers (UTUC), including cancers of renal pelvis and ureter (ICD-10 codes: C65 and C66), are relatively rare worldwide. UTUC accounts for less than 10% of all urothelial cancers [1]. In several aspects, UTUC in Taiwan is unique. Except Taiwan, men have higher incidence of UTUC than women. According to Cancer Incidence in Five Continents, Vol. XI [2], in the US, the annual incidence of cancer of renal pelvis in men was 0.6 per 100,000 population during year 2008-2012. During the same period, the incidence of cancer of renal pelvis in Taiwanese men was 2.1. It is noteworthy that Taiwanese females had extraordinarily high incidence of 2.1 per 100,000 population. Regarding cancer of ureter, both men and women in Taiwan have higher incidence than most western populations, 1.1 and 1.4 per 100,000 population, respectively [3]. The high incidence of UTUC in Taiwan has been attributed to several potential etiologies, including smoking, exposure to aristolochic acid, genetic factors, occupational exposures such as aromatic amines, and environmental factors such as Arsenic [4,5]. Due to these unusual features of UTUC in Taiwan, significanthas been undertaken [6]. Our group has published several research of surgical techniques for this important endemic cancer [7-14].

For localized high risk UTUC, the curative treatment option is radical nephroureterectomy (RNU) plus bladder cuff resection (BCR) with/without template lymphadenectomy [15-17]. Although European Association of Urology (EAU) guideline recommends open RNU as standard treatment, in the modern era of minimally invasive care, laparoscopic RNU+BCR with/without robotic assistance is feasible. In experienced hands, both laparoscopic and robotic RNU+ BCR provide similar oncological outcomes as open RNU. In addition, robotic RNU+BCR can limit the risk of post-operative complications and shorten hospital stay [16]. However, the EAU guideline provides precautions for minimally invasive RNU to minimize tumor spread along trocar routes as some reports have shown tumor metastasis under pneumoperitoneum condition during laparoscopic surgery [16,18,19].

Laparoscopic surgery is the most popular minimally invasive surgery (MIS) technique adopted for RNU+ BCR. However, laparoscopic RNU+ BCR is accompanied by barriers such as complex manipulation of instruments and challenging learning curve, especially for BCR. These barriers sometimes make surgeon to performed open or hybrid surgery. In a recent study, out of 1,808 patients with UTUC who underwent RNU, open surgery and laparoscopic hand-assisted were performed in 21.1% and 42.5%, respective. Total MIS either using robotic or laparoscopic RNU were done for 8.7% and 27.3%, respectively [6].

With the adoption and popularity of robotic surgery in urological area, RNU+ BCR has increasingly been done by robotic surgery. Some changes have been brought into the practice of robotic RNU+ BCR compared to traditional open approach. The most prominent changes are transperitoneal approach rather than retroperitoneal approach and flank rather than supine position. These modifications are advantageous for better visualization of anatomic landmark, larger space for multiple arms of robotic platform, and shorter learning curve [20,21].

Transperitoneal robotic partial nephrectomy is a well-established standard robotic procedure [22]. However, there are challenges when applying transperitoneal techniques in RNU. Due to the multi-quadrant nature of UTUC, patients sometimes need to be repositioned from flank to supine and robotic system requires re-docking. These procedures will lengthen the operation time. When working in limited

operation space, external clashing of robotic arms cannot be fully avoided. It is because the multi-arm design of the commonly used robotic surgical system. Another drawback of multi-arm robotic system is the requirement of 4 to 6 access ports on abdominal wall, i.e. more surgical wounds are created. Some rarely addressed topics are related to the shift from retroperitoneal to transperitoneal access. Now, there is an emerging trend back to retroperitoneal access for RNU+BCR with the novel single-port surgical system [20,21]. Some evidence supported the retroperitoneal access: less blood loss, shorter operation time and shorter hospitalization time [22]. More same-day discharges can be achieved by single-port system [23]. These advantages of retroperitoneal approach can only be implemented with the novel single-port system for easier manipulation within limited working space.

Recently, Dr Crivellaro's group developed a new technique of robotic RNU using single-port system, supine anterior retroperitoneal access (SARA) [20,21]. Briefly, patient is placed in supine position, a 3-cm incision is made at the McBurney point, and the da Vinci SP Surgical System is used to complete total robotic RNU+ BCR. Case reports from 2 patients showed low complication rate, less post-operative pain, and shorter hospitalization with the SARA RNU. With supine retroperitoneal approach, there is no need of patient reposition and re-docking of robot. Above-mentioned advantages of retroperitoneal access can be potentially achieved. Less respiratory stress is expected for the absence of pneumoperitoneum and lateral decubitus position [21].

In the initial report of 18 patients, 12 were partial nephrectomy, 2 each for radical nephrectomy, pyeloplasty, and nephroureterectomy [21]. Larger study of SARA technique is necessary for RNU+ BCR to verify its feasibility, safety and to identify its limitation(s) and areas for further potential improvement. Considering the current technical challenges of performing laparoscopic RNU+BCR or multiport robotic surgery in UTUC (a condition with higher incidence rates in Taiwan), this study is set forth to the above-mentioned goals of SARA RNU+ BCR using da Vinci SP system.

1.1.2 Animal and preclinical study

Prior to use SARA in human patients, the SP system has been evaluated for several operations in cadaveric models to determine the feasibility and technical approach that would be most advantageous for this system [24-27]. Given the ability of the SP system to operate within a small operative radius, this study aims to evaluate the performance and safety of the da Vinci SP® Surgical System for the surgical treatment of UTUC.

1.2 Investigational product

Da Vinci SP Surgical System, Model SP1098

The da Vinci SP® Surgical System, Model SP1098, uses advanced robotic technology to facilitate accurate movement of EndoWrist SP™ Instruments through a single surgical port. It is designed to enable complex surgery using a minimally invasive approach. The System includes three major subsystems (Surgeon Console, Vision Cart, Patient Cart), which are used with instruments and accessories. The system is software controlled.

The surgeon seated at the Surgeon Console controls all movement of the instruments and camera by using two hand controls and a set of foot pedals. The surgeon views the camera image on a three-dimensional (3D) viewer, which provides a view of patient anatomy and instrumentation, along with icons and other user interface features.

The Vision Cart includes supporting electronic equipment, such as the camera light source, video and image processing, and the networking hardware. The Vision Cart also has a touchscreen to view the camera image and adjust system settings.

The Patient Cart is the operative component of the da Vinci SP Surgical System. Its primary function is to support the positioning of the surgical port and to manipulate the surgical instruments and camera. The Patient Cart is positioned at the operating room table and contains an instrument arm that is positioned with respect to the target patient anatomy. The instrument arm contains four instrument drives that hold up to three surgical instruments and the camera. The patient-side assistant installs and removes the camera and instruments intra-operatively.

EndoWrist SP® Instruments:

Intuitive Surgical® EndoWrist SP Instruments are controlled by the da Vinci SP Surgical System, Model SP1098, and include flexible endoscopes, blunt and sharp endoscopic dissectors, scissors, forceps/pick-ups, needle holders, endoscopic retractors, electrocautery and accessories for endoscopic manipulation of tissue, including grasping, cutting, blunt and sharp dissection, approximation, ligation, electrocautery, and suturing through a single port.

The EndoWrist SP® Instruments and the catalog number used in this trial are listed below:

SP Endoscope (430077)

Monopolar Curved Scissors (a.k.a MCS) and MCS Tip (430004/430035)

Monopolar cautery instrument & hook (430007/400156)

Fenestrated bipolar forceps (430011)

Round tooth retractor (430002)

Medium-Large Clip Applier (430005)

Needle driver (430006)

Cadiere Forceps (430009)

Maryland bipolar forceps (430010)

1.3 Risks and benefits assessment

Risks:

1. Perioperative risks related to the surgeries: bleeding, wound infection, adjacent organ injury, wound dehiscence

2. Fail to perform the surgery successfully with SP system: conversion to multiport robotic or traditional endoscopic surgery or open surgery

Potential Benefits:

1. Cosmetic benefit: single incision or fewer scars at belly

2. Peri-operative benefits: shorter hospital stays, less complication, less pain and less analgesic use, less CO2 retention and oxidative stress related to pneumoperitoneum, improvement of disease symptoms and quality of life.

1.4 Regulatory

This study will be conducted in compliance with the protocol approved by the Institutional Review Board (IRB) / Research Ethics Committee (REC) of NTUH, and according to Good Clinical Practice standards and per Taiwan Health Authority regulations. No deviation from the protocol will be implemented without the prior review and approval of the IRB except where it may be necessary to eliminate an immediate hazard to a research subject. In such case, the deviation will be reported to the IRB as soon as possible.

2. Objectives and Endpoints

2.1 Study objectives

2.1.1 Primary objective

To investigate clinical feasibility of radical nephroureterectomy(RNU) and bladder cuff resection(BCR) using single-port robotic surgery

2.1.2 Secondary objectives

To evaluate safety, surgical outcomes, patient characteristics, and patient-reported outcomes of radical nephroureterectomy(RNU) and bladder cuff resection(BCR) using single-port robotic surgery

2.1.3 Other exploratory objectives (if any)

Not applicable

2.2 Study endpoints

2.2.1 Primary endpoint

Successful completion of RNU+ BCR without conversion to alternative surgery

2.2.2 Secondary endpoints

- Operative time (first skin incision to closure of wound)
- Console time
- Transfusion and estimated blood loss
- Length of hospital stay
- Complication (rate, in 30 days) (intraoperative and/or postoperative) (Clavien system)
- Readmission (rate, in 30 days)
- Reoperation (rate, in 30 days)
- Perioperative mortality (in 30 days)
- Pain score

2.2.3 Other exploratory endpoints (if any)

Not applicable

3. Study Design

3.1 Overall design

This prospective, interventional, non-randomized, single arm, clinical trial will investigate feasibility and safety of robot-assisted radical nephroureterectomy (RNU) + BCR using da Vinci SP Surgical System in Taiwan and provide initial evidence of retroperitoneal approach. All the investigators are well trained and have received proof of training after completing the training program for da Vinci SP system provided by Intuitive. This study includes single-arm supine anterior retroperitoneal approach (SARA) by single-port robotic natural orifice transluminal endoscopic surgery.

This study will be conducted in National Taiwan University Hospital, Taipei.

Informed consent will be provided to patient who has an indication of radical nephroureterectomy (RNU)+ BCR. Study participants will sign an informed consent before any study procedure begins. Eligibilities will be assessed during screening period (2 weeks) with blood test and other routine assessments. Eligible patient will undergo surgical intervention using da Vinci SP Surgical System. Post-operation follow-up will be performed according to time points specified in the study calendar.

3.1.1 Recruitment plan

This trial plans to recruit 20 evaluable patients at single trial site, NTUH. Assuming screening failure and drop-out of 5 patients, at least 25 patients will be screened (enrolled). Recruitment is estimated to complete within 1 year with recruitment rate of 0.5 patient per week.

3.2 Study calendar

Period	Screening	Operation period				Follow-up period	
Visit	Screening visit	Operation	POD 1	Discharge day	Follow-up 1	Follow-up 2	Follow-up 3
Day (window time)	-14 ~-1	0	1	n.a.	30 (±7)	90 (±14)	180 (±14)
Informed consent	X						
Medical history	X						
CBC D/C	X						
Biochemistry	X						
Other safety blood test	X						
Pre-operation routine test and imaging	X						
Operation		X					
Peri-operative outcomes		X	X	X			
Concomitant medications	X		X	X	X		
Analgesics use	X		X	X			
Pain assessment	X		X	X			
AE / Complication	X	X	X		X	X	X
Patient-reported outcomes	X		X		X		

Footnotes:

- POD: post-operation day
- CBC D/C: Complete blood count with differential count
- AE: adverse event

3.3 Criteria of Termination of the Trial

The trial shall be terminated by the investigator or the IRB when deemed necessary after evaluation. Incidents that may cause the termination of the trial include the encounter of life-threatening AE, fatal AE, serious non-compliance, etc. If 2 mortalities or 5 severe morbidities occur during the trial, the investigator will terminate the trial. A detailed written explanation of the reasons for the termination needs to be given to IRB and Health Authority as appropriate.

4. Study Population

4.1 Inclusion criteria

1. Age 20 years or more
2. Histologically or cytologically diagnosed upper tract urothelial cancer
3. indication of radical nephroureterectomy and ipsilateral bladder cuff resection, deemed feasible for robotic surgery
4. ASA physical status classification 1-2 and adequate organ function
5. Patients willing and able to comply with study protocol requirements and follow-up
6. With informed consent

4.2 Exclusion criteria

1. Synchronous bladder cancer
2. Distant metastasis of cancer
3. BMI ⩾30 or BMI <18.5
4. Unable to tolerate lateral decubitus or Trendelenburg position (relative)
5. Severe adhesion due to prior abdominopelvic surgery
6. Previous radiation treatment to the pelvic area
7. Active infectious disease
8. Severe concomitant illness that drastically shortens life expectancy or increases risk of therapeutic interventions, such as: Severe heart disease (NYHA functional class III-IV) or Severe lung disease (GOLD Group C-D)
9. Can’t follow trial-required procedures
10. Concomitant systemic or pelvic disease that increases the risk of surgery
11. Long-term use of anti-coagulant(s)
12. Patients with coagulopathy
13. Emergency surgery

4.3 Withdrawal criteria

1. Patients refuse to continue follow up per protocol during the study period
2. Patients developing mortality or morbidity during or within 30 days after the surgery that do not have consequential correlations with the surgical procedures (such as those resulting from natural disaster, war, or unexpected accidents)

5. Treatment

5.1 Treatment administration

Under general anesthesia, the patient will be positioned according to indicated procedures described below [21]:

The patient will be placed in supine position. A rubber roll will be placed under the flank of disease site to create a minor body tilt. Incision will be made at the McBurney point of 3 cm size, 3 cm medial and 3 cm caudal to the anterior superior iliac spine. Access to retroperitoneal space will be built by dissection of subcutaneous fat and separation of muscles. SP Access Port or trocar will be inserted into the incision and oriented towards the reference anatomy. Depending on the availability, Custom Remote Center may be used. Dissection of the retroperitoneal fat tissue will be performed towards the posterior portion of the retroperitoneal cavity until the quadratus lumborum and medially the iliopsoas muscle are exposed. Then dissection of a plane just above the psoas muscle will allow identification of the ureter, which will be followed until renal pelvis and renal hilum seen. Standard steps of RNU will be followed thereafter. The axis of the patient's dissection will be pivoted to the patient's legs for BCR. Standard surgical treatment for UTUC includes not only excision of the ipsilateral kidney and the whole ureter, but also consisting of resection of the intramural portion of the ipsilateral ureter, which is the most distal part of the whole specimen, and the surgery includes closure of the bladder wall defect after the BCR, which nicely demonstrates the beauty of the reconstructive power of the da Vinci robotic system.

5.2 Concomitant therapy

Medical treatment of underlying chronic diseases (such as diabetes or hypertension) is allowed.

6. Efficacy Assessments

- Primary endpoint: Success without conversion to alternative surgery: successful completion of radical nephroureterectomy and bladder cuff resection with da Vinci SP system (no conversion to conventional laparoscopic, multiport da Vinci surgery or open surgery; addition of access port to complete the procedure would not be considered as conversion.)
- Operative time (min): first skin incision to closure of wound
- Console time (min): the time when the surgeon starts the console work till the specimen is taken out from the patient
- Estimated blood loss (mL): measured at operating suite
- Length of hospital stay (day): the duration from operation day to the discharge day (included)
- Pain score: measured by Visual Analogue Scale (VAS)

Other assessments:

- Patient demographics and medical history
- Pathology assessment
- Body mass index, body weight
- Analgesic use(types: opioid or non-opioid, changes in post-operative period)

7. Safety Assessments

- Safety labs (complete blood count and other routine tests)
- Estimated blood loss (mL): measured at operating suite.
- Transfusion: record of blood product received.
- Complication (intraoperative and/or postoperative) (Clavien Dindo grading)
- Readmission (in 30 days)
- Reoperation (in 30 days)
- Perioperative mortality (in 30 days)

8. Adverse Event Reporting

Upon the occurrence of serious adverse events (SAE) which result in serious malfunctioning of the medical device, Dr. Jeff Shih-Chieh Chueh will report SAEs to the IRB of NTUH according to the Serious Adverse Event Reporting Procedures and Guidelines posted by NTUH. SAE reports to the IRB should include the following information when calling the Medical Monitor:

- Date and time of the SAE
- Date and time of the SAE report
- Name of reporter
- Call back phone number
- Affiliation/Institution conducting the study
- Protocol number
- Title of protocol
- Description of the SAE, including attribution to drug and expectedness

8.1 Definitions and reports of adverse events

All adverse events that occur after the informed consent is signed (including run-in) must be recorded on the adverse event CRF (paper and/or electronic) whether or not related to study agent. AE Data Elements including:

- AE reported date
- AE Verbatim Term
- CTCAE Term (v 5.0)
- Event onset date and event ended date
- Severity grade
- Attribution to study agent (relatedness)
- Whether or not the event was reported as a Serious Adverse Event (SAE)
- Action taken with the study agent
- Outcome of the event
- Comments

Identify the adverse event using the NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. The CTCAE provides descriptive terminology and a grading scale for each adverse event listed.

AEs will be assessed according to the CTCAE grade associated with the AE term. AEs that do not have a corresponding CTCAE term will be assessed according to their impact on the participant's ability to perform daily activities.

The possibility that the adverse event is related to study drug will be classified as one of the following: not related, unlikely, possible, probable, definite.

8.2 Serious Adverse Events

ICH Guideline E2A and GCP of Taiwan define serious adverse events as those events, occurring at any dose, which meet any of the following criteria:

- Results in death
- Is life threatening (Note: the term life-threatening refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe).
- Requires inpatient hospitalization (outside of planned combined treatment pathway) or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital abnormality/birth defect
- Events that may not meet these criteria, but which the investigator finds very unusual and/or potentially serious, will also be reported in the same manner.

8.3 Adverse event follow-up

All AEs, including lab abnormalities that in the opinion of the investigator are clinically significant, will be followed according to good medical practices and documented as such. Site staff should send follow-up reports as requested when additional information is available. Additional information should be entered on the IRB of NTUH of SAE form in the appropriate format. Follow-up information should be sent to NTUH IRB as soon as possible according to IRB's Serious Adverse Event Reporting Procedures and Guidelines.

9. Statistical Considerations

9.1 Sample size determination

This trial is not designed for registrational purpose, so that there is no formal testing or statistical calculation. This trial evaluates initial feasibility, not for efficacy or larger scale safety study. Therefore, this trial will not expose too many patients to pre-market SP Surgical System. Sample size is based on several factors: surgeon's experience of multi-port, pre-study training, and pre-clinical cadaver study of SP system. It is estimated that 20 patients is sufficient (passing learning curve or representative dataset) for this small feasibility study.

9.2 Planned statistical methods of analysis

Quantitative variables will be presented as mean±standard deviation (SD) and categorical variables will be presented as proportions. The Student t-test, Mann-Whitney U-test and Spearman rank correlation test will be used to analyze differences between groups of variables.

9.2.1 Efficacy analysis

Success rate for the completion of radical nephroureterectomy and bladder cuff resection with da Vinci SP System without conversion will be presented as proportions.

9.2.2 Safety analysis

All operated patients will be included in safety analysis. Related AE and complications will be described.

9.2.3 Analysis population

All operated patients will be included in analysis.

9.2.4 Missing, non-compliance, and others

Analysis will be carried on for available data after exclusion of the missing data.

If deviation(s) from the original statistical plan is identified, the investigator will follow the guideline of IRB to record and report such incident. The PI will report to IRB for with further review.

10. Direct Access to Source Data/Documents

Investigators permit IRB to access to the source data of experiment for trial-related monitoring, audits and regulatory inspection.

11. Ethical Considerations

This study will be conducted according to Taiwan and international standards of Good Clinical Practice for all studies. Applicable government regulations and NTUH research policies and procedures will also be followed.

This protocol and any amendments will be submitted to the NTUH Research Ethics Committee / Institutional Review Board (IRB) for formal approval to conduct the study. The decision of the IRB concerning the conduct of the study will be made in writing to the investigator.

All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. This consent form will be submitted with the protocol for review and approval by the IRB. The formal consent of a subject, using the IRB-approved consent form, will be obtained before that subject is submitted to any study procedure. This consent form must be signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent.

12. Data Handling and Keeping

The investigator shall accurately collect, record and report all data resulting from its conduct of the study in the manner, and pursuant to the schedule, set forth in the protocol. The investigators and the research assistants of this study will handle the research data. Clinical information, surgical image and parameters will be collected in NTUH. The data will be stored in computers of laboratory with an electronic encryption and in compliance with applicable regulations and regulatory agency requirements. The clinical and source data can only be assessed by clinical doctors and investigators of the study and kept for at least 5 years after the end of this study. A monitor may be appointed by NTUH and the investigator and who will be responsible for monitoring and reporting on the progress of the

study and for the verification of data generated from performance of this study. The monitor shall have qualifications and experience to enable a knowledgeable supervision of the Study. The monitor shall ensure that (a) the parties are adhering to the trail protocol, and (b) all data generated pursuant to the study are accurately and completely recorded and reported.

13. Financing, Insurance and Investigator Responsibilities

NTUH will provide sufficient funding for this clinical study, around NTD 5,000,000 to cover the study budget (sponsored by C-Sun Industry). Intuitive to provide NTUH with da Vinci SP Surgical System, and related instruments and accessories, materials and relevant fee of training program. During the study period of this clinical study, NTUH will maintain adequate levels of either insurance with a reputable insurer or reserves in order to self-insure at levels sufficient to support any possible occurrences of death or bodily injury to any person, or destruction or damage to any property. All data, information, inventions or discoveries (whether patentable or not), and materials derived as a direct result of the performance of the study, are the sole and exclusive property of Intuitive and can be published and/or utilized otherwise for further development.

All investigators would be able to evaluate and recruit potential clinical subjects. During the surgery, principal investigator would be the SP surgeon console operator, rest of the investigators can take the assistant role during the surgery.

14. References

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