NCT 01925677

Use of the Intuitive Surgical da Vinci® Single-Site™ with Instruments and Accessories for Single-Port Laparoscopic Nephrectomies

March 5, 2013

Protocol synopsis

Title of study: A six month, single-center, feasibility study of the use of the Intuitive Surgical da Vinci® Single-Site™ Instruments and Accessories for Single-Port Laparoscopic Nephrectomies

Purpose and rationale: After being informed of the potential risks and off-label use of the da Vinci Single-Site approach in our study, patients will undergo a robotic-assisted single-site donor nephrectomy performed by a two-surgeon team utilizing existing da Vinci instrumentation and Single-Site platforms. Renal mobilization and vascular dissection will be performed with manual laparoscopy performed for vascular division utilizing stapling devices.

Objectives: The primary objective is to measure the feasibility of the current Single-Site platform to perform donor nephrectomy prior to vascular division and kidney extraction.

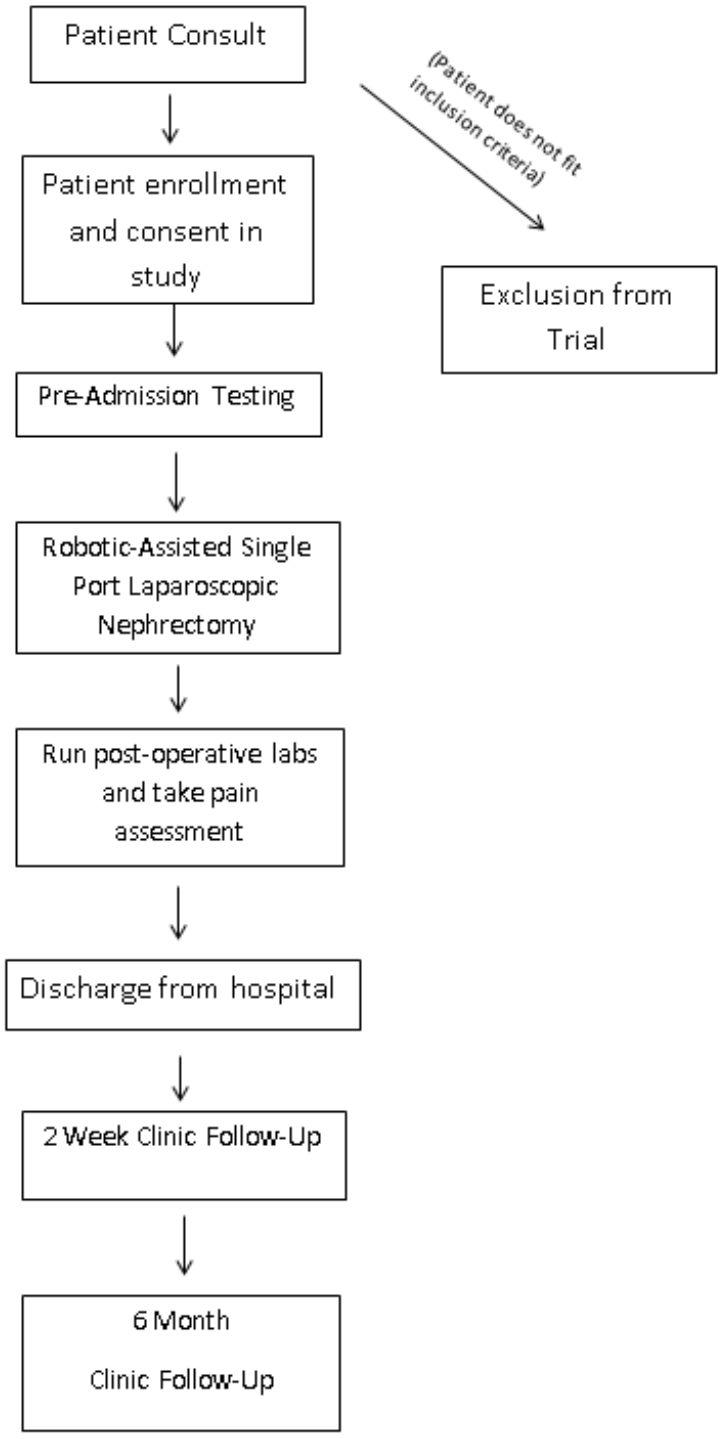
Population: The proposed study population consists of adults aged between18-70 who have been previously approved by the living donor transplant committee at the University of Maryland Medical Center as appropriate candidates for renal donation.

Inclusion criteria: The following criteria must be met in order for a patient to participate in the study. Male or female adults ages from 18 to 70 who are good general health, and who have a genuine altruistic motivation. The patient must also have compatible blood type with the recipient, a body mass index less than 35, and appropriate for left kidney donation. Approval by the Living Donor Center must also be met in order to participate in the trial.

Exclusion criteria: The following criteria will exclude any patients from participating in the clinical trial. Any patients suffering from cancer, diabetes, kidney disease, heart disease, liver disease, sickle cell disease, HIV or hepatitis, previous major abdominal surgery, or more than two left renal arteries.

Study design: After obtaining informed consent patients will be screened for eligibility. Patients will undergo a robotic-assisted single-incision laparoscopic donor nephrectomy with the use of the da Vinci Surgical System with the Single-Site platform.

Figure 1-1 Study Design



Efficacy assessments: Measurement of the ability of the current Single-Site platform to assist laparoscopic donor nephrectomy procedure prior to final extraction of the donor kidney.

Data analysis: Statistical analysis will be performed on ergonomic and other collected data during the operative procedures and compared to matched patients. The proposed study of 20 patients may not generate statistically significant conclusions; however, we believe our observations will provide valid conclusions that support the use and continued development of robotic single port donor nephrectomy.

Sample size justification: The sample size was determined to provide a pilot group that could potentially demonstrate the efficacy of the da Vinci Surgical System with the Single-Site platform in donor nephrectomies.

1.0 Background

Minimally invasive surgery has been an important factor responsible for the expansion of living renal donation since its advent over a decade ago. Presently, more than 6000 laparoscopic donor nephrectomies are performed annually in the United States. While the number of living kidney donors has plateaued over the last decade, the number of recipients awaiting transplantation has more than doubled to nearly 90,000. Refinements in minimally invasive surgical approaches may encourage additional suitable individuals to consider kidney donation.

Laparoendoscopic single site (LESS) surgery was introduced as one technique to further decrease the invasiveness of laparoscopic surgical approaches. We initiated our single-port donor nephrectomy program in 2009 and have reported the World's largest series. This series clearly supports the safety and improved outcomes associated with this approach. New instrumentation may further decrease the learning curve and operative times associated with single-port techniques. The robotic single-port platform has demonstrated feasibility in a variety of procedures.

Our center has performed over 200 single-port donor nephrectomies with standard laparoscopy and has reported patient benefits associated with a single port approach[1]. The single port robotic platform offers the potential to ameliorate the significant technical and ergonomic challenges that currently limit more widespread application of single port donor surgery.

2.0 Purpose and rationale

After being informed of the potential risks and off-label use of the da Vinci Single-Site approach in our study, patients will undergo a robotic-assisted single-site donor nephrectomy performed by a two-surgeon team utilizing existing da Vinci instrumentation and Single-Site platforms. Renal mobilization and vascular dissection will be performed with manual laparoscopy performed for vascular division utilizing stapling devices.

3.0 Objectives

3.1 Primary objective

The primary objective is to measure the feasibility of the current Single-Site platform to perform donor nephrectomy prior to vascular division and kidney extraction.

3.2 Secondary objectives

Secondary objectives include operative times, blood loss, and surgeon ergonomics as measured via techniques developed in our surgical simulation center.

4.0 Study design

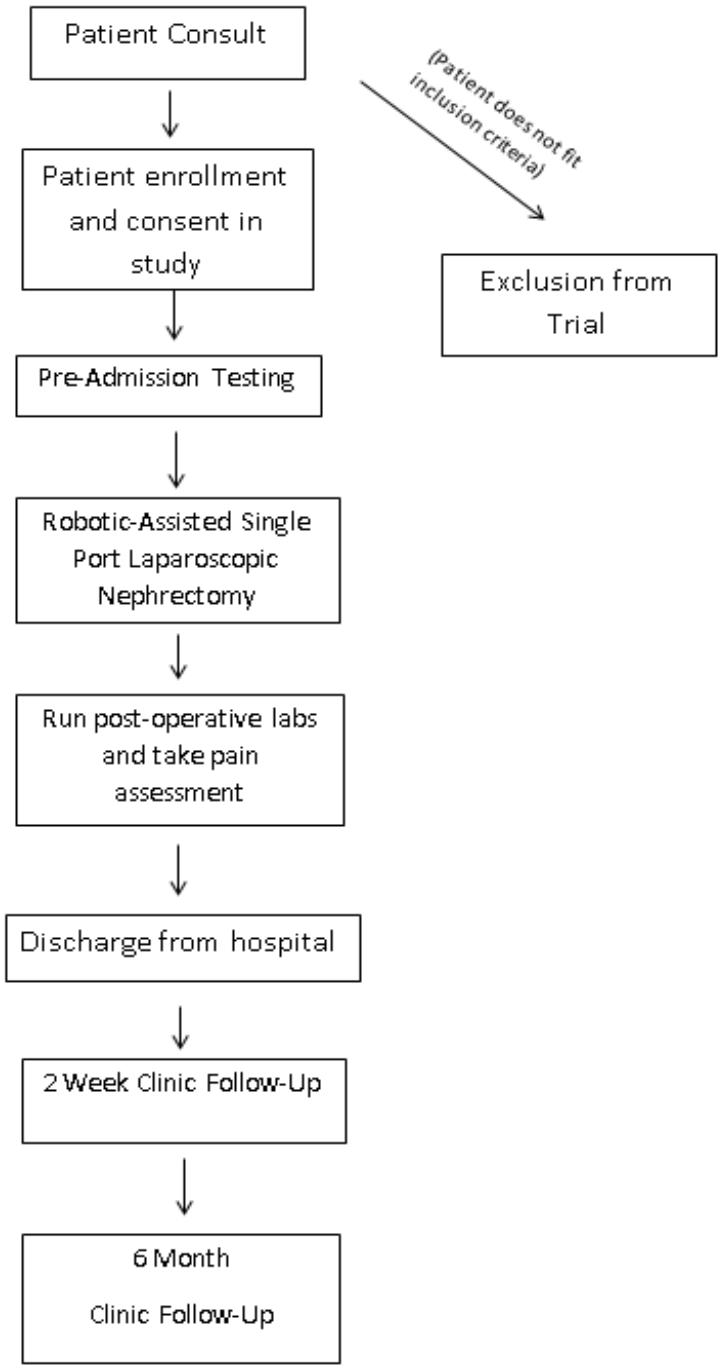
Hypothesis: We believe that the da Vinci system and its single port platform will offer solutions to the challenges of visualization, instrument articulation, and ergonomics that limit the widespread application of single-port donor nephrectomy as the preferred approach for renal donation.

Methods: We will perform an IRB-approved study of the use of the da Vinci Surgical System with Single-Site technology in donor nephrectomies. The IRB proposal and consent will be constructed to provide kidney donors with the opportunity to participate in our study. Patients will be informed of the potential risks and off-label use of the da Vinci Single-Site approach in our study. Because the standardized approach for renal donation at our center is single port donor nephrectomy, we anticipate enrollment of up to 20 patients for this study.

Patients will undergo robotic-assisted single-site nephrectomy performed by a two-surgeon team utilizing existing da Vinci instrumentation and Single Site platforms. Renal mobilization and vascular dissection will be performed with conversion to standardized laparoscopy for the final stages of vascular division with stapling devices and extraction. The primary objective is a feasibility measure of the ability of the current Single-Site platform to perform major portions of the procedure. Secondary objectives include operative times, blood loss, and surgeon ergonomics as measured via techniques developed in our surgical simulation center. Study cases will be compared to existing matched cohorts of single port donor nephrectomy cases performed by manual laparoscopy. The study population will include adults aged 18 to 70 of both genders who meet our center's criteria for renal donation and who consent to participate in the study. Our sample size of 20 patients is proposed to initiate this pilot study of the feasibility of robotic single port donor nephrectomy.

Statistical analysis will be performed on ergonomic and other collected data during the operative procedures and compared to matched patients. The proposed study of 20 patients may not generate statistically significant conclusions; however, we believe our observations will provide valid conclusions that support the use and continued development of robotic single port donor nephrectomy techniques.

Table 1 Study Design



5.0 Population

The proposed study population consists of adults aged between18-70 who have been previously approved by the living donor transplant committee at the University of Maryland Medical Center as appropriate candidates for renal donation.

5.1 Inclusion criteria

The following criteria must be met in order for a patient to participate in the study. Male or female adults ages from 18 to 70 who are good general health, and who have a genuine altruistic motivation. The patient must also have compatible blood type with the recipient, a body mass index less than 35, and appropriate for left kidney donation. Approval by the Living Donor Center must also be met in order to participate in the trial.

5.2 Exclusion criteria

The following criteria will exclude any patients from participating in the clinical trial. Any patients suffering from cancer, diabetes, kidney disease, heart disease, liver disease, sickle cell disease, HIV or hepatitis, previous major abdominal surgery, or more than two left renal arteries.

6.0 Treatments

The study is a feasibility study. Patients will undergo a donor nephrectomy with the assistance of the investigational device, the da Vinci Surgical System with the Single-Site Instruments and Accessories.

6.1 Investigational device

The investigational device, the da Vinci Surgical System with the Single-Site Instruments and Accessories will be used to perform major portions of the procedure prior to vascular division and extraction.

6.2 Treatment arms

During pre-admission testing, if the patient has met all inclusion/exclusion criteria, patients will be enrolled into the treatment group.

6.3 Treatment assignment

Once a potential study patient is identified and he/she fulfills the inclusion/exclusion criteria and the informed consent form is signed, the patient will be entered into the study. The patient will be assigned a patient identification number (see Section 6.5.1).

6.4 Treatment blinding

Not applicable

6.5 Treating the patient

6.5.1 Patient numbering

Each patient is uniquely identified in the study by a patient number. The first patient is assigned patient number 1, and subsequent patients are assigned consecutive numbers (e.g. the second patient is assigned patient number 2, the third patient is assigned patient number 3). Once assigned to a patient, a patient number will not be reused. If the patient fails to be enrolled for any reason, the reason for not being enrolled will be entered on the Screen Failure eCRF.

6.5.2 Use of the study device

The study site will be supplied with an investigational device by Intuitive Surgical Systems and it will be used by three qualified surgeons.

6.5.3 Study device supply, storage and tracking

The study device will be received by a designated person at the study site, handled and stored safely and properly, and kept in a secured location to which only the investigator and designated assistants have access. Upon receipt, all study devices will be stored according to the instructions specified on the device labels. Clinical supplies will be dispensed only in accordance with the protocol. Device labels will be in the local language and comply with all legal requirements. The investigator will maintain an accurate record of the shipment and dispensing of study device in a device accountability ledger. Monitoring of device accountability will be performed by the field monitor during site visits and at the completion of the trial. All unused study devices, packaging, and device labels will be destroyed in conformance to University of Maryland Medical Center policies.

6.5.4 Instructions using study device Not applicable.

6.5.5 Permitted study device adjustments and interruptions Not applicable.

6.5.6 Study device discontinuation and premature patient withdrawal Not applicable.

6.5.7 Emergency unblinding of treatment assignment Not applicable.

6.5.8 Study completion and post-study treatment

At study completion CRF page should be completed after the operation. Due to the nature of the study (a onetime exposure to the investigational device during the surgical procedure) withdrawal from the study cannot occur. Subjects who wish to withdraw from the study follow up will be permitted to do so.

7.0 Visit schedule and assessments

Table 7-1 lists all of the assessments and indicates with an “x” the visits when they are performed.

Table 1 Assessment schedule

	Baseline	Week		

Time Point	0	2	4	26
Visit Number	1	3	4	5
Informed Consent	X			
Background Information	X			
Inclusion/Exclusion	X			
Med Hist/Demography	X			
Vital Signs	X	X	X	X
Physical Exam	X	X	X	X
Laboratory Tests	X	X	X	X

7.1 Information to be collected on screening failures

Not Applicable

7.2 Patient demographics/other baseline characteristics

After informed consent has been signed and the patient's eligibility to participate in the study has been determined, baseline patient information will be obtained, such as date of birth, age, sex, race, full relevant medical history/current medical conditions.

A full physical examination will be made at baseline including vital signs, blood chemistry and hematology, serum creatinine, urinalysis, including a quantitative protein/creatinine ratio.

7.3 Efficacy

The observations to assess efficacy of the investigational device include the proportion of the surgical procedure able to be performed with the device, prior to standard laparoscopic techniques that will be employed in the final surgical steps. Efficacy will be specifically measured in operative time, blood loss, and successful completion of donation. Post-operative assessments will include patient satisfaction and recovery surveys. The efficacy variables selected are standard for this indication/patient population.

7.4 Safety

Safety assessments include blood loss, intraoperative complications or injuries to adjacent structures, and successful completion of donation surgery. These will be

compared to center defined rates for these safety parameters. The safety assessments selected are standard for this indication/patient population.

7.5 Other assessments

7.5.1 Resource utilization

For resource utilization, all relevant information about initial hospitalization and all follow-up hospitalizations post procdure (in the transplant study center or all other centers, if any) will be recorded. The hospitalization data will include the main reason for admission and duration of hospitalization and length of stay. All attempts will be made to collect RU variables in all patients throughout the duration of the study in order to avoid selection bias. There may also be circumstances when the collection of such data after completion of the study may be warranted. These data will be collected in the Hospitalization CRF and will be presented in a separate report.

7.5.2 Health-related Quality of Life

The SF-36 is a widely used instrument to measure generic health status. It is a 36-item questionnaire that yields an 8-scale health profile as well as summary measures of individual patients. It has proven useful in monitoring generic and specific populations, comparing the relative burden of different diseases, differentiating the health benefits produced by different treatments, and in screening individual patients. The purpose collecting SF-36 data in this study is to compare the final health status of those undergoing the robotic assisted single-incision laparoscopic donor nephrectomy.

The eight profiles (scales) are: bodily pain, general health, vitality, mental health, physical functioning, role-physical, role-emotional and social functioning. The two summary measures are physical health and mental health.

Patients will complete the questionnaire before other clinical assessments at any given visit. The SF-36 can be administered in 5 to 10 minutes with a high degree of respectability and quality. An appropriate person will be designated to facilitate self-administration. The administrator will not influence but will answer questions and address concerns to ensure that the questionnaire is filled out correctly and completely.

Completed questionnaires will be reviewed and examined by the investigator before the clinical examination for responses which may indicate potential AEs or SAEs. The investigator will review not only the responses to the questions in the questionnaires, but he or she will also review for any unsolicited comments written by the patient. If the occurrence of AEs or SAEs is confirmed, the physician will record the events as per instructions given in Section 7.5.1 of the protocol. Investigators will not encourage the patients to change the responses reported.

10 Data analysis

10.1 Sets for analysis

This study is not designed based on statistical power, thus statistical tests will not be performed as p-values would not be reliable and will lead to misinterpretation of the data.

All analyses will be descriptive.

10.2 Patient demographics/other baseline characteristics

Demographic and other baseline characteristics will be presented by treatment group. Continuous variables will be summarized by sample size, mean, standard deviation, median, minimum and maximum.

10.3 Analysis of the primary objective(s)

10.3.1 Variable

The primary objective is a feasibility assessment of the ability of the current Single-Site platform to perform major portions of the procedure prior to vascular division and extraction. This is a feasibility clinical study design to collect the primary evidence of safety and efficacy to support a marketing submission or application.

10.4 Analysis of secondary objectives

10.4.1 Efficacy (secondary)

Secondary objectives include operative times, blood loss, and surgeon ergonomics as measured via techniques developed in our surgical simulation center. Study cases will be compared to existing matched cohorts of single port donor nephrectomy cases performed by manual laparoscopy.

10.4.2 Safety

Safety variables to be assessed include discontinuation from study, discontinuation from treatment, renal function, AE/infection, SAE, notable events, laboratory tests, and vital signs.

Adverse events will be summarized by presenting, for each treatment group, the number and percentage of patients having any adverse event, having an adverse event in each organ system and having each individual adverse event. The same type of summaries will be provided for serious adverse events and for events suspected to be related to the study device. Any other information collected (e.g. severity or relatedness to study device) will be listed as appropriate.

Laboratory data will be summarized by baseline values to most extreme post-baseline values, by presenting summary statistics of raw data and change from baseline values (means, medians, standard deviations, ranges) and by the flagging of notable values in data listings.

Data from other tests (e.g. vital signs) will be listed, notable values will be flagged, and any other information collected will be listed as appropriate. Any statistical tests performed to explore the data will be used only to highlight any interesting comparisons that may warrant further consideration.

The data collected will be presented in listings, summary tables and graphs.

10.4.3 Resource utilization

Data related to Resource Utilization will be used for the purpose of economic evaluation which will be analyzed in a separate report.

10.4.4 Health-related Quality of Life

The change from baseline in the profile and summary scores of the SF-36 will be assessed in the treatment group.

10.5 Sample size calculation

This study is a pilot study of 20 patients without additional sample size calculation.

10.6 Power for analysis of critical secondary variables

Not applicable.

10.7 Interim analysis

Routine follow-up appointments will occur 2 weeks and 6 months after operation.