THE FEASIBILITY OF USING THE ULTRAVISION™ SYSTEM TO FACILITATE LOW IMPACT LAPAROSCOPIC SURGERY FOR THE TREATMENT OF ENDOMETRIOSIS

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Compliance Statement

This study will be conducted in full accordance with this protocol, all applicable Mercy Hospital St. Louis Institutional Review Board policies and procedures, International Conference on Harmonization guidelines for Good Clinical Practice and all applicable Federal and state laws and regulations including 45 CFR 46 and the HIPAA Privacy Rule.

THE FEASIBILITY OF USING THE ULTRAVISION™ SYSTEM TO FACILITATE LOW IMPACT LAPAROSCOPIC SURGERY FOR THE TREATMENT OF ENDOMETRIOSIS

Study Summary

Introduction and Background

The Ultravision™ System is an FDA-cleared medical device that removes surgical smoke by means of electrostatic precipitation from the visual field during laparoscopic surgical procedures. "Surgical smoke" refers to the suspended particulate matter that is generated as a by-product of the combustion and other processes that are associated with the use of energy-based surgical instruments. Surgical smoke can obscure (partially or totally) the surgeon's view of the operative field and this has obvious safety implications for the patient. In the case of laparoscopic procedures, which are increasing in popularity, the smoke is retained within the "closed abdomen" and this, coupled with the CO_2 pneumoperitoneum, presents additional challenges for the surgical team. The Ultravision™ System can therefore be considered an accessory to electrosurgical instruments to clear the surgical smoke generated during their use and as such will only be used when such devices are in use.

The ability to operate under "low impact" laparoscopic conditions has been shown by others to improve clinical outcomes by, for example, reducing post-surgical pain and with smaller incision sizes, improved cosmesis. For the purposes of this study "low impact" is defined as (1) a target pneumoperitoneal pressure of 10mm Hg; and (2) instead of 10mm and/or 12mm ports, the use of 3mm ports and one 5mm port. Using a standard insufflator, the combination of lower pneumoperitoneal pressure and smaller size ports creates visualization challenges for the surgeon due to the difficulty of preventing the buildup of surgical smoke within the abdomen. "Venting" or actively extracting the smoke through a trocar is known to be largely ineffective due to the narrow internal diameter of 3mm trocars, certainly unless the instrument is removed beforehand, which creates additional surgical challenges. Furthermore, operating under lower pressure can cause pneumoperitoneum to be lost upon venting of the smoke. The research question that is posed in this study is whether the Ultravison™ System, due to its unique mode of action which (unlike other smoke management approaches) provides smoke management without needing to extract or exchange CO_2, provides effective visual field clearing, thereby facilitating low impact laparoscopic surgery when using a conventional insufflator. In addition, Ultravision™ does not require CO_2 removal and replacement to achieve its intended use, thereby minimizing to the greatest extent possible patient CO_2 exposure. CO_2 is dry (effectively 0% relative humidity) and cold (typically 65F) and exposure is linked to postoperative pain and other adverse consequences such as patient cooling and tissue desiccation. Due its mode of action, Ultravision™ minimizes CO_2 exposure to the patient.

Laparoscopic surgery for the treatment of endometriosis is a common procedure for the removal of mild to moderate endometriosis. Diathermy is commonly used to remove the lesions which can be extensive, therefore this procedure presents an appropriate surgical procedure for this study.

Assessments in terms of surgical field visualization, CO_2 consumption, end tidal CO_2, patient satisfaction for cosmesis, and postoperative pain will be conducted in order to determine if the Ultravision™ System is effective in enabling laparoscopic surgery under low impact laparoscopic conditions. Adverse event information will be reported. The study is an open label single arm study.

Study Purpose

There are five main study objectives:

1. Demonstrate the feasibility of undertaking low impact laparoscopic surgery for endometriosis when using the Ultravision™ System.
2. Assess the impact of Ultravision on visual field clarity.
3. Determine the ability to complete the procedure while maintaining an abdominal pressure of $\leq$ 10mmHg.
4. Quantify the consumption of CO_2.
5. Collect data on additional clinical outcomes associated with the use of Ultravision and low impact surgery (i.e. end tidal CO_2 levels ($EtCO_2$), adverse events, cosmesis outcome, postoperative pain levels and pain medications).

Study Hypothesis

The primary hypothesis being tested in this study is that Ultravision facilitates the utilization of low impact laparoscopic surgery techniques whilst maintaining an adequate visual field throughout the procedure with low demand for CO_2 replenishment to maintain pneumoperitoneal pressure.

Study Population

The study will enroll patients indicated for laparoscopic surgery to treat endometriosis. Patients must meet all inclusion/exclusion criteria.

Study Design

This is a prospective single arm study. The study will enroll 20 patients. Comparisons to prior clinical trials and published literature will be made to assess the relative significance of the study results.

Study Endpoints

Success will be based on demonstration that the procedures using the Ultravision™ System achieves the following endpoints :

1. The ability to complete the procedure without increasing pneumoperitoneum due to visualization. Any increase beyond 10mm Hg and the reason for change will be recorded.
2. The quality of visualization in the laparoscopic field of view will be assessed by the investigator using a Visual Analog Scale (VAS).
3. Patient satisfaction with cosmesis outcome at the discharge follow-up visit assessed by means of a survey scaled from "very unsatisfied" to "very satisfied."
4. Post-Surgery Pain assessment based upon a Numerical Rating Scale (NRS) where 0 is "no pain at all" to 10 "worst pain imaginable" and the location of the pain using a body diagram.
5. Pain medication utilization

Other Data Collection

- End tidal CO_2 volume ($etCO_2$) (taken at the start of the procedure and at the completion of the procedure),
- Adverse Events,
- Electrosurgical instrument(s) used,
- Preoperative assessment: patient demographics, medical history, medication information, height and weight, pain (at intake visit)
- Number of endometriosis lesions resected

Study Size:

A sample size of 20 patients should provide a sufficient sample size for comparative analysis to prior clinical data relative to Ultravision and published peer reviewed clinical data on laparoscopy and low impact laparoscopy.

Duration of Study:

The target for the overall duration of the study is four months.

Data Analysis: Descriptive statistics for all endpoints will be applied to analyze the results.

Results from other studies conducted by Alesi as well as clinical data gleaned from the medical literature will be used to assess the relative significance of the study result.

1. STUDY PROTOCOL INTRODUCTION & BACKGROUND

The advantages of laparoscopic surgery are generally accepted in the medical community. However, as with any therapy or procedure the unique circumstances associated with this type of surgery are not without physiological consequences such as tissue desiccation and postoperative pain.[1] [2] The working space created by pneumoperitoneum using CO_2 is required to create the visual/working field but creates its own concerns regarding abdominal pressure and CO_2 absorption into the abdominal tissue.[3] The smoke generated by electrosurgical devices in the process of dissection of tissues during laparoscopy can obscure the surgical visual field which can impede the operating surgeon. It is often necessary to suspend the surgery to allow the smoke to dissipate, or more commonly open a laparoscopic port to vent the smoke into the room, adding to the operating time. It is also common to remove the laparoscope to clean the lens because it can be soiled by the smoke as well. In order to enhance the dissipation of smoke and maintain an adequate pneumoperitoneum it is often necessary to increase the flow of carbon dioxide (CO_2) from the insufflator. Surgical smoke handling during laparoscopic surgery results in an increase of the known risks to the patient of using excessive CO_2 as well as exposing the operating room staff to the smoke which may create a potential health concern.

The Ultravision™ Visual Field Clearing System provides a stable and clear visualization using electrostatic precipitation to remove the smoke from the visual field. This is accomplished with Ultravision without requiring venting of gas, that would otherwise be replaced to maintain the pneumoperitoneum operating pressure. Because it does not rely on gas flow for smoke clearing, CO_2 consumption is greatly reduced compared to other methods. Safety and feasibility studies have been carried out allowing it to be placed on the market in Europe, Japan and the United States. A randomized study of its clinical effectiveness showed that electrostatic-precipitation significantly improved visibility (reduction of visual impairment) and reduced

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[1] O'Malley C, Cunningham AJ, Physiologic Changes during laparoscopy, Anesthesiology Clinics of North America, 2001 Mar; 19(1): 1-19.

[2] Veekash G, Wei LX, Su M, Carbon dioxide pneumoperitoneum, physiologic changes and anesthetic concerns, Ambulatory Surgery, 162 July 2010.

[3] Srivastava A, Niranjan A, Secrets of laparoscopic surgery: Anaesthetic and surgical considerations, Journal of Minimum Access Surgery, 2010 Oct-Dec; 6(4): 91-94.

surgery time in laparoscopic cholecystectomy.[4] A similar study in laparoscopic hysterectomy and myomectomy reported similar results at lower pneumoperitoneal pressures (10mmHg). [5]

The ability to operate under low impact laparoscopic conditions has been shown by others to improve clinical outcomes by, for example, reducing post-surgical pain and improved cosmesis. [6] For the purposes of this study "low impact" is defined as (1) a target pneumoperitoneal pressure of 10mm Hg; and (2) the use of 3mm ports with one 5mm port. Using a standard insufflator, the combination of lower pneumoperitoneal pressure and smaller size ports creates visualization challenges for the surgeon due to the difficulty of preventing the buildup of surgical smoke within the abdomen. "Venting" or actively extracting the smoke through a trocar is known to be largely ineffective due to the narrow internal diameter of 3mm trocars, certainly unless the instrument is removed beforehand, which creates additional surgical challenges. In addition, due to its unique mode of action, Ultravision™, unlike other smoke clearing systems, does not require CO_2 removal and replacement to achieve its intended use. CO_2 exposure is linked to postoperative pain and other adverse consequences (i.e. patient cooling, tissue desiccation). Due its mode of action, Ultravision™ minimizes CO_2 exposure to the patient.

Laparoscopic surgery for the treatment of endometriosis is a common procedure for the removal of mild to moderate endometriosis. Diathermy is commonly used to remove the lesions which can be extensive, therefore this procedure presents an appropriate surgical procedure for this study. Diathermy devices are electrosurgical devices that deliver high frequency currents to heat tissue to aid in dissection of tissue and to control bleeding.

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[4] Ansell J., Electrostatic precipitation is a novel way of maintaining visual field clarity during laparoscopic surgery: a prospective double-blind randomized controlled pilot study. Surg, Endosc. (2014) 28: 2057-2065)

[5] Levine D., Investigator sponsored research, " A randomized, controlled study evaluating the effectiveness of the Ultravision™ Visual Field Clearing System in laparoscopic hysterectomy and myomectomy," Mercy Hospital St. Louis, November 2018.

[6] Yasir M, Kuldeep MS, Vigar HB, Aiman A, Masood I, Iqbal B, Evaluation of post-operative shoulder tip pain in low pressure versus standard pressure pneumoperitoneum during laparoscopic cholecystectomy, The Surgeon, Journal of the Royal Colleges of Surgeons of Edinburgh and Ireland, 10(2012) 71-74.

2. STUDY PURPOSE

The research question that is posed in this study is whether the Ultravison™ System provides effective visual field clearing thereby enabling low impact laparoscopic surgery when using a conventional insufflator with low demand for CO_2 replenishment to maintain pneumoperitoneal pressure.

3. INTENDED USE (PER INSTRUCTIONS FOR USE)

The Ultravision™ System is indicated for the clearance of smoke and other particulate matter that is created during laparoscopic surgery.

4. DEVICE DESCRIPTION

The Ultravision™ System is an accessory to electrosurgical instruments that is used to clear the surgical smoke generated during their use and as such will only be used when such devices are in use. An example of the effect of the Ultravision™ System during use to improve the visualization of the field of view is demonstrated in Figure 2 below:

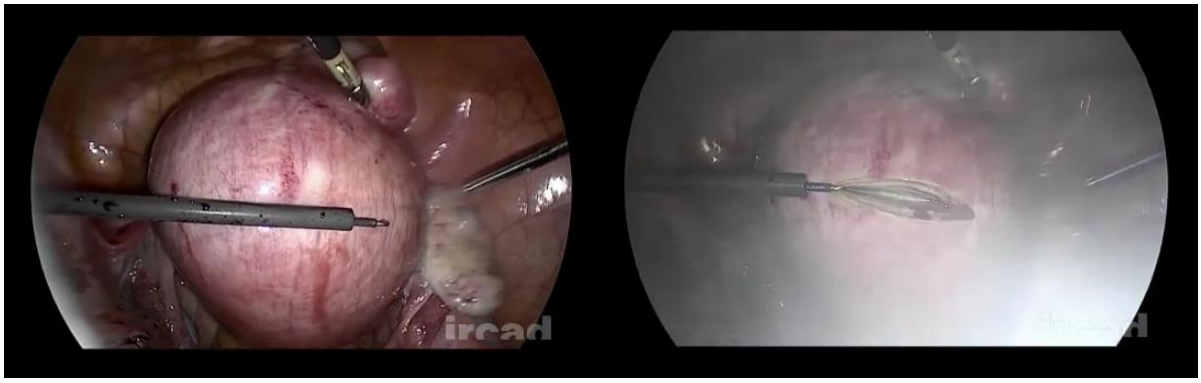

Figure 1. View before and during cutting with an electrosurgical instrument

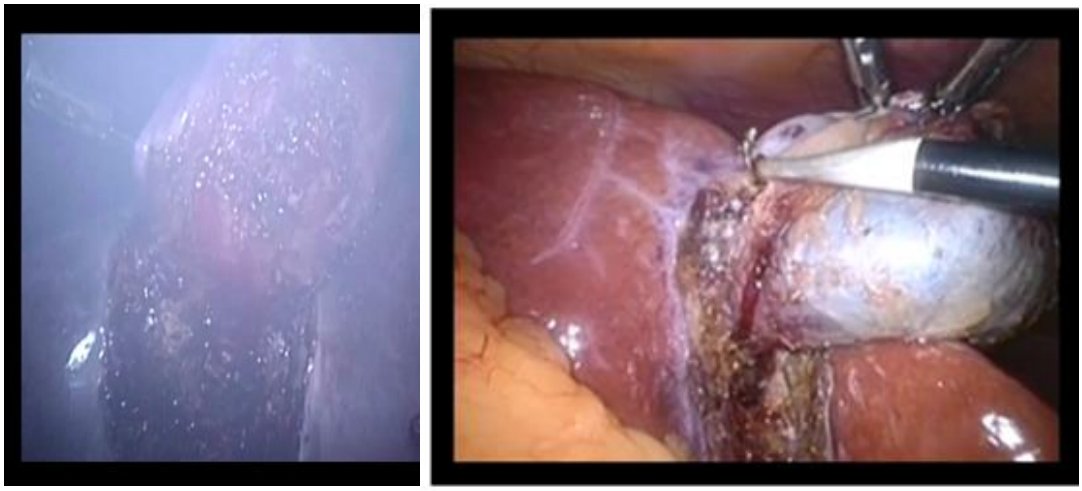

Figure 2. Electrosurgical smoke without (left hand image) and with (right hand image) Ultravision.

The system includes the following elements:

Standalone battery-operated generator unit

Figure 3. Ultravision Generator with battery pack

Ionwand™, which is introduced into the abdomen of the patient through either the Ultravision™ 5mm Trocar or a 2.5mm percutaneous catheter and provides the source of the electrons that create the negative ions that transiently charge the surgical smoke particles.

Figure 4. Ionwand, sterile assembly in package (top), 5mm Trocar (bottom)

Other accessories include a patient return adaptor and battery recharging station.

5. US REGULATORY STATUS

The Ultravision™ System obtained regulatory clearance through US FDA's De Novo Classification Process (DEN 150022). The system has been in distribution in Europe since January 2014 and in the US since December of 2016, over 250 systems are currently in use. To date there have been no incident or medical

device reports (patient injury reports) and there have been no product recalls. The Ultravision™ System and consumable items are being provided for this study free of charge.

6. STUDY DESIGN

This is a prospective nonrandomized study in patients undergoing laparoscopic surgery for endometriosis.

7. STUDY SIZE

The study will enroll 20 patients.

8. DURATION

The total duration of the study is expected to be approximately four months. Two months to enroll and two months to complete last follow-up visit and study report.

9. STUDY ENDPOINTS

To answer the research question posed the following data will be collected:

1. The ability to complete the procedure without increasing pneumoperitoneum due to visualization. Any increase beyond 10mm Hg and the reason for change will be recorded.
2. The quality of visualization in the laparoscopic field of view will be assessed by the investigator using a Visual Analog Scale (VAS).
3. Patient satisfaction with cosmesis outcome at the discharge follow-up visit assessed by means of a survey scaled from "very unsatisfied" to "very satisfied."
4. Post-Surgery Pain assessment based upon a Numerical Rating Scale (NRS) where 0 is "no pain at all" to 10 "worst pain imaginable" and the location of the pain using a body diagram.
5. Pain medication utilization

10. OTHER DATA COLLECTION

- End tidal CO_2 volume ($etCO_2$) (taken at the start of the procedure and at the completion of the procedure),
- Adverse Events,
- Electrosurgical instrument(s) used,
- Preoperative assessment: patient demographics, medical history, medication information, height and weight, pain (at intake visit)
- Number of endometriosis lesions resected

11. SUBJECT IDENTIFICATION & SELECTION

Potential subjects will be identified from the clinical practice of the participating investigator or by their respective research staff. Patients presenting to the clinical practice of the participating investigator for diagnosis or treatment consistent with the inclusion criteria will be informed about the study.

With referral from the treating physician/provider, patients scheduled for surgery prior to the start of the study may be contacted via telephone by a study team member to inform them of the study, assess their interest and assess their eligibility to participate. An IRB approved script will be used for such calls. For interested patients, a copy of the informed consent can be mailed or emailed to the patient for their review and consideration prior to their next clinic visit or the scheduled procedure.

Each new subject presenting for evaluation or inclusion is to be assessed for adherence to the following inclusion/exclusion criteria. Determination of whether subjects satisfy the criteria may be established by review of medical records, subject interview, physical examination, or testing as appropriate. A baseline form is used to collect subject screening information and baseline assessments. Patients are considered enrolled once it has been demonstrated that the inclusion/exclusion criteria have been met and the patient signs the informed consent.

The study allows for an intraoperative exclusion for excessive abdominal wall thickness or other anatomical characteristics that prevent the use of Ultravision. If this should occur, the patient will be withdrawn from the study. The withdrawal will be recorded on the withdrawal case report form. The patient will be replaced.

11.1. INCLUSION CRITERIA

Subjects MUST meet all the following:

I1	Is 18 years or older.
I2	Provide written informed consent prior to trial procedures after studies indicate that the patient needs the prescribed procedure.
I3	Agrees to attend all follow-up assessments.
I4	Is indicated for laparoscopic surgery for the treatment of endometriosis.
I5	Able to read and understand English

11.2. EXCLUSION CRITERIA

Subjects MUST not have any of the following:

E1	Existing comorbidities that would contraindicate them for laparoscopic surgery.
E2	Patient anatomy that is not compatible with the use of the Ionwand catheter i.e. abdominal wall thickness that exceeds the working length of the Ionwand catheter identified intraoperatively
E3	Patient with a BMI > 50
E4	Be pregnant

12. SUBJECT INFORMED CONSENT

A partial waiver of HIPAA Authorization is being requested for the purposes of initial screening for study eligibility and recruitment purposes. Identifiable health information to be accessed under this waiver will include contact information, demographics, and medical history. Only study team members will have access to this information. Safeguards to maintain privacy and confidentiality of information will be taken as described in the data collection and management section of the protocol. Patient inclusion could be substantially hindered without the ability to review patients' records for eligibility and recruitment purposes, particularly for patients who may have already been scheduled for surgery at the time the study begins.

Referred patients presenting for diagnosis or treatment consistent with the inclusion/exclusion criteria will undergo the informed consent process to authorize the gathering of data recorded on the Subject Screening & Enrollment Form. The study investigator will administer informed consent or may delegate the responsibility to a qualified individual as long as it is defined on the study responsibility log. When administering consent, it must be evident that the participant comprehends the nature of the study and the risks and benefits. Evidence is the patient is able to verbalize these topics in sufficient detail to confirm comprehension.

Completion of the informed consent does not constitute enrollment. Enrollment occurs once screening is complete and all criteria for participation have been met.

Subjects must document their consent for study participation by signing the Institutional Review Board approved Informed Consent Form. The informed consent process must be consistent with the Declaration of Helsinki. The subject must be given the opportunity to ask questions of, and receive answers from, study personnel prior to a request to sign the Informed Consent Form. This form is to be co-signed by the investigator. Failure to obtain consent prior to subject participation is considered a protocol deviation and must be reported to the Institutional Review Board.

Note that subjects will be asked to provide consent so that data related to their eligibility status data can be gathered.

After the subject and investigator sign the Informed Consent Form, the original is to be filed in the subject's study binder. Copies will be filed in the subject's medical record and the subject is also to be given a copy.

13. SCREENING & ENROLLMENT

Patient demographics and other baseline information will be collected to establish whether the patient meets the requirements for the study. It is assumed that a physical exam will be conducted as part of the standard of care. Only limited information on the patient's health status is collected for the study as defined in Table 1 below. Each patient will be assigned a unique study number. Baseline information will be collected, consistent with the standard of care. Baseline assessment is conducted at the preoperative visit.

Table 1
Baseline Assessment – Conducted at Pre-op visit

Type of Information	Data Sources	Time Frame
Date of Evaluation	Investigator Report	NA
Subject Age	Subject interview / Medical Record	NA
Height	Medical Record	NA
Weight	Medical Record	NA
Body Mass Index (BMI)	Medical Record	
Prior/Existing Medical Conditions	Subject interview & medical record	Within three months prior to surgery
Prior/Existing Medical Interventions	Subject interview & medical record	Within three months prior to surgery
Diagnosis Indicating Surgical Intervention	Investigator Report	Within three months prior to surgery
Current Pain Medications and Reason for Taking	Subject interview & medical record	Within three months prior to surgery

14. PREOPERATIVE PROTOCOL

Patients will be assessed preoperatively in accordance with the current standard of care.

Table 2
Pre-Surgery (Intake) Assessment

Type of Information	Data Sources
Date of Evaluation	Investigator Report
Completed Informed Consent	Investigator Report
Changes since baseline assessment • Medical conditions • Pain Medications • Medical interventions/Adverse Events	Medical Record/Patient Report
Pregnancy Test	Medical Record
Pain Assessment	Subject Report

Table 2 Pre-Surgery (Intake) Assessment	
Type of Information	**Data Sources**
Pain Medications	Subject Report

15. PROCEDURE PROTOCOL

The device is used in accordance with the instructions for use. An initial target pneumoperitoneal pressure setting of 10mmHg will be used for the procedure. At the discretion of the surgeon investigator, pressure will be adjusted as needed to accomplish the surgical procedure. A standard insufflator with 3mm ports and one 5 mm ports will be used for the procedure.

Table 3 Intraoperative/Procedure Information		
Type of Information	**Time Point**	**Data Sources**
Date of Procedure	Before opening	Patient Medical Record
Pneumoperitoneum pressure after camera trocar is inserted	Intraoperative	Investigator Report
Increase in pressure and reason for change	Intraoperative	Investigator Report
Adverse Events	Intraoperative	Investigator Report
Unplanned concomitant interventions or procedures	Intraoperative	Investigator Report
End tidal volume of CO_2 (etCO2), recorded at the beginning and end of the procedure.	Intraoperative	Investigator Report
Number of CO_2 liters consumed	At completion of the procedure	Investigator Report
Surgeon Survey on Quality of Visualization and Smoke Management	Immediately Post-operative	Investigator Report
Ultravision device(s) used (lot# and model #)	Immediately Post-operative	Investigator Report
Diathermy device(s) used	Immediately Post-operative	Investigator Report
Device Malfunction – recorded as an adverse event	Intraoperative	Investigator Report
Number of Endometriosis Lesions Resected	Post-operative	Operative Report / Investigator Report
Pain Assessment	Just Prior to discharge	Medical Record

Table 3 Intraoperative/Procedure Information		
Type of Information	**Time Point**	**Data Sources**
Pain Medications	Prescribed at discharge	Medical Record

16. SURGEON SURVEY

Immediately post procedure the investigator will be asked to provide feedback regarding visibility and smoke management during the procedure. Responses will be recorded on a VAS scale.

1. Overall quality of visualization.
2. How often was smoke management a negative factor during the procedure.

17. POST PROCEDURE FOLLOW-UP PROTOCOL

16.1 Post-operative days 1-7:

Subjects will be asked to complete a daily diary/self-assessment of pain. The assessment will include a pain rating, location of pain and medications taken for pain. The diary/self-assessment is included as a separate document.

16.2 Post-operative 2 week (± 3 days) follow up visit:

A 2 week follow up visit is current standard of care. At this visit, adverse events will be assessed. A final pain assessment will be administered during this visit.

16.3 Post-operative 4 week (± 1 week) follow up phone call:

Patient satisfaction with cosmesis (scar appearance) after the surgery will be collected by means of a telephone follow-up where a simple cosmesis satisfaction survey will be administered by a study team member.[7]

16.5 Unscheduled visit:

[7] Steinemann D, Raptis D, Lurje, Oberkofler C, Wyss R, Zehnder A, Lesurtel M, Vonlanthen R, Clavien P, Breitenstein S, Cosmesis and body image after single-[prt laparoscopic or conventional laparoscopic cholecystectomy: a multicenter double blinded randomized controlled trial (SPOCC-trial), BMC Surg. 2011; 11:24, September 2011.

A pain assessment and adverse event assessment will be performed at any unscheduled visit.

Additional evaluations will be completed at the discretion of the Principal Investigator based on the subject's presenting complaint.

18. ADVERSE EVENTS

18.1. ADVERSE EVENT CATEGORIES

For purposes of this protocol the adverse event definitions are derived from GCP standards and FDA Guidance.[8]

Table 4
Adverse Event Definitions

Adverse Event (AE)	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. Includes events related to the study device or comparator device, or the procedures involved.
Serious Adverse Event (SAE)	Adverse event that: ▪ Led to death ▪ Led to serious deterioration in the health of the subject, that: o Resulted in a life-threatening illness or injury, or o Resulted in a permanent impairment of a body structure or a body function, or o Required in-patient hospitalization or prolongation of existing hospitalization, or o Resulted in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function o Led to fetal distress, fetal death, or a congenital abnormality or birth defect Planned hospitalization for a pre-existing condition without serious deterioration in health, is not considered a serious adverse event. Hospitalization is defined as an admission greater than 24 hours
Adverse Device Effect (ADE)	Untoward and unintended response to a medical device or as a consequence of inadequate labeling and includes any event that is a result of user error.
Serious Adverse Device Effect (SADE)	Untoward medical occurrence that happens in a subject or other person, is related to the study device, comparator, or procedure, and is serious, but is not unanticipated

[8] Clinical Investigation of Medical Devices for Human Subjects - Part 1: General Requirements. ISO 14155-1. International Organization for Standardization. 2011.

Unanticipated Serious Adverse Device Effect (USADE)	Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, procedure, or comparator device if that incidence effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the risk analysis report of the plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

The signs, symptoms, and sequelae of an underlying adverse event (linked pathophysiologically to the AE) should not be reported as separate adverse events.

All adverse events, of any type, are to be recorded on an "Adverse Event Form". Adverse events are to be characterized by their severity, relatedness the surgical procedure, need for therapy, and resolution status.

Adverse events will initially be characterized as "serious" or "non-serious" by the study investigator.

18.2. ADVERSE EVENT ADJUDICATION

Events are to be initially judged by the investigator as to their relatedness to the study device, surgical procedure, or "other etiology". The classifications will be "not related", "probably not related", "undetermined", "probably related", or "related".

18.3. REPORTING OF ADVERSE EVENTS AND UNANTICIPATED PROBLEMS

Serious adverse events and Unanticipated Problems related to the research will be reported to the Mercy Institutional Review Board.

18.4. SUBSEQUENT SURGICAL INTERVENTIONS

Some complications may lead to a subsequent surgical intervention. The reason for each subsequent surgical intervention and the action taken is recorded on the case report form, along with the identification of the type subsequent surgical interventions accordingly. The exact type of intervention must be specified.

19. PATIENT WITHDRAWAL

A patient may choose to withdraw from participation in the study at any time without penalty. If a patient chooses to withdraw, they will still receive medical care consistent with the standard of care. The investigator may at their discretion withdraw a patient from participation or where intraoperative exclusions (defined in the I/E criteria) occur. Other examples include if the procedure necessitates conversion from laparoscopic to open technique, lack of adherence to visit schedule, adverse events, or safety concerns. For all withdrawals the date, point in the study, and reason for withdrawal will be recorded. Patients that withdraw prior to the procedure or are withdrawn from the study due to an intraoperative exclusion are replaced.

20. STUDY SUSPENSION/TERMINATION

If for any reason the principle investigator chooses to suspend or terminate the study, the IRB shall be informed of the decision and the basis of the decision.

21. STUDY MATERIALS

The Investigator is responsible for assuring that routine medical supplies, equipment, personnel, and facilities are available to successfully implement this study plan in a timely and efficient manner. Provisions should be made for research and medical staff to sufficiently accomplish:

- Screening of subjects to identify suitable study subjects,
- Conducting and obtaining informed consent,
- Scheduling for examinations and procedures,
- Coordination, monitoring, and source data verification,
- Case Report Forms,
- Investigational devices and
- Clinical study Plan and supporting study documentation.

22. PROVISION AND INVENTORY OF STUDY DEVICES

The device and required materials will be provided to the Investigator by Alesi Surgical Ltd.

23. DATA COLLECTION AND MANAGEMENT

The investigator and study team members as delegated are responsible for collecting the data from the study. Copies of all imaging documentation files will be collected and retained by the study team.

Case Report Forms (CRF) specifically created for this study will be used to collect all data. Case Report Forms shall reflect the contents of this study plan. The CRF and any amendment to it shall bear a version number and each page shall be identifiable by the number and identification of the subject whose data the CRF pertains. If/when it is necessary to amend the CRFs, the Investigator shall review the study protocol to determine if an amendment to this study protocol is necessary. All study protocol amendments require IRB notification. If the amendments are significant changes in the study design IRB review and approval may be required. The Investigator will work with the IRB for all changes to ensure the proper process for implementation of change occurs.

Manually entered information on any paper study documents must be legibly written in black ink only. If changes are required, a single line must be drawn through the incorrect information, the correct information written in, and the changes initialed and dated. The reason for the correction should be noted, unless obvious.

Use of white-out, obscuring incorrect data (scribbling-out), and additional comments written on the documents is prohibited.

The investigator must review sign and date each CRF or document review on a CRF review log; these responsibilities cannot be delegated to another person. The investigator is responsible for the accuracy and completeness of all study data.

All original imaging, laboratory, and procedural reports, etc., are considered source documents and will also be retained at the investigational site.

Study subjects will be identified by unique study identification numbers. The identification number is the 3-digit study number. A master key will contain the study identification number and patient identifier (as defined by the Study number, the patient ID number and the patient's initials). The master key will be stored in the study binder and kept in a secure, locked location in the Principal Investigator's office.

Study binders containing study data (including subject pain diaries) will be collected and stored in a secure, locked location in the Principal Investigator's office. Access to the records will be limited to the Lead Study Coordinator and the Principal Investigator only.

For analysis data may be extracted from case report forms and entered into Excel spreadsheets by a member of the study team. The spreadsheet(s) containing the study data set will not contain protected health information. Subjects will be identified by the 3-digit study number only (no initials). The study data set will be stored on a study team member's password-protected Mercy computer on a secure Mercy server.

Study data will not be removed from the site listed above at any time during the course of this study. Data extracted into spreadsheets may be shared outside of the facility for data analysis purposes. All shared data will be de-identified.

All public reporting of the results of this study will eliminate identifiable references to the subjects.

24. IMAGING DIAGNOSTICS

Any imaging performed for patients is considered consistent with standard of care.

25. DATA ANALYSIS PLAN

25.1. SAMPLE SIZE JUSTIFICATION

Ultravision is already cleared by the FDA for use in laparoscopic endometriosis. This post-market study is intended to evaluate user satisfaction and the relative impact the Ultravision™ System has on the procedure as opposed to demonstrating safety and efficacy. The sample size selected (20) is considered to be a sufficient quantity to establish whether or not low impact surgery is facilitated with the use of the

Ultravision™ System. This is designed as a single arm study to demonstrate feasibility of device use under low impact laparoscopy. The Ultravision will either enable the procedure to be completed as planned or not, therefore a control arm is not considered necessary to make this determination. In addition, incorporating a control arm using the same conditions without the use of Ultravision may not be in the best interest of the patient. The study design is considered to appropriate for the research question that is being posed.

25.2. DATA ANALYSIS

Data collected will be summarized using descriptive statistics. Results from other studies conducted by Alesi as well as clinical data gleaned from the medical literature will be used to assess the relative significance of the study results. Additional exploratory analysis may be conducted during data analysis.

26. TRAINING PROCEDURES

The Principal Investigator in the study is a current Ultravision user, no additional device training is required. To ensure compliance with the study plan and regulatory requirements as well as accurate data collection, site training will include a detailed review of this Investigational Plan, case report form (CRF) completion instructions, adverse event reporting, device handling and inventory, monitoring logistics, and regulatory requirements.

27. ADMINISTRATION

This study is being conducted as an "Investigator Sponsored" post-market study. The Principal Investigator holds ultimate responsibility for the design, conduct, analysis, and reporting of the results from this study and is the primary contact for all matters related to this investigational plan. The Principal Investigator is also accountable for monitoring this investigation and performing those actions necessary to protect the scientific credibility of the way this study is conducted.

28. REGULATORY COMPLIANCE

The Principal Investigator is responsible for ensuring that the study is implemented at their site according to the Investigator Agreement, this protocol, applicable laws, regulations, and any conditions of approval by either the respective Institutional Review Board. The Principal Investigator is also responsible for ensuring that this study is conducted in a scientifically credible and ethical manner. The Principal Investigator is responsible for the selection, training, and supervision of site-specific research personnel. The Principal Investigator shall always perform responsibilities in a manner which protects the rights, safety, and well-being of subjects.

The Principal Investigator and all research staff participating in this investigation are expected to adhere to this investigational plan, Good Clinical Practices, applicable privacy laws, the Declaration of Helsinki, and any approval requirements imposed by an Institutional Review Board. The study will be submitted for review and approval by the Mercy Institutional Review Board.

28.1. INSTITUTIONAL REVIEW BOARD

Subjects may not be enrolled into this study until legal authority to do so has been granted by the authorizing Institutional Review Board. A copy of all approval letters must be maintained in the site file.

28.2. GOOD CLINICAL PRACTICES

The principles of Good Clinical Practices defined in ISO 14155:2011-1 Clinical investigation of medical devices for human subjects – Part 1: General Requirements, Part 2: Clinical investigation plans will be adhered to in the design, conduct, analysis, and reporting of results of this investigation.

29. PRIVACY AND CONFIDENTIALITY

30. THIS STUDY IS TO BE PERFORMED IN ACCORDANCE WITH ALL APPLICABLE PRIVACY LAWS. ALL DATA AND INFORMATION CONCERNING SUBJECTS AND THEIR PARTICIPATION IN THIS TRIAL ARE CONSIDERED CONFIDENTIAL. ONLY AUTHORIZED INVESTIGATORS AND APPROVED STUDY PERSONNEL WILL HAVE ACCESS TO SOME PORTIONS OF THESE CONFIDENTIAL FILES. INSTITUTIONAL REVIEW BOARDS AND OTHER REGULATORY AUTHORITIES ALSO HAVE THE RIGHT TO INSPECT AND COPY RECORDS PERTINENT TO THIS TRIAL. RECORDS AND REPORTS

The following records and reports must be created and/or maintained by the parties as specified below.

30.1. INVESTIGATOR RECORDS

Records to be maintained by the investigator in a designated study file include:

- Site information
    - Site signature log
    - Responsibility log
    - Training and credentials of study personnel
- Device information

- Ultravision and diathermy device inventory log including: date, quantity, lot numbers of all devices, identification of all persons the device was used on, and final disposition
- Shipping documents

- Clinical study Plan/Protocol
  - Plan and all amendments
- Institutional Review Boards Records
  - Institutional Review Board Membership List
  - Submission to Institutional Review Boards
  - Approval letters
  - Notification of unanticipated adverse device events
  - updates/reports
  - Any other communication
- Screening and enrollment form
- Consent Form
  - Institutional Review Boards approved copy
  - Revised approved, consent forms
- Case Report Forms (CRFs)
  - Annotated CRF and/or CRF instructions (if applicable)
  - Blank CRFs and completion instructions (if applicable)
- Correspondence
  - All correspondence of material concern relating to the trial between the investigator and other parties (e.g. IRB).

The following records must be maintained for each subject enrolled in the trial:

- Signed Consent Form
- Completed CRFs
- Protocol Deviation Forms

- Complete medical records, including procedure reports, lab reports, professional notes, etc. for participating subjects.
- Records pertaining to subject death during the investigation (including death records, death certificate, and autopsy report, if performed)

30.2. INVESTIGATOR REPORTS

Traditional Investigator Reports such as progress reports are not applicable due to the acute nature of the investigation. The investigator shall be required to complete a summary report to Alesi Surgical, Ltd capturing their general observations.

30.3. RECORD RETENTION

Subject records, correspondence files, all supporting documentation, and reports must remain on file at the investigational site for a minimum of three years or in line with the Mercy's document retention policy (if longer) after the completion/termination of this or when it is no longer needed to support a marketing application, whichever is later.

31. RISK/BENEFIT ASSESSMENT

Medical treatment provided to the patient is within the standard of care for this type of procedure. Additional assessments for procedure data, end tidal CO_2 measures, post procedure pain assessments, pain medication, cosmesis result, and adverse event information do not introduce new risks to the patient. If necessary, the investigator will increase the pressure required to achieve adequate visualization/working space.

As surgical accessory devices, the Ultravision does not administer any medical treatment. The risks associated with its use are consistent with other surgical accessories used in laparoscopic surgery. The Ultravision™ System is required to undergo testing for sterility, biocompatibility, and electrical safety in order to demonstrate that such risks have been mitigated to acceptable levels. The benefits that are being evaluated in this study are quality of visualization under low impact laparoscopic conditions with the anticipated improvement in patient outcomes in terms of cosmesis and postoperative pain.

32. RELATED DOCUMENTS

The following documents are related to the proper execution of this protocol. They include the following document types:

A1. Subject Informed Consent
A2. Case Report Forms
A3. Pain Assessments
A4. Instructions for Use Labeling

A5. Recruitment Script

Study Data Collection Schedule

	Study Phase							
Data Collected	**Baseline & Enrollment**	**Pre-operative**	**Procedure**	**Discharge**	**Pain Diary Days 1-7 Post-Operative**	**14 Day ± 3 days Post-Operative Follow-up (clinic visit)**	**4 ± 1 week Telephone Survey**	**Unscheduled visit**
Informed Consent	X							
Inclusion/Exclusion Criteria	X							
Medicinal Allergies or Intolerance	X							
Prior /Existing Medical Conditions	X							
Prior/Existing Medical Interventions	X							
Diagnosis (Indicating Surgical Intervention)	X							
Current Drug Therapies and Reason	X	X						
Vital Signs	X	X						
Physical Exam	X							
Additional Diagnostic Testing – Prescribed by Investigator	X	X						X***
Pregnancy Test	X	X						
Procedure Data			X					
User Assessments			X					
Adverse Events		X*	X	X		X		X
Pain Medications		X		X**	X	X		X
Pain Assessment		X		X	X	X		X
Cosmesis Outcome							X	

*Compared to baseline assessment (new adverse medical events that occurred since baseline assessment was conducted)

Denotes pain medication prescription given at discharge* Additional evaluations will be completed at the discretion of the Principal Investigator based on the subject's presenting complaint.