A Comparative Study of CO_2 Exchange Patterns between Valve-free Trocar (AirSeal®) versus Standard Trocar (Endopath®) during Robotic Prostatectomies

Principal Investigator: Ronney Abaza, MD, FACS
OhioHealth Robotic Urologic Surgeon
Director of Robotic Surgery

Study Institution: OhioHealth Dublin Methodist Hospital
Medical Office Building
7450 Hospital Drive, Suite #300
Dublin, OH 43016

Grant Funded by: CONMED Corporation

NCT02114164

TABLE OF CONTENTS

1.0 – INTRODUCTION

1.1 – Background

Technological improvements are ongoing in minimally invasive surgery. Laparoscopic surgery has allowed for enhanced patient comfort and recovery in numerous procedures including cholecystectomies, gastric bypasses, and laparoscopic renal procedures. Laparoscopic surgeries must insufflate the abdomen in order to perform the necessary procedures of the surgery. In order to maintain space and vision, CO_2 must be used to inflate the abdomen with trocars being used as the entry points to the abdomen. These trocars are then connected to insufflation systems to increase intra-abdominal volume. Many different trocars have been used to accomplish this task.

Standard trocars (e.g. Endopath® Xcel® Bladeless System) are currently used for robotic prostatectomies at Dublin Methodist Hospital. The Xcel® trocars have been developed to reduce trauma to tissue during laparoscopic procedures due to their bladeless design, which allows for direct visualization of tissue layers during insertion and requires little force to penetrate the skin, providing for controlled access.[1, 2] The Xcel® Bladeless System presents a proprietary cannula ribbing with angled teeth that provides for more abdominal wall retention and reduces trocar slip-out.[3] It has been designed to reduce instrument drag force for quick and easy, one-handed exchange and is suited for various instrument sizes.[3] It also allows for extraction of larger specimens through its removable outer seal and reduces smudging when compared to older trocars.[3] However, the Endopath® Xcel® trocar has a standard "trap door" valve system that causes fluctuations in the intra-abdominal pressure during surgery. This occurs because any external pressure applied on the peritoneal cavity from the surgeon or due to contraction of abdominal muscles leads to a spike in intra-abdominal pressure. The valve on the port prevents the pneumoperitoneum from venting to keep pressures down. These pressure spikes may have physiologic implications for ventilation and carbon dioxide metabolism as well as potentially causing pain due to greater peritoneal "stretch."

A new class of valve-less trocars (i.e. the AirSeal® System) is seeking to replace the standard "trap door" valve and silicone valve trocars with a curtain of forced CO_2 gas that is collected, filtered, and then pumped back into the peritoneum to maintain the pressure differential.[4] The AirSeal® System consists of an insufflation, filtration, and recirculation system (AirSeal® iFS), a triple lumen filtered tube set, and a valve free trocar (AirSeal® Access Port). The device enables peritoneal access with a novel mechanism to maintain pneumoperitoneum without a mechanical seal. Specifically, the AirSeal® System creates a pressure barrier within the proximal housing of the cannula which acts as an invisible seal to maintain pneumoperitoneum during the course of surgery. It utilizes a re-circulation and filtration control unit (AirSeal® iFS) designed specifically for the AirSeal® Access Port to create and maintain the pressure barrier. The AirSeal® iFS is reusable and the AirSeal® Access Port and triple lumen filtered tube set are designed as single patient use devices. The AirSeal® System has applications in minimally invasive abdominal surgical procedures to establish a path of entry for laparoscopic instruments. The lack of a physical valve allows the AirSeal® port to vent immediately in the event of any pressure spikes as the port has a constant opening where the pneumoperitoneal gas may escape to keep pressures down. The implications of this benefit on patient outcomes is not yet fully characterized.

1.2 – Specific Aims/Rationale

Since its FDA clearance, the AirSeal® system has been used routinely in centers throughout the United States, including OhioHealth Dublin Methodist Hospital. The AirSeal® system has been observed by surgeons and anesthesia teams to provide a more gentle, stable, and consistent pneumoperitoneum.[5]

In studies observing valve-less trocar use, patients had blunted end-tidal CO_2 levels and CO_2 absorption rates (see Table 1 for definitions) compared with those found in transperitoneal laparoscopies using the conventional trocar.[6,7] The valve-less trocar has also been shown to eliminate stagnant surgical smoke as well as decrease operative time and CO_2 consumed.[6,7] A prospective analysis of these values in a head-to-head comparison between valve-less and conventional trocars is desired.

The primary observation to be made is the level of $PaCO_2$ in the arterial blood, specifically when the patient is insufflated and deflated during the surgery. As a result of the consistent pressure that the AirSeal® system maintains, CO_2 will be absorbed in lower levels when compared to the standard of care systems in which fluctuations in intra-peritoneum pressure are seen. Therefore, higher pressures will result in higher levels of CO_2 exchange in the blood, leading to increased vasodilation and lower pH levels.[8] Given the potential benefit of using valve-less trocars during robotic prostatectomies as demonstrated in other laparoscopic abdominal procedures, the aims of this study are:

Aim #1) Describe the perioperative CO_2 absorption rates between the conventional and valve-less trocar groups via the end-tidal CO_2 and $PaCO_2$, at baseline, 60 minutes intraoperatively, and immediately following surgery. Optimal intraoperative levels for $PaCO_2$ and end tidal CO_2 should be between 33-37 mmHg. These values are expected to slowly rise throughout surgery due to CO_2 absorption. The anesthesiologist will make specific adjustments and alter ventilation settings throughout the surgery to prevent the values from elevating further once they reach 37-38 mmHg. Between 33-36 mmHg, no adjustments are made. Therefore, we will also examine the valve and valve-less trocar groups on their ability to maintain acceptable arterial blood gas (ABG) levels by comparing the number of interventions required by the anesthesiologist during the procedure between groups.

Aim #2) Compare the maximum intraoperative pneumoperitoneal pressure (mmHg), smoke evacuation quality (categorical), and overall operative times (minutes) between the conventional and valve-less trocar groups.

Aim #3) Compare pain scores through discharge from the preoperative and post-anesthesia care units (PACU) by monitoring self-reported pain ratings using an 11-point numerical rating scale (NRS-11) and pain medication usage via morphine equivalent dose (MED) units.

Table 1. *Definitions of key variables.*

Variable	Definition	Unit
CO_2 absorption rate	Not directly measurable. We are using end tidal CO_2 and $PaCO_2$ to indirectly measure the absorption rate.	N/A
Arterial Blood Gases (ABGs)	Measurement of the pH level and the bicarbonate, oxygen, and carbon dioxide concentrations in arterial blood (HCO_3, PaCO2 & PaO_2); important in diagnosis of	N/A

	many respiratory diseases.	
HCO_3	Amount of bicarbonate in the arterial blood. This is used to aid in diagnosis of metabolic acidosis or alkalosis.	mmol/L
PaO_2	Partial pressure of oxygen in the arterial blood. This is the true measure of O_2 build in the blood.	mmHg
$PaCO_2$	Partial pressure of carbon dioxide in the arterial blood. This is the true measure of CO_2 build up in the blood, and reflects whether the lungs are keeping up in expelling the extra CO_2 from abdominal absorption.	mmHg
End tidal CO_2	The level of carbon dioxide in the air exhaled from the body, as measured by the ventilator. Essentially, this reflects the amount of CO_2 that the lungs are expelling due to CO_2 absorption from the insufflations. This increases over the course of the procedure.	mmHg
"Blunted" end tidal CO_2	A technical observation made regarding the shape of the end tidal CO2 curve on the capnogram displayed on the ventilator. This is an observation, not discretely measureable.	N/A
Tidal volume	The lung volume representing the normal volume of air displaced between normal inspiration and expiration when extra effort is not applied (i.e., normal/resting breathing).	ml
O_2 saturation	Measure of how much oxygen the blood is carrying as a percentage of the maximum it could carry.	%
Pneumoperitoneal pressure	Measurement of air or gas in the abdominal (peritoneal) cavity.	mmHg
Peak inspiratory pressure (PIP)	Point of maximal airway pressure.	mmHg
Positive end-expiratory pressure (PEEP)	Pressure maintained in airways at end of exhalation.	mmHg
Smoke evacuation quality	Smoke evacuation occurs during surgical procedures where there is tissue ablation. Smoke evacuation systems capture the plume (smoke comprised of carbonized cell fragments, water vapor, and hydrocarbons) from vaporized tissue near its origin before it becomes air-dispersed and deposits in the respiratory tracts of the surgical team.	Categorical *(see Appendix B)*

2.0 – METHODS

2.1 – Study Population

Adult male patients ≥ 18 years of age with prostate cancer who are eligible and electing to undergo robotic prostatectomy surgery at OhioHealth Dublin Methodist Hospital between March 1, 2016 and February 28 2017 (12 months). Exclusion criteria to robotic surgery include:

1) Cirrhosis or liver failure (Child-Pugh class A, B, or C) or clinical suspicion of liver failure
2) Ascites
3) Uncontrolled diabetes [as reported by the pre-anesthesia testing (PAT) physician]

4) Renal insufficiency (serum creatinine level > 3.0 mg/dl)

Exclusion criteria to participation in this study include:

5) Age < 18
6) Emergency surgery
7) Persons not capable of providing informed consent
8) Persons participating in any other research study involving an investigational drug or device or investigational surgical procedure that could interfere with the physiologic parameters being collected (for example, a study evaluating different anesthesia regimens that could confound study results).
9) Non English-speaking

2.2 – Hypothesis

It is hypothesized that the AirSeal® System will allow for lower CO_2 absorption rates than the Xcel® System. Furthermore, lower variance in pneumoperitoneal pressure will allow for less "over-pressure" events and peritoneal stretch, which may reduce postoperative pain. Pain will therefore also be assessed through self-report and post-operative pain medication usage (see Table 4 & Appendix A), and analyzed in comparison between both groups.

The term "over pressure" refers to times when the measured pressure in the peritoneal cavity exceeds the set pressure on the insufflator. In such cases, the standard insufflation systems will stop the flow of CO_2 into the abdomen through the port and will actively vent gas to reduce the pressure back to the set point (usually 10mmHg with a maximum of 20mmHg). This "over pressure" theoretically should not occur with the AirSeal® system because the lack of a valve on the port allows gas to escape immediately when the pressure rises (e.g. abdominal muscle contractions when anesthesia is light) so that the pressure does not exceed the set level. "Peritoneal stretch" refers to stretching of the peritoneum (lining of the abdominal wall) from insufflation of the abdomen. The higher the pressure of the pneumoperitoneum/intra-abdominal pressure, the more stretch there will be of the peritoneum with potentially more postoperative pain.

We intend to analyze the results of a total of 100 patients randomized to either the AirSeal® system or conventional trocars.

2.3 – Study Variables & Outcomes of Interest

The following data points are all routinely collected for patients who choose to undergo robotic prostatectomy, via the OhioHealth electronic medical record, CareConnect. We will collect similar data points for patients electing enrollment in this trial which include the following listed below (Tables 2-4). Data points which are not collected in the standard of care setting are noted below in **bold face type**. Only the study staff will have access to the database created solely for use in this study. Data will be de-identified following study completion, prior to statistical analysis.

Table 2. *Study Variables by Operative Time-point*
(a) Preoperative data [collected at the preoperative office/clinic visit, in the office setting, or in

the pre-anesthesia testing (PAT) office visit]:

1) Medical record number
2) Patient name
3) Patient date of birth
4) Phone number
5) Email address
6) Body mass index (BMI)
7) Weight (lb)
8) Medical history
9) Surgical history (major only)
10) Serum creatinine (most recent prior to surgery) (mg/dl)
11) Hemoglobin (g/dl)
12) Preoperative pain measured by the NRS-11 (Appendix A)

(b) Intraoperative data:

1) Details of the surgical procedure
2) The number, size(s), and locations of ports used (standard protocol vs. deviation from standard protocol)
3) Values obtained from anesthesia report at baseline, 60 minutes after insufflations, and at the end of procedure and mean and standard deviation calculated from continuously recorded values:
   a) End tidal CO_2 (mmHg)
   b) O_2 saturation (%)
   c) Respiratory rate
   d) Blood pressure
   e) Heart rate
   f) Tidal volume (ml)
   g) PIP (peak inspiratory pressure) (mmHg)
   h) PEEP (positive end-expiratory pressure) (mmHg)
4) **CO_2 absorption rate via arterial blood gases (ABGs) at baseline, 60 minutes after insufflations, and at the end of the procedure [$PaCO_2$ (mmHg), HCO_3 (mmol/L) & PaO_2 (mmHg)]**
5) **Number of times the anesthesiologist intervenes to adjust ventilation settings throughout the surgery to prevent the values from elevating further once they reach 37-38 mmHg**
6) Estimated blood loss (EBL, in ml)
7) Core body temperature (after trocar placement, at 30 minutes, at 60 minutes, and at end of procedure; Fahrenheit)
8) Insufflation time (minutes)
9) Insufflation pressure at which the procedure was performed (mmHg), and the total number (#), magnitude(s) (% increase in mmHg), and time(s) (hh:mm) of increased pressure episodes necessary to successfully complete the procedure
10) Procedure time (minutes from initial incision to closure)
11) Pneumoperitoneal pressure ranges (mmHg)

12) Smoke evacuation quality at the end of surgery (1-Below Average; 2-Average Amount; 3-Above Average) (Appendix B)
13) Number of times significant loss of pneumoperitoneum occurs (#), timepoint, and level of pressure adjustment (mmHg)
14) Scope cleanings (#)
15) Malfunctions of the AirSeal® System or control devices (# times)
16) Total amount of gas used during the procedure (liters)

(c) Postoperative data collected in the PACU through discharge:
1) Postoperative pain by the NRS-11 at multiple time points (Appendix A)
2) Postoperative parameters (as recorded by the PACU nurses as standard of care)
a) O_2 saturation (%)
b) Time in PACU (post anesthesia care unit) (hours)
c) Post-operative nausea and vomiting (presence/absence)
d) Vital signs (HR/RR/BP/temp) – *first recorded in PACU setting*
e) Use of post-operative pain medication (ketorolac, Percocet, Tylenol Extra Strength) , recorded as the total daily morphine equivalent dose ("MED", in mg/day)
3) Incidence of wound infection
4) Length of stay (targeting same day or next day discharge; 0 to 2)

(d) Postoperative data collected through postoperative Day 1
1) Postoperative parameters (standard of care)
a) Vital signs (HR/RR/BP/temp) – *first recorded in non-PACU setting*
b) Use of post-operative pain medication (ketorolac, Percocet, Tylenol Extra Strength), recorded as the total daily morphine equivalent dose ("MED", in mg/day)
2) Serum creatinine (mg/dl)
3) Hemoglobin (g/dl)
4) Urine output (ml; 1900-0700 hours postoperatively)
5) Incidence of wound infection

For item (b)2, a deviation from the standard port number/size(s)/locations would be due to body habitus, and will not have an effect the clinical outcomes for the patient. We will collect information on all surgical outcomes that occur until discharge from the PACU. The average amount of time spent in the PACU is roughly 1-2 hours. There will be no extended or long-term follow-up.

For item (b)3, continuous values will be exported into individual patients-specific Excel spreadsheets with the assistance of the CareConnect Systems Analysts. This is due to the fact that there are far too many data points (ET CO2, O2 saturation, RR, BP, HR, TV, PIP, PEEP, every 1 minute for 120 minutes) to be manually extracted and subsequently manually entered into the Data Collection Tool by study staff. The biostatistician will perform individual analyses on these data sets, and calculate means and standard deviations to be entered into the Data Collection Tool.

For item (d)4, we are evaluating for oliguria in the immediate post-operative period (1900-0700 hours). Oliguria is infrequently viewed as a complication of laparoscopic surgery. The rate of urine output in

healthy patients undergoing laparoscopic surgery is measured during the period of CO_2 pneumoperitoneum and for several hours after desufflation. For patients that are discharged prior to the completion of the urine output collection (i.e., prior to 0700 hours postoperatively), they will be instructed to take home their urine collection canister and collection instructions to complete measurements following discharge. The Research Coordinator will them call the patient the following morning for the urine output measurement.

Table 3. *Arterial Blood Gases (ABGs) monitoring schedule by anesthesiologist.*

Timepoint	**Definition**
Baseline	At insertion of the catheter
60 minutes	60 minutes after insufflations
End of the procedure	Immediately at the end of surgery

We will be measuring the trend in arterial blood gases over time (Table 3). Optimal intraoperative levels for $PaCO_2$ and end tidal CO_2 should be between 33-37 mmHg. These values are expected to slowly rise throughout surgery due to CO_2 absorption. The anesthesiologist will make specific adjustments and alter ventilation settings throughout the surgery to prevent the values from elevating further once they reach 37-38 mmHg. Between 33-36 mmHg, no adjustments are made.

Since the anesthesiologist will be adjusting ventilator settings at 37-38 mmHg to typically keep the end tidal CO_2 below 40 mmHg, we expect that there will not be a large amount of difference between standard and valve-less trocars regarding the ABGs. However, the ABGs will change over time, warranting the alteration of ventilator settings by the anesthesiologist. In other words, if the ABGs are same between the two groups but the anesthesiologist had to increase the respiratory rate or tidal volume to keep end tidal CO_2 low more so in the standard group than the valve-less, then we will conclude that the valve-less was better. Essentially, the ABGs are a sort of "control" whereby even if they are not different, it still allows us to know whether or not there was a real physiologic difference occurring, whether or not we saw a difference in the other measures that were adjusted in real time.

Table 4. *Pain monitoring schedule by Pre-op and PACU RNs using NRS-11.*

Timepoint	**Definition**
Baseline	Prior to surgery
Post-operatively	After surgery & after anesthesia completion
30 minutes post-operatively	30 minutes after surgical completion time (+/- 5 minutes)
60 minutes post-operatively	60 minutes after surgical completion time (+/- 5 minutes)
At discharge	Immediately prior to discharge from the PACU

Postoperative (post-anesthesia) pain will be evaluated at baseline, post operatively, once every thirty minutes for the first hour and every 8 hours until discharge (Table 4). Floor nurses (preoperative and PACU) will record pain scores reported by patients during structured interviews using an 11-point numerical rating scale (NRS-11), in which a rating of 0 corresponds to no pain, ratings of 1–3 indicate mild pain, 4-6 indicate moderate pain, and ratings of 7-10 correspond to severe pain (Appendix A).

Data will be collected using the forms in the Appendix. Data will be collected by a member of the research team (clinic nurse or clinical research coordinator). All data will be coded by subject number and de-identified. The designated clinical research coordinator will hold the key to subject codes in a locked cabinet and password-protected electronic file. Case reports formed with the coded key will be available only to the study staff.

Identifying information of participants will not be given to anyone not associated with the study unless explicit permission is obtained from a subject in writing. It will only be given as the law requires. The Office for Human Research Protections, Department of Health and Human Services, FDA, the IRB, and the study monitors may check records that identify subjects in order to verify data and monitor adherence to the study protocol. This might include medical records, case reports, the executed ICF, and other source documents. The key will not be made available to the study sponsor unless there is an adverse event (AE) or serious adverse event (SAE) related specifically to the study device warranting report to the FDA (MedWatch). The IRB will be notified under such circumstances.

The documents will be retained in a secure manner by the site principal investigator on password-protected files, media, and work-stations in secure office locations for a total of six years following the end of the study in accordance with institutional, state, FDA, and DHHS requirements, after which they will be destroyed.

2.4 – Study Design

This is a single-center, prospective, single-blind study. Subjects enrolled will be randomized to have their procedure performed using either the AirSeal® System or a conventional insufflator and trocar, all of which have been approved for use by the FDA's 510(k) process. The AirSeal® System is available at the Dublin Methodist Hospital. Following surgery, AirSeal® Access Port and filtered tube set will be discarded per standard institutional practice and policy.

Once a patient is identified as eligible via pre-screening, a member of the research study team will approach the patient for invitation into the study. Only research team members who are knowledgeable about the device and the procedures involved in the study will engage in a consent discussion with potential subjects. All research team members who will obtain consent from study subjects will be educated on the consent process and details of the research study.

Recruitment will occur either at the preoperative office/clinic visit, in the office setting, or in the pre-anesthesia testing office visit (PAT). The study will be explained to the potential subject with ample opportunity to ask questions and consider participation. Recruitment will occur prior to administration of any narcotic or sedative medications. Each potential subject will provide written informed consent prior to any research-related procedure, recording/documenting, or activity occurring. An individual's consent to participate will be documented on the IRB-approved informed consent form. The original executed consent form will be retained in the Principal Investigator's study files; a copy will be given to the subject to retain. The original copy will be will be kept in a locked cabinet along with all study documents that contain private subject information.

Following informed consent, patients will be randomized and prepared for surgery per standard institutional policy and practice. Prior to the start of the study, the study site will set up a computer based randomization system that will randomize subjects into either one of the two groups. Based on the randomization sequence, either the AirSeal® System or a conventional insufflator and trocar will be inserted per the surgeon's normal operative procedures and care (i.e., Endopath® port with standard insufflation). A total of one AirSeal® Access Port will be used on any one subject. For every control subject, one 5mm or larger port used will be designated and recorded as the "study" port. Dr. Abaza will be the only surgeon performing these procedures, eliminating variation in technique between surgeons. The AirSeal® port is 5mm in size and the standard insufflation port is 12mm in size, so the study population will not be subjected to larger port sizes than they would if off-study

Standard operative procedures will be followed regardless of randomization sequence or participation in the study (e.g., standard of care procedures). If a technical malfunction of the AirSeal® iFS or AirSeal® Access Port were to occur, the surgeon would replace both with a conventional insufflator and trocar. Documentation of the AirSeal® malfunction will be made and the subject will be followed for safety purposes, but no further study data will be recorded. All ports will be placed according to standard care. All clinical decisions will be made per standard practice and policy. One trocar per patient will be randomized between the Endopath and AirSeal® trocars. The other trocars used for the procedure will be standard (5 standard plus 1 randomized for a total of 6) and will not vary for patients on the study as compared with typical robotic prostatectomy patients.

A standardized anesthesia regimen will be followed in order to create a uniform population. The anesthesia regimen is typical for this type of surgery. Subjects will be given midazolam (2.0 mg) for pre-induction. Fentanyl (up to 1.5 mcg/kg), propofol (up to 2.0 mg/kg) and rocuronium (as needed for neuromuscular blockade) will be used for anesthesia. Anesthesia will be maintained with sevoflurane and/or deflurane and oxygen. Fentanyl (2-3 mcg/kg/hr or 0.7 mcg/kg boluses) will also be used for anesthesia maintenance. A dose of ondansetron (4 mg) will be given for nausea and vomiting prophylaxis and a dose of ketorolac (15-30 mg) will be given for pain prophylaxis. Glycopyrrolate and neostigmine will be used for anesthesia reversal. Postoperatively, ketorolac, oral Percocet, and/or Tylenol Extra Strength (ES) will be given as needed to treat pain. Ondansetron will also be given as needed for nausea control.

Along with standard anesthesia regimen, the anesthesiologist during the case will take arterial blood gases (ABGs). An arterial line will be placed since the subject is in the prone position to keep close surveillance on perfusion pressure. An arterial line is not placed in all robotic prostatectomy patients and is used in those who require more careful and continuous blood pressure monitoring. For the study, all patients who consent to participate will have an arterial line. An arterial line is a very small catheter similar to an IV catheter used in all surgical procedures but placed in an artery instead of a vein. It will be placed by anesthesia (not nursing). The risks are similar to an IV, such as bruising/bleeding/hematoma at the site of insertion. The arterial line will be removed at the end of the operation per routine practice unless required for postoperative blood pressure monitoring in PACU. The arterial line kit cost will be accounted for in the study budget. If in the opinion of the anesthesiologist an arterial line is not feasible, a 20 gauge needle catheter will be placed in the radial artery post-induction for samples to be taken intermittently during the surgery.

Samples will be taken at baseline beginning at insertion of the catheter, 60 minutes after insufflations, and at the end of the procedure. ABGs will be analyzed for $PaCO_2$, HCO_3, PaO_2 and pH. Study staff will document all values that are produced from ABGs. Data points (such as PIP, PEEP, end-tidal CO_2 etc.) from the anesthesia machine will be automatically uploaded into CareConnect. Subjects will undergo their surgical procedure regardless of participation in this study. The AirSeal® System is commercially available and in clinical use. There are no additional direct costs to participants in this study. The principal risk specifically associated with participation in this study is potential loss of confidentiality. Participants in this study are not exposed to any additional or different risks associated with the surgery. If randomized to the AirSeal® System, potential benefits to participation in the study include decreased need for port removal for removal of foreign bodies and native tissues, placement of prosthetics, and scope de-fogging and smoke evacuation.

As stated earlier, if a technical malfunction of the AirSeal® iFS or AirSeal® Access Port were to occur, the surgeon will replace both with a conventional insufflator and trocar. This is the same procedure that would take place should a technical malfunction occur with conventional insufflator and trocar. If the surgeon decides that the operation is not feasible with a standard insufflator and trocar (loss of insufflation/inconstant pressure with bleeding or anesthesia problems), then the surgeon can replace the standard insufflators with the AirSeal® iFS or AirSeal® Access Port. These events will be documented should they occur.

Patients will undergo standard insufflation (filling of the peritoneal cavity with CO_2 gas). After trocar placement, initial insufflation will be performed to 6mmHg in all patients. All procedures will be performed as per standard technique. If required, insufflation pressures will be increased up to 15mmHg per standard surgeon protocol. Increased insufflation pressure will be maintained either transiently (≤5 minutes to control bleeding or to improve access/visualization) or for the duration of the procedure as per surgeon need. The amount of time at each insufflation pressure will be measured. Procedures in which <5% of the case are performed above 8mmHg will be considered “low impact” procedures. We will compare CO_2 absorption rates between high pressure (>8mmHg) and low impact (≤8mmHg) procedures in the final analysis.

Study subjects will also be removed from the study if they revoke their informed consent. If, in the opinion of the surgeon/investigator, clinical observations made during the study suggest it may be unwise to continue, the surgeon/investigator may stop the study. In the event that the investigator chooses to discontinue or terminate the study, appropriate notification will be given to the IRB and sponsor.

The principal investigator also has the right to remove any subject from the study. Reasons for which a subject may be removed from the study include:

- Occurrence of a serious or intolerable adverse event
- The subject requests to be discontinued from the study
- Non-compliance with medication, protocol violation or unreliable behavior
- A protocol violation sufficiently serious as to require subject withdrawal
- Emergence of a clinically significant change in a laboratory parameter(s)

- General or specific changes in the subject's condition that render further treatment unreasonable or unsafe within the standards of clinical practice in the judgment of the Principal Investigator or treating physician

2.5 – Statistical Analysis

We will first compare the demographic and pre-operative clinical characteristics of the conventional and valve-less trocar groups to evaluate randomization fidelity. If any characteristics are found to be statistically significant between the groups, this will be accounted for in the analyses of the primary and secondary outcomes. We will describe all categorical variables as percentages and continuous variables with means and standard deviations.

Aim #1) Describe the perioperative CO_2 absorption rates between the conventional and valve-less trocar groups via the end-tidal CO_2 and $PaCO_2$, at baseline, 60 minutes intraoperatively, and immediately following surgery. We will also examine the valve and valve-less trocar groups on their ability to maintain acceptable ABG levels by comparing the number of interventions required by the anesthesiologist during the procedure between groups.

We will describe the change in CO_2 and $PaCO_2$ levels at 3 intervals: baseline to 60 minutes, 60 minutes to end of surgery, and baseline to end of surgery to examine the trends in both groups. We will compare the conventional and valve-less trocar groups on the number of interventions required by the anesthesiologist to maintain acceptable pressure using Poisson regression. If a significant number of patients required no intervention we will use a zero-inflated model. Statistical significance will be set at $p<.05$. We will also compare CO_2 absorption rates between high pressure (>8mmHg) and low impact (≤8mmHg) procedures.

Aim #2) Compare the maximum pneumoperitoneal pressure (mmHg), smoke evacuation quality (categorical), and overall operative times (minutes) between the conventional and valve-less trocar groups.

We will compare the conventional and valve-less trocar groups on maximum pneumoperitoneal pressure and overall operative time using t-tests or Wilcoxon rank sum tests. We will compare the groups on evacuation quality using a chi-square test. Statistical significance will be set at $p<.05$.

Aim #3) Compare pain scores through discharge from the preoperative and post-anesthesia care units (PACU) by monitoring self-reported pain ratings using an 11-point numerical rating scale (NRS-11) and pain medication usage via morphine equivalent dose (MED) units.

To evaluate our this outcome we will use a linear mixed model with pain score as the dependent variable and treatment group and time as independent variables. Mixed models are often preferred over a two-way ANOVA because they allow for incomplete data from participants and do not require a strictly normal distribution in the dependent variable. We will also examine the difference in MED units between groups using a t-test. Statistical significance will be set at $p<.05$.

3.0 – REFERENCES

1) Kolata RJ, Ransik M, Briggs L, Baum D. Comparison of wounds created by non-bladed trocars and pyramidal tip trocars in the pig. J Laparoendosc Adv Surg Tech. 1999;9:455-461.

2) McCarus SD, et al. Gynecological laparoscopy: improving laparoscopic herniation outcomes without trocar site fascial closure: a multicenter trial. Presented at: American College of Surgeons 90th Annual Clinical Congress; October 10-14, 2004: New Orleans, LA.

3) Ethicon Endo-Surgery. "Endopath Xcel Bladeless." *Xcel Bladeless*. Endopath, 2010. Web. 18 Sept. 2012. <http://www.ethiconendosurgery.com/xcelbladeless>.

4) Vilos GA, Ternamian A, Dempster J, et al., Society of Obstetricians and Gynaecologists of Canada. Laparoscopic entry: a review of techniques, technologies, and complications. *J Obstet Gynaecol Can.* 2007;29:433-465.

5) A new Valve-Less Trocar for Urology Laparoscopy: Initial Evaluation. Journal of Endourology 2009;23: 1535-39.

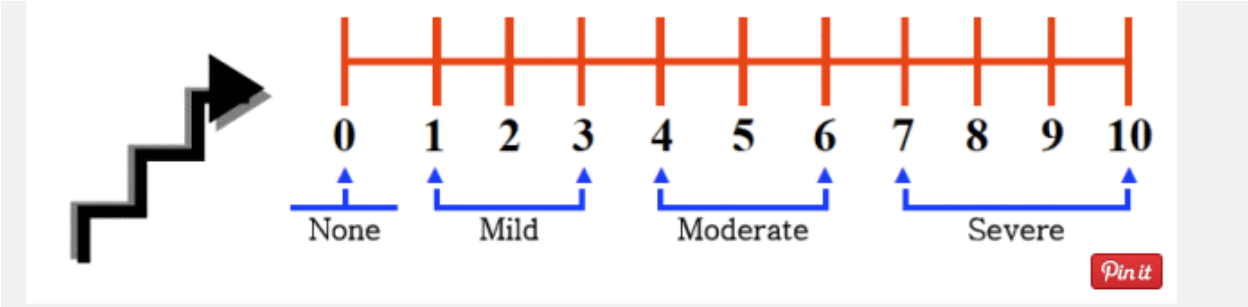
6) Herati et al. Use of the valveless trocar system reduces carbon dioxide absorption during laparoscopy when compared with standard trocars. Urology 2011; 5: 1126-1130.

7) Kadam PG, Marda M, Shah VR. Carbon dioxide absorption during laparoscopic donor nephrectomy: a comparison between retroperitoneal and transperitoneal approaches. *Transplant Proc.* 2008;40:1119-1121.

8) Dodd JW, Getov SV, Jones PW, Cognitive function in COPD. European Respiratory Journal 2010; 35:913-922.

4.0 – APPENDICES

A. Numerical Rating Scale (NRS-11)



Pain monitoring schedule by RN in PACU using NRS-11.	
Timepoint	**Definition**
Baseline	Prior to surgery
Post-operatively	After surgery & after anesthesia completion
30 minutes post-operatively	30 minutes after surgical completion time (+/- 5 minutes)
60 minutes post-operatively	60 minutes after surgical completion time (+/- 5 minutes)
At discharge	Immediately prior to discharge from the PACU

B. Smoke Evacuation Quality Questionnaire

For surgeon completion post-operatively (circle one):

1-Below Average **2-**Average Amount **3-**Above Average

C. Data Collection Forms *(see attached)*