minerva SURGICAL

Endometrial Ablation System

Operator's Manual

L0120 Rev. C

OPERATOR'S MANUAL

TABLE OF CONTENTS

CAUTION: FEDERAL (USA) LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN TRAINED IN THE USE OF THE MINERVA SYSTEM.

READ ALL INSTRUCTIONS, CAUTIONS AND WARNINGS PRIOR TO USE.

FAILURE TO FOLLOW ANY INSTRUCTIONS OR TO HEED ANY WARNINGS OR PRECAUTIONS COULD RESULT IN SERIOUS PATIENT INJURY.

THE MINERVA DISPOSABLE HANDPIECE MUST BE USED ONLY IN CONJUNCTION WITH THE MINERVA RF CONTROLLER AND THE MINERVA RF CONTROLLER MUST BE USED ONLY IN CONJUNCTION WITH THE MINERVA DISPOSABLE HANDPIECE.

THE MINERVA DISPOSABLE HANDPIECE IS NOT MADE FROM NATURAL RUBBER LATEX.

1.0 PHYSICIAN CHECKLIST

The Physician must:

- Have sufficient and adequate experience in performing procedures in the uterine cavity, such as IUD insertion or dilation and curettage (D&C) and hysteroscopy.
- Review and be familiar with the Instructions for Use (IFU).
- Be aware of the appropriate sequence of actions detailed in this Operator's Manual and the troubleshooting section in the event the system detects a high CO_2 flow rate during the Uterine Integrity Test, which may be indicative of a uterine perforation.
- Review the patient selection criteria for the Minerva clinical trials to determine which patients are appropriate for the Minerva procedure.

Adjunct personnel must be familiar with this Operator's Manual and other educational materials prior to using the Minerva Endometrial Ablation System.

2.0 SYSTEM DESCRIPTION

The Minerva Endometrial Ablation System is designed to treat abnormal uterine bleeding due to benign causes in pre-menopausal women for whom childbearing is complete. The System features a Minerva Disposable Handpiece which is positioned trans-cervically in the uterine cavity and connected to the Minerva RF Controller to deliver RF energy to ablate the endometrial lining of the uterus.

The Minerva Endometrial Ablation System is to be used by gynecologists with experience in performing blind intra-uterine manipulations and procedures.

The Minerva Endometrial Ablation System is a bipolar RF system that uses high voltage radio frequency (RF) electrical current at a frequency of 480 kHz to ionize argon gas that is fully contained and circulated within a sealed silicone membrane of the Plasma Formation Array (PFA). This stretchable silicone membrane is deployed in the uterine cavity. When the system is energized, the argon gas is ionized, turning it into plasma. It is this argon plasma that heats the interior surface of the silicone membrane. This energy, in the form of heat, is conducted through the silicone membrane to the tissue in contact with the membrane.

The combination of the heat conducted through the membrane wall from the plasma to the adjacent endometrial tissue, retained heated intra-cavitary moisture that fills gaps outside the array and a small amount of bipolar RF current travelling through the target tissue (and resultant heat), results in the ablation of endometrial tissue.

The Minerva Endometrial Ablation System consists of the Minerva Disposable Handpiece (with Desiccant), the Minerva RF Controller (with Footswitch and Power Cord), an argon (Ar) canister and a carbon dioxide (CO_2) canister. **Figure 1** shows the Minerva Disposable Handpiece and Minerva RF Controller.

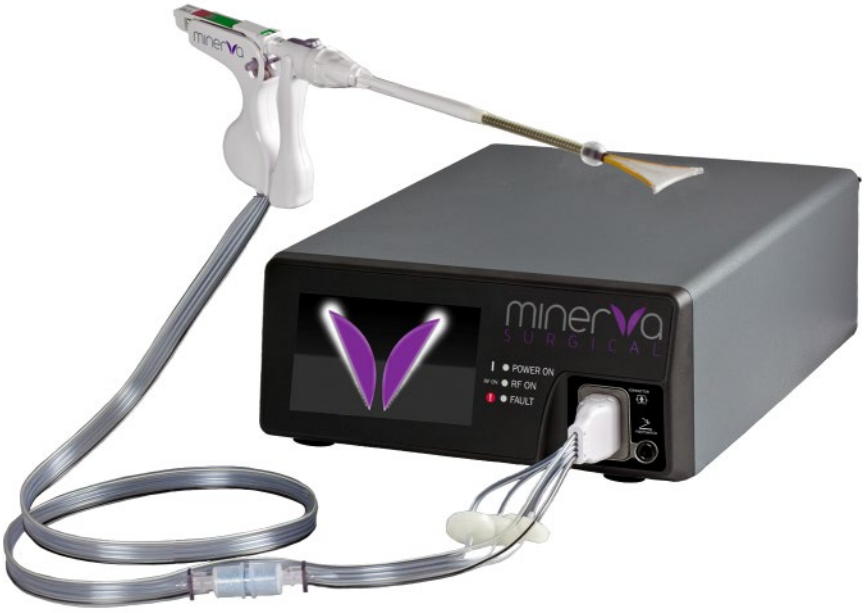


Figure 1: Minerva Disposable Handpiece and RF Controller

2.1 **Minerva Disposable Handpiece**

The Minerva Disposable Handpiece (**Figure 2**) is a single-patient, single-use component of the Minerva Endometrial Ablation System.

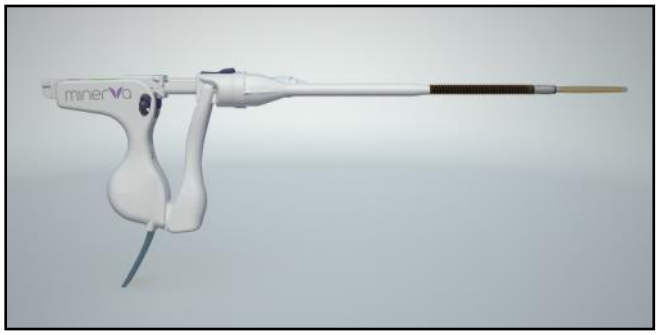


Figure 2: Minerva Disposable Handpiece

The Minerva Disposable Handpiece consists of the following:

- Plasma Formation Array (PFA): The PFA consists of an expandable metal frame, covered by a stretchable silicone membrane. The PFA is opened by a deployment mechanism using the handle, and the expanded frame acts as the internal electrode inside the membrane. A single tissue contacting electrode resides on the outer surface of the membrane. The final expanded triangular shaped PFA is intended to conform to the patient's uterine cavity (**Figure 3**). Argon gas inside the membrane is ionized by the RF energy delivered by the internal electrode. The RF current path extends through the internal electrode and is capacitively coupled through the membrane and uterine tissue to the single external electrode on the membrane surface. The heat generated from the ionized argon plasma allows for the controlled transfer of energy to the uterus for the purpose of endometrial tissue ablation. Intra-

cavitary moisture is not removed during the energy delivery process. Argon gas is fully contained within the Minerva Disposable Handpiece silicone membrane and is not released into the uterine cavity during the ablation procedure.

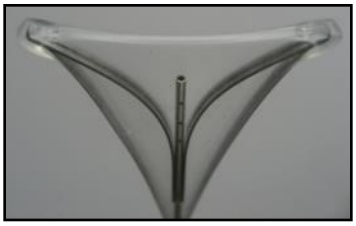


Figure 3: Plasma Formation Array (PFA)

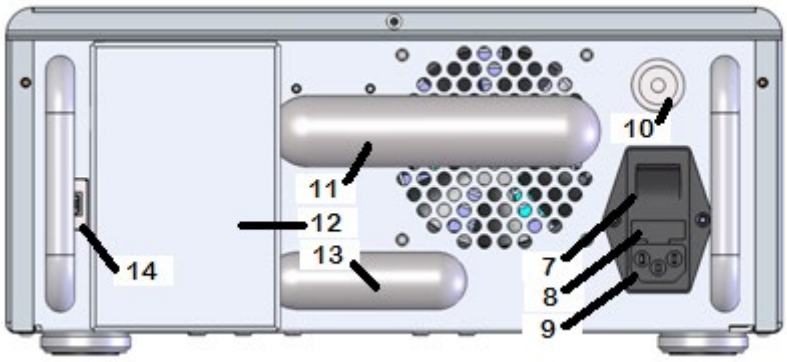
- Cervical Sheath: The Cervical Sheath contains the argon and CO_2 gas inflow/outflow circuits, electrical connections, insulation and mechanical connection between the PFA and the handle.
- Cervical Sealing Balloon: The Cervical Sealing Balloon is mounted on the outside of the Cervical Sheath and moves with the sheath when setting the PFA length sheath lock. When the sheath is locked to the calculated PFA length, the Cervical Sealing Balloon is positioned at the internal os to seal the uterine cavity for the Uterine Integrity Test (UIT) and to insulate the endocervical canal from possible thermal damage during the ablation cycle.
- Array Opening Indicator: This Red/Green Indicator is a mechanism which displays the progression of the PFA deployment/opening and does not indicate a dimension of the uterus.
- Handle: The handle assembly enables the deployment of the PFA. Additionally, the handle serves to electrically and pneumatically connect power and gas from the RF Controller to the PFA.
- Connecting Cord: The connecting cord consists of lumens for gas transfer and electrical power from the Minerva RF Controller to the Minerva Disposable Handpiece, as well as a proprietary connector. It also includes gas filters and a desiccant to prevent moisture from entering the RF Controller.

2.2 Minerva RF Controller

The Minerva RF Controller (**Figure 4** and **Figure 5**) is a controlled radio frequency (RF) power generator. The power provided to the Minerva Disposable Handpiece by the Minerva RF Controller is varied according to electro-physical changes in impedance characteristics of the uterine cavity during the ablation process. The system emits a maximum effective RF power of 40W at 480 kHz to perform its intended function. The Minerva RF Controller also controls the delivery of argon gas to the Minerva Disposable Handpiece. In addition, the Minerva RF Controller has a uterine integrity test (UIT) feature designed to assess possible defects of the uterus or the PFA using the introduction of CO_2 gas. The Minerva RF Controller includes a touch screen display and a footswitch. The Minerva RF Controller incorporates connections for the argon and CO_2 gas canisters on the back of the unit. The USB connection on the back of the unit is for use only by Minerva Surgical personnel. Handles located on the back of the unit facilitate transportation of the Minerva RF Controller.

1. Power On LED
2. RF On LED
3. FAULT LED
4. Footswitch Receptacle
5. Touch Screen Display
6. Disposable Handpiece Receptacle

Figure 4: Minerva RF Controller Front Panel



7. ON/OFF Switch
8. Fuse Drawer
9. Power Receptacle
10. Equipotential Ground Lug
11. Argon Canister
12. Argon and CO_2 Regulators
13. CO_2 Canister
14. USB Connector

Figure 5: Minerva RF Controller Back Panel

2.3 Desiccant

The Minerva desiccant is a non-sterile, single-patient use component that the user attaches in-line with the argon return line, prior to connecting the Minerva Disposable Handpiece to the Minerva RF Controller.

2.4 **CO_2 Canister**

The Minerva CO_2 canister is a 24-gram, CO_2 canister. It is attached to the regulator located on the back panel of the Minerva RF Controller.

2.5 **Argon (Ar) Canister**

The Minerva argon canister is a 25-gram, argon canister. It is attached to the regulator located on the back panel of the Minerva RF Controller prior to applying line voltage to the Minerva RF Controller (turning on the On/Off switch).

2.6 **Footswitch**

The Minerva Footswitch is a pneumatic switch that connects to the Minerva RF Controller front panel. It is used to activate the Minerva RF Controller and does not contain any electrical components.

2.7 **Power Cord**

The Minerva AC power cord, a medical grade cord, connects the Minerva RF Controller to the appropriate line voltage/power outlet. The receptacle for the power cord, the power input module, is located on the back panel of the Minerva RF Controller.

3.0 PRINCIPLES OF OPERATION

The Minerva Endometrial Ablation System is a bipolar RF system that uses high voltage radio frequency (RF) electrical current at a frequency of 480 kHz to ionize argon gas that is fully contained and circulated within a sealed silicone membrane. This stretchable silicone membrane of the Plasma Forming Array (PFA) is deployed in the uterine cavity. When the system is energized, the argon gas is ionized, forming plasma. It is this argon plasma that heats the interior surface of the silicone membrane. This energy, in the form of heat, is conducted through the silicone membrane and to the tissue in contact with the membrane. The combination of the heat conducted through the membrane wall from the plasma to the adjacent endometrial tissue, the retained heated intra-cavitary moisture that fills gaps around the surface of the array, and a small amount of bipolar RF current travelling through the target tissue (and resultant heat), results in the ablation of endometrial tissue.

The Minerva Disposable Handpiece is connected to the Minerva RF Controller, then inserted and positioned at the fundus of the uterine cavity. The handle of the Minerva Disposable Handpiece is actuated to expand the PFA. The Cervical Sealing Balloon is inflated to facilitate sealing of the endocervical canal. The UIT is performed to help assess the uterine cavity for possible uterine and Array defects. Upon successful completion of the UIT, the ablation cycle is initiated and plasma energy is delivered. After the ablation cycle is complete, the handle is unlocked to close the PFA, and the Cervical Sealing Balloon is deflated prior to removing the Minerva Disposable Handpiece from the uterus.

The Minerva RF Controller should be placed in proximity to the user and away from the sterile field. The Minerva RF Controller should be placed on a cart, to the left or right side of the user (the operator actuating the Minerva RF Controller is expected to be approximately within 1 meter of the Minerva RF Controller touch screen display). The Minerva RF Controller front panel should be facing the user, such that there is an unobstructed view of the touch screen. The footswitch should be connected to the connector on the Minerva RF Controller front panel and placed on the floor within easy reach of the user.

4.0 INDICATIONS FOR USE

The Minerva Endometrial Ablation System is intended to ablate the endometrial lining of the uterus in pre-menopausal women with menorrhagia (excessive bleeding) due to benign causes for whom childbearing is complete.

5.0 CONTRAINDICATIONS

The Minerva Endometrial Ablation System is contraindicated for use in:

- a patient who is pregnant or who wants to become pregnant in the future.
  PREGNANCIES FOLLOWING ABLATION CAN BE DANGEROUS FOR BOTH MOTHER AND FETUS.
- a patient with known or suspected uterine cancer or pre-malignant conditions of the endometrium, such as unresolved adenomatous hyperplasia.
- a patient with any anatomic condition (e.g., history of previous classical cesarean section or transmural myomectomy, including hysteroscopic and/or laparoscopic myomectomy performed immediately prior to the Minerva procedure) or pathologic condition (e.g., requiring long-term medical therapy) that could lead to weakening of the myometrium.
- a patient with a history of endometrial ablation and/or resection (including endometrial ablation/resection performed immediately prior to Minerva procedure) regardless of the modality by which it was performed.
  REPEAT ABLATION MAY RESULT IN SERIOUS PATIENT INJURY.
- a patient with active genital or urinary tract infection at the time of the procedure (e.g., cervicitis, vaginitis, endometritis, salpingitis or cystitis).
- a patient with an intrauterine device (IUD) currently in place and which is not removed prior to the Minerva procedure.
- a patient with a uterine cavity length less than 4 cm. The minimum Plasma Formation Array length is 4 cm. Treatment of a uterine cavity with a length less than 4 cm may result in thermal injury to the endocervical canal.
- a patient with a narrow uterine cavity.
- a patient where the Array Opening Indicator is in the Red Zone following deployment of the Minerva Disposable Handpiece.
- a patient with active pelvic inflammatory disease.
- a patient with undiagnosed vaginal bleeding.

6.0 WARNINGS

READ ALL INSTRUCTIONS CAREFULLY. FAILURE TO PROPERLY FOLLOW THE INSTRUCTIONS, WARNINGS, AND PRECAUTIONS MAY LEAD TO PATIENT OR USER INJURY.

THE MINERVA PROCEDURE IS INTENDED TO BE PERFORMED ONLY ONCE DURING A SINGLE OPERATIVE VISIT. THERMAL OR OTHER INJURIES TO THE BOWEL MAY OCCUR WHEN/IF MULTIPLE THERAPY CYCLES ARE PERFORMED DURING THE SAME OPERATIVE VISIT.

6.1 Uterine Perforation

- Use caution not to perforate the uterine wall when sounding, dilating or inserting the Minerva Disposable Handpiece.
- Activation of the Minerva Disposable Handpiece in the setting of a uterine perforation is likely to result in serious patient injury.
- The risk of uterine perforation is increased in patients with abnormal or obstructed uterine cavities including obstruction by fibroids that distort the uterine cavity.
- It has been reported in the literature that patients with a severely anteverted, retroflexed or laterally displaced uterus are at greater risk of uterine wall perforation during any intrauterine manipulation.
- If the Minerva Disposable Handpiece is difficult to insert into the cervical canal, use clinical judgment to determine whether or not further dilation is required. Forcibly advancing the Minerva Disposable Handpiece against resistance is likely to increase the risk of perforation or creation of a false passage. Sufficient dilation is required for safe insertion.

- To prevent injury to the endocervical canal, ensure the Plasma Formation Array is unlocked before removing the Minerva Disposable Handpiece from the uterus.
- Excessive force applied during placement of the Minerva Disposable Handpiece may result in tissue injury including perforation.
- Use caution during placement of the Minerva Disposable Handpiece in severe uterine angulations to prevent perforation.
- The Minerva System performs an integrity test to evaluate the integrity of the Minerva Disposable Handpiece and indirectly assess the integrity of the uterine cavity (Uterine Integrity Test) and sounds an alarm warning prior to treatment if the test fails. (See advisory note after Step 13.13).
- IF THE UTERINE INTEGRITY TEST FAILS AFTER REASONABLE ATTEMPTS TO IMPLEMENT THE TROUBLESHOOTING PROCEDURES (14.1.2-14.1.4), ABORT THE PROCEDURE.
- ALTHOUGH DESIGNED TO DETECT A PERFORATION OF THE UTERINE WALL, THIS TEST IS AN INDICATOR ONLY AND IT MIGHT NOT DETECT ALL PERFORATIONS. CLINICAL JUDGMENT MUST ALWAYS BE USED.
- IF A UTERINE PERFORATION IS SUSPECTED AND/OR CONFIRMED, THE PROCEDURE SHOULD BE TERMINATED IMMEDIATELY.
- For patients in whom the procedure was aborted due to a suspected uterine wall perforation, a work-up for perforation should be considered prior to discharge.
- **Post-treatment, any patient-reporting signs/symptoms that could indicate a serious complication, e.g., bowel injury, should be thoroughly evaluated without delay.**

6.2 **General Warnings**

- Endometrial ablation using the Minerva System is not a sterilization procedure. Therefore, the patient should be advised of appropriate birth control methods.
- Endometrial ablation is intended for use only in women who do not desire to bear children because the likelihood of pregnancy is significantly decreased following the procedure. Pregnancy following ablation may be dangerous for both mother and fetus.
- Endometrial ablation does not eliminate the potential for endometrial hyperplasia or cancer of the endometrium and may mask the physician’s ability to detect or make a diagnosis of such pathology.
- Patients who undergo endometrial ablation procedures who have previously undergone tubal ligation are at increased risk of developing post ablation tubal sterilization syndrome which can require hysterectomy. This can occur as late as 10 years post procedure.
- The Minerva procedure should not be performed concomitantly with placement of the Essure device.
- The safety and effectiveness of the Minerva System has not been evaluated in patients with the Essure device.

6.3 **Technical Warnings**

- The Minerva Disposable Handpiece is supplied sterile. Do not use the sterile single-patient use Minerva Disposable Handpiece if the packaging appears to be damaged or there is evidence of tampering.
- For single-use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the Minerva Disposable Handpiece and/or lead to failure of the Minerva Disposable Handpiece which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the Handpiece and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the Handpiece may lead to injury, illness or death of the patient.

- The used Minerva Disposable Handpiece must be treated as biohazardous waste and disposed of in accordance with hospital or clinic standard practice where the treatment is performed.
- If any hysteroscopy procedure is performed with hypotonic solution immediately prior to Minerva procedure, then the uterine cavity must be flushed with normal saline prior to treatment with the Minerva System. The presence of hypotonic fluid may reduce the efficiency of the Minerva System.
- Plugging the Minerva Disposable Handpiece into the Minerva RF Controller starts the pre-insertion Handpiece integrity check. CO_2 is delivered to the Minerva Disposable Handpiece to verify patency. THIS TEST TAKES APPROXIMATELY 10 SECONDS TO COMPLETE AND MUST BE PERFORMED WITH THE MINERVA DISPOSABLE HANDPIECE EXTERNAL TO THE PATIENT TO ELIMINATE THE RISK OF AIR OR GAS EMBOLISM AS WELL AS ANY FALSE READINGS. The Minerva RF Controller touch screen will display the progress of the test (Step 12.3.9). After the test image disappears, it is safe to insert the Minerva Disposable Handpiece.
- The Minerva Endometrial Ablation System may interfere with normal functions of some types of implanted pacemakers or implanted cardioverters/defibrillators. The Minerva System should not be used with patients who have pacemakers or other electrical implants. Check if the patient has pacemaker or implanted cardioverter/defibrillator prior to use. Consult the cardio-rhythm device manufacturer for information about the effects of RF energy on these devices.
- Care should be taken to ensure the patient does not contact metal parts which are earthed or which have an appreciable capacitance to earth, such as direct contact with the metal on tables.
- DANGER: EXPLOSION HAZARD. Do not use in the presence of a flammable anesthetic mixture. Do not use in the presence of flammable gases or liquids.
- Failure of the Minerva RF Controller could result in an unintended increase in output power.
- Do not use the Minerva System near or in a magnetic resonance (MR) environment.

6.4 **Cautions**

- A false passage can occur during any procedure in which the uterus is instrumented, especially in cases of a severe anteverted retroflexed or a laterally displaced uterus. Use caution to ensure that the Minerva Disposable Handpiece is properly positioned in the uterine cavity.
- Patients who have undergone endometrial ablation and are later placed on hormone replacement therapy should have a progestin included in their medication regimen in order to avoid the increased risk of endometrial adenocarcinoma associated with unopposed estrogen replacement therapy.
- The safety and effectiveness of the Minerva System has not been fully evaluated in patients:
    - with a uterine sound measurement greater than 10 cm;
    - with submucosal fibroids that distort the uterine cavity;
    - with bicornuate, septate or sub-septate uteri;
    - with medical (e.g., GnRH agonist) or surgical pretreatment; or
    - who have undergone a previous endometrial ablation including the Minerva endometrial ablation procedure.
- The Minerva System consists of the following components:
    - Single-patient use Minerva Disposable Handpiece with connecting cord and desiccant
    - Minerva RF Controller with footswitch and power cord
    - Minerva CO_2 canister
    - Minerva argon canister
- To ensure proper operation, never use other components with the Minerva System. Inspect the components regularly for damage, and do not use them if damage is

apparent. The use of any cables or accessories other than those specified in these instructions may result in increased emissions or decreased immunity of the Minerva RF Controller.

- The Minerva Disposable Handpiece should only be used by physicians trained in the use of the Minerva Disposable Handpiece.
- The Minerva Disposable Handpiece must be used only in conjunction with the Minerva RF Controller. No other handpieces can be used with the Minerva RF Controller.
- Patients must be informed of the risks and possible adverse events associated with the endometrial ablation procedure and use of the Minerva Endometrial Ablation System.
- The user should inspect the Minerva Disposable Handpiece for damage prior to use.
- The Minerva Desiccant is non-sterile, and the packaging should not be placed in the sterile field.
- Do not use the Minerva Desiccant if desiccant material is pink in color.
- The Minerva Disposable Handpiece must be external to (outside of) the patient before plugging the connecting cord into the appropriate port on the front panel of the Minerva RF Controller (Step 12.3.9).
- Do not use the Minerva Endometrial Ablation System in presence of volatile solvents or flammable anesthetics.
- In the event of a Minerva RF Controller failure, disconnect the Minerva Disposable Handpiece, use the ON/OFF Switch, or unplug the power cord to stop Argon and CO_2 flow, and RF energy delivery.
- Do not operate unit in a moist environment, as a shock hazard may exist. If liquids have entered the unit, the Minerva RF Controller must be returned to the manufacturer for testing prior to use.
- Interference produced by the operation of high-frequency equipment, such as the Minerva RF Controller, may adversely affect the operation of other electronic medical equipment such as monitors and imaging systems. If electromagnetic interference with other equipment is suspected, reorient the Minerva Disposable Handpiece or remove possible sources of interference (e.g., cellular phones, radios, etc.) from the room.
- It is recommended that any monitoring equipment or leads be placed as far as possible from the Plasma Formation Array when high frequency surgical equipment and physiological monitoring equipment are used simultaneously on the same patient. Needle monitoring electrodes are not recommended. Monitoring systems incorporating high frequency current-limiting devices are recommended for use.
- Do not use the Minerva Disposable Handpiece if wires are exposed as this increases the risk of an electrical shock or fire.
- Failure of the Minerva Endometrial Ablation System equipment could result in an unintended increase of output power.
- Use of accessories and cables, other than those specified for the Minerva Endometrial Ablation System, may result in increased emissions or decreased immunity of the system.
- Use only the hospital grade power cord and Minerva Footswitch supplied with the Minerva RF Controller.
- Removing screws and opening of the Minerva RF Controller will invalidate the warranty.
- The Minerva RF Controller contains no user serviceable parts. Return to manufacturer for repairs.
- Do not restrict the openings on the Minerva RF Controller enclosure, as they provide the required airflow for cooling.
- The patient should not come into contact with earthed metal parts or parts with appreciable capacitance to earth. The use of antistatic sheeting is recommended.

- Position the Minerva Disposable Handpiece connecting cord such that contact with patient or other electrical leads is avoided.
- Position the Minerva RF Controller on a flat surface for clinical use.
- Care should be taken not to damage the silicone membrane of the Plasma Formation Array during preparation and use.
- Careful measuring of the uterus is important for safe and proper Minerva Disposable Handpiece PFA length setting to prevent thermal injury to the endocervical canal.
- If during the ablation cycle the cervical balloon does not adequately seal the cervical canal, unintended thermal damage to the endocervical canal may occur as a result of hot fluid leaking from the uterine cavity into the canal. Use clinical judgment to continue with the ablation procedure if such a leak is suspected.
- During the ablation cycle, ensure the connection tubing is not kinked or twisted which could reduce the flow of argon gas and reduce the effect of ablation.
- During ablation, do not unlock the Minerva Disposable Handpiece handle or retract or remove the Minerva Disposable Handpiece.
- The Minerva RF Controller is for use without a neutral electrode.
- Use non-flammable agents for cleaning and disinfecting wherever possible.
- Flammable agents used for cleaning, disinfecting, or as solvents of adhesives should be allowed to evaporate before application of RF energy.
- Flammable solutions can pool under the patient or in body depressions such as the umbilicus, and in body cavities such as the vagina. Fluids pooled in the body depressions and cavities should be evacuated before the Minerva RF Controller is used.
- Endogenous gases (e.g., cotton and gauze saturated with oxygen) may be ignited by sparks produced during normal use of the Minerva RF Controller.
- Do not position the Minerva RF Controller such that it is difficult to connect/disconnect the Minerva Disposable Handpiece connector.
- To avoid risk of electric shock, the Minerva RF Controller must only be connected to a mains supply with protective earth.
- Do not modify the Minerva RF Controller without authorization from Minerva Surgical.
- The Minerva RF Controller needs special precautions regarding EMC and needs to be installed and put into service according to the EMC information provided in section 21.0.
- The use of Portable and Mobile RF Communications Equipment can affect the Minerva RF Controller.
- The Minerva RF Controller should not be used adjacent to or stacked with other equipment. If adjacent or stacked use is necessary, the Minerva RF Controller should be observed to verify normal operation in the configuration in which it will be used.
- The power cord connection to the Minerva RF Controller provides a means of isolation. The Minerva RF Controller should be positioned so as to provide easy access to the power cord connection in the event that the unit must be quickly unplugged.

7.0 MINERVA CLINICAL STUDIES

The Minerva Endometrial Ablation System was evaluated in two clinical studies, the Minerva Single-Arm Study and the Minerva Randomized Clinical Trial (RCT).

ADVERSE EVENTS

The Minerva Single-Arm Study was a prospective, multi-center, single-arm, international clinical study of 110 patients with menorrhagia. Adverse events were reported from the time of procedure through the 12-month follow-up study period. Two- and three-year safety was also evaluated by collecting gynecological adverse events in subjects who consented to long-term follow-up.

Additional safety and efficacy information is available from an ongoing RCT, evaluating the Minerva Endometrial Ablation System. The RCT is a prospective, controlled, randomized, multicenter, safety and effectiveness clinical study of 153 subjects (102 Minerva and 51 Rollerball) with menorrhagia. One year follow-up data are currently available. Long-term safety at two and three years is also being assessed by collecting gynecological adverse events.

Table 1 shows the number and percent of patients in each study who reported specific endometrial ablation-related adverse events and symptoms (one or more times) up to 3 years post-procedure (up to 1 year post-procedure in the RCT).

Table 1: Number and Percent of Patients with One or More Related* Adverse Events and Symptoms by Time of Occurrence

Adverse Event/Symptom	Minerva Single-Arm Study	Minerva Randomized Study	
	Minerva (n=110)	Minerva (n=102)	Rollerball (n=51)
Intra-operative Adverse Events and Symptoms			
Skin Rash and/or Itching or Burning Sensation	0 (0.0%)**	1 (1.0%)	0 (0.0%)
Post-operative Adverse Events and Symptoms (Recovery room to < 24 hours) * **			
Pelvic Cramping	64 (58.2%)	51 (50.0%)	23 (45.1%)
Vaginal Discharge and/or Unpleasant Vaginal Smell or Burning or Other Abnormal Sensation	15 (13.6%)	32 (31.4%)	16 (31.4%)
Bleeding or Spotting	8 (7.3%)	39 (38.2%)	15 (29.4%)
Nausea and/or Vomiting	17 (15.5%)	17 (16.7%)	8(15.7%)
Weakness, Fatigue, Sleepiness, Lack of Concentration, Dizziness	6 (5.5%)	5 (4.9%)	1 (2.0%)
Abdominal Pain and/or Bloating	10 (9.1%)	0 (0.0%)	0 (0.0%)
Circulatory Symptoms	4 (3.6%)	5 (4.9%)	3 (5.9%)
Headache	4 (3.6%)	0 (0.0%)	2 (3.9%)
Backache	3 (2.7%)	1 (1.0%)	0 (0.0%)
Fever	0 (0.0%)	1 (1.0%)	0 (0.0%)
Agitation	0 (0.0%)	1 (1.0%)	2 (3.9%)
Vulvar Pruritus	0 (0.0%)	1 (1.0%)	0 (0.0%)
Urinary Disturbance	0 (0.0%)	1 (1.0%)	1 (2.0%)
Post-operative Adverse Events and Symptoms (≥ 24 hours – 2 Weeks) * **			
Pelvic Cramping	12 (10.9%)	0 (0.0%)	0 (0.0%)
Abdominal Pain and/or Bloating	1 (0.9%)	3 (2.9%)	1 (2.0%)
Pelvic Pain	0 (0.0%)	1 (1.0%)	0 (0.0%)
Nausea and/or Vomiting	1 (0.9%)	0 (0.0%)	0 (0.0%)
Vaginal Discharge and/or Unpleasant Vaginal Smell or Burning or Other Abnormal Sensation	0 (0.0%)	1 (1.0%)	0 (0.0%)
Weakness, Fatigue, Sleepiness, Lack of Concentration, Dizziness	0 (0.0%)	1 (1.0%)	1 (2.0%)
Circulatory Symptoms	1 (0.9%)	0 (0.0%)	0 (0.0%)
Constipation	1 (0.9%)	0 (0.0%)	1 (2.0%)
Pelvic Inflammatory Disease	1 (0.9%)	0 (0.0%)	0 (0.0%)
Fever	1 (0.9%)	0 (0.0%)	0 (0.0%)
Endometritis or Endomyometritis	0 (0.0%)	1 (1.0%)	2 (3.9%)
Skin Rash and/or Itching or Burning Sensation	0 (0.0%)	1 (1.0%)	1 (2.0%)
Post-operative Adverse Events and Symptoms(>2 Weeks – 1 Year)			
Pelvic Inflammatory Disease	0 (0.0%)	1 (1.0%)	0 (0.0%)
Hematometra	0 (0.0%)	1 (1.0%)	0 (0.0%)
Dysmenorrhea	0 (0.0%)	0 (0.0%)	1 (2.0%)
Long-Term Follow-up Adverse Events and Symptoms	**(>1 Year – 3 Years) † (n=101)**	**>1 Year**	
Pelvic Cramping	2 (2.0%)	-	

* Possibly, probably, or highly probably related to Device or Procedure

** Percent of patients who reported specific endometrial ablation-related adverse events and symptoms

*** Ten patients in the Single-Arm Study and two patients in the RCT reported the same AE at the < 24 hours and the 24 hours – 2 Weeks visits
† Gynecologic Adverse Events during Long-Term Follow-up (2 and 3 years after the procedure)

Table 2 shows the frequency (number of occurrences) of endometrial ablation-related adverse events and symptoms reported during the 3-year follow-up period (up to 1-year post-procedure in the RCT). As an example, if the same patient reported two episodes of cramping, the table would reflect two occurrences.

Table 2: Number of Occurrences of Related* Adverse Events and Symptoms

Adverse Event/Symptom	Minerva Single-Arm Study	Minerva Randomized Study	
	Minerva (n=110)	Minerva (n=102)	Rollerball (n=51)
Intra-operative Adverse Events and Symptoms			
Skin Rash and/or Itching or Burning Sensation	0	1	0
Post-operative Adverse Events and Symptoms (Recovery room to < 24 hours)			
Pelvic Cramping	64	51	23
Vaginal Discharge and/or Unpleasant Vaginal Smell or Burning or Other Abnormal Sensation	16	32	16
Bleeding or Spotting	8	39	15
Nausea and/or Vomiting	21	19	9
Weakness, Fatigue, Sleepiness, Lack of Concentration, Dizziness	7	5	2
Abdominal Pain and/or Bloating	10	0	0
Circulatory Symptoms	4	5	3
Backache	3	1	0
Headache	4	0	2
Fever	0	1	0
Agitation	0	1	2
Vulvar Pruritus	0	1	0
Urinary Disturbance	0	1	1
Post-operative Adverse Events and Symptoms (≥ 24 hours – 2 Weeks)			
Pelvic Cramping	12	0	0
Abdominal Pain and/or Bloating	1	3	1
Pelvic Pain	0	1	0
Nausea and/or Vomiting	1	0	0
Vaginal Discharge and/or Unpleasant Vaginal Smell or Burning or Other Abnormal Sensation	0	1	0
Weakness, Fatigue, Sleepiness, Lack of Concentration, Dizziness	0	1	1
Circulatory Symptoms	1	0	0
Constipation	1	0	1
Pelvic Inflammatory Disease	1	0	0
Fever	1	0	0
Endometritis or Endomyometritis	0	1	2
Skin Rash and/or Itching or Burning Sensation	0	1	1
Post-operative Adverse Events and Symptoms (>2 Weeks – 1 Year)			
Pelvic Inflammatory Disease	0	1	0
Hematometra	0	1	0
Dysmenorrhea	0	0	1
Long-Term Follow-up Adverse Events and Symptoms	**(>1 Year – 3 Years) † (n=101)**	**>1 Year**	
Pelvic Cramping	2	-	

* Possibly, probably, or highly probably related to Device or Procedure
† Gynecologic Adverse Events during Long-Term Follow-up (2 and 3 years after the procedure)

7.1 Anticipated Post-Procedural Symptoms

For any endometrial ablation procedure, commonly reported postoperative events include the following:

- Postoperative cramping can range from mild to severe. This cramping will typically last a few hours and rarely continues beyond the first day following the procedure.
- When present, nausea and vomiting typically occur immediately following the procedure, are associated with anesthesia and can be managed with medication.
- Vaginal discharge
- Vaginal bleeding/spotting

7.2 Other Adverse Events

As with all endometrial ablation procedures, serious injury or death can occur.
The following adverse events could occur or have been reported in association with the use of other endometrial ablation systems and may occur when the Minerva Endometrial Ablation System is used:

- Post-ablation tubal sterilization syndrome
- Pregnancy-related complications
  NOTE: Pregnancy following endometrial ablation is very dangerous for both the mother and the fetus.
- Thermal injury to adjacent tissue, including bowel, bladder, cervix, vagina, vulva and/or perineum
- Perforation of the uterine wall
- Hemorrhage
- Hematometra
- Difficulty with defecation or micturition
- Uterine necrosis
- Air or gas embolism
- Infection or sepsis
- Complications leading to serious injury or death

8.0 MINERVA CLINICAL STUDIES SUMMARY

The Minerva Endometrial Ablation System was evaluated in two clinical studies, the Minerva Single-Arm Study and the Minerva RCT.

8.1 Minerva Single-Arm Clinical Study

The Minerva Single-Arm Study was a prospective, multi-center, single-arm, international clinical study of 110 patients with menorrhagia. Safety and effectiveness data were obtained for patients treated with the Minerva Endometrial Ablation System during the initial 12 months following the procedure as well as long-term at 2 and 3 years post-procedure.

8.1.1 Purpose

The safety and effectiveness of the Minerva Endometrial Ablation System was evaluated in premenopausal women who had completed childbearing and were suffering from menorrhagia secondary to benign causes.

8.1.2 Study Endpoints

The primary effectiveness measure was a validated menstrual diary scoring system developed by Higham (Higham JM, O'Brien PMS, Shaw RW *Br J Obstet Gynaecol* 1990; 97:734-9). Assessment of menstrual blood loss was performed using a pictorial blood loss assessment chart (PBLAC). Patient success was defined as a reduction in menstrual diary score from $\geq$150 pre-treatment to $\leq$ 75 at 12 months post-procedure.

Study success was based on a comparison between the Minerva Endometrial Ablation System and an Objective Performance Criterion (OPC). The OPC is 66% based on the lower bound of the 95% confidence interval of the average success rate for the five approved global endometrial ablation (GEA) devices.

The primary safety measure was based on the adverse events reported during the study.

Secondary endpoints included amenorrhea, anesthesia regimen, length of procedure (Minerva Disposable Handpiece insertion to Minerva Disposable Handpiece removal) and responses from a patient satisfaction questionnaire.

8.1.3 Methods

A prospective, multi-center, single-arm, international clinical study was conducted at seven clinical sites and included 110 patients diagnosed with menorrhagia. Menstrual diary scores were collected pre-operatively and monthly for 12 months post-procedure. Patients were treated at any time in their menstrual cycle. Patients received no endometrial pretreatment (e.g., hormone, dilation and curettage, or cycle timing).

Study subjects were required to meet the following key patient selection criteria:

Inclusion Criteria:

- Refractory menorrhagia with no definable organic cause
- Female subject from age 25 to 50 years
- Uterine sound measurement of 6.0cm to 10.0cm (external os to internal fundus)
- One of the following criteria:
  - Documented history of menorrhagia secondary to abnormal uterine bleeding (AUB).
  - If a pictorial blood loss assessment chart (PBLAC) scoring systems is used, a minimum PBLAC score of ≥150 for 1 month prior to study enrollment.
- Premenopausal at enrollment as determined by FSH measurement ≤ 40 mIU/ml
- Not pregnant and no desire to be pregnant in the future
- Patient agrees not to use hormonal contraception or any other medical intervention for bleeding during the study
- Able to provide written informed consent using a form that has been approved by the reviewing IRB/EC
- Subject agrees to follow-up exams and data collection, including ability to accurately use menstrual diaries for PBLAC analysis
- Subject demonstrates an understanding on how to use menstrual diaries.

Exclusion Criteria:

- Pregnancy or subject with a desire to conceive
- Endometrial hyperplasia as confirmed by histology
- Presence of active endometritis
- Active pelvic inflammatory disease
- Active sexually transmitted disease (STD), at the time of ablation
  Note: Treatment of STD documented in the chart serves as sufficient evidence of infection resolution. Patient may be considered for study enrollment.
- Presence of bacteremia, sepsis, or other active systemic infection
- Active infection of the genitals, vagina, cervix, uterus or urinary tract at the time of the procedure
- Known/suspected gynecological malignancy within the past 5 years
- Known clotting defects or bleeding disorders

- Untreated/unevaluated cervical dysplasia (except CIN I)
- Known/suspected abdominal/pelvic cancer
- Prior uterine surgery (except low segment cesarean section) that interrupts the integrity of the uterine wall (e.g., myomectomy or classical cesarean section)
- Previous endometrial ablation procedure
- Currently on medications that could thin the myometrial muscle, such as long-term steroid use (except inhaler or nasal therapy for asthma)
- Currently on anticoagulants
- Abnormal or obstructed cavity as confirmed by hysteroscopy or saline infusion sonohysterography (SIS), specifically:
    - Septate or bicornuate uterus or other congenital malformation of the uterine cavity
    - Pedunculated or submucosal myomas distorting the uterine cavity
    - Polyps likely to be the cause of the subject's menorrhagia
    - Intramural or subserosal myomas that distort the uterine cavity
- Presence of an intrauterine device (IUD) which the patient is unwilling to have removed at the time of the operative visit
- Presence of an implantable contraceptive device (e.g., Essure® or Adiana®).
- Subject currently on hormonal birth control therapy or unwilling to use a non-hormonal birth control post-ablation (including a Mirena® device).
- Subject who is within 6-weeks post-partum.
- Any general health condition which, in the opinion of the Investigator, could represent an increased risk for the subject
- Any subject who is currently participating or considers future participation in any other research of an investigational drug or device.

8.1.4 Patient Population

A total of 110 patients were enrolled at seven investigational sites. Patients were between the ages of 25 to 50, with 35.5% under or at the age of 40, and 64.5% 41 years of age or older. There were no statistical differences in demographic or gynecological history parameters among the seven investigational sites that had an effect on the ability to pool the results, as the pooling of the results was justified by the homogeneity of the primary endpoint (PBLAC Success) across sites.

This study was originally designed for 12 months of follow-up. After completion of the 12-month follow-up, the study protocol was amended to add long-term follow-up at 24 and 36 months following the procedure. Of the original 110 patients, re-consent for long-term follow-up was not obtained from 9 patients (all were study successes at the 12-month follow-up) reducing the Intent-to-Treat population to 101 patients for evaluation at 24 and 36 months. In addition, due to the length of time required to obtain regulatory approvals for the amendment for the long-term follow-up, 21 patients were not consented in time for the 24-month follow-up. The Intent-to-Treat population of 101 at 24 months includes: 72 patients who reported an outcome at 24 months, 5 screen failures, 1 aborted procedure, 2 withdrawals and 21 patients who could not be consented prior to the 24-month follow-up. At the 36-month follow-up, the Intent-to-Treat population includes: 93 patients reporting outcomes, 5 screen failures, 1 aborted procedure and 2 withdrawals. **Table 3** describes the accountability of subjects throughout the study period.

Table 3: Subject Accountability

	TOTAL
12-Month Follow-up	
• Enrolled	110
• Failed Inclusion/Exclusion Screen (not treated)	5
• Aborted procedure	1
• Completed Treatments	104
Intent to Treat Population	110
24-Month Follow-up	
• Re-consented in time and eligible for 24-month follow-up	72
• Failures from 12-month follow-up	
○ Failed Inclusion/Exclusion Screening	5
○ Aborted procedure	1
• Withdrew prior to visit for pelvic pain	1
• Withdrew for additional AUB treatment	1
• Not consented in time for 24-month follow-up	21*
24-Month Population	101
Re-consent not obtained	9**
36-Month Follow-up	
• Re-consented in time and eligible for 36-month follow-up	93
• Failures from 12-month follow-up	
○ Failed Inclusion/Exclusion Screening	5
○ Aborted procedure	1
• Withdrew prior to 24-Month visit for pelvic pain	1
• Withdrew at 24-Month visit for additional AUB treatment	1
36-Month Population	101
Re-consent not obtained	9**

* The regulatory bodies approved the amendment for long-term follow-up after the 24-month follow-up window for these 21 patients had closed.
** Re-consent for long-term follow-up was not obtained from 9 patients of the original 110 enrolled. Each of these patients was a study success at the 12-month follow-up.

Demographics and Gynecologic History

Table 4 presents the baseline demographic and gynecologic history parameters for the Intent-to-Treat Population (all enrolled subjects).

Table 4: Baseline Demographics and Gynecological History

Subject Characteristic	Total Subjects (N=110)
Age (yrs)	
Mean ± SD (Median)	42.0 ± 5.3 (43.2)
Range (min, max)	(29.3, 49.7)
Race/Ethnicity	
Hispanic**	23.6% (26)
Asian	0.9% (1)
Caucasian	75.5% (83)
African American	0% (0)
Body Mass Index (BMI) (Kg/m^2)	
Mean ± SD (Median)	28.2 ± 5.8 (27.3)
Range (min, max)	(18.0, 57.3)
Reproductive History	
Gravida	
Mean ± SD (Median)	2.8 ± 1.4 (3.0)
Range (min, max)	(0, 6)
Para	
Mean ± SD (Median)	2.3 ± 1.0 (2.0)
Range (min, max)	(0, 5)
Menstrual History	
Regular Cycle Pattern	86.4% (95)
Dysmenorrhea	59.1% (65)
PMS	72.7% (80)
PBLAC Score at baseline	
Mean ±SD (Median)	469.4 ± 337.2 (381.4)
Range (min, max)	(151.1, 2048.0)
Laboratory Testing	
FSH (IU/L)	
Mean ±SD (Median)	8.0 ± 7.2 (6.0)
Range (min, max)	(0.4, 38.0)

** Note: Hispanic is not a race; however, it is listed as such in the database to provide information on ethnicity of this subject population.

8.1.5 Results

Safety Endpoint
Adverse event information is described above in the “Adverse Events” Section, **Table 1** and **Table 2**.

Primary Effectiveness: Success Rates
Patient success at 12 months post-procedure is defined as a reduction in the PBLAC diary score from ≥150 pre-operatively to ≤75 post-procedure. Data presented in **Table 5** represent the success rates at one, two and three years post-procedure. At one year, the worst-case scenario is presented whereby each of the discontinued patients (five screening failures and one aborted procedure described in **Table 3** for

patient accountability) is counted as a “failures” for calculating the values listed in the table. At 2 and 3 years, long-term success rates were evaluated by asking each subject questions to assess their bleeding level. Due to the time lag in obtaining regulatory approvals and consenting subjects for long-term follow-up, there was a subset of subjects already past the window for their 24-month evaluation. As a result, 21 subjects had missed the 2-year follow-up. Subjects reporting a menstrual status of amenorrhea, spotting, hypomenorrhea, or eumenorrhea with no additional treatment for abnormal uterine bleeding (AUB) were considered a success in **Table 5**. A regression multiple imputation procedure was used to impute missing success/failures at the 24-month follow-up using the one-year success/failure variable as a predictor. One-hundred imputations were performed and the results were averaged to estimate the number of successes at two years and the associated success rate and 95% confidence interval (using Rubin’s method).

Table 5: Effectiveness: Success Rates (Intent-To-Treat Population)

Success Normal or Less Monthly Bleeding	**One Year* (Total N=110)**		**Two Years** (Total N=101)**		**Three Years** (Total N=101)**	
	n	**%**	**n**	**%**	**n**	**%**
Success N (%)	101	91.8	92.8+	91.9	94	93.1
95% CI	(85.0, 96.2)		(86.2, 97.6)		(86.2, 97.2)	

* Based on PBLAC Diary Scores

** Based on Telephone Questionnaires

+ Estimated number of successes using a regression multiple imputation procedure

The purpose of the primary effectiveness analysis was to determine if the true Minerva success rate is greater than the OPC of 66%. The null hypothesis was that the Minerva success rate was equal to or less than the OPC of 66%. Based on the success rate of 91.8% observed in the Minerva ITT population, the null hypothesis was rejected at the significance level of 0.025, and the 12-month follow-up success rate observed with the Minerva Endometrial Ablation System was demonstrated to be statistically significantly greater than the OPC of 66% (p-value <0.0001).

Secondary Effectiveness Endpoint: Amenorrhea

Amenorrhea Rates were also evaluated using PBLAC diary scores during the first 12 months (i.e., diary score of 0), and based on subject responses to questions during the long-term follow-up. Amenorrhea was based on menstrual bleeding during the 30-day time period prior to the follow-up phone contact or visit. **Table 6** below provides the Amenorrhea Rates at the initial 12 months, as well as long-term results determined by re-contacting subjects who consented to provide long-term follow-up between 4.5 and 5.2 years after the procedure (mean post-procedure time of 4.8 years).

Table 6: Amenorrhea Rates at 12 months and greater than 3 years post-treatment

Amenorrhea	One Year* (Total N=110)		>3 Years** (Total N=101)	
	n	%	n	%
N (%)	73	66.4	58	57.4
95% CI	(56.7, 75.1)		(47.2, 67.2)	

* Based on PBLAC Diary Scores

** Mean follow-up time 4.8 Years Based on Telephone Questionnaires

Secondary Effectiveness Endpoint: Patient Satisfaction

Patient satisfaction with the Minerva procedure was assessed and at 12 months of follow-up, out of those subjects who responded to the survey, 97.6% (81/83) were satisfied or very satisfied with the Minerva procedure. Patient satisfaction during long-term follow-up was reported as 97.2% (70/72) at 2 years, and 98.9% (92/93) at 3 years. In addition, at the 12-month follow-up interval 98.8% (82/83) of patients stated that they would recommend the procedure to a friend or a relative with the remaining 1.2% (1/83) reporting "Not Sure." At 2- and 3-year follow-up, all subjects (72/72 and 93/93, respectively) reported that they would definitely or maybe recommend the procedure.

Pre-menstrual symptoms and dysmenorrhea were evaluated at baseline and following the Minerva procedure. At the 12 months follow-up interval, reduction in pre-menstrual symptoms was reported by 80.8% (84/104). At 2 and 3-year follow-up, 65.3% (47/72) and 72% (67/93) of subjects reported a reduction in pre-menstrual symptoms, respectively. For the same time intervals 54.8% (57/104) of study subjects who were treated reported a reduction in dysmenorrhea at 12 months, and 48.6% (35/72), and 55.9% (52/93) at 2 and 3 years, respectively.

Secondary Endpoint: Procedure Time

Procedure time was determined for each patient by recording the time from insertion of the Minerva Disposable Handpiece to the time of removal. The mean procedure time was determined to be 3.9 ± 1.5 minutes.

Secondary Endpoint: Anesthesia Regimen

Anesthesia regimen was not dictated by the clinical protocol and was left to the discretion of each patient, clinical investigator, and attending anesthesiologist. Anesthesia regimen was also largely driven by the currently adopted guidelines specific to each medical facility/site. Anesthesia regimens used in the study are summarized in **Table 7**.

Table 7: Anesthesia Regimen (N=110)

Anesthesia Type	Total Subjects (N=110) % (N)
General	9.1% (10)
IV Sedation	11.8% (13)
Paracervical Block	9.1% (10)
IV Sedation/Paracervical Block	57.3% (63)
IV Sedation/Paracervical Block/ Other	12.7% (14)

8.1.6 Clinical Observations

Hysterectomy

During the 36-month follow-up period, one subject underwent hysterectomy between 12 and 24 months following the procedure for pre-existing pelvic pain unrelated to the endometrial ablation. No other hysterectomies were reported during the 3-year study period.

8.2 Minerva Randomized Clinical Trial (RCT) Summary

The Minerva Endometrial Ablation System is being evaluated in a prospective, controlled, randomized, multicenter, safety and effectiveness clinical study of 153 enrolled subjects with menorrhagia. One year follow-up data are currently available. Two- and three-year safety and effectiveness outcomes are being collected for this study.

The eligibility criteria (i.e., inclusion and exclusion criteria) for the Minerva RCT are similar to those for the Minerva Single-Arm study with a few exceptions (e.g., bleeding is assessed using the Alkaline Hematin method instead of PBLAC scores).

8.2.1 Study Objectives

The primary objective was to evaluate the safety and effectiveness of the Minerva Endometrial Ablation System compared to Rollerball ablation in reducing menstrual blood loss at 12 months post-treatment. An additional objective was to identify complications or adverse events that may occur in the subjects treated in this study. Subjects were randomized 2:1 to the Minerva Endometrial Ablation Device or the Rollerball Ablation Control arm, respectively. The two treatments were compared in a group of pre-menopausal women with menorrhagia (excessive uterine bleeding) from benign causes who no longer wished to retain fertility.

8.2.2 Study Design

The study was designed as a prospective, randomized (2:1), controlled, international, multicenter (13 sites) clinical investigation. The safety and effectiveness population consists of 153 enrolled subjects.

The primary effectiveness measure was a validated Alkaline Hematin method of measuring blood loss, assessing collected validated sanitary products (G.F. Ray, P. Burnett, D. Dadgar. Rapid quantitation of menstrual blood loss from feminine hygiene products. *Fertility and Sterility*, Volume 96, Issue 3, Supplement, Pages S281–S282, September 2011). Success was defined as a reduction in menstrual bleeding at 12

months to an Alkaline Hematin value of ≤80ml per cycle. Secondary endpoints included comparison of procedure time, patient satisfaction (as recorded by patient self-report), and amenorrhea rates between the two groups. Safety evaluation was based on the adverse events reported during the study, including device-related complications.

8.2.3 Patient Population

A total of 153 patients were enrolled in this study. Patients were between the ages of 25 to 50 with 35.3% under the age of 40 and 64.7% 41 years of age or older. There were no statistically significant differences in baseline characteristics or gynecological history parameters between the two treatment groups. **Table 8** describes the accountability of subjects throughout the study period.

Table 8: Subject Accountability

	Minerva	Rollerball	TOTAL
Intent to Treat Population	102	51	153
Enrolled but not Treated	0	0	0
Aborted Treatment	0	0	0
Completed Treatments	102	51	153
Population with 12-Month Data Available	99	44	143
• **Missed follow-up**	0	0	0
• **Withdrew for AE (Hysterectomy for PID)**	1	0	1
• **Withdrew for additional abnormal uterine bleeding (AUB) treatment**	1	5	6
• **Voluntary withdrawal for additional abnormal uterine bleeding (AUB) treatment**	1	2	3

Demographics and Gynecologic History

Table 9 presents the baseline demographic and gynecologic history parameters for the ITT population.

Table 9: Patient Demographics and Gynecologic History

Subject Characteristic	Minerva (n=102)	Rollerball (n=51)	p-value
Age (Years)			
Mean ± SD (Median)	42.6 ± 4.2 (42.9)	42.5 ± 4.7 (43.1)	0.97
Range (Min - Max)	31.6 – 50.1	32.3 - 49.3	
Race			
American Indian or Alaskan Native	1 (1.0 %)	0 (0.0 %)	1.00
Black or African American	3 (2.9 %)	2 (3.9 %)	
White	98 (96.1 %)	49 (96.1 %)	
Ethnicity			
Hispanic or Latino	30 (29.4 %)	15 (29.4 %)	1.00
Not Hispanic or Latino	72 (70.6 %)	36 (70.6 %)	
Body Mass Index (BMI) (kg/m^2)			
Mean ± SD (Median)	30.0 ± 7.1 (29.7)	28.8 ± 5.3 (28.6)	0.28
Range (Min - Max)	16.6 – 52.1	19.8 - 40.6	
Reproductive History			

Subject Characteristic	Minerva (n=102)	Rollerball (n=51)	p-value
Gravida			
Mean ± SD (Median)	3.1 ± 1.7 (3)	3.3 ± 1.5 (3)	0.65
Range (Min - Max)	0.0 – 10.0	0.0 - 7.0	
Para			
Mean ± SD (Median)	2.6 ± 1.3 (3)	2.5 ± 1.2 (2)	0.65
Range (Min - Max)	0.0 - 9.0	0.0 - 6.0	
Menstrual History			
Regular Cycle Pattern	97 (95.1 %)	48 (94.1 %)	1.00
Dysmenorrhea	57 (55.9 %)	32 (62.7 %)	0.49
PMS	66 (64.7 %)	35 (68.6 %)	0.72
Alkaline Hematin Score at Baseline			
Mean ± SD (Median)	310.2 ± 169.0 (247.5)	301.8 ± 176.1 (249.0)	0.78
Range (Min - Max)	161.5 – 1120.0	160.0 – 1026.1	
Laboratory Results - FSH (IU/L)			
Mean ± SD (Median)	7.5 ± 5.5 (6.0)	8.0 ± 6.3 (6.0)	0.60
Range (Min - Max)	1.0 – 30.0	2.0 – 35.3	

8.2.4 Results

Primary Safety Endpoint

Adverse event information is described above in the "Adverse Events" Section, **Table 1** and **Table 2**.

Primary Effectiveness Endpoint

Success Rates

The primary effectiveness objective for the Minerva Pivotal Study was the reduction of excessive uterine bleeding to normal levels or less as measured using the Alkaline Hematin (AH) method. In order to qualify for study entry, all subjects had to have pre-treatment AH values $\geq$ 160ml per cycle. Study success was achieved when bleeding was reduced to AH value of $\leq$ 80ml at 12 months after the endometrial ablation procedure. Data presented in **Table 10** represent the Success Rates based on the total number of 153 patients enrolled (Intent-to-Treat (ITT) Population) in the study.

Table 10: Effectiveness: Success Rates (Intent-To-Treat Population)

Randomization Arm	1 Year		
	Minerva N=102	Rollerball N=51	p-value
Success N (%)	95 (93.1%)	41 (80.4%)	0.02
95% CI	86.4%, 97.2%	66.9%, 90.2%	

The success rate at 1 year was 93.1% for the Minerva Test Group compared with 80.4% for the Rollerball Control Group, with a difference of -12.7% and upper 1-sided

97.5% confidence limit of -0.80%. Thus, the noninferiority null hypothesis was rejected because -0.80% is lower than 20%. The test for superiority of Minerva over Rollerball concluded that the success rate in the Minerva Test Group was statistically significantly greater than in the Rollerball Group (Fisher's exact test, p = 0.02).

Secondary Endpoint
Procedure Time
Procedure time was determined for each subject by recording the time of device insertion and the time of device removal. The mean procedure time for the Minerva procedure (3.1 ± 0.5 minutes) was statistically significantly less than the procedure time for the Rollerball ablation procedure (17.2 ± 6.7 minutes).

Additional Analyses
Amenorrhea
Table 11 below shows amenorrhea results at 1-year based on AH lab value classification, or subject certification of no bleeding during the 30-day period prior to the follow-up visit. The Amenorrhea rate at 1 year was 71.6% for the Minerva-treated subjects and 49% for those treated with Rollerball.

Table11: Amenorrhea Rates (Intent-To-Treat Population)

Randomization Arm	1 Year	
	Minerva N=102	Rollerball N=51
Amenorrhea* N (%)	73 (71.6%)	25 (49.0%)
95% CI	61.8%, 80.1%	34.8%, 63.4%

* Based on AH lab value or patient's written certification of no bleeding 30 days prior to 12-month visit.

Anesthesia
The anesthesia regimen was not dictated by the clinical protocol and was left to the discretion of each patient, clinical investigator and attending anesthesiologist. The type of anesthesia used in the Minerva procedure was nearly identical to the anesthesia regimen in the Rollerball ablation procedure.

Cervical Dilation
The mean cervical dilation for the Minerva procedure (6.8 ± 1.1mm) was statistically significantly less than the cervical dilation used for the Rollerball ablation procedure (9.3 ± 1.5 mm).

Patient Satisfaction
Patients were asked about their level of satisfaction with their endometrial ablation treatment for menorrhagia at study follow-ups. A total of 91.9% (91/99) of the Minerva patients versus 79.5% (35/44) of the Rollerball patients were "Satisfied" or "Very Satisfied" at 1 year post-procedure. Patients were also asked if they would recommend the procedure to a friend or relative. At 1 year after the endometrial ablation treatment, 94.9% (94/99) of the Minerva patients and 88.6% (39/44) of the

Rollerball ablation patients said “Maybe” or “Definitely” they would recommend the procedure to a friend or relative with a similar problem.

The reduction of Pre-menstrual symptoms at one year post-procedure was slightly higher in the subjects treated with the Minerva System 53.5% (53/99) compared to Rollerball ablation 43.2% (19/44). For the reduction in Dysmenorrhea one year after treatment however, the outcomes were similar for the two groups, with Minerva showing 46.5% (46/99) and Rollerball ablation 45.5% (20/44).

8.25 Clinical Observations

Hysterectomy

During the 12-month follow-up period, there were 6 reported hysterectomies, 3 (2.9%) in the Minerva patients and 3 (5.9%) in the Rollerball patients as described in **Table 12 below**.

Table12: Hysterectomies During the Study Period

Randomization Arm	Reason for Hysterectomy	Pathology Reported
Minerva N=102	Pelvic Inflammatory Disease (PID).	Acute salpingo-oophoritis
	Subject withdrew from study voluntarily to have a hysterectomy. Heavy uterine bleeding.	Multiple fibroids.
	Heavy uterine bleeding.	Multiple fibroids. Adenomyosis.
Rollerball N=51	Heavy uterine bleeding.	Multiple fibroids.
	Heavy uterine bleeding.	Adenomyosis.
	Heavy uterine bleeding.	Adenomyosis.

9.0 PATIENT SELECTION

Menorrhagia can be caused by a variety of underlying problems, including, but not limited to; endometrial cancer, myomas, polyps, drugs and abnormal uterine bleeding (anovulatory bleeding). Patients should always be screened and evaluated to determine the cause of excessive uterine bleeding before any treatment option is initiated. Consult medical literature relative to various endometrial ablation techniques, indications, contraindications, complications and hazards prior to the performance of any endometrial ablation procedure.

Patients with abnormal or obstructed uterine cavities were excluded from the clinical studies of the Minerva System. The risk of uterine perforation and serious complications (e.g., bowel injury) during endometrial ablation is likely increased in such patients.

10.0 PATIENT COUNSELING

As with any procedure, the physician needs to discuss risks, benefits and alternatives with the patient prior to performing endometrial ablation. Patient’s expectations should be set in a way that the patient understands that the aim of the treatment is the reduction in bleeding to normal levels.

The Minerva Endometrial Ablation System is intended for use only in women who do not desire to bear children because the likelihood of pregnancy is significantly decreased following the procedure. Patients of childbearing capacity should be cautioned of potential complications,

which may ensue if they should become pregnant. This counseling should include the need for post-procedure contraception where indicated. This procedure is not a sterilization procedure and subsequent pregnancies may be dangerous for the mother and fetus.

Vaginal discharge is typically experienced during the first few weeks following ablation and may last as long as a month. Generally, the discharge is described as bloody during the first few days; serosanguineous by approximately one week; then profuse and watery thereafter. Any unusual or foul-smelling discharge should be reported to the physician immediately. Other common post-procedural complications include cramping/pelvic pain, nausea and vomiting.

Uterine perforation should be considered in the differential diagnosis of any post-operative patient complaining of acute abdominal pain, fever, shortness of breath, dizziness, hypotension or any other symptom that may be associated with uterine perforation with or without damage to the adjacent organs of the abdominal cavity. Patients should be counseled that any such symptoms should be immediately reported to their physician.

11.0 PRETREATMENT PREPARATION OF PATIENT

The Minerva Endometrial Ablation System successfully treats a uterine cavity over a range of endometrium thickness. The lining of the uterus does not have to be thinned prior to the procedure, and the procedure may be performed during either the proliferative or the secretory phase of the cycle. The safety and effectiveness of the Minerva Endometrial Ablation System has not been fully and specifically evaluated in patients with medical or surgical pretreatment.

Active bleeding was not found to be a limiting factor when using the Minerva Endometrial Ablation System. It is recommended that a non-steroidal anti-inflammatory drug (NSAID) be given at least one hour prior to treatment and continued postoperatively to reduce intra-operative and post-operative uterine cramping.

12.0 SET-UP

12.1 Required items

The following items are required when using the Minerva Endometrial Ablation System:

- One sterile Minerva Disposable Handpiece (with Desiccant)
- One Minerva RF Controller (with Footswitch and Power Cord)
- One Argon Canister
- One CO_2 Canister

12.2 Patient Preparation

12.2.1 Prepare the patient for the anesthesia.
12.2.2 Place patient in dorsal lithotomy position.
12.2.3 Induce anesthesia according to standard practice.
12.2.4 Perform bimanual examination. Evaluate for severe ante-version or retro-version of the uterus.
12.2.5 Prepare and drape patient similar to prep for D&C.
12.2.6 Insert a speculum into the vagina.
12.2.7 Grasp the cervix with a tenaculum.
12.2.8 Take a sound measurement of the uterus to measure the length from fundus to external cervical os.

WARNING: The efficacy of the Minerva Endometrial Ablation System has not been evaluated in patients with a uterine sound measurement greater than 10 cm.

12.2.9 Determine the length of the cervical canal and dilate cervical canal to 7.0 mm.

Optional diagnostic hysteroscopy using normal saline or Ringers Lactate for distention media can be performed at this time.

12.2.10 Using the uterine sound and cervical canal measurements, consult the cavity length table (**Table 13**) to obtain the appropriate PFA length setting. Numbers marked with an asterisk represent adjusted dimensions that should reflect the Minerva Disposable Handpiece PFA length setting and while not observed in the clinical study, may be associated with a higher rate of failure to pass the uterine integrity test. Correct determination of the cavity length is important for safe and effective treatment. Overestimating the cavity length may result in thermal injury to the endocervical canal.

WARNING: Use caution not to perforate the uterine wall when sounding, dilating or inserting the Minerva Disposable Handpiece.

Table 13: Cavity Length Table

Cervical Canal Length (cm)	Uterine Sound Length (cm)										
	10	**9.5**	**9**	**8.5**	**8**	**7.5**	**7**	**6.5**	**6**	**5.5**	**5**
1	**Do Not Treat**			6.5*	6.5*	6.5	6	5.5	5	4.5	4
1.5			6.5*	6.5*	6.5	6	5.5	5	4.5	4	
2		6.5*	6.5*	6.5	6	5.5	5	4.5	4		
2.5	6.5*	6.5*	6.5	6	5.5	5	4.5	4			
3	6.5*	6.5	6	5.5	5	4.5	4				
3.5	6.5	6	5.5	5	4.5	4					
4	6	5.5	5	4.5	4						
4.5	5.5	5	4.5	4				**Do Not Treat**			
5	5	4.5	4								
5.5	4.5	4									
6	4										

* The value of 6.5 where indicated with an asterisk is not intended to reflect the numerical difference between the sound length and the length of the cervical canal. The value 6.5* is entered because it represents the maximum length to which the Minerva Disposable Handpiece Array can be extended.

CONTRAINDICATION: Do not treat a patient with a uterine cavity length that is less than 4 cm, as cervical canal damage may occur.

12.3 **Minerva Disposable Handpiece and Minerva RF Controller Preparation Procedure**

12.3.1 Open the sterile Minerva Disposable Handpiece package. Place the Minerva Disposable Handpiece, with the connecting cord and the syringe into the sterile field while being careful to keep the non-sterile suction line desiccant box out of the sterile field.

WARNING: Do not use the sterile single-patient use Minerva Disposable Handpiece if the packaging appears to be damaged or there is evidence of tampering.

CAUTION: Minerva Disposable Handpiece must be external to (outside of) the patient while performing all steps in section 12.3 and steps 13.1 through 13.5 in section 13.

12.3.2 Open the non-sterile suction line desiccant box and pouch. Remove the two end caps.

CAUTION: The argon return line desiccant contents are non-sterile and its packaging should not be placed in the sterile field.

CAUTION: If the argon return line desiccant is pink, replace it prior to initiating the ablation procedure.

12.3.3 Connect the desiccant to the two ports on the tubing of Minerva Disposable Handpiece (**Figure 6**). When properly connected you will feel or hear a click.

Figure 6: Desiccant Connection

12.3.4 Using the toggle switch on the back of the unit, turn on the Minerva RF Controller. **Figure 7** will appear on the touch screen display for 5 seconds.

Figure 7: Initial Screen

12.3.5 Adjust volume according to your preference.

12.3.6 Confirm your adequate familiarity with the Minerva Endometrial Ablation System Operator's Manual / Instructions for Use by pressing the green check mark on the touch screen display (**Figure 8**).

Figure 8: Confirmation Request Screen

12.3.7 Upon confirmation, screen image will change to display the status of argon (Ar) and CO_2 canisters (**Figures 9-12**) to indicate if there is sufficient gas to complete the procedure. If either one or both canister icons appear red, remove and replace with a new canister(s) until both canister icons are green.

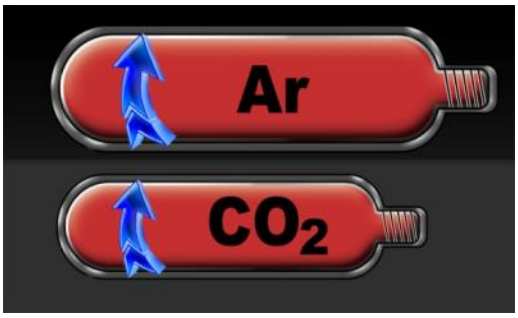


Figure 9: Replace Ar and CO_2

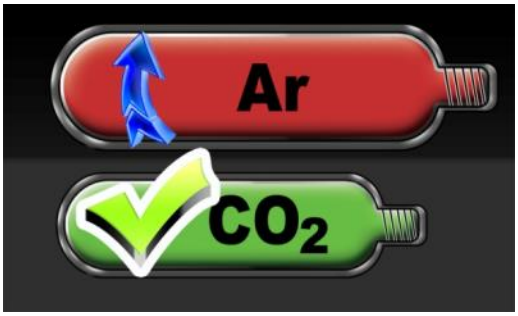


Figure 10: Replace Ar

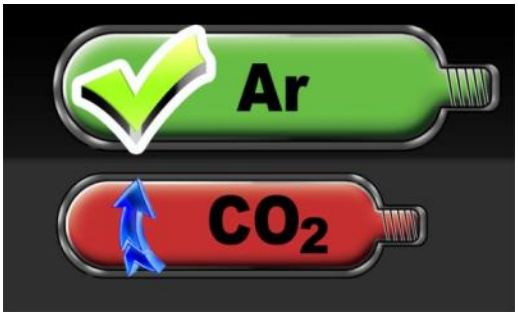


Figure11: Replace CO_2

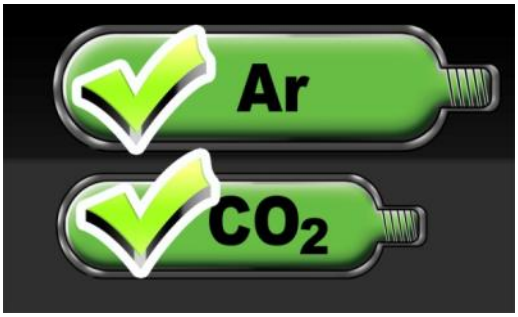


Figure 12: Sufficient Ar and CO_2

12.3.8 After both canister icons turn green, the screen will display the green canister status for 5 seconds after which the next screen (**Figure 13**) indicating that the Minerva Disposable Handpiece and Footswitch should be connected will appear.

Figure 13: Connect Minerva Disposable Handpiece and Footswitch

12.3.9 Connect the Minerva Disposable Handpiece connecting cord and foot-switch cord to the appropriate port on the front panel of the Minerva RF Controller. When connecting the Minerva Disposable Handpiece assure a snug fit such that the purple surface of the connector is not visible. When connecting the footswitch advance the black tubing over the nipple receptacle. At this time, the Minerva Disposable Handpiece test animation (**Figure 14**) will appear on the Minerva RF Controller touch screen display.

WARNING: Plugging the Minerva Disposable Handpiece into the Minerva RF Controller automatically starts a system test which takes approximately 7 seconds and must be performed with the Minerva Disposable Handpiece EXTERNAL to the patient.

CAUTION: Do not manipulate the Minerva Disposable Handpiece during the system test or test failure may result.

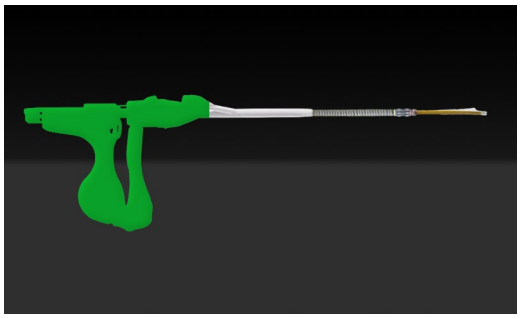


Figure 14: Minerva Disposable Handpiece Test

12.3.10 Successful completion of the tests will be reflected on the touch screen display (**Figure 15**).

Figure 15: Minerva Disposable Handpiece Test Successful

13.0 PROCEDURE

CAUTION: CO_2 continuously flows from the time that the Minerva Disposable Handpiece is plugged into the Minerva RF Controller until the Uterine Integrity Test portion of the procedure is complete.

WARNING: Use caution not to perforate the uterine wall when sounding, dilating or inserting the Minerva Disposable Handpiece.

13.1 **Using the uterine sound measurement and cervical canal measurements, consult the cavity length table as described in Step 12.2.10 above, to obtain the appropriate Plasma Formation Array length setting.**

CONTRAINDICATION: Do not treat a patient with a uterine cavity length that is less than 4 cm, as cervical canal damage may occur.

13.2 Adjust and lock the cavity length setting feature on the Minerva Disposable Handpiece (**Figure 16**) to the value obtained above (See step 12.2.10).

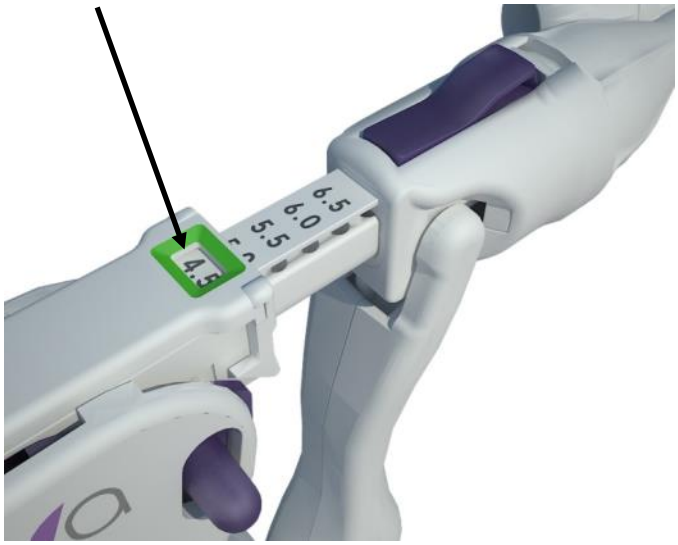


Figure 16: Minerva Disposable Handpiece PFA Length Setting Feature

13.3 Confirm that the cervix is dilated to at least 7.0 mm.
13.4 Maintain a slight traction on the tenaculum to minimize the angle of the uterus.
13.5 Press and hold the Green Button on the touch screen display (**Figure 17**) to draw vacuum on the PFA, thus minimizing the Minerva Disposable Handpiece tip insertion profile. The sheath of the Minerva Disposable Handpiece will not cover the PFA. Attempts to “sheath” the PFA will result in Minerva Disposable Handpiece damage.

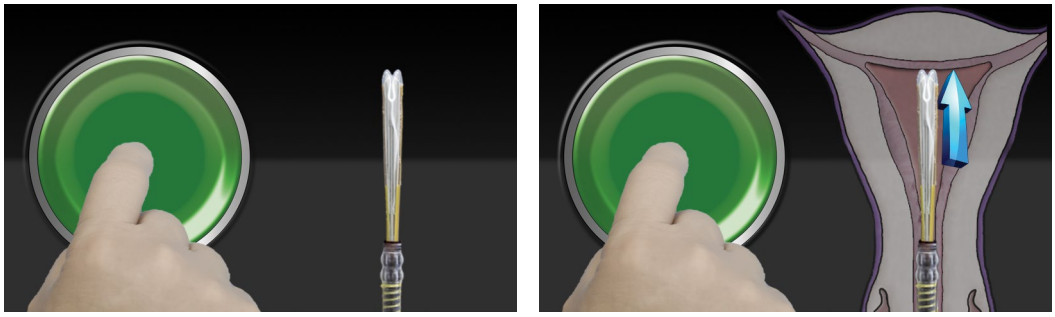


Figure 17: PFA Vacuum Button Screens

13.6 Angle the Minerva Disposable Handpiece in-line with the axis of the uterus as the Minerva Disposable Handpiece is inserted transcervically into the uterine cavity and advance the Minerva Disposable Handpiece until the distal tip of the PFA touches the fundus. Release the Green button on touch screen display of the Minerva RF Controller.

WARNING: If the Minerva Disposable Handpiece is difficult to insert into the cervical canal, use clinical judgment to determine whether or not further dilation is required. Forcibly advancing the Minerva Disposable Handpiece against resistance is likely to increase the risk of perforation or creation of a false passage. Sufficient dilation is required for safe insertion.

13.7 The touch screen display will change to the Minerva Disposable Handpiece deployment screen (**Figure 18**) upon release of the Green Button, to reflect steps 13.7 – 13.10 described below.

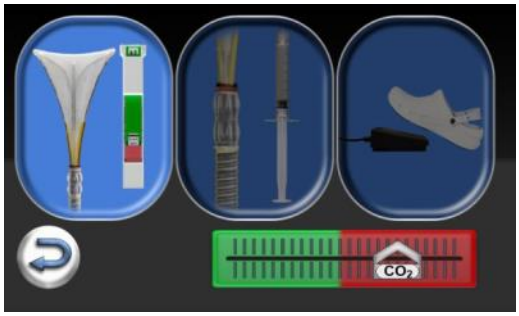


Figure 18: Minerva Disposable Handpiece Deployment

13.8 Maintain the distal tip of the PFA at the fundus. Slowly squeeze the Minerva Disposable Handpiece handle together while gently moving the Minerva Disposable Handpiece approximately 0.5 cm to and from the fundus until the Minerva Disposable Handpiece handle locks. DO NOT pull the deployed PFA back and away from the fundus. The Array Opening Indicator on the Minerva Disposable Handpiece should be in the Green zone (**Figure 19**).

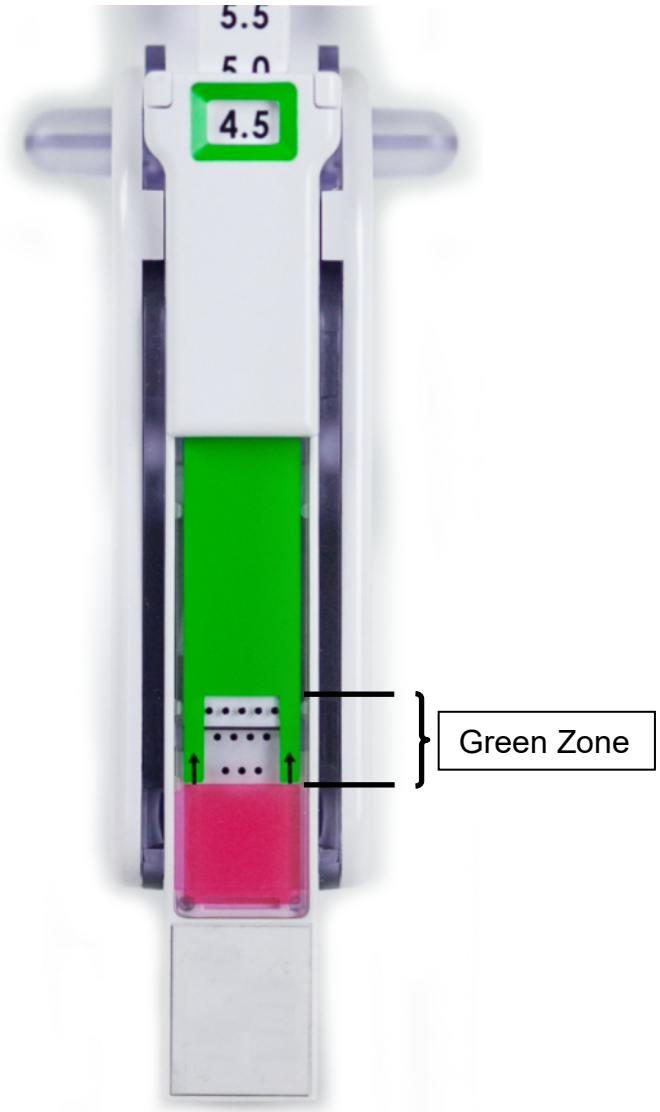


Figure 19: Array Opening Indicator Green Zone

NOTE: Once the Minerva Disposable Handpiece handle is locked, the uterus should move in conjunction with the Minerva Disposable Handpiece.

13.9 Gently move the Minerva Disposable Handpiece using anterior, posterior and lateral movements.

13.10 To complete placement, slightly pull back the Minerva Disposable Handpiece and then gently advance the Minerva Disposable Handpiece to the fundus. The Array Opening Black Indicator line on the Minerva Disposable Handpiece should now be in the Green Zone.

NOTE: The Black Indicator Line on the Array Opening Indicator displays the progression of the PFA deployment/opening and does not indicate a dimension of the uterus.

CONTRAINDICATION: Do not treat a patient if Array Opening Indicator is in the Red Zone following deployment of the Minerva Disposable Handpiece.

13.11 After connecting the sterile syringe (provided) to the inflation port on the sheath

(**Figure 20**), fully inflate the Cervical Sealing Balloon to seal the uterine cavity. Exercise caution not to damage the Cervical Sealing Balloon by over inflating and/or causing mechanical damage by use of other instruments. The position of the CO_2 arrow icon along the red-green scale near the bottom of the touch screen display indicates the likelihood of passing or failing the subsequent Uterine Integrity Test (UIT). If the CO_2 arrow icon is in the green zone, the CO_2 flow rate is sufficiently low that initiation of the UIT test is appropriate. If the CO_2 arrow icon is in the red zone, however, the CO_2 flow rate remains sufficiently high that the UIT test will not likely pass if initiated.

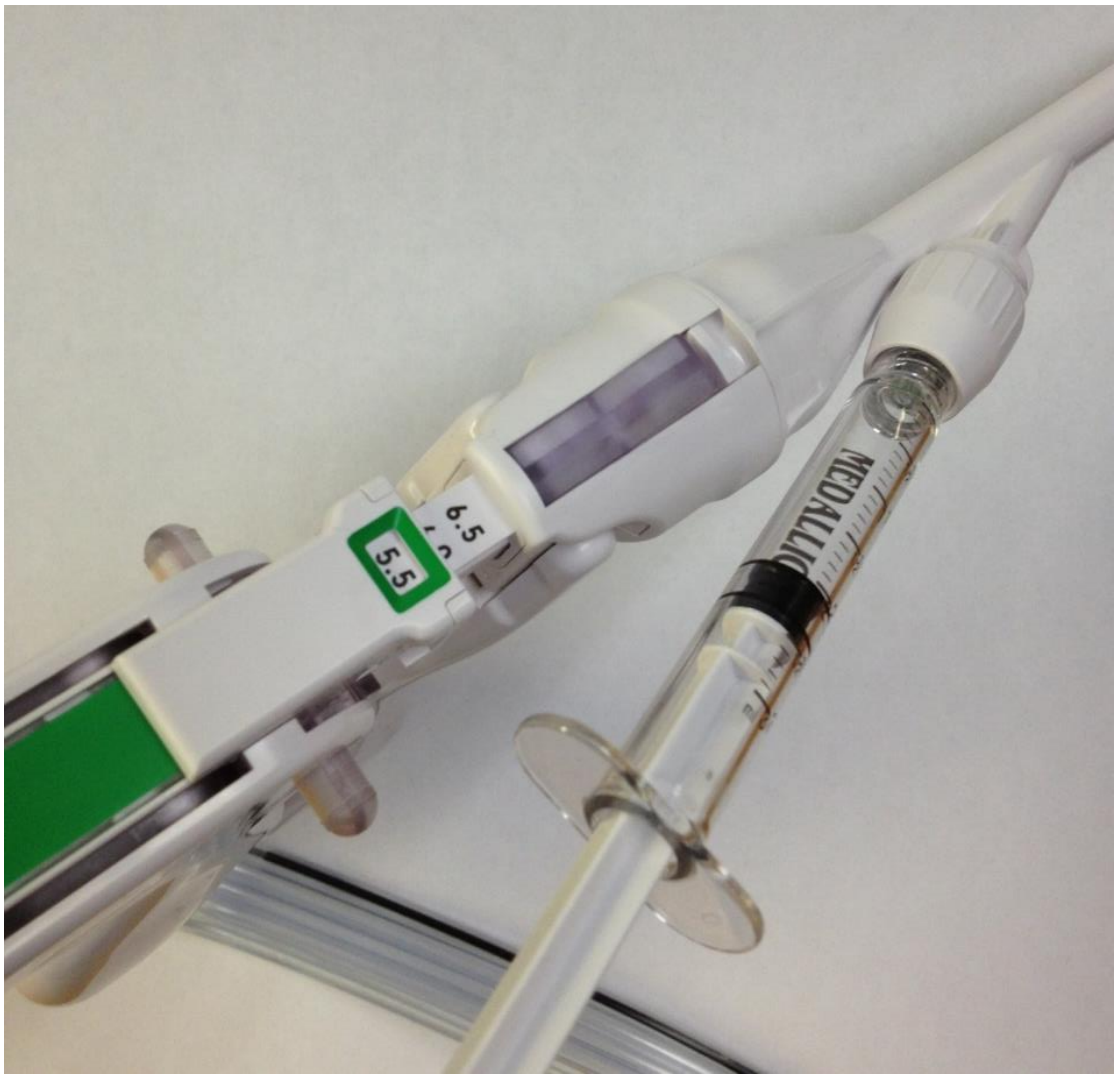


Figure 20: Syringe Connected to Inflation Port

13.12 Begin the uterine integrity test (UIT) procedure by stepping on and releasing the foot switch once. An animation indicating the progress of the UIT will appear on the touch screen display. See animation frame in (**Figure 21**)

Figure 21: Uterine Integrity Test Initiation

13.13 Upon successful completion of the UIT, the screen will switch (**Figure 22**) and the ablation procedure will start automatically.

Figure 22: Successful Uterine Integrity Test

NOTE: Power will not be applied to the Minerva Disposable Handpiece until the UIT passes. If the UIT fails, then the display on the Minerva RF Controller will indicate UIT Failure (Figure 23), and a rapid audible tone will sound. Consult the Troubleshooting section for more information.

Figure 23: Failed Uterine Integrity Test

13.14 Upon successful completion of the UIT, the screen will switch (**Figure 22**) and the ablation procedure will start automatically. The remaining ablation time will be displayed on the screen (**Figure 24**).

NOTE: Maintaining correct placement of the Minerva Disposable Handpiece PFA against the fundus is important for safe and effective treatment.

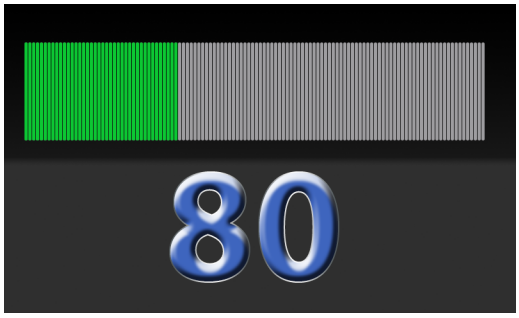


Figure 24: Remaining Ablation Time

13.15 During the ablation cycle, the blue “RF ON” LED on the front panel of the Minerva RF Controller will be ON. At the completion of the ablation cycle, this blue RF power delivery (RF ON LED) will switch off with the cessation of RF energy delivery.

NOTE: RF power delivery can be stopped at any time by pressing the foot switch. If Footswitch is accidently pressed, the cycle can be re-initiated by pressing the footswitch again.

13.16 Upon successful completion of the 2 minute ablation cycle, 2 images (**Figure 24** and **Figure 25**) will appear sequentially on the touch screen display.

Figure 24: Ablation Complete

Figure 25: Do Not Re-treat Warning

13.17 Using the supplied syringe deflate the Cervical Sealing Balloon.
13.18 Unlock and withdraw the Minerva Disposable Handpiece from the patient.

CAUTION: To avoid damaging the Minerva Disposable Handpiece, employ a gentle technique when retracting the Minerva Disposable Handpiece.

13.19 Using the toggle-switch, turn OFF the Minerva RF Controller.
13.20 Perform postoperative patient care according to standard procedures. The used Minerva Disposable Handpiece must be treated as biohazardous waste and disposed of in accordance with the standard practice of the clinic or hospital, where the treatment is performed.
13.21 Discharge the patient from the hospital or office as indicated by the managing physician.

WARNING: The Minerva procedure is indicated AS A SINGLE PROCEDURE ONLY. A repeat ablation either during the same operative visit or at a subsequent visit in the distant future is an absolute contraindication.

14.0 TROUBLESHOOTING

14.1 UIT Failure

14.1.1 If the UIT fails, a brief tone will sound and **Figure 26** will appear on the touch screen display.

WARNING: If a perforation is suspected, the procedure should be terminated immediately.

14.1.2 Return to the Minerva Disposable Handpiece deployment screen by pressing the "return" button in the lower left hand corner of the image on the touch screen display (**Figure 26**).

Figure 26: Uterine Integrity Test Failure and "Return" Button

14.1.3 Re-check for leaks between the cervix and Cervical Sealing Balloon by monitoring the CO_2 flow rate indicator image on bottom edge of the touch screen display (**Figure 27**).

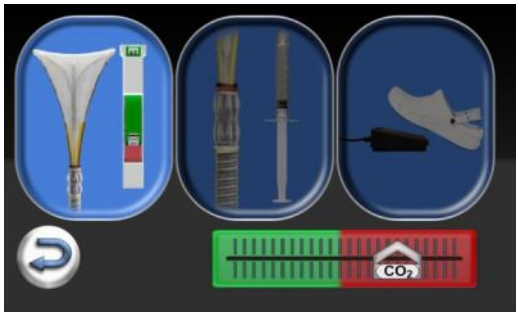


Figure 27: CO_2 Flow Rate Indicator

14.1.4 Remove the Minerva Disposable Handpiece from uterus and verify Cervical Sealing Balloon integrity by inflating the Cervical Sealing Balloon and checking for leaks. If the Cervical Sealing Balloon does not remain inflated, replace Minerva Disposable Handpiece. If the leak appears to be at the cervix and cannot be resolved by using the Cervical Sealing Balloon, use another tenaculum to grasp and tighten the cervix around the sheath. Repeat the UIT by stepping on and releasing the foot switch once the CO_2 indicator is in the green zone.

NOTE: CO_2 leakage may occur at the external cervical os due to the presence of an over-dilated cervix. Visible bubbles or the "hissing" sound of escaping gas may accompany CO_2 leakage under either of these conditions.

14.1.5 Apply good clinical judgment and consider stopping the procedure, if the UIT continues to fail after a reasonable number of attempts to implement the troubleshooting procedures (Steps 14.1.2 through 14.1.4 above)

NOTE: Removing the Minerva Disposable Handpiece from the uterine cavity after completing the UIT will require an additional UIT to be performed upon Minerva Disposable Handpiece re-insertion (whether or not the UIT previously passed) prior to initiating an ablation.

14.2 **Missing Desiccant**

14.2.1 If the desiccant is missing, **Figure 28** will appear on the touch screen display shortly after the Minerva Disposable Handpiece is connected the Minerva RF Controller.

Figure 28: Missing Desiccant

14.2.2 Attach both ends of the desiccant to the Minerva Disposable Handpiece cord.

14.3 **Minerva Disposable Handpiece Integrity Failure**

14.3.1 If the Minerva Disposable Handpiece fails the integrity test, **Figure 29** will appear on the touch screen display.

Figure 29: Minerva Disposable Handpiece Integrity Test Failure

14.3.2 This failure is an indication that something is obstructing the free flow of CO_2 through the Minerva Disposable Handpiece. Check for kinks in the Connector Cord tubing and/or inadvertent placement of a stool foot on the Minerva Disposable Handpiece cord. Disconnect and re-connect the Minerva Disposable Handpiece to re-start the test. If test fails for the second time, replace the Minerva Disposable Handpiece.

14.4 **Array Opening Indicator in Red Zone**

14.4.1 If the Array Opening Indicator is in the Red Zone after performing the seating procedure, close and remove the Minerva Disposable Handpiece from the uterine cavity. Inspect the Minerva Disposable Handpiece by opening in the air (outside of the patient's body). If the Array Opening Indicator is in the Red Zone when the Minerva Disposable Handpiece is deployed and locked in the air, replace the Minerva Disposable Handpiece. If the indicator is in the Green Zone, close the Minerva Disposable Handpiece and continue the procedure. If after performing the seating procedure the indicator is still in the Red Zone, rule out the possibility of uterine perforation or false passage.

14.4.2 Do not perform the procedure if the Array Opening Indicator is in the Red Zone.

14.5 **Footswitch Not Operational**

14.5.1 If the footswitch is not operational when pressing (initiating the procedure), make sure it is properly connected to the appropriate port on the front of the Minerva RF Controller, then re-attempt treatment initiation. If problem persists, contact Minerva Surgical Customer Service at 1-855-646-7874.

14.6 **Suspected Uterine Perforation**

14.6.1 *Prior to Application of Energy*:

- 14.6.1.1 Terminate the procedure
- 14.6.1.2 Assure patient stability
- 14.6.1.3 Consider patient work-up for perforation
- 14.6.1.4 Reschedule procedure, if appropriate

14.6.2 *During or after Application of Energy:*

- 14.6.2.1 Terminate the procedure
- 14.6.2.2 Assure patient stability
- 14.6.2.3 Rule out visceral injury
- 14.6.2.4 Reschedule procedure, if appropriate

14.7 **PFA Does Not Fully Deploy and Lock**

14.7.1 If the Minerva Disposable Handpiece does not lock, remove it from the uterus.

14.7.2 Inspect the Minerva Disposable Handpiece for damage;

14.7.3 Attempt to open and lock the Minerva Disposable Handpiece outside the patient; and

14.7.4 If damaged, then replace Minerva Disposable Handpiece.

14.7.5 If the Minerva Disposable Handpiece is not damaged, reinsert it into the patient's uterine cavity and attempt deployment; and

14.7.6 If unable to deploy the Minerva Disposable Handpiece to a width being in the GREEN ZONE, terminate the procedure.

14.7.7 Consider uterine perforation as a possible cause for not being able to deploy.

14.8 **Difficulty unlocking the Minerva Disposable Handpiece post-ablation**

14.8.1 If upon completion of the ablation cycle the Minerva Disposable Handpiece does not unlock using a single unlock lever, press on both levers simultaneously to unlock.

14.8.2 If the Disposable Handpiece does still not unlock, gradually withdraw the Minerva Disposable Handpiece from the patient.

15.0 ERROR MESSAGES

15.1 The user may encounter the error messages listed in **Table 14**.

Table 14: Error Messages

Error	Description	Required Action
Replace with a new Disposable Handpiece		
001	Handpiece Defect Error	Replace with new Disposable Handpiece
005		
011		
003	Argon Flow Related Error	
004		
007		
008		
009		
010		
012		
016		

Re-attempt using the same Disposable Handpiece		
002	If error occurs within 3 seconds after start of 120 second ablation countdown: Plasma Formation Error	Disconnect Disposable Handpiece, remove the device from the patient, re-connect the same device, re-insert, re-position, and re-attempt the start of ablation.
	If error occurs more than 3 seconds after start of 120 second ablation countdown: Membrane Defect Detected	Replace with a new Disposable Handpiece
006	Plasma Formation Error	Disconnect Disposable Handpiece, remove the device from the patient, re-connect the same device, re-insert, re-position, and re-attempt the start of ablation. If error recurs, replace with new Disposable Handpiece
013	Gas Canister Error	Disconnect Disposable Handpiece, remove the device from the patient, re-connect the same device, re-insert, re-position, and re-attempt the start of ablation.
014		
015	Pause Time Expired Error	Disconnect Disposable Handpiece, remove the device from the patient, re-connect the same device, re-insert, re-position, and re-attempt the start of ablation.

15.2 The user may encounter the system error messages listed in **Table 15**. The required action in all instances is to stop treatment and cycle the Minerva RF Controller power off and back on again. If the error is not cleared, contact Minerva Surgical customer service at 1-855-646-7874.

Table 15: System Error Messages

Error Codes	Description	Required Action
101 to 403	System Errors	Stop the treatment and turn the power off using the toggle switch on the back of the controller. Disconnect Disposable Handpiece and remove the device from the patient. Turn the power back on. When the error code clears, proceed with treatment. If the error code does not clear: • Note the error code displayed • Call Minerva Surgical Customer Service at 1-855-646-7874

16.0 REPLACEMENT INSTRUCTIONS

The Minerva RF Controller uses a pair of fuses located in a fuse drawer in the power input module. The fuses are Type T5AL, 250 V, 5 x 20mm each. The drawer can be accessed by using a flat-head screwdriver to pull it open. Disconnect the power cord prior to accessing the fuse drawer. If required, the fuse drawer may then be removed and the fuses changed. Assembly is the reverse of these steps.

Any potentially defective Minerva Surgical product must be returned to Minerva Surgical for evaluation. Follow the instructions in the Service Returns section (Section 23.0), for obtaining a returned goods authorization number (RGA #).

17.0 HOW SUPPLIED

- The Minerva Disposable Handpiece is supplied sterile.
- The Minerva Disposable Handpiece is intended for single-patient and single-use only. Do not re-sterilize the Minerva Disposable Handpiece.
- The Minerva RF Controller is supplied in a semi-ready-to-use state. The shipping box contains the Minerva RF Controller, Footswitch, and a detached power cord.
- Minerva argon and CO_2 canisters are supplied separately.

18.0 STORAGE, HANDLING AND DISPOSAL

- Store the Minerva Disposable Handpiece at room temperature in a clean and dry environment. Keep dry.
- Store the Minerva RF Controller at room temperature in a clean and dry environment. Keep dry.
- Handle both the Minerva RF Controller and Minerva Disposable Handpiece with care.
- Use the handles on the back of the RF Controller to facilitate moving or transport.
- Inspect the Minerva Disposable Handpiece and packaging to verify that no damage has occurred as a result of shipping. Do not use the Minerva Disposable Handpiece if damage has occurred or if the sterilization barrier has been damaged or broken.
- Dispose of used Minerva Disposable Handpieces in accordance with applicable regulations for the disposal of biohazardous material. There are no other limitations regarding the disposal of the Minerva components or accessories.

- Return the Minerva RF Controller to Minerva Surgical, Inc. for disposal.

19.0 STERILITY

- The Minerva Disposable Handpiece is sterilized using gamma irradiation. Do not use if the package is damaged or open.
- The Minerva RF Controller is supplied non-sterile and is not intended to be sterilized by the user. The Minerva RF Controller should be cleaned with a hospital grade disinfectant after each use.

20.0 TECHNICAL SPECIFICATIONS

Specifications

Mode of Operation: ..... Intermittent 120 seconds on 10 minutes shut off
Input: 100-240VAC, 50-60Hz, 300VA
Dimensions: ..... 14”(W) x 7”(H) x 22”(D) (35 x 17 x 55 cm)
Weight: ..... 25 lbs (11kg)
Output:..... 40W (80Wmax), 480 kHz, 250V max
Fuses:.....5x20mm Type “T” 5A/250V slow blow (Qty. 2; Schurter or equivalent), Type “L” - 50 A breaking capacity

Weight and dimensions indicated are approximate. Specifications are subject to change without notice.

Protection

Class 1, Type BF applied part, intermittent operation; Enclosure IPX0

Operating Conditions

Temperature: ..... 59°F to 95°F (15°C to 35°C)
Relative Humidity: ..... 25% to 75% relative, non-condensing
Atmospheric Pressure:..... 706 to 1082 cmH_2O (69 to 106 kPa)

Transport and Storage Requirements

Temperature: .....0°F to 140°F (-18°C to 60°C)
Relative Humidity: .....15% to 90% relative, non-condensing
Atmospheric Pressure:..... 510 to 1082 cmH_2O (50 to 106 kPa)

Output Power

Minerva Disposable Handpiece and RF Controller are for use exclusively with each other, and since the main component of system impedance is predominantly unrelated to the patient, no power curve is required or provided.

21.0 GUIDANCE AND MANUFACTURER’S DECLARATION

Emissions

The Minerva RF Controller (MIN180S) and Minerva Disposable Handpiece (MIN9770) are intended for use in the electromagnetic environment specified in **Table 16**. The user should ensure that both are used in such an environment.

Table 16: Emissions

Emissions Test	Compliance	Electromagnetic Environment— Guidance
RF CISPR11	Group 1	The RF Controller (MIN180S) with Minerva Disposable Handpiece (MIN9770) must emit electromagnetic energy in order to perform its intended function. Nearby electronic equipment may be affected when RF is energized. As per IEC 60601-2-2, test was performed in a mode with EUT switched on and in an idle state with the HF output not energized. CISPR 11 Group 1 limits were followed as per clause

		202.6.1.1.1
RF CISPR11	Class A	The RF Controller (MIN180S) with Handpiece (MIN9770) is suitable for use in all establishments other than domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonics EN 61000-3-2	Class A	
Flicker EN 61000-3-3	Complies	

Immunity

The Minerva RF Controller (MIN180S) and Minerva Disposable Handpiece (MIN9770) are intended for use in the electromagnetic environment specified in **Table 17**. The user should ensure that both are used in such an environment.

Table 17: Immunity

Immunity Test	IEC 60601 Test Level	Compliance Level	Electromagnetic Environment – Guidance
Electrostatic discharge (ESD) IEC 61000-4-2	± 6 kV contact ± 8 kV air	± 6 kV contact ± 8 kV air	Floors should be wood, concrete or ceramic tile. If floors are synthetic, the relative humidity should be at least 30%
Electrical Fast Transient (EFT) IEC 61000-4-4	± 2 kV Mains ± 2 kV I/Os	± 2 kV Mains ± 2 kV I/Os	Mains power quality should be that of a typical commercial or hospital environment.
Surge IEC 61000-4-5	± 1 kV Differential ± 2 kV Common	± 1 kV Differential ± 2 kV Common	Mains power quality should be that of a typical commercial or hospital environment.
Voltage Dips / Drop Outs IEC 61000-4-11	>95% dip for 0.5 cycle 60% dip for 5 cycles 30% dip for 25 cycles >95% dip for 5s	>95% dip for 0.5 cycle 60% dip for 5 cycles 30% dip for 25 cycles >95% dip for 5s	Mains power quality should be that of a typical commercial or hospital environment. If the user of the Minerva RF Controller (MIN180S) and Minerva Disposable Handpiece (MIN9770) requires continued operation during power mains interruptions, it is recommended that the Minerva RF Controller and the Minerva Disposable Handpiece be powered from an uninterruptible power supply or battery.
Power frequency (50/60 Hz) Magnetic Field IEC 61000-4-8	3 A/m	3 A/m	Power frequency magnetic fields should be that of a typical commercial or hospital environment.
Conducted RF IEC 61000-4-6 **Radiated RF IEC 61000-4-3**	3 Vrms 150 kHz to 80 MHz 3 V/m 80 MHz to 2.5 GHz	3 Vrms 3 V/m	Portable and mobile communications equipment should be separated from the Minerva RF Controller (MIN180S) and Minerva Disposable Handpiece (MIN9770) by no less than the distances calculated/listed below: $D=1.2\sqrt{P}$ 150kHz to 80MHz $D=1.2\sqrt{P}$ 80 to 800 MHz $D = 2.3\sqrt{P}$ 800 MHz to 2.5 GHz where P is the max power in watts of the transmitter and D is the recommended separation distance in meters. Field strengths from fixed transmitters, as determined by an electromagnetic site survey, should be less than the

			compliance levels. Interference may occur in the vicinity of equipment containing a transmitter.

Separation Distances

The Minerva RF Controller (MIN180S) and Minerva Disposable Handpiece (MIN9770) are intended for use in the electromagnetic environment in which radiated disturbances are controlled. The user can help prevent electromagnetic interference by maintaining a minimum distance between portable and mobile RF Communications Equipment and the Minerva RF Controller and Minerva Disposable Handpiece as recommended in **Table 18**, according to the maximum output power of the communications equipment.

Table 18: Separation Distances

Rated Max Output Power of transmitter (watts)	Separation distance according to frequency of transmitter (meters)		
	150 kHz to 80 MHz $D=1.2\sqrt{P}$	80 MHz to 800 MHz $D=1.2\sqrt{P}$	800 MHz to 2.5 GHz $D=2.3\sqrt{P}$
0.01	0.12	0.12	0.23
0.1	0.38	0.38	0.73
1	1.2	1.2	2.3
10	3.8	3.8	7.3
100	12	12	23

22.0 PARTS

Ordering information and related parts and accessories are found in **Table 19**.

Table 19: Parts List

Part Number	Description
MINCO2C	CO_2 Canister (5-pack)
MINARGC	Argon Canister (5-pack)
MINRFFS	Replacement Minerva RF Controller Footswitch
MINCRD1	Replacement Minerva RF Controller Power Cord (110 Volts, North America)
MINRGKT	RGA Biohazard Kit
MIN9770	Minerva Disposable Handpiece (single)
MIN3PAK	Minerva Disposable Handpieces (3-pack)
MIN180S	Minerva RF Controller

23.0 SERVICE RETURNS

Read these instructions prior to returning any used/unused potentially defective product to Minerva Surgical.

Contact Minerva Surgical Technical Support if the Minerva Disposable Handpiece or Minerva RF Controller fail to operate as intended. If product is to be returned to Minerva Surgical for any reason, Technical Support will issue a Returned Goods Authorization number (RGA #) and biohazard kit if applicable. Return the product according to the instructions provided with the Minerva Surgical-supplied biohazard kit.

Return the Minerva RF Controller according to the instructions provided by Minerva Surgical Technical Support. Be sure to clean the Minerva RF Controller before returning it and include all accessories in the box with the returned unit.

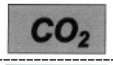
24.0 CALIBRATION AND PREVENTATIVE MAINTENANCE:

Calibration and Preventative Maintenance are not required for the Minerva RF Controller. Periodic verification of safety tests including leakage current in accordance with IEC 60601-1 is recommended in accordance with facilities internal procedures. The Minerva RF Controller is calibrated at the time of manufacture, and is equipped with a Power On Self Test (POST) function that verifies proper RF output each time it is powered on. Failure of the system to deliver proper RF output during this POST verification will result in an error. In the event of a POST failure, cycle power. If the POST failure is not cleared, contact Minerva Surgical customer service at 1-855-646-7874.

25.0 SYMBOLS

The symbols used on the Minerva RF Controller and Minerva Disposable Handpiece are listed in **Table 20**.

Table 20: Symbols list

Minerva Disposable Handpiece		Minerva RF Controller	
	Sterilized using irradiation		Power On
	Read Operator's Manual Prior To Use!		Power Off
	Do Not Reuse		Caution
	Do Not Resterilize		Equipotentiality
	Use By		Do Not Use in the Presence of Flammable Anesthetics
	Manufacturer		Type BF Applied Part
	Do Not Use if Package is Damaged		Risk of Electrical shock
	Keep Dry		Footswitch Connection
	Keep Away from Sunlight		Non-Ionizing Radiation
	Catalogue Number		Manufacturer
	Serial Number		Fuses
	Not Made with Natural Rubber Latex		Carbon Dioxide Canister
	MR Unsafe		Argon Canister
			Date of Manufacture

Manufactured by:
Minerva Surgical, Inc.
4255 Burton Drive
Santa Clara, CA 95054 USA
Phone: 1-855-646-7874
www.minervasurgical.com

Patents Pending