Minerva
Endometrial Ablation System

L0107 Rev. D

INSTRUCTIONS FOR USE (IFU)

MINERVA DISPOSABLE HANDPIECE AND DESICCANT SET

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MINERVA DISPOSABLE HANDPIECE AND DESICCANT SET

INSTRUCTIONS FOR USE

⚠ This document is a guide to the set-up and preparation of the Minerva Disposable Handpiece. This document is *not* a guide to the Minerva Endometrial Ablation System operation. Refer to the Minerva Endometrial Ablation System Operator's Manual for complete information on set-up, use, warnings, cautions, indications, contraindications and other relevant information.

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician trained in the use of the Minerva System.

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 Minerva Endometrial Ablation System Operator's Manual.
- Be aware of the appropriate sequence of actions detailed in the Minerva Endometrial Ablation System Operator's Manual 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 Minerva Endometrial Ablation System Operator's Manual and other educational materials prior to using the Minerva Endometrial Ablation System.

DEVICE DESCRIPTION

The Minerva Endometrial Ablation Set consists of the Minerva Disposable Handpiece and Desiccant (**Figure 1**).

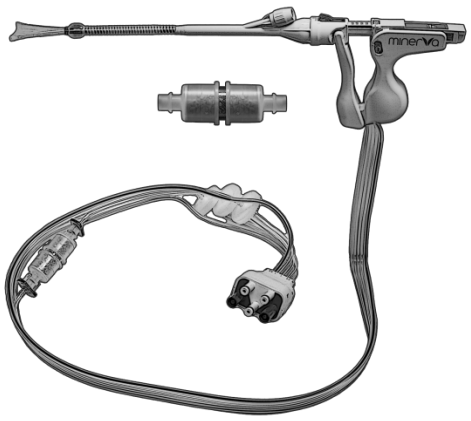

Figure 1: Minerva Endometrial Ablation Set

The Minerva Disposable Handpiece is a single-patient, single-use component of the Minerva Endometrial Ablation System. The 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. Refer to the Minerva Endometrial Ablation System Operator's Manual for a complete description.

INTENDED USE/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.

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 (PFA) 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

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.

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.
- IF THE UTERINE INTEGRITY TEST FAILS AFTER REASONABLE ATTEMPTS TO IMPLEMENT THE TROUBLESHOOTING PROCEDURES, 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.**

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.

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. 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.

CAUTIONS


Refer to Minerva Endometrial Ablation System Operator's Manual for complete information on the list of 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.
- 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 of the Operator's Manual.
- 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.

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)

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

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

MINERVA CLINICAL STUDIES SUMMARY

Minerva Single Arm Clinical Study

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.

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 ≤ 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 the amenorrhea rate, anesthesia regimen, length of procedure (Minerva Disposable Handpiece insertion to Minerva Disposable Handpiece removal), and responses from a patient satisfaction questionnaire.

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

1) Refractory menorrhagia with no definable organic cause
2) Female subject from age 25 to 50 years
3) Uterine sound measurement of 6.0cm to 10.0cm (external os to internal fundus)
4) One of the following criteria:
   A. Documented history of menorrhagia secondary to abnormal uterine bleeding (AUB).
   B. 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.
5) Premenopausal at enrollment as determined by FSH measurement ≤ 40 mIU/ml
6) Not pregnant and no desire to be pregnant in the future
7) Patient agrees not to use hormonal contraception or any other medical intervention for bleeding during the study
8) Able to provide written informed consent using a form that has been approved by the reviewing IRB/EC
9) Subject agrees to follow-up exams and data collection, including ability to accurately use menstrual diaries for PBLAC analysis
10) Subject who is literate or demonstrates an understanding on how to use menstrual diaries.

Exclusion Criteria

1) Pregnancy or subject with a desire to conceive
2) Endometrial hyperplasia as confirmed by histology
3) Presence of active endometritis
4) Active pelvic inflammatory disease
5) 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.
6) Presence of bacteremia, sepsis, or other active systemic infection
7) Active infection of the genitals, vagina, cervix, uterus or urinary tract at the time of the procedure
8) Known/suspected gynecological malignancy within the past 5 years
9) Known clotting defects or bleeding disorders
10) Untreated/unevaluated cervical dysplasia (except CIN I)
11) Known/suspected abdominal/pelvic cancer
12) Prior uterine surgery (except low segment cesarean section) that interrupts the integrity of the uterine wall (e.g., myomectomy or classical cesarean section)
13) Previous endometrial ablation procedure
14) Currently on medications that could thin the myometrial muscle, such as long-term steroid use (except inhaler or nasal therapy for asthma)
15) Currently on anticoagulants
16) Abnormal or obstructed cavity as confirmed by hysteroscopy or saline infusion sonohysterography (SIS), specifically:
    a. Septate or bicornuate uterus or other congenital malformation of the uterine cavity
    b. Pedunculated or submucosal myomas distorting the uterine cavity
    c. Polyps likely to be the cause of the subject's menorrhagia
    d. Intramural or subserosal myomas that distort the uterine cavity
17) Presence of an intrauterine device (IUD) which the patient is unwilling to have removed at the time of the operative visit
18) Presence of an implantable contraceptive device (e.g., Essure® or Adiana®).

19) Subject currently on hormonal birth control therapy or unwilling to use a non-hormonal birth control post-ablation (including a Mirena® device).
20) Subject who is within 6-weeks post-partum.
21) Any general health condition which, in the opinion of the Investigator, could represent an increased risk for the subject
22) Any subject who is currently participating or considers future participation in any other research of an investigational drug or device.

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 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 patients 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.

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 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 "failure" 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 Objective Performance Criterion (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-month 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)

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.

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 few exceptions (e.g., bleeding is assessed using the Alkaline Hematin method instead of PBLAC scores).

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.

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, and 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.

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			
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	

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 $\pm$ 0.5 minutes) was statistically significantly less than the procedure time for the Rollerball ablation procedure (17.2 $\pm$ 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).

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.

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.

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 up to 6 weeks. 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.

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.

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 Handpiece.
- The Minerva Desiccant is supplied non-sterile.
- The Minerva RF Controller is supplied in a semi-ready-to-use state. The shipping box contains the Minerva RF Controller, Minerva Footswitch, and a detached Power Cord.
- Minerva argon and CO_2 canisters are supplied separately.

WARNING This document is a guide to the setup and removal of the Minerva Disposable Handpiece and Desiccant Set. This document is ***not*** a guide to Minerva Endometrial Ablation System operation. Refer to the Minerva Endometrial Ablation System Operator's Manual for complete setup and use.

DIRECTIONS FOR USE

PRE-PROCEDURE

1. Open the sterile Minerva Disposable Handpiece package.
2. Place the Minerva Disposable Handpiece, with the connecting cord and the syringe into the sterile field while being careful to keep the non-sterile Desiccant pouch out of the sterile field.
3. Open the non-sterile Desiccant pouch. Remove the two end caps on the Desiccant.
4. Connect the Desiccant to the two ports on the tubing of the Connecting Cord. When properly connected you will feel or hear a click.

PROCEDURE

1. Complete the procedure by following the instructions described in the Minerva Endometrial Ablation System Operator's Manual.

POST-PROCEDURE

1. Using the supplied syringe, deflate the cervical balloon.
2. Unlock and withdraw the Minerva Disposable Handpiece from the patient.
3. Dispose the used Minerva Disposable Handpiece in accordance with hospital or clinic standard practice for biohazardous waste.

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