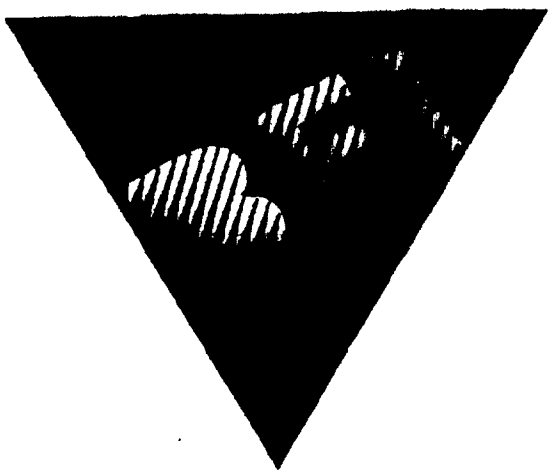
Hydro ThermAblator® (HTA®)

Installation & Operator's Manual

 # 55000-M



MEDICAL SYSTEMS

BEI Medical Systems Company, Inc.
100 Hollister Road
Teterboro, NJ 07608 USA
Phone: 201-727-4900
Fax: 201 727-4998
Mail: service@beimedical.com

EU Authorized Representative
NOT FOR SALES OR CUSTOMER SERVICE
QUALITY FIRST INTERNATIONAL LIMITED
20 Eversley Road Bexhill-on-Sea
East Sussex TN40 1HE
Phone: +44 (0) 208-522-1937
Fax: +44 (0) 208-522-1937

TABLE OF CONTENTS

TABLES

i **INTRODUCTION**

Carefully read this entire Operator's Manual, and view the Installation Operation video which is supplied with each HTA® unit, to become familiar with all of the HTA® features and controls before clinically using the equipment. This manual contains information about the proper procedures for inspecting, preparing, and operating the HTA®, and its care and storage after use. Failure to thoroughly understand and follow the instructions given in this manual may result in serious injury to the patient and/or the operator. Failure to follow the instructions written in this manual may result in damage to, or malfunction of, this equipment.

Follow the instructions contained within the operator's manuals of all equipment to be used in conjunction with the HTA® to avoid any possible hazard from equipment incompatibility.

Please contact BEI Medical Systems Company, Inc. for any questions about the information contained in this Operator's Manual, or for further information pertaining to the operation and safety of the HTA®. On site training is available upon request. Please contact BEI to make the necessary arrangements.

CAUTION - Federal Law restricts this device to sale by or on the order of a physician. The physician using the device must be trained in diagnostic hysteroscopy.

SECTION 1 Background and Clinical Information

BRIEF DEVICE DESCRIPTION

Hydro ThermAblator® (HTA®) is a software-controlled hysteroscopic thermal endometrial ablation system that consists of an operational unit, a heater canister, and a sterile procedure set. The procedure set consists of a sterile patient sheath assembly, a sterile cassette, a fluid level measurement reservoir, and a fluid collection bag. The system also requires the use of USP 0.9% saline, a standard hysteroscope, and a cervical-sealing tenaculum. It is designed to ablate the endometrial lining of the uterus by heating saline to a temperature of 90°C, by means of a heating element located in the external heater canister, and by recirculating this heated fluid through the uterus for a period of 10 minutes. The system includes various alarms and sensors to monitor the safe and effective delivery of the treatment therapy.

INDICATIONS

The HTA® is a hysteroscopic thermal ablation device intended to ablate the endometrial lining of the uterus in premenopausal women with menorrhagia (excessive uterine bleeding) due to benign causes for whom childbearing is complete.

CONTRAINDICATIONS

The device is contraindicated for use in a patient:

- who is pregnant or wants to be pregnant in the future, as pregnancy after ablation can be dangerous to both mother and fetus;
- who has known or suspected endometrial carcinoma or premalignant change of the endometrium, such as adenomatous hyperplasia;
- who has active pelvic inflammatory disease or hydrosalpinx;
- who has any anatomical or pathologic condition in which weakness of the myometrium could exist, such as, prior classic cesarean section or transmural myomectomy;
- who has an intrauterine device in place; or
- who has active genital or urinary tract infection, e.g., cervicitis, endometritis, vaginitis, cystitis, etc., at the time of treatment.

WARNINGS

NOTE: Failure to follow any instructions or to heed any warnings or precautions could result in serious patient injury.

General

- Although endometrial ablation with the HTA® significantly decreases the likelihood of pregnancy, it is not a sterilization procedure. The patient should be advised of appropriate birth control methods.

- Endometrial ablation does not eliminate the potential for endometrial hyperplasia or adenocarcinoma of the endometrium and may mask the physician's ability to detect or make a diagnosis of such pathology.

Technical

- The procedure set is provided sterile and is intended for single use only. Do not attempt to resterilize or reuse this component.

- The heater canister must be reprocessed after each treatment. Cross-patient contamination may result if this is not performed. The heater canister can be reprocessed up to 10 times, in accordance with the validated reprocessing procedures described in this manual (see page 61).

- Do not drape the sheath tubing over the patient's leg or place in contact with any part of the patient, as th tubing carries hot fluid.

- After the sheath has been placed in the patient during the startup phase, do not remove the sheath until post-treatment cooling cycle has been completed, as heated fluid may cause thermal injury to the patient See "Patient Cooling" section, Step 2 of manual (page 57).

- Excessive bleeding at the time of treatment may cause the tubing to become clogged. This condition ma cause a rise in the fluid level reservoir, triggering a high fluid level alarm. If the system cannot resolve thi condition, the procedure will be discontinued.

- The cassette must be properly installed, or the unit will not function properly and spillage of fluid will occu See "Cassette and Fluid level Measurement Reservoir Installation" section, after "INSTALLED" (page 44)

PRECAUTIONS

- Endometrial ablation procedures using the HTA® should only be performed by physicians trained in diagnostic hysteroscopy. Follow the user instructions in this manual to reduce the possibility of compromised safety, malfunction, and/or injury to the patient and/or user.

- To reduce risk of explosion, do not operate the HTA® in the presence of flammable anesthetics or oth flammable gas mixture.

- Ensure that the selected electrical supply outlet has a proper ground connection and complies with th HTA® input requirements, listed on the plate located on the rear of the unit. **Never** use a three (3) prong into a two (2) prong adapter.

- Do not connect any device rated higher than 3.15 amps at 220 VAC or 6.30 amps at 110 VAC to the auxiliary line cord located in the camera door (see Figure 15, Key Item #2, page 28).

- Never use the HTA® with equipment that has not been safety tested for excessive leakage current.

- The HTA® **MUST** only be connected to the patient using the patient sheath assembly provided in the Hydro ThermAblator® Procedure Set #55015.

- The HTA® control circuits are calibrated specifically for use with this sheath assembly. Use of any other hysteroscopic sheath assembly will lead to compromised safety of the patient and operator.

- Exercise care when handling liquids around this electrical equipment. Do not attempt to operate the HTA® if liquids have spilled on the unit.

- Ensure that the cable receptacle on the heater canister is completely dry. Do not operate the unit if liquid or saline has leaked into the thermistor interface of the heater canister. (See "Heater Canister Installation" section, Figure 22A, "Detail A" page 39).

- Follow hospital guidelines for handling contaminated fluids and disposables. At minimum, wear gloves and a mask at all times. Dispose of all disposables in appropriate containers. Clean and reprocess re-usables according to manufacturer's directions and hospital guidelines.

- Use caution when handling the fluid in the collection bag after treatment, as the fluid at this stage may still be **HOT** (approximately ≤ 45°C).

- Be certain that the height of the IV pole is properly adjusted to a height of 115 cm from the patient's uterus to the midpoint (80 mL) mark on the fluid level measurement reservoir (See Section 6, Step 11, page 46), as this height will allow proper fluid flow during the procedure.

- Leave the speculum in place throughout the treatment to avoid inadvertent sheath contact with patient.
- Patients who have undergone endometrial ablation and are later placed on hormone replacement therapy should have a progestin included in their regimen in order to avoid the increased risk of endometrial adenocarcinoma associated with unopposed estrogen replacement therapy.

The safety and effectiveness of the device has not been evaluated in patients:

- with a large uterine cavity (> 10.5 cm);
- with a small uterine cavity (< 6.0 cm);
- with submucosal myomas > 4 cm, bicornuate or full septate uterus;
- undergoing repeat endometrial ablation procedures (e.g., resection, ablation); or
- who are post-menopausal.

ADVERSE EVENTS

The HTA® device was evaluated in a randomized, prospective, multi-center clinical trial, comparing the HTA® to roller ball (RB) as the control arm. Adverse events for both study arms were reported from the time of procedure through the 1-year follow-up study period. The tables below describe these results:

Table 1a -- Adverse Events within 24 hours Post-Procedure

Adverse Event	HTA® Group n=184	RB Group n=85
uterine cramping	51 (28%)	21 (25%)
nausea	20 (11%)	2 (2%)
vomiting	20 (11%)	2 (2%)
abdominal pain	8 (4%)	2 (2%)
urinary tract infection	5 (3%)	2 (2%)
laceration	2 (1%)	2 (2%)
endometritis	2 (1%)	1 (1%)

Table 1b -- Adverse Events at 2 week Post-Procedure

Adverse Event	HTA® Group n=184	RB Group n=85
uterine cramping	37 (20%)	11 (13%)
transient change in appearance of cervical epithelium	19 (10%)	0 (0%)
vomiting	17 (9%)	2 (2%)
nausea	16 (9%)	4 (5%)
abdominal pain	6 (3%)	0 (0%)
urinary tract infection (UTI)	3 (2%)	0 (0%)
endometritis	1 (1%)	1 (1%)
thermal injury to extremity	1 (1%)	0 (0%)
vaginal infection	1 (1%)	0 (0%)
cervical laceration	1 (1%)	0 (0%)

Table 1c -- Adverse Events at 3, 6, and 12 months Post-Procedure*

Adverse Event	HTA® Group n=184	RB Group n=85
uterine cramping	25 (14%)	8 (9%)
vaginal infection	6 (3%)	2 (2%)
nausea	3 (2%)	0 (0%)
vomiting	3 (2%)	0 (0%)
abdominal pain	2 (1%)	1 (1%)
hematometra	1 (1%)	2 (2%)
urinary tract infection	1 (1%)	1 (1%)

* This table reports individual events. Multiple events may have occurred in the same patient.

Additional information related to some of these events is provided below:

- Peri-Operative Uterine cramping typically lasted a few days following ablation. Use of non-steroidal anti-inflammatory drugs (NSAIDs) prior to and following HTA® therapy was usually sufficient to manage cramping.
- Nausea and vomiting were generally attributed to certain types of general anesthesia.
- Asymptomatic alterations in cervical tissue, ranged from erythema to shallow ulcerations, and were resolved without treatment within 30 days following the ablation procedure.
- Patients with endometritis responded to a course of antibiotics.
- Hematometra was resolved with insertion of a uterine sound.
- Thermal injury to extremity involved a second degree burn in 1 HTA® subject. This burn occurred followin prolonged exposure of skin (lower leg) to the heated tubing of the HTA® during treatment. The subject was treated with topical antibiotics and dressing changes. The device was modified after the occurrence c this event to reduce this risk of injury.
- Other events, which occurred in no greater than 3% of subjects treated with the HTA®, included: diarrhea fever, headaches, abdominal distension, and post-ablation tubal sterilization syndrome.

In addition to the randomized, clinical study described above, a prototype of the HTA® was evaluated in a feasibility study, in which the following adverse events were reported:

- Fluid leakage into the vagina occurred in one subject, and was caused when the catheter sheath was withdrawn from the subject during the treatment cycle. This action caused the fluid to spill from the HTA® system and onto the perineum. **See Warnings section of manual.**
- Fluid leakage through fallopian tubes occurred in two subjects, and was caused when the fluid reservoir was elevated to a height greater than 115 cm above the uterus. This action increased the internal system pressure and intrauterine pressure. **See Precautions section of manual.**

POTENTIAL ADVERSE EFFECTS

The following adverse effects may potentially occur, but were not observed in clinical studies of the HTA®:

1. thermal injury to adjacent tissue;
2. heated saline escaping from the device system into the vascular spaces;
3. hemorrhage;
4. perforation of uterus;
5. complications with pregnancy (**NOTE**: pregnancy following endometrial ablation is dangerous to both the mother and the fetus); and
6. risks associated with hysteroscopy.

CLINICAL TRIALS SUMMARY

Purpose: The purpose of the study was to assess the safety and effectiveness of HTA® ablation, relative to RB ablation in terms of safety and effectiveness in the treatment of patients with menorrhagia due to benign causes in an anatomically normal uterine cavity.

Study Endpoints: The primary effectiveness endpoint was a validated diary scoring system (adapted from *Janssen CAH, Scholten PC, et al. based on "A Simple Visual Assessment Technique to Discriminate Between*

Menorrhagia and Normal Menstrual Blood Loss". Obstetrics & Gynecology, Vol. 85, No. 6, June 1995). Treatment success was defined as reduction in menses to a diary score of ≤ 75 in order to assure a return to eumenorrhea. Overall study success was a statistical difference of < 20% in the success rate between HTA® and RB in the reduction of excessive menstrual bleeding to at least normal levels. Secondary effectiveness endpoints evaluated were overall percent decrease in diary scores and responses from a quality-of-life questionnaire. Safety endpoints were adverse events associated with each procedure, including device-related complications, time of procedure, and type of anesthesia used.

Study Methods and Patients Studied: A randomized, prospective, multi-center clinical investigation was conducted at nine sites using investigators experienced with hysteroscopic roller ball endometrial ablation. Prior to acceptance in the study, subjects underwent a series of screening examinations which primarily documented bleeding status and uterine structure. Subjects were required to meet a set of entry criteria.

Key inclusion criteria for the study were:

- excessive uterine bleeding, as documented by the menstrual diary and calculation worksheet defined by Janssen (with a minimum score of 150);
- endometrial cavity measuring ≤ 10.5 cm;
- age ≥ 30 years; and
- previously failed, not tolerated, or refused medical therapy (i.e., Depo Provera, GnRH analogs, oral contraceptives, progestins, and Danocrine/Danazol) and as reported by the physician.

Key exclusion criteria for the study were:

- age > 50 years;
- active pelvic inflammatory disease;
- clotting defects, bleeding disorders, or anticoagulant treatments;
- abnormal pap smear that showed evidence of dysplasia; malignant pathology and/or simple hyperplasia, as documented by endometrial biopsy;
- history of gynecologic malignancy within the past 5 years;
- submucous myomas and/or polyps;
- intramural fibroids > 4cm, as documented on ultrasonogram, thought to be contributing to menorrhagia, such as those deforming the uterine cavity;
- congenital uterine anatomical anomaly, such as full septate or bicornate uterus;
- previous endometrial ablation procedure; and
- previous classic Cesarean section.

Subjects received one dose of Lupron 7.5mg on Cycle Day 21 ± 2 days. Treatment took place on Cycle Day 19 - 27 after injection. After completion of treatment, subjects were followed at 2 weeks, and 3, 6, and 12 months post-treatment.

Description of Patients: Two hundred seventy six subjects were enrolled in the the study. Baseline demographic and gynecological variables were statistically equivalent between the two groups with regard to age (HTA® 40.7 years, RB 40.6 years), race, body mass index, mean baseline diary score (HTA® 596.6, RB 585.5) and other criteria. The table below describes the accountability of subjects throughout the study period

Table 2 -- Subject Accountability

Subjects:	HTA®	RB	Total
enrolled in study	187	89	276
received no treatment	3	4	7
received incomplete treatment	7	0	7
for whom 12-month data not available:	10	2	12
received hysterectomy[1]	2	0	2
died in non-device-related events	2	0	2
lost to follow-up	6	2	8
for whom 12-month data are available	167	83	250

† Both subjects were ≥ 40 years old; reasons for hysterectomy were bleeding (1) and pain/myoma (1)

Results:

mary Effectiveness Endpoint

Results with respect to the primary effectiveness endpoint compared the pre-treatment and 1-year post-treatment bleeding scores for both HTA® and RB study groups, and are presented in the table below:

Table 3a -- Effectiveness: Diary Scores at 1 year

	HTA® n = 187*	RB n = 89*
number of successful subjects (diary score ≤ 75)	128	68
study success rate (# successful/total subjects)	68.4%	76.4%
number of subjects with amenorrhea (diary score = 0)	66	42
amenorrhea rate (# with diary score = 0/total subjects)	35.3%	47.1%

*This table presents the intent-to-treat results of the study data. See "Subject Accountability" section above fc accountability of all subjects enrolled in study.

Secondary Effectiveness Endpoint

Results with respect to the secondary endpoint of quality of life (QoL) compared QoL scores at pre-treatment and 12-months post-treatment for both HTA® and RB study groups, and are presented in the table below:

Table 3b -- Effectiveness: Quality of Life (QoL) at 1 year

	HTA®	RB
..mber of subjects who responded to questionnaire	167	83
QoL score (mean ± SD)†		
@ baseline	54.2 ± 13.5	53.3 ± 13.5
@ 1 year	13.0 ± 15.0	11.4 ± 15.2
leisure activities affected		
@ baseline	70.1%	66.3%
@ 1 year	21.6%	28.9%
work and activities of daily life affected		
@ baseline	90.4%	91.0%
@ 1 year	19.8%	20.0%

† The QoL information was obtained from the Ruta QoL questionnaire, with a scoring scale range of 2.6 - 89.5 A higher score is associated with increased menorrhagia (e.g., mild = 37.6; moderate = 46.7; and severe = 50.7).

Safety Endpoints

Results related to safety information were provided in terms of adverse event information, overall time of treatment, and type of anesthesia provided. Adverse event information is described in the "Adverse Events" section above. Overall mean treatment time was 26.4 ± 12.1 and 32.2 ± 12.2 for HTA® and RB, respectively.

Anesthesia was delivered at the discretion of the investigator and attending anesthesiologist. General anesthesia was administered to 55% and 76% of HTA and RB subjects, respectively. Of the HTA group, 30% subjects received a paracervical block with IV sedation as compared to 13% of the RB subjects. Fifteen and 9% of HTA and RB subjects, respectively, received paracervical block without IV sedation.

Conclusions: At 12 months of follow-up, HTA® Hysteroscopic ablation was demonstrated to be safe and effective, when compared to hysteroscopic roller ball ablation in (1) reduction of menstrual bleeding to a clinically acceptable level in menorrhagic women who had completed their childbearing and (2) improvement i reported quality of life (QoL), as measured by a validated QoL questionnaire (based on the *Ruta, DA et al. ssessment of Patients with Menorrhagia: How Valid is a Structured Clinical History as a Measure of Health Status?" Quality of Life Research, Vol. 4, p. 33-40* questionnaire).

PATIENT SELECTION

Menorraghia can be caused by a variety of underlying problems, including but not limited to, endometrial cancer, myomas, polyps, anovulation, drugs, and dysfunctional uterine bleeding. Patients should always be evaluated to determine the cause of their excessive uterine bleeding before any treatment option is initiated.

PATIENT COUNSELING

As with any procedure, the physician needs to discuss with the patient, the risks, benefits, and alternatives to endometrial ablation.

The device is intended for use only in women who do not desire to bear children because the likelihood of pregnancy is significantly decreased following this procedure. Patients of childbearing capacity should be counseled that endometrial ablation is not a sterilization procedure and should be provided an appropriate birt control method. Patients with childbearing capacity should be cautioned that serious potential complications may result to both mother and fetus if they should become pregnant.

Vaginal discharge is typically experienced during the first few days following ablation and may last as long as weeks. Generally, the discharge will be bloody during the first few days, then serosanguinous at one wee post-treatment, and watery thereafter.

PRETREATMENT PREPARATION OF PATIENT

The lining of the uterus should be thinned prior to HTA®. This can be accomplished by timing the menstrual cycle to the early proliferative phase or administering pretreatment drugs such as danocrine or GnRH agonists prior to performing the endometrial ablation. The optimum pretreatment regimes have not been determined at this time.

It is recommended that a non-steroidal anti-inflammatory drug (NSAID) be given at least one hour prior to treatment and continued post-operatively as necessary to reduce intra-operative and post-operative uterine cramping.

CLINICAL USE CHECKLIST

Prior to the use of the HTA® on a patient, the physician should complete the following checklist to better ensure safe and effective use of the device system. Note that this is not a comprehensive list, but attempts to cover some of the key issues before a physician uses the HTA®:

The physician must:

- be trained in diagnostic hysteroscopy;
- along with adjunctive personnel, review and be familiar with HTA® training material (manual, training video etc.);
- verify that HTA® fluid reservoir is positioned 115 cm above the patient's uterus;
- be able to perform diagnostic hysteroscopy with room temperature saline;
- be able to verify that uterine cavity is prepared for the ablation procedure and is able to identify cornu;
- along with adjunctive personnel, be able to initiate the heating process of HTA® treatment;
- be able to observe, confirm, and maintain proper placement of hysteroscopic tip; The tip should be positioned just inside of the internal os, and the sheath should not be advanced further into the uterine cavity during the treatment phase or pulled back out of the uterine cavity unit the cooling phase is complete;
- **NEVER** remove the sheath until the post-treatment cooling phase is complete, as confirmed by HTA® unit
- be aware of the appropriate sequence of actions, detailed in the Diagnostic and Troubleshooting section of this manual, to halt, resolve and/or continue the treatment, in the event the system detects a fluid loss of 1 mL; and
- be aware that, on the day of treatment, previously undetected pathology (e.g., submucous myomas), which may affect treatment results, may be present in the endometrial cavity.