Boston Scientific

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Genesys HTA ProCerva™

Procedure Set

Refer to the Genesys HTA™ System User's Manual for complete setup and use.

℞ ONLY

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician. The physician using the device must be trained in diagnostic hysteroscopy.

WARNING

Contents supplied STERILE using an ethylene oxide (EO) process. Do not use if sterile barrier is damaged. If damage is found, call your Boston Scientific representative.

For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device 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 device may lead to injury, illness or death of the patient.

After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.

INTRODUCTION

The Genesys HTA ProCerva Procedure Set consists of a disposable procedure sheath, a cassette, and a drainage bag. It is to be used only with the Genesys HTA System Operational Unit.

WARNING

This document is a guide to the setup and removal of the procedure set. This document is *not* a guide to system operation. Refer to the Genesys HTA System User's Manual for complete setup and use.

INTENDED USE/INDICATIONS FOR USE

The Genesys HTA System 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 system 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 pyosalpinx;
- who has hydrosalpinx;
- in whom a tight cervical seal cannot be established and maintained around the procedure sheath;
- who has any anatomical condition (e.g., history of previous classical cesarean section or transmural myomectomy) or pathologic condition (e.g., long term medical therapy) that could lead to weakening of the myometrium;
- who has an intrauterine device in place; or
- who has an active genital or urinary tract infection (e.g., cervicitis, endometritis, vaginitis, cystitis, etc.), at the time of treatment.

WARNINGS & CAUTIONS

To ensure the user is aware of all potential hazards and risks associated with the Genesys HTA System, carefully read all general warnings, technical warnings and cautions listed below.

Leakage of heated fluid can cause serious burn or injury to the tissue contacted, including tissue in or around the cervix, vagina, perineum, etc.

Failure to follow instructions or to heed any WARNINGS or CAUTIONS could result in serious patient or user injury.

General Warnings

- Although endometrial ablation with the Genesys HTA System 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.
- Patients who undergo endometrial ablation procedures who have previously undergone tubal ligation may be at increased risk of developing post ablation tubal sterilization syndrome which can require hysterectomy. This can occur as late as 10 years post-procedure.
- DO NOT perform same day HTA procedure and hysteroscopic tubal occlusion/sterilization. Ablation may cause intrauterine synechiae which can compromise (i.e. prevent) the 3-month confirmation test (HSG) for the tubal occlusion device. Women who have inadequate 3-month confirmation tests cannot rely on the tubal occlusion device for contraception.
- Bench and clinical studies have been conducted which demonstrate that the HTA procedure can be safely and effectively performed with nickel titanium tubal micro-inserts in place. However, the HTA procedure should only be performed after the 3-month tubal occlusion confirmation test.

Technical Warnings

- The Genesys HTA ProCerva Procedure Set is provided sterile and is intended for single use only. Do not attempt to resterilize or reuse any component of the procedure set.
- Scope adapters should be reprocessed in accordance with the validated cleaning and sterilization procedure provided in the Genesys HTA System User's Manual. Do not reuse any scope adapter that has not been cleaned and sterilized accordingly.
- Do not use excessive force when attaching the sheath to the scope adapter as such force may damage device components. Thermal injuries to patients have been reported in association with cracked or damaged procedure sheaths/adapters.
- Care must be taken with advancement and movement of the procedure sheath to avoid uterine perforation.
- The physician must maintain control of the procedure sheath (i.e., not hand it off to another individual) for the duration of the treatment to avoid compromising the cervical seal. A compromise of the cervical seal could result in fluid leakage through the cervix, which could result in thermal injury to surrounding tissue.
- Once heating has begun do not remove the procedure sheath until the post-treatment cooling cycle has been completed as confirmed by the display screen, as heated fluid may cause thermal injury to the patient.
- If system cooling is not possible (i.e., power loss), do not remove the procedure sheath from the patient until fluid in the uterus has cooled. It may take up to 10 minutes to ensure that fluid temperature in the uterus is below 45 °C. Exercise care when handling the procedure set, because the fluid may still be hot.
- Excessive menstrual clotting at the time of treatment may cause the Genesys HTA ProCerva Procedure Set to become clogged. This condition may trigger an alert. If the condition cannot be resolved, the procedure will be discontinued. To avoid clogging the fluid lines with blood clots, the procedure should not be scheduled during menses. Also, consideration should be given to pretreatment with drugs such as GnRH agonists prior to performing the endometrial ablation to help induce hypoestrogenic state.
- Do not place the procedure sheath tubing over the patient's leg or in contact with any part of the user's or patient's anatomy, as the tubing carries hot fluid and contact could result in thermal injury. The temperature of the tubing could be up to 55 °C.
- Ensure that the temperature of the fluid in the cassette is below 45 °C prior to disconnection of the Genesys HTA ProCerva Procedure Set.
- Do not look directly into the control unit's laser aiming beam. Light from the LED may cause retinal damage.
- Do not over-dilate the cervix.

Cautions

- Endometrial ablation procedures using the Genesys HTA System should be performed only by physicians trained in diagnostic hysteroscopy procedures. Follow all Genesys HTA System instructions to reduce the possibility of compromised safety, malfunction, and/or injury to the patient and/or the user.
- To avoid the risk of electric shock, ensure that the selected electrical supply outlet has a proper ground connection and complies with the information listed on the label located on the rear of the control unit.
- To reduce the risk of explosion, do not operate the Genesys HTA System in the presence of flammable anesthetics or a flammable gas mixture with air, oxygen, or nitrous oxide.
- Never use the Genesys HTA System with equipment that has not been safety tested for excessive leakage current.
- Exercise care when handling liquids around electrical equipment. Do not attempt to operate the Genesys HTA System if liquid has spilled onto the unit.
- The Genesys HTA System must be used only with the procedure sheath provided in the Genesys HTA ProCerva Procedure Set. Use of any other hysteroscopic procedure sheath sets will lead to compromised safety for the patient and user.
- Do not hang more than three liters of saline from the hook on the IV pole.
- Confirm that the vaginal speculum is an adequate size (width and length) to assure full separation of vaginal and vulvar tissue away from the procedure sheath, to avoid inadvertent thermal injury, and to provide visibility of the cervix. The temperature of the sheath at this location could be up to 65 °C.
- Do not rest the procedure sheath on the vaginal speculum during the procedure.
- Leave the vaginal speculum in place throughout the procedure.
- Confirm that the height of the control unit handle is properly adjusted to the height of the patient's uterus to allow proper fluid flow and pressure, during the procedure. The laser aiming beam can be used as a secondary means to assist with proper height adjustment.
- Ensure that the height of the control unit handle is no higher than the height of the patient's uterus or fluid leakage into the peritoneal cavity and vagina may occur during the procedure.

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- Do not grasp the procedure sheath with the tenaculum as doing so may damage the procedure sheath which could result in thermal injury.
- Throughout the procedure, carefully observe the junction of the procedure sheath with the external cervical os to confirm a tight cervical seal and that there is no fluid leakage.
- Be Aware: The fluid loss alarm signals a loss of at least 10 mL of fluid. Fluid losses in excess of 10 mL may occur in cases when the alarm is triggered.
- Use caution when handling the fluid in the drainage bag after treatment, as the fluid at this stage may still be hot.
- Follow hospital procedures for handling contaminated fluids and disposables.
- Do not attempt to repair or alter any components/parts of the Genesys HTA™ System. All repairs and servicing are to be performed only by authorized Boston Scientific service personnel. See the Warranty.
- Patients who have undergone endometrial ablation, who 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 irrespective of whether total amenorrhea has been achieved after ablation.
- Use Caution when performing the Genesys HTA System procedure on patients with nickel sensitivity, as the Genesys HTA ProCerva™ Procedure Set contains nickel.

The safety and effectiveness of the Genesys HTA System has not been evaluated in patients:

- with a large uterine cavity (> 10.5 cm);
- with a small uterine cavity (< 6.0 cm);
- with submucous myomas and/or polyps;
- with intramural fibroids > 4 cm, as documented on ultrasonogram, thought to be contributing to menorrhagia, such as those which distort the uterine cavity;
- with bicornuate or full septate uterus;
- undergoing repeat endometrial ablation procedures (e.g., resection, ablation); or
- who are post-menopausal.

ADVERSE EVENTS

The first generation HTA™ System was evaluated in a randomized, prospective, multi-center clinical trial, comparing the HTA System to Rollerball (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. Tables 1a, 1b, and 1c present these results.

Table 1a. Adverse Events within 24 Hours Post-Procedure

Adverse Events	HTA System Group n = 184	RB Group n = 85
Uterine cramping	51 (28%)	21 (25%)
Nausea	20 (11%)	4 (5%)
Vomiting	20 (11%)	2 (2%)
Abdominal pain	8 (4%)	2 (2%)
Urinary tract infection (UTI)	5 (3%)	2 (2%)
Laceration	2 (1%)	2 (2%)
Endometritis	2 (1%)	1 (1%)

Table 1b. Adverse Events at 2 Weeks Post-Procedure

Adverse Events	HTA System Group n = 184	RB Group n = 85
Uterine cramping	37 (20%)	11 (13%)
Transient change in appearance of the 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 Events	HTA System 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%)

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

Additional information related to some of the adverse events reported during the multi-center clinical trial 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 treatment with the HTA System 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 System subject. This burn occurred following prolonged exposure of skin (lower leg) to the heated tubing of the HTA System during treatment. The subject was treated with topical antibiotics and dressing changes. The system was modified after the occurrence of this event to reduce this risk of injury.
- Other events, which occurred in no greater than 3% of subjects treated with the HTA System, included: diarrhea, fever, headaches, abdominal distension, and post-ablation tubal sterilization syndrome.

During the development of the first generation HTA System, prior to the multi-center randomized clinical study described above, a prototype was evaluated in a feasibility study, in which the following adverse events were reported:

- Fluid leakage into the vagina occurred in one subject, when the procedure 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.[1]
- Fluid leakage through fallopian tubes occurred in two subjects, when the fluid reservoir was elevated to a height greater than 115 cm (45 inches) above the patient's uterus. This action increased the internal system pressure and intrauterine pressure.[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 the first generation HTA System:

- thermal injury to adjacent tissue, including cervix, vagina, vulva and/or perineum;
- heated saline escaping from the system into the vascular spaces;
- hemorrhage;
- perforation of uterus;
- complications with pregnancy (Note: Pregnancy following any endometrial ablation procedure is dangerous to both the mother and the fetus.);
- risks associated with hysteroscopy;
- post ablation tubal sterilization syndrome;
- infection or sepsis; and
- complications leading to serious injury or death.

CLINICAL TRIAL SUMMARY

Purpose: To evaluate the safety and effectiveness of the first generation HTA System in comparison to hysteroscopic Rollerball (RB) technique for endometrial ablation in women with menorrhagia due to benign causes for whom childbearing was complete.

Study Endpoints: The primary effectiveness endpoint was a validated pictorial menstrual blood loss 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 a reduction in menses from a diary score of > 150 to ≤ 75 at one year. Overall study success was defined as a statistical difference of < 20% in patient success rates between the HTA System and RB. Secondary effectiveness endpoints evaluated were overall percent decreases in diary scores and responses to a quality-of-life questionnaire. Safety endpoints were adverse events associated with each procedure, including system-related complications, time of procedure, and type of anesthesia used.

Study Methods and Patients Studied: A randomized (2:1), prospective, multi-center clinical investigation was conducted at nine sites using investigators experienced with hysteroscopic Rollerball 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 but > 6.0 cm;
- age ≥ 30 years; and
- previously failed, not tolerated, or refused medical therapy (i.e., Depo Provera™ Preparation, GnRH analogs, oral contraceptives, progestins, and Danocrine™ Suppressant/ 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 > 4 cm, 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 bicornuate uterus;
- previous endometrial ablation procedure; and
- previous classic cesarean section.

Subjects received one dose of Lupron™ Pharmaceutical 7.5 mg 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, 12, 24 and 36 months post-treatment.

Description of Patients: Two hundred seventy six subjects were enrolled in the study at a 2-1 ratio of HTA System vs. Rollerball respectively. Baseline demographic and gynecological variables were statistically equivalent between the two groups with regard to age (HTA System 40.7 years, RB 40.6 years), race, body mass index, mean baseline diary score (HTA System 596.6, RB 585.5) and other criteria. Table 2 describes the accountability of subjects throughout the study period.

[1] During the treatment cycle and during cooling when the fluid is hot, the display screen in the Genesys HTA System cautions the user not to remove the procedure sheath.

[2] The first generation HTA System was redesigned to address fluid leakage concerns resulting from the height of the fluid reservoir. The Genesys HTA System control unit is mounted on an adjustable-height pedestal that facilitates aligning the patient's uterus with the height of the control unit handle. A laser aiming beam from the control unit is a secondary means of ensuring proper height of the control unit.

Table 2. Subject Accountability

	HTA™ System	RB	TOTAL
Intent to Treat Population	**187**	**89**	**276**
No treatment received	-3	-4	-7
Incomplete treatments	-7	0	-7
Complete Treatments	**177**	**85**	**262**
Subjects not available at 12 month follow-up	-2	0	-2
Unrelated death	-6	-2	-8
Lost to follow-up	-2	0	-2
Hysterectomy†			
Population with 12-Month Data Available	**167**	**83**	**250**
Subjects not available at 24 month follow-up	-9	-7	-16
Lost to follow-up	-10*	-1	-11
Hysterectomy	-1	-2	-3
Repeat ablations			
Subjects Lost to Follow-up at 12 Months, returned at 24 Months	+4	+1	+5
Population with 24-Month Data Available	**151**	**74**	**225**
Subjects not available at 36 month follow-up	-5	-5	-10
Lost to follow-up	-7	-4	-11
Hysterectomy	-3	0	-3
Repeat ablations	-1	-1	-2
Uterine Artery Embolization			
Subjects Lost to Follow-up at 24 months, returned at 36 Months	+1*	+3	+4
Population with 36-Month Data Available	**136**	**67**	**203**

† Subjects were > 40 years old; reasons for hysterectomy were bleeding (1) and pain/myoma (1).
* One subject previously reported as having a hysterectomy, returned at 36 months and had not received a hysterectomy.

Primary Effectiveness Endpoint

Success was based on a reduction in excessive uterine bleeding to normal levels or better. A success at 12 months post-treatment is defined as a reduction in diary score from ≥ 150 pre-treatment to ≤ 75. Success at 24 and 36 months is defined as amenorrhea (no bleeding), hypomenorrhea (light bleeding), or eumenorrhea (normal menstrual bleeding) as reported by subject via questionnaire. Results at 12, 24 and 36 months post-treatment are presented in Table 3a for the Intent to Treat (ITT) Population.

Table 3a. Effectiveness: Bleeding Rates for the Intent to Treat Population

Intent to Treat Population: n = 276	HTA System n = 187			RB n = 89		
Months post treatment	**12[a]**	**24[b]**	**36[b]**	**12[a]**	**24[b]**	**36[b]**
Number of successful subjects	128	139	127	68	68	62
Study success rate	68%	74%	68%	76%	76%	70%
Number of subjects with Amenorrhea	66	70	72	42	34	31
Amenorrhea rate	35%	37%	39%	47%	38%	35%

Note: Intent to Treat (ITT) population represents all subjects enrolled in the study including those considered as failures because they were not available for follow-up, did not receive treatment, and/or received partial treatment. Therefore, the ITT group represents a worst case scenario for effectiveness. See Subject Accountability section for complete accounting of all subjects enrolled in the study.
a Based on diary score.
b Based on questionnaire response.

Secondary Effectiveness Endpoint

Quality of Life (QOL) information was obtained by comparing QOL scores obtained via questionnaire at pre-treatment and at 12, 24, and 36 months post-treatment. These scores were compared and the results are presented in Table 3b.

Table 3b. Effectiveness: Quality of Life (QOL)

	HTA System	RB
Number of subjects who responded @ 1 year	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%
Number of subjects who responded @ 2 years	151	74
QOL score at 2 years++	11.0	10.0
Number of subjects who responded @ 3 years	136	67
QOL score at 3 years++	5.0	4.5

† 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).
++There is no standard deviation noted for 2 years or 3 years.

In addition, 98% of HTA System subjects and 97% of RB subjects reported satisfaction with their treatments at 36 months post treatment.

Safety Endpoint: Adverse event information is described in the *Adverse Events*. Overall mean treatment time was 26.4 ± 12.1 minutes and 32.2 ± 12.2 minutes for the HTA System and RB groups, respectively. Anesthesia was delivered at the discretion of the investigator and attending anesthesiologist. General anesthesia was administered to 55% and 76% of the HTA System and RB subjects, respectively. Paracervical block with IV sedation was administered to 30% and 13% of the HTA System and RB subjects, respectively; and paracervical without IV sedation was administered to 15% and 9% of the HTA System and RB subjects, respectively.

POST-APPROVAL STUDY SUMMARY

Study Objective

To prospectively collect data on the use of the Genesys HTA™ System under normal clinical use.

Primary Endpoint

Clinically significant subject burn with the Genesys HTA System.

Secondary Endpoint

Technical complaint with the Genesys HTA System (i.e. disposable and hardware issues).

Primary Statistical Hypothesis

The subject rate of clinically significant burns with the Genesys HTA System is not significantly greater than 1%.

Study Design and Patients Studied

A multi-center, single-arm, performance goal, prospective registry study with a planned number of 1,325 subjects and up to 100 study sites was conducted using investigators experienced with the HTA System. All enrolled subjects were required to meet the approved indications for use of the Genesys HTA System prior to acceptance in the study. Potential study subjects meeting any of the labeled Contraindications were excluded from the study.

Total Number of Enrolled Study Sites and Subjects

Eighteen (18) sites participated in the study. A total of 1,014 subjects were enrolled. 992 subjects were in the Intent-to-Treat (ITT) population, 931 subjects were in the Evaluable Population, and 61 subjects were in the Incomplete Population.

Total enrollment was less than the planned number of 1,325 due an interim analysis using the O'Brien-Fleming stopping rule. This rule followed the group-sequential analysis decision rules for efficacy where enrollment could cease early if the rate of clinically significant burns for the registry was low and significantly less than the 1.0% stated in the protocol.

The rate of clinically significant burns for the 820 Evaluable subjects at the time of the first group-sequential decision rule (0.1%) (1/820) was statistically significantly lower ($p<0.005$) than the hypothesis rate of 1.0%. This result enabled the study to not require any additional subject enrollment and it ceased at 1,014 subjects.

Study Visits and Follow-up Requirements

Study visits were all in-person and were limited to investigators reviewing the eligibility requirements with the subject, obtaining Informed Consent, and performing the procedure; all could be performed same-day. Any additional study visits were related to follow-up only and as scheduled in the protocol, only required for subjects that experienced a burn. Follow-up visits for subjects that experienced a burn were scheduled ≥ 21days post-procedure.

Final Primary Endpoint Findings

Study success was based on the subject rate of clinically significant burns being not significantly greater than 1%.

Clinically significant burns were defined as:

Deep 2nd degree: Burns that:

- Involve both internal anatomy (e.g. vagina, cervix) and external anatomy (e.g. vulva, perineum, buttocks) or
- Require medical or surgical intervention (e.g., a prescription, systemic antibiotics, debridement, skin grafting, etc.); over-the-counter treatments (e.g. topical burn treatments) or prophylactic medications (medications not intended for treatment of the burn but given per the treating physician's standard practice for prophylaxis, even if these are prescription medications) would not fulfill these criteria (and hence their usage alone would not make these clinically significant burns).

3rd degree: Full Thickness

- Any burns that cannot be verified to satisfy the criteria for non-clinically significant burns with follow-up ≥ 21 days after the procedure.

Non-Clinically Significant Burns were captured in the study, but were not included in the primary endpoint calculation. To be considered a non-clinically significant burn it must meet the following criteria:

1st degree: Superficial burns that are verified to be limited to 1st degree burns through follow-up ≥ 21 days after the procedure.

Superficial 2nd degree: Burns that are verified through follow-up ≥ 21 days after the procedure and do NOT:

- Involve both internal anatomy (e.g. vagina, cervix) and external anatomy (e.g. vulva, perineum, buttocks) and
- Require medical or surgical intervention (e.g., a prescription, systemic antibiotics, debridement, skin grafting, etc.)

As described in Table 4, four (4) burns were experienced in the study. Three (3) were considered non-clinically significant and one (1) was deemed clinically significant (due to internal and external anatomy involvement) as defined per the protocol. All of the burns occurred during the procedure, none required intervention, three (3) resolved without any residual effects, and one (1) was recovering/resolving at follow up.

As defined in Table 5, one (1) clinically significant burn was experienced in the study (0.1%), meeting the Primary Statistical Hypothesis that the subject rate of clinically significant burns with the Genesys HTA System be no greater that 1.0%. The clinically significant burn rate experienced in the study (0.1%) was significantly lower ($p<.005$) than the Primary Statistical Hypothesis.

Table 4. Registry Study – Burn Listings (N=931)

Initial Burn Classification	Onset Timing	Internal Anatomy Involved	External Anatomy Involved	Potential Cause	Action Taken	Medication Given	Type of Intervention	Outcome	Change from Initial Assessment	Clinically Significant
1st Degree	During procedure	Cervix	No	Patient Anatomy	Medication Given-Prophylactic Antibiotic Gel	Yes	None	Recovering/ Resolving	No	No
1st Degree	During procedure	Cervix	No	Poor Cervical Seal	No additional action taken	No	None	Resolved without residual effects	No	No
Superficial 2nd Degree	During procedure	Cervix	No	Other	Medication Given-Prophylactic Antibiotics, Estrogen Cream	Yes	None	Resolved without residual effects	No	No
Superficial 2nd Degree	During procedure	Vagina	Perineum	Inadvertent Movement of the Sheath, Poor Cervical Seal, Other	Medication Given-Silvadene Cream	Yes	None	Resolved without residual effects	No	Yes

Table 5. Primary Endpoint – Burn Rate (ITT, Evaluable and Incomplete Population) for the Final Analysis (N=931)

	ITT Population (N=992)	95% CI	Evaluable Population (N=931)	95% CI	Incomplete Population (N=61)	95% CI
Any Burns at Procedure	0.4% (4/992)	[0.1%,1.0%]	0.2% (2/931)	[0.0%,0.8%]	3.3% (2/61)	[0.4%,11.3%]
Clinically Significant Burns	0.1% (1/992)	[0.0%,0.6%]	0.1% (1/931)	[0.0%,0.6%]	0% (0/61)	[0.0%,5.9%]
Superficial 2nd Degree involve with internal anatomy and external anatomy and require medical or surgical intervention	0.1% (1/992)	[0.0%,0.6%]	0.1% (1/931)	[0.0%,0.6%]	0% (0/61)	[0.0%,5.9%]
Deep 2nd Degree	0% (0/992)	[0.0%,0.4%]	0% (0/931)	[0.0%,0.4%]	0% (0/61)	[0.0%,5.9%]
3rd Degree	0% (0/992)	[0.0%,0.4%]	0% (0/931)	[0.0%,0.4%]	0% (0/61)	[0.0%,5.9%]
Clinically Non-significant Burns	0.3% (3/992)	[0.1%,0.9%]	0.1% (1/931)	[0.0%,0.6%]	3.3% (2/61)	[0.4%,11.3%]
1st Degree	0.2% (2/992)	[0.0%,0.7%]	0% (0/931)	[0.0%,0.4%]	3.3% (2/61)	[0.4%,11.3%]
Superficial 2nd Degree	0.1% (1/992)	[0.0%,0.6%]	0.1% (1/931)	[0.0%,0.6%]	0% (0/61)	[0.0%,5.9%]
Deep 2nd Degree	0% (0/992)	[0.0%,0.4%]	0% (0/931)	[0.0%,0.4%]	0% (0/61)	[0.0%,5.9%]
3rd Degree	0% (0/992)	[0.0%,0.4%]	0% (0/931)	[0.0%,0.4%]	0% (0/61)	[0.0%,5.9%]
Overall Clinically Significant Burns at follow-up days >= 21 days*	0.1% (1/992)	[0.0%,0.6%]	0.1% (1/931)	[0.0%,0.6%]	0% (0/61)	[0.0%,5.9%]
Superficial 2nd Degree involve with internal anatomy and external anatomy and require medical or surgical intervention	0.1% (1/992)	[0.0%,0.6%]	0.1% (1/931)	[0.0%,0.6%]	0% (0/61)	[0.0%,5.9%]
Deep 2nd Degree	0% (0/992)	[0.0%,0.4%]	0% (0/931)	[0.0%,0.4%]	0% (0/61)	[0.0%,5.9%]
3rd Degree	0% (0/992)	[0.0%,0.4%]	0% (0/931)	[0.0%,0.4%]	0% (0/61)	[0.0%,5.9%]
*Including clinically significant burns at procedure and clinically significant burns at >= 21 days upgraded from clinically non-significant burns at procedure.						

Table 6 – Serious Adverse Device Effects
MedDRA Outcome (ITT, Evaluable and Incomplete Population) for the Final Analysis (N=931)

	ITT Population (N=992)	95% CI	Evaluable Population (N=931)	95% CI	Incomplete Population (N=61)	95% CI
Subjects with at least one Serious adverse event	0.1% (1/992)	[0.0%,0.6%]	0.1% (1/931)	[0.0%,0.6%]	0% (0/61)	[0.0%,5.9%]
Injury, poisoning and procedural complications (System Organ Class)	0.1% (1/992)	[0.0%,0.6%]	0.1% (1/931)	[0.0%,0.6%]	0% (0/61)	[0.0%,5.9%]
Thermal burn (Preferred Term)	0.1% (1/992)	[0.0%,0.6%]	0.1% (1/931)	[0.0%,0.6%]	0% (0/61)	[0.0%,5.9%]

Final Secondary Endpoint Findings

Seventeen (17) procedures involved a technical complaint and were stopped prior to completion. Fourteen (14) of these technical complaints were related to fluid leak, either a visible fluid leak or an inability to obtain an adequate seal. Thirteen (13) of these incomplete procedures were stopped prior to the delivery of heated saline phase.

Serious Adverse Device Effects (SADEs)

Per the approved protocol, an SADE is an adverse device effect resulting in any of the consequences characteristic of a serious adverse event, or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made, or if circumstances had been less opportune. Only one SADE was reported for the study (0.1%). See Table 6. The SADE represents the one (1) clinically significant burn experienced in the study.

Study Strengths and Limitations

Strengths

- Prospective multicenter study
- Real time peri-procedural data
- Active safety reporting
- Women with patulous cervix included
- Collected all burn and SADE events
- All burns investigated
- Large sample size

Limitations

Technical malfunction reporting may have been inconsistently assessed by the sites. Some sites may have misinterpreted appropriate fluid loss alarms as technical issues when in fact the alarm was not a technical issue with the device but rather how the device is intended to perform. The alarm may have been triggered by a clinical use issue, but reported as a technical issue and artificially inflating the overall technical issue rate.

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 Genesys HTA™ System 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 counseled on the use of an appropriate birth control method. Patients with childbearing capacity should be cautioned that serious potential complications may result to both mother and fetus in the event of a pregnancy.

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

PRETREATMENT PREPARATION OF PATIENT

- The endometrium should be in a basal state prior to Genesys HTA System treatment. This can be accomplished by timing the menstrual cycle to the early proliferative phase or administering pretreatment drugs such as GnRH agonists prior to performing the endometrial ablation.
- As with any hysteroscopic procedure, the bladder should be empty.
- The usual vaginal preparation for hysteroscopy should be employed.
- 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 Genesys HTA System on a patient, the physician should complete the following checklist to better ensure safe and effective use of the system. Note that this is not a comprehensive list, but an attempt to cover some of the key issues before a physician uses the Genesys HTA System.

The physician must:

- along with ancillary personnel, thoroughly read and understand all directions for use, Indications and Contraindications supplied with the Genesys HTA System (including the Genesys HTA System User's Manual) and those for compatible accessories to be used with the Genesys HTA System;
- be trained to perform diagnostic hysteroscopy;
- be able to verify that the uterine cavity is properly prepared for the ablation procedure and be able to identify the cornu;
- be able to observe, confirm, and maintain proper placement of the hysteroscopic tip beyond the internal os and be able to maintain control of the procedure sheath throughout the entire procedure;
- neither advance nor withdraw the procedure sheath into or out of the uterine cavity once heating has begun until the cooling is complete.
- be aware of the appropriate sequence of actions to halt, resolve and/or continue the treatment, in the event the Genesys HTA System detects a fluid loss of 10 mL; and
- be aware that, on the day of treatment, previously undetected pathology (e.g., submucous myomas), may be present in the endometrial cavity which may affect treatment results.

HOW SUPPLIED

Contents supplied STERILE using an ethylene oxide (EO) process. Store in a cool, dry, dark place. Do not use if package is damaged or opened. See product labeling for expiration date. Do not use product beyond its expiration date.

The Genesys HTA ProCerva™ Procedure Set is supplied in a box containing these Directions for Use and two sealed trays. One tray contains the procedure sheath and sheath cap, while a second tray contains the cassette and drainage bag.

DEVICE DESCRIPTION

The Genesys HTA ProCerva Procedure Set consists of a procedure sheath (with sheath cap), cassette, and drainage bag (Figure 1).

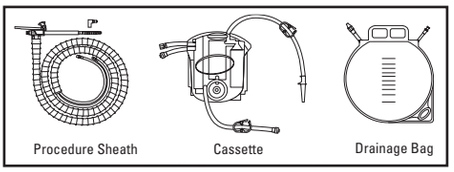

Figure 1. Procedure Set

The procedure sheath circulates the saline to and from the uterus during the procedure. The procedure sheath contains two lumens (one for fluid delivery and one for fluid return), a cervical seal assist feature that aids the user in gaining and maintaining a cervical seal, and tubing that attaches the procedure sheath to the cassette. A sieve tip on the end of the procedure sheath is intended to minimize the occurrence of occlusion due to uterine debris. The procedure sheath also includes a tenaculum stabilizer that, when engaged, allows the physician to hold the procedure sheath and tenaculum with one hand.

A hysteroscope (not supplied) is inserted into the procedure sheath to provide visualization during the procedure. Various scope adapters (sold separately) are available to ensure proper connection between the hysteroscope and procedure sheath.

A sheath cap is included for priming the system.

The cassette interfaces with the control unit to facilitate heating, cooling, and distribution of saline throughout the procedure. The cassette contains an internal fluid sensor for fluid measurement during the procedure. The procedure sheath serves as the fluid conduit between the cassette and the uterine cavity. Effluent is collected in the drainage bag.

DIRECTIONS FOR USE

WARNING

The following section is a guide to the setup and removal of the procedure set. This section is *not* a guide to system operation. Refer to the Genesys HTA System User's Manual for complete setup and use.

Pre-Procedure

1. Examine the procedure set and insert the cassette into the control unit as follows:
   A. Examine the Genesys HTA ProCerva Procedure Set package for damage. Do not use if the package is opened or damaged.
   B. Open the procedure set package and remove the contents.
   C. Inspect each tray for damage. Do not use if the procedure sheath or cassette trays are open or damaged.
   D. Peel open the cassette tray and remove the cassette and drainage bag from the tray and inspect. Do not use if the contents are damaged.
   E. Facing the cassette slot, position the cassette above the cassette slot with the Boston Scientific logo facing away from control unit.
   F. Slide the cassette down until it is fully seated in the control unit. The top of the cassette should be flush with the top of the control unit, and the two blue LED indicators behind the cassette should illuminate, indicating that the cassette is properly inserted.
2. Hang the drainage bag, attach and engage the cassette as follows;
   A. Attach the drainage bag to the right side of the control unit by placing the rigid handle of the drainage bag onto both of the drainage bag hooks.
   B. Connect the drain line luer fitting from the cassette to the drainage bag.
   C. After the drainage bag is connected, press the *Engage Cassette* button to engage the cassette to the control unit.
3. Setup the saline supply bag and confirm tubing clamps are open as follows:
   A. Hang a 3L bag of 0.9% Normal Saline from the IV pole hook.
   B. Spike the saline bag.

   Note: Ensure that the saline bag ports are pulled away from the bag and into a vertical position, and that the saline spike has sufficiently penetrated the bag port to facilitate flow.

   C. Confirm that the cassette's supply and drain lines are unclamped.
4. Peel open the procedure sheath tray. Place its contents onto the sterile field and inspect for damage. Do not use if the contents are damaged. Observing sterile technique, connect the procedure sheath inflow and outflow tubing connectors to the matching color-coded sheath connections on the cassette (male and female luer style, Purple – Purple and Yellow – Yellow).

   Note: Prior to attaching the luer fittings from the procedure sheath to the cassette, twist the procedure sheath tubing ¼ turn counterclockwise. This may decrease the likelihood of kinked tubing.

5. Attach the scope adapter to the procedure sheath and insert the scope as follows:
   A. Attach the sterilized scope adapter to the proximal end of the procedure sheath.

   Note: Seat the scope adapter fully onto the procedure sheath. There will be resistance due to an O-ring on the procedure sheath.

   B. Turn the knurled knob on the scope adapter approximately 2 ¼ turns to secure the scope adapter to the procedure sheath.

   Note: Do not over-tighten the scope adapter, as doing so may cause damage to the procedure sheath.

   C. Carefully guide the distal end of the hysteroscope through the procedure sheath until it stops in the scope adapter and secure appropriately.
6. Attach the sheath cap to the tip of the procedure sheath. To prevent leakage, ensure that the sheath cap fully covers the sieve tip area and openings of the distal tip.
7. Press the *Fill System* button to advance to System Preparation.

Procedure

Complete the procedure by following the instructions on the control unit display screen and referring to the Genesys HTA System User's Manual.

WARNING

Once heating has begun maintain a stable sheath position and do not remove the procedure sheath until the post-treatment cooling cycle has been completed as confirmed by the display screen, as heated fluid may cause thermal injury to the patient.

If heated fluid leaks onto the patient, flush the area with cool saline. It is important to assess the area in order to determine if a burn is present. If a burn is present, determine the severity and an appropriate treatment should be made per the standard of care at your facility. It is also recommended that the area be assessed again at follow-up.

Post-Procedure

1. When prompted by the system, withdraw the procedure sheath from the patient.
2. Reattach the sheath cap to the distal tip of the procedure sheath to prevent fluid from spilling.

   Note: If the sheath cap has inadvertently been discarded, pinch the supply line tubing clamp and the drain line tubing clamp to help contain the fluid.

Caution: Use caution when handling the fluid in the drainage bag after treatment, as the fluid at this stage may still be hot.

3. Clamp and remove the saline bag after the procedure:
   A. Pinch the tubing clamp on the supply line.
   B. Detach the saline bag from the cassette's supply line tubing.
   C. Remove the saline bag and dispose in accordance with hospital procedures.
4. Clamp, disconnect, and cap the drainage bag after the procedure:
   A. Pinch the tubing clamp connected to the cassette's drain line.
   B. Disconnect the luer fitting from the inlet tubing.
   C. Connect the tethered luer cap to the inlet tubing on the drainage bag and close to prevent contents from spilling.

   Note: If hazardous fluids are spilled during removal, clean up in accordance with hospital procedures.

D. Open the drain valve on the drainage bag and discard the contents in accordance with hospital procedures.

E. Safely dispose of the drainage bag and contents in accordance with hospital procedures.

5. Once prompted by the system, pull the cassette straight up to remove. Ensure the cassette is held upright and handle carefully to prevent contamination from residual fluids.

Note: At the end of the procedure the disposable procedure set components may contain approximately 270 mL of fluid.

6. Remove the hysteroscope and scope adapter from the procedure sheath and route both for sterilization according to hospital procedures.
7. Dispose of the cassette and procedure sheath according to hospital safe disposal procedures.

WARRANTY

Boston Scientific Corporation (BSC) warrants that reasonable care has been used in the design and manufacture of this instrument. **This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether express or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular purpose.** Handling, storage, cleaning and sterilization of this instrument as well as other factors relating to the patient, diagnosis, treatment, surgical procedures and other matters beyond BSC's control directly affect the instrument and the results obtained from its use. BSC's obligation under this warranty is limited to the repair or replacement of this instrument and BSC shall not be liable for any incidental or consequential loss, damage or expense directly or indirectly arising from the use of this instrument. BSC neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this instrument. **BSC assumes no liability with respect to instruments reused, reprocessed or resterilized and makes no warranties, express or implied, including but not limited to merchantability or fitness for a particular purpose, with respect to such instruments.**

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Do not use if package is damaged.

Recyclable Package

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