DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

Memorandum

Date · DEC 12 1997

From Deputy Director, Office of Device Evaluation (HFZ-400)
Center for Devices and Radiological Health (CDRH)

Subject Premarket Approval of GyneCare, Inc.'s THERMACHOICE™ UTERINE BALLOON THERAPY™ (UBT) SYSTEM - ACTION

To The Director, CDRH
ORA _____

ISSUE. Publication of a notice announcing approval of the subject PMA.

FACTS. Tab A contains a FEDERAL REGISTER notice announcing:

(1) a premarket approval order for the above referenced medical device (Tab B); and

(2) the availability of a summary of safety and effectiveness data for the device (Tab C).

RECOMMENDATION. I recommend that the notice be signed and published.

Kimber C. Richter

Kimber C. Richter, M.D.

Attachments
Tab A - Notice
Tab B - Order
Tab C - S & E Summary

DECISION

Approved ✓ Disapproved _____ Date December 12, 1997

Prepared by J. Michael Kuchinski, CDRH, HFZ-470, 12-5-97, 594-1180

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DRAFT

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[DOCKET NO. _____]

Gynecare, Inc. Premarket Approval of ThermaChoice™ Uterine Balloon Therapy™ (UBT) System

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its approval of the application by GyneCare, Inc., Menlo Park, CA, for premarket approval, under the Federal Food, Drug, and Cosmetic Act (the act), of the ThermaChoice™ Uterine Balloon Therapy™ (UBT) System. After reviewing the recommendation of the Obstetrics and Gynecology Devices Panel, FDA's Center for Devices and Radiological Health (CDRH) notified the applicant, by letter of December 12, 1997, of the approval of the application.

DATES: Petitions for administrative review by (insert date 30 days after date of publication in the FEDERAL REGISTER).

ADDRESSES: Written requests for copies of the summary of safety and effectiveness data and petitions for administrative review to the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857.

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FOR FURTHER INFORMATION CONTACT:

Colin M. Pollard,
Center for Devices and Radiological Health (HFZ-470),
Food and Drug Administration,
9200 Corporate Blvd.,
Rockville, MD 20850,
301-594-1180.

SUPPLEMENTARY INFORMATION: On June 17, 1997, GyneCare, Inc., Menlo Park, CA., submitted to CDRH an application for premarket approval of the ThermaChoice™ Uterine Balloon Therapy™ (UBT) System. The system is a 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 child bearing is complete.

On October 6, 1997, the Obstetrics and Gynecology Devices Advisory Panel of the Medical Devices Advisory Committee, an FDA advisory committee, reviewed and recommended approval of the application.

On December 12, 1997 CDRH approved the application by a letter to the applicant from the Director of the Office of Device Evaluation, CDRH.

A summary of the safety and effectiveness data on which CDRH based its approval is on file in the Dockets Management Branch (address above) and is available from that office upon written request. Requests should be identified with the name of the device and the docket number found in brackets in the heading of this document.

Opportunity for Administrative Review

Section 515(d)(3) of the act, (21 U.S.C. 360e(d)(3)) authorizes any interested person to petition, under section 515(g) of the act, for administrative review of CDRH's decision to approve this application. A petitioner may request either a formal hearing under 21 CFR part 12 of FDA's administrative practices and procedures regulations or a review of the application and CDRH's action by an independent advisory committee of experts. A petition is to be in the form of a petition for reconsideration under 21 CFR 10.33(b). A petitioner shall identify the form of review requested (hearing or independent advisory committee) and shall submit with the petition supporting data and information showing that there is a genuine and substantial issue of material fact for resolution through administrative review. After reviewing the petition, FDA will decide whether to grant or deny the petition and will publish a notice of its decision in the FEDERAL REGISTER. If FDA grants the petition, the notice will state the issue to be reviewed, the form of the review to be used, the persons who may participate in the review, the time and place where the review will occur, and other details.

Petitioners may, at any time on or before (insert date 30 days after date of publication in the FEDERAL REGISTER), file with the Dockets Management Branch (address above) two copies of each petition and supporting data and information, identified with the name of the device and the docket number found in brackets in the heading of this document. Received petitions may

be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 515(d), 520(h) (21 U.S.C. 360e(d), 360j(h))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.10) and redelegated to the Director, Center for Devices and Radiological Health (21 CFR 5.53).

Dated:_____.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Susan M. Aloyan
Director, Regulatory Affairs and Quality Assurance
GyneCare, Inc.
Ethicon, Inc.
a Johnson & Johnson Company
235 Constitution Drive
Menlo Park, California 94025

DEC 12 1997

Re: P970021
ThermaChoice™ Uterine Balloon Therapy™ (UBT) System
Filed: June 17, 1997
Amended: August 21 and 29, October 21, November 3 and 25, 1997

Dear Ms. Aloyan:

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the ThermaChoice™ Uterine Balloon Therapy™ (UBT) System. This device is indicated for the treatment of menorrhagia (excessive uterine bleeding) due to benign causes in premenopausal women for whom child bearing is complete. We are pleased to inform you that the PMA is approved subject to the conditions described below and in the "Conditions of Approval" (enclosed). You may begin commercial distribution of the device upon receipt of this letter.

The sale, distribution, and use of this device are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that to ensure the safe and effective use of the device that the device is further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii), (1) insofar as the labeling specifies the requirements that apply to the training of practitioners who may use the device as approved in this order and (2) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

In addition, in order to gather long-term safety and effectiveness data, you must conduct a postmarket approval study that will continue to follow subjects from the Gynecare Uterine Balloon Therapy™ (UBT) Efficacy Study for a period of three years from the time of treatment. The protocol should address the following parameters:

- Need for hysterectomy or repeat ablation for continued or recurrent menorrhagia
- Assessment of patient's menstruation pattern
- Adverse events and/or complications
- Quality of Life Questionnaire
- Patients' pregnancy and contraception status
- Diagnosis of malignancy of the uterus

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Reports will be submitted annually. Please be advised that the results of the long-term data must be included in the labeling.

Expiration dating for this device has been established and approved at thirteen months. This is to advise you that the protocol you specified in the PMA is considered an approved protocol for the purpose of verifying the tentative expiration date and extending the expiration dating as provided by 21 CFR 814.39(a)(8).

CDRH will publish a notice of its decision to approve your PMA in the FEDERAL REGISTER. The notice will state that a summary of the safety and effectiveness data upon which the approval is based is available to the public upon request. Within 30 days of publication of the notice of approval in the FEDERAL REGISTER, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act (the act).

Failure to comply with the conditions of approval invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form.

All required documents should be submitted in triplicate, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

PMA Document Mail Center (HFZ-401)
Center for Devices and Radiological Health
Food and Drug Administration
9200 Corporate Blvd.
Rockville, Maryland 20850

If you have any questions concerning this approval order, please contact Mr. Colin M. Pollard at (301) 594-1180.

Sincerely yours,

Kimber Richter

Kimber Richter, M.D.
Deputy Director
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

Issued: 5-2-95

CONDITIONS OF APPROVAL

APPROVED LABELING. As soon as possible, and before commercial distribution of your device, submit three copies of an amendment to this PMA submission with copies of all approved labeling in final printed form to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration (FDA), 9200 Corporate Blvd., Rockville, Maryland 20850.

ADVERTISEMENT. No advertisement or other descriptive printed material issued by the applicant or private label distributor with respect to this device shall recommend or imply that the device may be used for any use that is not included in the FDA approved labeling for the device. If the FDA approval order has restricted the sale, distribution and use of the device to prescription use in accordance with 21 CFR 801.109 and specified that this restriction is being imposed in accordance with the provisions of section 520(e) of the act under the authority of section 515(d)(1)(B)(ii) of the act, all advertisements and other descriptive printed material issued by the applicant or distributor with respect to the device shall include a brief statement of the intended uses of the device and relevant warnings, precautions, side effects and contraindications.

PREMARKET APPROVAL APPLICATION (PMA) SUPPLEMENT. Before making any change affecting the safety or effectiveness of the device, submit a PMA supplement for review and approval by FDA unless the change is of a type for which a "Special PMA Supplement-Changes Being Effected" is permitted under 21 CFR 814.39(d) or an alternate submission is permitted in accordance with 21 CFR 814.39(e). A PMA supplement or alternate submission shall comply with applicable requirements under 21 CFR 814.39 of the final rule for Premarket Approval of Medical Devices.

All situations which require a PMA supplement cannot be briefly summarized, please consult the PMA regulation for further guidance. The guidance provided below is only for several key instances.

A PMA supplement must be submitted when unanticipated adverse effects, increases in the incidence of anticipated adverse effects, or device failures necessitate a labeling, manufacturing, or device modification.

A PMA supplement must be submitted if the device is to be modified and the modified device should be subjected to animal or laboratory or clinical testing designed to determine if the modified device remains safe and effective.

A "Special PMA Supplement - Changes Being Effected" is limited to the labeling, quality control and manufacturing process changes specified under 21 CFR 814.39(d)(2). It allows for the addition of, but not the replacement of previously approved, quality control specifications and test methods. These changes may be implemented before FDA approval upon acknowledgment by FDA that the submission is being processed as a "Special PMA Supplement - Changes Being Effected." This acknowledgment is in addition to that issued by the PMA Document Mail Center for all PMA supplements submitted. This procedure is not applicable to changes in device design, composition, specifications, circuitry, software or energy source.

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Alternate submissions permitted under 21 CFR 814.39(e) apply to changes that otherwise require approval of a PMA supplement before implementation of the change and include the use of a 30-day PMA supplement or annual postapproval report. FDA must have previously indicated in an advisory opinion to the affected industry or in correspondence with the applicant that the alternate submission is permitted for the change. Before such can occur, FDA and the PMA applicant(s) involved must agree upon any needed testing protocol, test results, reporting format, information to be reported, and the alternate submission to be used.

POSTAPPROVAL REPORTS. Continued approval of this PMA is contingent upon the submission of postapproval reports required under 21 CFR 814.84 at intervals of 1 year from the date of approval of the original PMA. Postapproval reports for supplements approved under the original PMA, if applicable, are to be included in the next and subsequent annual reports for the original PMA unless specified otherwise in the approval order for the PMA supplement. Two copies identified as "Annual Report" and bearing the applicable PMA reference number are to be submitted to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850. The postapproval report shall indicate the beginning and ending date of the period covered by the report and shall include the following information required by 21 CFR 814.84:

(1) Identification of changes described in 21 CFR 814.39(a) and changes required to be reported to FDA under 21 CFR 814.39(b).

(2) Bibliography and summary of the following information not previously submitted as part of the PMA and that is known to or reasonably should be known to the applicant:

> (a) unpublished reports of data from any clinical investigations or nonclinical laboratory studies involving the device or related devices ("related" devices include devices which are the same or substantially similar to the applicant's device); and
>
> (b) reports in the scientific literature concerning the device.

If, after reviewing the bibliography and summary, FDA concludes that agency review of one or more of the above reports is required, the applicant shall submit two copies of each identified report when so notified by FDA.

ADVERSE REACTION AND DEVICE DEFECT REPORTING. As provided by 21 CFR 814.82(a)(9), FDA has determined that in order to provide continued reasonable assurance of the safety and effectiveness of the device, the applicant shall submit 3 copies of a written report identified, as applicable, as an "Adverse Reaction Report" or "Device Defect Report" to the PMA Document Mail Center (HFZ-401), Center for Devices and Radiological Health, Food and Drug Administration, 9200 Corporate Blvd., Rockville, Maryland 20850 within 10 days after the applicant receives or has knowledge of information concerning:

(1) A mixup of the device or its labeling with another article.

(2) Any adverse reaction, side effect, injury, toxicity, or sensitivity reaction that is attributable to the device and

(a) has not been addressed by the device's labeling or

(b) has been addressed by the device's labeling, but is occurring with unexpected severity or frequency.

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(3)Any significant chemical, physical or other change or deterioration in the device or any failure of the device to meet the specifications established in the approved PMA that could not cause or contribute to death or serious injury but are not correctable by adjustments or other maintenance procedures described in the approved labeling. The report shall include a discussion of the applicant's assessment of the change, deterioration or failure and any proposed or implemented corrective action by the applicant. When such events are correctable by adjustments or other maintenance procedures described in the approved labeling, all such events known to the applicant shall be included in the Annual Report described under "Postapproval Reports" above unless specified otherwise in the conditions of approval to this PMA. This postapproval report shall appropriately categorize these events and include the number of reported and otherwise known instances of each category during the reporting period. Additional information regarding the events discussed above shall be submitted by the applicant when determined by FDA to be necessary to provide continued reasonable assurance of the safety and effectiveness of the device for its intended use.

REPORTING UNDER THE MEDICAL DEVICE REPORTING (MDR) REGULATION. The Medical Device Reporting (MDR) Regulation became effective on December 13, 1984, and requires that all manufacturers and importers of medical devices, including in vitro diagnostic devices, report to FDA whenever they receive or otherwise became aware of information that reasonably suggests that one of its marketed devices

(1)may have caused or contributed to a death or serious injury or

(2)has malfunctioned and that the device or any other device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

The same events subject to reporting under the MDR Regulation may also be subject to the above "Adverse Reaction and Device Defect Reporting" requirements in the "Conditions of Approval" for this PMA. FDA has determined that such duplicative reporting is unnecessary. Whenever an event involving a device is subject to reporting under both the MDR Regulation and the "Conditions of Approval" for this PMA, you shall submit the appropriate reports required by the MDR Regulation and identified with the PMA reference number to the following office:

Division of Surveillance Systems (HFZ-531)
Center for Devices and Radiological Health
Food and Drug Administration
1350 Piccard Drive, 340
Rockville, Maryland 20850
Telephone (301) 594-2735

Events included in periodic reports to the PMA that have also been reported under the MDR Regulation must be so identified in the periodic report to the PMA to prevent duplicative entry into FDA information systems.

Copies of the MDR Regulation and an FDA publication entitled, "An Overview of the Medical Device Reporting Regulation," are available by written request to the address below or by telephoning 1-800-638-2041.

Division of Small Manufacturers Assistance (HFZ-220)
Center for Devices and Radiological Health
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

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SUMMARY OF SAFETY AND EFFECTIVENESS DATA:
ThermaChoice™ Uterine Balloon Therapy™ System

I. GENERAL INFORMATION

DEVICE GENERIC NAME:	Thermal Balloon Endometrial Ablation Therapy
DEVICE TRADE NAME:	ThermaChoice™ Uterine Balloon Therapy™ (UBT) System
APPLICANT'S NAME AND ADDRESS:	Gynecare, Inc. 235 Constitution Drive Menlo Park, CA 94025
PREMARKET APPROVAL APPLICATION (PMA) NUMBER:	P970021
DATE OF PANEL RECOMMENDATION:	October 6, 1997
DATE OF NOTICE OF APPROVAL TO THE APPLICANT:	DEC 12 1997

II. INDICATIONS FOR USE

The ThermaChoice™ Uterine Balloon Therapy™ (UBT) System is a 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 child bearing is complete.

III. DEVICE DESCRIPTION

The following includes a pictorial representation of the UBT System and a brief description of the device including the functional components and the properties of the device relevant to the treatment of menorrhagia.

The ThermaChoice™ Uterine Balloon Therapy™ (UBT) System is a software controlled device designed to ablate endometrial tissue by thermal energy heating of sterile injectable fluid (5% dextrose in water) within a latex balloon. The ThermaChoice™ UBT System consists of a controller with power cord, single-use sterile catheter, and umbilical cable.

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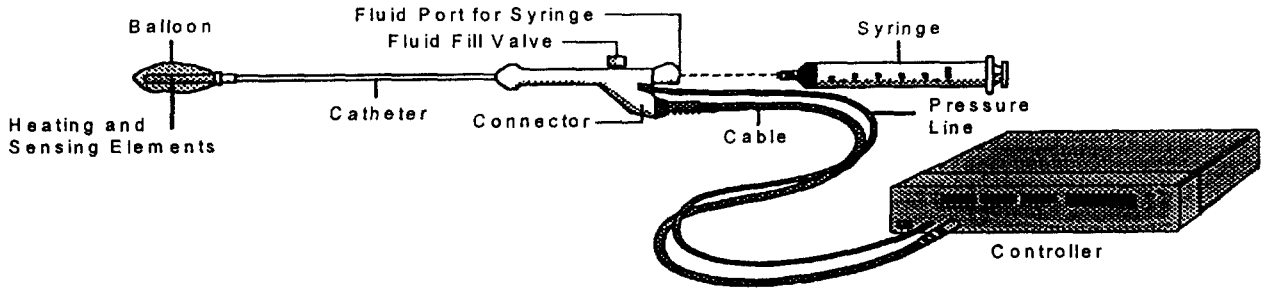
Figure 1 - ThermaChoice Uterine Balloon Therapy System



The umbilical cable connects the catheter electronically to the controller. The single-use catheter is supplied sterile and includes a shielded heating element and two thermocouples surrounded by a balloon which has a tube for fluid pressure measurement. The tube connects to a pressure port located on the front panel which is connected to a pressure transducer internal to the controller.

A microprocessor in the controller controls indicators, displays, alarms and catheter functions. The software contained in this medical device completely controls time and temperature for thermal ablation. The software converts sensor inputs and provides for the display of temperature, pressure, and therapy time. During normal operation, the software controls the heater, calculates the therapy time, provides alerts and user messages to prompt the required user input. For safety purposes, the software provides hazard warning and automatic shutdowns for specific hardware and user errors. In addition, specific hardware backups provide safety shutdown in the event of software failure.

During use, the catheter is inserted into the uterus and the latex balloon at the distal tip is filled with 2 to 30 mL of sterile, injectable fluid (5% dextrose in water). Fluid pressure is manually adjusted to 160-180 mmHg (optimal) for 30-45 seconds. The heating element within the balloon can be manually activated if the pressure is above 150 mmHg. The system achieves endometrial ablation by maintaining the fluid temperature at 87°C (188°F) for an 8 minute cycle. At the completion of the heat cycle, the fluid inside the balloon is withdrawn and the balloon catheter is removed from the uterus. The balloon catheter is then disconnected from the umbilical cable and discarded. The balloon catheter is not intended for reuse.

Safety features incorporated into the device will stop the procedure should pressure variations occur that are greater than 210 mmHg or less than 45 mmHg after device activation. In addition, if the temperature inside the balloon exceeds 95°C (203°F) for 2 seconds, or falls below 75°C (167°F) for 15 seconds, or is unable to reach 87°C (188°F) within 4 minutes of pre-heating, the controller will shut down the heating element and the procedure will terminate.

IV. CONTRAINDICATIONS, WARNINGS, AND PRECAUTIONS

CONTRAINDICATIONS

- A patient who is pregnant or who wants to become pregnant in the future.
- A patient with a history of latex allergy or who has demonstrated a sensitivity to latex material.
- A patient with known or suspected endometrial carcinoma (uterine cancer) or pre-malignant change of the endometrium such as unresolved adenomatous hyperplasia.
- A patient with any anatomic or pathologic condition in which weakness of the myometrium could exist, such as history of previous classical cesarean sections or transmural myomectomy.
- A patient with active genital or urinary tract infection at the time of procedure (e.g., cervicitis, vaginitis, endometritis, salpingitis, or cystitis).
- A patient with an IUD currently in place.

WARNINGS

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

- 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.
- Endometrial ablation using the ThermaChoice™ UBT System is not a sterilization procedure. Pregnancies after ablation can be dangerous for both mother and fetus.
- Endometrial ablation procedures using the ThermaChoice™ UBT System should be performed only by medical professionals who have experience in performing procedures within the uterine cavity such as IUD insertion or dilation and curettage (D & C) and having adequate training and familiarity with the ThermaChoice™ system.
- Endometrial ablation procedures do 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.
- The UBT balloon catheter is for single use only — do not reuse, or resterilize.
- Do not treat patients for more than one 8 minute therapy cycle in a given treatment session because of the potential for transmural injury to the uterus or injury to adjacent viscera.
- Use caution not to perforate the uterine wall when sounding the uterus or inserting the UBT balloon catheter. If a perforation is present, the procedure should be terminated immediately.

PRECAUTIONS

- The UBT balloon catheter, controller, and umbilical cable are designed as a system. To ensure proper function, never use other components with the UBT system.

- A starting pressure of 160 - 180 mmHg is recommended and typically requires 6-15 cc of fluid and may require as much as 30 cc. **Titration to achieve a stable pressure (no fluctuations greater than ± 10 mmHg for at least 30 sec) prior to activating the heating element is critical to proper functioning of the device. When inserting fluid, do not exceed a pressure of 200 mmHg.** Typically, pressure levels decline slowly during the course of the procedure as the uterus relaxes. If a pressure of 160 - 180 mmHg cannot be reached with 30 cc or less of fluid, or if there is a rapid drop in pressure, remove balloon catheter and check for catheter leak and/or uterine perforation. **Never add additional fluid during a therapy cycle. Rapid loss of pressure during a therapy cycle may indicate a uterine wall defect is present. Adding additional fluid to the balloon may create (or exacerbate if already present) a uterine wall defect such as perforation.**
- Those 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 ThermaChoice™ UBT System has not been fully evaluated in patients:
  - ◊ with a large uterine cavity (>30 cc in volume or uterine sound >10 cm);
  - ◊ with a small uterine cavity (<2 cc in volume or uterine sound < 6 cm);
  - ◊ with submucosal myomas, a bicornuate or septate uterus or a previous endometrial resection/ablation;
  - ◊ undergoing repeat endometrial ablation procedures; and,
  - ◊ who are post-menopausal.

V. ADVERSE EFFECTS OF THE DEVICE ON HEALTH

In a study of 134 patients treated with UBT, (intent to treat randomized UBT patients (n=131) plus 3 patients initially randomized to rollerball group but treated with UBT), adverse events were reported as: **endometritis** (3 cases), **urinary tract and vaginal infection** (1 case), and **post-coital bleeding** (1 case). Endometritis was reported in 2.1% of patients. Infections and post-coital bleeding were each reported at rates of less than 1.0%. The overall rate of postoperative adverse events was 3.7%. Treatment to resolve these adverse events included administration of antibiotics for the infections and dilatation and curettage (D&C) for the one case of post-coital bleeding. (See **Table 3.**)

Pelvic Cramping

Post-treatment pelvic cramping described as mild, moderate or severe, was reported by 91.8% (123/134) of the UBT patients. No medical intervention was required for these patients. (See **Table 1.**)

Table 1
Pelvic Cramping Related to Uterine Balloon Therapy

Reported Severity	Occurrences n = 134	Percentage (%)
None	11	8.2
Mild	46	34.3
Moderate	64	47.8
Severe	13	9.7

Nausea/Vomiting
There were 32 reports of nausea/vomiting (23.9%) in the immediate recovery period following the UBT procedure, i.e., within 24 hours of the procedure. There was 1 report of severe nausea/vomiting following a UBT the required medical intervention.

Perforation of the Uterus and Hematometra
Although these were not reported in the U.S. clinical trial, there was one report each of uterine perforation and hematometra from an international experience of approximately 3000 patients treated with the UBT System.

Vaginal Discharge
Patients were asked to report any vaginal discharge for the first 30 days following the UBT procedure. A total of 74.6% (100/134) of the patients experienced serosanguineous discharge. No medical intervention was required.

Other Potential Adverse Effects
The following adverse effects might be expected (potential), but have not yet been observed in the clinical study of the ThermaChoice™ UBT System:

- **Rupture of the Uterus**
- **Thermal Injury to Adjacent Tissue**
- **Heated Liquid Escaping into the Vascular Spaces and/or Cervix, Vagina, Fallopian Tubes, and Abdominal Cavity**
- **Electrical Burn**
- **Allergic Reaction to Latex**
- **Hemorrhage**
- **Infection**
- **Pregnancy** - Pregnancy following endometrial ablation is dangerous for both the mother and fetus.
- **Post-Ablation-Tubal Sterilization Syndrome** - This is a complication following endometrial ablation in women who have also previously undergone tubal ligation. The pathophysiology of this condition is believed to be related to the regeneration of endometrium in the cornual areas of the uterus. Blood from these glands can flow back into the proximal fallopian tubes in cases where the lower uterine segment is extensively scarred. The proximal oviduct becomes filled with blood and fluid causing symptoms similar to those of an ectopic pregnancy.

VI. ALTERNATE PRACTICES OR PROCEDURES

The following alternate practices and procedures are currently available to treat excessive uterine bleeding:

- **Drug Therapy**
  Drug therapy using estrogen-progestogen combinations, such as those found in oral contraceptives or progestogens (progesterone) by themselves are most often employed for the treatment of menorrhagia. Other classes of drugs used include androgens such as danocrine, GnRh agonists, non-steroidal anti-inflammatory drugs (NSAIDs) and anti-fibrinolytic medications.
- **Dilatation and Curettage (D&C)**
  D&C is generally used in conjunction with drug therapy and is performed as a diagnostic or therapeutic procedure in which the uterine contents are either scraped away by an instrument or removed through vacuum aspiration.
- **Hysteroscopic Endometrial Ablation**
  Hysteroscopic endometrial ablation is a minimally invasive surgical procedure which utilizes a resectoscope or operating hysteroscope, a video monitor, a fluid distention medium such as glycine or sorbitol, and a surgical ablation device such as an electrode loop, rollerball or laser.
- **Hysterectomy**
  The most common surgical procedure, and only definitive treatment performed for excessive menstrual bleeding, is hysterectomy.

VII. MARKETING HISTORY

The ThermaChoice™ Uterine Balloon Therapy™ (UBT) System (formerly EASy™) became commercially available in January, 1995, for international market. To date, the UBT system is available to 30 countries in six continents. The UBT system has not been withdrawn from any market due to any reason related to the safety or efficacy of the device.

VIII. SUMMARY OF PRECLINICAL STUDIES

A. LABORATORY STUDIES (NONCLINICAL STUDIES)

- **PERFORMANCE TESTING MECHANICAL**

Volume-to-Burst Test - 61 devices were tested to determine the level of safety and point of failure by comparing burst volume to actual use volume. The actual maximum use volume is 30 cc and the average burst volume was 4010 cc and the average maximum pressure was 30 lb.

Volume Burst Pressure Test - 60 devices were tested to determine the level of safety and point of failure by comparing burst pressure to actual use pressure. The actual use pressure is 160-180mmHg and the average burst pressure was 719 lb. There were no failures reported.

Balloon Attachment Pull Test - 60 devices were pull tested to determine if the device met the design specification of 1 lb. pull force without balloon detachment and leakage. The average applied pull force was 1.07 lb. There were no failures reported.

Balloon Insertion Test - 65 devices were push tested to determine if the device met the design specification of 2.25 lb. without any failures. The average insertion force was 4.1 lb. There were no failures reported.

Balloon Attachment Twist Test - 62 devices were twisted 360° around the catheter axis and returned to original position to determine the level of failure. All tested units survived the twist test. There were no failures reported.

Catheter Tube 90 Degree Bend Test - 46 devices were tested by the bend test. The bend test was conducted by bending the catheter 90° in one direction, then back to the original position, and then bending the device 90° in the opposite direction. This cycles was repeated for 8 cycles. 45 catheters survived the test without any failure. 1 catheter was cracked but no leakage was observed.

Catheter Tip Deflection Test - 46 devices were deflected at the catheter's end to determine if the device would meet a 0.5 inch deflection. The force at maximum deflection (0.5 in) was measured and the average force was 6 lb. There were no failures reported.

Pressure Line Pull Strength - 60 devices were tested to determine the force necessary to pull the pressure line from the device is 5 lb. The average force was found to be 8.5 lb. There were no failures reported.

- **PERFORMANCE TESTING ELECTROMAGNETIC COMPABILITY**

Emissions And Susceptibility (Immunity) - Testing was performed by two independent test houses for emissions and susceptibility (immunity). This testing was based on the EN 5501, and IEC 801-2, 3, 4, and 5 standards. There were instances of recoverable device failure which were determined to be clinically acceptable.

- **PERFORMANCE TESTING ELECTRICAL SAFETY**

Electrical Safety Testing - Electrical safety testing was performed based on IEC 601 1. The testing performed included temperature rise, dielectric strength, leakage current, and impact testing. The device passed this testing without failure.

- **PERFORMANCE TESTING HEATING ELEMENT AND SENSORS**

  Heating Element and Sensors - The heating element and sensors are tested to confirm accuracy and response time. These components performed to the design specification.

- **SOFTWARE VALIDATION**

  Software Validation - Software validation addressed the following items: device hazard analysis, software requirements specification, requirements for validation traceability analysis, software test and validation procedures. All documents were presented and evaluated. As a result, the software presented with this medical device should operate safely and effectively for the specified software requirements.

- **HAZARD ANALYSIS VERIFICATION TESTING**

  Hazard Analysis - Hazard Analysis has been conducted on the product, including controller, catheter, umbilical cable and power cord. Failure Mode and Effect Analyses (FMEA) has also been performed on the controller, the catheter, the umbilical cable and the power cord. These FMEAs helped in product development to identify potential failure modes and severity of failure, and thus, helped to eliminate or reduce their occurrence through design and design changes. These tests have also been used in performing QC tests on the device during manufacture and to validate the device design.

- **MICROBIOLOGICAL (STERILITY) TESTING**

  Microbiology tests are performed on a regular basis to monitor the overall sterilization process of the disposable UBT catheter and to assess and requalify the sterilization cycle. Biological Indicator testing is used to monitor every sterilized lot. Bioburden testing is periodically performed to monitor the manufacturing procedures and revalidation is to be conducted as appropriate. Other testing were performed to assure that the integrity of the packaging pouch will be maintained during the sterilization process and during shipping. These tests insure seal integrity of the pouch containing the sterile, single-use catheter.

- **MATERIAL SAFETY (TOXICOLOGY)**

  Biocompatibility/Toxicity Testing
  Biocompatibility testing was conducted on the sterilized UBT catheter assembly to assure that the materials were safe for use in a medical device which involves tissue contact. Components of the UBT catheter passed the following biocompatibility tests: Cytotoxicity (MEM elution L-929 mouse fibroblast cells), Hemolysis (rabbit blood), Systemic Toxicity (mouse), Sensitization (dermal, saline and cottonseed oil in rabbits), Vaginal Irritation, Pyrogenicity (rabbit), and Mutagenicity (Ames *Salmonella*). Following minor modifications to the device, additional Cytotoxicity

studies were performed to ensure biocompatibility. Biocompatibility testing were performed in accordance with Good Laboratory Practices (GLP) on final finished devices except the Mutagenicity and Hemolysis testing.

- **SHELF LIFE VALIDATION**

Shelf life studies include an accelerated aging study to establish the 13-month Shelf Life for the UBT catheter. The accelerated aging study has been completed, and a real time aging study is underway.

Real time aging under the UBT Catheter (P/N 00325)-Aging Study - Master Protocol, includes real time testing to address balloon expansion to failure and balloon twist testing, functional testing, pull strength (5 lb pull force), seal integrity, sterility test, and product packaging evaluation. These tests will verify the latex membrane's (balloon), and packaging system's integrity and the catheter's properties over time.

- **ANIMAL STUDY**

Gynecare conducted an animal study to evaluate potential effects of bursting of the UBT balloon during an ablation procedure. This study evaluated the histological effects on porcine uterine and cervical tissue from 1 animal, after the balloon was intentionally burst during an endometrial ablation procedure. The temperature of the uterine surface was measured prior to the procedure. The UBT balloon catheter was inserted into the uterus and heated to a temperature of 87°C (188°F). The uterine surface and cervix temperature were recorded. Hysteroscopic scissors (1 mm diameter) were then inserted through the cervical os to puncture the balloon. The temperature of the extravasated fluid was recorded. The pig was euthanized and the uterus and surrounding tissues were removed for histological examination. The thermocouple readings from the uterine surface showed an increase from 32.8°C prior to the procedure to 33.3°C during the procedure when the balloon temperature was 87°C. Histological evaluation of the tissue samples showed that only the inner uterine surface adjacent to the balloon exhibited thermal damage. No thermal injury occurred in the mid portion of the uterus or the uterus near the cervical os. Thermal injury to uterine sites not adjacent to balloon placement did not occur. Nevertheless, given the differences between the porcine model in relation to the human uterus and that 1 animal was evaluated, this test model's applicability in humans is limited.

VIII. SUMMARY OF CLINICAL STUDIES

A. *Ex Vivo* and FEASIBILITY CLINICAL STUDIES

- **Extirpated Uteri Studies**

Gynecare conducted two clinical studies to evaluate use of the UBT System on freshly excised human uteri. The study objectives of the first study were to measure the temperature at the serosal, myometrial and endometrial surfaces of the human uterus

during *ex vivo* ablation and to evaluate the depth of ablation using histological techniques. Following ablation, the excised human uteri were compared histologically to a control uterus that had undergone a "sham" endometrial ablation procedure. This study was intended to develop the techniques for taking temperature measurements and preparing samples for histological evaluation during an *in vivo* study to be conducted.

In a second study, the UBT catheter was compared to modified catheters for future R&D prototype development. The preceding study showed that serosal temperatures remained within a safe, physiological range during UBT and both studies showed that the depth of thermal injury following UBT was sufficient to produce thermal necrosis without risking transmural injury.

- **Feasibility Study**
  Gynecare conducted a feasibility study under investigational device exemptions (IDE) Number G940155 to evaluate the safety of the UBT system by examining the thermal effects on uteri immediately after ablation. The study was conducted to assess that the heat applied during the ablation procedure is localized to the endometrium and superficial myometrium without affecting deeper tissue. A total of 12 thermocouples were placed on the external and internal surfaces of the uterus in order to measure the serosal, myometrial and endometrial temperatures during eight ablation procedures (and one sham procedure) which took place immediately prior to scheduled hysterectomy. Macroscopic and microscopic observations were made to determine the uniformity and depth of ablation. Histology was performed on tissue taken from similar uterine sites as were the temperature measurements attained during the procedure.

  Study results were comparable to those observed in the extirpated uteri studies in that thermal cellular injury to the endometrium after UBT was sufficient to conclude that the desired clinical effect could be anticipated. Furthermore, there was no histologic evidence or temperature elevation noted at the serosal level which might cause concern for a potential risk of transmural injury to adjacent structures.

B. UNITED STATES MULTI-CENTER CLINICAL INVESTIGATION

- **Study Objectives**
  The study objectives were to identify any complications or adverse effects that may occur as a result of using the UBT system, and to evaluate the safety and effectiveness of the UBT system compared with hysteroscopic endometrial ablation (rollerball ablation) in eliminating or reducing excessive menstrual bleeding from benign causes in women who no longer wished to retain fertility.

- **Study Hypothesis**
  The clinical study proposed that UBT is as safe and effective as the hysteroscopic rollerball procedure in treating excessive uterine bleeding.

- **Study Design**
  This study was designed as a randomized, prospective, multi-center clinical investigation to evaluate a minimum of 216 women with excessive uterine bleeding at 14 investigational sites in order to determine the safety and effectiveness of the UBT endometrial ablation system as compared to rollerball ablation. Uterine bleeding as documented in patient diaries pursuant to the validated methods of Higham[1] et al., was defined as the primary study endpoint.

- **Study Procedure Methods**
  Demographic information and gynecological history were recorded, and patients were evaluated for a minimum of 1 month prior to the procedure to determine their suitability for study entry. Subjects were to have at least a three-month documented history of menorrhagia complicated by failed medical therapy due to inadequate response, side effects, non-compliance or contraindications. Patients were examined at regular intervals up to one year and will continue to be followed for a total of three years post-procedure. All patients signed Patient Informed Consent.

  Uterine bleeding was documented in patient diaries and subsequently scored by the investigator in the assessment of patient bleeding. All complications and adverse events were documented and reported. Protocol deviations and device failures were also recorded. Patients completed Quality-of-Life Questionnaires prior to the procedure and at 6, 12, 24 and 36 months after the procedure.

  Patient inclusion criteria included:

  - ◊ pre-menopausal females over 30 years of age and in good general health;
  - ◊ history of excessive uterine bleeding for a minimum of 3 months pre-procedure and failed traditional medical therapy;
  - ◊ completed menstrual diary score greater than 150 for at least one month;
  - ◊ uterine cavity sound measure between 4 and 10 cm; and,
  - ◊ normal Pap smear and benign endometrial pathology (biopsy) within 6 months of procedure.

  Because endometrial ablation is known to significantly reduce fertility, the population was limited to study subjects for whom child bearing was complete.

  Patient exclusion factors included:

  - ◊ previous endometrial ablation procedure or previous uterine surgeries or any uterine surgery in which thinning of the uterine musculature occurs;
  - ◊ submucous fibroids, polyps or septate uterus as determined by hysterography, hysteroscopy, or ultrasonography within 6 months;

[1] Higham, J.M., O'Brian, P.M.S., Shaw, R.W. Assessment of menstrual blood loss using pictorial chart. British Journal of Obstetrics and Gynaecology 1990;97:734-739.

- ◊ active pelvic inflammatory disease (PID), or recurrent chronic PID, active inflammatory bowel disease, active genital or urinary tract infection;
- ◊ sensitivity to latex.; and,
- ◊ pregnant or wants to become pregnant.

- **Study Period and Population**

  Following FDA and IRB approvals, the first patient was randomized into the study in December, 1995 and treated in January, 1996. All patients were entered into the study by September 30, 1996. Final one-year follow-up was completed in September, 1997.

  Once patient eligibility was confirmed and written informed consent was obtained, each woman was stratified by appropriate age grouping ($\leq$ 40 or > 40 years) and randomized into either the UBT treatment group or the rollerball control group.

  A total of 275 women were randomized in this study, 137 into the UBT group and 138 into the rollerball control group. Three groups of patients have been defined for analysis:

  - ◊ Intent-to-Treat Group (all randomized patients; n=275);
  - ◊ Safety Evaluation Group (all anesthetized patients; n=260);
  - ◊ Efficacy Evaluation Group (all patients completing one-year follow-up; n=239).

- **Demographics and Gynecological History**

  Baseline pre-procedure demographics and gynecological history are summarized in **Table 2.**

  From the analyses of the demographic and gynecologic history variables, it was concluded that baseline variables were equivalent between the UBT and rollerball treatment groups. As a result, it was valid to compare the procedure outcomes of the two groups.

  Analyses of the baseline variables in the Intent-to-Treat group (all patients randomized into the study) demonstrated that only those variables normally associated with age (age, onset of menorrhagia, number of years with menorrhagia and uterine cavity length) were found to be different across the two age strata. All other baseline variables (above Table) did not vary as a function of age. Therefore, no important or unexpected differences between the two age groups due to baseline demographic or gynecological factors were found to prevent pooling of the data across age strata.

  With no unexpected or unexplained differences in variables found among sites, it was also concluded that pooling results from all sites was valid.

Table 2 Demographic and Gynecological History.
Comparison Between UBT and Rollerball Ablation Treatment Groups

Demographic Characteristic and Gynecological History	Uterine Balloon Therapy	Hysteroscopic Rollerball
Race		
Caucasian	81.8%	80.4%
African American	13.9%	13.0%
Other, e.g., Hispanic, Asian, etc.	4.3%	6.6%
Age	40.4 (± 4.8)	40.7 (± 5.0)
Body Mass Index (BMI kg/m^2) (Obesity defined as BMI > 27.3 kg/m^2.)	29.1 (± 7.8)	28.2 (± 6.9)
Age at the onset of menorrhagia	29.6 (± 9.8)	29.7 (± 9.7)
Menstrual diary scores	552.5 (± 712.2)	570.5 (± 562.1)
Baseline diary scores	73-4590	155-3650
Bleeding cycle length (days)	6.9 (± 3.2)	7.2 (± 2.6)
Uterine cavity depth (cm)	8.5 (± 1.3)	8.6 (± 1.2)
Anteverted Uterine position	59.1%	63.8%
Hemoglobin	12.7 (± 1.4) g/dl	12.5 (± 1.6) g/dl
Hematocrit	37.8% (± 3.8)	37.1% (± 4.1)
Pre-menstrual syndrome (PMS)	91.2%	91.3%
Dysmenorrhea (painful menses)	92.7%	95.0%
Menstrual bleeding prevents working outside home	39.7%	41.9%

- **Device Procedural Incidents**
  Product procedural incidents were reported in 18.7% (25/134) of attempted Uterine Balloon Therapy™ procedures and 10.3% (13/126) of the attempted rollerball cases; none of the incidents jeopardized patient safety. The procedural incidents ranged from equipment failures to user or other procedural errors where the procedure discontinued or delayed and resulted in lengthening the procedure. The incidents were the results of multiple issues and included catheter priming problems, pressure titration problems (over or under pressure), patient response variations, clinical experience with a new product, packaging, and in some cases, design shortcomings. Modifications to both catheter and controller have been implemented to address many of the issues reported.

- **Operative Time**
  The time elapsed for each ablation procedure was calculated in the Safety Evaluation group as the number of minutes between the time of completion of surgical preparation to the time that the ablation device was removed from the uterus. Recorded times included a pre-ablation three-minute suction curettage in all cases. Recorded times also included time necessary for trouble-shooting device performance incidents.

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The mean UBT time of procedure was 27.4 (± 11.8) minutes as compared to 39.6 (± 14.7) minutes for rollerball. The percentage of UBT cases that were completed in 30 minutes or less, 71.0% (93/131), was significantly higher than the 28.6% (36/126) of rollerball cases which were completed in 30 minutes.

- **Anesthesia**

  The study protocol did not dictate what type of anesthesia was to be used; the decision was left up to the investigator, anesthesiologist and patient. Looking at the Safety Evaluation group, 53.7% (72/134) of the UBT procedures were completed with general anesthesia while 84.1% (106/126) of the rollerball cases were performed with general anesthesia. Intravenous sedation was used in 38.8% (52/134) of the UBT cases as compared to 14.3% (18/126) of the rollerball cases.

- **UBT-Related Adverse Events**

  There were no intra-operative adverse events and four post-operative adverse events related to Uterine Balloon Therapy (Safety Evaluation group). In a study of 134 patients treated with UBT, (intent to treat randomized UBT patients (n=131) plus 3 patients initially randomized to the rollerball group but treated with UBT), adverse events were reported as: **endometritis** (3 cases), **urinary tract and vaginal infection** (1 case), and **post-coital bleeding** (1 case). Endometritis was reported in 2.1% of patients. Infections and post-coital bleeding were each reported at rates of less than 1.0%. The overall rate of postoperative adverse events was 3.7%. The single report of post-coital bleeding resulted from a polypoid endometrial inflammatory response. Treatment to resolve these adverse events included administration of antibiotics for the infections and dilatation and curettage (D&C) for the one case of post-coital bleeding. (See **Table 3.**)

Table 3 - Adverse Events Related to Uterine Balloon Therapy™ and Rollerball Ablation

Safety at 12 Months		
	THERMACHOICE (n = 134)	ROLLERBALL (n = 126)
Intraoperative Adverse Events	None (0%)	2 fluid overloads 1 cervical laceration 1 uterine perforation (3.2%)
Postoperative Adverse Events	1 post-coital bleeding 3 endometritis 1 UTI (3.7%)	1 endometritis 1 hematometra 1 PATSS[1] (2.4%)
Mean Procedure Time (minutes)	27.4**	39.6**
Cases Performed Under General Anesthesia	53.7%**	84.1%**

[1]PATSS = post-ablation-tubal sterilization syndrome.
*Not statistically different (P > 0>05). ** Statistically significant (P< 0.05).

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- **Anticipated Clinical Events Post-Ablation**
  There are several clinical events that are normal and expected consequences of endometrial ablation, either by rollerball or uterine balloon therapy. These responses include pelvic cramping (See Table 1.), vaginal discharge and nausea/vomiting. These types of adverse events would be anticipated with this type of procedure.

- **Efficacy at One Year: Diary Scores**
  Study results demonstrated that the two treatment groups had the same therapeutic outcome twelve months following ablation, as measured by diary scores of ≤ 75. There were 239 patients completing twelve months of follow-up (125 UBT and 114 RB) who were included in the Efficacy Evaluation Group. Two patients who had hysterectomies (1 UBT and 1 RB) for menorrhagia prior to completing follow-up were included in success/failure calculations as treatment failures. The overall success rates as measured by menstrual diary scores twelve months post-procedure were comparable in the Efficacy Evaluable Groups and are shown in Table 4. The UBT group showed an 80.2% (101/126) success rate compared to 84.3% (97/115) for the rollerball group. The difference is not statistically significant.

Table 4 - Success Rate at Twelve Months (Efficacy Evaluable Group)

Twelve Month Evaluation Success Rate	UBT n=126*	RB n=115*
No. Diary Score ≤ 75 (%) 95% Confidence Interval	**101 (80.2%)** (73.2%, 87.2%)	**97 (84.3%)** (77.6 %, 90.9%)

*Two patients, 1 UBT and 1 RB, considered treatment failures in primary endpoint analysis for having a hysterectomy prior to one-year follow-up as a result of continued menorrhagia.

The success rates for the age group strata in UBT-treated patients (Efficacy Evaluation Group) were the same: 79.7% (51/64) and 80.6% (50/62) for the ≤ 40 years and > 40 years age groups, respectively. The rollerball age success rates were 90.9% (50/55) in the younger group and 78.3% (47/60) in the older patients. A comparison of the effectiveness at 12 months between the study arms is summarized in Table 5.

- **Efficacy at One Year: Quality-of-Life Improvements**
  Secondary endpoint measurements involving Quality-of-Life issues were also found to be similar between the UBT and rollerball groups. Specific results for several of the secondary endpoints involving Quality-of-Life variables one year post-ablation are listed in Table 5, below.

Impact on Life

Answers to pre-procedure questions indicated that 70.3% of the UBT patients and 78.6% of the rollerball patients felt menorrhagia had a severe impact on their life (ranking of 8 to 10). Only 2 (1.6%) women in the UBT group and 1 (0.9%) in the rollerball group ranked the impact of excessive bleeding before ablation from 1 to 3,

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or as having only a slight impact. Twelve months after ablation the women completed the same questionnaire at which time only 3.2% (4/125) of the UBT-treated women and 1.8% (2/114) of the rollerball group reported menorrhagia as having a major impact on their life.

Hemoglobin

The rate of anemia was decreased in both the UBT and rollerball groups following the procedures. A total of 122 of the 125 UBT cases had twelve-month hemoglobin values available. Of these, 9.0% (11/122) had low hemoglobin values twelve months post-ablation compared to 26.3% (36/137) prior to the procedure. In the rollerball group, 8.8% (10/114) were anemic at one year, compared to 29.7% (41/138) before ablation.

Hematocrit

Of all women randomized to UBT, 29.9% (41/137) had abnormally low hematocrit values prior to ablation. In the rollerball Intent-to-Treat group, 29.7% (41/138) had low hematocrit levels before surgery. Following ablation, 11.6% (14/121) of the UBT-treated group with twelve-month blood test results had low hematocrits as compared to 10.6% (12/113) of the rollerball group.

Premenstrual Symptoms

Both treatment groups demonstrated comparable decreases in reports of pre-menstrual symptoms following ablation. In the UBT-treatment group, 91.2% (125/137) reported PMS symptoms prior to ablation, while 72.8% (91/125) reported symptoms twelve months following the procedure. In the rollerball group, 91.3% (126/138) had PMS symptoms prior to the procedure as compared to only 71.9% (82/114) twelve months afterwards.

Dysmenorrhea

A total of 70.4% (88/125) of the UBT-treated patients and 75.4% (86/114) of the rollerball group reported a decrease in dysmenorrhea twelve months post-operatively. Only 4.8% (6/125) of the UBT and 1.8% (2/114) of the rollerball patients reported an increase in their dysmenorrhea symptoms.

Patient Satisfaction

All but five UBT patients and one rollerball patient expressed some degree of satisfaction twelve months after their ablation procedure. Specifically, 85.6% (107/125) of women treated with UBT were "very satisfied" twelve months post-operatively, compared to 86.7% (98/113) of women treated with rollerball. A total of 10.4% (13/125) of the UBT-treated group reported being "satisfied" at twelve months, while 12.4% (14/113) of the rollerball group claimed they were "satisfied". Only one patient (0.9%) in the rollerball group reported being "dissatisfied" compared to 4.0% of the women treated with UBT being "dissatisfied" at twelve months after their procedure.

Work Outside the Home

Both treatment groups demonstrated reductions in the number of women prevented from working outside the home because of menorrhagia. While 39.7% (54/136) of the UBT treatment group answered that they couldn't work outside the home because of bleeding pre-ablation, only 4.0% (5/124) did so twelve months post-UBT. In the rollerball group, 41.9% (57/136) of the women were prevented from working outside the home before therapy, but this decreased to 2.7% (3/112) twelve months after rollerball ablation.

Table 5 - Effectiveness Comparison at 12 Months for Uterine Balloon Therapy and Rollerball Ablation

Effectiveness at 12 Months	THERMACHOICE (n = 125)	ROLLERBALL (n = 114)
Study Success Rate (Diary Score ≤ 75)	80.2%*	84.3%*
Decrease to Normal Bleeding Levels or Less (Diary Score ≤ 100)	84.8.%*	89.5%*
Mean Percent Decrease in Diary Scores	85.5 ± 22.5**	91.7 ± 12.0**
% Patients with ≥ 90% Reduction in Diary Scores	61.6%*	68.4%*
% Patients with Diary Scores = 0	13.2%**	27.2%**
Quality of Life		
% Patients with Anemia Pre/Post *(HCT)*	29.9% / 11.6%*	29.7% / 10.6%*
Satisfaction: Very Satisfied / Satisfied	85.6% / 10.4%*	86.7% / 12.4%*
% Patients with Reduction in Dysmenorrhea	70.4%*	75.4%*
Inability to Work Outside the Home Pre/Post	39.7%* / 4.0%*	41.9%* / 2.7%*
% Patients Reporting Severe Impact on Life Pre/Post	70.3%* / 3.2%*	78.6%* / 1.8%*

*Not statistically different (P > 0.05). **Statistically significant (P < 0.05)

C. Multi-center International Study

The results of a multi-center international study and other international experience were presented, however, because protocols and data collection were not fully documented, these studies were not used to support the safety and effectiveness of the UBT System. Nevertheless, a total of 336 pre-menopausal patients were treated and followed in the International Uterine Balloon Therapy Trial using the recommended protocol of an 8-minute therapy time and at least 150 mmHg start pressure (160-180 mmHg preferred). Patient follow-up at 6 months is reported, with a total of 7.4% (25/336) of the women having had hysterectomies since their ablation procedures, and 4.5% (15/336) having had repeat ablations. There were no intra-operative adverse events or any major post-operative complications attributable to the ThermaChoice™ device. Specifically, adverse events included mild vaginal, bladder, or uterine infections and hematometra for a total rate of approximately 3%.

Approximately 3000 women (including non-study patients) have been treated with the UBT device outside of the United States. From this experience, a uterine

perforation was reported with the attending physician opting to perform a hysterectomy, even though the patient was in stable condition. The patient recovered with no further sequellae.

X. CONCLUSIONS DRAWN FROM THE STUDIES

The pre-clinical and clinical data provide reasonable assurance that the ThermaChoice™ Uterine Balloon Therapy™ is safe and effective when used as indicated in accordance with the directions for use.

XI. PANEL RECOMMENDATIONS

At an advisory meeting held on October 6, 1997, the Obstetrics and Gynecology Devices Panel recommended that the Gynecare, Inc., PMA for the ThermaChoice™ Uterine Balloon Therapy™ (UBT) System be approved subject to the following:

1. Resolution of the potential issue of introducing air during catheter priming;
2. Resolution of remaining software issues regarding specification system requirements, validation test plan, and test results;
3. Submission of the Final Report on the pivotal clinical study, including results of the 1 year follow-up on the remaining study subjects and final data analysis;
4. Development of final proposed labeling for both professional and patient, including modification of the indications for use statement; and,
5. Development of a post-approval study in order to gather long-term safety and effectiveness data.

Gynecare provided information to resolve the remaining engineering and clinical questions. In addition, the post-approval study will address:

- need for hysterectomy or repeat ablation for continued or recurrent menorrhagia;
- assessment of patient's menstruation pattern;
- adverse events and/or complications;
- Quality of Life Questionnaire;
- patients' pregnancy and contraception status; and,
- diagnosis of malignancy of the uterus

XII. FDA DECISION

An FDA inspection of the Gynecare, Inc. manufacturing facility was completed on June 2, and October 2, 1997, and the sterilization facility's inspection was completed on December 11, 1996. It was determined that the manufacturer was in compliance with and has an acceptable Good Manufacturing Practices (GMP) program.

CDRH concurred with the Obstetrics and Gynecology Devices Panel's recommendation. Based on a review of the data contained in the PMA, CDRH determined that the ThermaChoice™ Uterine Balloon Therapy™ (UBT) System is safe and effective as a 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 child bearing is complete. Furthermore, the applicant agreed to the postapproval requirement to follow subjects enrolled in the efficacy study for a period of three years from the time of treatment. The applicant will also ensure that physician education is available to new physician users, pursuant to the ThermaChoice™ Physician Training Plan.

CDRH issued an approval order for the stated indication for the applicant's PMA for the ThermaChoice™ Uterine Balloon Therapy™ (UBT) System on DEC 12 [illegible].

XIII. APPROVAL SPECIFICATIONS

Directions for use: See the Device Labeling.

Hazards to Health from Use of the Device: See Indication, Contraindications, Warnings, Precautions and Adverse Events in the labeling.

Post-approval Requirements and Restrictions: See approval order.

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U.S. Pat. Nos. 4,949,718; 5,105,808; 5,159,925; 5,460,628; 5,449,380
and other patents pending.
PN00383 Rev. A9 (1997-12-12)

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weitere Patente angemeldet.
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THERMACHOICE™

Uterine Balloon Therapy

ThermaChoice UBT System Operating Manual

Gynecare inc.

technology for women's healthcare

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Gynecare™

THERMACHOICE™

Uterine Balloon Therapy

Thermal Balloon Ablation System

Read all directions, cautions and warnings prior to use.

This manual provides directions for using the ThermaChoice Uterine Balloon Therapy (UBT) System.

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician with appropriate training.

Caution: This product contains natural rubber latex which may cause allergic reaction

DEVICE DESCRIPTION

The ThermaChoice UBT System is a software controlled device designed to ablate uterine tissue by thermal energy. The system is comprised of a single-use balloon catheter, a reusable controller, umbilical cable, and power cord. The ThermaChoice catheter is designed for use only with the ThermaChoice controller.

The balloon catheter is 1) connected to the controller, 2) inserted through the cervix i the uterus, 3) filled with sterile, injectable fluid (5% dextrose in water) carefully stabi ing the pressure to 160-180 mmHg pressure, and 4) activated to thermally ablate endometrial tissue by maintaining a temperature of approximately 87°C (188°F) for minutes.

INDICATIONS

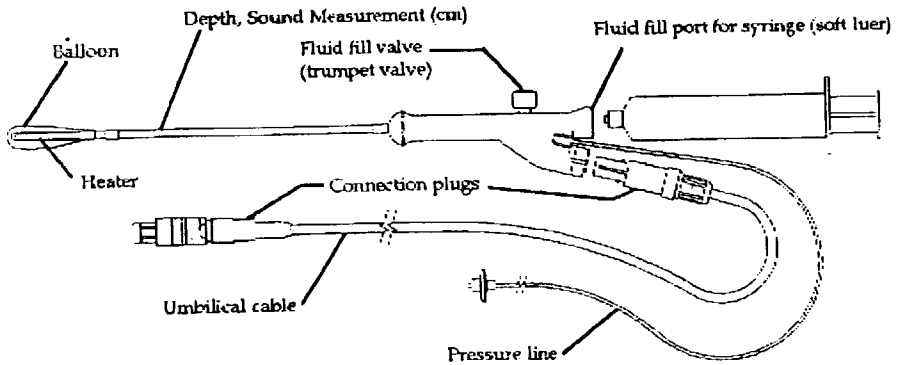
The ThermaChoice UBT system is a thermal ablation device intended to ablate the endometrial lining of the uterus in premenopausal women with menorrhagia (excessi uterine bleeding) due to benign causes for whom childbearing is complete.

CONTRAINDICATIONS

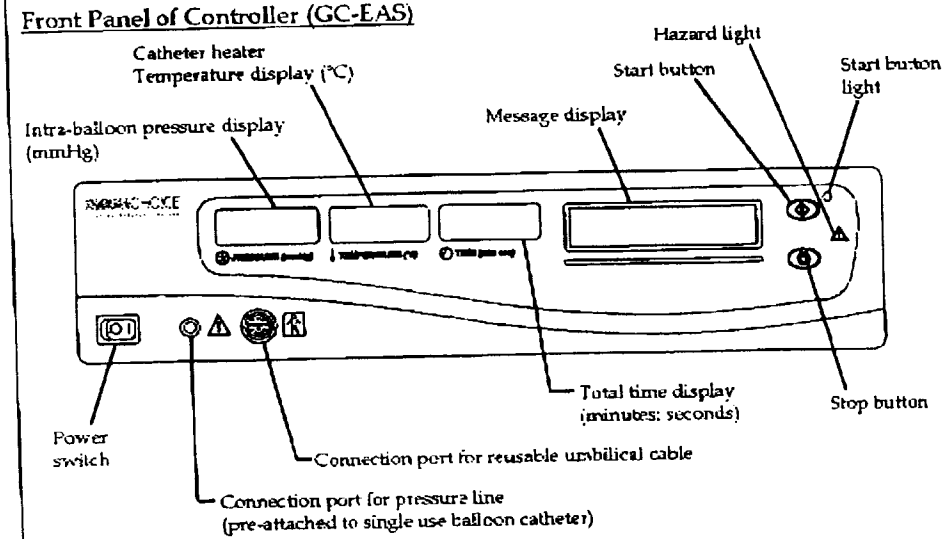
The device is contraindicated for use in:

- A patient who is pregnant or who wants to become pregnant in the future.
- A patient with a history of latex allergy or who has demonstrated a sensitivity to latex material.
- A patient with known or suspected endometrial carcinoma (uterine cancer) or premalignant change of the endometrium such as unresolved adenomatous hyperplasia.
- A patient with any anatomic or pathologic condition in which weakness of the myometrium could exist, such as history of previous classical cesarean sections or transmural myomectomy.
- A patient with active genital or urinary tract infection at the time of procedure (e.g., cervicitis, vaginitis, endometritis, salpingitis, or cystitis).
- A patient with an intrauterine device (IUD) currently in place.

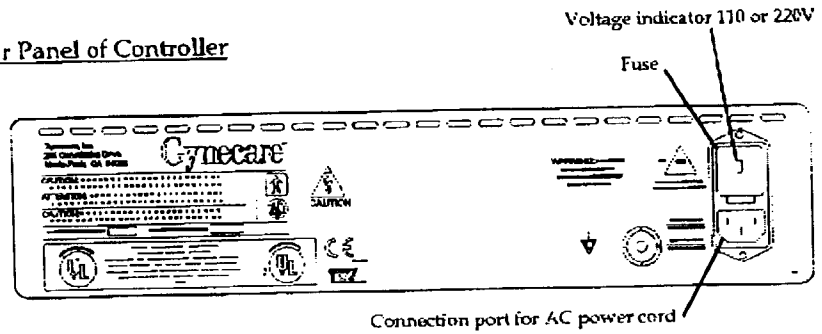
Single-Use Balloon Catheter (GC-EAC) and Umbilical Cable (GC-EAU)



Front Panel of Controller (GC-EAS)



Rear Panel of Controller



DESCRIPTION OF SYMBOLS

Front Panel of Controller

Off (power: disconnection from the mains)

On (power: connection to the mains)

Start Button — Stop Button

indicates hazard condition and termination of procedure (see ERROR MESSAGES section) Red light: when on, attention, consult operator's manual

INSERT CATHETER
FILL CATHETER — Message Display- displays prompts and error messages

Displays pressure inside balloon in mmHg

Displays heater temperature inside balloon in °C

Displays total running time for preheat and therapy in MINUTES: SECONDS

Rear Panel of Controller

(see SPECIFICATIONS for additional information)

Voltage indicator (110 or 220V)

Connection port for power cord

Location of Fuses; Type and value rating

Equipotentiality

Type BF Equipment

Cover to be removed by qualified service personnel only

Danger: Risk of explosion if used in the presence of flammable anesthetics!

Notified body TUV Product Services, Munich

0123

WARNINGS

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

- 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.
- Endometrial ablation using the ThermaChoice UBT System is not a sterilization procedure. Pregnancies after ablation can be dangerous for both mother and fetus.
- Endometrial ablation procedures using the ThermaChoice UBT System should be performed only by medical professionals who have experience in performing procedures within the uterine cavity such as IUD insertion or dilation and curettage (D&C) and having adequate training and familiarity with the ThermaChoice system.
- Endometrial ablation procedures do 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.
- The UBT balloon catheter is for single use only — do not reuse, or resterilize.
- Do not treat patients for more than one therapy cycle in a given treatment session because of the potential for transmural injury to the uterus or injury to adjacent viscera.
- Use caution not to perforate the uterine wall when sounding the uterus or inserting the UBT balloon catheter. If a perforation is present, the procedure should be terminated immediately.

PRECAUTIONS

The UBT balloon catheter, controller, and umbilical cable are designed as a system. To ensure proper function, never use other components with the UBT system.

A starting pressure of 160 - 180 mmHg is recommended and typically requires 6-15 cc of fluid and may require as much as 30 cc. **Titration to achieve a stable pressure (no fluctuations greater than ± 10 mmHg for at least 30 sec) prior to activating the heating element is critical to proper functioning of the device. When inserting fluid, do not exceed a pressure of 200 mmHg.** Typically, pressure levels decline slowly during the course of the procedure as the uterus relaxes. If a pressure of 160 - 180 mmHg cannot be reached with 30 cc or less of fluid, or if there is a rapid drop in pressure, remove balloon catheter and check for catheter leak and/or uterine perforation. Never add additional fluid during a therapy cycle. Rapid loss of pressure during a therapy cycle may indicate a uterine wall defect is present. Adding additional fluid to the balloon may create (or exacerbate if already present) a uterine wall defect such as a perforation.

Those 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 ThermaChoice UBT system has not been fully evaluated in patients:

- with a large uterine cavity (>30 cc in volume or uterine sound >10 cm).
- with a small uterine cavity (< 2 cc in volume or uterine sound < 6 cm).
- with submucosal myomas, a bicornuate or septate uterus or a previous endometrial resection/ablation.
- undergoing repeat endometrial ablation procedures.
- who are post-menopausal.

ADVERSE EVENTS

In a study of 134 women, the most frequent events that have been reported following completion of the procedure include:

- Cramping/pelvic pain - Post-treatment cramping was reported in 91.8% of the patients which ranged from mild to severe as reported during the intra-operative period and immediate post-operative period. This cramping will typically last a few hours and rarely continues beyond the first day following ablation. The use of non-steroidal anti-inflammatory drugs (NSAIDs) prior to and following Uterine Balloon Therapy is usually sufficient to manage cramping and pelvic pain.
- Nausea and Vomiting - Nausea and vomiting were reported for 23.9% of the patients in the immediate hours following the procedure. This may be attributed to general anesthesia, and can be easily managed with medication.
- Endometritis was reported in 2.1% of patients. All patients responded to a course of oral antibiotics.
- Post-procedure symptoms such as pain, fever, nausea, vomiting, difficulty with defecation or micturition were reported. Failure of such symptoms to resolve over a reasonable period of time warrants evaluation by appropriate medical personnel.
- Hematometra was reported in 0.6% of patients treated in clinical studies conducted outside of the United States. In all patients, the hematometra was resolved with insertion of a uterine sound.
- A single perforation of the uterus was reported in a procedure conducted outside the United States.

OTHER POTENTIAL ADVERSE EFFECTS

The following adverse effects might be expected (potential), but have not yet been observed in clinical studies of the ThermaChoice UBT System:

1. **Rupture of the Uterus**
2. **Thermal Injury to Adjacent Tissue**
3. **Heated Liquid Escaping Into the Vascular Spaces and/or Cervix, Vagina, Fallopian Tubes, and Abdominal Cavity.**
4. **Electrical Burn**
5. **Allergic Reaction to Latex**
6. **Hemorrhage**
7. **Infection**
8. **Pregnancy** - Pregnancy following endometrial ablation is dangerous to both mother and fetus.

9. **Post-ablation-tubal sterilization syndrome** - This is a complication following endometrial ablation in women who have also previously undergone tubal ligation. The pathophysiology of this condition is believed to be related to the regeneration of endometrium in the cornual areas of the uterus. Blood from these glands can flow back into the proximal fallopian tubes in cases where the lower uterine segment is extensively scarred. The proximal oviduct becomes filled with blood and fluid causing symptoms similar to those of an ectopic pregnancy.

CLINICAL TRIAL

Conclusions: At twelve months of follow-up, balloon ablation was demonstrated to be at least as safe (with fewer intraoperative complications, less use of general anesthesia, and shorter procedure times), and as effective as hysteroscopic rollerball ablation in reducing menstrual bleeding to a clinically acceptable level in menorrhagic women who had completed their childbearing. Furthermore, statistically equivalent and significant reductions in patient-reported dysmenorrhea (mild, moderate, severe menstrual cramps), PMS symptoms (mild, moderate, severe common PMS symptoms), and overall impact of menses on lifestyle (scale of 1-10; 1 = none, 10 = severe) were experienced by both groups.

Purpose: The use of balloon thermal ablation for the treatment of menorrhagia for benign causes in an anatomically normal uterine cavity was compared with rollerball electrosurgical endometrial ablation with regard to safety and effectiveness. The primary effectiveness measure was a validated diary scoring system (adapted from Higham JM, O'Brien PMS, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. Br J Obstet Gynaecol 1990;97:734-9). Success was defined as the reduction of excessive menstrual bleeding to normal flow or less. Secondary endpoints evaluated were overall percent decrease in diary scores and responses from a quality-of-life questionnaire. The endpoints for safety were based on the evaluation of adverse events associated with each procedure, including device-related complications, time of procedure, and type of anesthesia used.

Methods: This randomized, prospective, multicenter clinical investigation was conducted at 14 sites using investigators highly experienced with hysteroscopic rollerball endometrial ablation. All patients were ≥ 30 years old, premenopausal, and had completed childbearing. All had an anatomically normal uterine cavity > 4 cm and < 10 cm.

Three months of documented menorrhagia for benign causes was a requirement for inclusion and was confirmed with a diary score of at least 150 points. Endometrial biopsy and pap smear were required to rule out (pre)malignant uterine disease. No uterine thinning medications could be used for three months prior to treatment, and all patients underwent a three-minute suction curettage just prior to treatment. Selection of anesthesia regimen was left to the individual investigators. Treatment success was defined as reduction in menses to a diary score less than or equal to 75 in order to assure a return to eumenorrhea. In the original Higham study, a diary score of 100 had an 86% sensitivity and an 81% specificity for true menorrhagia for benign causes as determined by chemical analysis of the saturated pads.

Description of Patients: Two hundred seventy-five patients were randomized, 260 evaluated for safety, 255 of whom were eventually treated with either ThermaChoice Uterine Balloon Therapy (131) or rollerball ablation (124). A total of 125 UBT-treated patients and 114 rollerball-treated patients were available for Efficacy Evaluation by having completed twelve-month follow-up. Baseline demographic and gynecologic variables were statistically equivalent between the two groups with regard to age (U 40.2 years, RB 40.9 years), race, body mass index, mean baseline diary score (UBT 552.5, RB 570.5) and other criteria.

Results:

Table 1. Effectiveness at 12 Months

	THERMACHOICE (n = 125)	ROLLERBALL (n = 114)
Study Success Rate (Diary Score ≤ 75)	80.2%*	84.5%*
Decrease to Normal Bleeding Levels or Less (Diary Score ≤ 100)	84.8%*	89.5%*
Mean Percent Decrease in Diary Scores	85.5 ± 22.5**	91.7 ± 12.0**
% Patients with > 90% Reduction in Diary Scores	61.6%*	68.4%*
% Patients with Diary Scores = 0	15.2%**	27.2%**
Quality-of-Life		
% Patients with Anemia Pre/Post (HCT)	29.9% / 11.6%*	29.7% / 10.6%*
Satisfaction: Very Satisfied / Satisfied	85.6% / 10.4%*	86.7% / 12.4%*
% Patients with Reduction in Dysmenorrhea	70.4%*	75.4%*
Inability to Work Outside the Home (Pre/Post-Treatment Score)	39.7%* / 4.0%*	41.9%* / 2.7%*
% Patients Reporting Severe Impact on Life Pre/Post	70.3%* / 3.2%*	78.6%* / 1.8%*

*Not statistically different (P > 0.05). **Statistically significant (P < 0.05)

Table 2. Safety at 12 Months

	THERMACHOICE (n = 134)	ROLLERBALL (n = 126)
Intra-operative Adverse Events	None (0%)	2 fluid overloads 1 cervical laceratı 1 uterine perfora (3.2%)
Post-operative Adverse Events	1 post-coital bleeding 3 endometritis 1 UTI (3.7%)	1 endometritis 1 hematometra 1 PATSS† (2.4%)
Mean Procedure Time (minutes)	27.4**	39.6**
Cases Performed Under General Anesthesia	53.7%**	84.1%**

†PATSS = post-ablation-tubal-sterilization syndrome *Not statistically different (P > 0.05).
**Statistically significant (P < 0.05)

PATIENT SELECTION

Menorrhagia can be caused by a variety of underlying problems including but no limited to, endometrial cancer, myomas, polyps, anovulation, drugs, and dysfunc uterine bleeding. Patients should always be evaluated to determine the cause of th excessive uterine bleeding before any treatment option is initiated.

Consult medical literature relative to various endometrial ablation techniques, indi tions, contraindications, complications, and hazards prior to the performance of a endometrial ablation procedures.

- Documented diagnosis of menorrhagia for benign causes
- Completed childbearing
- Premenopausal
- Normal pap smear and endometrial biopsy

need opening sentence here

- Anatomically normal uterine cavity: standard sonography, saline infusion sonography, hysteroscopy, or hysterosalpingography within 6 months prior to performing UBT should be used to rule out submucous fibroids, large polyps, and congenital abnormalities.
- Uterine cavity depth of 6-10 cm
- Failed or contraindicated medical therapy.

PATIENT COUNSELING

As with any procedure the physician needs to discuss risks, benefits and alternatives with the patient prior to performing 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 birth control method. Patients with childbearing capacity should be cautioned of the potential complications which may ensue if they should become pregnant.

Vaginal discharge is typically experienced during the first few days following ablation and may last as long as a few weeks. Generally, the discharge is described as bloody during the first few days; by approximately one week, serosanguinous, then profuse and watery thereafter.

PRETREATMENT PREPARATION OF PATIENT

The lining of the uterus should be thinned prior to UBT. This can be accomplished by timing the menstrual cycle to the early proliferative phase, administering pretreatment drugs such as danocrine or GnRH agonists, or performing suction or sharp curettage immediately 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.

DIRECTIONS FOR USE

Please read all directions, cautions and warnings prior to use.

1.0 SET-UP

1.1. The following items are required for use of the UBT System.

UBT System	Reorder # Number
1 sterile disposable UBT balloon catheter and syringe (30cc)	GC-EAC
1 umbilical cable	GC-EAU
1 controller	GC EAS
1 power cord	GC-EAP

Medical Supplies

5Xcc sterile injectable 5% dextrose in water (D5W)
sterile drape for umbilical cord
tenaculum, (weighted) speculum
uterine sound, cervical dilator(s)

1.2 Open the sterile package containing the UBT balloon catheter and syringe. Disinfect umbilical cable as described at the end of this manual.

1.3 Make sure that the controller power is off before making the connection (Steps 1.4 - 1.5).

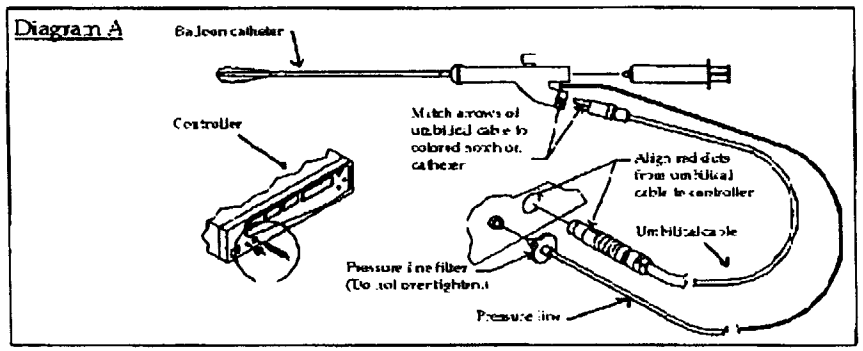
1.4 Plug the power cord into the back of the controller and into the wall outlet.

1.5 The umbilical cable includes a connector plug at each end to connect the balloon catheter to the controller. Visually inspect the cable and connector plugs to ensure there are no defects or signs of wear. Drape umbilical cable with sterile drape and attach cable to the connector at the proximal end of the balloon catheter (match arrows of cable to colored notch on catheter). Attach the opposite end of the cable to the connection port on the front panel of controller. (Align red dots from umbilical cable to controller). (See Diagram A).

Note: When oriented correctly, the cable plugs will fit into the connectors easily and securely.

1.6 Connect the pressure line (pre-attached to balloon catheter) to the connection port (luer lock) on the front panel of controller. Tighten 1/4 turn only; do not over-tighten (See Diagram A). Periodically clean the entrance of the controller's port using a cotton swab with 50% ethyl alcohol.

Diagram A



1.7 TURN ON the controller POWER. The Message Display will read:

Message Display: REV. N.NN
Note: N.NN = software revision level
WARMING UP

After a few seconds, the Message Display will alternate between the following messages:

Message Display: PRIME CATHETER

and

INSERT CATHETER
FILL CATHETER

The pressure line MUST be connected to the controller BEFORE the balloon catheter is filled with fluid, or the device may not function properly.

2.0 CATHETER PRIMING

2.1 **FILL** the 30cc syringe with approximately 15-20cc of sterile injectable 5% dextrose in water (D_5W).

Use only sterile injectable 5% dextrose in water (D_5W). Use of other fluids may compromise system.

2.2 **CONNECT** syringe to the port in the proximal end of the balloon catheter. Do not overtighten syringe when connecting.

2.3 Point balloon catheter tip downward.

2.4 Press trumpet valve on top of balloon catheter handle and fill with 5-10cc of D_5W.

2.5 Press trumpet valve and evacuate fluid and air from balloon to a negative pressure of -150 to -200 mmHg (indicated by pressure display on controller).

Note: You may need to purge air from syringe several times to attain desired negative pressure. You must release trumpet valve to maintain negative pressure. Air should be completely evacuated to optimize the function of the device.

2.6 The negative pressure creates a low-profile balloon insertion (balloon is drawn tight against catheter tip). Do not go beyond -300 mmHg. Check that negative pressure is maintained for at least 10 seconds before proceeding.

If negative pressure cannot be maintained for 10 seconds, remove balloon catheter and replace.

3. PRESSURE TITRATION

3.1 Fill syringe to 30cc with D_5W, purge air, and connect to balloon catheter (do not overtighten).

3.2 Using appropriate sterile technique and cervical/vaginal preparation, dilate cervix to 5mm if necessary.

3.3 Measure depth of uterus.

3.4 Wet outside of balloon with D_5W.

3.5 After sounding uterus, and wetting the balloon, SLOWLY INSERT BALLOON CATHETER into uterus until tip is touching the fundus. Ensure depth indicated by markings on catheter is consistent with previous sound measurement. Use a tenaculum to hold cervix if necessary.

Ensure cervical dilation to 5mm and do not use excessive force during insertion, as such force can cause the balloon to tear or the catheter to perforate the uterine wall.

3.6 Press trumpet valve on top of balloon catheter and fill balloon slowly to pressure of 160-180 mmHg using 2-30cc of D_5W (Release trumpet valve to allow pressure to stabilize). Incrementally add small volumes to achieve a stable pressure (no fluctuations greater than ± 10 mmHg) of 160-180 mmHg for a minimum of 30 seconds. The pressure of the balloon against the uterine wall often precipitates uterine relaxation, thereby temporarily decreasing pressure.

For optimal results, it is extremely important to allow pressure to stabilize to 160-180 mmHg for 30-45 seconds before pressing START (◇) button. The pressure will ultimately stabilize with careful titration.

Note: Once the heater is activated, the pressure may initially rise 10-20 mmHg; the pressure may then drop slowly for the remainder of the procedure. The ending balloon pressure may be as low as approximately 100 mmHg, and is typically between 120-150 mmHg.

Note: Activation pressure for the procedure is ≥ 150 mmHg. The procedure cannot start until the pressure is over 150 mmHg.

Note: It is recommended that for very small uteri, pressure titration should occur towards the lower end of the range (i.e. 160 mmHg) to minimize any potential for overpressure readings during the heating process.

Do not over pressurize balloon during titration. The controller can not display pressure > 300 mmHg.

Optimal balloon volume depends on the potential volume of the uterine cavity and is typically 6-15cc at >160 mmHg (at start) and may be as great as 30cc. If pressure level cannot be reached with 30cc of fluid, remove balloon catheter and check for uterine perforation and/or balloon catheter leak. Replace balloon catheter if necessary.

4. TREATMENT

4.1 Message Display:

READY PRESS START

When a steady pressure of 160-180 mmHg is maintained, press START (◇) button on controller to activate heater.

Do not add fluid once heater is activated, as this could result in patient injury. Hold balloon catheter immobile during procedure (with valve oriented upwards).

4.2 After the start button is pressed, the controller activates the heater to achieve treatment temperature of 87°C (188°F) within 4 minutes. (This preheat cycle may take up to 4 minutes, but is usually 15-45 seconds.)

PREHEATING TO 87°C

Note: If the treatment temperature of 87°C is not reached within 4 minutes, the controller will terminate the procedure. Remove fluid, remove catheter.

4.3 Message Display:

THERAPY CYCLE 87°C 8 MIN.

Once 87°C is reached, you will hear an audible alarm that indicates automatic activation of the 8 minute therapy cycle. Time elapsed is shown on the "TOTAL TIME" display (preheat + 8 minute therapy time).

Note: Pressure may rise slightly with initial heating. It is common to then see the pressure fall gradually during procedure.

4.4 When the treatment cycle is completed, the Message Display will alternate between the following messages:

CYCLE COMPLETE REMOVE CATHETER

and

TURN POWER OFF

4.5 The controller automatically terminates the heater at the end of the treatment (cycle) and an audible alarm will sound. Total treatment time will be displayed on controller (preheat time plus 8 minute therapy time).

5. POST-TREATMENT

5.1 Wait approximately 30 seconds for fluid to cool and then remove fluid by drawing back on syringe while depressing trumpet valve. Remove all fluid from balloon. Remove balloon catheter. Check that entire fluid volume is with drawn.

5.2 Disconnect catheter pressure line from controller.

5.3 Disconnect umbilical cable from catheter by holding grey shell and pulling back.

5.4 Disconnect umbilical cable from controller by holding stainless steel ribbed shell and pulling back. Do not pull on the cable itself.

5.5 Discard catheter. Retain umbilical cable and disinfect for next case.

5.6 Power must be turned off before beginning another procedure.

OPERATING PARAMETERS / ALARM AND DISPLAY MESSAGES

The controller is designed to monitor time, temperature and pressure within parameters preset at the factory.

- ALERT. If the temperature and/or pressure increases or falls beyond a level pre-set at the factory, the controller will sound a short audible alert.
- HAZARD ALARM/TERMINATION OF PROCEDURE (HEATER SHUT OFF LIMITS). If the temperature and/or pressure increases or falls outside the operating parameters, the controller will sound an alarm, terminate the procedure and display an error message. Additionally, if the controller detects a system failure, the procedure will be terminated. If the procedure is terminated, the Message Display will display a message indicating the cause.

The following chart explains operating parameters for temperature, time, and pressure:

	Standard	Range	Alarm/Heater Shut Off Limits	
Temperature	87°C	75-90°C	Over Under	≥95°C for 2 sec or be- ≤75°C for 15 sec*
Pressure	Titrate to 160-180 mmHg before starting procedure; Activation Pressure (Minimum starting pressure) ≥ 150 mmHg	45-210 mmHg	Over Under	≥210 mmHg ≤45 mmHg
Time	8 minute therapy cycle after reaching 87°C (preheat phase)		Over	>4 minute pre-heat

*or failure to achieve temperature of 87°C within 4 minute preheat phase.

When parameters extend outside the normal operating range, the controller sounds an audible alert (intended only as warning signals to the clinician). These values are listed below and reside between normal operating and termination parameters (see previous chart):

		Alert (Warning)
Temperature	Over	> 90°C & < 95°C for 2 seconds
	Under	< 83°C for 2 seconds
Pressure	Over	> 200 mmHg & < 210 mmHg for 2 seconds
	Under	> 45 mmHg & < 70 mmHg for 2 seconds

ERROR MESSAGES

Under electrostatic discharge to the controller or abnormal line voltage conditions, i.e. surge and fast transients, the system may terminate the procedure. The message display may be blank or may indicate an error code. If any of these occur turn off the power to the controller and restart the procedure.

In addition to the operating messages listed in the "Directions," the Message Display also provides messages which indicate conditions under which the controller either will not begin treatment or will terminate treatment after the heating cycle has been initiated.

Prior to pressing START (◇) – the following error messages indicate conditions under which the controller will not begin therapy cycle until corrected:

MESSAGE DISPLAY	REASON	ACTION
CONNECT CATHETER	Balloon catheter and/or umbilical cable is not connected.	Connect balloon catheter. Ensure connections are secure.
CATHETER ERROR REPLACE CATHETER	Balloon catheter and/or umbilical cable is not functioning properly.	Replace balloon catheter and/or umbilical cable.
SYSTEM ERROR TURN POWER OFF	System is not functioning properly.	Return controller for repair.

After pressing START (◇) – the following error messages indicate conditions under which the controller will terminate the procedure and disable the heating element after the therapy cycle has begun:

MESSAGE DISPLAY	REASON	ACTION
CATHETER ERROR END PROCEDURE	Balloon catheter is not functioning properly.	Remove fluid. Remove balloon catheter.
SYSTEM ERROR or HEATER ERROR and END PROCEDURE	System is not functioning properly.	Remove fluid. Remove balloon catheter. Return controller for repair.
PREHEAT ERROR or OVERHEAT ERROR or PRESSURE ERROR and END PROCEDURE	Treatment temperature and/or pressure is outside standard operating parameters.	Remove fluid. Remove balloon catheter.

WARRANTY

Gynecare, Inc., warrants the original purchase of the Gynecare UBT System Controller shall be free of defects in material and workmanship when used as intended under normal surgical conditions and in conformance with its directions for use and maintenance instructions. The obligation of Gynecare, Inc., under this warranty shall be limited to the repair or replacement, each at no charge, at the option of Gynecare, Inc., within one year from the date of purchase, if examination shall disclose to the satisfaction of Gynecare, Inc., that the controller does not meet this warranty.

THIS WARRANTY IS MADE IN LIEU OF ALL OTHER WARRANTIES EXPRESSED OR IMPLIED INCLUDING THE WARRANTIES OF MERCHANTABILITY AND FITNESS FOR USE AND ALL OTHER OBLIGATIONS AND LIABILITIES ON THE PART OF GYNECARE. GYNECARE, INC., NEITHER ASSUMES NOR AUTHORIZES ANY OTHER PERSON TO ASSUME FOR IT, ANY OTHER LIABILITY IN CONNECTION WITH THE SALE OF A GYNECARE CONTROLLER. THIS WARRANTY SHALL NOT APPLY TO A GYNECARE CONTROLLER OR ANY PART THEREOF WHICH HAS BEEN SUBJECT TO ACCIDENT, NEGLIGENCE, ALTERATION, ABUSE, OR MISUSE, NOR TO ANY GYNECARE, INC., CONTROLLER THAT HAS BEEN REPAIRED OR ALTERED BY ANYONE OTHER THAN AN AUTHORIZED GYNECARE SERVICE PERSON, MAKES NO WARRANTY WHATSOEVER WITH REGARD TO ACCESSORIES OR PARTS USED IN CONJUNCTION WITH THE GYNECARE, INC. CONTROLLER AND NOT SUPPLIED AND MANUFACTURED BY GYNECARE, INC. THE TERM "ORIGINAL PURCHASER", AS USED IN THE WARRANTY, SHALL BE DEEMED TO MEAN THAT PERSON OR ORGANIZATION AND ITS EMPLOYEES, IF APPLICABLE, TO WHOM THE GYNECARE CONTROLLER WAS SOLD BY GYNECARE, INC. THIS WARRANTY MAY NOT BE ASSIGNED OR TRANSFERRED IN ANY MANNER.

Should any Gynecare, Inc. controller become inoperable after the one year period on this Warranty or should damage occur which is not covered under the terms of this Warranty, Gynecare, Inc. will, upon request, be willing to repair the controller, if possible, for an appropriate handling and repair charge.

SERVICE

Should the UBT System Controller become inoperable contact Gynecare's Customer Service Department for instructions and a return material authorization number. Clean and repackage the controller appropriately and return it for repair, servicing and/or modification to the authorized locations listed below. If the controller is not under warranty, an appropriate handling and repair charge will be established after receipt and examination of the controller.

For service, technical support or reorder information, contact in the U.S.:
Gynecare, Inc.
Ethicon, Inc.
A Johnson & Johnson Company
235 Constitution Drive
Menlo Park, CA 94025
Phone: (650) 614-2500
Toll Free: (800) 336-4963
Fax: (650) 462-6742

Note: Any device related incidence or problems which are felt to represent a safety issue, should be reported to Gynecare's Customer Service Department or Authorized European Representative.

AUTHORIZED EUROPEAN REPRESENTATIVE

ETHICON France
une divson ETHNOR S.A.
192 Avenue Charles De Gaulle
92523 Neuilly sur Seine Cedex
France
Tel: 01/46 41 59 90

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Tel: 0131-453 5555

ETHICON S.P.A.
Via del Mare 56
00040 Pomezia
Roma
Italia
Tel: 06/911 944 32

ORDERING INFORMATION AND RELATED PARTS AND ACCESSORIES

Reorder Number	Description
GC-EAS	UBT System Controller
GC-EAC	UBT Balloon Catheter (sterile, single-use)
GC-EAU	UBT Umbilical Cable (reusable up to 20 applications)
GC-EAP	UBT Power cord (specify country)
GC-EAM	UBT System Manual
GC-EAI	UBT Instruction card

SPECIFICATIONS (CONTROLLER AND UMBILICAL CABLE)

Power Requirements	110 to 120 V; 50/60 Hz; 2A; 3-wire grounded system or 220-240V; 50/60 Hz; 1A; 3-wire grounded system
Mains Fuses	110-120VAC, 5x20mm T3A 250V Slow blow 220-240VAC, 5x20mm T1.6A 250V Slow blow
Heater Fuses	T5A 250V
Dimensions	Height 10.2cm (4in.), width 41.2cm (16.25in.), depth 37.0cm (14.56 in.)
Weight	6.9 kg (15.3 lb) (controller only)
Case	Aluminum and impact-resistant plastic
Umbilical Cable	Length 152 cm (60 in.)

MAINTENANCE

1.0 CALIBRATION:

Every time the UBT system is powered up, the controller zeros out the offsets that may be present on the measurement circuitry, and therefore automatically provides a single point calibration. In addition, the pressure sensor utilized in the controller is internally calibrated and temperature compensated and is accurate and stable over the operating range. These sensors are of differential type, and therefore measure the balloon pressure relative to the outside atmosphere. In addition to the internal means of calibration, it is possible to ensure the proper operation of the system against other calibrated devices. This procedure is recommended to be performed on an annual basis. The procedure also needs to be carried out if it is believed that the system is behaving unexpectedly.

Note: There are no calibration adjustments on the controller. If the unit does not meet the calibration requirements, it needs to be sent back to the manufacturer.

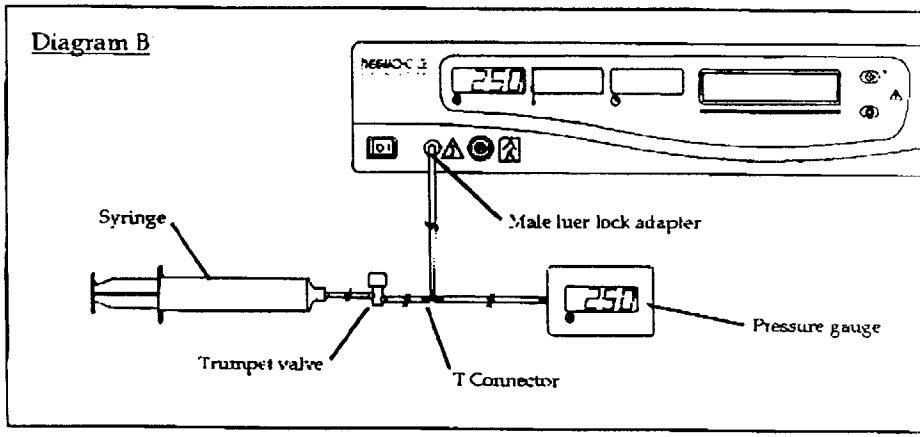
1.1. PRESSURE CALIBRATION

1.1.1. Equipment List

The following equipment list or equivalent is needed to perform the procedure:

1. Pressure meter: DigiMano model DPM 2000PS. NETECH Corporation, 60 Bethpage Drive, Hickville, NY 11801, Telephone: (800) 547-6557/ (Any calibrated, NBS traceable pressure gauge with a range of at least ± 6 psi can be used).
2. Syringe: PN 309562, Becton-Dickinson. State Surgical Supply, 3380 Vincent Rd. # C, Pleasant Hill, CA 94523, Telephone: (510) 284-1060.
3. Trumpet valve: PN S5402601, Braun Medical, Inc., 824 Twelfth Ave, PO Box 4027, Bethlehem, PA 18018-0027, Telephone: (610) 266-0500.
4. T connector: PN T20-1, Value Plastics, Inc., 3350 Eastbrook Dr., Fort Collins, CO 805 Telephone: (970) 223-0953.
5. Tubing: 0.093 ID, 0.156 OD, Norton Performance Plastics Corp, PO Box 3660, Akron OH 44309-3660, Telephone: (800) 798-1539.
6. Male luer lock adapter: PN B0850402, Braun Medical, Inc., 824 Twelfth Ave., PO Box 4027, Bethlehem, PA 18018-0027, Telephone: (610) 266-0500.

Diagram B



1.1.2. Procedure

1. With no attachments to the luer lock, apply power to the controller. The pressure display should read 0±10 mmHg.
2. Assemble the digital pressure gauge, the tubing, the T connector, the trumpet valve, the male luer lock adapter, and the syringe as shown in Diagram B, and connect to the connection port (luer lock) of the controller.
3. While depressing the trumpet valve, apply vacuum to the system using the syringe until the gauge reads approximately -250 mmHg.
4. Release the trumpet valve. The controller pressure reading should be within ± 10 mmHg of the gauge reading.
5. While depressing the trumpet valve, apply pressure to the system until the reading on the digital display meter indicates a pressure of approximately 250 mmHg.

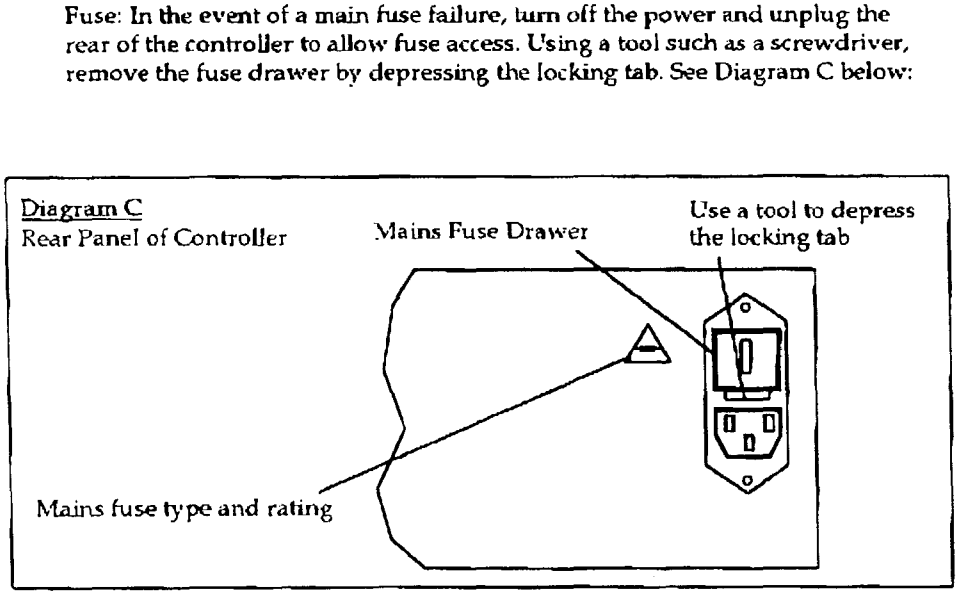
6. Release the trumpet valve. The controller pressure reading should be within ± 10 mmHg of the gauge reading.

1.2. TEMPERATURE CALIBRATION

1. Obtain a calibrated digital or glass thermometer.
2. Place this thermometer in close proximity to a new UBT catheter tip and allow them to come to thermal equilibrium with the ambient.
3. Connect the catheter to the controller using the umbilical cable as described earlier in the manual.
4. Power up the controller.
5. Note the thermometer reading and compare to that of the controller. The readings should be within ± 5 degrees Celsius.
6. Insert the balloon end of the catheter along with the thermometer in 80-90 degree Celsius water.
7. Allow a few minutes for the catheter and the thermometer to come to thermal equilibrium.
8. Compare the two temperature readings. They should be within ± 5 degrees Celsius.

2.0 FUSE REPLACEMENT:

Fuse: In the event of a main fuse failure, turn off the power and unplug the rear of the controller to allow fuse access. Using a tool such as a screwdriver, remove the fuse drawer by depressing the locking tab. See Diagram C below:



Replace both fuses with the same type and rating as specified on the rear of the controller. Reinsert the fuse drawer until the locking tab snaps into place. Reconnect the power cord and restore power to the controller. If a fuse fails again, disconnect all power to the controller and return it to Gynecare.

All other service must be performed by appropriately qualified technical personnel. Field repair, other than the controller's external fuse replacement voids all warranties and may not be performed without express authorization from Gynecare.

3.0 CLEANING: CONTROLLER SYSTEM

It is good practice to routinely clean the exterior surface of the device.

1. Disconnect all umbilical cables and unplug the power cord from the wall outlet before cleaning.
2. Use a cloth dampened with 50% water and 50% isopropyl alcohol, or a mild, nonabrasive detergent (such as commercially available dish cleaning liquid) mixed with water.
3. Periodically clean the entrance of the controller's port (luer lock) using a cotton swab with 50% isopropyl alcohol.

Do not autoclave, ETO sterilize, or immerse the controller or umbilical cable in a liquid. Do not allow liquids to enter the controller during cleaning.

4.0 DISINFECTION: UMBILICAL CABLE

The UBT Umbilical Cable is packaged non-sterile. After each use, the cable should be disinfected. To disinfect, wipe down the cable with a damp cloth using a solution of 50% water and 50% isopropyl alcohol. Use only 50% water and 50% isopropyl alcohol. Ensure that the cable and connectors are completely dry. Inspect the cable and the connector plugs before each use for signs of wear and replace if necessary. The umbilical has been validated for 20 cycles. Following 20 uses, discard the cable, and replace.

5.0 POWER CORD

Users in North America operating from a nominal 120 Vac system must select a Type SJT, SJTO, SJO, or SJE, Hospital Grade cord set. The power supply cord must be marked 'Grounding Reliability can only be achieved when the equipment is connected to an equivalent receptacle marked "Hospital Grade" or "Hospital Only"".

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PN00513 Rev. A9 (1997-12-12)

Gynecare ™
THERMACHOICE™
Uterine Balloon Therapy

Thermal Balloon Ablation Catheter and Syringe (Single-Use)

Read all directions, cautions and warnings prior to use.

This instructions for use provides directions for using the ThermaChoice Uterine Ballo Therapy (UBT) Catheter.

Caution: Federal law (USA) restricts this device to sale by or on the order of a physici with appropriate training.

Caution: This product contains natural rubber latex which may cause allergic reacti

DEVICE DESCRIPTION

The ThermaChoice UBT System is a software controlled device designed to ablate uterine tissue by thermal energy. The system is comprised of a single-use balloon catheter, a reusable controller, umbilical cable, and power cord. The ThermaChoice catheter is designed for use only with the ThermaChoice controller.

The balloon catheter is 1) connected to the controller, 2) inserted through the cervix the uterus, 3) filled with sterile, injectable fluid (5% dextrose in water) carefully stal ing the pressure to 160-180 mmHg pressure, and 4) activated to thermally ablate endometrial tissue by maintaining a temperature of approximately 87°C (188°F) fo minutes.

INDICATIONS

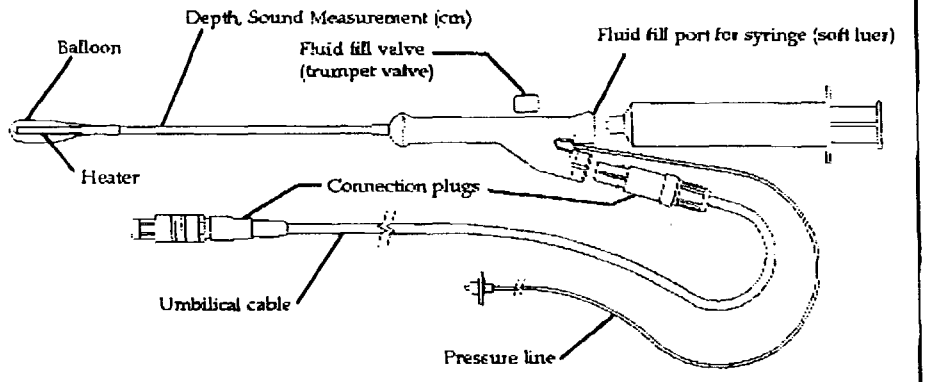
The ThermaChoice UBT system is a thermal ablation device intended to ablate the endometrial lining of the uterus in premenopausal women with menorrhagia (excess uterine bleeding) due to benign causes for whom childbearing is complete.

CONTRAINDICATIONS

The device is contraindicated for use in:

- A patient who is pregnant or who wants to become pregnant in the future.
- A patient with a history of latex allergy or who has demonstrated a sensitivity to latex material.
- A patient with known or suspected endometrial carcinoma (uterine cancer) or pr malignant change of the endometrium such as unresolved adenomatous hyperplasia.
- A patient with any anatomic or pathologic condition in which weakness of the myometrium could exist, such as history of previous classical cesarean sections or transmural myomectomy.
- A patient with active genital or urinary tract infection at the time of procedure (e.g., cervicitis, vaginitis, endometritis, salpingitis, or cystitis).
- A patient with an intrauterine device (IUD) currently in place.

Single-Use Balloon Catheter (GC-EAC) and Umbilical Cable (GC-EAU)



WARNINGS

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

- 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.
- Endometrial ablation using the ThermaChoice UBT System is not a sterilization procedure. Pregnancies after ablation can be dangerous for both mother and fetus.
- Endometrial ablation procedures using the ThermaChoice UBT System should be performed only by medical professionals who have experience in performing procedures within the uterine cavity such as IUD insertion or dilation and curettage (D&C) and having adequate training and familiarity with the ThermaChoice system.
- Endometrial ablation procedures do 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.
- The UBT balloon catheter is for single use only — do not reuse, or resterilize.
- Do not treat patients for more than one therapy cycle in a given treatment session because of the potential for transmural injury to the uterus or injury to adjacent viscera.
- Use caution not to perforate the uterine wall when sounding the uterus or inserting the UBT balloon catheter. **If a perforation is present, the procedure should be terminated immediately.**

PRECAUTIONS

The UBT balloon catheter, controller, and umbilical cable are designed as a system. To ensure proper function, never use other components with the UBT system.

A starting pressure of 160 - 180 mmHg is recommended and typically requires 6-15 cc of fluid and may require as much as 30 cc. **Titration to achieve a stable pressure (no fluctuations greater than ± 10 mmHg for at least 30 sec) prior to activating the heating element is critical to proper functioning of the device. When inserting fluid, do not exceed a pressure of 200 mmHg.** Typically, pressure levels decline slowly during the course of the procedure as the uterus relaxes. If a pressure of 160 - 180 mmHg cannot be reached with 30 cc or less of fluid, or if there is a rapid drop in pressure, remove balloon catheter and check for catheter leak and/or uterine perforation. Never add additional fluid during a therapy cycle. Rapid loss of pressure during a therapy cycle may indicate a uterine wall defect is present. Adding additional fluid to the balloon may create (or exacerbate if already present) a uterine wall defect such as a perforation.

Those 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 ThermaChoice UBT system has not been fully evaluated in patients:

- with a large uterine cavity (>30 cc in volume or uterine sound >10 cm).
- with a small uterine cavity (< 2 cc in volume or uterine sound < 6 cm).
- with submucosal myomas, a bicornuate or septate uterus or a previous endometrial resection/ablation.
- undergoing repeat endometrial ablation procedures.
- who are post-menopausal.

ADVERSE EVENTS

In a study of 134 women, the most frequent events that have been reported following completion of the procedure include:

- Cramping/pelvic pain - Post-treatment cramping was reported in 91.8% of the patients which ranged from mild to severe as reported during the intra-operative period and immediate post-operative period. This cramping will typically last a few hours and rarely continues beyond the first day following ablation. The use of non-steroidal anti-inflammatory drugs (NSAIDs) prior to and following Uterine Balloon Therapy is usually sufficient to manage cramping and pelvic pain.
- Nausea and Vomiting - Nausea and vomiting were reported for 23.9% of the patients in the immediate hours following the procedure. This may be attributed to general anesthesia, and can be easily managed with medication.
- Endometritis was reported in 2.1% of patients. All patients responded to a course of oral antibiotics.
- Post-procedure symptoms such as pain, fever, nausea, vomiting, difficulty with defecation or micturition were reported. Failure of such symptoms to resolve over a reasonable period of time warrants evaluation by appropriate medical personnel.
- Hematometra was reported in 0.6% of patients treated in clinical studies conducted outside of the United States. In all patients, the hematometra was resolved with insertion of a uterine sound.
- A single perforation of the uterus was reported in a procedure conducted outside the United States.

OTHER POTENTIAL ADVERSE EFFECTS

The following adverse effects might be expected (potential), but have not yet been observed in clinical studies of the ThermaChoice UBT System:

1. **Rupture of the Uterus**
2. **Thermal Injury to Adjacent Tissue**
3. **Heated Liquid Escaping Into the Vascular Spaces and/or Cervix, Vagina, Fallopian Tubes, and Abdominal Cavity.**
4. **Electrical Burn**
5. **Allergic Reaction to Latex**
6. **Hemorrhage**
7. **Infection**
8. **Pregnancy** - Pregnancy following endometrial ablation is dangerous to both mother and fetus.
9. **Post-ablation-tubal sterilization syndrome** - This is a complication following endometrial ablation in women who have also previously undergone tubal ligation. The pathophysiology of this condition is believed to be related to the regeneration of endometrium in the cornual areas of the uterus. Blood from these glands can flow back into the proximal fallopian tubes in cases where the lower uterine segment is extensively scarred. The proximal oviduct becomes filled with blood and fluid causing symptoms similar to those of an ectopic pregnancy.

CLINICAL TRIAL

Conclusions: At twelve months of follow-up, balloon ablation was demonstrated to be at least as safe (with fewer intraoperative complications, less use of general anesthesia, and shorter procedure times), and as effective as hysteroscopic rollerball ablation in reducing menstrual bleeding to a clinically acceptable level in menorrhagic women who had completed their childbearing. Furthermore, statistically equivalent and significant reductions in patient-reported dysmenorrhea (mild, moderate, severe menstrual cramps), PMS symptoms (mild, moderate, severe common PMS symptoms), and overall impact of menses on lifestyle (scale of 1-10; 1 = none, 10 = severe) were experienced by both groups.

Purpose: The use of balloon thermal ablation for the treatment of menorrhagia for benign causes in an anatomically normal uterine cavity was compared with rollerball electrosurgical endometrial ablation with regard to safety and effectiveness. The primary effectiveness measure was a validated diary scoring system (adapted from Higham JM, O'Brien PMS, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. Br J Obstet Gynaecol 1990;97:734-9). Success was defined as the reduction of excessive menstrual bleeding to normal flow or less. Secondary endpoints evaluated were overall percent decrease in diary scores and responses from a quality-of-life questionnaire. The endpoints for safety were based on the evaluation of adverse events associated with each procedure, including device-related complications, time of procedure, and type of anesthesia used.

Methods: This randomized, prospective, multicenter clinical investigation was conducted at 14 sites using investigators highly experienced with hysteroscopic rollerball endometrial ablation. All patients were ≥ 30 years old, premenopausal, and had completed childbearing. All had an anatomically normal uterine cavity ≥ 4 cm and ≤ 10 cm.

Three months of documented menorrhagia for benign causes was a requirement for inclusion and was confirmed with a diary score of at least 150 points. Endometrial biopsy and pap smear were required to rule out (pre)malignant uterine disease. No uterine thinning medications could be used for three months prior to treatment, and all patients underwent a three-minute suction curettage just prior to treatment. Selection of anesthesia regimen was left to the individual investigators. Treatment success was defined as reduction in menses to a diary score less than or equal to 75 in order to assure a return to eumenorrhea. In the original Higham study, a diary score of 100 had an 86% sensitivity and an 81% specificity for true menorrhagia for benign causes as determined by chemical analysis of the saturated pads.

Description of Patients: Two hundred seventy-five patients were randomized, 260 evaluated for safety, 255 of whom were eventually treated with either ThermaChoice Uterine Balloon Therapy (131) or rollerball ablation (124). A total of 125 UBT-treated patients and 114 rollerball-treated patients were available for Efficacy Evaluation by having completed twelve-month follow-up. Baseline demographic and gynecological variables were statistically equivalent between the two groups with regard to age (UBT 40.2 years, RB 40.9 years), race, body mass index, mean baseline diary score (UBT 552.5, RB 570.5) and other criteria.

Results:

Table 1. Effectiveness at 12 Months

	THERMACHOICE (n = 125)	ROLLERBALL (n = 114)
Study Success Rate (Diary Score ≤ 75)	80.2%*	84.3%*
Decrease to Normal Bleeding Levels or Less (Diary Score ≤ 100)	84.8%*	89.5%*
Mean Percent Decrease in Diary Scores	85.5 + 22.5**	91.7 + 12.0**
% Patients with > 90% Reduction in Diary Scores	61.6%*	68.4%*
% Patients with Diary Scores = 0	15.2%**	27.2%**
Quality-of-Life		
% Patients with Anemia Pre/Post (HCT)	29.9% / 11.6%*	29.7% / 10.6%*
Satisfaction: Very Satisfied / Satisfied	85.6% / 10.4%*	86.7% / 12.4%*
% Patients with Reduction in Dysmenorrhea	70.4%*	75.4%*
Inability to Work Outside the Home (Pre/Post-Treatment Score)	39.7%* / 4.0%*	41.9%* / 2.7%*
% Patients Reporting Severe Impact on Life Pre/Post	70.3%* / 3.2%*	78.6%* / 1.8%*

*Not statistically different (P > 0.05). **Statistically significant (P < 0.05)

Table 2. Safety at 12 Months

	THERMACHOICE (n = 134)	ROLLERBALL (n = 126)
Intra-operative Adverse Events	None (0%)	2 fluid overloads 1 cervical laceration 1 uterine perforation (3.2%)
Post-operative Adverse Events	1 post-coital bleeding 3 endometritis 1 UTI (3.7%)	1 endometritis 1 hematometra 1 PATSS[1] (2.4%)
Mean Procedure Time (minutes)	27.4**	39.6**
Cases Performed Under General Anesthesia	53.7%**	84.1%**

[1]PATSS = post-ablation-tubal-sterilization syndrome *Not statistically different ($P > 0.05$).
**Statistically significant ($P < 0.05$)

PATIENT SELECTION

Menorrhagia 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.

Consult medical literature relative to various endometrial ablation techniques, indications, contraindications, complications, and hazards prior to the performance of any endometrial ablation procedures.

- Documented diagnosis of menorrhagia for benign causes
- Completed childbearing
- Premenopausal
- Normal pap smear and endometrial biopsy
- Anatomically normal uterine cavity: standard sonography, saline infusion sonography, hysteroscopy, or hysterosalpingography within 6 months prior to performing UBT should be used to rule out submucous fibroids, large polyps, and congenital abnormalities.
- Uterine cavity depth of 6-10 cm
- Failed or contraindicated medical therapy.

PATIENT COUNSELING

As with any procedure the physician needs to discuss risks, benefits and alternatives with the patient prior to performing 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 birth control method. Patients with childbearing capacity should be cautioned of the potential complications which may ensue if they should become pregnant.

Vaginal discharge is typically experienced during the first few days following ablation and may last as long as a few weeks. Generally, the discharge is described as bloody during the first few days; by approximately one week, serosanguinous; then profuse and watery thereafter.

PRETREATMENT PREPARATION OF PATIENT

The lining of the uterus should be thinned prior to UBT. This can be accomplished by timing the menstrual cycle to the early proliferative phase, administering pretreatment drugs such as danocrine or GnRH agonists, or performing suction or sharp curettage immediately 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.

DIRECTIONS FOR USE

Please read all directions, cautions and warnings prior to use.

1.0 SET-UP

1.1. The following items are required for use of the UBT System.

UBT System	Reorder # Number
1 sterile disposable UBT balloon catheter and syringe (30cc)	GC-EAC
1 umbilical cable	GC-EAU
1 controller	GC EAS
1 power cord	GC-EAP

Medical Supplies

50cc sterile injectable 5% dextrose in water (D_5W)
sterile drape for umbilical cord
tenaculum, (weighted) speculum
uterine sound, cervical dilator(s)

1.2 Open the sterile package containing the UBT balloon catheter and syringe. Disinfect umbilical cable as described at the end of this manual.

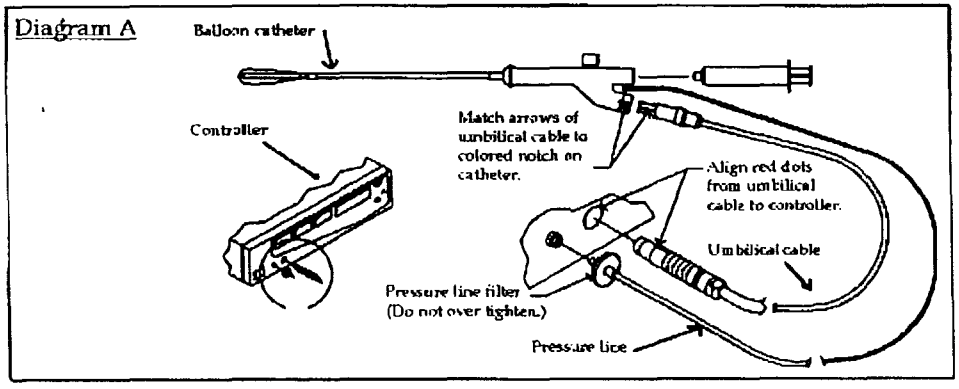
1.3 Make sure that the controller power is off before making the connection (Steps 1.4 - 1.6).

1.4 Plug the power cord into the back of the controller and into the wall outlet.

1.5 The umbilical cable includes a connector plug at each end to connect the balloon catheter to the controller. Visually inspect the cable and connector plugs to ensure there are no defects or signs of wear. Drape umbilical cable with sterile drape and attach the cable to the connector at the proximal end of the balloon catheter (match arrows of cable to colored notch on catheter). Attach the opposite end of the cable to the connection port on the front panel of controller. (Align red dots from umbilical cable to controller). (See Diagram A).

Note: When oriented correctly, the cable plugs will fit into the connectors easily and securely.

Diagram A



1.6 Connect the pressure line (pre-attached to balloon catheter) to the connection port (luer lock) on the front panel of controller. Tighten 1/4 turn only; do not over-tighten (See Diagram A). Periodically clean the entrance of the controller's port, using a cotton swab with 50% ethyl alcohol.

1.7 TURN ON the controller POWER. The Message Display will read:

Message Display:
Note: N.NN = software revision level

REV. N.NN WARMING UP

After a few seconds, the Message Display will alternate between the following messages:

Message Display:

PRIME CATHETER

and

INSERT CATHETER FILL CATHETER

The pressure line MUST be connected to the controller BEFORE the balloon catheter is filled with fluid, or the device may not function properly.

2.0 CATHETER PRIMING

2.1 FILL the 30cc syringe with approximately 15-20cc of sterile injectable 5% dextrose in water (D_5W).

Use only sterile injectable 5% dextrose in water (D_5W). Use of other fluids may compromise system.

2.2 CONNECT syringe to the port in the proximal end of the balloon catheter. Do not overtighten syringe when connecting.

2.3 Point balloon catheter tip downward.

2.4 Press trumpet valve on top of balloon catheter handle and fill with 5-10cc of D_5W.

2.5 Press trumpet valve and evacuate fluid and air from balloon to a negative pressure of -150 to -200 mmHg (indicated by pressure display on controller).

Note: You may need to purge air from syringe several times to attain desired negative pressure. You must release trumpet valve to maintain negative pressure. Al should be completely evacuated to optimize the function of the device.

2.6 The negative pressure creates a low-profile balloon insertion (balloon is drawn tight against catheter tip). Do not go beyond -300 mmHg. Check that negative pressure is maintained for at least 10 seconds before proceeding.

If negative pressure cannot be maintained for 10 seconds, remove balloon catheter and replace.

3. PRESSURE TITRATION

3.1 Fill syringe to 30cc with D_5W, purge air, and connect to balloon catheter (do not overtighten).

3.2 Using appropriate sterile technique and cervical/vaginal preparation, dilate cervix to 5mm if necessary.

3.3 Measure depth of uterus.

3.4 Wet outside of balloon with D_5W.

3.5 After sounding uterus, and wetting balloon, **SLOWLY INSERT BALLOON CATHETER** into uterus until tip is touching the fundus. Ensure depth indicated by markings on catheter is consistent with previous sound measurement. Use tenaculum to hold cervix if necessary.

Ensure cervical dilation to 5mm and do not use excessive force during insertion, as such force can cause the balloon to tear or the catheter to perforate the uterine wall.

3.6 Press trumpet valve on top of balloon catheter and fill balloon slowly to pressure of 160-180 mmHg using 2-30cc of D_5W (Release trumpet valve to allow pressure to stabilize). Incrementally add small volumes to achieve a stable pressure (no fluctuations greater than ± 10 mmHg) of 160-180 mmHg for a minimum of 30 seconds. The pressure of the balloon against the uterine wall often precipitates uterine relaxation, thereby temporarily decreasing pressure.

For optimal results, it is extremely important to allow pressure to stabilize to 160-180 mmHg for 30-45 seconds before pressing START (◇) button. The pressure will ultimately stabilize with careful titration.

Note: Once the heater is activated, the pressure may initially rise 10-20 mmHg; the pressure may then drop slowly for the remainder of the procedure. The ending balloon pressure may be as low as approximately 100 mmHg, and is typically between 120-150 mmHg.

Note: Activation pressure for the procedure is ≥ 150 mmHg. The procedure cannot start until the pressure is over 150 mmHg.

Note: It is recommended that for very small uteri, pressure titration should occur towards the lower end of the range (i.e. 160 mmHg) to minimize any potential for overpressure readings during the heating process.

Do not over pressurize balloon during titration. The controller can not display pressure > 300 mmHg.

Optimal balloon volume depends on the potential volume of the uterine cavity and is typically 6-15cc at >160 mmHg (at start) and may be as great as 30cc. If pressure level cannot be reached with 30cc of fluid, remove balloon catheter and check for uterine perforation and/or balloon catheter leak. Replace balloon catheter if necessary.

4. TREATMENT

4.1 Message Display:

READY PRESS START

When a steady pressure of 160-180 mmHg is maintained, press START (◇) button on controller to activate heater.

Do not add fluid once heater is activated, as this could result in patient injury. Hold balloon catheter immobile during procedure (with valve oriented upwards).

4.2 After the start button is pressed, the controller activates the heater to achieve treatment temperature of 87°C (188°F) within 4 minutes. (This preheat cycle may take up to 4 minutes, but is usually 15-45 seconds.)

PREHEATING TO 87°C

Note: If the treatment temperature of 87°C is not reached within 4 minutes, the controller will terminate the procedure. Remove fluid, remove catheter.

4.3 Message Display:

THERAPY CYCLE 87°C 8 MIN.

Once 87°C is reached, you will hear an audible alarm that indicates automatic activation of the 8-minute therapy cycle. Time elapsed is shown on the "TOTAL TIME" display (preheat + 8 minute therapy time).

Note: Pressure may rise slightly with initial heating. It is common to then see the pressure fall gradually during procedure.

4.4 When the treatment cycle is completed, the Message Display will alternate between the following messages:

CYCLE COMPLETE REMOVE CATHETER

and

TURN POWER OFF

4.5 The controller automatically terminates the heater at the end of the treatment (cycle) and an audible alarm will sound. Total treatment time will be displayed on controller (preheat time plus 8 minute therapy time).

5. POST-TREATMENT

5.1 **Wait approximately 30 seconds for fluid to cool** and then remove fluid by drawing back on syringe while depressing trumpet valve. Remove all fluid from balloon. Remove balloon catheter. Check that entire fluid volume is with drawn.

5.2 Disconnect catheter pressure line from controller.

5.3 Disconnect umbilical cable from catheter by holding grey shell and pulling back.

5.4 Disconnect umbilical cable from controller by holding stainless steel ribbed shell and pulling back. Do not pull on the cable itself.

5.5 Discard catheter. Retain umbilical cable and disinfect for next case.

5.6 Power must be turned off before beginning another procedure.

ORDERING INFORMATION AND RELATED PARTS AND ACCESSORIES

Reorder Number	Description
GC-EAS	UBT System Controller
GC-EAC	UBT Balloon Catheter (sterile, single-use)
GC-EAU	UBT Umbilical Cable (reusable up to 20 applications)
GC-EAP	UBT Power cord (specify country)
GC-EAM	UBT System Manual
GC-EAI	UBT Instruction card

*THERMA*CHOICE™

Uterine Balloon Therapy™

• **What is ThermaChoice™ Uterine Balloon Therapy™?** It is a new outpatient procedure to reduce excessive menstrual bleeding. Unlike hysterectomy, which takes out the entire uterus, the procedure just destroys the lining of the uterus by the use of heat.

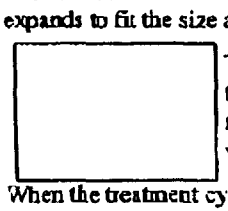
• **What can I expect from ThermaChoice?** In most cases, bleeding during your period will be reduced to moderate or light flow. Some women may experience spotting; a few may experience no bleeding at all. Clinical data has shown that up to 15% of patients may not respond to ThermaChoice therapy and may require additional treatment.

• **Am I a candidate for ThermaChoice?** Your doctor must rule out abnormal uterine conditions like some fibroids, and your pap smear and biopsy must also be normal. This is not a treatment for uterine cancer. **If you still want to have children, ThermaChoice is not an option since the uterine lining is destroyed during therapy.**

• **How does ThermaChoice work?**

First, a soft flexible balloon attached to a thin catheter (tube) is inserted into the vagina, through the cervix and placed gently into the uterus.

Then the balloon is inflated with a sterile fluid which expands to fit the size and shape of your uterus.



The fluid in the balloon is heated to 87° C (degrees) or 188° F and maintained for eight minutes while the uterine lining is treated.

When the treatment cycle is complete, all the fluid is withdrawn from the balloon and the catheter is removed. Nothing stays in your uterus.

Your uterine lining has been treated and will slough off like a period in the next 7-10 days.

(PANEL 3)

A New Treatment Alternative

Can I get pregnant after treatment? This therapy should not be used if you ever want to have children--in fact, pregnancies after ablation can be dangerous for **both fetus and mother.** Since there is a chance pregnancy could occur, contraception or sterilization should be used after treatment. Please discuss these options with your physician.

• **What will I feel during the procedure?** About an hour before therapy, your physician may give you medication which minimizes cramping during and after the procedure. You may also be given a mild sedative to help you relax. In most cases, you will be awake during the procedure and may experience cramping and/or discomfort. Your doctor may use a local anesthesia to numb the cervix and the uterus. Sometimes patients want to be "put to sleep" using general anesthesia after which you may experience some nausea. This is an option for you to discuss with your doctor.

• **What will I feel after the procedure?** You may feel mild or moderate cramping like a menstrual period, and if needed, your doctor will give you a mild medication to make you more comfortable. After 1-4 hours in the recovery room, you should arrange to be driven home where you can take it easy for the rest of the day.

• **What can I expect after I go home?** Most women can return to work and family commitments by the next day. Sexual activity can be resumed after your first check-up, usually 7-10 days. Most patients have a pinkish and watery vaginal discharge for about 2 weeks, sometimes as long as a month. In some cases, the first few periods after the procedure may continue to be heavy but will begin to improve thereafter.

• **Are there any post-procedure complications for which I should call my physician after I get home?** You should call your physician if you develop a fever of 100.4° Fahrenheit or over, worsening pelvic pain that is not relieved by ibuprofen (e.g. Advil) or other medication prescribed by your physician, nausea, vomiting, bowel or bladder problems, and/or a greenish vaginal discharge.

(PANEL 2)

• **What are the risks of ThermaChoice?** The procedure may pose some rare, but possible, safety risks including blood loss, heat burn of internal organs, electrical burn, perforation (hole) or rupture of the wall of the uterus, or leakage of heated fluid from the balloon into the cervix or vagina. Collection of blood or tissue in the uterus and/or fallopian tubes during the months post-procedure is also possible and may require an outpatient procedure to correct the problem.

As with any type of uterine procedure, there may also be the risk of infection, usually easily managed with oral antibiotic therapy.

Caution: This product contains natural rubber latex which may cause allergic reactions.

What you should know about excessive menstrual bleeding

• **I bleed so heavily every month, I can't leave home. Is this normal?** Heavy bleeding is not normal, but it is common. One out of every 5 women has unusually heavy bleeding, also called **menorrhagia.** Women just like you have described symptoms of unmanageable bleeding, flooding, clotting and a constant need to change pads or tampons which quickly become soaked. You feel tired, worry about embarrassing accidents and are frustrated when your periods rule your life.

• **What causes menorrhagia?** The most common cause is hormonal imbalance, especially in women 35-45, prior to menopause. Benign (non-cancerous), uterine growths, such as fibroids or polyps, infection, or chronic illness can also cause excessive bleeding.

• **How is excessive bleeding evaluated?** In order to find the cause of bleeding and determine the right treatment for you, your doctor will take a thorough history and may perform tests which provide information about the lining of your uterus. Talk to your doctor about which tests are appropriate for your specific needs.

(PANEL 1)

What other treatments are available for me?

- **Drug therapy** (such as low dose birth control pill or other hormones) is frequently prescribed for excessive bleeding caused by hormonal imbalance. It is often used among women who wish to retain fertility and can be effective in decreasing bleeding without the need for surgery. Repeated, long term dosing is usually required. Minor side effects are common and may include headache, breast tenderness, and weight gain. Major complications are rare.

- **Dilation and curettage** (D&C) is typically the first surgical step if drug therapy fails. The top layer of the uterine lining is scraped away which may reduce bleeding, usually for only a few cycles. D&C is typically performed in an outpatient surgery setting under general anesthesia. If a polyp (small overgrowth) is removed, the problem may be corrected.

- **Hysteroscopic endometrial ablation** destroys and removes the uterine lining with an electrosurgical instrument or laser. The procedure may be performed under general or regional anesthesia, and involves an instrument used to view the uterus (hysteroscope), and a heat source which is inserted through the hysteroscope into the uterus. The procedure is typically performed in 30-60 minutes. Most women return to work in two to three days. This method will reduce heavy bleeding approximately 85% of the time, with light or normal reduction in some patients and elimination of bleeding in others. Risks may include accidental uterus perforation, bleeding, infection, or heart failure due to the quantity of fluids used during the procedure.

- **Hysterectomy** (removal of the uterus) provides a cure for excessive bleeding. It is major surgery which is usually performed under general anesthesia. Several days in the hospital and up to six weeks recovery are most common.

Talk with your doctor...understand all your options.

(PANEL 3)

*THERMA*CHOICE™

Uterine Balloon Therapy™

- A new minimally invasive choice for you and your doctor to consider in the treatment of excessive menstrual bleeding, ThermaChoice has the potential to offer.
  - An alternative to hysterectomy or other major surgical procedures
  - An outpatient procedure; no hospital stay
  - Less need for general anesthesia
  - A fast recovery, with a return to normal activity within two days for most patients
  - Reduced bleeding

Talk with your doctor if you have specific questions about ThermaChoice and about your options to treat excessive bleeding.

GYNECARE™

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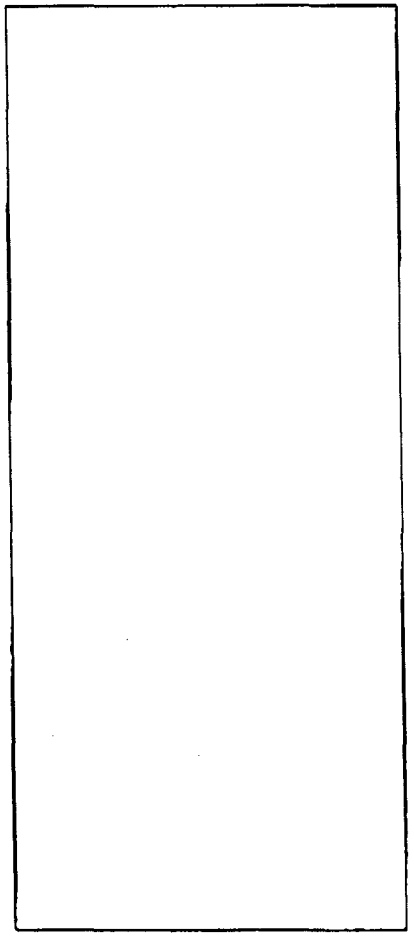
(PANEL 2)

Excessive Menstrual Bleeding



You Don't Have to Live With It Anymore!

(PANEL 1)