OBJECTIVE: To provide an overview of the approved second-generation endometrial ablation technologies.

STUDY DESIGN: Data from the FDA Summary of Safety and Effectiveness Data were compared for Thermachoice, HydroThermablator, Her Option and Novasure devices.

RESULTS: At 12 months' follow-up, Novasure and HydroThermablator had the highest amenorrhea rates. Thermochoice and Novasure had the highest success rates at 12 months. Novasure had the lowest adverse event rates in the first 24 hours, between 24 hours and 2 weeks and between 2 weeks and 1 year of follow-up.

CONCLUSION: Summary of Safety and Effectiveness Data, obtainable on the FDA Web site, offers objective data for comparing second-generation endometrial ablation technologies.

Keywords: menorrhagia, endometrium, summary of safety and effectiveness data, endometrial ablation.

Endometrial ablation (EA), as a treatment for women symptomatic for menorrhagia, has been demonstrated to be safe and effective.1-7 Success with first-generation endometrial ablation (FGEA) procedures requires that physicians be experienced hysteroscopists. Employing a neodymium-YAG laser, wire-loop or rollerball electrode with radio-frequency (RF) electrosurgical generator, the operative hysteroscopist must meticulously treat the endometrium surrounding the uterine cavity to ensure a safe and satisfactory clinical outcome.8

Owing to issues that include a prolonged learn-
ing curve, inconsistent clinical results and the potential for serious complications (such as hemorrhage and fluid intravasation) FGEA has not been widely adopted by the gynecologic community.\textsuperscript{9-11} Responding to an unmet need, the medical device industry has now developed second-generation endometrial ablation (SGEA) technologies that are characterized by ease of use and consistent results among treating physicians as compared to FGEA procedures. Four SGEA systems have received Food and Drug Administration (FDA) approval and are being marketed in the United States (ThermaChoice UBT\textsuperscript{®}, Gynecare, Somerville, New Jersey; HydroThermablator\textsuperscript{®} [HTA], Boston Scientific, Natick, Massachusetts; Her Option\textsuperscript{®}, American Systems, Minnetonka, Minnesota; and NovaSure\textsuperscript{®}, Novacept, Palo Alto, California). Their availability represents a positive development for physicians and patients; however, the costs associated with their acquisition have created a dilemma for many physicians and administrators of ambulatory surgical facilities and hospitals. How does one choose between SGEA technologies? Though well-intentioned, physicians and health care administrators are often unprepared or unqualified to make such important decisions. The decision-making process that demands objectivity is more often characterized by trial and error, happenstance and great subjectivity. Even if physicians and their institutions have equal and ready access to all the SGEA technologies during an evaluation period, pressures exerted by sales and marketing personnel from the various medical device companies often dictate a prompt purchasing decision be made.

The purpose of this paper is to provide a brief overview of the approved SGEA technologies and to introduce the gynecologic community to a powerful source of evidence-based and objective information regarding SGEA devices. Provided by FDA and available for each of the SGEA devices, Summary of Safety and Effectiveness Data\textsuperscript{12-15} (SSED) documents detail aspects of safety, efficacy, performance and other clinical use issues of importance.

\textbf{SGEA Technologies Overview}

The ThermaChoice UBT\textsuperscript{®} System is a software-controlled device that accomplishes endometrial tissue ablation using thermal energy from heated sterile fluid (5\% dextrose in water) within a latex balloon. The ThermaChoice UBT\textsuperscript{®} System consists of a controller and single-use sterile catheter and umbilical cable.

During use, the catheter is inserted into the uterus, and the balloon at the distal tip is filled with up to 30 mL of fluid. Pressure within the balloon is manually adjusted and must be stabilized between 160 and 180 mm Hg before the heating element within the balloon is manually activated. The treatment cycle begins once a temperature of 87°C has been reached. Endometrial ablation is achieved by maintaining pressure within the balloon between 150 and 180 mm Hg and fluid temperature at 87°C during an 8-minute treatment cycle. Upon completion of the treatment cycle, the balloon is deflated and the balloon catheter withdrawn from the uterus. The system allows automatic shutdown if balloon pressure rises to \textgreater 210 mm Hg or falls to \textless 45 mm Hg during the treatment cycle. In addition, the procedure will self-terminate if the temperature inside the balloon exceeds 95°C for 2 seconds or falls below 75°C for 15 seconds or if a temperature of 87°C cannot be achieved after 4 minutes of preheating. The present design of the commercially available device employs a silastic balloon and intraballoon impellor to circulate the heated fluid.

The HTA\textsuperscript{®} makes use of USP 0.9\% saline for uterine distension and a single-use, polycarbonate sheath with inflow and outflow channels through which a standard, 3-mm-outside-diameter, rigid hysteroscope is inserted. During operation, the HTA\textsuperscript{®} system is first primed with 300 mL of room temperature saline, which is subsequently circulated within the uterine cavity for 2 minutes. Activation of the heating element signals the beginning of the treatment phase. When the saline temperature reaches 80°C, a 10-minute treatment cycle ensues. During the treatment phase, fluid freely circulates between the uterine cavity and the system reservoir, where it is warmed to a maximum temperature of 90°C. Following the treatment cycle, a post-treatment flush takes place. Approximately 1 minute is required to achieve adequate cooling to allow safe withdrawal of the hysteroscope from the uterine cavity. Intrauterine pressure is limited to 50–55 mm Hg to minimize the potential for fluid passing into the peritoneal cavity through patent fallopian tubes. (The opening pressure of a fallopian tube is estimated to be \textgreater 70 mm Hg.) The system will sound an alarm and terminate the procedure if it recognizes a loss of 10 mL from the circulating volume of 300 mL.

The Her Option\textsuperscript{®} system consists of a console in
which is stored a compressor, user interface and microprocessor. A reusable cryoprobe and single-use, disposable catheter, which covers the cryoprobe during use, completes the system. The probe is inserted into the uterine cavity and directed toward either cornu. Active freezing is initiated by depressing the freeze button on the control unit. Freezing continues until the freeze button is again depressed or until a maximum of 10 minutes of treatment time has elapsed. The heat button is then pressed to thaw the probe, allowing its removal. The user then reinserts the device to the opposite cornu and initiates a second freeze cycle. To monitor the position of the cryoprobe and advance of the iceball and to protect against ablation of an inappropriate myometrial depth, transabdominal ultrasound imaging is mandatory throughout the ablation procedure.

The NovaSure® system consists of a disposable device, RF controller and foot switch. The controller delivers RF energy to ablate the endometrium. The system continuously monitors tissue impedance (resistance to the flow of electrical current) and automatically terminates the procedure when a tissue impedance of 50 ohms is achieved. The disposable, 3-dimensional, bipolar ablation device is inserted transcervically into the uterine cavity. Uterine cavity length, determined by preoperative sounding, and width, measured by the device, are key entered into the RF controller to automatically calculate the power level required for treatment of a uterine cavity of any given size. Depressing the foot switch first activates a cavity integrity assessment cycle intended to automatically identify an unrecognized uterine perforation. When satisfied with the results of the cavity integrity evaluation, the operator again depresses the foot switch to initiate the treatment cycle. RF energy delivery averages 90 seconds, but treatment is limited to 2 minutes in all cases.

**SSED Documents**

The FDA has as its mission the promotion and protection of public health. All medical devices, including SGEA technologies, are subject to FDA approval or clearance. Only after undertaking and completing an investigational trial, intended to demonstrate safety and effectiveness, can a medical device manufacturer seek marketing approval through a lengthy and arduous premarket approval (PMA) application process. As part of this exercise, manufacturers of SGEA technologies are required to submit to the FDA volumes of information related to engineering, manufacturing, sterilization, bio-compatibility, and preclinical and clinical use. Much of FDA’s focus is appropriately directed at data generated during the pivotal clinical study (commonly referred to as the Phase III, or PMA, trial). If FDA grants approval for a medical device, it must then generate a document entitled “SSED,” which summarizes the many tens of thousands of pages of data that have been submitted by the manufacturer and reviewed by the agency and its designated expert. An SSED document is available for each of the endometrial ablation technologies and can be found on the official FDA Web site:


The SSED document precisely identifies the indications and contraindications for use of each device/system, states precautions and warnings, provides a full description of each system and addresses currently available alternative therapy. A strong emphasis is placed on the description of adverse events and potential complications that were observed in the pivotal trial or may be associated with use of a particular product in a commercial setting. Study design, inclusion/exclusion criteria and clinical results are summarized in a concise, easily understood fashion.

The PMA trial design employed by each SGEA manufacturer was, with a few notable exceptions, remarkably similar. In all 4 trials the investigational device was compared to rollerball endometrial ablation, the control procedure.

The ThermaChoice UBT® system was the first to be studied. The study design employed a one-to-one randomization schedule. For the HTA®, Her Option® and NovaSure® trials, FDA allowed a 2:1 randomization schedule so as to obtain more data points on the investigational products.

With respect to inclusion criteria, the HTA® investigational trial included patients with uterine sounding lengths of up to 10.5 cm as compared to 10 cm for the other 3 devices. Patients found at screening to have intracavity pathology (submucosal fibroids, polyps) were excluded from treatment in all protocols except the one utilized for the NovaSure® device, in which submucosal fibroids and polyps <2 cm in diameter were nonexclusionary. The
HTA® protocol allowed inclusion of patients with intramural fibroids < 4 cm in diameter that did not cause distortion of the uterine cavity and were thought by the investigator not to be responsible for complaints of menorrhagia. The Her Option® study allowed inclusion of patients with intramural fibroids < 2 cm in diameter. All protocols excluded patients found to have congenital uterine abnormalities (e.g., T shaped or bicornuate); however, the HTA® protocol allowed inclusion of patients with subseptate uteri. Endometrial pretreatment regimens varied between the protocols. Patients undergoing treatment with the ThermaChoice UBT® system were required to undergo suction dilatation and curettage for 3 minutes. Patients enrolled in the HTA® trial had endometrial pretreatment utilizing an intramuscular dose of Lupron (TAP Pharmaceutical, Lake Forest, Illinois), 7.5 mg, whereas those in the Her Option® trial received Lupron, 3.75 mg. Patients undergoing NovaSure® treatment received no hormonal or mechanical pretreatment of the endometrium, nor was the procedure timed to any particular menstrual cycle day.

Two hundred seventy-five patients were enrolled and randomized in the ThermaChoice® study, with 137 assigned to the investigational arm. The HTA® study enrolled a total of 276 patients, with 187 assigned to HTA® treatment. The Her Option® study enrolled a total of 279 patients, with 193 undergoing the investigational procedure. One hundred seventy-five of 265 patients in the NovaSure® study were randomized to the investigational arm. Data on patient demographics for each of the test arms are found in Table I.

In all the SGEA protocols, anesthesia regimens employed during the investigational procedure were left to the discretion of the patient and physician. However, data were collected in each trial on the type of anesthesia employed (i.e., local, intravenous sedation, epidural, general). Local anesthesia, plus or minus intravenous sedation, was used in 38.8% of patients undergoing the ThermaChoice

Table I  Demographics and Gynecologic History

<table>
<thead>
<tr>
<th>Variable</th>
<th>ThermaChoice® (n = 137)</th>
<th>HTA® (n = 187)</th>
<th>Her Option® (n = 193)</th>
<th>NovaSure® (n = 175)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>40.4 ± 4.8</td>
<td>40.7 ± 5.2</td>
<td>41.2 ± 5.1</td>
<td>39.7 ± 5.5</td>
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<tr>
<td>Body mass index</td>
<td>29.1 ± 7.8</td>
<td>29.0 ± 7.4</td>
<td>29.3 ± 8.4</td>
<td>27.6 ± 6.3</td>
</tr>
<tr>
<td>No. of pregnancies</td>
<td>Not available</td>
<td>Not available</td>
<td>2.5 ± 1.2</td>
<td>2.7 ± 1.3</td>
</tr>
<tr>
<td>No. of full-term deliveries</td>
<td>Not available</td>
<td>Not available</td>
<td>2.4 ± 1.2</td>
<td>2.2 ± 1.1</td>
</tr>
<tr>
<td>Baseline diary score</td>
<td>552.5 ± 712.2</td>
<td>596.6 ± 787.6</td>
<td>570 ± 441</td>
<td>562 ± 381</td>
</tr>
<tr>
<td>Uterine sounding length (cm)</td>
<td>8.5 ± 1.3</td>
<td>8.5 ± 1.3</td>
<td>8.0 ± 1.1</td>
<td>8.8 ± 0.8</td>
</tr>
</tbody>
</table>

Values are given as mean ± SD.

Figure 1  Adverse events reported in the first 24 hours.
UBT® procedure and 45% of patients undergoing HTA®. Of the Her Option® patients, 39% received a combination of paracervical block and conscious sedation as compared to 73% of NovaSure® patients.

According to the SSED documents, the ThermaChoice® procedure (including the 3-minute suction dilatation and curettage) lasted an average of 27.4 ± 11.8 minutes. Overall treatment time for the HTA® averaged 26.4 ± 12.1 minutes. NovaSure® procedure time (device insertion to removal) averaged 4.2 ± 3.5 minutes. Time during which energy was delivered was measured in 48 of the NovaSure® patients and averaged 84 ± 25 seconds. No data on the length of the procedure were reported in the SSED document for Her Option® patients.

Adverse event data were collected, analyzed and reported for each of the SGEA technologies, and although the SSED documents are quite uniform in reporting data, some variability exists with respect to the types of minor adverse events reported as well as their temporal relationship to performance of the ablation procedure. In all 4 SGEA trials, the most common complaints were nausea, vomiting, uterine cramping and abdominal pain. Figures 1–3 are a summary of these data points spread in the time domain. Except for a uterine perforation observed in one patient undergoing the Her Option®
ablation procedure, no serious intraoperative complications were observed with use of any of the investigational SGEA devices.

Patients enrolled in all 4 trials were required to utilize validated sanitary products to allow precision in quantifying uterine blood loss before and after the procedure (pictorial blood loss assessment chart [PBLAC]). In each of the 4 trials, treatment success was defined as a PBLAC score of $\leq 75$. (Normal menstrual bleeding equates to a score of $\leq 100$.) Amenorrhea required a PBLAC score of 0. For all patients except those enrolled in the ThermaChoice® trial, data were calculated for the intent-to-treat group, which included all patients randomized regardless of whether or not they actually received treatment. For the purpose of statistical analysis in the HTA®, Her Option®, and NovaSure® clinical trials, patients lost to follow-up were automatically considered failures even if their last PBLAC score, as recorded in the menstrual diary, suggested treatment success. Patients in the HTA®, Her Option®, and NovaSure® trials who required additional medical/surgical intervention for treatment of menorrhagia were considered failures. In contrast, in the ThermaChoice UBT® trial, amenorrhea and success rates were calculated after excluding patients who were either lost to follow-up or randomized but not treated. Additional data on outcomes associated with use of each SGEA technology are summarized in Table II.

### Discussion

For physicians wishing to offer patients endometrial ablation, there now exist valuable new technologies. Four SGEA devices have demonstrated adequate safety and effectiveness in clinical trials to be cleared for commercial use in the United States by FDA. However, all SGEA technologies are not created equal. Significant differences exist in mechanism of action, ease of use and clinical outcome. Although the learning curve for each SGEA procedure is significantly shorter than with rollerball ablation, the physician performing these procedures requires adequate in-servicing and a reasonable amount of clinical experience before competence is ensured. In evaluating and comparing 1 system to another, a physician is wise to obtain as much hands-on experience as possible. However, such clinical experience is often limited by inadequate clinical material or colored by the subjectivity imposed by industry salespeople and marketing personnel. Articles appearing in peer-reviewed medical journals and opinions of physicians expert in the field of endometrial ablation can be valuable sources of information; however, with them there exists the potential for significant subjectivity. The vast majority of issues related to an SGEA system’s performance are reflected in the SSED documents. The fact that the PMA trial design employed by each SGEA manufacturer was similar makes the SSED documents extremely valuable in assessing and comparing the different ablation devices. These documents provide objective and unbiased information on indications, contraindications and need for endometrial pretreatment and data generated in scientifically sound, randomized trials detailing anesthesia regimens, length of procedures, amenorrhea rates, success rates, adverse events and complications. Because they are generated by the FDA and are rich in information substantiated by evidence-based clinical data, SSED documents provide a unique resource for physicians seeking objectivity. One must also note that changes made by manufacturers in device design and performance after FDA approval may not be reflected in SSED documents. This information can be found in the current product information available from each of the SGEA manufacturers.

### Table II Clinical Outcomes at the 12-Month Follow-up

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ThermaChoice® (n = 126)</th>
<th>HTA® (n = 187)</th>
<th>Her Option® (n = 193)</th>
<th>NovaSure® (n = 175)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amenorrhea (%)</td>
<td>13.2*</td>
<td>35.3</td>
<td>22.2</td>
<td>36.0</td>
</tr>
<tr>
<td>Success (%)</td>
<td>80.2*</td>
<td>68.4</td>
<td>67.4</td>
<td>77.7</td>
</tr>
<tr>
<td>Hysterectomy (%)</td>
<td>1</td>
<td>2</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Patient satisfaction (%)</td>
<td>96*</td>
<td>Not available</td>
<td>86</td>
<td>92</td>
</tr>
<tr>
<td>Patient would recommend procedure (%)</td>
<td>Not available</td>
<td>Not available</td>
<td>98</td>
<td>95</td>
</tr>
</tbody>
</table>

*Data for ThermaChoice® were calculated for patients with 12 months’ data available and not for the intent-to-treat group.
Conclusion

SSED documents, available on the FDA Web site, are highly informative and offer an objective source of data, allowing a comparison of the indications, performance and clinical results associated with SGEA technologies. They offer great value to the reader who faces the need to make an informed decision on what device he/she should consider employing in his/her day-to-day practice and provide a legitimate estimate of the clinical results that can be expected.

References