ENDOMETRIAL ABLATION: PAST, PRESENT, AND FUTURE
PART II

MORRIS WORTMAN, M.D., F.A.C.O.G.
DIRECTOR AND CLINICAL ASSOCIATE PROFESSOR OF GYNECOLOGY
Endometrial Ablation: Past, Present, and Future
Part II

MORRIS WORTMAN, MD, FACOG
DIRECTOR AND CLINICAL ASSOCIATE PROFESSOR OF GYNECOLOGY
CENTER FOR MENSTRUAL DISORDERS
UNIVERSITY OF ROCHESTER MEDICAL CENTER
ROCHESTER, NEW YORK

ABSTRACT

Endometrial ablation (EA) is the most commonly performed surgical procedure for the management of abnormal uterine bleeding unresponsive to medical therapy. In well-selected subjects, EA provides a safe, inexpensive, and convenient alternative to hysterectomy with a rapid return to normal function.

The first generation of EA techniques were introduced in 1886 by Professor Sneguireff of Moscow. He was the first to apply super-heated steam to the uterine cavity to vaporize the endometrial basalis. This method—known as atmocausis—was refined by Ludwig Pincus of Danzig in 1895, and he went on to perform over 800 procedures. As the 20th century brought forth other energy sources—electricity, X-ray, radium, and even cryogenics—they were each used, in turn, to accomplish endometrial ablation.

In 1981, Dr. Milton Goldrath successfully performed EA by co-locating a neodymium-doped yttrium aluminum garnet (Nd:YAG) laser with a rod-lens hysteroscope to achieve photovaporization of the endometrium. The accomplishment of EA under direct visualization defined the second generation of EA.

The challenges and risks of second-generation technology, however, were soon apparent, and though this practice continues today, it appears to be confined to a relatively small number of devoted and highly-skilled sub-specialists.

The late 1990s saw increasing interest in safe, affordable, and easily-mastered EA technology. The result was a return to blind technology but modified with a variety of features that brought unprecedented safety to EA, even permitting its selected in-office application. This third generation of EA techniques and devices has propelled the growth of EA in the 21st century.

Although much has been accomplished in the quest for safe, affordable, convenient, and easily-mastered EA, the future requires refinement of patient selection criteria, management strategies for late-onset endometrial ablation failures (LOEAFs), as well as minimally invasive methods for reducing them.
Global Endometrial Ablation

Dr. Harry Reich reported the first innovations in gynecologic surgery. In 1989, the continuous flow gynecologic resectoscope cleared the US Food and Drug Administration and soon supplanted the neodymium-doped yttrium aluminum garnet (Nd:YAG) laser for accomplishing endometrial ablation (EA). The low-cost resectoscope, powered by a standard electrosurgical unit, enabled EA technology to spread to an increasing number of community and medium-sized hospitals. That same year, Dr. Harry Reich reported the first laparoscopic hysterectomy, a minimally invasive endoscopic technique to accomplish hysterectomy. These two modalities—advanced laparoscopic and hysteroscopic surgery—would dramatically influence gynecologic practice and bring increasingly safe, minimally-invasive, and low-cost solutions to common gynecologic maladies.

By the early 1990s, despite great interest in resectoscopic endometrial ablation, the complications associated with this approach were undeniable. Arieff et al. and Baggish et al. both reported numerous cases of fatal hypotensive encephalopathy resulting from fluid and electrolyte disturbances. Uterine perforation and visceral injuries—coupled with the difficulties in mastering a complex surgical technique—limited EA’s growth and potential for impacting hysterectomy rates in the United States.

In 1990, recognizing the complexity of hysteroscopic endometrial ablation techniques, Phipps et al. treated 33 subjects utilizing a 10-mm diameter radiofrequency thermal probe (Rocket Medical plc, London, United Kingdom). The authors employed both straight and curved probes of lengths varying from 50–70 mm in a technique reminiscent of the one described by Bardenheuer in 1937. Despite the relative simplicity of the technique, two serious complications—vaginal burns that resulted in vesico-vaginal fistulae—occurred prompting the authors to modify their procedure. In 1994, Neuwirth et al. introduced a thermal balloon which was intended to conform to the uterine cavity and was “designed to produce endometrial ablation blindly.” Neuwirth et al. treated 10 subjects in a study designed to demonstrate the safety of the device. These approaches—the radiofrequency probe and the thermal balloon—are recognized today as the beginning of non-resectoscopic endometrial ablation (NREA) and are often referred to as “global” endometrial ablation or GEA. Some authors have also referred to these techniques as second-generation EA which is an unfortunate misnomer that fails to recognize the history of EA. These latest techniques are, in fact, third-generation EA procedures.

Between Phipps’ reports in 1990 and 2018, there have been at least 10 different NREA systems that direct energy into the uterine cavity in an attempt to selectively destroy the regenerative endometrial basalis. All of these systems eliminate the use of large volumes of distention media and all but one—hydrothermal ablation—are blind techniques reminiscent of first-generation EA devices introduced in the late 19th and early 20th centuries. Two of the NREA techniques are iterative and involve the blind introduction of probes—one is a microwave and the other a cryo-probe—to accomplish endometrial destruction “bit by bit.” The remaining eight techniques seek to cause the near simultaneous destruction of the entire endometrium. With the exception of hydrothermal ablation, described below, the other nine techniques and devices represent a return—albeit far more sophisticated—to the methods first employed in the late 19th century.

I. Thermal Balloon

THERMACHoice® Uterine Balloon Therapy System

In 1997, The US Food and Drug Administration (FDA) issued the first premarket approval for a non-resectoscopic endometrial ablation device—the THERMACHoice® Uterine Balloon Therapy System (Gynecare, Inc., Somerville, New Jersey). The THERMACHoice® system, first introduced in 1995 in other parts of the world, consisted of a disposable 16 cm long x 4.5 mm diameter catheter that housed a latex balloon, heating element, and thermocouple (Fig. 1). The original catheter was inflated with 5% dextrose in water, was heated to 87°C, and maintained an intrauterine pressure of 160–180 mm Hg for eight minutes. The THERMACHoice® underwent several modifications in 1999 and 2004. In 1999, a silicone balloon with an internal impeller was approved to provide more uniform distribution of heat within the uterine cavity. The last version—THERMACHoice® III—incorporated a silastic balloon; a more flexible material with improved elasticity designed to enhance contact at the uterine cornua. However, in 2015, the THERMACHoice® III catheter was recalled by the FDA because of an issue related to the catheter’s purported two-year shelf life and has since been permanently withdrawn from...
worldwide distribution.

In a large randomized multicenter study comparing thermal uterine balloon therapy with hysteroscopic rollerball endometrial ablation, Meyer et al. reported 12-month follow-up data on 239 women and demonstrated similar outcomes. However, while the incidence of complications was 3.2% in the rollerball EA group, there were none in the THERMACHOICE® group. Another large study of the THERMACHOICE® system was conducted by Kumar et al. who followed 253 women for up to 11 years. During a median follow-up interval of 71 months (S. D. 42), 84% percent of subjects successfully avoided a hysterectomy while the vast majority of women reported significant improvement in their symptoms.

The successful in-office application of THERMACHOICE® has been reported by Chapa et al. who performed THERMACHOICE® III procedures on 148 patients under parametrial block using dilute mepivacaine and oral anxiolysis. Although the THERMACHOICE® provided an excellent alternative to resectoscopic endometrial ablation, the system proved unsuitable for in-office use because of its relatively long treatment cycle and the requirement for high intrauterine pressures.

However, the advantages of the system—minimal cervical dilation, simplicity of use, and very low risk of complications—were responsible for propelling the GEA market. Another benefit of the THERMACHOICE® system, compared to its resectoscopic predecessors, was the elimination of expensive medical preparation of the endometrium and substituting a brief suction curettage just prior to the procedure.

Cavaterm™ and Cavaterm Plus™

The Cavaterm™ (Veldana Medical SA, Morges, Switzerland) thermal balloon was first tested on extirpated uteri in 1992, introduced into clinical trials by Pnn Medical SA (former Wallsten Medical SA, Vaud, Switzerland) in 1993, and approved for use in 1995. Although the Cavaterm™ is unavailable in the United States, it is used in many European countries. The system has two components, a central unit (Fig. 2) and a balloon catheter (Fig. 3). The catheter is a highly-flexible, antiallergenic silicone balloon designed to conform to the uterine cavity by adjusting its length from 4–8 cm. Subsequent to its introduction, the Cavaterm™ original 8 mm diameter catheter was reduced to 6 mm and reintroduced as the Cavaterm™ Plus. The Cavaterm™ Plus balloon is filled with 5% dextrose in water heated to 78°C at an intrauterine pressure of 230–240 mm Hg for a 10-minute treatment cycle. A pressure relief valve is automatically activated if an overpressure is sensed, thus adding an important safety feature.

Like the THERMACHOICE®, endometrial preparation may be performed with a simple suction curettage and is associated with very low complication rates. Vilos et al. notes that “the device emphasizes the concept that a sustained high intraballoon pressure causes reduction in uterine blood flow, which in turn enhances deeper penetration of heat resulting in deeper endometrial necrosis.” The manufacturer recommends that if the balloon position is in doubt, the operator may utilize an intraoperative abdominal ultrasound examination to confirm the proper position of the balloon prior to the initiation of the treatment cycle. Although the Cavaterm™ system has been utilized in the presence of leiomyomas less than 2 cm in diameter, it is not approved for such use.

Friberg et al. conducted the first clinical trials in 116 women who were followed for 10–46 months. The success rate—defined as amenorrhea, minimal or normal bleeding at the time of the patient’s worst days of flow—was 94% in women whose uteri did not contain submucous leiomyomas. The hysterectomy avoidance rate for women without submucous leiomyomas was 85% at 49 months.

MenoTreat™ Thermal Balloon

The MenoTreat™ device (Atos, Medical AB, Hörby, Sweden)—a third thermal balloon ablation device—is available in many European countries and consists of a controller and disposable silicone balloon catheter. During an 11-minute treatment cycle, heated saline (85°C) is circulated through the inflated balloon at 200 mm Hg. As with other balloon ablation devices, the procedures are most often performed with the adjuvant use of intravenous sedation or general anesthesia. The efficacy of the MenoTreat™ system is comparable to other balloon ablation systems.

Thermablate Endometrial Ablation System™

The Thermablate EAS™ system (Ido- man Teoranta Ltd., Toronto, Canada) is the final example in this category of thermal balloon ablation systems and consists of a handheld treatment control.
unit (TCU; Fig. 4), a disposable silicone balloon catheter, and a power supply. “The objectives [in designing] the Thermablate EAS™ system [was] to shorten procedure times, provide more uniform and consistent treatment, improve clinical outcomes, perform the procedure under no or minimal analgesia/anesthesia outside the operating room, and reduce costs compared to existing [second] generation endometrial ablation techniques.”

The balloon is housed in a flexible 12 cm long x 6 mm diameter catheter that is introduced through the cervix and subsequently filled with pre-heated glycerin (173°C) prior to initiating a 15-second balloon integrity test. After confirming the balloon’s reliability, the catheter is deflated and reintroduced for a treatment cycle lasting just over two minutes at an intrauterine pressure of 220 mm Hg during which the glycerin is kept at 100–150°C.

Karmamdis et al. reported the results of 72 premenopausal women with menorrhagia who were treated with the Thermablate EST™ device and followed for up to two years. The combined amenorrhea and hypomenorrhea rates at three, six, 12, and 24 months were 39%, 73%, 77%, and 70% respectively.

Some of the manufacturer’s contraindications are listed in Table I and are representative of those reported for nearly all thermal balloon EA devices.

The manufacturer notes that

<table>
<thead>
<tr>
<th>Contraindications to the use of the Thermablate™ system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterus sounds to &lt;8 cm or &gt;12 cm</td>
</tr>
<tr>
<td>Uterine cavity with significant distortion</td>
</tr>
<tr>
<td>Intramural leiomyomas &gt;3.0 cm</td>
</tr>
<tr>
<td>Intracavitary lesions (Type 0 or 1 submucous myoma or polyp of any size)</td>
</tr>
<tr>
<td>Septate uterus</td>
</tr>
<tr>
<td>Previous classical cesarean section or transmural myomectomy</td>
</tr>
<tr>
<td>A history of 3 or more lower segment cesarean sections</td>
</tr>
<tr>
<td>Linear scar (from cesarean Section) thickness &lt;8 mm</td>
</tr>
<tr>
<td>A previous endometrial ablation</td>
</tr>
<tr>
<td>Desire to retain fertility</td>
</tr>
</tbody>
</table>
“Patients requiring further treatment after thermal balloon ablation should be treated medically, by resectoscopic endometrial ablation, or by hysterectomy. Repeat resectoscopic ablation resection should be attempted only by experienced hysteroscopists since the complications may be severe.” The manufacturer also recommends that a diagnostic hysteroscopy should be performed just prior to treatment to ensure that cervical dilation has not caused a uterine perforation. Alternatively, one can “use ultrasonic surveillance during the treatment to check for correct balloon position inside the uterine cavity.” The system was approved for use in Canada in 2003 and is presently used throughout Europe, Southeast Asia, Australia, and many other countries around the world.

II. Radiofrequency Endometrial Ablation (RFA)

There are currently two endometrial ablation devices that utilize radiofrequency (RF)—the NovaSure® (Hologic Inc., Bedford, Massachusetts) and the Minerva® Endometrial Ablation System (Minerva Surgical Inc., Redwood City, California). The Minerva® device, in addition to RF current, also utilizes two additional methods of energy application to achieve endometrial ablation. The NovaSure System®

In September 2001, the NovaSure® Impedance Controlled Endometrial Ablation System was approved and introduced by Novacept Inc. (Palo Alto, California). The system, consisting of a controller (Fig. 5) and an 8 mm diameter disposable probe (Fig. 6), delivers radiofrequency bipolar energy dispersed through a triangular-shaped gold-plated porous mesh which conforms to the uterine cavity (Fig. 7) and is designed to deliver deeper coagulation at the mid-body of the uterus—where endometrium is thickest—and shallower desiccation at the thinner cornua. The device is also equipped with an adjustment sheath to protect the endocervical canal.

Prior to the initiation of treatment, the disposable probe allows measurement of both uterine cavity length and width (intracornual distance) as shown in Figure 8 and automatically delivers power based on these variables. The NovaSure® device also incorporates a Cavity Integrity Assessment System (CIAS)—a feature designed to detect a uterine wall defect—which averts energy discharge in the event of a uterine perforation. The CIAS utilizes a hysteroslactor-type of technology which insufflates carbon dioxide into the uterine cavity. Once the intrauterine pressure of 50 mm Hg is reached and maintained for four seconds, the device is activated and maintains an energy output which is controlled by concomitantly monitoring tissue impedance. The procedure, which averages 90 seconds, is automatically terminated when overall tissue impedance reaches 50Ω—a value consistent with superficially ablated myometrium. Another feature of the NovaSure® is its use of continuous suction during the treatment cycle.

![Figure 7. NovaSure® conforming to the uterine cavity.](image)

![Figure 8. NovaSure® handpiece with measuring devices.](image)

![Figure 9. Market share of GEA devices by manufacturer.](image)
which provides a two-fold benefit; first, it draws the endometrium into contact with the bipolar mesh and, second, it removes debris and steam which are byproducts of vaporized endometrium.

In 2017, Hologic Inc. released a redesigned version of the original NovaSure® device—the NovaSure® ADVANCED—which offers a slimmer 6 mm diameter catheter designed to minimize cervical dilation and improve patient comfort in an office-based setting. The updated device is also equipped with an acorn-shaped cervical seal designed to increase the sealing surface within the endocervical canal and improve its working length. The NovaSure® ADVANCED device has been available in Europe, Canada, and Australia since 2016.

The NovaSure® system is the most commercially successful GEA device worldwide.25 The US market share in 2016 was 57.1%26 (Fig. 9). By February 2017, the company reported the sale of 2.5 million devices since its introduction.27 Compared to other NREA systems, the advantages of the NovaSure® device include the need for only minimal cervical dilation, a relatively short treatment cycle, low complication rate, a uterine integrity test, and automated self-termination of the treatment sequence. Additionally, NovaSure® is able to achieve a reproducible depth of ablation, independent of endometrial thickness, thereby obviating the need for expensive endometrial preparation.28 In fact, the ability to perform endometrial ablation without endometrial preparation distinguishes the NovaSure® System from all previous devices.

NovaSure® is the subject of numerous investigational studies including four prospective randomized clinical trials comparing it with the THERMACHOICE® EAS,29-32 a double-blind randomized trial comparing it to Cavaterm™,31 a trial comparing it to a microwave endometrial ablation (MEA) system (previously produced by Microsulis Medical Limited, Denmead, United Kingdom),34 as well as a pivotal trial comparing it to “roller-ball” endometrial ablation.35

Sabbah and Desaulniers36 suggested that the NovaSure® endometrial ablation procedure may have a significant clinical role in the treatment of menorrhagia in women with grade I and II submucous leiomyomas up to 3 cm in greatest dimension. In their study of 65 women, they were able to demonstrate a significant reduction in menstrual blood loss in nearly 95% of subjects. However, their data is confined to a follow-up period of only 12 months. Although the NovaSure® instructions for use (IFU) do not specifically mention the presence of leiomyomas as a contraindication, the manufacturer lists the presence of submucosal fibroids that distort the uterine cavity as a precaution for use.37

Minerva® Endometrial Ablation System

The Minerva® Endometrial Ablation System was approved by the FDA in mid-2015 and—like NovaSure®—employs radiofrequency current but additionally incorporates two additional features to accomplish endometrial ablation.38 Since Minerva® is relatively new, at the time of this writing, there are fewer clinical studies and publications available for analysis.

The system has two major modules—a proprietary controller unit (Fig. 10) and a disposable handpiece (Fig. 11). The handpiece, in turn, has a plasma formation array (PFA), a cervical sheath, and a cervical sealing balloon (Fig. 12). The PFA is composed of an expandable metal frame which is covered by an elastic silicone membrane. During activation, the PFA’s metal frame acts as the internal electrode while two laterally placed tissue-con-
tacting electrodes of the same polarity reside on the outer surface of the membrane. The expanded triangular-shaped PFA is filled with argon gas and is intended to conform to the patient’s uterine cavity.

The disposable handpiece requires cervical dilation to 7 mm. Once inserted and positioned, the device arms expand to deploy a silicone balloon. After the cervical balloon is inflated and the controller unit verifies the adequacy of the cervical seal, the uterine integrity test is initiated. During the integrity test, carbon dioxide is instilled into the uterine cavity from the device’s main sheath to 28 strategically positioned delivery ports that allow the detection of a uterine perforation as small as a 21-gauge needle. Upon successful completion of the uterine integrity test, and after the anatomic requirements of the uterus have been confirmed, the silicone balloon is filled with argon gas and the controller is activated. During the two-minute treatment cycle, bipolar radiofrequency energy is utilized for two purposes. First, it is delivered directly to the target tissue and, second, it is utilized to ionize argon gas transforming it into plasma which is subsequently used to heat endometrium through the membrane. Unlike the NovaSure® system, which evacuates heated liquids, the Minerva® system utilizes them to fill the uterine interstices that may have been otherwise left untreated, thereby augmenting the EA process. The three methods by which Minerva® accomplishes endometrial ablation are summarized in Table II.

These three methods operate in a simultaneous and complimentary fashion. During the procedure, the power level is limited to a maximum of 40 Watts and is automatically adjusted downwards as a function of changing tissue impedance. One of the possible, but unproven, benefits of the Minerva® system is that it may provide some advantage in treating the uterus with an irregular surface or one that contains deeply recessed uterine cornua such as those demonstrated in Figures 13 and 14.

The Minerva® system is the first endometrial ablation system to be evaluated and approved by the FDA’s new Objective Performance Criterion (OPC) control, which represents a composite of success rates for all previous FDA-approved non-resectoscopic endometrial ablation systems (THERMACHoice®, NovaSure®, Genesys Hydro ThermAblator® [HTA] System, [Boston Scientific Corp., Natick, Massachusetts], Her Option®, and MEA). In 2015, Laberge et al. published a multicenter single-arm study, which included a total of 105 subjects using the OPC methodology. The study revealed a one-year post-procedure success rate (PBLAC <75) of 96.2%, with 69.5% of the patients reporting amenorrhea (PBLAC score 0). The patient satisfaction at one year was 97.6%, statistically superior to that of the OPC control group. None of the subjects required hysterectomy by the end of the first year.

Subsequently, Laberge et al. published the results of a double-arm randomized controlled trial (RCT) which included 153 subjects enrolled at 13 clinical sites including eight academic and five private medical centers in the United States, Canada, and Mexico. The primary objective of the study was to evaluate the safety and efficacy of the Minerva® EAS compared with hysteroscopic rollerball ablation in reducing menstrual blood loss as measured by the alkaline hematin (AH) method at 12 months post-treatment, as well as the occurrence of any adverse events. In this study, success was defined as a reduction in menstrual bleeding from >160 mL pretreatment to <80 mL at 12 months post-treatment. Laberge et al. randomized 153 subjects to two groups: 102 subjects in the Minerva® EAS test group and 51 subjects in the rollerball endometrial ablation control group. Investigators utilized a variety of anesthetic and analgesic techniques including general anesthesia, intravenous sedation (with or without paracervical block), and spinal block. The mean procedure time for the Minerva® subjects was 3.1 minutes while the mean procedure time for the rollerball EA group was 17.2 minutes. The success rate—defined by the reduction of menstrual bleeding to less than or equal to 80 mL/month—was 93.1% at one year compared to 80.4%
for the rollerball group (p=0.02). The amenorrhea rate for the Minerva® group was 71.6% and 49% for the rollerball group (p=0.01). Patient satisfaction was 91.9% for the Minerva® group and 79.5% for the rollerball group (p <0.05). The authors concluded that the Minerva® efficacy was statistically significantly superior to the rollerball EA group as measured by success rate, amenorrhea rate, and patient satisfaction at one year. A comparison between the features of the two FDA-approved radiofrequency devices is shown in Table III.

### III. Heated Free Fluid Under Hysteroscopic Control

The HydroThermAblator® (HTA)—first produced and distributed by BEI Medical Systems Co. (Teterboro, New Jersey)—gained FDA approval in 2001 and remains the sole global endometrial ablation device and procedure performed under direct hysteroscopic control. HTA utilizes normal saline heated to 90°C which is passed into the endometrial cavity under a gravity-based system to facilitate endometrial ablation. The arrangement calls for a three-liter bag of normal saline placed at a height of 115 cm above the uterus to create an intrauterine pressure of 50–55 mm Hg—well below the 70 mm threshold at which heated saline might pass through the tubal ostia. HTA consists of a control unit, an outflow fluid pump, and an adjustable support pole on a mobile base. The system is connected by insulated inflow and outflow tubing to a standard 2.9 mm hysteroscope which is encased by a disposable 7.8 mm insulated sheath. The controller contains a microprocessor to regulate both the temperature of infused saline and treatment time while monitoring both pres-
sure and flow. HTA also incorporates an important safety feature to alert the operator and interrupt therapy if more than 10 mL of fluid is lost from the system.

The HTA procedure begins with a diagnostic hysteroscopy utilizing normal saline kept at room temperature. After confirming a tight cervical seal, normal saline, heated to 90°C, is introduced at 300 mL/min at an intrauterine pressure of 50–55 mm Hg and circulated for 10 minutes through a closed-loop system. The procedure is performed entirely under hysteroscopic control and is observed on a video display (Figs. 15 and 16) allowing the physician to monitor all phases of the process. This is followed by a one-minute cooling cycle before the instruments are removed.

The current generation of hydrothermal ablation systems was approved in 2010 with various safety features. The primary objective was to reduce the likelihood of clinically significant vaginal and vulvar burns. The advantages and disadvantages of the HTA system are reviewed in Table IV.

Most of the currently available clinical trials, and all of those designed for FDA approval, were performed on women following pretreatment with leuprolide acetate. In a clinical trial reported by Corson et al., 42 276 women were randomized to two groups in a 2:1 distribution. The first group consisted of 187 women who were treated with HTA while the second was comprised of 89 subjects treated with rollerball EA. The primary endpoint, or "success rate," of the study was a Janssen score—a standardized pictorial menstrual diary—of <75 one year following treatment. At the end of 12 months, success rates were 77% for HTA and 82% for rollerball while amenorrhea rates were reported to be 40% and 51% respectively.

One of the troubling issues of the first-generation HTA system was a substantial number of reports of deep second and third degree burns estimated at 0.32% as determined by a passive (user) reporting system. 43 The incidence of these burns was reduced to 0.14% with the release of the ProCerva™ Sheath (Boston Scientific Corp., Natick, Massachusetts). The most recent iteration of the HTA (Hydro ThermAblator®) was approved for clinical use in 2010 "with an improved design to deliver the same therapeutic benefits as the earlier HTA system, improved operator performance, and impart new safety features for the benefit of the patient and the device operator." 43 Specifically, the new system incorporated features to reduce the likelihood of fluid leaks and subsequent vulvar, vaginal, and cervical burns. The Genesys system’s ProCerva™ sheath includes a "cervical seal assist”—a finned silicone tube at the distal end used to maintain a tight seal between the distal portion of the device and the endocervical canal.

Since the Hydro ThermAblator® is not a fixed geometry system, some have advocated its applicability in women with menorrhagia and submucous leiomyomas. Glasser et al., 44 in an off-label use study, reported on 22 subjects with menorrhagia who were known to have submucous leiomyomas <4 cm in diameter. He described an overall success rate—defined as requiring no additional medical or surgical intervention—of 91%. Twelve subjects (54%) reported complete amenorrhea, five (23%) described oligomenorrhea, and three (14%) became eumenorrheic. There were two (9%) failures. A 60-month follow up of the original group of 22, along with an additional 11 patients, had a hysterectomy rate of 12%. A larger retrospective study by Hachmann-Nielsen et al., 45 on 160 consecutive women who underwent HTA between 2004 and 2008, indicated that HTA was associated with a high rate of amenorrhea with or without submucous leiomyomas. Of the subjects studied, submucous myomas were

<table>
<thead>
<tr>
<th>Table IV</th>
<th>Hydro ThermAblator® system advantages and disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td><strong>Disadvantages</strong></td>
</tr>
</tbody>
</table>
| Possible use in the presence of anomalies  
Possible use with selected submucous leiomyomas  
Hysteroscopic control during and after treatment  
8 mm of dilation  
Association with vaginal and cervical burns  
Physician must maintain a prolonged fixed position  
Endometrial preparation required | **Note that none of the non-resectoscopic endometrial ablation devices are approved for use with uterine anomalies or leiomyomas** |

---

Figure 17. AEGEA™ Vapor System controller unit.

Figure 18. AEGEA™ system treatment of irregular uterine cavity.
Figure 19. Cryoendometrial ablation with Her Option®.

noted in 33 women (24.3%). However, there was a significantly reduced success rate for women with submucous myomas >3 cm. As is the case with all other GEA devices, the HTA is not specifically approved for the treatment of submucous leiomyomas.

IV. Heated Water Vapor

The AEGEA™ Adaptive Vapor Ablation System (Aegia Medical Inc., Redwood City, California) achieved FDA approval in late-2017 and is a fully automated vapor delivery and safety monitoring system reminiscent of “atmocausis”—the application of superheated steam—first described over 120 years ago by Professor Sneguireff of Moscow,46 and later refined by Ludwig Pincus of Danzig.47-49 The AEGEA™ system creates and circulates steam at low pressure within the endometrial cavity for approximately 140 seconds—a 20 second “saline flush” and a 120 second treatment time.

The AEGEA™ Vapor System includes a vapor generator (Fig. 17) and a disposable procedure kit (Fig. 18). The single-use kit includes a 5.8 mm probe with a soft flexible tip as well as supply and drain accessories that deliver water to, and collect it from, the generator. The catheter contains three inflatable balloons which provide a secure seal at the endocervical canal while properly anchoring the Vapor Probe tip within the uterine cavity. The device also incorporates both a Uterine Cavity Integrity Test (UCIT) and a Device Lumen Patency Test (DLPT). The UCIT prevents the discharge of caustic steam through an accidental uterine perforation or into the endocervical canal while the DLPT is designed to insure proper probe tip placement within the uterine cavity.

The procedure begins with measurement of the uterus from fundus to the cervical canal using a sounding device after which the vapor probe’s “cervical slide collar” is adjusted placing the internal balloon just beyond the internal cervical os. Once the catheter and cervical collar are properly positioned, both the internal and external balloons are inflated, thereby preventing the escape of water vapor into the vagina. During the procedure, intrauterine pressure is maintained between 20 and 52 mm Hg and the cervical canal temperature is monitored with a thermocouple. The procedure, which takes four minutes to accomplish, includes a twominute vapor treatment. The AEGEA™ System is intended to treat women with normal, as well as non-uniform, uterine cavities including women with uterine anomalies50 and leiomyomas—however, as with other NREA systems, the AEGEA™ is not specifically approved for either.

The pivotal trial was a prospective, single-arm, non-randomized, multicenter study conducted at 14 investigation sites. Between May 2014 and May 2015, 155 patients were treated. The primary effectiveness endpoint was a reduction in menstrual blood loss as measured by a validated Pictorial Blood Loss Assessment Chart (PBLAC) of <75 at one year following treatment. The AEGEA Vapor System was judged to be effective in 122 subjects (78.7%) at one year with 30 (19.4%) reporting amenorrhea. At 12 months, 90.8% of subjects available for follow up reported being very satisfied (70.2%) or satisfied (20.6%).51

V. Microwave Endometrial Ablation (MEA)

The technique of microwave endometrial ablation owes its origins to the work of Phipps et al.,52 who, in 1990, reported the treatment of 42 subjects with a radiofrequency probe placed in the endometrial cavity in energy doses varying from 330 kJ to 660 kJ. Phipps’ probe utilized electromagnetic energy at 27.12 MHz to heat the endometrium and destroy the basalis. The technique’s clear advantage was in eliminating the use of distention fluid which was both cumbersome and carried potential risks. Phipps’ report stimulated interest in the use of microwaves as a potentially safer energy source. Microwaves are non-ionizing waveforms that are absorbed in tissues where they energize water molecules and cause tissue heating. A domestic microwave oven, for instance, uses a frequency of 2.3 GHz to penetrate deeply into food. However, if the frequency is increased, the result is a shorter wavelength with reduced penetration.

The potential for a microwave endometrial ablation probe prompted the formation of a research team in 1992 at the University of Bath, Microwave Physics Department in conjunction with the Royal United Hospital departments of Gynaecology and Medical Physics.53 The team sought to develop an intrauterine probe—operating in the microwave energy spectrum—that would provide safe EA with a reduced power output and treatment times. The first clinical trials began in 1994 and were reported by Sharp et al. in 1995.54 The probe was designed to be 8 mm in diameter—sufficiently small to facilitate passage into the uterine cavity and large enough to minimize the risk of uterine perforation. The depth of microwave tissue heating was to be restricted to 6 mm with a low total energy dosage to minimize the risks of peripheral tissue heating. The team developed a 9.2 GHz probe that would deliver microwave energy through an 8 mm dielectrically-loaded waveguide. The probe was fitted with a thermocou-
ple positioned at the tip to constantly measure and record endometrial surface temperatures.

In the original clinical trials, microwave endometrial ablation was performed following endometrial preparation with either danazol or Goscrelin and was carried out utilizing both general and paracervical block anesthesia. During the procedure, the microwave applicator was inserted until the tip reached the fundus and was then activated after which the cavity was treated from the fundus toward the lower uterine segment with a side-to-side motion to treat the entire endometrial surface. The temperature at the applicator-tissue interface was 100°C which produced micro-pockets of superheated steam. The mean treatment time was 3.5 minutes but varied with the endometrial surface area—the presence of leiomyomas tended to increase treatment times while pretreatment with GnRH agonists typically shortened them.

A report by Cooper et al. compared 123 patients treated with MEA to 132 women undergoing transcervical resection of the endometrium. At 12 months, the amenorrhea and patient satisfaction rates were 40% and 78%, respectively, for MEA-treated women while TCRE-treated women reported 40% and 76%—nearly identical outcomes. At the two-year follow up, the amenorrhea rates were 47% for the MEA group and 41% for TCRC with patient satisfaction rates of 76% and 67%, respectively.

MEA provided many advantages compared to the technique described by Phipps et al. The short treatment time and low power (30 watts) meant a very low energy dosage (average 4.2 kJ)—approximately 1% of what had been utilized by Phipps et al. MEA also incorporated continuous thermometry.

The MEA system was approved in the UK in 1996 and was produced and distributed by Microsulis Medical Limited. The device earned FDA approval in the United States in 2003. However, in 2011, Microsulis Medical Limited sold its MEA system to Hologic Inc., and the system has since been removed from the market.

VI. Cryoendometrial Ablation

Cryoaablation of the endometrium is unique among other global ablation technologies which utilize thermal energy to heat the endometrium. Cryosurgery causes endometrial destruction by three separate mechanisms. First, coagulation necrosis is caused by intracellular and extracellular ice crystal formation which results in the rupture of cells walls. Second, cryoaablation causes avascular necrosis of the endometrium by producing capillary obstruction and stasis. Third, cryoaablation causes intracellular and extracellular dehydration. The first use of cryosurgery within the uterine cavity was described by Cahan and Brockenier in 1967 at Memorial Sloan Kettering Cancer Center utilizing a 6 mm curved stainless-steel liquid-nitrogen-cooled probe. The treatment cycle called for five separate freeze-thaw positions within the endometrial cavity. The limitations of this early technology included the difficulty in controlling liquid nitrogen and in monitoring temperatures during the treatment cycle. Additional studies on endometrial cryoaablation were carried out by Droegemueller and his colleagues working first with Freon and then nitrous oxide. Nitrous oxide brought the probe temperature to -50°C, but the probe designs were insufficient to cause predictable and total endometrial destruction. In 1992, Pitroff et al. reported 15 cases in which saline was used to improve contact between the nitrous-oxide-cooled cryoprobe and the endometrium. This allowed temperatures of approximately -40°C at the endometrial surface. Pitroff’s improvements are still utilized in today’s Her Option® (American Medical Systems Inc., Minnetonka, Minnesota) endometrial ablation system.

In 2001, the US Food and Drug Administration approved the Her Option® In-Office Cryoaablation Therapy. Her Option® (Fig. 19) utilizes a propriety compressed gas mixture that generates temperatures between -90 and -120°C at the probe tip. In 2010, Cooper Surgical Inc. (Danbury, Connecticut) acquired the Her Option® Office Cryoaablation Therapy System. The system consists of a small portable console along with a disposable 5.5 mm cryoprobe. The probe is echogenic, allowing for constant ultrasound guidance, and is equipped with a surface temperature monitoring system that allows for continuous direct temperature measurements during freezing and rewarming phases. Finally, the probe has an auxiliary port which allows small amounts of saline to be injected to improve contact between the cryoprobe and endometrium. Ultrasound monitoring is recommended during cryoaablation as it assures the operator of proper probe placement and allows one to measure the developing “iceball”. A variety of techniques have been described with respect to probe placement and freeze patterns.

In 2003, Duleba et al. reported a prospective randomized study of 279 women comparing endometrial cryoaablation (N=193) to rollerball EA (N=86). In this study, all subjects were pretreated with a gonadotropin-releasing hormone and the procedures were carried out under sonographic guidance. One of the study’s observations was that minimal analgesia was required for women undergoing cryoaendometrial ablation. At 12 months, the success rates—defined as a PBAC score <-75—were 67.4% and 73.3%, respectively, for cryoaendometrial and electrosurgical ablation.

Endometrial Ablation: Where are we now?

When Goldrath et al. reintroduced second-generation endometrial ablation in the 1980s, they each envisioned EA under visual—hysteroscopic—control. The growth of these late 20th century techniques required solving three separate problems:

- Addressing the technical challenges of hysteroscopic endometrial ablation,
- Minimizing the incidence of serious intraoperative complications—dissention fluid mismanagement, uterine perforation, and visceral injury, and
- The demonstration of long-term efficacy.

Minimizing technical challenges and intraoperative complications of endometrial ablation

Paradoxically, the 21st century success of endometrial ablation was the result of replacing second-generation, hysteroscopically-controlled EA with non-hysteroscopic modalities—the so-called global endometrial ablation (GEA), or third-generation devices. Until these devices and techniques were introduced and refined, EA was practiced by only a few devoted and early proponents.
of minimally invasive gynecologic endoscopy. However, the lack of adequate training, fluid management systems, and protocols soon gave way to unfortunate and well-publicized complications.3-7 It was the implementation of GEA—in many ways a return to the principles of first-generation techniques—that enabled endometrial ablation to gain widespread acceptance in the gynecologic community.

GEA device manufacturers have simplified the technique and reduced the risks associated with EA and accomplished it by eliminating operative hysteroscopy and its associated risks.8,9 Risk reduction has also been further enhanced with the adoption of uterine cavity integrity tests (UCITs) prior to the application of thermal energy. These intraoperative assessments have been incorporated into the NovaSure®, Minerva®, and AEGA systems. Based on utilization estimates from the most widely distributed GEA device—NovaSure® ADVANCED—the approximate rate of reported thermal bowel injury is less than one per 25,000 procedures.7,58

These improvements have propelled the use of endometrial ablation as a minimally invasive surgical technique for abnormal uterine bleeding (AUB). In 2008, GEA, or third-generation EA, constituted the most common surgical treatment for heavy menstrual bleeding in the United States and, by 2016, the US. GEA market improved to over half a million units sold annually.70 Although all of the NREA devices have been shown to reduce menorrhagia and improve short-term quality of life scores,12,29,41,44 there is still a relative lack of reliable information regarding the long-term impact of these techniques 10–30 years postoperatively.

Demonstration of long-term efficacy

Longinotti et al.,71 in a now-famous study of 3681 women who underwent both resectoscopic and third-generation procedures, reported that 26% of women eventually required hysterectomy by their eighth postoperative year. Though some of these hysterectomies were performed for issues such as vaginal prolapse or adnexal pathology, the most common reason for subsequent uterine extirpation was intractable vaginal bleeding (51.6%) followed by cyclic pelvic pain (20.3%). Remarkably, the study revealed no relationship between the type of EA and the ensuing requirement for hysterectomy. However, this conclusion is limited by the study’s design.

Late-onset endometrial ablation failures typically presents in one of three ways—recurrent abnormal uterine bleeding, cyclic pelvic pain, or the inability to adequately evaluate and sample the endometrium in the presence of abnormal uterine bleeding.71,74 While the majority of women who undergo EA are able to successfully avoid hysterectomy, the precise number of women who require medical treatment for persistent vaginal bleeding or cyclic pelvic pain is unknown.

The most important determinant of long-term efficacy and hysterectomy avoidance appears to be proper patient selection. Risk factors of LOEAF include relative youth (women under the age of 35 years), severe dysmenorrhea, unexplained pelvic pain, and the presence of submucous leiomyomas or a uterus with an enlarged surface area.66 There is also evidence that EA procedures performed in outpatient centers under intravenous sedation and analgesia may provide women with better outcomes than those performed in an office-based setting. Wishall et al.,76 in a retrospective cohort study of 300 patients who underwent EA between 2007 and 2013, found that operating room-based procedures decreased the subsequent risk of hysterectomy by 76% (adjusted OR 0.24, 95% CI 0.07–0.77). However, randomized prospective studies on whether or not the incidence of LOEAFs are affected by the type of analgesia and sedation utilized have not been published.

Another incompletely unresolved issue with respect to “long-term efficacy” is whether or not EA may mask or delay the diagnosis of endometrial cancer. In 1987, DeCherney et al.,77 forewarned that the consequence of failing to destroy a “nest of endometrial tissue” during EA could result in a sequestered island of endometrial carcinoma (EC) inaccessible to standard biopsy techniques, possibly delaying or obscuring the diagnosis. In 1993, Copperman et al.,78 described the first case of post-ablation endometrial carcinoma (PAEC) in a 56-year-old who presented with postmenopausal bleeding five years following a resectoscopic EA. Several authors have since reported cases of PAEC.79,80 Dood et al.,81 conducted a retrospective cohort study in nearly 500 outpatient general practices in the UK who were treated for abnormal uterine bleeding between 1994 and 2010. Of the 234,721 women who met the study criteria, 4776 underwent endometrial ablation while the remainder received medical management. The authors observed no difference in endometrial cancer rates in the two groups. However, the study is limited by its retrospective nature and its failure to investigate the effect of prior EA exposure on histology and stage. Although there is no data to suggest that PAECs present at advanced stages of disease, it is clear that the assessment of the uterine cavity in women with abnormal uterine bleeding following an EA is unreliable by traditional methods—hysteroscopy, endometrial biopsy, and sonography.72,79

Endometrial Ablation: The Future

As endometrial ablation technology matures, several issues will require attention by physicians, manufacturers, and professional organizations.

Clarifying the role of EA in women with abnormal uterine bleeding

The gynecologic landscape has undergone many significant changes since the early 1980s when EA first emerged from blind, first-generation techniques. Hysteroscopic and resectoscopic EA were introduced at a time when fewer medical and surgical options existed for women requesting treatment for AUB. In the early 1980s, neither the levonorgestrel-releasing intrauterine system (LNG-IUS) nor the laparoscopic hysterectomy, were available. With the introduction of those technologies, physicians were required to develop algorithms that offered safe, economical, and minimally invasive treatment strategies in a patient-centered approach.

The LNG-IUS was first developed by Luukkanen et al. in 1977 and approved by the FDA in 2000 as a contraceptive device—the Mirena® IUD (Bayer Healthcare Pharmaceuticals, Wayne, New Jersey). In 2009, the Mirena® IUD was also sanctioned for the management of heavy menstrual bleeding (HMB) and remains the only LNG-IUS device currently available in the US with this approval. The LNG-IUS has since become an important addition to the gynecologic armamentarium for managing women with AUB. In a review of 13 randomized controlled trials com-
paring conservative surgery or hysterectomy to medical therapy, Marjoribanks et al.\textsuperscript{41} concluded that there was no demonstrable difference in satisfaction rates between surgery and LNG-IUS, though the latter is more often associated with vaginal bleeding and spotting. The authors reported that while “oral medication suits a minority of women in the long term [that] the LNG-IUS device provides a better alternative to surgery in most cases.” This finding supports the notion that the treatment for AUB should begin with minimally invasive and reversible medical approaches as a first-line management strategy.

In addition to changes in the medical management of menstrual disorders, the surgical approaches have changed as well. With the invention of the laparoscopic hysterectomy,\textsuperscript{2} some have advocated for uterine extirpation as a first-line surgical approach to managing women with abnormal uterine bleeding. In 2015, Zuppi et al.\textsuperscript{86} observed that after a mean follow up of 14.4 years, 29% of women treated with endometrial ablation underwent additional surgery, whereas no patients after laparoscopic subtotal hysterectomy (LSH) suffered symptom recurrence. The authors concluded that “because of an improved quality of life and lower reoperative rate, LSH (laparoscopic supracervical hysterectomy) should become the treatment of choice in women with abnormal uterine bleeding resistant to medical treatment and should be proposed to all women instead of HEA (hysteroscopic endometrial ablation).” While Zuppi et al. right-fully advocates for hysterectomy’s definitive role in treating AUB, their statement asks us to accept the premise that LSH—a far more invasive, morbid, and expensive procedure—should be the initial surgical approach for women who are resistant to medical management. Unfortunately, this deeply flawed conclusion fails to consider the many factors that determine the appropriateness of any patient-centered management strategy. These variables include the patient’s age, emotional predisposition to hysterectomy, a history of previous abdominal procedures, coexisting morbidities, medical insurance coverage, and whether or not she can accept a comparatively long period of recovery.

As the risks, benefits, costs, and limitations of each of these medical and surgical treatment modalities is clarified, the role of EA will be more completely understood.

**Improving patient education, selection, and informed consent**

Most women, when given the best available information and guidance in selecting treatment options, often select an appropriate management strategy. Proper patient counseling for a woman considering EA requires an honest assessment of her specific risk factors for developing a late-onset endometrial ablation failure (LOEAF).\textsuperscript{72} All issues that increase a woman’s chance of developing a late-onset failure—age, leiomyomas, uterine size, severe dysmenorrhea, or unexplained pelvic pain\textsuperscript{2}—need to be scrupulously presented. For patients who are considering an office-based EA, they should also be provided with a realistic expectation of the pain that may be associated with procedures performed under minimal sedation or local anesthesia. Important-ly, both the patient and the physician should have a clear strategy for managing intolerable pain.

Issues of informed consent regarding endometrial ablation are different from most gynecologic procedures which typically focus on immediate complications. In addition to discussing issues related to intraoperative complications—which are uncommon with modern EA—attention should be focused on the incidence and presenta-tion of LOEAFs. In the author’s experience, accurate information best allows the woman to participate in the treatment modality best suited for her cir-cumstances and lifestyle.

**Protocols for long-term follow up of women who undergo endometrial ablation**

As of this writing, specialty groups, such as ACOG and the American Association of Gynecologic Laparoscopists (AAGL), have not yet developed protocols for following women who have undergone endometrial ablation. In 1991, McLucas\textsuperscript{87} suggested that subsequent to EA, women “should be encouraged to undergo a baseline ultrasound three months after ablation and then annually as part of their health maintenance.” The author (MW) incor-porated this practice in 1994 and has found annual sonography to be helpful for detecting asymptomatic areas of endometrial regrowth and hematome-trae—often a precursor to symptomatic LOEAF. Women should be reminded—at the time of their annual examination—to report any changes in their menstrual pattern as well as any unexplained pelvic pain. Whether or not annual ultrasound examinations are cost-effective is a subject that requires further investigation. However, the author has found that an annual ultrasound examination and review of LOEAF-associated symptoms is extremely helpful in reducing both anxiety and unnecessary emergency room visits for women who experience unant-icipated pelvic pain or vaginal bleeding.

The management of abnormal perimenopausal or post-menopausal bleeding

Irregular vaginal and postmenopausal bleeding is often encountered in women with a prior history of endometrial ablation. Ahonkallio et al.\textsuperscript{88} demonstrated the limitations of endometrial sampling and sonohysterography following EA. The authors evaluated 57 women (ages 47–52) who had undergone a previous EA for the treatment of heavy uterine bleeding with both endometrial biopsy and sonohysterography. An endometrial sampling could not be obtained in 23% of subjects using a Pipelle\textsuperscript{8} device (Cooper Surgical Inc., Trumbull, Connecticut). During sono hysterography, the uterine cavity distended regularly in only 16% of women and did not distend at all in 42% of subjects. In 18% of attempts, the sonohysterography catheter did not enter the uterine cavity at all. Ahonkallio et al. concluded that endometrial assessment is compromised following EA and that intrauterine adhesions may diminish the reliability of endometrial sampling. AlHilli et al.\textsuperscript{89} studied 91 patients who had undergone radiofrequency EA and who underwent subsequent transvaginal ultrasound examinations. Symptomatic patients (69.2%) were significantly more likely than asymptomatic patients to have an endometrial thickness of 3 mm or more, a heterogeneous endometrial echotexture, and leiomyomas. Unfortunately, sonographic criteria that might obviate the need for endometrial sampling have not yet been established and physicians are often left with few guidelines for managing women with recurrent perimenopausal or postmenopausal bleeding who have undergone an EA.

Although the author (MW) has described ultrasound-guided reopera-
tive hysteroscopic surgery as a technique for evaluating women who require endometrial biopsy. This method is impractical and should be utilized only by the most experienced hysteroscopists. Unfortunately, many women who require endometrial sampling, following an LOE, presently require a hysterectomy for a proper histologic diagnosis. There is clearly a need to improve both non-invasive and minimally invasive techniques to evaluate women who have undergone EA and who require endometrial assessment.

Innovations for reducing the incidence of late-onset endometrial ablation failures (LOEAFs): EA/LNG-IUS

Although patient selection remains the most important tool for reducing the incidence of LOEAFs, five authors have demonstrated improved success rates of EA with the postoperative insertion of an LNG-IUS.

In 1997, Römert reported a series of 26 subjects with refractory hypermenorrhea who were treated with rollerball endometrial ablation (RBEA). Thirteen of the subjects were treated with RBEA alone while the remaining 13 women underwent RBEA followed by the insertion of an LNG-IUS. After nine months, 54% of women in the RBEA group reported amenorrhea compared to 92% of women who received combined therapy. In 2000, Hans Bratschi reported the results of 99 subjects treated with both hysteroscopic endometrial resection and an LNG-IUS and reported amenorrhea or hypomenorrhea in 95.9% of subjects who were followed for at least 18 months—a rate far superior to what might be expected with any ablation or resection technique alone.

In 2003, Maia et al. reported the results of a retrospective observational study in which 95 women were identified with pelvic pain, menorrhagia, and an ultrasound diagnosis of adenomyosis. All of the subjects underwent endometrial resection (EMR). In the 42 women who underwent EMR alone, the incidence of amenorrhea at 12 months was only 9%, whereas 100% of the 53 subjects who underwent both EMR followed by the insertion of a Mirena intrauterine device reported amenorrhea (p <0.001). The authors noted that the rates of amenorrhea in their study were significantly greater than literature reports in which Mirena was used alone and not in association with endometrial resection to treat adenomyosis.

An observational study by Vaughan et al. reviewed the outcomes of 105 women who were offered both a thermal balloon EA and an LNG-IUS and followed for a mean duration of 25 months. Fifty-three (50.5%) of the cohort described menses “lighter than normal,” while 49 (46%) subjects reported amenorrhea. Ninety-five (90.5%) subjects described their treatment as a “complete success” and two (1.9%) subjects felt the treatment was a failure. Only one subject required a hysterectomy during the follow-up period.

In 2015, Papadakis et al. reported the results of combined EA and LNG-IUS on the incidence of late-onset failure. In this prospective cohort study, 23 women with HMB and secondary dysmenorrhea were treated with both endometrial ablation—thermal balloon or radiofrequency device—and an LNG-IUS and were monitored for four years. Their results were compared to a cohort of 65 women who underwent EA alone. Treatment failure was defined as persistent pain, bleeding, or the requirement for a hysterectomy. Of the 23 women who underwent the combined EA/LNG-IUS treatment, none underwent hysterectomy for treatment failure at four years, while 24% of women who underwent EA alone required uterine extirpation. Although persistent HMB was not significantly different between the two groups, the group that underwent combined treatment reported significantly less postoperative pain.

These studies certainly suggest that additional research is warranted in clarifying the role of combined EA/LNG-IUS treatment in women who have not adequately responded to medical management alone for HMB and who are at high risk for developing LOEAF. The potential benefits of this combined EA/LNG-IUS approach include (a) providing contraception to women who have not undergone a sterilization procedure and (b) suppression of any residual endometrium in women who undergo EA. Importantly, the LNG-IUS may provide a platform around which postoperative fibrosis is allowed to occur, possibly preventing complete obstruction and sequestration of residual endometrial tissue. It needs to be emphasized that the use of the LNG-IUS in the setting of EA is an off-label application not approved by the Food and Drug Administration and that removal of the device may present some challenges.

CONCLUSIONS

Since Soranus of Ephesus first introduced the use of uterine astringents in the second century, the deliberate destruction of the endometrium has been offered as a minimally invasive approach for managing intractable uterine bleeding unresponsive to contemporary medical interventions. The late 19th century witnessed the introduction of first-generation endometrial ablation as superheated steam that was utilized to cause thermal destruction of the endometrium—atmoscaeus. As other energy sources and methods became available—electrosurgery, radium, X-rays—each was given an opportunity to remediate intractable uterine bleeding while avoiding major intra-abdominal surgery. During the early 20th century—a time when both hysterectomy and anesthesia were far riskier than today—the ability to perform EA in an office-based setting had clear rewards.

Early practitioners of EA were soon aware of the immediate risks and benefits of EA and even described the occurrence of late-onset complications. In the midst of a hysterectomy epidemic, the 1980s saw renewed interest in EA as a variety of minimally invasive endoscopic techniques were introduced. These second-generation modalities allowed EA under direct visual control. The earliest of these techniques utilized Nd:YAG laser energy delivered through a quartz fiber that was co-located with a hysteroscope. This technique was soon supplanted by the more affordable resectoscope which required only inexpensive and readily available electrosurgery. Unfortunately, the enthusiasm for these second-generation techniques was soon dampened by reports of severe complications resulting from uterine perforation, fluid mismanagement, and a scarcity of adequate training.

In the latter part of the 20th century, a variety of EA devices were introduced that obviated the need for hysteroscopic control and fluid distention. With the
exception of hydrothermal ablation, these techniques—like their first-generation counterparts—were “blind” and reminiscent of late 19th century practices. Despite the lack of visual control, these third-generation techniques were equipped with a variety of innovative safeguards that produced excellent results with unprecedented safety. The combination of safety, efficacy, and affordability has propelled third-generation—or “global”—endometrial ablation to remarkable growth in the early part of the 21st century.

In the decades ahead, use of EA in the United States is forecast to increase at an annual rate of 5.5% from 2016 to 2024. In this setting, a variety of questions remain in the ever-changing landscape of menstrual disorder remedies. Can we reduce EA failures with proper patient selection or by combining EA with LNG-IUS? How do we follow women who may require periodic evaluation following EA? How can we safely manage women who may require evaluation for AIB or postmenopausal bleeding following EA? As advocates for women’s health, our primary responsibility continues to be the search for effective patient-centered and cost-effective strategies. Though medicine and technology will continually evolve, these remain achievable and worthwhile goals.

Author’s Disclosures

Dr. Wortman is a consultant for Ocon Medical Ltd.

References

37. NovaSure ADVANCED Impedance Controlled Endometrial Ablation System. Instruc-
Endometrial Ablation: Past, Present, and Future Part II

WORTMAN


86. Zuppi E, Centini G, Lazzeri L, et al. Hyste,rosccopic endometrial resection versus laparoscopic supracervical hysterectomy for abnormal uterine bleeding: long-term follow up of a ran-
87. McClusky B. Intrauterine applications of the
88. Ahonkallio SJ, Liakka AK, Martikainen HK,
et al. Feasibility of endometrial assessment after
thermal ablation. Eur J Obstet Gynecol Reprod
Uterine ultrasound findings after radiofrequency
endometrial ablation: correlation with symp-
90. Wortman M, Daggett A, Deckman A.
Ultrasound-guided reoperative hysteroscopy for
managing global endometrial ablation failures. J
Minim Invasive Gynecol 2014;21:238–44.
91. Römer TH. A prospective study on comb-
ined hysteroscopic-local hormonal therapy of
recurrent refractory hypermenorrhea. Ge-
92. Bratschi HU. Hysteroscopic Endometrial
tion of Mirena after Endometrial Resection in
Patients with Adenomyosis. J American Assoc
Gynecol Laparosc 2003;10:512–16.
94. Vaughan D, Byrne P. An evaluation of the
simultaneous use of the levonorgestrel-releasing
intrauterine device (LNG-IUS, Mirena®) com-
bined with endometrial ablation in the manage-
ment of amenorrhea. J Obstet Gynaecol
95. Papadakis EP, El-Nashar SA, Laughlin-Tom-
maso SK, et al. Combined endometrial ablation
and levonorgestrel intrauterine system in
women with dysmenorrhea and heavy menstru-
al bleeding: novel approach for challenging
cases. J Minim Invasive Gynecol 2015;22:
1203–7.