

NovaSure™ GEA Technology Overview. Analysis of Worldwide Clinical Results

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Summary

The NovaSure™ GEA is a system developed for treatment of women suffering from menorrhagia secondary to DUB. This technology provides for a customized, controlled, contoured endometrial ablation, without the need for concomitant hysteroscopic visualization and/or endometrial pre-treatment. Average treatment time is ninety (90) seconds. Active bleeding, at the time of treatment, is not found to be a limiting factor for use of this technology. The NovaSure™ GEA technology has been evaluated in a large number of patients, under different clinical protocols, and has been shown to be both safe, and effective yielding a high patient satisfaction rate. The results of these clinical studies are summarized in this publication.

Introduction

Hysterectomy is currently the leading treatment method for patients symptomatic for menorrhagia. Over 600,000 hysterectomies are performed every year in the U.S. alone. Although efficacious, hysterectomy has a number of potentially serious drawbacks. Higher morbidity and mortality rates, and high direct and indirect costs top the list¹.

Ablation of the endometrial lining of the uterus is a less invasive and aggressive method, and, as such, may be a better alternative for a sizeable number of patients. Because of lower morbidity and mortality rates and significantly lower procedure costs², endometrial ablation is increasingly being adopted by the gynecological community worldwide³. Although hysteroscopically directed endometrial ablation has been proven

successful in the management of DUB, the procedure is not performed by the vast majority of gynecologists owing to its perceived technique related difficulties and inherent risks. The risks associated with the hysteroscopic approach are well known. Among these are uterine wall perforation, intravasation of fluid distention media, hyponatremia, encephalopathy, and death^{4,5,6,7}.

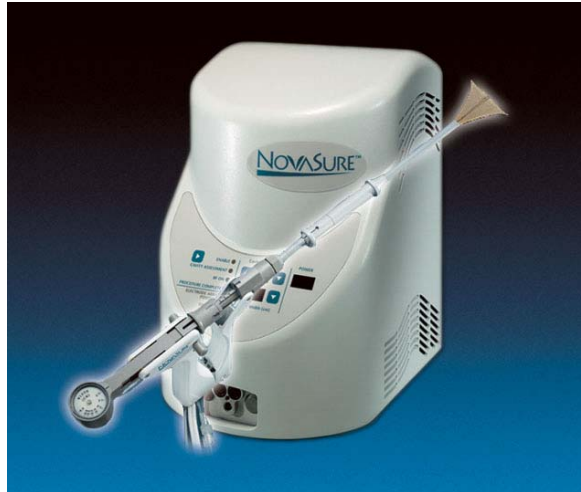
Easy-to-perform global ablation techniques have made it easier for more gynecologists to test the waters of endometrial ablation and operative hysteroscopy⁸. These less complicated methods of endometrial ablation employ differing agents and energy sources to permanently destroy the endometrial lining. Included among these are LASER energy (ESC Sharplan “ELITT”⁹), Nd:YAG single fiber LASER¹⁰, Monopolar RF energy (“Vesta DUB”¹¹), high temperature (Gynecare “ThermaChoice®”^{12, 13}, Wallsten “CavaTerm”¹⁴, BEI “HTA”), sub zero temperature (CryoGen “Her Option”¹⁵), microwave energy (Microsulus “MEA”¹⁶). The technology employed, energy source, treatment time, procedural risks and outcomes vary from one method to another. Large-scale studies have been, and continue to be undertaken, in order to assess their safety and efficacy.

Global, or second-generation endometrial ablation technologies (SEATs), are significantly easier to use and minimize, or actually eliminate, the need for hysteroscopy. However, there are a number of limiting factors for each system that need to be considered. The labeling information for most SEATs calls for either mechanical or hormonal pre-treatment of the endometrium. Many SEATs lack a reliable safety mechanism that ensures that energy is not delivered in cases of undetected uterine perforation or after creation of false passage. Treatment time, although reduced from that required for rollerball endometrial ablation, is still prolonged for many SEATs. Owing to the need for significant amounts of analgesia/anesthesia for many SEATs, their use in an office setting appears limited. The NovaSure™ Global Endometrial Ablation (GEA) System successfully addresses many of the drawbacks of other global ablation techniques.

Description of the NovaSure™ GEA System

The NovaSure™ GEA System (Picture 1) consists of a single use, 3-Dimensional bipolar ablation device and Radio Frequency Controller that enables a controlled endometrial ablation in an average of 90 seconds without the need for concomitant hysteroscopic visualization.

Endometrial “pre-treatment” of any kind (mechanical, hormonal, or cycle timing) is not required when using NovaSure™ GEA. The technology is easily employed in the actively bleeding patient.



Picture 1

The NovaSure™ GEA disposable ablation device consists of a conformable, bipolar, metalized, porous, fabric mesh, mounted on an expandable metal frame. Integral to the hand-held device is the Intrauterine Measuring System (IMD) used to determine uterine cavity width (cornu-to-cornu distance). The unique geometry of the electrode allows for a controlled depth of ablation, characterized by a more shallow depth at the cornu and lower uterine segment, and a deeper ablation in the mid-body of the uterus. The NovaSure™ GEA device can treat uteri with sounding lengths up to 12 cm. During its insertion into the uterine cavity, the ablation electrode is housed in a protective sheath. The sheath is then withdrawn into the endocervical canal, allowing for full and proper intrauterine deployment of the fan-shaped device. During the ablation procedure, the protective sheath then occupies the full length of the cervical canal, protecting the fragile endocervical tissues from injury.

The NovaSure™ GEA Controller contains a constant power output generator with a maximum power delivery of 180 watts. Measurement of uterine cavity length (determined by traditional sounding), and width (which is measured by the GEA device at the time of device deployment), are entered into the controller, which automatically calculates the unique power output required to assure an optimal, confluent endo-myometrial ablation. Throughout the short procedure, the depth of ablation is controlled continuously by monitoring tissue impedance (resistance).

An important component, unique to the NovaSure™ GEA, is a vacuum pump, contained within the RF Controller. This provides continuous

suction allowing for the removal of steam, blood and other byproducts of ablation from the cavity. As opposed to balloon ablation technologies, in which pressure distends the uterine cavity, the NovaSure™ GEA system's use of constant vacuum, assures intimate contact between the ablation electrode and the endometrium. Vaporization of the endometrial layer is a low impedance process owing to this tissue's high liquid content. Once the ablation process reaches the myometrial layer, tissue impedance (resistance) rises rapidly until 50 Ohms is reached (equivalent to the impedance of the ablated superficial myometrium). This signals the NovaSure™ generator to automatically terminate the ablation process. This automatic feedback mechanism is a key aspect of the NovaSure™ GEA technology, and, differentiates it from other global ablation technologies. With NovaSure™ GEA, the ablation process is based, not on temperature and time, but on specific, well-analyzed physical characteristics (electrical conductivity) of tissue, allowing for a well controlled, consistent and rapid ablation process that is unique to any given uterus.

A Cavity Integrity Assessment System is another integral part of the NovaSure™ GEA System. This automatic safety feature assists the physician in the timely detection of an inadvertent uterine wall perforation, and prevents energy delivery in such cases. The Cavity Integrity Assessment System utilizes the same technology employed by conventional hysteroflators, in which there is an inverse relationship between flow rate and pressure. CO₂ is delivered into the uterine cavity at a safe flow rate and pressure. Once the controller determines that this pressure is maintained, over a period of 7 seconds, thus confirming uterine wall integrity, it signals the generator to proceed with the ablation process. Another valuable aspect of the NovaSure™ GEA system is its portability and light weight, allowing the system to be easily transferred from one treatment facility to another.

Clinical Trials and Subjects

There have been a number of clinical trials conducted worldwide, intended to assess the safety, efficacy and other aspects of the NovaSure™ GEA technology. To this point, approximately 1000 patients have undergone the NovaSure™ procedure. Some of these patients were treated outside of clinical protocols since the product is currently commercially available in Canada and Europe.

The remaining women were study subjects in thirteen different clinical trials conducted worldwide under a variety of protocols with different aims and end points. Three were Grade A Randomized Controlled Trials. In these, the NovaSure™ GEA system was compared to the "gold

standard" rollerball, Cavaterm™ balloon and ThermaChoice® balloon. The remaining studies were Grade B and C studies. Some clinical trials are still underway. In all of the trials, women assigned to the NovaSure™ GEA procedure received no pretreatment with pharmaceutical agents (birth control pills, GnRH, e.t.c) or mechanical means (i.e. D&C); neither was the procedure timed to a particular menstrual cycle day. Procedures were performed even if patients were actively bleeding on the day of treatment. The uterine cavity was evaluated by means of hysteroscopy or sonohysteroscopy to exclude patients with submucous fibroids and/or polyps that would significantly distort the uterine cavity. Hereditary malformations of the uterine cavity (T-shaped, unicornuate, septate) as well as a history of classical Cesarean Section or myomectomy were exclusion criteria in these studies. Uterine cavity size was limited to a maximum uterine sounding length of 10 cm and averaged 9.4 cm. The average cornu-to-cornu distance was 3.98 cm, ranging from 2.3 – 5.5 cm. FSH levels were determined, prior to the procedure, to assure the pre-menopausal status of study subjects. Remaining diagnostic evaluation of the patient was similar to that which is standard for women deemed to be candidates for endometrial ablation.

Methods

The NovaSure™ GEA procedure is performed as follows:

A speculum is inserted into the vagina to visualize the cervix which is then grasped with a tenaculum. The cavity is sounded and the measurement recorded. Cervical dilation to 7.5mm is accomplished with Hegar dilators. Cervical length is assessed during dilation. The uterine cavity length (sound measurement minus length of the cervix) is entered into the RF Controller. The NovaSure™ GEA device is inserted, deployed, and properly seated in the uterine cavity. The cornu-to-cornu measurement is determined by the Intrauterine Measurement Device (IMD) feature on the disposable device, and entered into the RF Controller. This allows for a precise and automatic calculation of the power requirement for optimal treatment of the uterine cavity. The RF Controller is activated by depressing the foot switch. Following a seven second perforation detection cycle, the ablation process begins. At the conclusion of the ablation cycle (average time 85 seconds), the RF Controller automatically terminates energy delivery. The device is closed and withdrawn from the cavity. The tenaculum and vaginal speculum are removed to conclude the procedure. Treatment time is measured from the initiation, to the conclusion, of RF energy application.

During clinical trials, all adverse events and/or complications, both during and after the procedure, were recorded. Post-operative and dis-

charge times were recorded. Following surgery, all patients were required to maintain a menstrual diary for 12 months. Even if the patient had achieved amenorrhea, continuation of the diary was still required. Follow-up visits were undertaken at 6 and 12 months. Menstrual blood loss was assessed before, and after treatment, using a pictorial blood assessment chart (PBLAC) and method described by Higham et al.¹⁷.

PBLAC scoring to assess the amount of bleeding allowed correlation with the approved WHO classification (amenorrhea, hypomenorrhea, eumenorrhea and menorrhagia). Post-treatment menstrual diaries were evaluated on a monthly basis. FSH determinations at 12 months post-ablation, allowed for the exclusion of subjects from the treatment success group, who had become amenorrheic, but who had also entered menopause.

Results

Average patient age was 42 years and all patients had completed childbearing at the time of the procedure. The average number of pregnancies prior to the ablation was 2.86. Uterine position was described as: anteverted – 51%, retroverted – 23%, and mid-position – 26%.

The average PBLAC score before treatment was 715, a figure that is 7 times higher than the upper limit for menstrual bleeding according to the Higham score¹⁷.

The majority of patients (75%) were treated using an anesthesia regimen consisting of para-cervical block (PCB) with, or without, light IV sedation. A sizeable number of patients underwent the ablation procedure in an office setting.

Of the patients treated in these clinical trials, there were no serious intra-operative complications. In one of the earliest trials, one patient experienced a superficial cervical burn, which was healed in 3 weeks time with no sequelae. The majority of the patients were discharged 1-2 hours post-procedure. Five hundred forty (540) patients have completed their 6-month follow-up visit. Forty-eight percent (48%) were amenorrheic (PBLAC=0), 22% experienced spotting (PBLAC= 1-10), 12% were hypomenorrheic (PBLAC=11-30) and 9% were eumenorrheic (PBLAC=31-100), and 9% remained menorrhagic (PBLAC=100+).

Four hundred sixty-seven (467) patients have completed their 12-month follow-up visit. Fifty-one percent (51%) reported amenorrhea (PBLAC=0), 23% experienced spotting (PBLAC= 1-10), 11% were hypomenorrheic (PBLAC=11-30), and 8% were eumenorrheic (PBLAC=31-100). Only 7% were menorrhagic (PBLAC=100+). See table 1.

Conclusions

1. Clinical results indicate that the NovaSure™ GEA system can be

Table 1. 6 & 12 Months Results after NovaSure GEA Ablation

	6 months follow-up (N=540)	12 months follow-up (N=467)
Amenorrhea (PBLAC=0)	48%	51%
Spotting (PBLAC=1-10)	22%	23%
Hypomenorrhea (PBLAC=11-30)	12%	11%
Eumenorrhea (PBLAC=31-100)	9%	8%
Menorrhagia (PBLAC=100+)	9%*	7%*

* Patients undergoing hysterectomy, or having additional surgical interventions for menorrhagia, were considered failures and included in the "Menorrhagia" group.

The re-treatment rate in this large study population is low (1%). The majority of additional surgical interventions (hysterectomies) were due to continuous bleeding and/or patient dissatisfaction with the procedure outcome. Several patients underwent hysterectomy for complaints of pain. In each of these cases, there was pathologic confirmation of either adenomyosis and/or endometriosis. In one patient, the re-treatment procedure was rollerball ablation. There were no other medical/surgical interventions (i.e. D&C, drug therapy). The procedure success rate, defined as reduction in bleeding to a PBLAC score of 100 or less, was 91% and 93% at 6 and 12 months respectively. Treatment times averaged 89 seconds, and ranged from 40 to 120 seconds. Patient satisfaction, as assessed in the FDA trial, was 98%.

successfully used as an effective method of treatment for women with menorrhagia secondary to DUB.

2. The NovaSure™ GEA system proved to be a safe and effective modality in the management of patients suffering from excessive menstrual bleeding.

3. The system employs unique safety features allowing for a very low complication rate.

4. Endometrial pretreatment appears unnecessary for success of the NovaSure™ GEA.

5. The NovaSure™ GEA procedure is rapidly accomplished (89 seconds average treatment time) and can easily be performed, under IV sedation and paracervical block anesthesia, in an office setting.

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