Clinical Performance Characteristics of the Adiana® System for Permanent Contraception: The First Year of Commercial Use

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In 2009, the Adiana® System for Permanent Contraception was approved by the US Food and Drug Administration and became the second device on the market for hysteroscopic sterilization. This article outlines the basics of the Adiana procedure as it relates to the initial 12-month clinical experience following commercial launch. Safety, efficacy, and practical applications are explored to provide a better understanding of product performance characteristics in the first year of actual clinical use.
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Female sterilization began in the late 19th century and has seen its most significant change with the introduction of laparoscopy. By the abandonment of open laparotomy to achieve tubal occlusion, women have been able to avoid hospitalization and prolonged recoveries. According to the Centers for Disease Control and Prevention (CDC), from 2006 to 2008, female sterilization was the contraception of choice for 17% of all women.[1] In women aged 30 to 44 years, female sterilization was the leading method of contraception. In 2009, there were 700,000 cases of laparoscopic sterilization; the most common method was bipolar coagulation.[1,2]

Nonetheless, laparoscopy has its own disadvantages and risk of complications. The most significant morbidity is associated with the use of electrical energy and inadvertent thermal damage to the bowel. Introduction of trocars into the abdominal cavity carries substantial risk of injury to intra-abdominal organs and blood vessels. Based on the Collaborative Review of Sterilization (CREST) study,

the rate of unintended major surgery was 0.9 per 100 procedures.[3]

Compared with laparoscopic sterilization, hysteroscopic sterilization is intended to reduce the risk of injury as no instruments are inserted into the abdominal cavity. Intraoperative complications with a hysteroscopic procedure most often involve the risk of uterine perforation and fluid deficit. The first product for hysteroscopic sterilization was introduced in 2002, with the US Food and Drug Administration's (FDA) approval of Essure® Permanent Birth Control System (Conceptus Incorporated, Mountain View, CA), a nickel titanium and polyethylene terephthalate device. Despite this profound advance as a sterilization option for women, the literature contains several reports of uterine perforations that occurred with use of the first hysteroscopic sterilization system.[4-7] Concerns about complications related to uterine perforation remain, and devices for hysteroscopic sterilization continue to evolve; the Essure product has been redesigned from earlier versions, newer novel devices are in development or in clinical trials, and yet others have been approved for use. The most recent introduction to the hysteroscopic sterilization market is the Adiana® System for Permanent Contraception (Hologic, Inc., Bedford, MA).

The Adiana clinical trial, Evaluation of the Adiana System for Transcervical Sterilization (EASE), carefully evaluated the safety profile of the procedure and device. In this prospective, observational study of 770 women, no uterine or tubal perforations, expulsions, injuries related to matrix placement, excessive pain, or bleeding occurred. There was one case of hyponatremia that resolved without complication.[8]

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The Adiana Procedure

The Adiana system achieves tubal occlusion by tissue ingrowth into a silicone matrix placed within the lumen of the fallopian tubes bilaterally. The Adiana matrix is a biocompatible implant composed of fully cured silicone. Silicone has been shown to be safe and well tolerated for such diverse uses as contraception,[9,10] cardiac valves,[11,12] and reconstructive surgery.[13-16] The Adiana matrix is housed within the tip of the delivery catheter (Figure 1).

Proper matrix placement requires the catheter to be situated approximately 1.4 cm into the intramural portion of the fallopian tube. Through use of a hysteroscope with a 5-Fr operating channel, the Adiana delivery catheter is used to cannulate the fallopian tube. Once the catheter is placed through the tubal ostia, a position detection array (PDA) indicates if the catheter is both correctly positioned inside the fallopian tube and in contact with the tubal mucosa. After the device position is confirmed by the PDA, the distal tip of the catheter delivers less than 3 W of bipolar radiofrequency energy to the electrode array (Figure 2). Thermocouples in the

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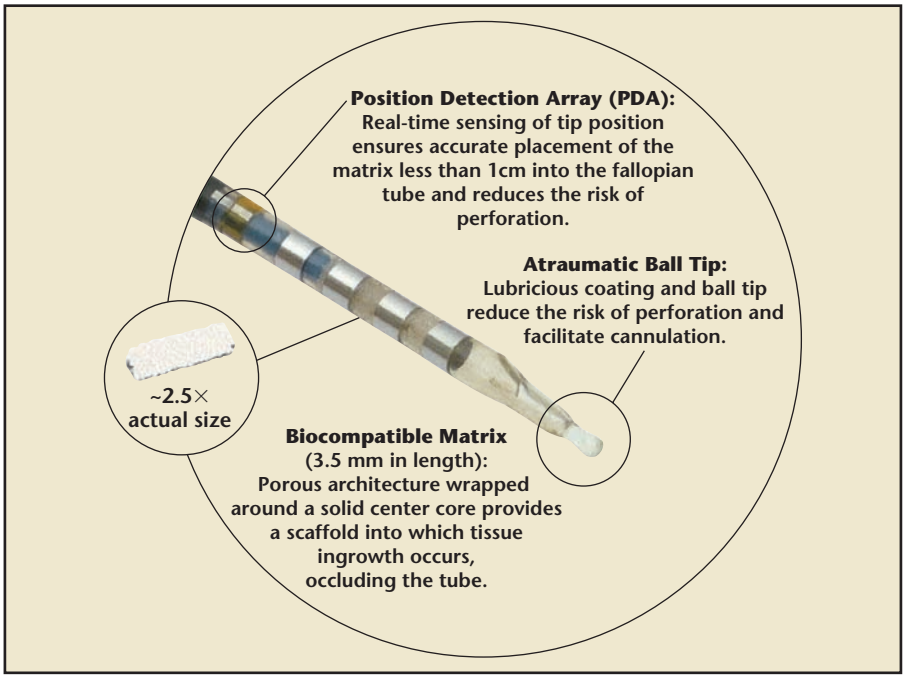
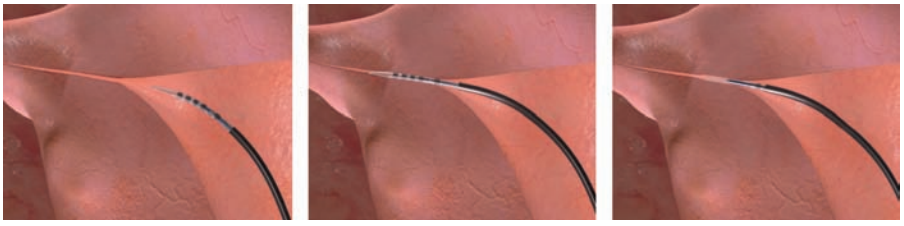
Figure 1. *The Adiana® System for Permanent Contraception (Hologic, Inc., Bedford, MA) delivery catheter.*





(A) (B) (C)

Figure 2. *The Adiana® System for Permanent Contraception (Hologic, Inc., Bedford, MA) procedure. (A) Position the catheter: The catheter is passed hysteroscopically just inside the fallopian tube, eliminating the need for incisions. The position detection array (PDA), located on the catheter tip, alerts the physician when the catheter is in the correct location within the tube. (B) Deliver radiofrequency energy: The catheter applies very low-level bipolar radiofrequency (RF) energy (< 3 W) within the intramural portion of the fallopian tube to create a superficial lesion approximately 500 μm in depth. This prepares the fallopian tube to accept the matrix. (C) Release the matrix: The catheter delivers a silicone polymer matrix that remains within the RF-treated portion of the fallopian tube. The matrix provides a substrate for tissue ingrowth, leading to tubal occlusion and permanent tubal sterilization.*

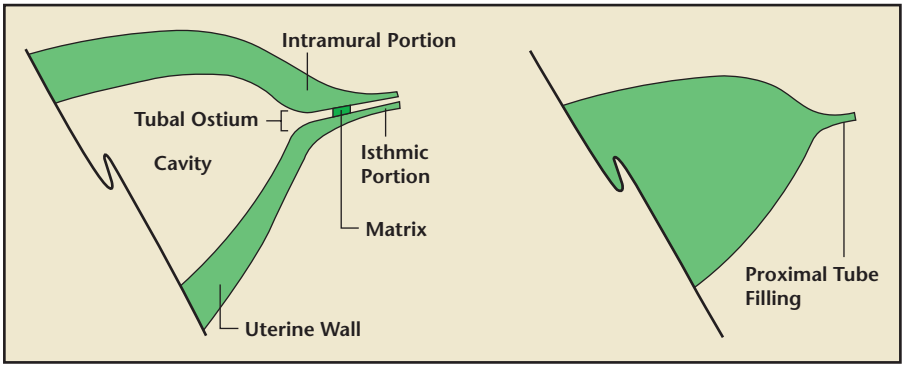


Figure 3. *Implanted matrix location and image depicting contrast media filling the proximal tube.*

catheter tip are used as part of a feedback loop that maintains a constant temperature of 64°C for 60 seconds, creating a superficial lesion within the fallopian tube. The generator has a liquid crystal display (LCD) that tells the surgeon that the delivery of radiofrequency energy is complete.[17]

After the radiofrequency energy is delivered, the surgeon deploys the matrix into the tubal lumen in the region where the lesion was formed. The endothelial damage provided by the radiofrequency energy encourages a tissue ingrowth response consisting primarily of fibroblasts infiltrating the porous structure of the silicone matrix, thereby resulting in occlusion in about 3 months.[18]

As with other hysteroscopic sterilization products, confirmation of tubal occlusion 3 months following the Adiana procedure is accomplished by a hysterosalpingogram (HSG). The confirmatory HSG for tubal occlusion after Adiana requires 6 images obtained with low-pressure instillation of contrast media: a scout film, minimal fill, partial fill, full fill, and right and left lateral oblique views. For the test to be conducted properly, the HSG operator should advance the contrast media beyond the cornua into the fallopian tube to the location of the Adiana matrix (Figure 3).[17]

Commercial Use

Adiana was first made commercially available in January 2009 for hysteroscopic sterilization procedures in Europe, and was subsequently approved by the FDA in July 2009. In 2010, the Adiana product instructions for use (IFU) were revised to allow the device to be used in women 6 weeks after a pregnancy.

Worldwide adoption of the procedure has been rapid. Physicians interested in using the Adiana device complete didactic, surgical, and practical training on both the surgical procedure and the HSG confirmation test prior to purchasing the device or controller. Through June 30, 2010, approximately 6334 units (2 devices/unit for bilateral sterilization) were shipped to physicians trained to use the Adiana device.[19]

In July 2010, a project was initiated to assess physician experience with the training programs and clinical performance of the Adiana product. All US-based surgeons who have completed the Adiana training program were sent an invitation to participate in an online survey. Information was collected to evaluate Adiana's clinical performance characteristics, including bilateral placement rate, compliance with HSG, and the observed rate of tubal occlusion. A secondary aim of the survey was to gather information on pregnancies among patients with Adiana implants. This information was used in part to calculate a commercial-use efficacy rate.

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Of the 337 clinicians registered in the database, 168 (49.9%) responded to the e-mail request and 156 (46.3%)

completed the survey. The responses represent the experience of approximately 1500 cases. Bilateral occlusion rates were high; 80% of physicians responding to the survey reported 3-month bilateral occlusion rates in excess of 85%. Unilateral and inconclusive results were found to occur very infrequently and were reported to occur less than 5% of the time (Hologic, unpublished data). These rates of occlusion are consistent with those observed in the EASE trial.[8]

Using the number of reported pregnancies and commercial units sold adjusted for utilization and the timeline imposed by the HSG procedure, a statistical model was developed to provide an estimate of efficacy in the commercial-use population. This rate was compared with the 12-month efficacy rate reported in the EASE trial.[8] This method permits an estimation of the 1-year probability of pregnancy, although many women in the commercial-use population have been relying on the Adiana system for less than 12 months. Based on industry experience, an assumption was made that, conservatively, 75% of the monthly shipped devices are used in surgery that month; this translates to approximately 4750 procedures performed during this 18-month time period. Assuming all patients had a consistent fecundity rate in the first year of being able to rely on the device for contraception, the pregnancy rate at 1 year can be estimated based on the number of reported pregnancies divided by the patient-relying years, which equates to a 1-year pregnancy rate of 0.57%.[19] The 1-year pregnancy rate in the EASE clinical trial was 1.07% for all women relying on the Adiana system for contraception.[8,20]

Safety in Commercial Use

Since the introduction of the Adiana procedure for hysteroscopic sterilization, 2 significant adverse events have been reported.[21] In the first event, 1 patient required antibiotics and salpingectomy to treat a postprocedure infection following off-label use for bilateral hydrosalpinx. In the other event, excess fluid absorption of nonionic distension media led to the empiric administration of furosemide and patient observation. There have been no reported cases of uterine perforation, expulsion, or pain reported to the Manufacturer and User Facility Device Experience (MAUDE) database.

In a recently published case report, Gimpelson and Wagner[25] noted a successful completion of hysteroscopic sterilization using the Adiana system after failed attempts to bilaterally place the Essure system. Although the first Essure coil was easily placed in the right ostium, the second coil could not be passed beyond 2.4 cm into the left ostium. The authors completed the procedure by successfully placing an Adiana matrix in the left ostium.

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Because the Adiana matrix is composed of cured silicone, it is unlikely that either an allergic response or an adverse reaction to the matrix material would occur. The Adiana implant does not contain a metal component and therefore may represent a logical choice of sterilization method for women with a known or potential nickel allergy.[22] It is estimated that between 10% and 30% of women are at risk for having a nickel allergy.[23,24]

Reported Ease of Use

The delivery catheter was designed to reduce the likelihood of uterine perforations. The soft and pliable construction of the catheter tip allows it to flex with the contours of the patient's anatomy. This tip also has a rounded end and a curvature to facilitate fallopian tube cannulation. In addition, the catheter shaft is designed to bend and buckle if resistance is encountered so as to limit the amount of force that is transmitted to the tissue.

In-Office Procedure

The Adiana device and procedure have been shown to be well tolerated by patients. The procedure can be performed in either an office setting or the operating room (OR). In fact, a significant portion of procedures in the EASE trial were performed in a physician's office. Presthus and colleagues[26] recently reviewed this data and compared patients undergoing Adiana placement in an office setting with patients who had the Adiana procedure performed in the OR. Among the 725 women treated, 220 procedures were performed in the office and 505 occurred in the OR. There were no differences between the 2 groups in bilateral placement or Adiana reliance at 3 months and 6 months. The average duration of the procedure was slightly longer in the office group, but women treated in the office had a shorter recovery time, returned to work sooner, and reported lower pain

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values compared with women who had the Adiana procedure performed in the OR.[26]

Although there are few data to assess where the procedure is conducted, it is interesting to note that approximately 50% of units are sold to private practice providers, whereas the remainder are shipped to institutions.[19] In addition to the potential benefits to patients and providers, procedures performed in the office may ultimately translate to a benefit in cost savings to the health care system.[27]

HSG

The final component of the Adiana procedure is the confirmatory HSG. The FDA requires that all patients have a confirmatory HSG at 3 months postprocedure. Unlike an HSG to evaluate infertility, the HSG procedure to confirm tubal occlusion after Adiana relies on a low-pressure instillation of contrast media. Furthermore, the intent of the HSG after the Adiana procedure is to identify proximal tubal occlusion (Figure 3) rather than examine for uterine abnormalities or distal tubal disease.

Despite these differences, the overall technique to adequately assess tubal occlusion is similar. Only an HSG catheter should be used for the confirmatory HSG. Left- and right-side markers are applied to distinguish the patient's anatomic orientation. It is recommended that dye be passed through the catheter prior to uterine cavity placement to eliminate air bubbles. The speculum should be removed during the procedure and an adequate cervical seal should be obtained. Because the matrix is placed approximately 10 mm within the intramural portion of the fallopian tube, contrast media should be infused to the point where the uterine cavity is completely filled, each cornua is opacified, and each cornua is distended (Figure 4). If the uterus is initially in the retroverted or anteverted position, it may be necessary to apply downward traction to the tenaculum or catheter balloon to obtain a posterior/anterior (P/A) view.[19]

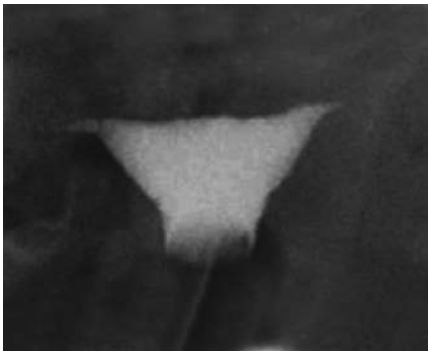

Figure 4. *Hysterosalpingogram demonstrating proximal tubal filling that confirms bilateral tubal occlusion 3 months after Adiana® System for Permanent Contraception (Hologic, Inc., Bedford, MA) procedure.*

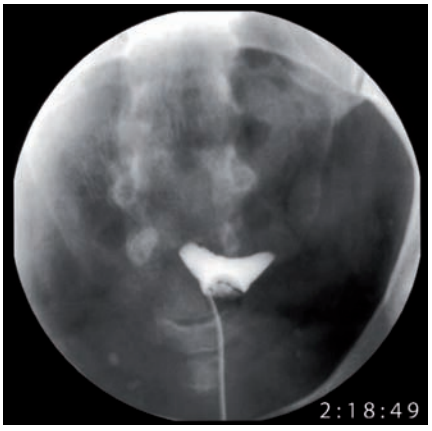

Figure 5. *Cornual obstruction seen bilaterally. Proximal tubal filling not achieved.*

Cornual obstruction is commonly encountered during HSG for infertility and may be seen during the Adiana occlusion confirmation. Possible causes include tubal spasm, mucus or debris plugging, and lodging of air bubbles in the cornual region (Figure 5). Hurd and colleagues[28] have suggested that unilateral cornual obstruction during HSG is often resolved by rotating the patient in such a way that the obstructed tube is inferior. In their series of 24 patients, this maneuver resulted in 63% resolution rate.

Tubal spasm often occurs with injection of contrast media during the HSG. With spasm, dye is unable to pass beyond the tubal ostia and can lead to an incorrect interpretation of the tubal occlusion. Other factors, including inadequate visualization of the tubes, absence of a cervical seal, and failure to follow the guidelines in the IFU, may lead to an inaccurate diagnosis of occlusion and expose the patient to a risk of an unintended pregnancy.

To emphasize the importance of the HSG procedure and interpretation, it should be noted that 3 of the 6 pregnancies in the EASE trial were secondary to improperly performed or misinterpreted HSG studies.[17,23]

Other Intrauterine Procedures

With no hormones, metal, or foreign body protruding into the uterine cavity, the Adiana system may be preferable for women who may require future gynecologic procedures. Evaluating data from the EASE trial, Herbst and colleagues[29] noted that women who have undergone the Adiana procedure were able to subsequently undergo common diagnostic and therapeutic intrauterine procedures including hysteroscopy, endometrial biopsies, dilation and curettage, endometrial ablation, intrauterine device insertion, and in vitro fertilization (IVF); no sequelae or adverse effects were reported in

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these subjects. Since 2004, 18 patients from the EASE study have had an endometrial ablation and 15 of those patients had the ablation after a confirmatory HSG. These patients have continued to rely on the Adiana system for contraception.

Currently, the IFU contains a warning that global endometrial ablation cannot be performed concomitantly with hysteroscopic sterilization by either the Essure coil or an Adiana matrix. Recently, the American College of Obstetricians and Gynecologists (ACOG) released a committee opinion explicitly stating that "health care providers should follow the manufacturers' instructions and not perform same-day endometrial ablation and hysteroscopic sterilization."[30]

Beyond the First Year: Future Trends and Challenges

The Adiana sterilization system has demonstrated strong adoption and performance characteristics in its first year of commercial use. This safe and effective method of permanent birth control can be performed in the setting of the physician's office, providing patients with convenience and reduced times in recovery and return to work. The absence of hormones, metal, or an intrauterine foreign body may position it as the preferred option for women who may require intrauterine gynecologic procedures in the future.

Clearly, the confirmatory HSG is a challenging yet critical element to the success of this process. Worldwide, the interest in identifying a method to optimize or replace the HSG may provide new ways to evaluate the success of the hysteroscopic sterilization procedure.

Future areas of investigation will include the use of Adiana implants in women with hydrosalpinges, in women undergoing IVF, and to provide additional information about the safety of intrauterine procedures following Adiana placement, as well as continued longitudinal data regarding the efficacy of the Adiana product in commercial use.

Overall, hysteroscopic sterilization represents a less invasive option for women who elect this procedure over laparoscopic sterilization. The Adiana System for Permanent Contraception is a recent and successful addition to other permanent sterilization methods. ■

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Main Points

- Compared with laparoscopic sterilization, hysteroscopic sterilization is intended to reduce the risk of injury as no instruments are inserted into the abdominal cavity.
- The Adiana system achieves tubal occlusion by tissue ingrowth into a silicone matrix placed within the lumen of the fallopian tubes bilaterally.
- As with other hysteroscopic sterilization products, confirmation of tubal occlusion 3 months following the Adiana procedure is accomplished by a hysterosalpingogram.
- Since the introduction of the Adiana procedure for hysteroscopic sterilization, only 2 significant adverse events have been reported.
- The delivery catheter was designed to reduce the likelihood of uterine perforations. The soft and pliable construction of the catheter tip allows it to flex with the contours of the patient's anatomy.
- With no hormones, metal, or foreign body protruding into the uterine cavity, the Adiana system may be preferable for women who may require future gynecologic procedures.

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