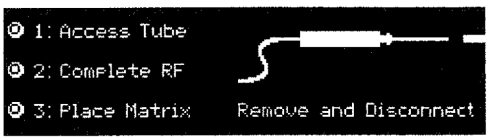
- The "Progress Tone" sounds every 5 seconds during RF energy delivery.
- If the entire 60 second duration lesion is successfully completed, the RF Generator transitions to the *Place Matrix* Mode. If the treatment is halted, the display will indicate the Total RF Treatment time up until the RF treatment was halted. The maximum total allowable RF time is 120 seconds per fallopian tube.

Place Matrix Step

- After successful RF energy delivery, the Place Matrix step is displayed. The "Place Matrix Tone" sounds and the screen displays the following image:

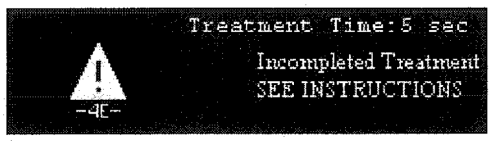
- When the Matrix is ejected without error, the "Matrix Placed Tone" is sounded. Once the Matrix is ejected, the "Remove and Disconnect the Catheter" screen is shown:



- Once the RF Generator sounds the Matrix release tone, the used Delivery Catheter may be disconnected.
- If the Delivery Catheter is disconnected before the Matrix is ejected, an Error is triggered. (See *Error and Fault Modes* below)

ERROR and FAULT Modes

- A detailed description of these two modes is contained in the RF Generator Specification and Installation Manual.
- This ERROR mode is displayed upon detection of any **recoverable** error. The system displays the corresponding error message, and upon pressing the Reset button, transitions to either the Access Tube step (if a Delivery Catheter is connected) or to the *Connect Catheter* step.
- A sample error screen is shown below. In this example, the error code is "4E" and this occurred after 5 seconds of RF energy delivery:



- The FAULT mode is displayed when any **unrecoverable** error condition occurs during any mode. The system will need to be power cycled off and on to proceed. A sample FAULT screen appears as follows:

Contact Cytyc Technical Services for repair instructions if the problems persist.

5. TROUBLESHOOTING GUIDE

While the Adiana Transcervical Sterilization System procedure is not complicated, unusual cases may present unique challenges. The Cytyc Training Program with troubleshooting guide contains a description of some of the challenges that can occur when using the Adiana Transcervical Sterilization System. Some of these challenges include:

- Visualizing the Ostia
- Placing the device up to the Black Mark band (cannulation)
- PDA Contact Challenges
- RF Treatment Challenges
- Delivery Catheter Stability
- Matrix ejection failure (no Matrix placed)

6. HOW SUPPLIED

Sterilization

The Delivery Catheter with implantable Matrix and accessory Introducer is supplied sterile through moist heat (steam) sterilization and is intended for SINGLE USE ONLY. The device will remain sterile for the duration of the labeled shelf life so long as the unit packaging is unopened and undamaged.

Packaging and Contents

The Delivery Catheter with implantable Matrix and accessory Introducer are provided in packaging that is separate from the RF Generator.

Components of the Adiana Transcervical Sterilization System

Component Name	Description
Delivery Catheter	Delivery Catheter with implantable Matrix and integral cord for attachment to the RF Generator via the Catheter Cable
Split Introducer with mandrel	Use aid for insertion into hysteroscope
ID Number Tag	Identifies product identification
Instructions For Use, Adiana Transcervical Sterilization System	Provides customer with necessary information for product use
RF Generator	An RF energy generator that guides the operator through the implantation procedure and delivers controlled RF energy through the Delivery Catheter
Footswitch	Attachment that allows for hands-free control of the RF treatment
RF Generator Cable	Cable assembly that connects the Delivery Catheter to the RF Generator

Storage and Handling

The storage life of the Delivery Catheter with Matrix is one year from the date of manufacture.

Do not use product past the recorded expiration date. Expired product should be discarded. The Expiration Date is marked on the package outer label and on the tray lid label.

Handle system components with care. Do not submerge the RF Generator, the Delivery Catheter handle or cable connections in fluid. The Adiana Transcervical Sterilization System components have all been tested for reliability, however, excessive exposure to fluid or rough handling can cause errors or damage.

MRI Safety

The Matrix has been determined to be Magnetic Resonance Imaging (MRI) Safe. It will not produce substantial image artifacts that would adversely affect an MRI examination.

Shipping and Storage Environment

Shipping and Storage environment: -30 to 50°C, relative humidity 10% to 90%, non-condensing.

Operating environment: 10 to 40 °C, relative humidity 20% to 80%, non-condensing.

Limited Warranty

Should the Adiana Transcervical Sterilization System become inoperable, contact Cytyc Inc., Customer Service Department for instructions and a Return Goods Authorization Number. Clean and repackage the device appropriately and return it for repair, servicing, and /or modification to the authorized location listed below. If the device is not under warranty, an appropriate handling and repair charge will be established at receipt and examination of the device.

7. LABELING SYMBOLS

Alternating Current	~
Attention: consult accompanying documents	!
Catheter	
Contrast, Display	
Dangerous Voltage	
Down / Decrease Volume or Contrast	
Up / Increase Volume or Contrast	
Earth Ground	
Footswitch	
Fuses	
Reset	R
Start RF Treatment / Stop RF Treatment (Non-Ionizing Radiation)	
Power ON / OFF	
Volume, Audio Speaker	

VII. B. ADIANA RF GENERATOR – SPECIFICATION AND INSTALLATION MENU

Adiana RF Generator

Specification and Installation Manual

Caution: Federal law restricts this device to sale by or on the order of a physician.

Caution: This manual is not intended to be used as a complete "Instructions For Use." Do not attempt to use the Adiana RF Generator without first reading both the *Adiana Transcervical Sterilization System Instructions for Use* and the *Adiana RF Generator Specification and Installation Manual* and understanding them both in their entirety.

Manufactured and Distributed by:

Cytyc Surgical Products
250 Campus Drive
Marlborough, MA 01752

(508) 263-2900

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1. Introduction

The Adiana RF Generator is designed to be used in conjunction with the Adiana Delivery Catheter (Delivery Catheter) for the purpose of providing permanent female contraception. The RF Generator produces radiofrequency energy which is delivered through the Delivery Catheter into the fallopian tube. During treatment the physician uses Delivery Catheter to place the Adiana Matrix within the fallopian tube. Tissue in-growth then occurs into the implanted Matrix, resulting in blockage of the fallopian tube.

To stimulate a healing response which causes tissue in-growth into the Matrix, a superficial lesion is created using no more than 3 Watts of power. To ensure a well defined lesion, the RF output is controlled to maintain a pre-set temperature as monitored by a thermocouple positioned within the Delivery Catheter.

Designed to be used exclusively with the Delivery Catheter, the RF Generator is a microprocessor-controlled, bipolar electrosurgical generator with automatic temperature control and a unique tissue contact sensor.

During use, the RF Generator prompts the operator to perform certain actions. The Generator also senses various inputs, controlling the delivery of energy as well as sensing proper Delivery Catheter position and delivery of the Matrix. During treatment, the RF Generator guides the operator through the various steps of the procedure via the on-screen display.

2. Indications for Use

The Adiana RF Generator is indicated for use only with the Adiana Delivery Catheter for women who desire permanent birth control (female sterilization) by occlusion of the fallopian tubes.

3. RF Generator Warnings and Precautions

⚠ This symbol alerts the user that further information is essential for proper use, and this manual should be referenced for clarification.

The safe and effective use of RF energy is highly dependent upon factors under control of the operator. There is no substitute for a proper training. It is important that the operating instructions supplied with this product be read, understood and followed before use.

3.1. Warnings

- The voltage selector and the power entry module must be set to the same voltage to prevent generator malfunction and potential instrument damage. The voltage selector is factory set and should not be changed by the user.
- Do not use this device in the presence of flammable anesthetics, other flammable gases, near flammable fluids such as skin prepping agents and tinctures, flammable objects, or with oxidizing agents.
- Observe appropriate fire precautions at all times.
- Do not use this device in oxygen enriched atmospheres, nitrous oxide (N_2O) atmospheres, or in the presence of other oxidizing agents.
- While using this device during a procedure, the patient should not be allowed to come into direct contact with grounded metal objects such as surgical table frame, the instrument table, etc.
- When the RF Generator is activated, the conducted and radiated electrical fields may interfere with other electrical medical equipment.
- Place any monitoring electrodes as far as possible from the surgical electrodes when RF surgical equipment and physiological monitoring equipment are used simultaneously on the same patient.
- Electrosurgery should be used with caution in the presence of internal or external pacemakers or implantable cardioverter defibrillators. Interference produced with the use of an electrosurgical device can cause devices such as a pacemaker to enter an asynchronous mode or can block the pacemaker entirely. Consult the pacemaker manufacturer or hospital Cardiology department for further information when use of the RF Generator is planned in patients with cardiac pacemakers.

- This equipment has been tested and found to comply with the limits for medical devices to the IEC 60601-1-2:2001. These limits are designed to provide reasonable protection against harmful interference in a typical medical installation. This equipment generates, uses, and can radiate radio frequency energy and, if not installed and used in accordance with the instructions, may cause harmful interference to other devices in the vicinity. However, there is no guarantee that interference will not occur in a particular installation. If this equipment does cause harmful interference to other devices, (which can be determined if the harmful effect on the other device is alleviated by turning this equipment off and on), the user is encouraged to try to correct the interference by one or more of the following measures:
-
- - Reorient or relocate the receiving device.
- - Increase the separation between the equipment.
- - Connect the equipment into an outlet on a circuit different from that to which the other device(s) are connected.
- - Consult the manufacturer or field service technician for help.

3.2. Precautions

- Do not activate the RF generator until the Delivery Catheter is properly positioned in the patient.

- The activation tone and light are important safety features. Do not obstruct the activation light. Do not disable the audible tone.

- Do not remove the cover of the RF Generator as there is a potential for electrical shock.

- Refer to authorized personnel for service should the RF Generator cease to operate

- Use only the Adiana pneumatic footswitch with RF Generator.

- The mains power cord of the RF Generator must be connected to a properly grounded receptacle. Extension cords and/or adapter plugs must not be used.

- Do not wrap the instrument cable around metal objects. Wrapping cables around metal objects may induce hazardous currents.

4. Installation and Set Up

Inspect the RF Generator for any signs of physical damage to the front panel, chassis or cover. **If any physical damage is found, DO NOT USE THE UNIT AND CONTACT CYTYC FOR SERVICING.** See Section 13 for product return information.

4.1. Preparing the RF Generator for Use

- The RF Generator may be placed on a mounting cart or on any sturdy table or platform. It is recommended that carts have conductive wheels. Refer to hospital procedures or local codes for detailed information.

- Provide at least four to six inches of space around the sides and top of the RF Generator for convection cooling. Under continuous use for extended periods of time, it is normal for the top and rear panel to be warm.

4.2. Accessories

4.2.1 Power Cord

- The RF Generator is shipped with an approved Hospital Grade mains power cord.
-
- Do not use extension cords or three-prong to two-prong adapters. The mains power cord assembly should be periodically checked for damaged insulation or connectors.
-
- Plug the RF Generator into a grounded receptacle (extension cords and/or adapter plugs must not be used).

4.2.2 Delivery Catheter Cable

- The Catheter Cable is a custom cable assembly used to connect the Delivery Catheter to the front receptacle labeled "CATHETER" on the RF Generator. When connecting the cable to the front panel, ensure the connection is secure by pressing until the connector 'clicks'.

4.2.3 Foot Pedal

- The RF Generator can be controlled by an external foot pedal. The foot pedal is pneumatic and has a guard housing. Depressing the footswitch is equivalent to pressing the RF button on the RF Generator front panel.
-
- The foot pedal connects to the back of the RF Generator.
-

5. Cleaning and Disinfection Instructions

5.1. Cleaning and Disinfecting

5.1.1 RF Generator

- The RF Generator may be disinfected using isopropyl alcohol and water solution applied with a cloth. Use a mild detergent and damp cloth to clean the RF Generator cover, front panel, and power cable. The RF Generator is not sterilizable.
-
- Do not spray or pour liquids directly on the unit.

5.1.2 Catheter Cable

- Use a mild detergent and damp cloth, followed by a disinfectant to clean the Delivery Catheter cable after use. Inspect the cable for any signs of physical damage. Ensure that the cable is dry following cleaning and before use.

5.1.3 Foot Switch

- To clean the foot switch, use a mild detergent, followed by a disinfectant to clean. The foot switch is not sterilizable.

6. RF Generator Operation

The RF Generator produces up to 3 watts of RF energy, which is delivered through the Delivery Catheter. In addition to delivering RF energy, the Delivery Catheter is also utilized to place the Matrix within the fallopian tube. Tissue in-growth, stimulated by the RF lesion, fills the spaces in the Matrix, occluding the fallopian tube and providing permanent contraception.

The RF Generator automatically senses the position of the Delivery Catheter within the fallopian tube via a Position Detector Array (PDA) built into the Delivery Catheter. The System determines if the impedance values from the Catheter indicate that there is circumferential tubal contact. If the PDA, which is proximal to the RF electrode array on the Delivery Catheter, is not in 4 points of circumferential contact, the System will determine which of four PDA electrodes are not in contact and will graphically display this on the display screen.

The RF Generator automatically controls tissue temperature via temperature sensors within the Catheter, and delivers energy for a pre-determined time. Once the energy has been properly delivered, the System monitors the Catheter to ensure that the operator has delivered the Matrix.

The RF Generator has a display screen that provides visual cues, along with auditory cues, to guide the physician through the treatment process. The operator can interact with the generator through either the front panel control buttons and/or the foot switch.

6.1. Quick Usage Overview

This section provides an abbreviated overview of a typical treatment with the System and is provided only as a general orientation to the typical clinical use of the System. A typical treatment with the System is completed as follows:

- Set up Equipment. Prepare the patient as described in the Adiana Transcervical Sterilization System Instructions for Use.
- Connect the Delivery Catheter to the RF Generator via the Catheter Cable.
- Place Delivery Catheter into hysteroscope. Advance into the uterus.
- Place the Catheter into fallopian tube until the black mark on the shaft reaches the tubal ostium.
- Monitor the PDA Display on the RF Generator display screen which will indicate when all four quadrants of the PDA are in tissue contact. When the tip of the catheter is in adequate contact with the fallopian tube, the

System will prompt the user to deliver RF Energy.

- ONCE IN PROPER CONTACT MINIMIZE MOTION OF THE CATHETER.

- Press the "RF" button on the RF Generator or depress the footswitch. The System will begin controlled RF energy delivery for 60 seconds. MINIMIZE MOTION OF THE CATHETER. Excessive movement will trigger a fault.. The display will count down the time from 60 seconds to zero, with an audible tone every 5 seconds.

- At the end of the RF energy delivery, the System will prompt the user to deliver the Matrix. DO NOT MOVE THE CATHETER PRIOR TO DELIVERING THE MATRIX. Deliver the Matrix as described in the Deliver Catheter Instructions for Use.

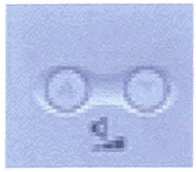
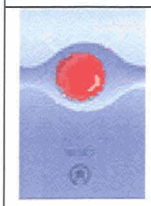
- The System will then prompt the user to remove and disconnect the Catheter. The procedure is then repeated on the contralateral fallopian tube.

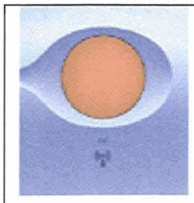
6.2. Front Panel Controls

The front panel contains the main procedural controls as well as the Display screen. A description of the control buttons and their functions are given below. Refer to Figures 1 and 2 below for location and description of each item on the front panel.

Figure 1: Radiofrequency Generator Front Panel

Figure 2: Front Panel Buttons

Graphic Example	Description
	Power Switch -- This switch controls both the On and OFF power. Shown lighted, which indicates that the Power is ON.
	Volume Down – Decreases the volume of the audio speaker. A single depression of the key decreases the value incrementally. Continuous depression decrements the volume to the minimum allowable value. Up – Increases the volume of the audio speaker. Continuous depression increments the volume to the maximum allowable value.
	RESET Stops the output of Radiofrequency energy during On Mode. Also Resets the RF Generator after an Error occurs. The switch is shown here flashing RED which indicates that the RF Generator has entered an error mode and may be reset by pressing this button.

	RF - Starts and stops the output of Radiofrequency energy. The switch is unlit and an Amber color when RF energy is NOT being delivered. The switch flashes when the PDA senses complete (4 quadrant) tissue contact. The switch remains lit constantly during RF delivery. (Shown with RF Power OFF.)

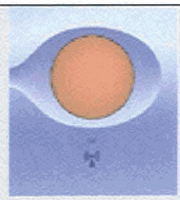
Front Panel Displays

	Display - In RF ON mode, displays the total remaining treatment time as the Generator counts down the Time from 60 seconds to zero. If a Treatment is halted, the display will indicate the Total RF Treatment Time up until the RF Treatment was halted.

Front Panel Indicators

- Other than the Display there are two visual indicators on the front of the generator: the RF On Button/Indicator and the Error/Fault/Indicator/Reset Button. The operation of these two indicators is described below:
-
- RF Treatment "On" Indicator
-
-

Figure A:

Figure B 

There are three indications that the RF output is active and that the treatment is proceeding:

- The Display will show "RF On" and displays a countdown of treatment time remaining (Figure A).
- The RF button (Figure B) remains lit over the course of the treatment.
- An audio tone sounds once every five seconds of elapsed time

Error Indicator

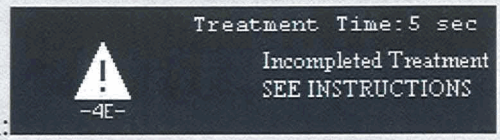
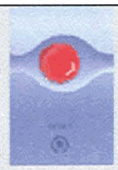
Figure A: 

Figure B: 

There are three indications that an error has occurred:

- The Attention symbol (exclamation point) is displayed along with an error message (Figure A).
- The Reset button flashes red (Figure B).
- The Error tone sounds.

Front Panel Receptacle

	Used to connect one end of the Catheter Cable. This is a 14-pin connector, designed ONLY for use with the Adiana Catheter Cable.

6.3. Rear Panel Controls

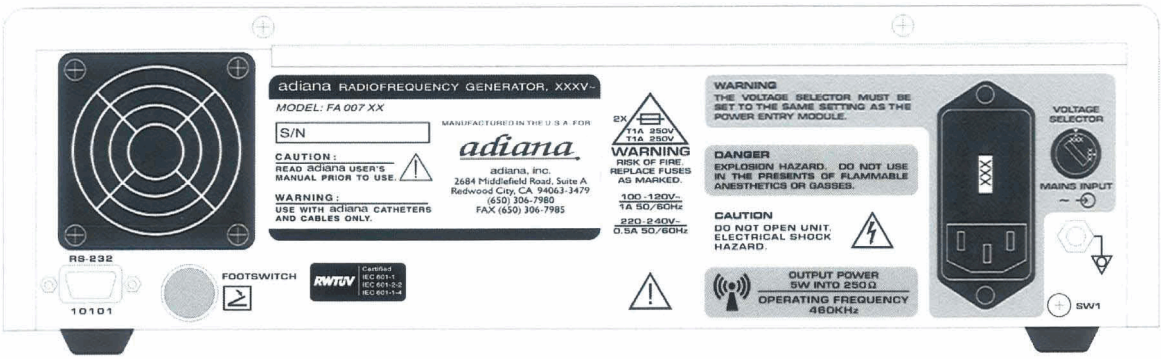
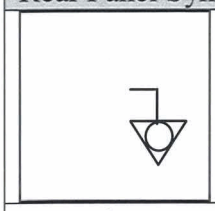
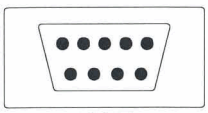
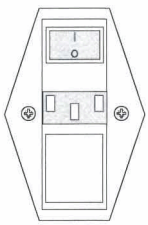


Figure 3: Ad Radiofrequency Generator rear panel,

Figure 4: Rear Panel Functions

Rear Panel Symbol	Description
	Equipotential Ground Stud -- Provides a means of securely linking the earth grounds of the Generator to other grounded equipment. Multi-Contact Corp. POAG-S 6 type.
RS232  10101	RS-232 Port – For Service Use Only.
	AC power inlet -- IEC inlet power entry module with fuses, EMI filter, and AC switch.
VOLTAGE SELECTOR	Voltage Selector – SERVICE ONLY: This switch configures the Generator to either 110V~ or 220V~, in conjunction with internal setting of the Power Entry Module. The configuration may only be changed by qualified service personnel with the appropriate tools. Unauthorized tampering with this switch setting could damage instrument and will void the warranty.

Rear Panel Symbol	Description

Rear Panel Receptacle

	Footswitch Receptacle – Used to connect Adiana Footswitch to the Adiana RF Generator.

7. Tones

There are six unique tones that the System generates to provide the user with auditory cues that supplement the visual indicators. These are described below:

Progress Tone:

- Sounds when the RF Generator is first turned on.
- Sounds whenever progress is made toward completing the procedure. It is accompanied by new information on the display.
- Sounds every five seconds during the application of the RF treatment

Non-Progress Tone:

- Sounds whenever an incorrect action occurs. This can occur when the Catheter loses contact during placement into the fallopian tube, or when an inappropriate key is pressed (for instance, pressing the Reset key when there is no need to Reset). The display indicates the next appropriate action.

Place Matrix Tone:

- Sounds at the end of the RF treatment as a reminder to place the Matrix.

Matrix Placed Tone:

- Sounds after the Matrix has been released from the Delivery Catheter.

Error Tone:

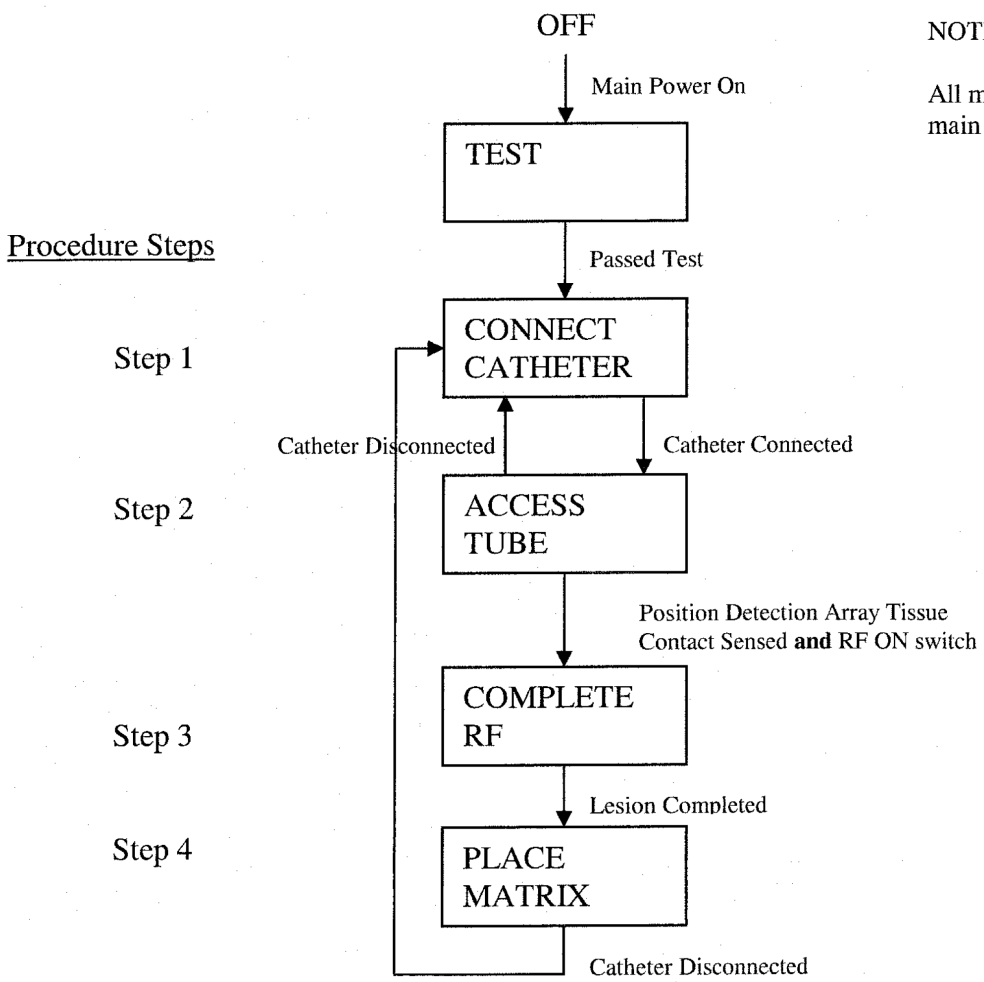
- Sounds whenever an error is encountered during the procedure. It is accompanied by an error message on the display.

Fault Tone:

- Sounds when the RF Generator detects a problem during one of its ongoing self-checks. It is accompanied by an error message on the display.

8. RF Generator Modes

The sequence of modes of operation for the RF Generator are shown in the following flowchart and presented in detail in Table 1 below.



NOTES:

All modes transition to OFF when main power is switched off.

Table 1: RF Generator Mode Sequence

Mode	Description	LED Display		Screen Display	Switches	Tone
		LED	Description			
Off Mode	When the Main Power is turned off in any mode, all power to the generator is turned off. When the Main Power switch is first switched on, the Generator transitions to the Power On Self Test mode.					
Power On Self Test Mode	When main power switch is turned on, the System performs internal self-tests. If the test fails, unit goes to FAULT mode. If test passes, System enters *Connect Catheter* mode	RF Reset	ON ON	adiana version 1.x Displays the Adiana logo and the software version string as shown Screen display is held for 2 seconds	When the System is performing internal tests, all switches are disabled, (except tone volume and display brightness) and do not respond to user.	Generator emits a "Progress Tone".
Connect Catheter Mode	This mode is entered automatically after a successful internal self-test. It will also be entered from either the *Access Tube* or *Complete RF* modes if	RF Reset	Off Off	Connect Catheter ...	All switches are inactive (do not respond to user). When pressed, they generate a "Non-Progress Tone".	The "Progress Tone" sounds upon entering the *Connect Catheter*

Mode	Description	LED Display		Screen Display	Switches	Tone
		LED	Description			
	the catheter is disconnected.					Mode.
Access Tube Mode	This mode is entered upon connecting the Delivery Catheter while in the *Connect Catheter* Mode.	RF Reset	ON if tubal contact is complete; OFF otherwise OFF	 When the Position Detector Array (PDA) senses no tubal contact, the Generator displays the above graphic. When the PDA senses partial tissue contact, the information is displayed and continuously updated. Each quadrant corresponds to each of the four contacts on the catheter (here only 2 sides are in contact). The tubal contact is complete when	RF Button is inactive *until* all 4 PDA contacts are satisfied. If the PDA senses full tubal contact, the display will show "Start RF Treatment" Pressing either the RF Button or the foot swich will cause the RF generator to move to the Complete RF Mode if the PDA has sensed sufficient 4-quadrant contact.	The "Progress Tone" sounds upon entering the *Access Tube* Mode. The "Progress Tone" sounds upon transitioning form incomplete to complete contact. Also, the "Non-Progress" tone sounds upon transitioning from complete to

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Mode	Description	LED Display		Screen Display	Switches	Tone
		LED	Description			
				the PDA senses sufficient tissue contact on all four sides of the catheter as in the above example		incomplete contact.
Complete RF Mode	This mode is entered when either the RF button is pressed or the Foot Switch is pressed, AND there is complete contact around the tip of the Adiana catheter while in the *Access Tube* mode. If the full duration lesion is completed successfully, the Generator transitions to the Place Matrix Mode. If the treatment is halted, the display indicates the total RF treatment Time up	RF Reset	Remains constantly lit over Treatment Time OFF	1: Access Tube RF On... Hold Steady 2: Complete RF 35sec 3: Place Matrix The display counts down and continuously updates the time remaining until the end of the RF application as seen in the above graphic.	Reset Switch – If pressed during RF delivery, the System terminates RF Delivery and the display shows Error Code 40. RF Switch – If pressed, the System terminates RF Delivery and the display shows Error Code 40. Foot Switch – If pressed during RF delivery, the System terminates RF Delivery and the display shows	The "Progress Tone" sounds every 5 seconds during RF Delivery.

Mode	Description	LED Display		Screen Display	Switches	Tone
		LED	Description			
	until the RF Treatment was halted.				Error Code 40.	
Place Matrix Mode	This mode is entered following the *Complete RF* Mode after normal completion of the RF delivery. The System senses the Matrix ejection, and then transitions to the *Connect Catheter* Mode when the catheter is disconnected. If the catheter is disconnected before the Matrix is ejected, an error is triggered.	RF Reset	OFF OFF	1: Access Tube 2: Complete RF 3: Place Matrix ...Hold Catheter Steady Place the Matrix screen 1: Access Tube 2: Complete RF 3: Place Matrix Remove and Disconnect Remove and Disconnect the Catheter screen Prior to Matrix ejection, the Place Matrix screen is displayed. After the Matrix is ejected the display prompts the user to Remove and Disconnect the catheter and animates the screen.	Reset Switch – Inactive; it will not respond to user. When pressed, a "Non Progress" Tone is heard. RF Switch – Inactive; it will not respond to user; when pressed, a "Non Progress" tone is heard. Foot Switch – Inactive; it will not respond to user. When pressed, a "Non Progress" tone is heard.	The "Place Matrix" Tone sounds upon entering the Place Matrix Mode. When the Matrix is ejected without error, the "Matrix Placed" tone is sounded.
ERROR Mode	This mode is entered upon detection of any **recoverable error** conditions during any mode, excluding the FAULT mode. The System displays the corresponding error	RF Reset	OFF Blinks once per second	Treatment Time: 5 sec Incompleted Treatment SEE INSTRUCTIONS -4E- This is an example of an ERROR screen. Note: There is a distinct error message associated with individual errors or faults. The corresponding	Reset Switch – When pressed, the error is cleared and transitions to either the Connect Catheter mode or the Access Tube mode (depending	The "Error Tone" sounds upon entering this mode.

Mode	Description	LED Display		Screen Display	Switches	Tone
		LED	Description			
	message, and upon Reset button press, transitions to the *Access Tube* Mode if the error occurred in the Complete RF Mode. Otherwise the System transitions to the *Connect Catheter* mode.			Error Message will be displayed along with the symbol shown above. For the purpose of this example, an error is shown which would occur if a catheter were disconnected during RF treatment. The triangle-symbol in the LED display will flash once per second.	on whether or not a catheter is connected.) RF Switch – Inactive; it will not respond to user; when pressed, a "Non Progress" tone is heard. Foot Switch – Inactive: it will not respond to user. When pressed, a "Non Progress" tone is heard.	
FAULT Mode	This mode is entered upon detection of any **unrecoverable error** condition during any mode. The System is inoperable in the mode until the AC mains power is cycled off, then on.	RF Reset	OFF ON continuously	 This is an example of a FAULT display. The corresponding error code is displayed. The triangle symbol blinks.	All switches are inactive, i.e., do not respond to user. When pressed, a "Non Progress" tone is heard. A power cycle is required to reset this fault.	The "Fault Tone" sounds upon entering this mode.

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9. Detailed Procedural Instructions

9.1. Before turning the RF Generator on

Plug the RF Generator into electrical line power.

9.2. Turn the Generator On

- RF Generator will perform an internal self test and then display the CONNECT CATHETER message.

- Insert the Catheter Cable into the socket on the right side of the front panel which is labeled "Catheter". MAKE SURE CONNECTOR IS INSERTED ALL THE WAY AND LOCKED INTO POSITION.
- Connect a sterile, single use, Delivery Catheter to the RF Generator via a Catheter Cable.
- Connect the Delivery Catheter to the Cather Cable.

  Note: The Catheter Cable has unique connectors that mate with the Delivery Catheter and the RF Generator, respectively. It can only be connected one way.

- Once the Catheter is connected, the RF Generator transitions to the ACCESS TUBE Mode.

9.3. ACCESS TUBE

After the Delivery Catheter is connected, the RF Generator will enter ACCESS TUBE mode and the following display will be shown.

- Insert the Delivery Catheter through the hysteroscope into the uterus.
- **Note:** The RF Generator uses the Position Detection Array (PDA) to determine tissue contact. Position Detection Array information is displayed and continuously updated.
- While in the Access Tube Mode, once the Delivery Catheter is positioned correctly in the fallopian tube, when complete PDA tubal contact is obtained, the RF Generator will indicate complete PDA contact and will indicate "Start RF Treatment".

9.4. Delivering RF Energy - The Complete RF mode

- Once full PDA contact is obtained, and the Delivery Catheter is properly positioned with the Black Mark at the tubal ostium, press the RF Button (or the foot switch).

- The Progress Tone sounds and the display will show Complete RF. The following screen is displayed.

- MINIMIZE MOTION OF THE CATHETER. Excessive movement will trigger a fault...

- The RF button illuminates with an Amber color.

- The RF Generator measures and monitors relevant parameters such as power, current, voltage, and impedance. The RF Generator displays Remaining Treatment time and highlights the "2: Complete RF" bar on the display menu.
- If the Matrix is ejected prior to RF treatment (See Matrix Eject Sensor section) then Error message 4E is displayed and the RF Generator waits

for the Reset button to be pressed before returning to CONNECT CATHETER Mode. Other fault codes are possible, and a complete list is included in Table 2, below.

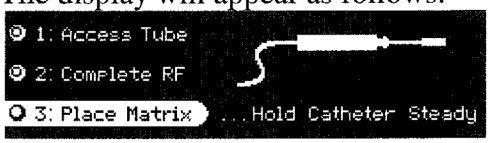
- If a RF Treatment is halted, the display will indicate the Total RF Treatment Time that elapsed prior to halting treatment.
-
- To immediately end the RF Treatment before complete treatment time has elapsed, depress either, the Reset button, the ON button or the footswitch.

- The System transitions to the *Place Matrix* Mode upon time expiration.

9.5. Place Matrix Mode –Delivery of the Matrix

- By directly visualizing the Delivery Catheter in the ostium, ensure that the Delivery Catheter position has not moved during RF delivery. HOLD THIS POSITION using continuous visual reference to the hysteroscopic image of the catheter in the fallopian tube ostium.

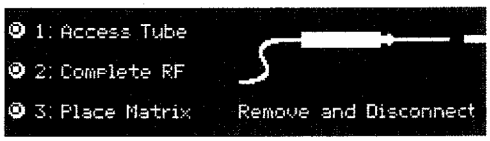
The display will appear as follows.



- After RF treatment is complete, but the Matrix is not yet ejected, the RF Generator displays the "Place Matrix … Hold Steady" and animates the image above.

- As described in the Adiana System Instructions for Use, the operator releases the matrix by depressing the Matrix release button on the Delivery Catheter. The RF Generator will sound a tone after the matrix has been released.

- After the Matrix has been ejected, the display prompts the user to remove the Delivery Catheter, as in the following.



- After the Matrix is ejected, the RF Generator displays the text "Remove and Disconnect" and animates the image of the catheter.

10. Troubleshooting

10.1. Problem: No RF Power Output

- RF Generator is not plugged in
- RF Generator is not turned on
- RF Generator is in CONNECT CATHETER mode
- Fault in Delivery Catheter, Delivery Catheter cable, or footswitch
- No Delivery Catheter connected
- RF Generator is in Fault mode
- RF Generator is still in Place Matrix mode
- Delivery Catheter was previously used

10.2. Internal RF Generator Failures

Error Events and Messages: In addition to graphics and other text that indicate Position Detection Array status and overall procedure status, Table 2 below shows text messages that are displayed for errors that occur in each MODE. Instructions are provided for each error event.

10.3. Error Event Codes and Instructions

Error Events, in the phase in which they occur, the displayed message, and physician instructions, are listed below in Table 2.

Table 2: Error Events and Instructions

Mode	Error#	Error Event	Error Message	Instructions
Off		(none)	(display off)	
Test	1A-K	Power On Self Test Errors	"System Error. Turn Unit Off. See Instructions"	Disconnect the catheter and Power unit off, and then Power it on again. If the error reoccurs, contact Cytyc or refer servicing to qualified Cytyc personnel.
Connect Catheter	2A	Catheter Connection Status error	"Bad Connection. Replace Catheter or Cable"	Disconnect and discard catheter. Press Reset button and connect a new catheter per display instructions and continue with the procedure. If the error reoccurs, disconnect the catheter and replace the cable. Press Reset button, reconnect the catheter per display instructions, and continue with procedure.
	2D	Detect Ejected Matrix	"No Matrix Present. Replace Catheter"	Disconnect and discard catheter. Press Reset button and connect a new catheter per display instructions and continue with the procedure.
Access Tube	3A	Catheter Connection Status error	"Bad Connection. Replace Catheter or Cable"	Disconnect and discard catheter. Press Reset button and connect a new catheter per display instructions and continue with the procedure. If the error reoccurs, disconnect the catheter and replace the cable. Press Reset button, reconnect the catheter per display instructions, and continue with procedure.
	3B	Main Array Low Impedance	"Bad Connection. Replace Catheter or Cable"	Disconnect and discard catheter. Press Reset button and connect a new catheter per display instructions and continue with the procedure. If the error reoccurs, disconnect the catheter and replace the cable. Press Reset button, reconnect the catheter per display instructions, and continue with procedure.

Mode	Error#	Error Event	Error Message	Instructions
	3D	Detect Ejected Matrix	"Unexpected Matrix Ejection. See Instructions"	This refers to the condition when the Matrix has been deployed during the access tube mode and RF energy has not yet been applied: A) If the Matrix is not yet placed in the fallopian tube, disconnect and discard the catheter. Press Reset button button, connect a new catheter and repeat the procedure. B) If the Matrix was placed in the fallopian tube, abandon the procedure and refer patient to an alternative treatment.
	3E	Position Detection Array Low Impedance	"Bad Connection. Replace Catheter or Cable" or " PDA Low Impedance"	Reposition the catheter. Press Reset and Continue with the procedure. If the error reoccurs, Disconnect the catheter. Press reset and Replace the catheter. Connect the catheter again per display instructions and continue with the procedure. If the error reoccurs, Disconnect the Cable. Press Reset and Replace the cable. Connect the catheter per display instructions and continue with the procedure.
	3G	PDA_TEST_ID Out of Limit Error	"System Error Turn Unit Off SEE INSTRUCTIONS"	Disconnect the catheter and Power unit off, and then Power it on again. If the error reoccurs, contact Cytyc or refer servicing to qualified Cytyc personnel.
Complete RF	4A	Catheter Connection Status error	"Treatment Time: xx sec Bad Connection. Replace Catheter or Cable"	Disconnect and discard catheter. Press Reset and connect a new catheter per display instructions and continue with the procedure. If the error reoccurs, disconnect the cable. Press Reset and reconnect the catheter again per display instructions and continue with procedure. NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube

Mode	Error#	Error Event	Error Message	Instructions
	4B	Catheter Connection Status error	"Treatment Time: xx sec Catheter Disconnected. Restart RF Treatment"	Press Reset button and reconnect the catheter. Continue with the procedure. NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube
	4C	Main Array Low Impedance	"Treatment Time: xx sec Bad Connection. Replace Catheter or Cable"	Disconnect and discard catheter. Press Reset button and connect a new catheter per display instructions and continue with the procedure. If the error reoccurs, disconnect the catheter and replace the cable. Press Reset button, reconnect the catheter per display instructions, and continue with procedure. NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube.
	4D	Main Array High Impedance	"Treatment Time: xx sec Bad Connection. Replace Catheter or Cable"	Disconnect and discard catheter. Press Reset button and connect a new catheter per display instructions and continue with the procedure. If the error reoccurs, disconnect the catheter and replace the cable. Press Reset button, reconnect the catheter per display instructions, and continue with procedure. NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube

Mode	Error#	Error Event	Error Message	Instructions
	4E	Detect Ejected Matrix	"Treatment Time: xx sec Incomplete Treatment. See Instructions"	This refers to the condition when the Matrix has been deployed during the RF cycle: A) If the Matrix was not placed in the fallopian tube, disconnect and discard the catheter. Press Reset button and connect a new catheter. Repeat the procedure PROVIDED total RF delivery is 120 seconds or less per tube. (NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube) B) If the Matrix was placed in the fallopian tube, abandon the procedure and refer patient to an alternative treatment.
	4F	Position Detection Array Insufficient Contact	"Treatment Time: xx sec Movement Detected. Restart RF Treatment"	Reposition the catheter. Press Reset and continue with the procedure. NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube
	4G	Temp1/Time1 error	"Treatment Time: xx sec Temperature Fault. Restart Treatment"	Reposition the catheter, press the Reset button and continue with the procedure NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube
	4H	Temp2/Time2 error		
	4I	Temp3/Time2 error		
	4J	Temp4 error		
	4K	Temp5 error		
	4L	Miswired TC	"Treatment Time: xx sec Catheter Fault. Replace Catheter"	Disconnect and discard catheter. Press Reset button and connect a new catheter per display instructions and continue with the procedure. NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube

Mode	Error#	Error Event	Error Message	Instructions
	4M	Low Impedance Position Detection Array	"Treatment Time: xx sec Bad Connection. Replace Catheter or Cable"	Disconnect and discard catheter. Press Reset button and connect a new catheter per display instructions and continue with the procedure. If the error reoccurs, disconnect the catheter and replace the cable. Press Reset button, reconnect the catheter per display instructions, and continue with procedure. NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube
	4O	RF Off Command	"Treatment Time: xx sec Treatment Halted by User. Restart RF Treatment"	Reposition the catheter. Press Reset and continue with the procedure NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube
Place Matrix	5A	Open TC1 and Open TC2 before Matrix Ejection	"Treatment Time: xx sec Catheter Disconnected. Restart RF Treatment Before Placing Matrix"	Press Reset button, reconnect the catheter per display instructions, and repeat the procedure. NOTE: Do not exceed a cumulative total of 120 seconds of RF on a single fallopian tube
Any State	0A-Q	Internal Reference Value Errors	"Treatment Time: xx sec System Error Turn Unit Off SEE INSTRUCTIONS"	Error 0A-Q (FAULT Any state) Disconnect the catheter and Power unit off, and then Power it on again. If the error reoccurs, contact Cytyc or refer servicing to qualified Cytyc personnel.

11. Technical specifications

11.1. RF Output

RF energy: 460KHz + 10KHz

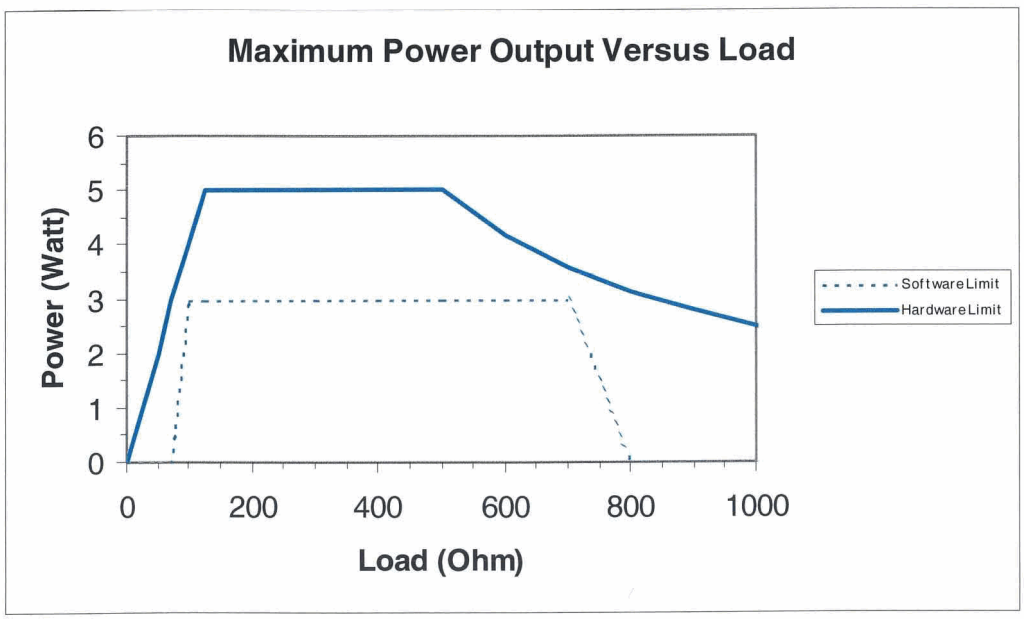
Maximum power: 5 Watts, software limited to 3W

Maximum voltage: 50 Vrms

Maximum current: 0.2 Arms

The output is isolated from earth ground and is intended for use with the bipolar Delivery Catheter. No neutral electrode pad is used with this RF Generator.

The RF Generator automatically adjusts its output level to the proper setting; there are no manual power control settings.



11.2. Mechanical Specifications

Size: 14"W x 18"D x 4.25"H (341 mm x 456 mm x 108 mm)

Weight: 20 lb. (9 kg) maximum.

11.3. Environmental Specifications

Operational temperature: 10°C to 40°C

Storage temperature: -30°C to 50°C

Operational Humidity: 20% to 80%, non-condensing

Storage Humidity: 10% to 90% non-condensing

11.4. AC Ratings

Fusing: T1A, 250V, 100 – 240V~, 50/60 Hz

Current:

- 100 – 120V~ / 50/60 Hz configuration: 1.0 Amp

- 220 – 240 V~ / 50 Hz configuration: 0.5 Amp

11.5. Footswitch Specifications

Pneumatic

11.6. Connectors Information

Patient Connections

- Isolated Patient Connection
-
- 14-pin connector

•

MAINS INPUT

- Standard IEC/UL Power Cable Connection

RF OUTPUT

- Connection through Catheter Connector Only

11.7. Guidance and Manufacturer's Declaration—Electromagnetic Emissions

The FA 007 01 RF Generators are intended for use in the electromagnetic environment specified below. The customer or the user of theRF Generator should assure that it is used in such an environment.

Emissions Test	Compliance	Electromagnetic Environment— Guidance
RF emissions CISPR11	Group 2	The Generator must emit electromagnetic energy in order to perform its intended function. Nearby electronic equipment may be affected.
RF emissions CISPR11	Class A	The equipment is suitable for use in all establishments other than domestic and those directly connected to the public low-voltage power supply network that supplies buildings used for domestic purposes.
Harmonic emissions IEC 61000-3-2	Class A	
Voltage fluctuations/ flicker emissions IEC 61000-3-3	Complies	

12. Labeling Symbols

Alternating Current	~
Attention: consult accompanying documents	
Catheter	
Contrast, Display	
Dangerous Voltage	
Down / Decrease Volume or Contrast	
Up / Increase Volume or Contrast	
Earth Ground	
Footswitch	
Fuses	
Reset	
Start RF Treatment / Stop RF Treatment (Non-Ionizing Radiation)	
Power ON / OFF	
Volume, Audio Speaker	

13. Warranty and Return Information

Contact Cytyc Corporation for Warranty Statement and Specific Return Authorization Instructions.

Cytyc Surgical Products
250 Campus Drive
Marlborough, MA 01752

800-XXX-XXXX

VII. C. PATIENT BROCHURE

The
Adiana Transcervical Sterilization System

DRAFT-
Pending Final Review of SSED and System IFU

Patient Information Brochure

IMPORTANT
This product is intended to prevent pregnancy.
It does not protect against HIV infection and other sexually transmitted diseases.

This brochure is designed to provide important information regarding permanent female contraception using a device known as the Adiana Transcervical Sterilization System. Use of this medical device requires discussion with a qualified doctor. It is important that you read this booklet carefully and discuss its contents with your doctor.

The Adiana Transcervical Sterilization System

Your choice about permanent birth control

You are reading this brochure because you are considering choices about permanent birth control (female sterilization). Sterilization is intended to prevent pregnancy for the rest of your life.

However, this information is not intended to be comprehensive as all women have individual needs and concerns. Your doctor will advise you whether the procedure is appropriate for you with regards to your circumstances and medical history.

The Adiana Procedure is intended to permanently prevent pregnancy, and is similar to other permanent birth control procedures such as tubal ligation ("having your tubes tied") or vasectomy. Since the Adiana Procedure requires no incision (unlike tubal ligation) it is gentler on your body because it can be performed without general anesthesia, does not involve cutting through the skin and recovery is quick.

What is the Adiana Procedure?

[Insert Procedure and Mechanism Description]

Is Adiana right for you?

The Adiana Procedure is only appropriate if you are sure you don't want any more children, would like to have permanent birth control and believe you will not change your mind. If there is any chance you may want to have children in the future, you should choose another form of birth control. You should avoid making this choice during times of stress, such as a divorce or after a miscarriage, and NEVER under pressure from a partner or others.

You should be aware that there are other methods of birth control, both temporary/reversible and permanent.

Other Options

The table on the following page shows pregnancy rates for various birth control methods. Consult with your doctor to find out more about these alternative methods and whether the Adiana Procedure is a suitable option for you. It is your right to decide what method suits you. If, at any time before the Adiana Procedure, you decide not to have it, you should tell your doctor and cancel the procedure. You do not have to provide any explanation or reason for your decision.

If you decide you want the Adiana Procedure, you will have a general examination and laboratory tests to confirm that you are a good candidate for the procedure. It may turn out that the Adiana Procedure is not an option for you.

Pregnancy Rates for Birth Control Methods
(For One Year of Use)

The following table provides estimates of the percent of women likely to become pregnant while using a particular contraceptive method for one year. These estimates are based on a variety of studies.

"Typical Use" rates mean that the method either was *not always used correctly* or was *not used with every act of sexual intercourse* (e.g., sometimes forgot to take birth control pill as directed and became pregnant), or was *used correctly* but *failed anyway*.

"Lowest Expected" rates mean that the method was *always used correctly* with *every act of sexual intercourse but failed anyway* (e.g., always took a birth control pill as directed but still became pregnant).

Method	Typical Use Rate of Pregnancy	Lowest Expected Rate of Pregnancy
Sterilization:		
Male Sterilization	0.15%	0.1%
Female Sterilization	0.5%	0.5%
Hormonal Methods:		
Implant *(Norplant ™ and Norplant ™ 2)*	0.05%	0.05%
Hormone Shot *(Depo-Provera™)*	0.3%	0.3%
Combined Pill *(Estrogen/Progestin)*	5%	0.1%
Minipill *(Progestin only)*	5%	0.5%
Intrauterine Devices (IUDs):		
Copper T	0.8%	0.6%
Progesterone T	2%	1.5%
Barrier Methods:		
Male Latex Condom[1]	14%	3%
Diaphragm[2]	20%	6%
Vaginal Sponge *(no previous births)*[3]	20%	9%
Vaginal Sponge *(previous births)*[3]	40%	20%
Cervical Cap *(no previous births)*[2]	20%	9%
Cervical Cap *(previous births)*[2]	40%	26%
Female Condom	21%	5%
Spermicide: *(gel, foam, suppository, film)*	26%	6%
Natural Methods:		
Withdrawal	19%	4%
Natural Family Planning *(calendar, temperature, cervical mucus)*	25%	1-9%
No Method:	85%	85%

[1] Used Without Spermacide [2] Used With Spermacide [3] Contains Spermacide

Data adapted from: Trussell J. Contraceptive efficacy. In Hatcher RA, Trussell J. Stewart F, et al Contraceptive Technology: Seventeenth Revised Edition. New York. NY: Ardent Media, 1998.

The Adiana Procedure: Key Considerations

The procedure should be considered irreversible
There are no data on the safety or effectiveness of surgery to reverse the Adiana Procedure. It is only meant to be used by women who are certain they no longer want to have children.

Like all methods of birth control, the Adiana Procedure should not be considered 100% effective
No method of birth control is 100% effective and there is a small chance you could become pregnant.

There is a waiting period after the procedure
A confirmatory test, consisting of a pelvic x-ray and dye test (hysterosalpingogram, HSG), will be performed three months after the procedure to determine if your tubes are occluded. Based on the results of the HSG exam, your doctor will advise you whether the Adiana Matrix can be relied on for permanent birth control. Because of this 3-month waiting period, you will need to talk to your doctor (before the procedure is performed) about alternative contraceptive options to cover this time.

The Adiana Procedure is newer than other procedures
Adiana is one of the newest methods of permanent birth control, so it hasn't been studied in as many women or for as long as most birth control methods.

As with all procedures, there are risks associated with the Adiana Procedure
You should be aware of these risks and discuss them in detail with your doctor before you make your decision. There is a list of risks detailed in this brochure. Many of them are rare. You should talk to your doctor about the likelihood of these risks, particularly in relation to your own situation.

What is the Adiana Procedure like for women?
A clinical trial of the effectiveness of the Adiana Procedure was conducted in women from the United States, Australia, and Mexico. This trial involved approximately 645 women. Based on data from these trials, the Adiana Procedure is:

- effective
- quick
- highly rated by women

Effective
If the Adiana Procedure is completed successfully, the one-year effectiveness rate 98.9%.

Quick
The average procedure time was about 11 minutes in the clinical trial.

Highly rated by women

- 98% of women rated their tolerance of the procedure as 'well' to 'excellent'.
- General anesthesia was not required by any women in the clinical trial.
- 94% of women resumed their normal activities within one day of the procedure. After two days, 98% of women were back at work.
- One year after the procedure, women rated the Adiana System very highly. Overall, over 500 women have used the Adiana System for more than a year and 99% have rated their overall comfort as 'good' to 'excellent'.

Risks and adverse events of the Adiana Procedure

As with all procedures, there are risks associated with the Adiana Procedure and Matrix. The Safety Summary below includes detailed information on the known or possible risks associated with the Adiana System. There may be more risks that have not yet been identified. If you decide to have the procedure, your doctor will provide more detailed information about these risks and their likelihood for your particular circumstances. Many of these risks are rare.

This section is not intended to be a substitute for a thorough discussion with you doctor about whether this treatment is right for you. Please read this section carefully, then talk to your doctor.

SAFETY SUMMARY

[This section to be completed following discussion and review of the Adiana System SSED with FDA Staff]

Glossary

Anesthesia - Partial or complete loss of sensation with or without loss of consciousness.

Cervix - The neck of the uterus.

Contraceptive - Any process, device or method that prevents conception (pregnancy).

Ectopic Pregnancy - Implantation of the fertilized egg outside of the uterus.

Effectiveness - Producing, or able to produce a desired effect.

Expulsion - To force something out.

Fallopian Tubes - The tubes that carry the eggs from the ovary to the uterus.

Hysterosalpingogram (HSG) - An x-ray of the uterus and ovaries after filling the organs with dye.

***In vitro* Fertilization** - Fertilizing an egg outside of the living body (in a test tube).

Occlusion - To close up or block off.

Perforation - Making a hole through something.

Permanent - Not able to change back and forth.

Reversible - Able to change back and forth.

Tubal Ligation - Permanent female sterilization by means of cutting and tying the fallopian tubes.

Uterus - An organ of the female reproductive system for containing and nourishing the embryo and fetus (baby) from the time the fertilized egg is implanted to the time of birth of the fetus.

Vasectomy - Permanent male sterilization by means of removal of all or a segment of the vas deferens (the tube that transports the sperm).

Cytyc Surgical Products
250 Campus Drive
Marlborough, MA 01752

(508) 263-2900

VII. D. ADIANA SYSTEM HSG PROTOCOL

Adiana HSG PROTOCOL

Overview

The Adiana Procedure requires hysterosalpingography (HSG) to be performed at the end of the 3 month Waiting Period in order to assess tubal occlusion. ONLY after bilateral tubal occlusion is confirmed on HSG, should the patient be instructed to discontinue alternative birth control and rely exclusively on the implanted Adiana matrices. The determination of categorical fallopian tube occlusion usually requires a minimum of six x-ray films. The HSG procedure can be done quickly and is usually well tolerated by the patient. It is important to become familiar with the contents of this manual before performing HSGs for tubal occlusion confirmation.

Equipment

Fluoroscopy

Required equipment includes a standard image intensifier and x-ray equipment, including spot film/flat plate capabilities. While most modern fluoroscopy equipment provides real time video display of live images, *film* images will provide higher resolution images which will help ensure that fine resolution structures or contrast will be identified. DO NOT rely on prints from fluoroscopy video frames unless they provide equal resolution to film images.

Instruments

A serrated cannula or balloon tipped catheter is needed for the procedure to ensure adequate cervical seal and prevent contrast medium leakage past the cervix.

Pressure Valve Syringe

Contrast media is typically applied at pressures of approximately 150-200mm Hg. During the Adiana EASE clinical trial, many investigators found a pressure mediating syringe (Bonchek Vein Distention System, 200mmHg) to be useful for limiting distension pressure.

Contrast Agents

HSGs can be performed with a variety of contrast materials. Water soluble agents are preferable since oil-based agents are dense, have been known to have adverse effects, and can obscure visualization.

Technique

Normal patient preparation and HSG techniques, as customary for your institution, should be employed. The following is presented as additional guidance.

It is extremely important to create a seal at the cervix to avoid leakage of contrast material and to maintain adequate pressure throughout the procedure.

Sterile Field
The cervical canal or endometrial cavity should be accessed using aseptic technique.

Patient Placement
The patient should be positioned supine at the end of the fluoroscopic table in a modified lithotomy position.

View and Clean Cervix
A sterile double bladed metal speculum is inserted into the vagina to provide a clear view of the cervix. The cervix is cleaned with a disinfectant and the excess is wiped with a dry swab or sponge to prevent its passage into the uterine cavity. It is important to remove the metal speculum during x-ray exposure to prevent the image of the speculum from overlying potential contrast media spill or cervical leakage.

Sealing Cervix and Injecting Contrast Medium
Care should be taken to minimize cervical dilation so that a good cervical seal is easy to achieve and maintain throughout the HSG.

Optimize Fluoroscopic View
Six radiographs are recommended in order to unequivocally demonstrate tubal occlusion. For this procedure, the entire uterine cavity is gradually filled with enough contrast media to challenge both cornu to achieve full extension with clear visibility. The uterine cavity silhouette should be apparently seen and no critical structures should overlay confounding objects.

Images

For the first four pictures the fluoroscopy beam should approximate anterior/posterior (A/P) projection and should focus on visualization of the uterus. If needed, reposition the image camera and inject additional dye only if necessary. The last two images should focus on visualization of the right and left fallopian tubes. A suggested sequence is described below.

(1) Scout radiograph
The first picture should be taken prior to dye injection to ensure a normal uterine cavity without adhesions and/or other pathologies.

[Insert Image 1- Scout Radiograph]

(2) Partial Fill
A second picture should be taken as the dye is injected to confirm proper position of the uterus and adequate anatomical visualization.

[Insert Image 2 – Partial fill of uterine cavity with radiopague dye]

(3) Cervical seal/ Complete Fill
A third picture should be taken as additional contrast media is injected to confirm a good cervical seal and indicate complete filling of the uterine cavity.

[Insert Image 3- Fully distended uterine filling]

(4) Cornual visualization
A fourth picture is suggested to demonstrate maximal distension of the cornual area and adequate filling of the uterine cavity. If necessary for full cornual visualization, a tenaculum can be used to apply tension to the cervix. However, too much tension on the cervix can trigger a vagal reaction.

[Insert Image 4- Fully filled cornua]

(5) Right Lateral Oblique – To better capture the right fallopian tube and create separation from underlying structures, ask patient to rotate slightly, placing right the knee on the left side of her body for a right lateral oblique radiograph.

[Insert Image 5 - right lateral oblique radiograph]

(6) Left Lateral Oblique
Repeat the procedure on the left side.

[Insert Image 6- Left lateral oblique radiograph]

Confirm HSG Quality

Develop and check the quality of the films. It is essential to confirm that films are of adequate quality for unequivocal confirmation of tubal occlusion.

NOTE: Film resolution exceeds the resolution present on most video displays. Always review developed films prior to making a determination of occlusion.

Evaluating HSGs

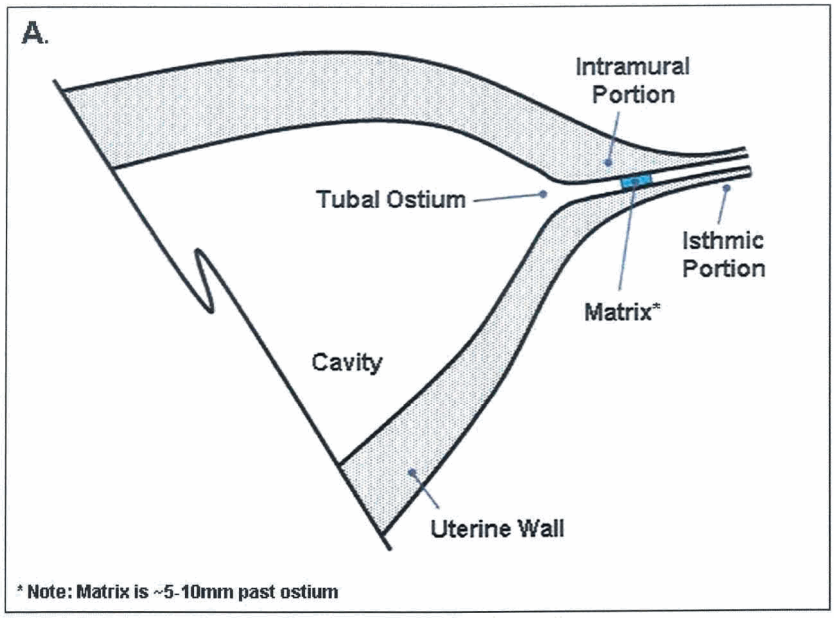
When evaluating the HSG, it is important to first confirm that the appropriate radiographs described above are provided, a good A/P image of the uterine silhouette is obtained, and the uterus is maximally distended in at least one view. The HSG will need to be immediately repeated if:

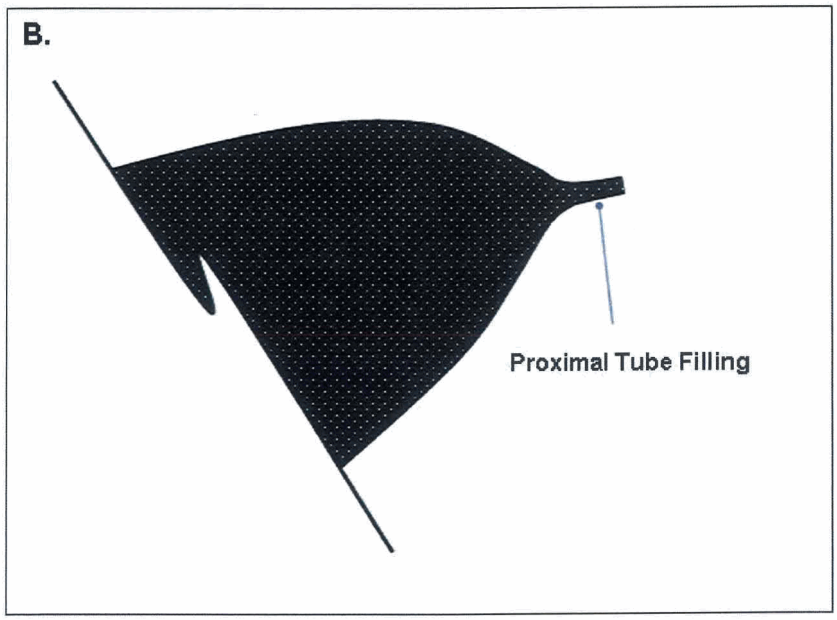
1. The appropriate sequence of radiographs has been captured but one or both uterine cornua are not maximally distended;
2. The projection of the silhouette is fundal rather than A/P;
3. The appropriate sequence of radiographs was not taken, and/or the uterine cornua are not distended or are otherwise obscured making evaluation of the image impossible or equivocal.

Interpreting Images

Adiana Matrix Location

The Adiana Matrix is delivered into the intramural portion of the fallopian tube. The following drawing depicts the Matrix location (A), as well as the resulting HSG image (B):



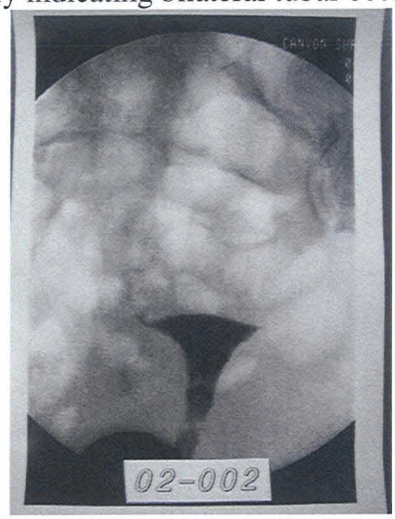


The Matrix is typically located 10mm into the fallopian tube, and proximal tubal filling may occur. Drawing B shows a typical HSG image.

Confirmed Tubal Occlusion

The observation of occlusion should be based upon the correct interpretation of satisfactory HSGs. It is important to verify proper visualization of the both cornua and maximum distension of the uterus. Correct placement (tubal occlusion) is indicated by a total blockage of contrast medium at the Matrix. Contrast medium should not be seen in the fallopian tubes beyond the Matrix. See Figure below.

HSG clearly indicating bilateral tubal occlusion



[Insert Image 6 – Bilateral Occlusion]

When there is unequivocal bilateral tubal occlusion, the patient can be advised to discontinue reliance on the alternative birth control, and begin relying on the Adiana System for permanent contraception.

Incomplete Cornual Filling

Incomplete corneal filling or poor image capture can prevent adequate visualization of the entire uterine cavity. This can be the result of too little dye or not allowing adequate time for dye to fill the cavity. Uterine spasm may be the result of too much tenaculum tension on the cervix or over-pressurization of the uterine cavity. Allow time for the spasm to resolve.

Image 7 -Incomplete Uterine Filling

Image 8 – Uterine Spasm

Avoid Over-pressurization
Aggressive pressures may open occluded tubes

[Image 9 – Opened Tube]

Tubes Proximally Filled
When tubes appear to be filled proximally to an excessive length (e.g. over 10-15mm) and a deeper placement of the Matrix is suspected, transvaginal ultrasound (TVUS) can be used to clarify findings. If ultrasound confirms that the Matrix is deeply placed in relation to the cornua, and the HSG otherwise shows occlusion, the tube may be appropriately judged to be occluded. If the TVUS does not correlate well with the HSG, a repeat HSG should be considered or the patient should choose another method for permanent contraception.

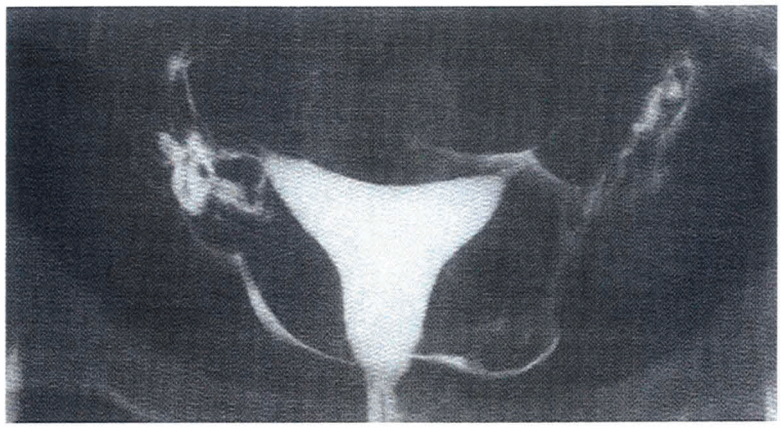
Contrast Media Distal to Matrix location
When media is seen beyond the Matrix, it is important to differentiate non-occluded tubes from peritubal extravasation. In this circumstance, it is important to note:

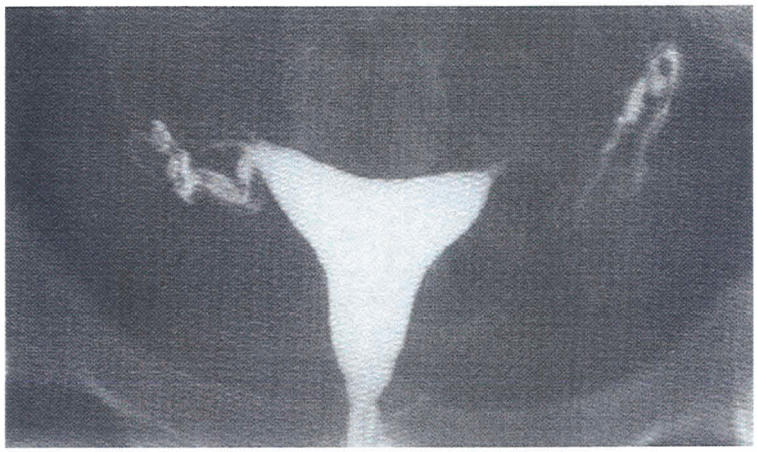
- degree of opacification in distal tube – will be indicative of whether tube is patent or simply represents overlying tissue shadow
- speed to achieve opacification – if freely opacifies, then tube assumed to be patent rather than contrast forced out of tube
- peritoneal spill – will signify tubal patency
- time to appearance of dye distal to matrix – if dye appears distal to matrix quickly after uterine cavity filling, this is indicative of tubal patency

[Image 10- Intravasation in area around matrix]

Normal Unblocked Tubes

In the images below, note the unique character of the dye: finely defined contrast within the isthmic portion, broad filling within the febrial portion, and diffuse spread within the organs in the peritoneal cavity.





Patient Management

When there is unequivocal bilateral tubal occlusion, the patient can be advised to discontinue reliance on the alternative birth control, and begin relying on the Adiana System for permanent contraception.

Patients with patent or inconclusive HSGs should be advised to continue relying on alternate contraception for an additional three months. They should be advised NOT to rely on the Adiana System for contraception at this time.

The HSG protocol should be repeated in three months. If bilateral occlusion has not been achieved at that time, the patient should be counseled to seek an alternate means of contraception.

Repeat Tests

If results are equivocal or patent after three months of waiting, advise the patient to continue using alternative contraception. Repeat the HSG in three months. (If the HSG was non-diagnostic due to technical issues, an immediate repeat may be considered.) If the fallopian tubes are not occluded at six months post implantation, the patient should seek an alternate means of contraception.

Adiana HSG PROTOCOL

Overview

The Adiana Procedure requires hysterosalpingography (HSG) to be performed at the end of the 3 month Waiting Period in order to assess tubal occlusion. ONLY after bilateral tubal occlusion is confirmed on HSG, should the patient be instructed to discontinue alternative birth control and rely exclusively on the implanted Adiana matrices. The determination of categorical fallopian tube occlusion usually requires a minimum of six x-ray films. The HSG procedure can be done quickly and is usually well tolerated by the patient. It is important to become familiar with the contents of this manual before performing HSGs for tubal occlusion confirmation.

Equipment

Fluoroscopy

Required equipment includes a standard image intensifier and x-ray equipment, including spot film/flat plate capabilities. While most modern fluoroscopy equipment provides real time video display of live images, *film* images will provide higher resolution images which will help ensure that fine resolution structures or contrast will be identified. DO NOT rely on prints from fluoroscopy video frames unless they provide equal resolution to film images.

Instruments

A serrated cannula or balloon tipped catheter is needed for the procedure to ensure adequate cervical seal and prevent contrast medium leakage past the cervix.

Pressure Valve Syringe

Contrast media is typically applied at pressures of approximately 150-200mm Hg. During the Adiana EASE clinical trial, many investigators found a pressure mediating syringe (Bonchek Vein Distention System, 200mmHg) to be useful for limiting distension pressure.

Contrast Agents

HSGs can be performed with a variety of contrast materials. Water soluble agents are preferable since oil-based agents are dense, have been known to have adverse effects, and can obscure visualization.

Technique

Normal patient preparation and HSG techniques, as customary for your institution, should be employed. The following is presented as additional guidance.

It is extremely important to create a seal at the cervix to avoid leakage of contrast material and to maintain adequate pressure throughout the procedure.

Sterile Field
The cervical canal or endometrial cavity should be accessed using aseptic technique.

Patient Placement
The patient should be positioned supine at the end of the fluoroscopic table in a modified lithotomy position.

View and Clean Cervix
A sterile double bladed metal speculum is inserted into the vagina to provide a clear view of the cervix. The cervix is cleaned with a disinfectant and the excess is wiped with a dry swab or sponge to prevent its passage into the uterine cavity. It is important to remove the metal speculum during x-ray exposure to prevent the image of the speculum from overlying potential contrast media spill or cervical leakage.

Sealing Cervix and Injecting Contrast Medium
Care should be taken to minimize cervical dilation so that a good cervical seal is easy to achieve and maintain throughout the HSG.

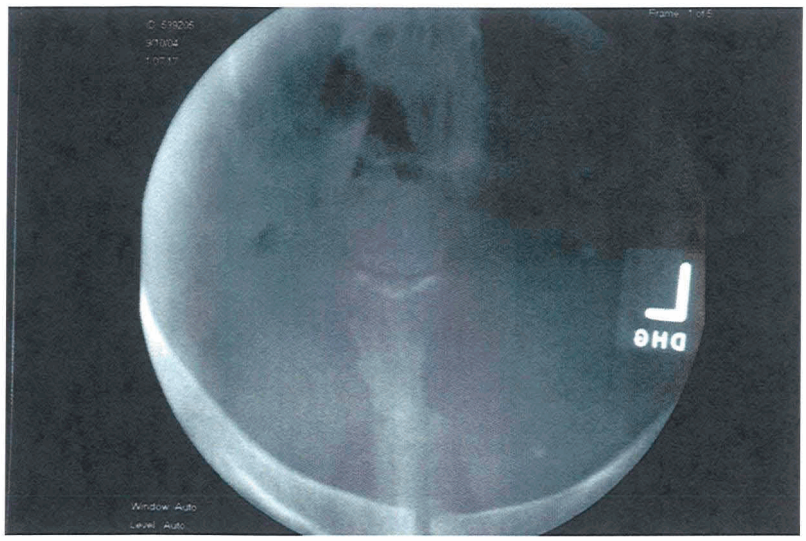
Optimize Fluoroscopic View
Six radiographs are recommended in order to unequivocally demonstrate tubal occlusion. For this procedure, the entire uterine cavity is gradually filled with enough contrast media to challenge both cornu to achieve full extension with clear visibility. The uterine cavity silhouette should be apparently seen and no critical structures should overlay confounding objects.

Images

For the first four pictures the fluoroscopy beam should approximate anterior/posterior (A/P) projection and should focus on visualization of the uterus. If needed, reposition the image camera and inject additional dye only if necessary. The last two images should focus on visualization of the right and left fallopian tubes. A suggested sequence is described below.

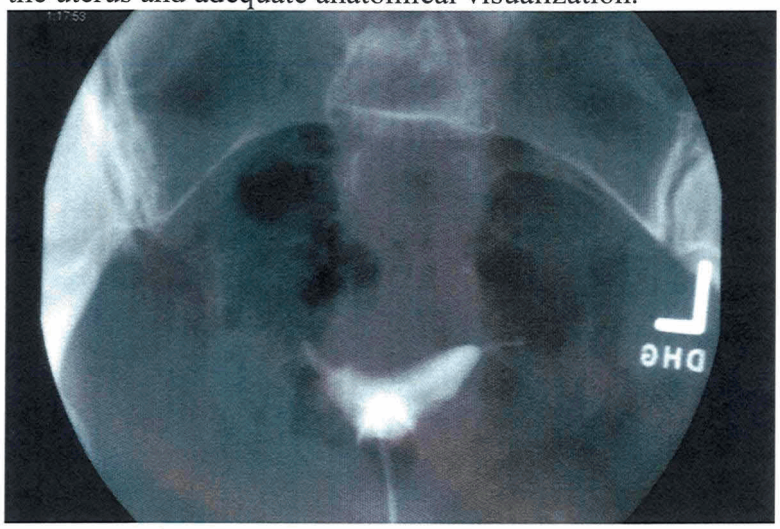
(1) Scout radiograph

The first picture should be taken prior to dye injection to ensure a normal uterine cavity without adhesions and/or other pathologies.



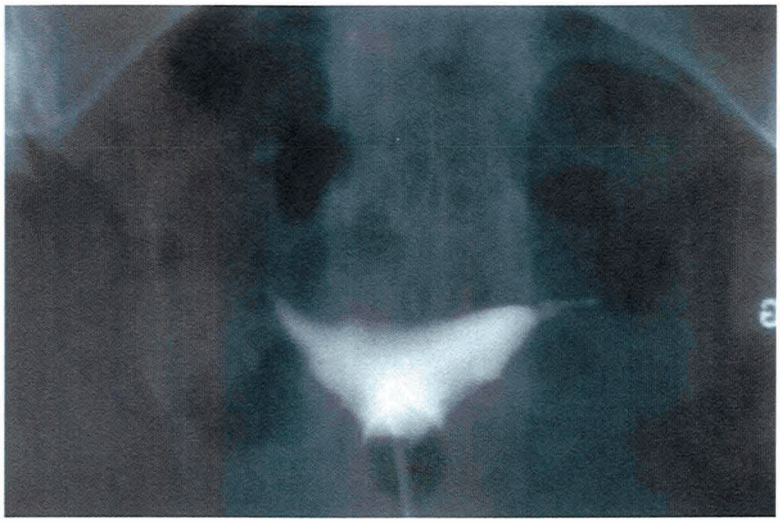
(2) Partial Fill

A second picture should be taken as the dye is injected to confirm proper position of the uterus and adequate anatomical visualization.



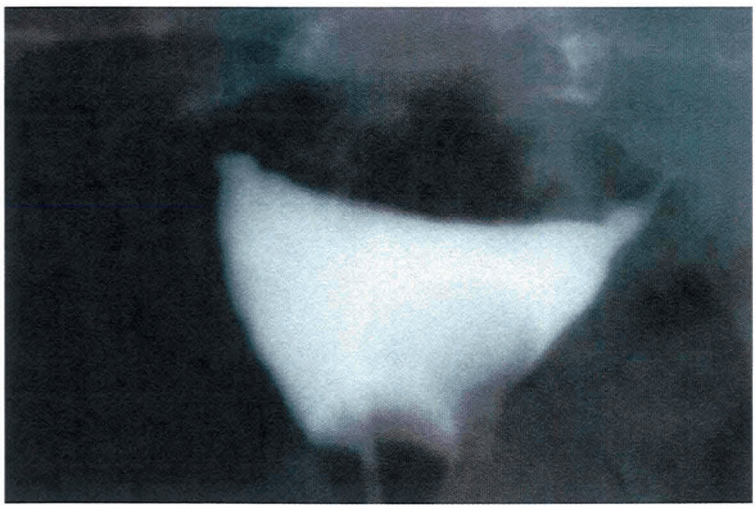
(3) Cervical seal/ Complete Fill

A third picture should be taken as additional contrast media is injected to confirm a good cervical seal and indicate complete filling of the uterine cavity.

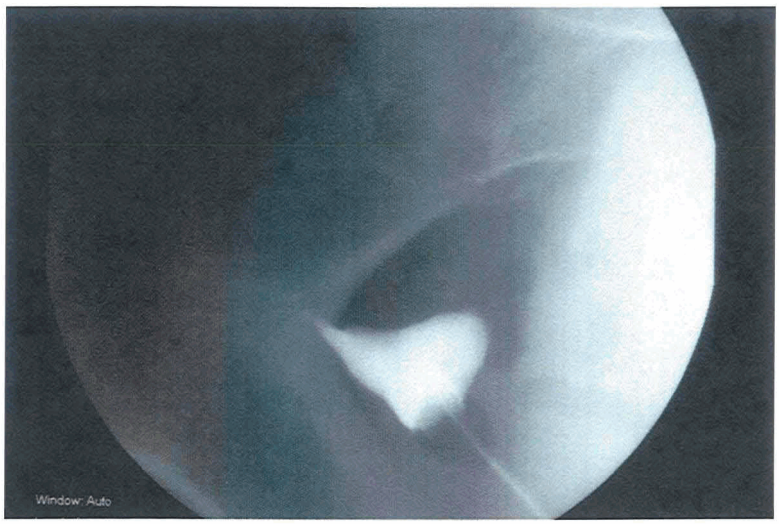


(4) Cornual visualization

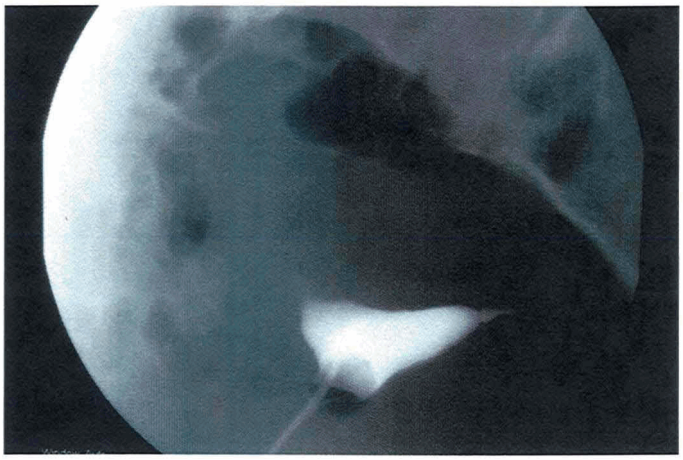
A fourth picture is suggested to demonstrate maximal distension of the cornual area and adequate filling of the uterine cavity. If necessary for full cornual visualization, a tenaculum can be used to apply tension to the cervix. However, too much tension on the cervix can trigger a vagal reaction.



(5) Right Lateral Oblique – To better capture the right fallopian tube and create separation from underlying structures, ask patient to rotate slightly, placing right the knee on the left side of her body for a right lateral oblique radiograph.



(6) Left Lateral Oblique
Repeat the procedure on the left side.



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Develop and check the quality of the films. It is essential to confirm that films are of adequate quality for unequivocal confirmation of tubal occlusion.

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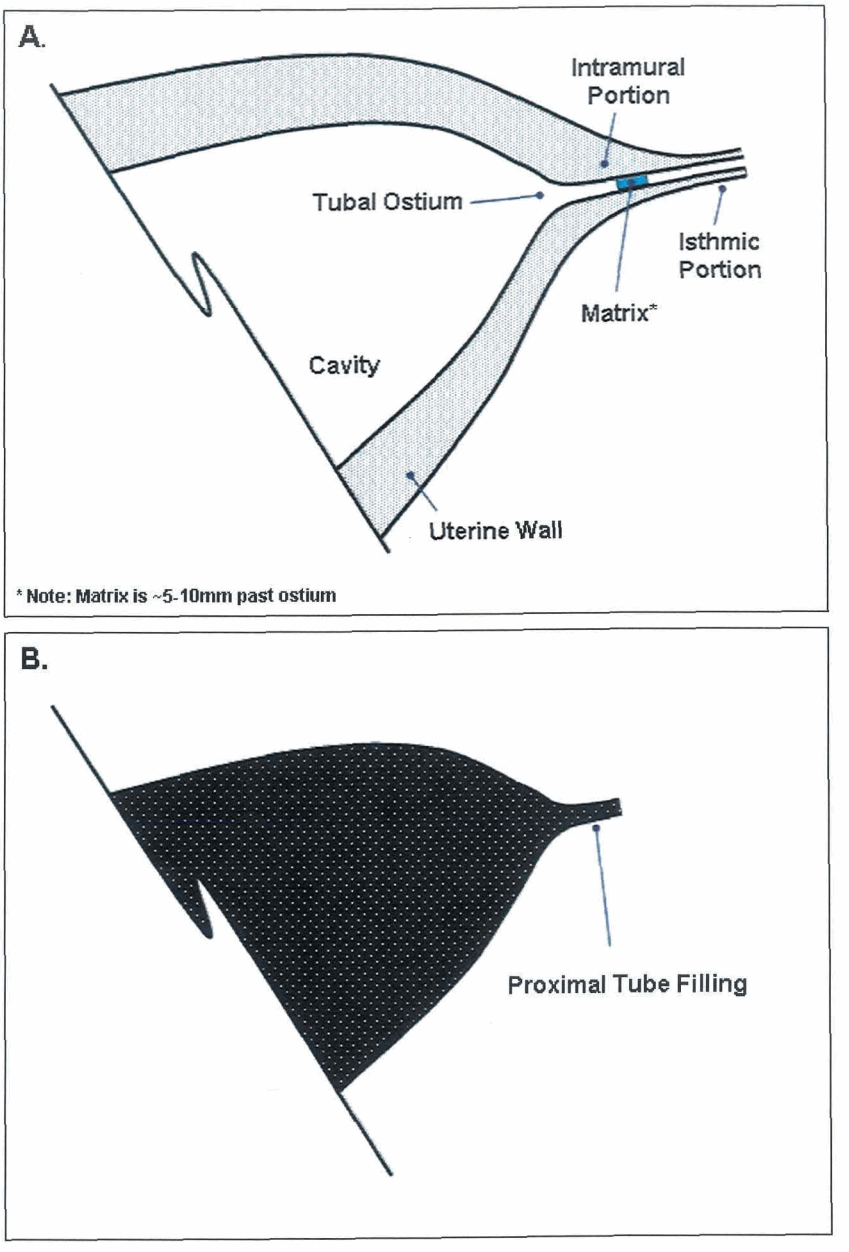
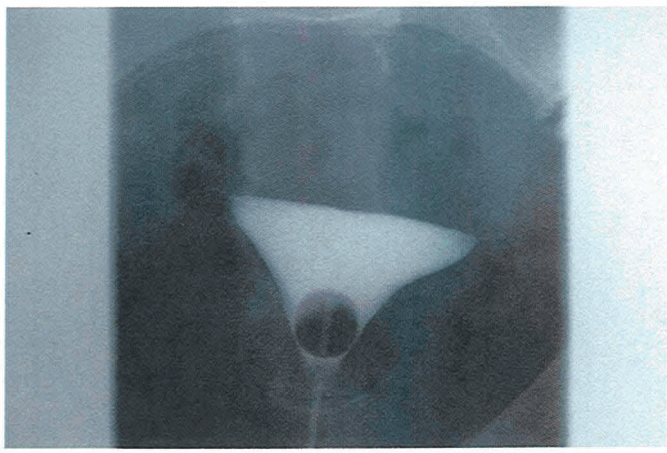


The Matrix is typically located 10mm into the fallopian tube, and proximal tubal filling may occur. Drawing B shows a typical HSG image.

Confirmed Tubal Occlusion

The observation of occlusion should be based upon the correct interpretation of satisfactory HSGs. It is important to verify proper visualization of the both cornua and maximum distension of the uterus. Correct placement (tubal occlusion) is indicated by a total blockage of contrast medium at the Matrix. Contrast medium should not be seen in the fallopian tubes beyond the Matrix. See Figure below.

HSG clearly indicating bilateral tubal occlusion



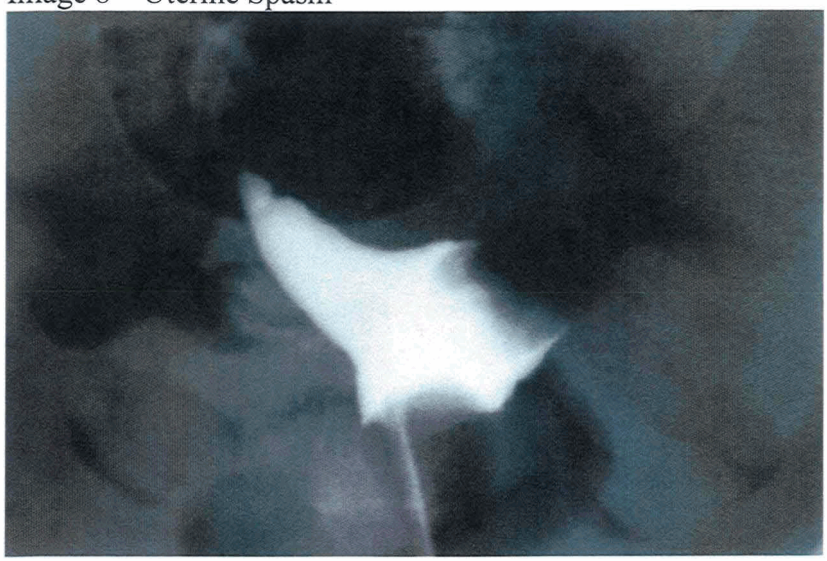
When there is unequivocal bilateral tubal occlusion, the patient can be advised to discontinue reliance on the alternative birth control, and begin relying on the Adiana System for permanent contraception.

Incomplete Cornual Filling

Incomplete corneal filling or poor image capture can prevent adequate visualization of the entire uterine cavity. This can be the result of too little dye or not allowing adequate time for dye to fill the cavity. Uterine spasm may be the result of too much tenaculum tension on the cervix or over-pressurization of the uterine cavity. Allow time for the spasm to resolve.

Image 7 -Incomplete Uterine Filling

Image 8 – Uterine Spasm



Avoid Over-pressurization

Aggressive pressures may open occluded tubes [Image 9 – Opened Tube]

Tubes Proximally Filled

When tubes appear to be filled proximally to an excessive length (e.g. over 10-15mm) and a deeper placement of the Matrix is suspected, transvaginal ultrasound (TVUS) can be used to clarify findings. If ultrasound confirms that the Matrix is deeply placed in relation to the cornua, and the HSG otherwise shows occlusion, the tube may be appropriately judged to be occluded. If the TVUS does not correlate well with the HSG, a repeat HSG should be considered or the patient should choose another method for permanent contraception.

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When media is seen beyond the Matrix, it is important to differentiate non-occluded tubes from peritubal extravasation. In this circumstance, it is important to note:

- degree of opacification in distal tube – will be indicative of whether tube is patent or simply represents overlying tissue shadow
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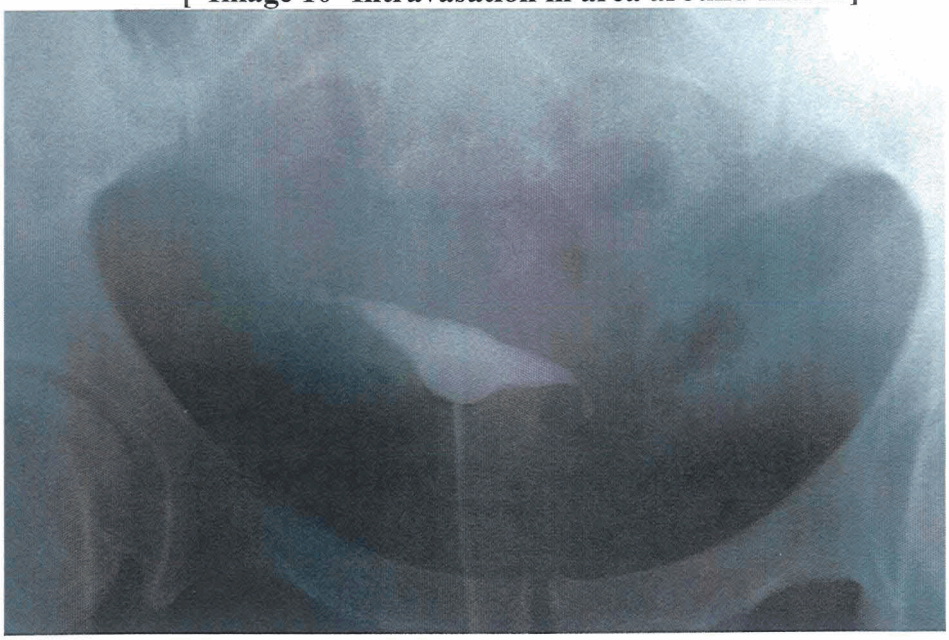
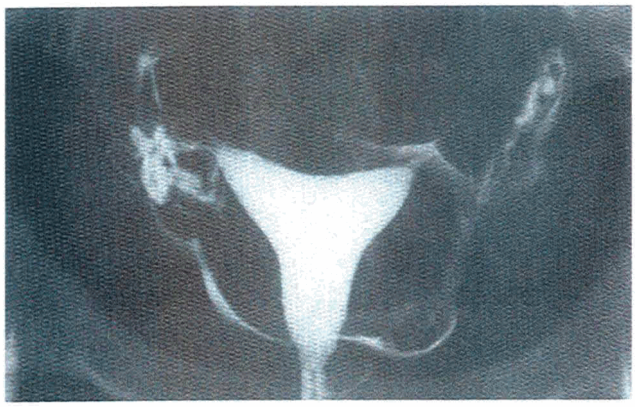
- peritoneal spill – will signify tubal patency
- time to appearance of dye distal to matrix – if dye appears distal to matrix quickly after uterine cavity filling, this is indicative of tubal patency

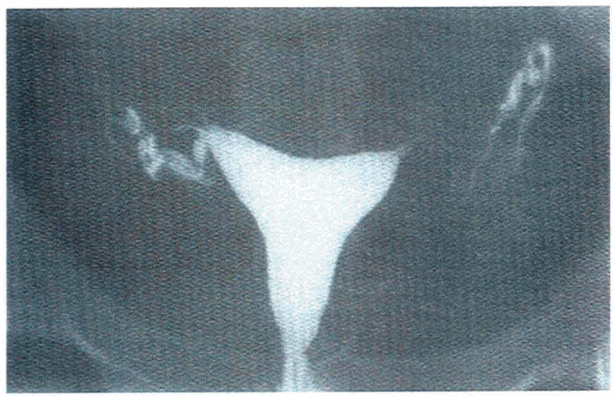
[Image 10- Intravasation in area around matrix]



Normal Unblocked Tubes

In the images below, note the unique character of the dye: finely defined contrast within the isthmic portion, broad filling within the febrial portion, and diffuse spread within the organs in the peritoneal cavity.





Patient Management

When there is unequivocal bilateral tubal occlusion, the patient can be advised to discontinue reliance on the alternative birth control, and begin relying on the Adiana System for permanent contraception.

Patients with patent or inconclusive HSGs should be advised to continue relying on alternate contraception for an additional three months. They should be advised NOT to rely on the Adiana System for contraception at this time.

The HSG protocol should be repeated in three months. If bilateral occlusion has not been achieved at that time, the patient should be counseled to seek an alternate means of contraception.

Repeat Tests

If results are equivocal or patent after three months of waiting, advise the patient to continue using alternative contraception. Repeat the HSG in three months. (If the HSG was non-diagnostic due to technical issues, an immediate repeat may be considered.) If the fallopian tubes are not occluded at six months post implantation, the patient should seek an alternate means of contraception.

VII. E. PRODUCT LABELS

5. Labeling

A variety of labeling components will accompany the Adiana Transcervical Sterilization System. There are two principal components of the system, the Adiana Delivery Catheter and the Adiana RF Generator. Labeling has been organized into the following categories:

Applied Labeling (detailed in Section 5.1)

- Adiana Delivery Catheter Applied Labeling
  Pigtail Serial Number Tag
  Pouch and Box Label
  Catheter Cable Label

- Adiana RF Generator Applied Labeling
  Front and rear panel labels
  Software display screens

System Labeling (to accompany product) (detailed in Section 5.2)

- Summary of Safety and Effectiveness
- System Instructions for Use
- RF Generator Specification and Installation Manual
- Patient Information Brochure (to be fully completed following finalization of SS&E)

A table containing brief description, part number, and location within this PMA module of the above labeling is provided in Table 5.1 below. Following this table a discussion of each labeling component, and the content, is provided. Larger labels/documents are provided within the appendices.

[redacted]

[redacted]

5.1 Applied Labeling

5.1.1 Delivery Catheter Applied Labeling

- Pigtail Serial Number Tag

The Cytyc Pigtail Serial Number Tag [redacted] provided in Appendix 10.

- Pouch and Box Label

The Delivery Catheter Product Label [redacted] The label specification with label image and manufacturing procedures are provided in Appendix 10.

- Delivery Catheter Cable Label

The Delivery Catheter Cable Label is supplied [redacted] A sample of the label is provided in Appendix 10.

5.1.2 RF Generator Applied Labeling

Labeling for the RF Generator is [redacted] Some of the labeling is [redacted] to the front and rear panels. Other labeling is [redacted] Samples of the front and rear panels, sample [redacted] images and specifications for each image are included in Appendix 11.

- Front Panel

The front panel of the RF Generator contains the LCD display and [redacted] labels.

Figure 5.1: RF Generator front panel, Part Number FA 007 01

- Rear Panel

The rear panel of the RF Generator is illustrated below in Figure 5.2. The rear panel carries relevant warnings and electrical safety information as well as functional elements that are shown in Figure 5.2 and listed in Table 5.2 below:

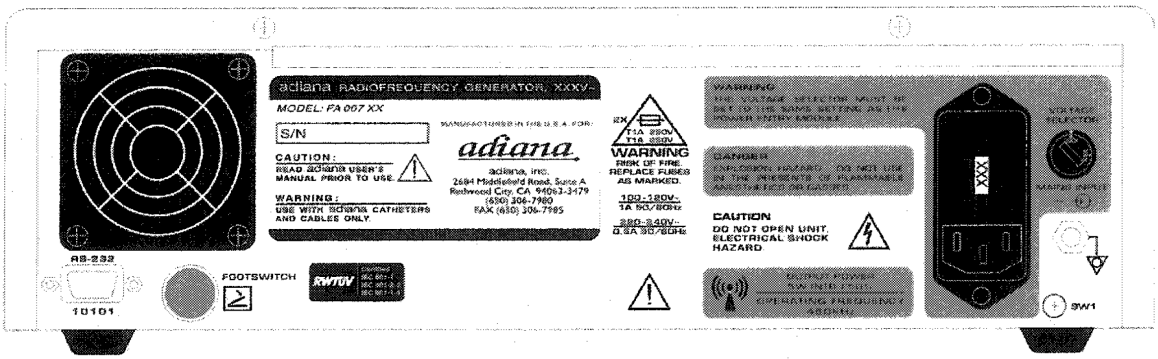
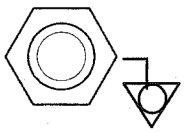
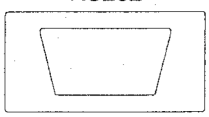
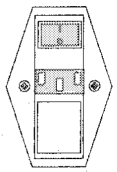
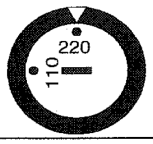
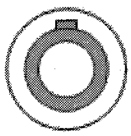


Figure 5.2: RF Generator Rear Panel FA 007 01 (110VAC)

Table 5.2: Rear Panel Functional Elements

Rear Panel	Description
	**Equipotential Ground Stud** -- Provides a means of securely linking the earth grounds of the Generator to other grounded equipment.
RS232  10101	**RS-232 Port** – For Service Use Only.
	**AC power inlet** -- IEC inlet power entry module with fuses, EMI filter, and AC switch.
VOLTAGE SELECTOR 	**Voltage Selector** – SERVICE ONLY: This switch configures the Generator to either 110V~ or 220V~, in conjunction with internal setting of the Power Entry Module. The configuration may only be changed by qualified service personnel with the appropriate tools.
	**Footswitch Receptacle –** Used to connect Adiana Footswitch to the Adiana RF Generator.

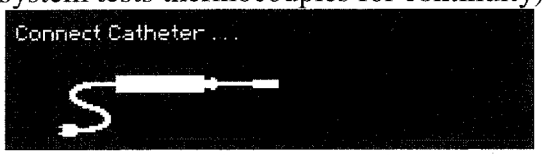
- RF Generator Software Screens

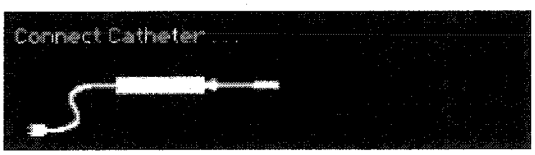
The RF Generator utilizes a menu driven display to guide the user through the various steps of the Adiana Procedure. As the RF Generator transitions from one mode to the next it continuously checks for errors in the catheter, as well as within the generator itself.

Images of RF Generator screens are shown below in Figures 5.3 through 5.10. Information describing the significance of each image is contained in PMA Module 2. Additional procedural description is provided in the RF Generator Specification and Installation Manual in Appendix 14 of this PMA Module.

Figure 5.3: Display for Power On Mode
(while system performs self-test)

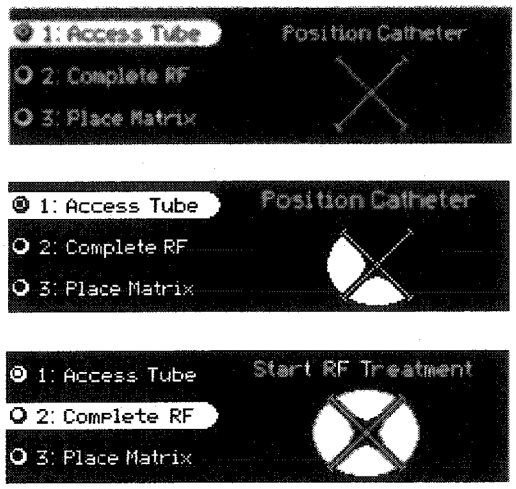
Figure 5.4: Display for Connect Catheter Mode
(while system tests thermocouples for continuity)





(image appears to move, indicating catheter action)

Figure 5.5: Display for Access Tube (as the system monitors the Position Detector Array (PDA)



Note: Any combination of three quadrants can be illuminated. When all 4 quadrants are in contact, the image indicates that the RF treatment should be started.

Figure 5.6: Complete RF Display
(with countdown timer for 60 second duration)

(Display increments from "60" to "0")

Figure 5.7: Place Matrix Display
(signals the operator to release the Matrix)

Figure 5.8: Remove and Disconnect
(signals the operator to remove and disconnect catheter)

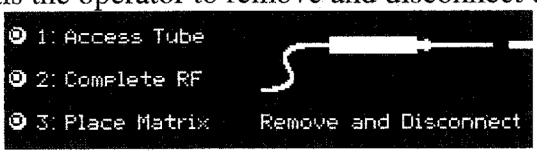
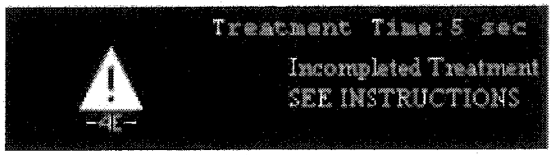


Figure 5.9: Display for Error Mode during RF Generator emission



Note: Error code can reference any error; treatment time will be between 1 and 59 seconds. Error codes are provided in the RF Generator Specification and Installation Manual.

Finally, for any unrecoverable error, the following screen display is shown:

Figure 5.10: Display for Fault Mode detection of *unrecoverable error*

The corresponding error code is displayed. The triangle symbol blinks. The system is inoperable in this mode until the AC mains power is cycled off, then on.

5.2 System Labeling

System labeling is comprised of the following:

- Draft Summary of Safety and Effectiveness
- Draft Adiana Transcervical Sterilization System Instructions for Use to be provided with both the Delivery Catheter and RF Generator
- Draft RF Generator Specification and Installation Manual to be provided with the RF Generator
- Patient Information Brochure to be provided by the Physician or by Cytyc upon patient request (Draft will be completed upon finalization of SS&E)

The following documents are overviewed below. Draft versions are included in the Appendices.

5.2.1 Summary of Safety and Effectiveness

Adiana's Summary of Safety and Effectiveness contains a data summary from the EASE Clinical Trial as well as a brief summary of the material submitted in the three previous PMA Modules. A draft version of the Summary of Safety and Effectiveness can be found in Appendix 12.

5.2.2 Adiana Transcervical Sterilization System Instructions for Use

The System Instructions for Use contains Device Descriptions for both the Delivery Catheter with Matrix and RF Generator, Contraindications, Warnings and Precautions, Adverse Events and Clinical Information (to be inserted upon agreement with FDA), Directions for Use, Handling and Warranty Information. A draft of the System IFU and Patient Implant Card are included in Appendix 13.

5.2.3 RF Generator Specification and Installation Manual

The RF Generator Specification and Installation Manual is to be provided with each RF Generator along with a Systems Instruction for Use. The document contains Warnings and Precautions specific to the use of the RF Generator, Installation set-up information, information about device accessories, operation of the RF Generator, troubleshooting, technical specifications, and warranty. A draft of the RF Generator Specification and Installation Manual is provided in Appendix 14.

5.2.4 Patient Information Brochure

The Patient Information Brochure is to be provided to patients as part of the physician-patient conversation about use of this device. The brochure may be distributed by the physician or by Cytyc upon request. The brochure contains patient – oriented information describing how the Adiana Transcervical Sterilization System works, risks and benefits, information about alternative contraceptive choices, what to expect, and a glossary. A complete Patient Information Brochure will be submitted to FDA upon finalization of the Summary of Safety and Effectiveness and the Instructions for Use.

5.2.5 HSG Protocol

Performing and accurately interpreting HSGs has been an important aspect of the Adiana Procedure. To ensure that physicians who interpret HSGs for commercial product are successful, a written HSG protocol has been developed.

A draft version of the HSG protocol can be found in Appendix 16.

VIII. TRAINING PROGRAM (PROPOSED)

VIII. A. PHYSICIAN TRAINING (SYSTEM AND HSG)

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6.0 TRAINING

This section contains a description of the design and delivery of physician training for the Adiana Transcervical Sterilization System (Adiana System) that was employed throughout the EASE clinical trial. In addition, proposed commercial training will be presented.

6.1 Physician Training Overview (EASE Study)

During the trial, Cytyc provided training for two "tiers" of EASE trial investigators. The first tier (i.e. "Tier One") was comprised of the initial six investigational sites (October 2002), and the second tier ("Tier Two") consisted of investigators who were trained as part of the expansion of the trial to the remaining investigational sites in late 2003. As the trial progressed, minor changes to the training were made based on feedback and results in the trial.

For participation in the EASE trial, Cytyc selected investigators with prior experience in operative hysteroscopy. Some physicians had prior experience with tubal cannulation, but the majority did not. Additionally, these investigators had previous hands-on experience with hysterosalpingography, as well as familiarity with transcervical sterilization principles. The training associated with the EASE trial was designed to further familiarize the investigators in the principles and practice of hysteroscopy in conjunction with the Adiana Transcervical Sterilization System as well as with specifics on the execution of the EASE clinical trial. This training included written materials, didactic presentations, hands-on experience with Hysteroscopic Trainers, and clinical practice.

Tier One training was conducted in two separate sessions with specific investigators attending either session. Training was conducted on-site at the [redacted] The first session took place in October 2002 and included investigators [redacted] The second session took place on November 2002 and included [redacted]

[redacted] was selected as the initial training site because the investigator at this site, [redacted] had years of experience with Cytyc product development studies, having been involved from the early phases. The facilities there were properly set up to facilitate group training and allow participants to observe clinical use. Additionally, the clinical staff in [redacted] were experienced researchers and trainers; knowledgeable in good clinical practices and follow-up; and prepared to assist as necessary.

By the end of the Tier One training, investigators were expected to:

- Understand and be able to explain Adiana System technology, including: counseling patients
- Successfully perform the Adiana Procedure, including: setting up appropriate equipment and preparing the patient
- Successfully perform follow up evaluation, including: performing and interpreting HSGs
- Follow up and manage difficult cases

After the first year of the trial (150 patients and 200 patient-months of wear) FDA approved the expansion of the EASE trial, and a second group of trial sites was added to the study (Tier Two) in 2003. Prior to training the second tier of investigators, Tier One investigators were asked to assist in improving the training program. Based on information gathered from early trial experiences, and on a protocol change, Tier Two training was developed and presented to the newly added investigators. Additions made to the Tier Two training program are detailed below.

The majority of Tier Two training took place at the [redacted] over the course of four sessions held between October, 2003 and November 2003. Doctors trained in these sessions included: [redacted] This training included written materials, didactic presentations, hands-on experience with Hysteroscopic Trainers, and clinical practice.

The final group of Tier Two training included [redacted] and [redacted] who were unable to attend the meetings in [redacted] Therefore, they were trained at their respective offices. For their training, each investigator received written training materials, a full didactic PowerPoint presentation delivered by the Cytyc clinical staff, and in-depth discussion of the procedure. All three physicians were trained on Hysteroscopic Trainers prior to performing the procedure in the clinic. After completion of this training, each investigator observed placement of the device by a previously trained clinician. To complete their training, each investigator actually performed the implantation while under observation of the Cytyc clinical staff.

[redacted] were involved with product development and performed the Adiana Procedure in the earlier hysterectomy studies; thus, they were fully experienced in the use of the Adiana System and did not require further clinical training for the purpose of the clinical trial. [redacted] had been working with Cytyc since 1998 and [redacted] since 1999.

Before embarking on Tier Two training, Cytyc considered the technical and clinical issues that had arisen during the first year of the EASE trial and revised the protocol accordingly. This was addressed in [redacted] Among other approved protocol changes, §10.8 was added to clarify case management procedures when treatment results were unsuccessful in a first treatment attempt. Cytyc

wanted Tier Two investigators to be familiar with these activities, and training modules were expanded to incorporate this additional information. In addition to the previous Tier One training requirements, Tier Two investigators received additional instructions in:

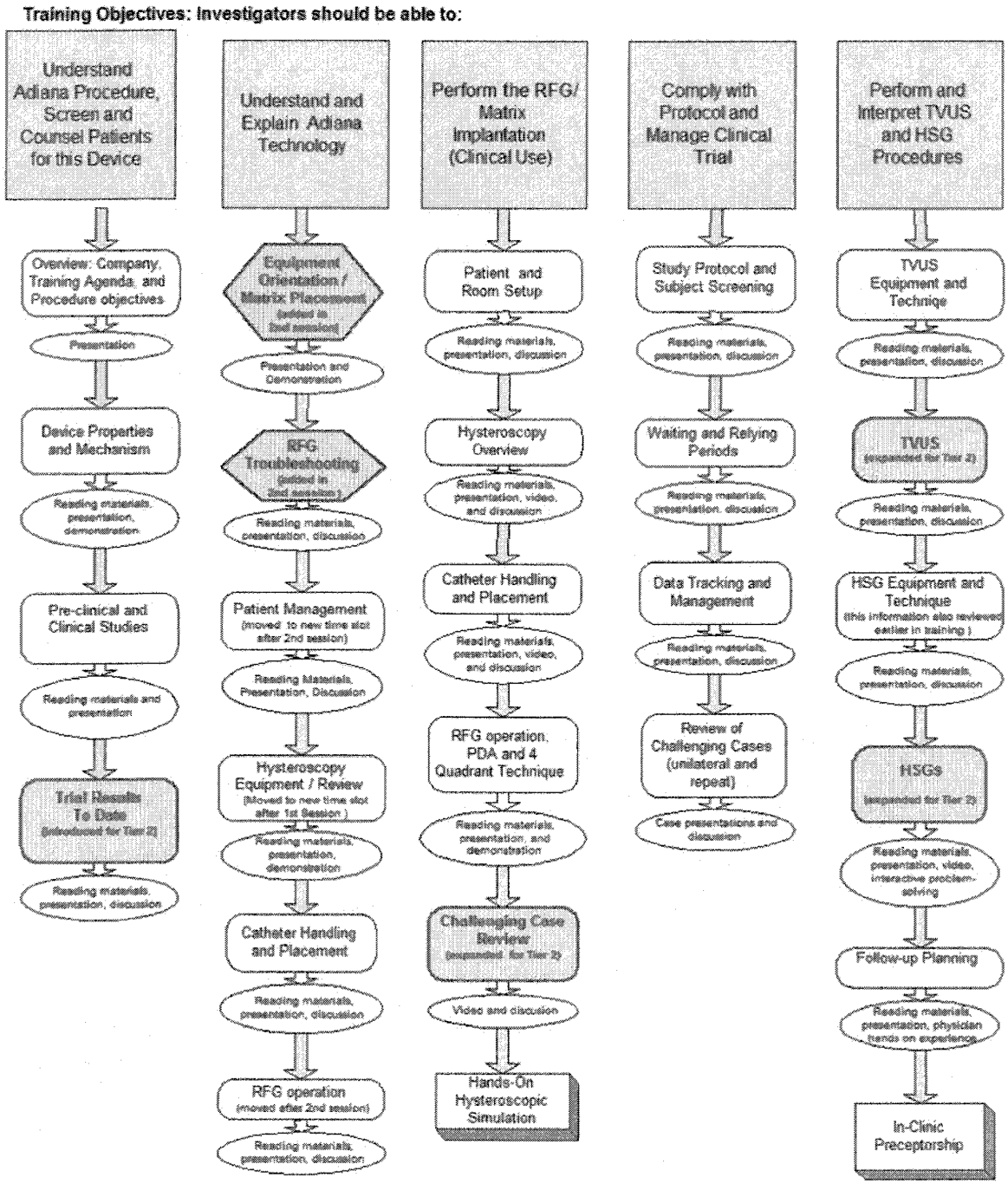
- Matrix placement in atypical cases
- Use of transvaginal ultrasound (TVUS) to effectively identify matrices and perform measurements
- Case management where hysterosalpingogram (HSG) was equivocal

A schematic cverview and detailed training discussion for Tiers One and Two are provided below:

6.1.1 Schematic Overview

Figure 6.1 below provides a schematic view of Cytyc Training that was conducted during the course of the EASE clinical trial. Each major training objective is highlighted at the top of the diagram. The training modules and delivery mechanisms to achieve the objectives are specified below each. Modules that were added for the second session of Tier One are shown in green and modules that were added for Tier Two training are shown in blue.

Figure 6.1: EASE Trial Investigator Training Overview:



6.1.2 General Training Overview (Tiers One and Two)

This section includes a description of the Investigator training and "lessons learned" that were ultimately implemented in the design of the commercial training program.

Trainers

EASE investigator training was created and conducted by Cytyc clinical staff, including [redacted] Cytyc Medical Director, [redacted], also contributed to the training program. As Cytyc staff had actively participated in product development and in performing hysterectomy studies, they were well versed in Adiana technology and assumed the role as trained representatives. Training was also conducted by both [redacted] These individuals had participated in numerous OUS Adiana patient treatments and were extremely experienced in the Adiana technique. (Subsequently, following all training, [redacted] began treating patients in the EASE IDE Trial in January 2004, [redacted] began treating patients in December 2004.

Content

Didactic information selected for the EASE investigator training program was based upon knowledge requirements necessary for understanding the principles and design of the Adiana System. It was an investigator qualification requirement for the trial that they be acquainted with hysteroscopic technique. Tier One training focused more on the "ideal case". However, as the EASE trial proceeded and protocol changes were introduced, additional information was included in Tier Two training to address troubleshooting for the more challenging cases.

Didactic Classroom Methods

EASE investigator training included didactic presentations, hands-on practice with Hysteroscopic Trainers, and actual clinical experience with preceptors. Didactic material was collected and organized into modules that would assist in the comprehension of defined learning objectives. Questions were addressed both during and subsequent to the delivery of each module. Following the completion of each module, trainers elicited discussion about the information that had just been presented. Whenever possible, video and live demonstrations were also provided. Additionally, a Hysteroscopic Trainer was utilized to provide hands-on practice before proceeding to clinic. PowerPoint handouts to facilitate note-taking and organization of discussions were distributed prior to any training. Additionally, all investigators received training in the RF Generator and Delivery Catheter Instructions for Use.

Hysteroscopic Trainer Instruction

Following didactic training, all investigators practiced the Adiana Procedure hands-on, using a Hysteroscopic Trainer [redacted]; See Appendix 18). This

unique model, used to train other hysteroscopic transcervical sterilization systems, provides a simulated uterus that allows the use of complete hysteroscope set up (fluid, hysteroscope, camera, and catheter) in a rubber model with realistic tubal ostia. The Trainer provides an excellent simulation of hysteroscope placement and movement, Delivery Catheter use, and tubal cannulation. The Trainer was operated in conjunction with a Wolf Office Hysteroscopy System and provided investigators the opportunity to become more familiar with and "rehearse" the Adiana Procedure. Equipped with an endocamera, camera controller, camera head, optical coupler, video cables, fiber optic light source, and monitor, the Wolf hysteroscope enabled investigators to observe their internal positions on the video monitor and visually navigate throughout the procedure.

During hysteroscopic simulated training, Cytyc trained representatives (trainers) provided both, proactive assistance, offering step by step explanation of the procedure, and reactive assistance, monitoring, guidance and explanation whenever an error or difficulty occurred. Cytyc trained representatives monitored physician performance and reiterated warnings and precautions that had already been described in the classroom.

By completion of the hysteroscopic simulation training, investigators were required to demonstrate that they were able to:

- Observe the necessary precautions to prevent injury during hysteroscopy and transcervical sterilization
- Successfully operate an hysteroscope in utero and identify fallopian tube ostia
- Successfully perform the entire Adiana Procedure in both normal and challenging cases.

The Trainer enabled the investigator to practice correct maneuvering of the hysteroscope and the hysteroscope/catheter assembly, both under normal circumstances and with challenging cases. Investigators were not permitted to attempt live cases until they were able to successfully perform the Adiana Procedure in simulation. This determination was made by a Cytyc trained representative.

Clinical Proctoring

Investigators received proctoring support during hands-on training at peri-hysterectomy and healthy patient access studies in [redacted] Each physician was proctored for approximately 3 patients (6 'tubes') during this phase of training. After completing this phase, each investigator had the option of requesting a Cytyc trained representative be present at their respective investigational site during procedures, to ensure that they were following the procedural instructions that they had received during training.

The final three Tier Two investigators were unable to attend training in Monterrey. In lieu of this, they received didactic training and experiential practice with a Hysteroscopic Trainer at their respective facilities and they did not perform clinical training cases prior to EASE patient treatments. After observing cases in the

operating room with a previously trained investigator, each of the three physicians (whom were co- or sub- investigators at their respective sites) went on to perform the procedure independently. Their initial procedure occurred in the presence of a Cytyc trained representative.

Investigator Meetings

Formal investigator meetings were held annually at the American Association of Gynecologic Laparoscopists (AAGL) in 2002, 2003, 2004, 2005, and 2006. Agendas at these meetings included review of EASE results to date, review of warnings and precautions including the importance of vigilance and repeated discussions with patients about the risk of pregnancy and ectopic pregnancy, clinical technique challenges, lessons learned with video examples, protocol issues, enrollment and reporting, and discussion of training. At many of these meetings, investigators formally presented their experiences with patients and newly discovered treatment tips.

6.2 EASE Trial Physician Training – Tier One

6.2.1 Overview

Training activities included a presentation overview of Cytyc, Inc., its clinical and regulatory strategies, the EASE protocol, study timelines and training topics to be covered. The Adiana System, procedure objectives, device properties and mechanisms were also reviewed. The investigators were walked through the procedure and results from *in vitro* testing, Pre-Hysterectomy and Peri-hysterectomy clinical studies were also discussed. Based on a few questions that had surfaced following the Tier One training session, the second Tier One presentation included additional information on RF Generator troubleshooting, (i.e., interpreting RF Generator error codes) and facilitation of tubal access..

A *Clinical Use* module was reviewed, which covered a range of topics including: patient screening, preparing a treatment room for the procedure, and anesthesia requirements. Although the investigators were already familiar with hysteroscopy, this technique was also reviewed. Proper catheter handling and placement was also discussed. Additionally, videos were shown to further elucidate both the hysteroscopy and the Adiana Procedure. Patient follow-up including TVUS (as it related to data collection under the EASE protocol) and HSG evaluations were also reviewed.

These didactic presentations were followed by guided, hands-on experience with Hysteroscopic Trainers, with which investigators applied previously learned didactic information and practiced the Adiana Procedure. (See Hysteroscopic Trainer above)

The EASE clinical trial protocol, site management and trial compliance requirements were presented with an interactive discussion. Topics included case scheduling, site

management details, and patient screening. Waiting and Wearing Period requirements were reviewed along with electronic data collection (EDC) data collection and management.

TVUS and HSG evaluation protocols were presented including when TVUS should be performed, instructions on TVUS interpretation, and an overview of HSG equipment and technique. This included HSG instructions on proper HSG procedural technique and interpretation of images.

Following the didactic trainer and Hysteroscopic Trainer instruction, investigators went to the [redacted] to observe and practice the Adiana Procedure. Each physician had the opportunity to treat approximately six fallopian tubes, from both healthy and peri-hysterectomy cases. All physicians quickly showed a complete understanding of the Adiana Procedure. In the estimation of the trainers presenting the course material, there were no physicians that were believed to be lacking in the skills to execute the Adiana Procedure or lacking in the ability to execute the EASE clinical trial at their respective investigational site.

6.2.2 Overall Tier One Training Assessment

Tier One training was assessed by Cytyc trained representatives who noted investigator learning and comprehension patterns. It was noted that hysteroscopists with more experience seemed to readily grasp the technique ahead of non-experienced users. Questions of understanding of the Adiana Procedure from these experienced investigators did not emerge until later in the trial, and these focused mainly on the challenging cases (anatomical anomalies) and equivocal HSGs. Additionally with all investigators there was continuous discussion of the new experimental anesthesia protocols. It was concluded that Tier One training had been overly targeted to the ideal case and that there had been gaps in the area of challenging cases and the interpretation of equivocal HSGs. It was determined that training needed to include instruction for the handling of failed access for one or both tubes, non-occlusion, and patient management in difficult cases, as well as understanding of treatment time limits, effective use of the hysteroscope, and use of TVUS. As a result of Tier One training and the experiences learned, Tier Two training was revised to include increased emphasis on challenging cases, on performing TVUS, and on interpreting equivocal HSGs.

6.3 EASE Trial Physician Training - Tier Two

6.3.1 Overview

As the EASE clinical trial had been underway for one year when Tier Two training was executed, results of the trial to date were additionally presented. Also, based on information collected over the course of the year, training topics and delivery were further modified based on investigator feedback. These modifications included expanded presentation of case reviews, and a protocol for handling atypical TVUS and HSG evaluations. The Adiana System, device mechanism, procedure objectives and device properties were also reviewed and demonstrated.

Results from *in vitro* testing and preclinical studies were discussed; however, emphasis was placed on the EASE clinical trial endpoints and results to date, specifically, percentages of patients successfully treated, procedure time, and use of anesthetics. At the time of the Tier Two presentations, there had been no pregnancies to date. Nevertheless, investigators were reminded to continue to counsel their patients about the possibility of pregnancy.

The *Clinical Use* training module covered a range of topics from patient screening, preparing a room for this procedure, anesthesia requirements and case management. Hysteroscopy was carefully reviewed prior to any discussions related to the Adiana Procedure. Catheter handling and placement were also broken into steps and discussed. For Tier Two, videos displaying various approaches to treating unexpected anatomical findings from early EASE cases were shown to further elucidate both hysteroscopy and the Adiana Procedure. Patient follow-up including TVUS and HSG technique were also reviewed.

The discussion of case management was expanded to address the lessons learned and troubleshooting experiences encountered by Tier One investigators. Patient screening, setup, and preparation for the procedure were also discussed in greater detail. Videos were shown that depicted various unusual clinical situations, including access issues with suggestions for catheter placement and Matrix release. Additional RF Generator troubleshooting for device and human error were presented and solutions to a variety of problems were discussed. Various patient protocol follow-up requirements (i.e., unilateral placement, or no matrix placed) were reviewed.

Site management and trial compliance information was presented in the same manner as for Tier One training, including case scheduling, site management details, patient screening; and CRF completion. Waiting and Wearing Period requirements were discussed and data collection and management protocols were clarified.

TVUS and HSG technique and troubleshooting were discussed in greater detail than for Tier One. Additional topics included greater explanation of the use of TVUS within the EASE protocol. HSG was also covered in more depth including procedural technique and interpretations. Videos depicting various anatomical anomalies were

shown and investigators discussed how to best proceed with each condition. Equivocal HSGs were presented and various courses of action discussed.

6.3.2 EASE trial physician training - summary

Cytyc trained representatives observed the first implantations of many Tier Two investigators. As in Tier One, it was determined that additional discussion of how to facilitate tubal access and case management for challenging cases would be helpful.

In summary, all investigators were able to successfully perform the Adiana Procedure. At subsequent investigator meetings, discussions focused on equivocal HSGs and various anesthetic combinations. The Adiana Procedure itself and technique were discussed only in light of anatomical anomalies and management of cases where technical challenges occurred signifying that this was not a critical concern for the investigators. Overall, investigators indicated that they were pleased with their training and that it was sufficient to enable them to perform the Adiana Procedure.

6.4 Proposed Physician Training for Marketed Device

Cytyc recognizes the significance of effective training for the Adiana System once it is released for commercial distribution. Patient safety as well as product effectiveness will depend upon a consistent fully operational training program. To address this, Cytyc has developed an integrated training curriculum that targets physician learning needs prior to using the marketed device. Many factors have been taken into consideration in the design of this program including information gathered from investigators during the EASE trial and training approaches used for other currently approved transcervical sterilization products. The sections below describe the factors that have been used as a basis for this program.

6.4.1 Basis for Training

Feedback Gathered from Investigators

During the EASE trial training sessions and at investigator meetings, Cytyc investigators spoke openly about their learning needs. Some investigators delivered presentations to the others on problems they had encountered and lessons learned. During all of these sessions it was concluded that needs existed for:

- Guidance for challenging cases (e.g. when to try again and when to stop, strategies for dealing with accessing difficulties)
- General procedure suggestions (e.g. avoiding catheter kinking, equipment stability during the procedure)
- Guidance for interpreting HSGs, and in particular, equivocal HSGs
- Keeping current on new and better ways to achieve patient comfort during treatment

It was also revealed that investigators who were skilled hysteroscopists encountered little difficulty at mastering the Adiana Procedure technique. Those who were less experienced in hysteroscopy had more difficulty, primarily with orientation of the operative field of view in the hysteroscope and coordination of catheter movements within the field of view; however, they were still able to accomplish initial patient treatments with no discernable 'learning curve' as expressed by clinical results. (Reference Clinical Report R0071, Section 8.3.1).

Feedback Gathered from Trial Results

The EASE trial bilateral placement rate was 94.6% (initial placement attempt), and physicians encountered minimal difficulty with the hysteroscopic technique and with the Adiana System. More significant challenges were posed by the interpretation of equivocal HSGs and by the management of anatomically difficult cases. In general, adverse events were minimal and anticipated. However, physicians remained cognizant of the need to maintain open communication with patients concerning the possibility of pregnancy and in particular, ectopic pregnancy.

6.4.2 Proposed Commercial Training

It is Cytyc's intention to provide a comprehesive training program for all physicians who require it. This includes training for both the Adiana Transcervical Sterilization Procedure and the Adiana HSG Procedure. Training for these two procedures will be delivered separately. An overview of both training programs is provided below.

1. Adiana Transcervical Sterilization System Training

Once commercialized, Cytyc will market devices exclusively to physicians who have successfully completed the Cytyc training program. To be eligible for Cytyc training, physicians shall be certified in the field of gynecology by a national organization (for example, the American College of Obstetrics and Gynecology in the USA) or be qualified for certification, and shall be experienced in the use of operative hysteroscopy at the physician's primary clinical facility. Physicians who have not yet achieved competency in hysteroscopy will need to obtain training externally. Cytyc will generate and provide a list of resources for training in hysteroscopy.

The following provides information describing the proposed program for training in the Adiana System. In order to reach an optimal balance between providing ample background information and customized training aimed at the correct learning level, Cytyc will deliver training that targets two different physician experience levels:

Track One: Physicians currently performing hysteroscopic sterilization

Track Two: Experienced hysteroscopists (defined as those who have operative hysteroscopy privileges at their clinical facility)

Physicians who are not competent hysteroscopists will not be eligible to procure the Adiana System and will not be trained in the Adiana technique.

Track One: Physicians currently performing hysteroscopic sterilization

As a result of their experience with currently commercialized transcervical sterilization devices, many physicians are already competent in this type of procedure- principally with the use of a hysteroscope to visualize and assess the tubal ostia; with the manipulation of catheters through the working channel; and with cannulation of the fallopian. Due to the much shorter cannulation depth as compared to the alternative commercially available product, cannulation with the Adiana System appears to be less challenging for users (this is supported by the higher acute tubal access rate with the Adiana System as compared to Essure (95% vs 86%) and from physician feedback). Additionally, the RF Generator has internal safety mechanisms and through its user display, simply guides the physician through the procedure. This minimizes the need for extensive training preparation. For these reasons, formal proctorship by Cytyc representatives for this group will not be required. Therefore, physicians experienced at transcervical sterilization will only participate in didactic training as well as training with a hysteroscopic simulator. In addition, they will have the option for proctorship by a Cytyc trained representative during their first few cases. Based on this, Track One training will be the same as Track Two with the exception that proctored cases with a Cytyc Representative are not required.

Track Two: Experienced hysteroscopists who demonstrate competence in hysteroscopic technique but who lack experience in transcervical sterilization

The second group of physicians, designated as "Track Two" will have experience in hysteroscopy but may not yet be competent at transcervical sterilization.
After their didactic training and Hysteroscopic Trainer use, these individuals will be required to perform their initial clinical procedures in the presence of a Cytyc trained representative. Based on the experience from the EASE trial, it is anticipated that treatment of approximately three patients would be necessary for the clinician to achieve this objective. Therefore, Track Two training will provide the additional; case observation in addition to didactics and Hysteroscopic Trainer experience.

Physicians (in either training program) will not be authorized to procure product from Cytyc until all relevant aspects of the appropriate training program have been completed. As part of this required training, physicians will complete a questionnaire to evaluate training effectiveness. Documentation of completion of either training program (as applicable) will be required. Once a clinician has successfully completed all portions of either training program, they will be eligible for purchasing product without constraint.