Directions for Use

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NATRELLE® Silicone-Filled Breast Implants and *NATRELLE INSPIRA*® Breast Implants

Smooth surface implants

Allergan Aesthetics

an AbbVie company

WARNING:

- Breast implants are not considered lifetime devices. The longer people have them, the greater the chances are that they will develop complications, some of which will require more surgery.
- Breast implants have been associated with the development of a cancer of the immune system called breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). This cancer occurs more commonly in patients with textured breast implants than smooth implants, although rates are not well defined. Some patients have died from BIA-ALCL.
- Patients receiving breast implants have reported a variety of systemic symptoms such as joint pain, muscle aches, confusion, chronic fatigue, autoimmune diseases and others. Individual patient risk for developing these symptoms has not been well established. Some patients report complete resolution of symptoms when the implants are removed without replacement.

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

The sale and distribution of this device is restricted to users and/or user facilities that provide information to patients about the risks and benefits of this device in the form and manner specified in the approved labeling provided by Allergan.

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INTRODUCTION

Directions to the Physician
The information supplied in this Directions for Use document is intended to provide physicians an overview of essential information about *NATRELLE*® Silicone-Filled Breast Implants and *NATRELLE INSPIRA*® Breast Implants, including the indications for use, contraindications, warnings, precautions, important factors for a patient to consider, adverse events, other reported conditions, instructions for use, and a summary of Allergan's core clinical study results.

Patient Counseling and Informed Decision Information
You should review this document prior to counseling the patient about breast implant surgery with *NATRELLE*® Silicone-Filled Breast Implants or *NATRELLE INSPIRA*® Breast Implants. Please familiarize yourself with the content of this document and resolve any questions or concerns prior to proceeding with use of the device. As with any surgical procedure, breast implantation is NOT without risks. Breast implantation is an elective procedure, and the patient must be well counseled and understand the risk/benefit relationship.

Each patient should receive Allergan's patient brochure ***NATRELLE® Silicone-Filled Breast Implants and NATRELLE INSPIRA® Breast Implants: Important Factors Breast Augmentation and Reconstruction Patients Should Consider*** and be informed that Allergan's patient labeling, ***Breast Augmentation/Reconstruction with NATRELLE® Silicone-Filled Breast Implants and NATRELLE INSPIRA® Breast Implants***, is available online (www.allerganlabeling.com) during her initial visit/consultation. She should be advised of the potential complications and that medical management of serious complications may include additional surgery and explantation. The patient should be advised to wait at least 1-2 weeks after reviewing and considering this information before deciding whether to have this surgery, unless an earlier surgery is deemed medically necessary.

In order to formally record a successful informed decision process, the ***Acknowledgement of Informed Decision and Patient Decision Checklist*** document (available separately and within the patient labeling document at: www.allerganlabeling.com) should be signed by both the patient and the surgeon. A copy should be provided to the patient and another copy retained in the patient's file.

For detailed instructions regarding patient counseling and informed consent, please see the section "Patient Counseling Information: Important Factors, Possible Adverse Events and Other Reported Conditions" on page 9.

Certification

Certification via Allergan's ***Physician Certification Program*** specific to *NATRELLE*® Silicone-Filled Breast Implants is required in order to gain access to these implants. Please see the section "Preoperative Education, Planning, and Preparation" in the Instructions for Use, visit https://www.allerganssurgicaleducation.com/, or contact your local Hospital or Surgical Sales Representative or the Allergan Customer Care Department for detailed training information.

Device Tracking

NATRELLE® Silicone-Filled Breast Implants and *NATRELLE INSPIRA*® Breast Implants are subject to Device Tracking per federal regulation. This means that the implanting physician is required to report to Allergan the serial number of the implanted device(s), the date of surgery, information relating to the implanting physician's practice, and information on the patient receiving the implant(s). This information should be recorded on the **Device Tracking Form** supplied by Allergan with each silicone gel-filled breast implant. Following surgery, the form should be returned to Allergan, using the contact information provided on the form. Unless the patient chooses to opt-out, as part of Allergan's Device Tracking Program, the patient's personal information (including name, address, phone number, date of birth, email, and social security number) will also be provided to Allergan, any of its vendors/third parties providing device tracking services on its behalf, and any relevant regulatory authorities for device tracking purposes, in accordance with applicable laws and regulations. As part of Allergan's Device Tracking Program, Allergan may share this information with the implanting physician and may occasionally be asked to release this information to a third party, such as the FDA. If the patient chooses to participate in Allergan's Device Tracking Program but DOES NOT want Allergan to release patient specific information, the patient may opt-out of this sharing. Please note that there may be instances where Allergan is legally required to share the information as per federal regulation.

Allergan strongly recommends that all patients receiving *NATRELLE*® Silicone-Filled Breast Implants or *NATRELLE INSPIRA*® Breast Implants participate in Allergan's Device Tracking program. This will help ensure that Allergan has a record of each patient's contact information. Patients should be encouraged to complete the Device Tracking Form and return it to Allergan so that they can be contacted in the event of a recall or other problems with the implants.

Device tracking information can also be provided electronically via the AbbVie Device Management Portal, the National Breast Implant Registry, or the Aesthetic One app. To use the AbbVie Device Management Portal, go to devicemanagement.abbvie.com to register and start data entry. For the National Breast Implant Registry, go to thepsf.org/NBIR to register and start data entry. To use the Aesthetic One app, go to www.aestheticone.org to register and start data entry.

DEVICE DESCRIPTION

NATRELLE® Silicone-Filled Breast Implants and *NATRELLE INSPIRA*® Breast Implants are constructed with barrier shell technology resulting in a low diffusion silicone elastomer shell and are filled with silicone gel. All styles are single "lumen" round design and consist of a shell, a patch, and silicone gel fill. Allergan has approval for 3 types of silicone gel fillers: *Responsive* silicone gel, *SoftTouch* silicone gel, and *Highly Cohesive* silicone gel. Allergan's *Responsive* silicone gel is a softer gel than Allergan's *SoftTouch* silicone gel, which is softer than Allergan's *Highly Cohesive* silicone gel. This document includes round implants filled with each of the three gel types.

NATRELLE® Silicone-Filled Breast Implants are filled with *Responsive* silicone gel. They are dry heat sterilized and are available with a smooth surface. Table 1 provides an overview of the styles and sizes of *NATRELLE*® Silicone-Filled Breast Implants.

Table 1: *NATRELLE*® Silicone-Filled Breast Implants

Style Number	Breast Implant Description	Size Range
Style 10	Smooth shell surface, *Responsive* silicone gel, moderate profile	120cc – 800cc
Style 15	Smooth shell surface, *Responsive* silicone gel, moderate-plus profile	155cc – 752cc
Style 20	Smooth shell surface, *Responsive* silicone gel, high profile	120cc – 800cc
Style 40	Smooth shell surface, *Responsive* silicone gel, moderate profile	80cc – 560cc
Style 45	Smooth shell surface, *Responsive* silicone gel, extra-high profile	120cc – 800cc

In general, *NATRELLE INSPIRA*® Breast Implants have a higher fill than *NATRELLE*® Silicone-Filled Breast Implants and are filled with *Responsive* silicone gel, *SoftTouch* silicone gel, and *Highly Cohesive* silicone gel. They are also dry heat sterilized and are available with a smooth surface.

Table 2 provides an overview of the styles and sizes of *NATRELLE INSPIRA*® *Responsive* Breast Implants. Table 3 provides an overview of the styles and sizes of *NATRELLE INSPIRA*® *SoftTouch* Breast Implants. Table 4 provides an overview of the styles and sizes of *NATRELLE INSPIRA*® *Cohesive*™ Breast Implants.

Table 2: *NATRELLE INSPIRA*® *Responsive* Breast Implants

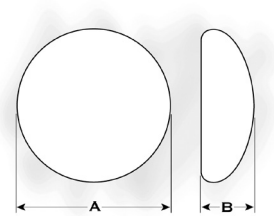
Style Name	Breast Implant Description	Size Range
Style SRL	Smooth shell surface, *Responsive* silicone gel, low profile	110cc – 610cc
Style SRLP	Smooth shell surface, *Responsive* silicone gel, low plus profile	125cc – 640cc
Style SRM	Smooth shell surface, *Responsive* silicone gel, moderate profile	140cc – 755cc
Style SRF	Smooth shell surface, *Responsive* silicone gel, full profile	180cc – 770cc
Style SRX	Smooth shell surface, *Responsive* silicone gel, extra-full profile	200cc – 800cc

Table 3. *NATRELLE INSPIRA® SoftTouch* Breast Implants

Style Name	Breast Implant Description	Size Range
Style SSL	Smooth shell surface, *SoftTouch* silicone gel, low profile	110cc – 610cc
Style SSLP	Smooth shell surface, *SoftTouch* silicone gel, low plus profile	125cc – 640cc
Style SSM	Smooth shell surface, *SoftTouch* silicone gel, moderate profile	140cc – 755cc
Style SSF	Smooth shell surface, *SoftTouch* silicone gel, full profile	180cc – 770cc
Style SSX	Smooth shell surface, *SoftTouch* silicone gel, extra-full profile	200cc – 800cc

Table 4. *NATRELLE INSPIRA® Cohesive* Breast Implants

Style Name	Breast Implant Description	Size Range
Style SCL	Smooth shell surface, *Highly Cohesive* silicone gel, low profile	110cc – 610cc
Style SCLP	Smooth shell surface, *Highly Cohesive* silicone gel, low plus profile	125cc – 640cc
Style SCM	Smooth shell surface, *Highly Cohesive* silicone gel, moderate profile	140cc – 755cc
Style SCF	Smooth shell surface, *Highly Cohesive* silicone gel, full profile	180cc – 770cc
Style SCX	Smooth shell surface, *Highly Cohesive* silicone gel, extra-full profile	200cc – 800cc



A = Width; B = Projection

Round Breast Implant

INDICATIONS

NATRELLE® Silicone-Filled Breast Implants and *NATRELLE INSPIRA*® Breast Implants are indicated for women for the following:

- **Breast augmentation for women at least 22 years old.** Breast augmentation includes primary breast augmentation to increase the breast size, as well as revision surgery to correct or improve the result of a primary breast augmentation surgery.
- **Breast reconstruction.** Breast reconstruction includes primary reconstruction to replace breast tissue that has been removed due to cancer or trauma or that has failed to develop properly due to a severe breast abnormality. Breast reconstruction also includes revision surgery to correct or improve the result of a primary breast reconstruction surgery.

CONTRAINDICATIONS

Breast implant surgery should not be performed in:

- Women with active infection anywhere in their body
- Women with existing cancer or pre-cancer of their breast who have not received adequate treatment for those conditions
- Women who are currently pregnant or nursing

WARNINGS

There is a boxed warning on all breast implants. Please see the cover page.

AVOID DAMAGE DURING SURGERY

- Care should be taken to avoid the use of excessive force and to minimize handling of the implant during surgical insertion.
- Data accumulated from Allergan's retrieval study analyses of explanted ruptured silicone gel-filled breast implants, observations of surgeries, and a review of the published literature indicate that the forcing of implants through too small an opening or applying concentrated localized pressure on the implants may result in localized weakening of the breast implant shell potentially leading to shell damage and possible implant rupture.
- An incision should be of appropriate length to accommodate the style, size, and profile of the implant. Typically, the incision needed for silicone-filled breast implants will be longer than the one made for a saline breast augmentation. This longer incision will reduce the potential for creating excessive stress to the implant during insertion. The unique nature of the more cohesive gel in the *SoftTouch* and *Highly Cohesive* silicone-filled breast implants requires an even larger incision to reduce excessive stress on the implant during insertion and minimize the potential for gel fracture (fissure in the gel) or deformation (change in shape).

- Care should be taken when using surgical instruments in proximity with the breast implant, including scalpel, sutures, and dissection instrumentation.
- Silicone gel-filled breast implants are prone to unintended instrument trauma during implantation or during explantation.[44,2] Shell failure can result from damage by scalpels, suture needles, hypodermic needles, hemostats, and Adson forceps and has been observed in explanted device shells using scanning electron microscopy.[1] Allergan's (retrieval study) analyses of explanted devices have identified unintended surgical instrument damage as one potential cause of shell failure and thus implant rupture.
- Do not treat capsular contracture by closed capsulotomy or forceful external compression, which will likely result in implant damage, rupture, folds, and/or hematoma.
- Use care in subsequent procedures such as open capsulotomy, breast pocket revision, hematoma/seroma aspiration, and biopsy/lumpectomy to avoid damage to the implant.
- Re-positioning of the implant during subsequent procedures should be carefully evaluated by the medical team and care taken to avoid contamination of the implant. Use of excessive force during any subsequent procedure can contribute to localized weakening of the breast implant shell potentially leading to decreased device performance.
- Do not contact the implant with disposable, capacitor-type cautery devices.
- Do not alter the implants or attempt to repair or insert a damaged prosthesis.
- Do not re-use or re-sterilize any breast implant that has been previously implanted. Breast implants are intended for single use only.
- Do not place more than one implant per breast pocket.
- Do not use the periumbilical approach to place the implant.
- Do not use microwave diathermy in patients with breast implants. Microwave diathermy has been reported to cause tissue necrosis, skin erosion, and implant extrusion.

PRECAUTIONS

Specific Populations

Safety and effectiveness have not been established in patients with the following:

- Autoimmune diseases (e.g., lupus and scleroderma)
- A compromised immune system (for example, currently receiving immunosuppressive therapy)
- Planned chemotherapy following breast implant placement
- Planned radiation therapy to the breast following breast implant placement
- Conditions or medications that interfere with wound healing and blood clotting
- Reduced blood supply to breast tissue

- Clinical diagnosis of depression or other mental health disorders, including body dysmorphic disorder and eating disorders. Please discuss any history of mental health disorders prior to surgery. Patients with a diagnosis of depression, or other mental health disorders, should wait until resolution or stabilization of these conditions prior to undergoing breast implantation surgery.

Additional Precautions

- Preoperative Planning - Proper surgical planning such as allowance for adequate tissue coverage, implant placement (i.e., submuscular *vs.* subglandular), incision site, implant type, etc., should be made preoperatively. For detailed instructions on proper preoperative planning, please refer to section "Preoperative Education, Planning and Preparation" on page 44.
- Back-up Implants - It is advisable to have more than one size breast implant in the operating room at the time of surgery to allow for flexibility in determining the appropriate size implant to be used. A back-up implant should also be available.
- Surgical Mesh - The use of surgical mesh or acellular dermal matrix together with the breast implant has not been studied in the Core Study.
- Explantation - If it is necessary to perform explantation of the implant, care must be taken to minimize manipulation of the product (particularly in regards to sharp-edged openings). Explanted devices should be returned to Allergan for evaluation. Contact Allergan's Product Surveillance Department at 1.800.624.4261 for an Explant Kit and explant return instructions.

PATIENT COUNSELING INFORMATION: IMPORTANT FACTORS, POSSIBLE ADVERSE EVENTS AND OTHER REPORTED CONDITIONS

General Patient Counseling Information

As with any surgical procedure, breast implantation is NOT without risks. Breast implantation is an elective procedure, and the patient must be well counseled and understand the risk/benefit relationship of these products and procedures.

At the time of consultation, provide patients with a printed copy of the breast augmentation and reconstruction brochure, ***Important Factors Breast Augmentation and Reconstruction Patients Should Consider*** (available by contacting your Sales Representative or the Allergan Customer Care Department at 800.766.0171). Additionally, instruct the patient to read the patient labeling, ***Breast Augmentation/Reconstruction with NATRELLE® Silicone-Filled Breast Implants and NATRELLE INSPIRA® Breast Implants*** (available at: www.allerganlabeling.com), prior to making the decision to proceed with surgery.

1. The patient labeling (available at: www.allerganlabeling.com) is intended as the primary means to relate uniform risk and benefit information to assist your patient in making an informed decision about primary breast augmentation and revision-augmentation, or primary reconstruction and revision-reconstruction surgery (as applicable), but it is not intended to replace consultation with you.
2. Each patient should receive Allergan's patient brochure and be informed that the patient labeling is online during her initial visit/consultation to allow her sufficient time prior to surgery to read and adequately understand the important information on the risks, follow-up recommendations, and benefits associated with silicone-filled breast implant surgery.
3. Each patient should be informed that there is a boxed warning for all breast implants.
4. It is important that all patients seeking to undergo elective surgery have realistic expectations that focus on improvement rather than perfection.
5. Request that your patient openly discuss with you, prior to surgery, any history that she may have of depression or other mental health disorders.
6. Allow the patient at least 1-2 weeks after reviewing and considering this information before deciding whether to have this surgery, unless an earlier surgery is deemed medically necessary.
7. Discuss with the patient the warnings, precautions, important factors to consider, possible adverse events, and Allergan's core clinical study results.
8. Advise the patient of the possible adverse events and other reported conditions. Explain that medical management of serious adverse events may include additional surgery and explantation.

In order to formally record a successful informed decision process, review the ***Acknowledgement of Informed Decision and Patient Decision Checklist*** document (available separately and within the patient labeling document at: www.allerganlabeling.com). The document should be signed by both the patient and the surgeon and then retained in the patient's file.

Important Factors to Convey to Patients

Below are some of the important factors (Table 5), possible adverse events (Table 6), and other conditions (Table 7) your patients need to be aware of when considering *NATRELLE*® Silicone-Filled Breast Implants or *NATRELLE INSPIRA*® Breast Implants. The patient labeling provides additional information on important factors for patients.

Table 5: Important Factors to Convey to Patients

Insurance coverage

- Patients should check with their insurance company regarding coverage issues before undergoing surgery
- Insurance coverage may differ based on whether breast implants are being used for breast reconstruction or breast augmentation
- Patients should be advised that health insurance premiums may increase, insurance coverage may be dropped, and/or future coverage may be denied based on the presence of breast implants
- Diagnostic procedures will add to the cost of having breast implants, and patients should be told that these costs may exceed the cost of their initial surgery over their lifetimes and that these costs may not be covered by their insurance carrier
- Treatment of complications may not be covered

Smoking

- Smoking may interfere with the healing process

Radiation to the Breast

- Allergan has not tested the effects of radiation therapy in patients who have breast implants. The literature suggests that radiation therapy may increase the likelihood of capsular contracture, necrosis, and implant extrusion

Breast Examination Techniques

- Patients should perform breast self-examinations monthly and be shown how to distinguish the implant from their breast tissue
- The patient should not manipulate or squeeze the implant excessively
- The patient should be told that the presence of lumps, persistent pain, swelling, hardening, or change in the implant shape may be signs of symptomatic rupture of the implant. If the patient has any of these signs, she should be told to report them and possibly have an MRI evaluation to screen for rupture

Screening Mammography

- Presurgical mammography with a follow-up mammogram after implantation may be performed to establish a baseline for routine future mammography in augmentation patients
- Patients should be instructed to undergo routine mammography exams as per their primary care physician's recommendations. The importance of having these exams should be emphasized. The current recommendations for preoperative/screening mammograms are no different for women with breast implants than for those women without implants
- Patients should be instructed to inform their mammographers about the presence, type, and placement of their implants
- Breast implants may complicate the interpretation of mammographic images by obscuring underlying breast tissue and/or by compressing overlying tissue
- Accredited mammography centers, technicians with experience in imaging patients with breast implants, and use of displacement techniques are needed to adequately visualize breast tissue in the implanted breast

Imaging Screening for Breast Implant Rupture

- Breast implant rupture is considered "silent" when it occurs without any other problems, signs, or symptoms. Breast implant rupture is considered "symptomatic" when it is accompanied by changes in the look or feel of the breast and/or breast implant. Advise your patient that she will need to have regular imaging to screen for rupture even if she is having no problems.
- For asymptomatic patients, the first ultrasound or magnetic resonance imaging (MRI) should be performed at 5-6 years postoperatively, then every 2-3 years thereafter. For symptomatic patients or patients with equivocal ultrasound results for rupture at any time postoperatively, an MRI is recommended.
- If your patient has symptoms of breast implant rupture (described in Table 6) or equivocal ultrasound results at any time postoperatively, you should recommend that she has an MRI to determine whether rupture is present.[3,4] Provide your patient with a list of MRI facilities in her area that have:
  - at least a 1.5 Tesla magnet,
  - a dedicated breast coil, and
  - a radiologist experienced with breast implant MRI films for signs of rupture
- If rupture is noted via imaging , then you should advise your patient to have her implant removed

Avoiding Damage During Treatment

- Patients should inform other treating physicians of the presence of implants to minimize the risk of damage to the implants

Mental Health and Elective Surgery

- It is important that all patients seeking to undergo elective surgery have realistic expectations that focus on improvement rather than perfection. Request that your patient openly discuss with you, prior to surgery any history that she may have of depression or other mental health disorders.

POSSIBLE ADVERSE EVENTS

Potential adverse events that may occur with silicone gel-filled breast implant surgery include: implant rupture, capsular contracture, reoperation, implant removal, pain, changes in nipple and breast sensation, infection, scarring, asymmetry, wrinkling, implant displacement/migration, implant palpability/visibility, breastfeeding complications, hematoma/seroma, implant extrusion, necrosis, delayed wound healing, breast tissue atrophy/chest wall deformity, calcium deposits, and lymphadenopathy.

Table 6 contains a description of these adverse events. For specific adverse event rates/outcomes for *NATRELLE*® Silicone-Filled Breast Implants, refer to the Core Study section below on page 22.

Table 6: Possible Adverse Events

Rupture

- *Breast implants are not lifetime devices.*
- Breast implants rupture when the shell develops a tear or hole. Ruptures can occur at any time after implantation, but they are more likely to occur the longer the implant is implanted.
- The following things may cause implants to rupture: damage by surgical instruments, stressing the implant during implantation and weakening it, folding or wrinkling of the implant shell, excessive force to the chest (e.g., during closed capsulotomy, which is contraindicated), trauma, compression during mammographic imaging, and severe capsular contracture. Breast implants may also simply wear out over time. Laboratory studies have identified some of the causes of rupture for Allergan's product. It is not conclusively known whether these tests have identified all causes of rupture. Laboratory studies to identify any additional causes of rupture are ongoing.
- Silicone gel-filled implant ruptures are most often silent. This means that most of the time neither you nor your patient will know if the implant has a tear or hole in the shell. MRI examination is currently the best method to screen for rupture. See Table 5 for additional information regarding Rupture screening.
- Sometimes there are symptoms associated with gel implant rupture. These symptoms include hard knots or lumps surrounding the implant or in the armpit, change or loss of size or shape of the breast or implant, pain, tingling, swelling, numbness, burning, and hardening of the breast.
- When MRI signs of rupture are found (such as subcapsular lines, characteristic folded wavy lines, teardrop sign, keyhole sign, noose sign), or ultrasound findings of rupture, or if there are signs or symptoms of rupture, you should remove the implant and any gel you determine your patient has, with or without replacement of the implant. It also may be necessary to remove the tissue capsule.
- There are also consequences of rupture. If rupture occurs, silicone gel may either remain within the scar tissue capsule surrounding the implant (intracapsular rupture), move outside the capsule (extracapsular rupture), or move outside the breast (gel migration). There is also a possibility that rupture may progress from intracapsular to extracapsular and beyond.
- Rupture information from the Allergan Core Study
  - In Allergan's Core Study, there was a MRI screening cohort who had regular MRIs to screen for breast implant rupture whether or not they were symptomatic (i.e., MRI cohort) and a non-MRI screening cohort who were not screened with breast implant MRIs (i.e., non-MRI cohort).
  - The rupture rates in the MRI cohorts were 9.3% for primary augmentation, 5.4% for revision-augmentation, 35.4% for primary reconstruction, and 0% for revision-reconstruction. The rupture rate for the whole MRI cohort in the Core Study (including augmentation, revision-augmentation, reconstruction, and revision-reconstruction patients) through 10 years was 13.0% for patients and 7.7% for implants.
  - Across all patients in the Core Study, all ruptures were intracapsular with the exception of 3 cases of extracapsular gel (one rupture progressed to extracapsular gel following exploratory surgery to confirm the rupture and then implant replacement was delayed).
  - The cumulative rupture rates for the MRI and non-MRI cohorts are as follows:

Cumulative Risk of First Occurrence of Implant Rupture By Patient MRI Cohort

	Augmentation[a]	Revision-Augmentation[b]	Reconstruction[c]	Revision-Reconstruction[d]
4 weeks	0.0%	0.0%	0.0%	0%
6 months	0.7% (0.1, 4.5)	0.0%	0.0%	0%
1 year	0.7% (0.1, 4.5)	0.0%	0.0%	0%
2 years	0.7% (0.1, 4.5)	0.0%	0.0%	0%
3 years	2.0% (0.7, 6.1)	0.0%	0.0%	0%
4 years	2.8% (1.0, 7.2)	0.0%	2.3% (0.3, 15.4)	0%
5 years	5.0% (2.4, 10.1)	0.0%	11.9% (5.1, 26.2)	0%
6 years	5.0% (2.4, 10.1)	0.0%	11.9% (5.1, 26.2)	0%
7 years	7.4% (4.0, 13.2)	0.0%	19.4% (10.2, 35.1)	0%
8 years	7.4% (4.0, 13.2)	0.0%	25.7% (14.6, 42.9)	0%
9 years	9.3% (5.3, 15.8)	5.4% (1.4, 20.0)	35.4% (22.1, 53.6)	0%
10 years	9.3% (5.3, 15.8)	5.4% (1.4, 20.0)	35.4% (22.1, 53.6)	0%

[a] 12 silent ruptures, 1 symptomatic
[b] 1 silent rupture, 1 symptomatic
[c] 13 silent ruptures, none symptomatic
[d] no silent ruptures, none symptomatic. Kaplan-Meier risk calculations are not applicable because of the low sample size in the Revision-Reconstruction cohort

Cumulative Risk of First Occurrence of Implant Rupture By Patient Non-MRI Cohort

	Augmentation[a]	Revision-Augmentation[b]	Reconstruction[c]	Revision-Reconstruction[d]
4 weeks	0.0%	0.0%	0.0%	0%
6 months	0.0%	0.0%	0.0%	0%
1 year	0.0%	0.0%	0.0%	0%
2 years	0.6% (0.1, 3.8)	1.8% (0.2, 11.8)	0.0%	0%
3 years	2.2% (0.8, 5.8)	1.8% (0.2, 11.8)	0.0%	0%
4 years	4.6% (2.3, 8.9)	1.8% (0.2, 11.8)	0.0%	0%
5 years	10.5% (6.7, 16.1)	3.9% (1.0, 14.8)	6.7% (1.0, 38.7)	0%
6 years	10.5% (6.7, 16.1)	3.9% (1.0, 14.8)	6.7% (1.0, 38.7)	0%
7 years	11.1% (7.2, 16.9)	3.9% (1.0, 14.8)	6.7% (1.0, 38.7)	0%
8 years	11.7% (7.7, 17.6)	3.9% (1.0, 14.8)	6.7% (1.0, 38.7)	0%
9 years	12.3% (8.2, 18.3)	3.9% (1.0, 14.8)	18.3% (4.6, 58.0)	0%
10 years	13.7% (9.3, 19.9)	10.0% (3.8, 25.4)	18.3% (4.6, 58.0)	6.7% (0.2, 31.9)

[a] 3 symptomatic
[b] 2 symptomatic
[c] 1 symptomatic
[d] none symptomatic. Kaplan-Meier calculations are not applicable because of the low sample sizes in the Revision-Reconstruction cohort

- Rupture information from the International MRI Study[5]
  - Further rupture rate information on Allergan implants is provided from a published European study known as the International MRI Study. Silent rupture data were collected via a single MRI on 77 augmentation, 11 reconstruction, and 18 revision patients implanted with smooth and textured *NATRELLE*® implants by 5 surgeons. The average age of the implants was approximately 11 years. Silent rupture was found in approximately 15% of the combined group of augmentation, reconstruction, and revision patients and 8% of the implants. There was one possible case of extracapsular rupture with the remainder classified as intracapsular ruptures. No cases of migrated gel were found.
- Rupture information from the Large Post-approval Study
  - Additional information on rupture was collected through 2 arms Allergan's post-approval Breast Implant Follow-up Study (BIFS): the BIFS-arm and the NBIR-arm. The NBIR arm of the study is now complete. Additional information on the study is provided on page 41.

- Additional rupture information from literature
  - Studies of Danish women evaluated with MRI involving a variety of manufacturers and implant models showed that about three-fourths of implant ruptures are intracapsular and the remaining one-fourth are extracapsular.[6] Additional studies of Danish women indicate that over a 2-year period, about 10% of the implants with intracapsular rupture progressed to extracapsular rupture as detected by MRI.[3] In about half of these cases of progression from intracapsular to extracapsular rupture, the women had experienced trauma or mammography. In the other half, no cause was given. In the women with extracapsular rupture, after 2 years, the amount of silicone outside the scar tissue capsule increased for about 14% of these women.

Capsular Contracture

- Patients should be advised that capsular contracture may be more common following infection, hematoma, and seroma, and the chance of it happening may increase over time
- Capsular contracture occurs more commonly in revision patients than in primary augmentation or reconstruction patients
- Capsular contracture is also a risk factor for implant rupture, and it is one of the most common reasons for reoperation
- Patients should also be advised that additional surgery may be needed in cases where pain and/or firmness are severe. This surgery ranges from removal of the implant capsule tissue to removal and possible replacement of the implant itself. This surgery may result in loss of breast tissue. Capsular contracture may happen again after these additional surgeries.

Reoperation

- Patients should be advised that additional surgery to their breast and/or implant will likely be necessary over the course of their lives. Additional surgeries to the patients' breasts will likely be required, either because of implant rupture, other complications, or unacceptable cosmetic outcomes. Patients may decide to change the size or type of their implants, requiring a reoperation, or they may have a reoperation to improve or correct their outcome
- Patients should be advised that their risk of future complications increases with revision surgery as compared to primary augmentation or reconstruction surgery
- There is a risk that implant shell integrity could be compromised inadvertently during reoperation surgery, potentially leading to product failure

Implant Removal

- Implants are not considered lifetime devices, and patients likely will undergo implant removal(s), with or without replacement, over the course of their lives
- When implants are explanted without replacement, changes to the patient's breasts may be irreversible

Lactation

- Breast implant surgery may interfere with the ability to successfully breastfeed, either by reducing or eliminating milk production
- Breastfeeding difficulties have been reported following breast surgery, including breast reduction and breast augmentation
- A periareolar surgical approach may further increase the chance of breastfeeding difficulties

Pain

- Pain of varying intensity and length of time may occur and persist following breast implant surgery
- In addition, improper size, placement, surgical technique, or capsular contracture may result in pain
- Patients should be advised to contact their surgeon if there is significant pain or if pain persists

Changes in Nipple and Breast Sensation

- Sensation in the nipple and breast can increase or decrease after implant surgery, is typically lost after complete mastectomy where the nipple itself is removed, and can be severely lessened by partial mastectomy
- Radiation therapy also can significantly reduce sensation in the remaining portions of the breast or chest wall
- The placement of breast implants for reconstruction may further lessen the sensation in the remaining skin or breast tissue
- The range of changes varies from intense sensitivity to no feeling in the nipple or breast following surgery
- While some of these changes can be temporary, they can also be permanent, and may affect the patient's sexual response or ability to breastfeed

Infection

- In rare instances, acute infection may occur in a breast with implants
- The signs of acute infection include erythema, tenderness, fluid accumulation, pain, and fever
- Very rarely, Toxic Shock Syndrome, a potentially life-threatening condition, has been reported in women after breast implant surgery. It is characterized by symptoms that occur suddenly and include high fever (102°F, 38.8°C or higher), vomiting, diarrhea, a sunburn-like rash, red eyes, dizziness, lightheadedness, muscle aches, and drops in blood pressure, which may cause fainting
- Patients should be advised to contact a physician immediately for diagnosis and treatment for any of these symptoms

Unsatisfactory Results

- Patients should be informed that dissatisfaction with cosmetic results related to such things as scar deformity, hypertrophic scarring, capsular contracture, asymmetry, wrinkling, implant displacement/migration, incorrect size, and implant palpability/visibility may occur
- Careful surgical planning and technique can minimize, but not preclude, the risk of such results
- Pre-existing asymmetry may not be entirely correctable
- Revision surgery may be indicated to maintain patient satisfaction but carries additional considerations and risks

Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

- Based on information reported to global regulatory agencies and found in medical literature, an association has been identified between breast implants and the development of anaplastic large cell lymphoma (ALCL), a type of non-Hodgkin's lymphoma. Women with breast implants may have a very small but increased risk of developing Breast Implant Associated ALCL (BIA-ALCL) in the fluid or scar capsule adjacent to the implant, with documented potential for local, regional, and distant spread of the cancer with mortality reported in rare cases.
- BIA-ALCL has been reported globally in patients with an implant history that includes Allergan's and other manufacturers' breast implants with various surface properties, styles, and shapes. Most of the cases in the literature reports describe a history of the use of textured implants.
- You should consider the possibility of BIA-ALCL when a patient presents with late onset, persistent peri-implant seroma. In some cases, patients presented with capsular contracture or masses adjacent to the breast implant. When testing for BIA-ALCL, collect fresh seroma fluid and representative portions of the capsule, and send to a laboratory with appropriate expertise for pathology tests to rule out ALCL, including immunohistochemistry testing for CD30 and ALK (anaplastic lymphoma kinase). If your patient is diagnosed with peri-implant BIA-ALCL, develop an individualized treatment plan in coordination with a multi-disciplinary care team. Because of the small number of cases worldwide, there is no worldwide consensus on the treatment regimen for peri-implant BIA-ALCL. However, the National Comprehensive Cancer Network (NCCN) recommends surgical treatment that includes implant removal and complete capsulectomy ipsilaterally as well as contralaterally, where applicable.[32]
- Report *all confirmed cases* of BIA-ALCL to the FDA (https://www.fda.gov/Safety/MedWatch). In some cases, the FDA may contact you for additional information. The FDA will keep the identities of the reporter and the patient confidential.
- FDA also recommends reporting cases of BIA-ALCL to the PROFILE Registry (https://www.thepsf.org/research/clinical-impact/profile.htm) where you can submit more comprehensive case data. This will help provide a better understanding of the etiology of BIA-ALCL.
- For additional information on FDA's analysis and review of BIA-ALCL, please visit www.fda.gov/medical-devices/breast-implants/questions-and-answers-about-breast-implant-associated-anaplastic-large-cell-lymphoma-bia-alcl

Additional Complications

- After breast implant surgery the following may occur and/or persist, with varying intensity and/or for a varying length of time: hematoma/seroma, implant extrusion, necrosis, delayed wound healing, and breast tissue atrophy/chest wall deformity
- Calcium deposits can form in the tissue capsule surrounding the implant with symptoms that may include pain and firmness
- Lymphadenopathy has also been reported in some women with implants

OTHER REPORTED CONDITIONS

Patients receiving breast implants have reported a variety of signs and symptoms such as joint pain, muscle aches, confusion, chronic fatigue, autoimmune diseases and others. Individual patient risk for developing these symptoms has not been well-established. Some patients report complete resolution of symptoms when the implants are removed without replacement.

There have been reports in the literature of other conditions in women with silicone gel-filled breast implants. Many of these conditions, which are discussed below in Table 7, have been studied to evaluate their potential association with breast implants. Furthermore, there is the possibility of risks, yet unknown, which in the future could be determined to be associated with breast implants. It should also be noted that the cited references include data from augmentation and/or reconstruction patients, as well as from a variety of manufacturers and implant models.

Table 7: Other Reported Conditions

Connective Tissue Disease (CTD)

Potential Conditions

- Connective tissue diseases include diseases such as lupus, scleroderma, rheumatoid arthritis, and fibromyalgia
- There have been a number of published epidemiological studies (1988-2007) which have looked at whether having a breast implant is associated with having a typical or defined connective tissue disease
- A 2007 study concluded that the weight of the evidence did not support a causal association between implants and definite or atypical CTD.[7] The study size needed to conclusively rule out a smaller risk of connective tissue disease among women with silicone gel-filled implants would need to be very large (based on literature published from 1988-2016).[4,8,9,10,12, 13, 14,15,16,17,18] The published studies taken together show that breast implants are not significantly associated with a risk of developing a typical or defined connective tissue disease.[4,8,14,15] These studies do not distinguish between women with intact and ruptured implants. Only one study (2003) evaluated specific connective tissue disease diagnoses and symptoms in women with silent ruptured versus intact implants, but the study was too small to rule out a small risk[9]

Signs and Symptoms

- Scientific expert panels and literature reports published between 2000 and 2004 have found no evidence of a consistent pattern of signs and symptoms in women with silicone breast implants[4,19,20,21,22]
- Having these rheumatological signs and symptoms does not necessarily mean that a patient has a connective tissue disease; however, you should advise your patient that she may experience these signs and symptoms after undergoing breast implantation
- If a patient has an increase in these signs or symptoms, you should refer your patient to a rheumatologist to determine whether these signs or symptoms are due to a connective tissue disorder or autoimmune disease,
- Please see systemic symptoms information in the Boxed Warning on the cover page.

Cancer

Breast Cancer

- Reports in the medical literature (1995-2007) indicate that patients with breast implants are not at a greater risk than those without breast implants for developing breast cancer[7,23,24,25,26,27]
- Reports (2000-2004) have suggested that breast implants may interfere with or delay breast cancer detection by mammography and/or biopsy; however, other reports in the published medical literature indicate that breast implants neither significantly delay breast cancer detection nor adversely affect cancer survival of women with breast implants[23,26,28,29,30]
- A large follow-up study published in 2009 reported no evidence of an association between breast implants and cancer, and even showed a decreased incidence of breast cancer compared to the general population[31]

Brain cancer

- A study, published in 2001, has reported an increased incidence of brain cancer in women with breast implants as compared to the general population[33]
- The incidence of brain cancer, however, was not significantly increased in women with breast implants when compared to women who had other plastic surgeries
- A review of 4 large studies, published in 2009, in women with cosmetic implants and an additional long-term follow-up study published in 2003 concluded that the evidence does not support an association between brain cancer and breast implants[31,34]
- A 2007 epidemiological review also lent support to the lack of causation between implants and any type of cancer[7]

Respiratory/ lung cancer

- Studies published between 2001 and 2009 reported an increased incidence of respiratory/lung cancer in women with breast implants[31,33,35]
- Other studies (published 1997-2003) of women in Sweden and Denmark have found that women who get breast implants are more likely to be current smokers than women who get breast reduction surgery or other types of cosmetic surgery[36,37,38]
- Several large studies, published between 2000 and 2006, have found no association between breast implants and respiratory/lung cancer[23,39,40,41,42]

Cervical/ vulvar cancer

- Two studies (2001, 2007) reported an increased incidence of cervical/vulvar cancer in women with breast implants[33,35]
- Another long-term follow-up study (2009) showed equivalent incidences of cervical cancer in women with breast implants compared to the general population[31]
- Other recent large studies (published between 2000-2006) concluded that the evidence does not support an association between reproductive system cancers and breast implants[23,39,40,41,42]

Other cancers

- There have been several studies published between 2000-2007 that examined the risk of other types of cancers, e.g., thyroid cancers, urinary system cancers, sarcoma, endocrine cancer, connective tissue cancer, cancer of the eye, and unspecified cancers in women with breast implants. All of those studies found no increased risk in women with breast implants[9,20,33,35,39,40,41,42]

Other Conditions

Neurological Disease, Signs, and Symptoms

- Some women with breast implants have complained of neurological symptoms (such as difficulties with vision, sensation, muscle strength, walking, balance, thinking or remembering things) or diseases (such as multiple sclerosis), which they believe are related to their implants. A scientific expert panel report (Institute of Medicine, 2000) found that the evidence for a neurological disease or syndrome caused by or associated with breast implants is insufficient or flawed.[4] Further review (2007) of the epidemiologic evidence also failed to find an association between implants and neurologic disease[7]

Suicide

- In several studies (2001-2004), a higher incidence of suicide was observed in women with breast implants[43,44,45,46]
- The reason for the observed increase is unknown, but it was found that women with breast implants had higher rates of hospital admission due to psychiatric causes prior to surgery, as compared with women who had breast reduction or in the general population of Danish women[44]

Effects on Children

- It is not known if a small amount of silicone may pass through from the breast implant silicone shell into breast milk during breastfeeding. Although currently there are no established methods for accurately detecting silicone levels in breast milk, a study published in 2000 measuring silicon (one component in silicone) levels did not indicate higher levels in breast milk from women with silicone gel-filled implants when compared to women without implants[47]
- In addition, concerns have been raised regarding potential damaging effects on children born to mothers with implants. Two studies, published in 2001 and 2002, in humans have found that the risk of birth defects overall is not increased in children born after breast implant surgery.[48,49] Although low birth weight was reported in a third study, other factors (for example, lower pre-pregnancy weight) may explain this finding.[50] This author recommended further research on infant health. A 2007 review of the evidence did not find that offspring of women with implants were at an increased risk for esophageal disorders, rheumatic diseases, or congenital malformations[7]

Potential Health Consequences of Gel Bleed

- Small quantities of low molecular weight (LMW) silicone compounds, as well as platinum (in zero oxidation state), have been found to diffuse (bleed) through an intact implant shell (2001 and 2003).[4,34] evidence is mixed as to whether there are any clinical consequences associated with gel bleed. For instance, studies published in 2000 and 2005 on implants implanted for a long duration have suggested that such diffusion may be a contributing factor in the development of capsular contracture[4] and lymphadenopathy.[51] However, evidence against gel bleed being a significant contributing factor to capsular contracture and other local complications is provided by the fact that there are similar or lower complication rates for silicone gel-filled breast implants than for saline-filled breast implants. Saline-filled breast implants do not contain silicone gel and, therefore, gel bleed is not an issue for those products. Furthermore, toxicology testing has indicated that the silicone material used in Allergan's implants does not cause toxic reactions when large amounts are administered to test animals. It should also be noted that studies reported in the literature (1987-1999) have demonstrated that the low concentration of platinum contained in breast implants is in the zero oxidation (most biocompatible) state[52,53,54,55]
- Allergan provided testing to identify the gel diffusion constituents (including the platinum species [or other catalysts]), the rate that the gel constituents diffuse out, and how that rate changes over time. Over 99% of the LMW silicones and platinum stayed in the implant. The overall body of available evidence supports that the extremely low level of gel bleed is of no clinical consequence.

ALLERGAN'S CORE STUDY

The Allergan *NATRELLE*® Silicone-Filled Breast Implant Core Study is the primary set of clinical data used to establish a reasonable assurance of safety and effectiveness of the *NATRELLE*® Silicone-Filled Breast Implants and *NATRELLE INSPIRA*® Breast Implants for breast augmentation, reconstruction, and revision. Please note that Core Study assessed both BIOCELL textured and smooth breast implants. BIOCELL textured breast implants were recalled in July 2019 due to a higher risk associated with BIA-ALCL and are no longer manufactured or marketed.

A summary of the Core Study is presented below. More information can also be found in the *NATRELLE*® Silicone-Filled Breast Implants Summary of Safety and Effectiveness Document (SSED) on the FDA's website *http://www.accessdata.fda.gov/cdrh_docs/pdf2/P020056b.pdf*.

Study Overview

The Allergan Core Study was a prospective,10-year, multicenter, single arm, observational clinical study conducted across 47 investigational sites in 715 women undergoing breast augmentation, reconstruction, and revision operations. Patients were enrolled between January 6, 1999 and June 30, 2000 and were serially followed at 0-4 weeks, 6 months, 1 year, and annually through 10 years. Patients in the MRI cohort were screened for breast implant rupture with scheduled MRIs at 1, 3, 5, 7, and 9 years. The final results through 10 years of patient follow-up are being reported.

Safety assessments included local complications rates, and effectiveness assessments including change in breast size (Augmentation patients only), patient and physician satisfaction with outcome (all patients), and quality of life (all patients).

The 715 women enrolled in the Allergan Core Study included 455 primary augmentation patients, 147 revision-augmentation patients, 98 primary reconstruction patients, and 15 revision-reconstruction patients.

The 10-year follow-up rates by cohort are 66.8% (280) for Primary Augmentation, 63.8% (74) for Revision-Augmentation, 75.4% (46) for Primary Reconstruction, and 80% (8) for Revision-Reconstruction.

A total of 264 patients were enrolled in the MRI arm of the Core Study to screen for breast implant rupture. This included 158 primary augmentation patients, 50 revision-augmentation patients, 51 primary reconstruction patients, and 5 revision-reconstruction patients.

The 10-year MRI compliance rate for the final MRI was 73.9% for the Primary Augmentation cohort, 77.8% for the Revision-Augmentation cohort, 76.1% for the Primary Reconstruction cohort, and 100% for the Revision-Reconstruction cohort.

Patient Demographics and Baseline Characteristics

Demographic information for the Core Study with regards to race is as follows: 86% of the Core Study patients were Caucasian; 5% were Hispanic; 3% were Asian; <1% were African American; and 5% were other or unknown. The median age at surgery was 34 years for Primary Augmentation patients, 42 for Revision-Augmentation patients, 48 years for Primary Reconstruction patients, and 54 years for Revision-Reconstruction patients. Approximately 56% of the Core Study patients were married. Approximately 83% had some college education.

Table 8: Patient Demographics by Cohort

	Primary Augmentation (N = 455)	Revision-Augmentation (N = 147)	Primary Reconstruction (N = 98)	Revision-Reconstruction (N = 15)
Race:				
Caucasian	83.6%	86.6%	93.9%	93.3%
Hispanic	7.0%	2.7%	2.0%	6.7%
Asian	3.9%	2.0%	3.1%	0%
African American	0%	0.7%	1.0%	0%
Other	3.3%	2.0%	0%	0%
Not Provided	2.2%	6.0%	0%	0%
Median Age[a]	34	42	48	54
Median Weight[a] (Range)	124 (90 - 200)	125 (95 - 189)	135 (91 - 222)	135 (116 - 180)
Married	48.1%	63.3%	76.5%	66.7%
College Education[b]	83.5%	85.0%	76.5%	66.7%

[a] At time of surgery

[b] Includes some college education, college graduates, post-college education

With respect to surgical characteristics in the Core Study, for Primary Augmentation patients, the most frequently used devices were smooth implants (59%), and the most common incision site was inframammary (46%). Over half of Primary Augmentation patients (54.9%) enrolled for augmentation only, and the remaining patients enrolled for augmentation with accompanying conditions as follows: 23.7% asymmetry, 15.8% ptosis, and 5.5% aplasia.

For Revision-Augmentation patients, the most frequently used devices were smooth implants (57%), and the most common incision site was inframammary (64%).

For Primary Reconstruction patients, the most frequently used devices were textured implants (64%), and the most common incision site was the mastectomy scar (59%).

For Revision-Reconstruction patients, the most frequently used devices were textured implants (56%), and the most common incision site was mastectomy scar (52%).

Table 9: Surgical Baseline Characteristics by Cohort

	All Cohorts (N = 1348)	Primary Augmentation (N = 908)	Revision-Augmentation (N = 288)	Primary Reconstruction (N = 127)	Revision-Reconstruction (N = 25)
Style Number					
40 (smooth)	44.5%	45.8%	46.9%	32.3%	32.0%
45 (smooth)	11.6%	13.2%	10.1%	3.9%	12.0%
110 (textured)	30.6%	26.9%	33.3%	52.0%	28.0%
120 (textured)	13.2%	14.1%	9.7%	11.8%	28.0%
Placement Site[a]					
Submuscular	69.1%	69.7%	60.4%	82.7%	76.0%
Subglandular	29.0%	29.6%	38.9%	6.3%	8.0%

[a] Other placement sites included subcutaneous and subtissue flap

As a note, supplemental safety information was also obtained from Allergan's Adjunct Study, the Danish Breast Implant Registry, an international clinical MRI study, and the literature to help assess long-term rupture rate and the consequences of rupture for this product. The literature, which had the most available information on the consequences of rupture, was also used to assess other potential complications associated with silicone gel-filled breast implants. The key literature information is referenced in this document.

Effectiveness Results

Effectiveness assessments included change in breast size (Primary Augmentation patients only), patient and physician satisfaction with outcome (all patients), and quality of life (QoL) (all patients). QoL is comprised of measures of self-esteem, body image, and general health outcomes assessed at baseline and Years 1, 2, 4, 6, 8, and 10. Change in breast size was assessed by cup/circumferential chest size measurements. Patient satisfaction was based on a 5-point scale assessment of satisfaction with implants at the time of follow-up visits. The QoL measures were the SF-36, Rosenberg Self Esteem Scale, the Body Esteem Scale, and the Rowland Expectation Scale.

Primary Augmentation Patients

For Primary Augmentation patients, 396 (87%) of the original 455 patients had a breast measurement within 18 months of surgery. Of these 396 patients, 41% increased by 1 cup size; 45% increased by 2 cup sizes; 8% increased by more than 2 cup sizes; and 5% had no increase or decrease for a variety of reasons including improving the shape and fullness of the breast, to correct congenital asymmetry, or atypical pre-implant breast measurement.

Of the original 455 patients, 279 (61.3%) provided a satisfaction rating at 10 years after implantation. Of these 279 patients, 86.0% indicated that they were definitely satisfied with their breast implants, 8.2% indicated they were somewhat satisfied, 2.2% indicated that they were neither satisfied nor dissatisfied, 1.8% were indicated they were somewhat dissatisfied, and 1.8% indicated they were definitely dissatisfied.

Physician satisfaction with patient results was rated in 279 cases (61.3%) at 10 years. Physicians reported being definitely satisfied with the breast implants in 88.9% of cases, somewhat satisfied in 5.7% of cases, neither satisfied nor dissatisfied in 1.4% of cases, somewhat dissatisfied in 2.9% of cases, and definitely dissatisfied in 1.1% of cases.

For Primary Augmentation patients, scores on the SF-36, which measures mental and physical health, showed a slight improvement in one scale (Reported Health Transition) and a slight worsening in six scales (Role Emotional Problems, Role Physical Health Problems, General Health, Social Functioning, Vitality, and Mental Health) after 10 years compared to before breast implantation, although all scales remained higher than the general U.S. female population. There was no significant change on the Rosenberg Self-Esteem Scale at 10 years. Scores on the Rowland Expectation instrument showed significant improvement in "self image," "social relations," and "daily living" at 10 years. Patient responses to questions on the Body Esteem Scale generally showed decreases in weight concern and physical condition and an increase with regard to sexual attractiveness.

Revision-Augmentation Patients

Revision-Augmentation patients did not undergo a measurement of breast cup size change because they were undergoing replacement of an existing breast implant.

Of the original 147 Revision-Augmentation patients, 74 (50.3%) provided a satisfaction rating at 10 years. Of these 74 patients, 73.0% indicated they were definitely satisfied with their breast implants, 10.8% indicated that they were somewhat satisfied, 2.7% indicated that they were neither satisfied nor dissatisfied, 6.8% indicated they were somewhat dissatisfied, and 6.8% indicated that they were definitely dissatisfied.

Physician satisfaction with patient results was rated in 74 cases (50.3%) at 10 years. Physicians reported being definitely satisfied with the breast implants in 75.7% of cases, somewhat satisfied in 8.1% of cases, neither satisfied nor dissatisfied in 5.4% of cases, somewhat dissatisfied in 6.8% of cases, and definitely dissatisfied in 4.1% of cases.

For Revision-Augmentation patients, the SF-36, which measures mental and physical health, showed no significant changes in all but one scale (Vitality), which decreased after 10 years. Scores on the Rowland Expectation instrument showed significant improvement in "self image," "social relations," and "daily living" at 10 years. Patient responses to questions on the Rosenberg Self Esteem Scale showed no changes 10 years after receiving implants. Patient responses to questions on the Body Esteem Scale regarding overall body image showed no changes, but a decrease with regard to physical condition was shown.

Primary Reconstruction Patients

Of the original 98 Primary Reconstruction patients, 43 (43.9%) provided a satisfaction rating at 10 years after implantation. Of these 43 patients, 67.4% indicated that they were definitely satisfied with their breast implants, 23.3% indicated that they were somewhat satisfied, and 9.3% indicated that they were neither satisfied nor dissatisfied.

Physician satisfaction with patient results was rated in 44 cases (44.9%) at 10 years. Physicians reported being definitely satisfied with the breast implants in 75.0% of cases, somewhat satisfied in 20.5% of cases, neither satisfied nor dissatisfied in 2.3% of cases, and somewhat dissatisfied in 2.3% of cases.

For Primary Reconstruction patients, scores on the SF-36, which measures mental and physical health, showed no changes after 10 years compared to before breast implantation. Scores on the Rowland Expectation instrument showed significant improvement in "self image" and "social relations" at 10 years. Patient responses on the Rosenberg Self Esteem Scale, and Body Esteem Scale showed no significant changes.

Revision-Reconstruction Patients

Of the original 15 Revision-Reconstruction patients, 8 (53.3%) provided a satisfaction rating at 10 years. Of these 8 patients, 87.5% were definitely satisfied with their breast implants and 12.5% were definitely dissatisfied with their breast implants.

Physician satisfaction with patient results was rated in 7 cases (46.7%) at 10 years. Physicians reported being definitely satisfied with the breast implants in 85.7% of cases and somewhat dissatisfied in 14.3% of cases.

For revision-reconstruction patients, statistical analyses were not performed on QoL results due to the small sample size though results were generally similar on the SF-36, which measures mental and physical health, Rosenberg Self Esteem Scale, and Body Esteem Scale and higher on the Rowland Expectation instrument after 10 years.

Safety Results

The cumulative complication rates at Years 3, 5, 7, and 10 are presented below in Tables 10-13. The reasons for reoperation at Years 3, 5, 7, and 10 and reasons for implant removal at Years 3, 5, 7, and 10 are presented in Tables 14-17 and Tables 18-21, respectively.

Table 10: Kaplan-Meier Risk Rates By Patient for Augmentation Cohort (N = 455)

Complication[a,b,c]		Year 3	Year 5	Year 7	Year 10
Any complication (including reoperation)[d]		25.3% (21.5, 29.6)	28.5% (24.5, 33.0)	30.5% (26.3, 35.1)	32.9% (28.6, 37.7)
Any reoperation		19.9% (16.4, 23.9)	25.5% (21.7, 29.8)	30.2 (26.1, 34.8)	36.1% (31.6, 40.9)
Implant removal with or without replacement		6.8% (4.8, 9.6)	11.3% (8.7, 14.7)	13.6% (10.7, 17.2)	20.9% (17.2, 25.2)
Implant removal with replacement		6.1% (4.2, 8.8)	9.3% (6.9, 12.4)	11.1% (8.4, 14.5)	18.6% (15.0, 22.8)
Implant removal without replacement		0.7% (0.2, 2.2)	2.3% (1.2, 4.3)	2.8% (1.6, 5.0)	2.8% (1.6, 5.0)
Asymmetry		2.7% (1.6, 4.8)	2.7% (1.6, 4.8)	3.0% (1.8, 5.1)	3.3% (2.0, 5.6)
Breast pain		8.3% (6.1, 11.3)	8.8% (6.5, 11.9)	10.5% (8.0, 13.9)	11.5% (8.7, 15.0)
Breast/skin sensation changes		1.6% (0.8, 3.3)	1.6% (0.8, 3.3)	1.6% (0.8, 3.3)	1.6% (0.8, 3.3)
Capsular contracture III/IV		10.7% (8.2, 14.0)	13.0% (10.1, 16.5)	16.2% (12.9, 20.1)	18.9% (15.4, 23.1)
Delayed wound healing		1.1% (0.5, 2.7)	1.1% (0.5, 2.7)	1.1% (0.5, 2.7)	1.1% (0.5, 2.7)
Hematoma		1.6% (0.7, 3.2)	1.6% (0.7, 3.2)	1.6% (0.7, 3.2)	1.6% (0.7, 3.2)
Hypertrophic scarring/ scarring		3.7% (2.2, 5.9)	4.2% (2.6, 6.5)	4.2% (2.6, 6.5)	4.2% (2.6, 6.5)
Implant malposition		5.4% (3.6, 7.9)	5.9% (4.0, 8.5)	5.9% (4.0, 8.5)	6.9% (4.8, 9.7)
Implant palpability/visibility		1.4% (0.6, 3.0)	1.6% (0.8, 3.4)	1.6% (0.8, 3.4)	1.6% (0.8, 3.4)
Implant rupture	MRI Cohort	2.0% (0.7, 6.1)	5.0% (2.4, 10.1)	7.4% (4.0, 13.2)	9.3% (5.3, 15.8)
	Non-MRI Cohort	2.2% (0.8, 5.8)	10.5% (6.7, 16.1)	11.1% (7.2, 16.9)	13.7% (9.3, 19.9)
Nipple complications		5.1% (3.4, 7.6)	5.7% (3.9, 8.3)	6.0% (4.1, 8.7)	6.3% (4.3, 9.1)
Ptosis		0.9% (0.3, 2.4)	1.7% (0.8, 3.5)	2.0% (1.0, 3.9)	2.0% (1.0, 3.9)
Seroma		1.8% (0.9, 3.5)	1.8% (0.9, 3.5)	1.8% (0.9, 3.5)	1.8% (0.9, 3.5)

Table 10: Kaplan-Meier Risk Rates By Patient for Augmentation Cohort (N = 455)

Complication[a,b,c]	Year 3	Year 5	Year 7	Year 10
Swelling	7.8% (5.6, 10.6)	7.8% (5.6, 10.6)	8.9% (6.6, 12.0)	9.2% (6.8, 12.4)
Wrinkling/Rippling	0.9% (0.4, 2.5)	1.5% (0.7, 3.2)	1.5% (0.7, 3.2)	1.8% (0.8, 3.7)
Other complications[e]	0.2% (0.0, 1.6%)	0.2% (0.0, 1.6%)	0.2% (0.0, 1.6%)	0.2% (0.0, 1.6%)

[a] Includes reports of only ≥ moderate severity for all complications except for reoperation, implant removal, implant extrusion, implant rupture, and pneumothorax
[b] There were no reports of the following complications: capsule calcification, irritation, lymphadenopathy, pneumothorax
[c] The following complications occurred at a rate less than 1.0% at all timepoints: bruising, gel migration, implant extrusion, infection, lymphedema, redness, skin rash, tissue necrosis
[d] 141 primary augmentation patients experienced at least one complication
[e] Other complications include flexion of pectoral muscle creating a deforming band obliquely beneath areola

Table 11: Kaplan-Meier Risk Rates By Patient for Revision-Augmentation Cohort (N = 147)

Complication[a,b,c]	Year 3	Year 5	Year 7	Year 10
Any complication[d] (including reoperation)	32.4% (25.4, 40.8)	34.0% (26.8, 42.5)	37.6% (30.0, 46.3)	38.6% (30.9, 47.5)
Any reoperation	32.4% (25.4, 40.8)	36.8% (29.4, 45.3)	40.7% (33.0, 49.3)	46.0% (38.0, 54.9)
Implant removal with or without replacement	11.4% (7.2, 18.0)	18.1% (12.6, 25.6)	24.4% (18.0, 32.5)	32.4% (25.0, 41.3)
Implant removal with replacement	10.1% (6.1, 16.4)	16.1% (10.9, 23.5)	21.8% (15.6, 29.8)	30.1% (22.8, 39.0)
Implant removal without replacement	2.3% (0.7, 6.8)	3.1% (1.2, 8.0)	4.0% (1.7, 9.4)	4.0% (1.7, 9.4)
Asymmetry	2.8% (1.1, 7.4)	5.3% (2.5, 10.7)	5.3% (2.5, 10.7)	6.5% (3.2, 12.8)
Breast pain	7.6% (4.3, 13.4)	8.5% (4.9, 14.5)	10.5% (6.3, 17.2)	11.7% (7.1, 18.8)
Breast/skin sensation changes	1.4% (0.3, 5.4)	2.2% (0.7, 6.6)	2.2% (0.7, 6.6)	2.2% (0.7, 6.6)
Bruising	2.1% (0.7, 6.3)	2.1% (0.7, 6.3)	3.0% (1.1, 7.8)	3.0% (1.1, 7.8)
Capsular contracture III/IV	16.8% (11.4, 24.1)	18.4% (12.8, 26.0)	20.2% (14.3, 28.1)	28.7% (21.3, 37.9)
Hematoma	2.1% (0.7, 6.3)	2.1% (0.7, 6.3)	2.1% (0.7, 6.3)	2.1% (0.7, 6.3)
Hypertrophic scarring	5.8% (2.9, 11.3)	6.6% (3.5, 12.3)	6.6% (3.5, 12.3)	6.6% (3.5, 12.3)

Table 11: Kaplan-Meier Risk Rates By Patient for Revision-Augmentation Cohort (N = 147)

Complication[a,b,c]		Year 3	Year 5	Year 7	Year 10
Implant malposition		4.4% (2.0, 9.5)	6.0% (3.1, 11.7)	6.0% (3.1, 11.7)	6.0% (3.1, 11.7)
Implant palpability/visibility		4.3% (2.0, 9.4)	6.0% (3.0, 11.6)	6.0% (3.0, 11.6)	6.0% (3.0, 11.6)
Implant rupture	MRI Cohort	0%	0%	0%	5.4% (1.4, 20.0)
	Non-MRI Cohort	1.8% (0.2, 11.8)	3.9% (1.0, 14.8)	3.9% (1.0, 14.8)	10.1% (3.8, 25.4)
Infection		1.4% (0.3, 5.4)	1.4% (0.3, 5.4)	1.4% (0.3, 5.4)	1.4% (0.3, 5.4)
Nipple Complications		1.4% (0.3, 5.4)	1.4% (0.3, 5.4)	1.4% (0.3, 5.4)	1.4% (0.3, 5.4)
Ptosis		1.5% (0.4, 5.8)	4.0% (1.7, 9.3)	4.9% (2.2, 10.5)	4.9% (2.2, 10.5)
Seroma		5.0% (2.4, 10.1)	5.0% (2.4, 10.1)	6.0% (3.0, 11.7)	6.0% (3.0, 11.7)
Swelling		6.3% (3.3, 11.8)	7.2% (3.9, 13.0)	8.2% (4.6, 14.5)	8.2% (4.6, 14.5)
Wrinkling/Rippling		4.6% (2.1, 9.9)	5.4% (2.6, 11.0)	5.4% (2.6, 11.0)	5.4% (2.6, 11.0)
Other complications[e]		0.7% (0.1, 4.9)	0.7% (0.1, 4.9)	0.7% (0.1, 4.9)	0.7% (0.1, 4.9)

[a] Includes reports of only ≥ moderate severity for all complications except for reoperation, implant removal, implant extrusion, implant rupture, and pneumothorax

[b] There were no reports of the following complications: capsule calcification, gel migration, implant extrusion, lymphadenopathy, lymphedema, pneumothorax, tissue/skin necrosis

[c] The following complications occurred at a rate less than 1.0% at all timepoints: delayed wound healing, irritation, redness, skin rash,

[d] 53 revision-augmentation patients experienced at least one complication

[e] Other complications include herniation following an auto accident

Table 12: Kaplan-Meier Risk Rates By Patient for Reconstruction Cohort (N = 98)

Complication[a,b]	Year 3	Year 5	Year 7	Year 10
Any complication (including reoperation)[c]	34.2% (25.5, 44.8)	37.3% (28.1, 48.4)	42.4% (32.4, 54.0)	47.0% (36.1, 59.3)
Any reoperation	43.0% (33.7, 53.5)	49.2% (39.5, 59.9)	54.3% (44.4, 64.9)	71.5% (61.2, 81.0)
Implant removal with or without replacement	19.9% (13.2, 29.5)	27.1% (19.1, 37.5)	29.6% (21.3, 40.3)	53.5% (42.8, 64.9)
Implant removal without replacement	3.5% (1.1, 10.6)	7.6% (3.5, 16.3)	7.6% (3.5, 16.3)	13.6% (7.1, 24.9)
Implant removal with replacement	16.8% (10.6, 25.9)	20.7% (13.7, 30.6)	24.8% (17.0, 35.3)	48.0% (37.1, 60.1)

Table 12: Kaplan-Meier Risk Rates By Patient for Reconstruction Cohort (N = 98)

Complication[a,b]		Year 3	Year 5	Year 7	Year 10
Asymmetry		17.0% (10.8, 26.3)	19.9% (12.9, 29.8)	19.9% (12.9, 29.8)	23.2% (15.4, 33.9)
Breast pain		3.1% (1.0, 9.3)	3.1% (1.0, 9.3)	4.8% (1.8, 12.6)	6.8% (2.8, 16.1)
Breast/skin sensation changes		1.0% (0.1, 7.1)	1.0% (0.1, 7.1)	1.0% (0.1, 7.1)	1.0% (0.1, 7.1)
Bruising		1.0% (0.1, 7.1)	1.0% (0.1, 7.1)	1.0% (0.1, 7.1)	1.0% (0.1, 7.1)
Capsular contracture III/IV		13.2% (7.7, 22.2)	16.1% (9.8, 25.8)	20.9% (13.4, 31.8)	24.6% (16.2, 36.2)
Delayed Wound Healing		1.0% (0.1, 7.2)	1.0% (0.1, 7.2)	1.0% (0.1, 7.2)	1.0% (0.1, 7.2)
Hematoma		0	1.5% (0.2, 10.4)	1.5% (0.2, 10.4)	1.5% (0.2, 10.4)
Hypertrophic scarring		5.5% (2.3, 12.7)	5.5% (2.3, 12.7)	5.5% (2.3, 12.7)	5.5% (2.3, 12.7)
Implant extrusion		1.0% (0.1, 7.1)	1.0% (0.1, 7.1)	1.0% (0.1, 7.1)	1.0% (0.1, 7.1)
Implant malposition		2.3% (0.6, 8.9)	2.3% (0.6, 8.9)	2.3% (0.6, 8.9)	2.3% (0.6, 8.9)
Implant palpability/visibility		2.5% (0.6, 9.6)	4.1% (1.3, 12.1)	4.1% (1.3, 12.1)	6.4% (2.3, 16.8)
Implant rupture	MRI Cohort	0%	11.9% (5.1, 26.2)	19.4% (10.2, 35.1)	35.4% (22.1, 53.6)
	Non-MRI Cohort	0	6.7% (1.0, 38.7)	6.7% (1.0, 38.7)	18.3% (4.6, 58.0)
Infection		3.2% (1.0, 9.5)	3.2% (1.0, 9.5)	3.2% (1.0, 9.5)	3.2% (1.0, 9.5)
Nipple Complications		3.3% (1.1, 9.8)	3.3% (1.1, 9.8)	3.3% (1.1, 9.8)	3.3% (1.1, 9.8)
Redness		2.1% (0.5, 8.3)	2.1% (0.5, 8.3)	2.1% (0.5, 8.3)	2.1% (0.5, 8.3)
Seroma		0	0	0	2.3% (0.3, 15.4)
Skin rash		2.0% (0.5, 7.9)	2.0% (0.5, 7.9)	2.0% (0.5, 7.9)	2.0% (0.5, 7.9)
Swelling		7.1% (3.5, 14.4)	7.1% (3.5, 14.4)	7.1% (3.5, 14.4)	7.1% (3.5, 14.4)
Tissue/skin necrosis		2.3% (0.6, 8.8)	2.3% (0.6, 8.8)	2.3% (0.6, 8.8)	2.3% (0.6, 8.8)
Wrinkling/Rippling		5.7% (2.4, 13.2)	8.7% (4.2, 17.4)	10.2% (5.2, 19.6)	10.2% (5.2, 19.6)
Other complications[d]		1.0% (0.1, 7.1)	1.0% (0.1, 7.1)	1.0% (0.1, 7.1)	1.0% (0.1, 7.1)

[a] Includes reports of only ≥ moderate severity for all complications except for reoperation, implant removal, implant extrusion, implant rupture, and pneumothorax

[b] There were no reports of the following complications: capsule calcification, gel migration, irritation, lymphadenopathy, lymphedema, pneumothorax, ptosis

[c] 39 primary reconstruction patients experienced at least one complication

[d] Other complications include complications such as upper pole crescent deformity

Table 13: Cumulative Incidence Rates for Revision-Reconstruction Cohort (N = 15)[a]

Complication[a,b,c]		Year 3	Year 5	Year 7	Year 10
Any complication (including reoperation)[d]		40.0% (16.3, 67.7)	40.0% (16.3, 67.7)	46.7% (21.3, 73.4)	46.7% (21.3,73.4)
Any reoperation		33.3% (11.8, 61.6)	33.3% (11.8, 61.6)	40.0% (16.3, 67.7)	46.7% (21.3, 73.4)
Implant removal with or without replacement		0%	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	20.0% (4.3, 48.1)
Implant removal without replacement		0%	0%	0%	6.7% (0.2, 31.9)
Implant removal with replacement		0%	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	13.3% (1.7, 40.5)
Asymmetry		6.7% (0.2, 31.9%)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)
Bruising		6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)
Capsular contracture III/IV		0%	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)
Implant malposition		6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	13.3% (1.7%, 40.5%)	13.3% (1.7, 40.5)
Implant palpability/visibility		6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)
Implant rupture	MRI Cohort	0%	0%	0%	0%
	Non-MRI Cohort	0%	0%	0%	6.7% (0.2, 31.9)
Seroma		6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)
Skin rash		6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)	6.7% (0.2, 31.9)
Other complications		0%	0%	0%	0%

[a] Due to the small sample size in the Revision-Reconstruction cohort, Kaplan-Meier risk rates were not computed. Cumulative incidence of First Occurrence of Complications with 95% confidence intervals are shown.

[b] Includes reports of only ≥ moderate severity for all complications except for reoperation, implant removal, implant extrusion, implant rupture, and pneumothorax

[c] There were no reports of the following complications: breast pain, breast/skin sensation changes, capsule calcification, delayed wound healing, gel migration, hematoma, hypertrophic scarring, implant extrusion, infection, irritation, nipple complications, lymphadenopathy, lymphedema, pneumothorax, ptosis, redness, tissue/skin necrosis, wrinkling/rippling

[d] 7 revision-reconstruction patients experienced at least one complication

Table 14: Main Reasons for Reoperation for Primary Augmentation Cohort

Main Reason for Reoperation[a]	Year 3 N= 115 Reoperations in 89 Patients	Year 5 N= 153 Reoperations in 113 Patients	Year 7 N= 180 Reoperations in 132 Patients	Year 10 N=221 Reoperations in 153 Patients
Asymmetry	4 (3.5%)	5 (3.3%)	5 (2.8%)	5 (2.3%)
Biopsy	11 (9.6%)	13 (8.5%)	22 (12.2%)	28 (12.7%)
Breast Mass/Cyst/Lump	1 (0.9%)	1 (0.7%)	3 (1.7%)	4 (1.8%)
Breast pain	1 (0.9%)	2 (1.3%)	3 (1.7%)	3 (1.4%)
Capsular contracture	37 (32.2%)	43 (28.1%)	48 (26.7%)	55 (24.9%)
Delayed wound healing	3 (2.6%)	3 (2.0%)	3 (1.7%)	3 (1.4%)
Hematoma/seroma	9 (7.8%)	10 (6.5%)	12 (6.7%)	13 (5.9%)
Implant extrusion	1 (0.9%)	1 (0.7%)	1 (0.6%)	1 (0.5%)
Implant malposition	18 (15.7%)	24 (15.7%)	26 (14.4%)	27 (12.2%)
Implant palpability	0	1 (0.7%)	1 (0.6%)	1 (0.5%)
Implant rupture (suspected)	1 (0.9%)	7 (4.6%)	12 (6.7%)	29 (13.1%)
Infection	0	2 (1.3%)	2 (1.1%)	2 (0.9%)
Necrosis	1 (0.9%)	1 (0.7%)	1 (0.6%)	1 (0.5%)
Nipple complications (unplanned)	1 (0.9%)	1 (0.7%)	1 (0.6%)	1 (0.5%)
Patient request for style/size change	5 (4.3%)	9 (5.9%)	9 (5.0%)	12 (5.4%)
Ptosis	16 (13.9%)	20 (13.1%)	21 (11.7%)	25 (11.3%)
Scarring/hypertrophic scarring	5 (4.3%)	8 (5.2%)	8 (4.4%)	8 (3.6%)
Wrinkling/rippling	1 (0.9%)	2 (1.3%)	2 (1.1%)	3 (1.4%)

[a] The reoperation rate excludes planned secondary surgeries. If more than one reason for a given reoperation was reported, the following hierarchy was used to determine a primary reason for that reoperation: rupture, infection, capsular contracture, extrusion, necrosis, hematoma/seroma, delayed wound healing, breast pain, implant malposition, wrinkling, palpability/visibility, asymmetry, breast tissue contour deformity, ptosis, scarring, nipple complications, device injury/iatrogenic, breast cancer mass, biopsy, and patient request for style/size change.

Table 15: Main Reasons for Reoperation for Revision-Augmentation Cohort

Main Reason for Reoperation[a]	Year 3 N=74 Reoperations in 46 Patients	Year 5 N= 90 Reoperations in 52 Patients	Year 7 N= 98 Reoperations in 57 Patients	Year 10 N= 108 Reoperations in 63 Patients
Asymmetry	3 (4.1%)	3 (3.3%)	3 (3.1%)	3 (2.8%)
Biopsy	6 (8.1%)	8 (8.9%)	8 (8.2%)	9 (8.3%)
Breast Cancer mass	1 (1.4%)	2 (2.2%)	3 (3.1%)	3 (2.8%)
Breast pain	1 (1.4%)	1 (1.1%)	1 (1.0%)	1 (0.9%)
Breast tissue contour deformity	1 (1.4%)	1 (1.1%)	1 (1.0%)	1 (0.9%)
Capsular contracture	12 (16.2%)	17 (18.9%)	20 (20.4%)	26 (24.1%)
Delayed wound healing	2 (2.7%)	2 (2.2%)	2 (2.0%)	2 (1.9%)
Device Injury – Iatrogenic or Traumatic	1 (1.4%)	1 (1.1%)	1 (1.0%)	1 (0.9%)
Hematoma/seroma	12 (16.2%)	13 (14.4%)	13 (13.3%)	13 (12.0%)
Implant extrusion	1 (1.4%)	1 (1.1%)	1 (1.0%)	1 (0.9%)
Implant malposition	8 (10.8%)	11 (12.2%)	11 (11.2%)	12 (11.1%)
Implant palpability/visibility	1 (1.4%)	1 (1.1%)	1 (1.0%)	1 (0.9%)
Implant rupture (suspected)	4 (5.4%)	4 (4.4%)	5 (5.1%)	7 (6.5%)
Infection	2 (2.7%)	2 (2.2%)	3 (3.1%)	3 (2.8%)
Nipple Complications (unplanned)	3 (4.1%)	3 (3.3%)	3 (3.1%)	3 (2.8%)
Patient request for style/size change	3 (4.1%)	3 (3.3%)	3 (3.1%)	3 (2.8%)
Ptosis	5 (6.8%)	8 (8.9%)	9 (9.2%)	9 (8.3%)
Scarring/hypertrophic scarring	6 (8.1%)	7 (7.8%)	7 (7.1%)	7 (6.5%)
Wrinkling/rippling	1 (1.4%)	1 (1.1%)	2 (2.0%)	2 (1.9%)
Other	1 (1.4%)	1 (1.1%)	1 (1.0%)	1 (0.9%)

[a] The reoperation rate excludes planned secondary surgeries. If more than one reason for a given reoperation was reported, the following hierarchy was used to determine a primary reason for that reoperation: rupture, infection, capsular contracture, extrusion, necrosis, hematoma/seroma, delayed wound healing, breast pain, implant malposition, wrinkling, palpability/visibility, asymmetry, breast tissue contour deformity, ptosis, scarring, nipple complications, device injury/iatrogenic, breast cancer mass, biopsy, and patient request for style/size change.

Table 16: Main Reasons for Reoperations for Reconstruction Cohort

Main Reason for Reoperation[a]	Year 3 N= 55 Reoperations in 41 Patients	Year 5 N= 65 Reoperations in 46 Patients	Year 7 N= 76 Reoperations in 50 Patients	Year 10 N= 94 Reoperations in 62 Patients
Asymmetry	8 (14.5%)	11 (16.9%)	12 (15.8%)	15 (16.0%)
Biopsy	4 (7.3%)	4 (6.2%)	8 (10.5%)	8 (8.5%)
Breast cancer	0	0	0	0
Breast Mass/Cyst/Lump	2 (3.6%)	2 (3.1%)	3 (3.9%)	3 (3.2%)
Breast pain	0	0	0	0
Breast tissue contour deformity	2 (3.6%)	2 (3.1%)	2 (2.6%)	2 (2.1%)
Capsular contracture	9 (16.4%)	10 (15.4%)	10 (13.2%)	12 (12.8%)
Delayed wound healing	1 (1.8%)	1 (1.5%)	1 (1.3%)	1 (1.1%)
Hematoma/seroma	6 (10.9%)	7 (10.8%)	8 (10.5%)	8 (8.5%)
Implant extrusion	2 (3.6%)	2 (3.1%)	2 (2.6%)	2 (2.1%)
Implant malposition	13 (23.6%)	14 (21.5%)	15 (19.7%)	16 (17.0%)
Implant rupture (suspected)	0	0	2 (2.6%)	14 (14.9%)
Infection	0	0	0	0
Necrosis	1 (1.8%)	1 (1.5%)	1 (1.3%)	1 (1.1%)
Nipple complications (unplanned)	1 (1.8%)	1 (1.5%)	1 (1.3%)	1 (1.1%)
Patient request for style/size change	2 (3.6%)	3 (4.6%)	3 (3.9%)	3 (3.2%)
Ptosis	2 (3.6%)	3 (4.6%)	4 (5.3%)	4 (4.3%)
Scarring/hypertrophic scarring	2 (3.6%)	3 (4.6%)	3 (3.9%)	3 (3.2%)
Wrinkling	0	1 (1.5%)	1 (1.3%)	1 (1.1%)

[a] The reoperation rate excludes planned secondary surgeries. If more than one reason for a given reoperation was reported, the following hierarchy was used to determine a primary reason for that reoperation: rupture, infection, capsular contracture, extrusion, necrosis, hematoma/seroma, delayed wound healing, breast pain, implant malposition, wrinkling, palpability/visibility, asymmetry, breast tissue contour deformity, ptosis, scarring, nipple complications, device injury/iatrogenic, breast cancer mass, biopsy, and patient request for style/size change.

Table 17: Main Reasons for Reoperations for Revision-Reconstruction Cohort

Main Reason for Reoperation[a]	Year 3 N= 7 Reoperations in 5 Patients	Year 5 N=8 Reoperations in 5 Patients	Year 7 N= 9 Reoperations in 6 Patients	Year 10 N=12 Reoperations in 7 Patients
Asymmetry	0	1 (12.5%)	1 (11.1%)	2 (16.7%)
Biopsy	0	0	0	1 (8.3%)
Breast tissue contour deformity	0	0	0	0
Capsular contracture	1 (14.3%)	1 (12.5%)	1 (11.1%)	2 (16.7%)
Delayed wound healing	0	0	0	0
Hematoma/seroma	0	0	0	0
Implant malposition	0	0	0	0
Implant rupture (suspected)	0	0	0	0
Infection	0	0	0	0
Nipple complications (unplanned)	5 (71.4%)	5 (62.5%)	5 (55.6%)	5 (41.7%)
Patient request for style/size change	0	0	0	0
Ptosis	0	0	1 (11.1%)	1 (8.3%)
Scarring/hypertrophic scarring	1 (14.3%)	1 (12.5%)	1 (11.1%)	1 (8.3%)
Wrinkling	0	0	0	0
Other	0	0	0	0

[a] The reoperation rate excludes planned secondary surgeries. If more than one reason for a given reoperation was reported, the following hierarchy was used to determine a primary reason for that reoperation: rupture, infection, capsular contracture, extrusion, necrosis, hematoma/seroma, delayed wound healing, breast pain, implant malposition, wrinkling, palpability/visibility, asymmetry, breast tissue contour deformity, ptosis, scarring, nipple complications, device injury/iatrogenic, breast cancer mass, biopsy, and patient request for style/size change.

Table 18: Main Reasons for Implant Removal for Augmentation Cohort

Main Reason for Implant Removal[a]	Year 3	Year 5	Year 7	Year 10
	N= 57 Explants in 30 Patients	N= 92 Explants in 49 Patients	N= 107 Explants in 58 Patients	N=156 Explants in 84 Patients
Asymmetry	3 (5.3%)	6 (6.5%)	7 (6.5%)	7 (4.5%)
Biopsy	0	0	1 (0.9%)	1 (0.6%)
Breast cancer	1 (1.8%)	1 (1.1%)	2 (1.9%)	2 (1.3%)
Breast pain	0	2 (2.2%)	4 (3.7%)	5 (3.2%)
Breast tissue contour deformity	0	1 (1.1%)	1 (0.9%)	1 (0.6%)
Capsular contracture	25 (43.9%)	31 (33.7%)	36 (33.6%)	50 (32.1%)
Hematoma/seroma	0	0	0	0
Implant extrusion	1 (1.8%)	1 (1.1%)	1 (0.9%)	1 (0.6%)
Implant malposition	8 (14.0%)	11 (12.0%)	11 (10.3%)	11 (7.1%)
Implant rupture (suspected)	1 (1.8%)	5 (5.4%)	10 (9.4%)	27 (17.3%)
Infection	0	2 (2.2%)	2 (1.9%)	2 (1.3%)
Patient request for style/size change	12 (21.1%)	22 (23.9%)	22 (20.6%)	31 (19.9%)
Ptosis	4 (7.0%)	6 (6.5%)	6 (5.6%)	12 (7.7%)
Wrinkling	2 (3.5%)	4 (4.4%)	4 (3.7%)	6 (3.9%)

[a] If more than one reason for a given implant removal was reported, the following hierarchy was used to determine a primary reason for that removal: rupture, infection, capsular contracture, extrusion, necrosis, hematoma/seroma, delayed wound healing, breast pain, implant malposition, wrinkling, palpability/visibility, asymmetry, breast tissue contour deformity, ptosis, scarring, nipple complications, device injury/iatrogenic, breast cancer mass, biopsy, and patient request for style/size change.

Table 19: Main Reasons for Implant Removal for Revision-Augmentation Cohort

Main Reason for Implant Removal[a]	Year 3	Year 5	Year 7	Year 10
	N= 29 Explants in 16 Patients	N= 46 Explants in 25 Patients	N= 61 Explants in 33 Patients	N=78 Explants in 42 Patients
Asymmetry	0	1 (2.2%)	1 (1.6%)	1 (1.3%)
Biopsy	0	0	0	0
Breast cancer mass	0	1 (2.2%)	2 (3.3%)	2 (2.6%)
Breast pain	1 (3.5%)	1 (2.2%)	1 (1.6%)	1 (1.3%)
Capsular contracture	5 (17.2%)	12 (26.1%)	18 (29.5%)	28 (35.9%)
Implant extrusion	0	0	0	0
Implant malposition	5 (17.2%)	10 (21.7%)	10 (16.4%)	14 (18.0%)
Implant palpability/visibility	1 (3.5%)	1 (2.2%)	1 (1.6%)	1 (1.3%)
Implant rupture (suspected)	3 (10.3%)	3 (6.5%)	4 (6.6%)	6 (7.7%)
Infection	1 (3.5%)	1 (2.2%)	2 (3.3%)	2 (2.6%)
Patient request for style/size change	7 (24.1%)	8 (17.4%)	10 (16.4%)	11 (14.1%)
Ptosis	2 (6.9%)	4 (8.7%)	6 (9.8%)	6 (7.7%)
Scarring/hypertrophic scarring	2 (6.9%)	2 (4.4%)	2 (3.3%)	2 (2.6%)
Wrinkling/rippling	0	0	2 (3.3%)	2 (2.6%)
Other	2 (6.9%)	2 (4.4%)	2 (3.3%)	2 (2.6%)

[a] If more than one reason for a given implant removal was reported, the following hierarchy was used to determine a primary reason for that removal: rupture, infection, capsular contracture, extrusion, necrosis, hematoma/seroma, delayed wound healing, breast pain, implant malposition, wrinkling, palpability/visibility, asymmetry, breast tissue contour deformity, ptosis, scarring, nipple complications, device injury/iatrogenic, breast cancer mass, biopsy, and patient request for style/size change.

Table 20: Main Reasons for Implant Removal for Reconstruction Cohort

Main Reason for Implant Removal[a]	Year 3	Year 5	Year 7	Year 10
	N= 23 Explants in 19 Patients	N= 31 Explants in 25 Patients	N= 34 Explants in 27 Patients	N= 57 Explants in 44 Patients
Asymmetry	3 (13.0%)	7 (22.6%)	7 (20.6%)	12 (21.1%)
Breast cancer	0	0	0	0
Breast pain	0	0	0	0
Breast tissue contour deformity	0	0	0	0
Capsular contracture	6 (26.1%)	7 (22.6%)	7 (20.6%)	10 (17.5%)
Hematoma/seroma	1 (4.4%)	1 (3.2%)	1 (2.9%)	1 (1.8%)
Implant extrusion	1 (4.4%)	1 (3.2%)	1 (2.9%)	1 (1.8%)
Implant malposition	8 (34.8%)	9 (29.0%)	10 (29.4%)	12 (21.1%)
Implant rupture (suspected)	0	0	2 (5.9%)	15 (26.3%)
Infection	0	0	0	0
Necrosis	1 (4.4%)	1 (3.2%)	1 (2.9%)	1 (1.8%)
Patient request for style/size change	3 (13.0%)	4 (12.9%)	4 (11.8%)	4 (7.0%)
Ptosis	0	0	0	0
Wrinkling	0	1 (3.2%)	1 (2.9%)	1 (1.8%)

[a] If more than one reason for a given implant removal was reported, the following hierarchy was used to determine a primary reason for that removal: rupture, infection, capsular contracture, extrusion, necrosis, hematoma/seroma, delayed wound healing, breast pain, implant malposition, wrinkling, palpability/visibility, asymmetry, breast tissue contour deformity, ptosis, scarring, nipple complications, device injury/iatrogenic, breast cancer mass, biopsy, and patient request for style/size change.

Table 21: Main Reasons for Implant Removal for Revision-Reconstruction Cohort

Main Reason for Implant Removal[a]	Year 3	Year 5	Year 7	Year 10
	N=0 Explants	N= 1 Explant in 1 Patient	N= 1 Explant in 1 Patient	N= 3 Explants in 3 Patients
Asymmetry	N/A	1 (100%)	1 (100%)	2 (66.7%)
Breast tissue contour deformity	N/A	0	0	0
Capsular contracture	N/A	0	0	1 (33.3%)
Delayed wound healing	N/A	0	0	0
Implant malposition	N/A	0	0	0
Implant rupture (suspected)	N/A	0	0	0
Infection	N/A	0	0	0
Patient request for style/size change	N/A	0	0	0
Wrinkling	N/A	0	0	0

[a] If more than one reason for a given implant removal was reported, the following hierarchy was used to determine a primary reason for that removal: rupture, infection, capsular contracture, extrusion, necrosis, hematoma/seroma, delayed wound healing, breast pain, implant malposition, wrinkling, palpability/visibility, asymmetry, breast tissue contour deformity, ptosis, scarring, nipple complications, device injury/iatrogenic, breast cancer mass, biopsy, and patient request for style/size change.

Other Clinical Safety Outcomes

Below is a summary of clinical findings from the Core study with regard to connective tissue disease (CTD), CTD signs and symptoms, cancer, lactation complications, reproductive complications, and suicide. These issues, along with others, are being further evaluated as part of an Allergan post-approval study of patients followed through 10 years.

CTD Diagnoses

Five Primary Augmentation patients (1.1%) were reported to have a new diagnosis. Two had a diagnosis of rheumatoid arthritis at 7 months and at 3 years after implantation, 2 patients had a diagnosis of fibromyalgia at 3 years and 4.5 years after implantation, and 1 patient had a diagnosis of Raynaud Syndrome 5 years after implantation. Two Revision-Augmentation patients (1.4%) were reported to have a new diagnosis of fibromyalgia (at 10 months) and rheumatoid arthritis (after nearly 8 years). There were 2 Primary Reconstruction patients (2.0%) who reported CTDs through 10 years. One patient had a new diagnosis of an undifferentiated CTD at 3 months after implantation, and 1 patient with a new diagnosis of rheumatoid arthritis at 5.5 years after implantation. No Revision-Reconstruction patients had new diagnoses of a CTD through 10 years. It cannot be determined whether or not these CTD diagnoses were caused by the implants because there was no comparison group of similar women without implants.

CTD Signs and Symptoms

In the Core Study, self-reported signs and symptoms were collected in the categories of General, Gastrointestinal, Neurological, Urinary, Global, Pain, Fatigue, Fibromyalgia, Joint, Muscular, Skin, and Other. For Primary Augmentation patients at 10 years, statistically significant increases after accounting for age were found for the symptom categories of Skin, Urinary, and Other. For Primary Reconstruction patients at 10 years, statistically significant increases after accounting for age were found in the symptom category of Skin. For Revision-Augmentation and Revision-Reconstruction patients, no significant increases were found.

The Core Study was not designed to evaluate cause and effect associations because there is no comparison group of women without implants, and because other contributing factors, such as medications and lifestyle/exercise, were not studied. Therefore, it cannot be determined whether this increase was due to the implants or not, based on the Core Study. However, a patient should be aware that she may experience an increase in these symptoms after receiving breast implants.

Cancer

There were 4 Primary Augmentation patients (0.9%) with a new diagnosis of breast cancer through 10 years in the Allergan Core Study. In Primary Augmentation patients, there was 1 report of brain cancer and 1 report of thyroid cancer. There was 1 Revision-Augmentation patient ((0.7%) with a new diagnosis of breast cancer. There were no reports of other cancers in Revision-Augmentation patients.

There were 13 Primary Reconstruction patients (13.3%) with recurrence of breast cancer through 10 years. For Revision-Reconstruction patients, there were no reports of new diagnoses or reoccurrence of breast cancer. There were no reports of other cancers in Primary Reconstruction or Revision-Reconstruction patients.

Lactation Complications

Eighteen (23%) of the 78 Primary Augmentation patients who attempted to breastfeed following breast implantation in the Core Study through 10 years reported difficulty with breastfeeding. The most common difficulty was inadequate milk production. For the 20 Revision-Augmentation patients who attempted to breastfeed after receiving breast implants, 6 (30%) had difficulty breastfeeding, 5 due to inadequate milk production and 1 due to pain. One of the 98 Primary Reconstruction patients attempted to breastfeed following breast implantation in the Core Study through 10 years and did not experience any difficulties. No Revision-Reconstruction patients attempted to breastfeed after receiving breast implants.

Reproduction Complications

Thirty-six (8.0%) of the Primary Augmentation patients in the Allergan Core Study reported a reproduction problem through 10 years, most commonly miscarriage. Six (4.0%) Revision-Augmentation patients experienced a reproduction problem, most commonly miscarriage, through 10 years. Two (2%) Primary Reconstruction patients reported a reproduction problem through 10 years. No revision-reconstruction patients experienced a post-implantation reproduction problem.

Suicide

There was 1 report of suicide in the Primary Augmentation patients and 2 reports of suicide in the Revision-Augmentation patients in the Core Study through 10 years. There were no reports of suicide in the Primary Reconstruction and Revision-Reconstruction patients.

Additional Analyses

Detection of Breast Implant Rupture

Implant rupture was identified from 3 sources:

- Physician Exam
- Evidence of Rupture observed by the physician upon reoperation or device explant
- Devices identified as ruptured via MRI (options included "ruptured," "indeterminate," "unreadable film," "no evidence of rupture") for those patients participating in the serial MRI portion of this study

Detection of Breast Implant Rupture: Physician Exam

In some cases, implant ruptures were suspected based on physician exam. The implants were either confirmed to be ruptured upon explant, confirmed as non-ruptured upon explant, or confirmed as non-ruptured on MRI and not explanted. Table 22 includes information by cohort.

Table 22: Resolution of Rupture Suspected Based on Physician Exam

	Suspected Rupture based on Physician Exam	Rupture Confirmed on Explant	Non-Rupture Confirmed on Explant	Non-Ruptured Assessed on MRI
Augmentation	10	4	2	4
Revision-Augmentation	9[a]	2	2	4
Reconstruction	1	1	0	0
Revision-Reconstruction	0	0	0	0

[a] One suspected rupture was unconfirmed

ALLERGAN'S POST-APPROVAL STUDIES

Additional clinical safety and effectiveness data on *NATRELLE*® Silicone-Filled Breast Implants are being gathered through the BIFS post-approval study via two separate study arms: the BIFS-arm and the NBIR-arm. The NBIR-arm of the study was completed in 2022, and a summary of results is provided below.

BIFS-001 NBIR Arm Post-Approval Study

The purpose of the BIFS-001 NBIR-Arm was to collect reoperation data on *NATRELLE*® Silicone-Filled Breast Implants in the post-market environment. Data were collected only when NBIR-arm subjects returned to their implanting physician (i.e., study investigator) for a reoperation. Information on the reasons for reoperation was collected.

Summary of the Post-Approval Study Methods

Study Population

The NBIR-Arm consisted of subjects who were originally enrolled in the large cohort BIFS-001 post-approval clinical study. After all subjects had been implanted with their study devices for at least 5 years, the study was divided into 2 arms: the BIFS-arm and the NBIR-arm. Subjects were transferred into the NBIR-arm if they did not meet continuation criteria for annual follow-up through the BIFS-arm (e.g., not completing baseline or Years 1, 2, 3, and 4 follow-up questionnaires; not meeting original enrollment criteria such as being free of target diseases at baseline; or not being enrolled at a study site selected through cluster sampling methodology to continue follow-up through the BIFS-arm).

Data Source

Data from NBIR-arm subjects were collected when a subject returned to the study investigator for a reoperation. Reasons for reoperation were obtained. To maximize data collection, all study investigators were contacted at the end of the study to request entry of any reoperations that had not been previously provided. Of the 953 sites contacted, 283 were responsive.

Key Study Endpoints

The key study endpoint was the number of subjects with a reported reoperation. Information on the reasons for reoperation and whether an explant occurred were also collected.

Total number of Enrolled Study Sites and Subjects

The NBIR-arm consisted of 50,584 subjects including 36,732 subjects implanted with *NATRELLE*® Silicone-Filled Breast Implants and 13,852 subjects implanted with saline breast implants at 953 study sites. Of the 36,732 subjects implanted with *NATRELLE*® Silicone-Filled Breast Implants, 26,779 (72.9%) had undergone augmentation, 5,314 (14.5%) had undergone revision-augmentation, 4,024 (11.0%) had undergone reconstruction, and 615 (1.7%) had undergone revision-reconstruction. Of the 13,852 subjects implanted with saline breast implants, 12,858 (92.8%) had undergone augmentation, 827 (6.0%) had undergone revision augmentation, 140 (1.0%) had undergone reconstruction, and 27 (0.2%) had undergone revision-reconstruction.

Study visits and length of follow-up

Subjects in the NBIR-arm had been implanted with their study devices for at least 5 years and were followed for 10 years post-implantation. Data were collected only when they returned to their implanting physician (i.e., study investigator) for a reoperation.

Summary of the Post-Approval Study Results

Final safety findings (key endpoints)

Among subjects implanted with *NATRELLE*® Silicone-Filled Breast Implants, 180 (0.5%) had a reported reoperation. Among subjects implanted with saline breast implants,10 (<0.1%) had a reported reoperation.

All reasons for reoperation by frequency and percentage among patients who underwent reoperation are presented in Table 23. Of note, subjects may have undergone reoperation for more than one reason and may have had more than one reoperation. Thus, the total number of reasons exceed the number of patients who had a reoperation.

Table 23. Reasons for Reoperation

Reasons for Reoperation[a]	Silicone N=180 patients with reoperation n (%)[b]	Saline N=10 patients with reoperation n (%)[b]
Complications		
Capsular Contracture	72(40%)	1(10%)
Extracapsular Extravasation	3(1.7%)	0
Hematoma	1(0.6%)	0
Infection	3(1.7%)	0
Ptosis	21(11.7%)	0
Scarring	2(1.1%)	0
Seroma	3(1.7%)	0
Skin Necrosis	0	0
Wound Problems	0	0
Wrinkling/Rippling	12(6.7%)	1(10%)
Device Maintenance		
Correction of Asymmetry	39(21.7%)	0
Device Migration	10(5.6%)	0
Implant Malposition	16(8.9%)	1(10%)
Suspected Rupture/Deflation[c]	33(18.3%)	6(60%)
Patient Request/Other		
Patient wish change shape/size/style	79(43.9%)	4(40%)
Need for Biopsy	2(1.1%)	0
Staged Reconstruction	0	0
Tumor	3(1.7%)	0
Other	59(32.8%)	1(10%)
Missing	0	0

a Subjects may have more than one reason for reoperation.

b Percentages are based on subjects who had a reoperation.

c Rupture occurring in silicone and deflation in saline implants.

Most of the reoperations involved implant removal (175 subjects implanted with *NATRELLE*® Silicone-Filled Breast Implants and 10 subjects implanted with saline breast implants). No subjects in the NBIR-Arm reported BIA-ALCL in the capsule around breast implants.

Final effectiveness findings (key endpoints)

Effectiveness was not assessed for the NBIR-arm.

Study Strength and Weaknesses

The BIFS-001 NBIR-arm followed 50,000 subjects who were originally enrolled in the large cohort BIFS-001 post-approval clinical study through 10 years of implantation to assess the occurrence of reoperations in the post-market environment. Though there were no mandatory follow-up visits, study investigators had the opportunity to provide reoperation data either when it occurred or retrospectively.

However, the number of reoperations reported in the BIFS-001 NBIR-arm is low compared to the reoperation rates reported in the premarket Core Study (Tables 14-17). The difference may reflect possible missing reports of reoperation due to the lack of mandatory follow-up visits for the NBIR-arm. In contrast, the CORE study required annual in-office visits with the investigator. Furthermore, the study was limited to data obtained from study investigators only. Over the course of 10 years, subjects may have seen other medical practitioners instead of their implanting surgeon for a reoperation. Thus, the results may represent an underestimation of reoperations occurring in the post-market environment.

INSTRUCTIONS FOR USE

This product is intended for **single use only**. Do not reuse explanted implants.

Preoperative Education, Planning and Preparation

Education

ALLERGAN ACADEMY® Educational Materials are available through https://www.allergansurgicaleducation.com/ to supplement surgical knowledge of the dimensional techniques recommended for use with *NATRELLE*® Silicone-Filled Breast Implants and *NATRELLE INSPIRA*® Breast Implants.

Please contact your local plastic surgery sales representative or the Allergan Customer Care Department for further information on the **ALLERGAN ACADEMY**® or any other Allergan physician education initiatives.

Planning & Preparation

The size of the device may be determined preoperatively by means of dimensional planning or intraoperatively with the help of temporary sizer devices.

Proper surgical planning such as allowance for adequate tissue coverage, implant placement

(i.e., submuscular *vs.* subglandular), incision site, implant type, etc., should be made preoperatively.

Implant Size Selection

- Note that larger implants, subglandular placement, and an insufficient amount of skin/tissue available to cover the implant may cause the implant to be more palpable.
- Available tissue must provide adequate coverage of the implant.
- Carefully evaluate breast implant size and profile, incision placement, pocket dissection, and implant placement criteria with respect to the patient's anatomy and desired physical outcome.
- Select an implant consistent in size with the patient's chest wall dimensions, including base width measurements, bearing in mind the laxity of the tissue and the projection of the implant.
- A thorough discussion should be conducted with the patient, employing appropriate visual aids such as imaging, sizing implants, or other options to clarify her objectives and reduce the incidence of reoperation for size change.

Implant Placement

- Note that the possible risks of submuscular implant placement may include longer surgery, longer recovery, more postoperative pain, and greater difficulty when performing some reoperation procedures than subglandular placement. The possible benefits of submuscular implant placement may be less palpable implants, less likelihood of capsular contracture,[4] and easier imaging of the breast for mammography. Also, submuscular placement may be preferable if the patient has thin or weakened breast tissue.
- Note that subglandular placement may make surgery and recovery shorter, may be less painful, and may be easier to access for reoperation than the submuscular placement. However, this placement may result in more palpable implants, greater likelihood of capsular contracture,[57,58] and increased difficulty in imaging the breast with mammography.

Incision Site Selection

- Note that a periareolar incision, located around the border of the areola, involves cutting through the breast tissue and may be associated with a higher likelihood of breastfeeding difficulties as compared to the other incision sites.[59] Additionally, a periareolar incision may carry an increased risk of infection and change in sensation.
    - The inframammary incision is generally less concealed than the periareolar, but it is associated with less breastfeeding difficulty than the periareolar incision site.
    - The axillary incision is less concealed than the periareolar site.
- Take special care during breast reconstruction procedures carried out via the mastectomy scar to make sure that appropriate amounts of healthy tissue are available to cover the implant and that the implant is properly sized and positioned based upon careful preoperative planning.

- The periumbilical approach has not been studied in the pivotal study and should not be used for a wide variety of reasons, including potential damage to the implant shell.

Be aware that the unique nature of higher cohesive gels may require a larger incision compared to the incision size required for other silicone-filled implants to avoid skin edge trauma, gel fracture, or implant deformation. Gel fracture has been observed in *NATRELLE*® 410 implants filled with *Highly Cohesive* silicone gel, In Allergan's *NATRELLE*® 410 Pivotal Study, gel fracture occurred at a rate of less than 1%. To ensure an adequate incision length for *SoftTouch* and *Highly Cohesive* implants, an incision should be a minimum of 5.0 cm. For implants larger than 300 cc, an additional 0.5 cm of incision length should be added for each 50 cc of additional volume (e.g., for a 335 cc implant, use an incision length of 5.5 cm).

Intraoperative Device Examination and Handling

Examination of Silicone Gel-Filled Breast Implants

Prior to use, examine the breast implant for evidence of any particulate contamination, damage, or loss of shell integrity. If satisfactory, return the breast implant to the inner thermoform tray and cover it with the lid until implanted to prevent contact with airborne contaminants.

DO NOT implant any device that may appear to have particulate contamination, damage, or loss of shell integrity. A sterile back-up implant must be readily available at the time of surgery.
DO NOT implant any device that may appear to have leaks or nicks.
DO NOT implant damaged or contaminated breast implants.

Sterile Product

Each sterile silicone gel-filled breast implant is supplied in a sealed, double primary package. Sterility of the implant is maintained only if the thermoform packages, including the package seals, are intact. Use standard procedures to maintain sterility during transfer of the breast implant to the sterile field. Remove the breast implant and accessories from their packages in an aseptic environment and using talc-free gloved hands.

DO NOT use the product if the thermoform packages or seals have been damaged.
DO NOT resterilize the product.

Avoid unnecessary exposure of the breast implant to lint, talc, sponges, towels, skin oils, and other contaminants.

Prior to use, keep the breast implant in the inner thermoform and covered to prevent contact with airborne and surgical field particulate contaminants.

How to Open Sterile Product Package

Product identification stickers accompanying each device are provided within the internal product packaging. The stickers provide product-specific information and are designed to be attached to the patient's chart for identification purposes. Stickers are also included for the Device Tracking

Form and the patient's Device Identification Card.

Each sterile silicone gel-filled breast implant is supplied in a sealed, double primary package. Sterility of the implant is maintained only if the thermoform packages, including the package seals, are intact. Use standard procedures to maintain sterility during transfer of the breast implant to the sterile field.

Follow the steps below to remove the breast implant and accessories from their packages in an aseptic environment and using talc-free, gloved hands.

1. Peel open the lid of the outer thermoform package.
2. Invert the outer thermoform package over the sterile field, allowing the sealed inner thermoform package to gently fall into the field.
3. Peel open the lid of the inner thermoform package using the pull-tab.
4. Gently retrieve the breast implant. Prior to use, examine the breast implant for evidence of any particulate contamination, damage, or loss of shell integrity. If satisfactory, return the breast implant to the inner thermoform tray and cover it with the lid until implanted to prevent contact with airborne contaminants.

Device Implantation and Explantation Considerations

The implantation of silicone gel-filled breast implants involves a variety of surgical techniques. Therefore, use the method which your practice and discretion dictates to be best for the patient, and is consistent with this product insert data sheet. Some of the important surgical considerations that have been identified include the following:

<u>General</u>

- **NOTE:** Have more than one size breast implant in the operating room at the time of surgery to allow for flexibility in determining the appropriate size implant to be used. Back-up breast implants should be available during the procedure.
- **NOTE:** Smoking may interfere with the healing process.
- **DO NOT** use more than one implant per breast.
- **DO NOT** damage the breast implant with sharp surgical instruments such as needles and scalpels, blunt instruments such as clamps and forceps, or by overhandling and manipulation during introduction into the surgical pocket.
- **DO NOT** use excessive force during breast implant placement. Excessive force upon insertion of the implant may cause implant rupture or, for implants filled with *SoftTouch or Highly Cohesive* silicone gel, cause gel fracture.

- **DO NOT** manipulate the implant for either radial expansion, compression, or dissection of the pocket.

Surgical Placement

- Ensure incision is sufficiently large to facilitate insertion without excessive manipulation and handling of the device and to avoid damage to the device. Inadequate pocket dissection increases the risk of rupture and implant malposition.
- Plan out the pocket dissection preoperatively and perform pocket dissection accurately and with minimal trauma.
- Create a well-defined, dry pocket of adequate size and symmetry to allow the implant to be placed flat on a smooth surface.
- Obtain excellent hemostasis to avoid postoperative hematoma. Persistent, excessive bleeding must be controlled before implantation.
- Any postoperative evacuation of hematoma or seroma must be conducted with care to avoid breast implant contamination, or damage from sharp instruments.
- Consider use of a sterile delivery assistance sleeve (available separately) to assist with placement of the breast implant.
- Securely close the incision for the placement of the implant in several layers, whenever possible. The use of drains should be in accordance with the surgeon's own clinical judgment.

Explantation

- **NOTE:** If it is necessary to perform explantation of the implant, care must be taken to minimize manipulation of the product (particularly in regards to sharp-edged openings).
- **NOTE:** Explanted devices should be intraoperatively assessed by the explanting surgeon to identify the presence or absence of implant rupture, gel migration, and device deformity or gel fracture for implants filled with *Highly Cohesive* silicone gel. Explanted devices should be returned to Allergan for evaluation. Contact Allergan's Product Surveillance Department at 1.800.624.4261 for an Explant Kit and explant return instructions.

Method for Removing Ruptured Silicone Gel from the Surgical Pocket

- **Ruptured breast implants must be reported and should be returned to Allergan. In the event of breast implant rupture, contact Allergan Product Surveillance Department at 1.800.624.4261.**

- In the event of breast implant rupture, the following technique is useful for removal of the silicone mass.
  - Wearing double talc-free surgical gloves on one hand, use the index finger to penetrate the silicone mass. With the other hand, exert pressure on the breast to facilitate manipulation of the silicone mass into the double-gloved hand.
  - Once the silicone is in hand, pull the outer glove over the silicone mass and remove.
  - To remove any residual silicone, blot the surgical pocket with gauze sponges.
  - Avoid contact between surgical instruments and the silicone. If contact occurs, use isopropyl alcohol to remove the silicone from the instruments.

DOCUMENTATION THE PHYSICIAN SHOULD PROVIDE TO THE PATIENT

Breast implantation is an elective procedure and the patient must be well counseled on the risk-benefit relationship. The surgeon should provide each prospective patient with the following:

- *Patient Brochure and Patient Labeling*

  Designed specifically for Augmentation and for Reconstruction patients, the Patient Brochure, ***NATRELLE® Silicone-Filled Breast Implants and NATRELLE INSPIRA® Breast Implants: Important Factors Breast Augmentation and Reconstruction Patients Should Consider*** should be given to the patient during her initial visit/consultation to allow sufficient time for review. The surgeon and the patient should also discuss Allergan's patient labeling, ***Breast Augmentation/Reconstruction with NATRELLE® Silicone-Filled Breast Implants and NATRELLE INSPIRA® Breast Implants***, which is available online (www.allerganlabeling.com). These documents should be used to facilitate patient education on the risks and benefits of silicone gel-filled breast implant surgery and should be discussed with the patient during initial visit/consultation to allow sufficient time for review prior to making the decision to proceed with surgery. You should verify that the patient has an adequate understanding of the information.

- *Device Identification Card*

  Enclosed with each silicone gel-filled breast implant is Allergan's Device Identification Card. To complete Allergan's Device Identification Card, place one device identification sticker for each implant on the back of the card. Stickers are located on the internal product packaging attached to the label. If a sticker is unavailable, the lot number, catalog number, and description of the device may be copied by hand from the device label. Patients should be provided with these cards for personal reference. They should record their device identification information on the Device Identification Card.

- *Acknowledgement of Informed Decision and Patient Decision Checklist*

  In order to document a successful informed decision process, the ***Acknowledgement of Informed Decision and Patient Decision Checklist*** document (available separately at: www.allerganlabeling.com should be signed by both the patient and the surgeon. A copy should be provided to the patient and a copy should be retained in the patient's file.

ADDITIONAL SPECIFIC PRODUCT INFORMATION

Returned Goods Policy
Product returns should be handled through your Hospital or Surgical Sales Representative or the Allergan Customer Care Department at 800.766.0171. Return value is based on time limitations. All package seals must be intact to be eligible for return. Returned products may be subject to a restocking charge.

Reporting and Return of Explanted Devices
The reason for explantation should be reported and the explanted device returned to Allergan. In the event of an explantation, please contact Allergan's Product Surveillance Department at 1.800.624.4261 for an Explant Kit and explant return instructions.

ConfidencePlus® Limited Warranty
The *ConfidencePlus®* Limited Warranty provides lifetime replacement and limited financial reimbursement in the event of shell leakage or breakage resulting in implant rupture, subject to certain conditions as fully discussed in the *ConfidencePlus®* literature. Our *ConfidencePlus®* Premier Limited Warranty program applies automatically to every Allergan *NATRELLE®* Silicone-Filled Breast Implant or *NATRELLE INSPIRA®* Breast Implant recipient subject to the conditions discussed in the *ConfidencePlus®* literature. For more information, please visit www.cppwarranty.com or contact Allergan's Product Surveillance Department at 1.800.624.4261.

Product Ordering
To order directly in the U.S.A. or for product information, please contact your local Allergan Hospital or Surgical Sales Representative or the Allergan Customer Care Department at 1.800.766.0171.

Reporting Problems
The U.S. Food and Drug Administration (FDA) requires healthcare providers to report serious injuries involving medical devices (defined as those that need medical or surgical intervention to prevent permanent damage) to the manufacturer and/or to FDA. In addition, injuries or complications can be voluntarily reported directly by the patient to FDA's MedWatch.

If you have a patient who has experienced one or more serious problems related to her breast implants, you are encouraged to report the serious problem(s) to the FDA through the MedWatch

voluntary reporting system for her. Examples of serious problems include disability, hospitalization, harm to offspring, and medical or surgical intervention to prevent lasting damage.

You are also required to report any product problem or serious adverse event to Allergan. Deaths must be reported to Allergan and FDA. To report, use MedWatch form 3500, which may be obtained through FDA's website at https://www.fda.gov/Safety/MedWatch/. You may also call 1.888. INFO.FDA (1.888.463.6332), 10am-4pm Eastern Time, Monday through Friday. **Keep a copy of the completed MedWatch form for your records.**

This information reported to MedWatch is entered into databases to be used to follow safety trends (patterns) of a device and to determine whether further follow-up of any potential safety issues related to the device is needed.

The National Breast Implant Registry

The Plastic Surgery Foundation has developed the National Breast Implant Registry in collaboration with the FDA, patients and breast implant manufacturers to strengthen the post-market surveillance infrastructure for current and future breast implant devices in the United States. The National Breast Implant Registry, first launched in 2018, is a quality improvement initiative and safety surveillance registry that collects clinical, procedural and outcomes data at the time of operation and any subsequent reoperations for all US patients receiving breast implants. The National Breast Implant Registry allows surgeons to register implants with the manufacturers for the purpose of device tracking while also submitting data to the registry. Go to thepsf.org/NBIR to register and start data entry.

GRAPHICAL SYMBOLS

The following symbols appear in the package labels for *NATRELLE*® Silicone-Filled Breast Implants, *NATRELLE INSPIRA*® *Responsive* Breast Implants, *NATRELLE INSPIRA*® *SoftTouch* Silicone-Filled Breast Implants, and *NATRELLE INSPIRA*® *Cohesive* Silicone-Filled Breast Implants.

	Prior to using this device refer to the Directions for Use (DFU) Document at www.allerganlabeling.com or request a copy by calling 800-678-1605
	Dry Heat Sterilized
	For Single Use Only
	Expiration Date (YYYY-MM-DD)
	Lot
	Catalog Number
	Serial Number
	Not Made With Natural Rubber Latex
(01)	Global Trade Item Number
(17)	Expiration Date
(21)	Serial Number

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L034rev15 11/2024