Breast implant illness

4th Edition - 2023

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Preface

The 4th edition of the e-book *Breast Implant Illness* contains important updates, including a section on the new FDA guidelines on tumor risk associated with breast implants. Explantation is still in high demand and patients want to be well informed.

There are many possible reasons for explantation. The surgical indications are related to contracture, rupture, seroma or lymphoma. Also, some patients attribute a wide range of symptoms to the implants and seek a surgical solution. Or they may want to remove the implants simply because they have changed their minds about wearing them and would rather not go through another surgery when the time comes to have them replaced.

There is a growing perception that breast implants can be removed whenever the patient so wishes. Rather than replacing the implants at regular intervals, some patients decide to have them removed altogether.

The decision to remove the implants should be preceded by careful consideration and acceptance, with health and well-being as the priority.

Patients who come to the surgeon for explantation are not looking to be judged, but to be heard, understood and helped.

Enjoy the book!

Autoimmune/autoinflammatory syndrome induced by adjuvants

Introduction

'Autoimmune/autoinflammatory syndrome induced by adjuvants' is abbreviated as ASIA. Adjuvants are materials foreign to the body which can trigger chronic inflammation.

First described in 2011 by the Israeli physician Yehuda Shoenfeld, ASIA encompasses autoimmune diseases with similar symptoms caused by adjuvants (1). The list of these diseases and their triggers include siliconosis (silicone), macrophagic myofasciitis (aluminium hydroxide), Gulf War illness (squalene) and vaccine-related events (aluminium hydroxide). ASIA has also been associated with substances like iodine, mercury, mineral oil and titanium (2, 3).

Silicone was first used for medical purposes in 1947 to make bandages and has since become widely employed in a number of materials and prostheses. At first, it was considered an inert and stable substance, with a texture mimicking human tissue and resistant to degradation (4, 5).

However, researchers eventually realized that injectable silicone could cause severe local reactions and even reactions in locations far from the implant site, suggesting the material was not as immunologically inert as originally believed (6, 7).

In fact, since the 1960s, the use of breast implants in reconstructive and esthetic surgery has been shown to pose a risk of breast implant illness (BII) (8).

Other studies, though their results remain inconclusive, indicate that breast implant patients may also be at heightened risk of rheumatoid arthritis, Sjögren's syndrome, Raynaud's syndrome and scleroderma (9).

Symptoms

The most common symptoms of ASIA are arthritis, myalgia, fatigue and neurological manifestations. Table 1 shows a more detailed list of symptoms (10), but there may be others not listed.

Symptoms usually appear a few years after implantation.

Table 1: ASIA syptoms.

Myalgia, myositis, muscle weakness	Sleep disorders	Mood changes
Arthralgia or arthritis	Vertigo	Food intolerance
Chronic fatigue	Light and sound sensitivity	Fibromyalgia symptoms
Neurological manifestations	Swallowing difficulties	Irritable bowel
Cognitive changes, memory loss	Hair loss	Shortness of breath
Fever	Dry hair and skin	Night sweats
Dry mouth and eyes	Headache	Genital infection
Anxiety	Depression	Skin lesions

Source: the author.

Diagnosis

To establish a diagnosis, at least 2 major criteria, or 1 major criterion and 2 minor criteria, from Table 2 are required (1). For example, a patient developing arthritis after breast implantation meets the requirements for a diagnosis of ASIA.

Diagnosis is essentially clinical, meaning physical examination and medical history taking. There are no specific diagnostic laboratory markers for ASIA.

Table 2: Diagnostic criteria for ASIA.

Major criteria
Exposure to external stimuli (vaccine, silicone) preceding symptoms
Presence of clinical manifestations
- Myalgia, myositis or muscle weakness
- Arthralgia or arthritis
- Chronic fatigue, sleep disorders
- Neurological manifestations
- Cognitive changes, memory loss
- Fever, dry mouth
Elimination of the external stimuli improves symptoms
Biopsy of affected organs shows typical changes
Minor criteria
Presence of specific antibodies against the adjuvant (silicone)
Other manifestations such as irritable bowel syndrome
Specific HLA
Development of autoimmune disease such as scleroderma

Source: Shoenfeld, 2011

Risk groups

ASIA may affect patients with intact or ruptured implants. Silicone from the implant may be found in body regions far from the breast, such as the lymph nodes. The older the implant, the higher the risk of ASIA.

The risk groups for ASIA include (11):

— Patients with vitamin D deficiency (12)

— Patients with history of autoimmune reactions to adjuvants (silicone, vaccines)

— Patients with diagnosed autoimmune disorders (rheumatoid arthritis, scleroderma etc.)

— Patients with history of allergy and atopic disorders

— Patients predisposed to autoimmune disorders (family history of autoimmune disorders) (13)

Disease mechanism

ASIA occurs due to the presence of adjuvants (foreign materials) in the body which trigger chronic inflammation and the release of inflammatory substances (13).

The inflammatory substances triggered by the presence of adjuvants cause ASIA symptoms such as arthralgia, fatigue and fever.

Controversies

ASIA has been the object of controversies due to the broadness and lack of specificity of the diagnostic criteria. In fact, the criteria will identify many patients with unrelated autoimmune diseases and persons with similar symptoms but no autoimmune disease (14).

There is also some controversy over the disease mechanism. Some researchers believe the illness is caused by the toxicity of the silicone itself, rather than by the organism's autoimmune response to the presence of the foreign material (15).

Finally, some authors don't think the breast implant should be considered an adjuvant unless it is rupured. Moreover, throughout our lives we are exposed to an array of foreign substances, even to silicone in certain products, making it difficult to determine whether the implant has the effect of an adjuvant (16).

Treatment

ASIA may be treated surgically and/or with drugs such as corticoids, immunosuppressants and biological medications like adalimumab. Medication is rarely enough, though.

The gold standard surgical treatment is removal of the breast implant along with its capsule, a procedure sometimes referred to as *en bloc* explantation. Over the years, the organism forms a capsule around the implant. This is a normal and expected process.

The capsule is a collagen structure which forms around the breast implant in nearly every implant recipient. The most appropriate technical term for the procedure is total intact capsulectomy, but social media have popularized the expression *en bloc* explantation (17).

In patients with ASIA, the entire capsule should be removed because it contains silicone particles which might contaminate the breast tissue in case of rupture. By examining a biopsy of the capsule, the pathologist can identify normal changes in the implant (Figure 1) and detect the presence of silicone particles (Figure 2) (18).

Figure 1: A pathologist's report of a breast implant capsule biopsy showing normal findings.

Microscopic findings:

Right breast capsule: breast implant capsule with fibrosis and synovial metaplasia. No malignancy identified

Left breast capsule: breast implant capsule with fibrosis and synovial metaplasia. No malignancy identified

Source: the author.

Figure 2: Evidence of silicone particles in a breast implant capsule biopsy.

Microscopic findings:

Right breast capsule: fibrotic capsule with exogenous refringent material consistent with silicone. No malignancy identified

Left breast capsule: fibrotic capsule with exogenous refringent material consistent with silicone. No malignancy identified

Source: the author.

The terms used to describe the surgical removal of silicone implants and their capsules can be rather confusing. The following definitions are the most common:

Capsulotomy: The capsule is incised to make more room for the implant replacement. Thus, the capsule is not removed.

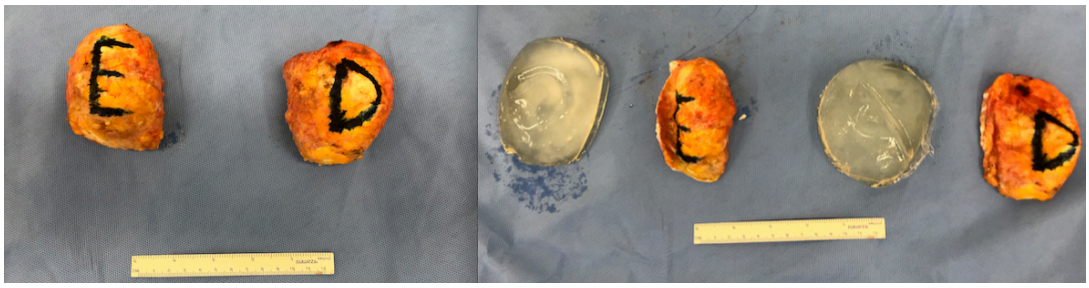
Partial capsulectomy: The capsule is partly removed.

Total capsulectomy: All the capsule is removed. Many surgeons use 'total capsulectomy' and '*en bloc* explantation' as synonyms, but total capsulectomy does not necessarily mean the capsule and the implant are removed in one piece. For example, the surgeon may open the capsule, remove the implant, and leave the capsule for later removal.

Total intact capsulectomy: The implant and the capsule are removed in one piece without rupturing the capsule or contaminating the surgical field with silicone. This is the ideal procedure for patients with breast implant illness (Figure 2).

***En bloc* explantation**: This term should be limited to a procedure in which the implant and the capsule are removed in one piece from patients with anaplastic large cell lymphoma (ALCL), leaving a so-called safety margin (removing the tissue adjacent to the capsule to ensure no tumor cells are left behind in the breast tissue (Figure 3).

Figure 3: *En bloc* explantation. Left: implants with capsules still attached. Right: implants removed from their capsules.



Source: the author

En bloc explantation does not always resolve ASIA symptoms. In some patients, symptoms improve as a result of the explantation, but in others they improve only temporarily, or not at all (13).

The medical literature shows that *en bloc* explantation alleviates

the most common systemic symptoms, such as arthralgia, myalgia, fatigue and memory loss, benefiting 50-100% of patients (19, 20, 21).

The mechanical aspects of the implant can trigger symptoms like breast pain and the sensation of hardening from contracture. In 75% of such cases explantation is curative (19).

On the other hand, if the patient has developed an autoimmune condition because of the silicone, surgery should be combined with medication. In any case, it is important to stress that explantation alone may not be enough to resolve ASIA symptoms.

Explantation helps relieve ASIA symptoms by removing the cause (silicone) triggering the inflammatory response.

The reason why some patients still have symptoms after explantation is that silicone particles remain in lymph nodes and other body tissues to which they have been carried by cells. The continued presence of silicone particles in these tissues maintains the inflammatory response, even after explantation.

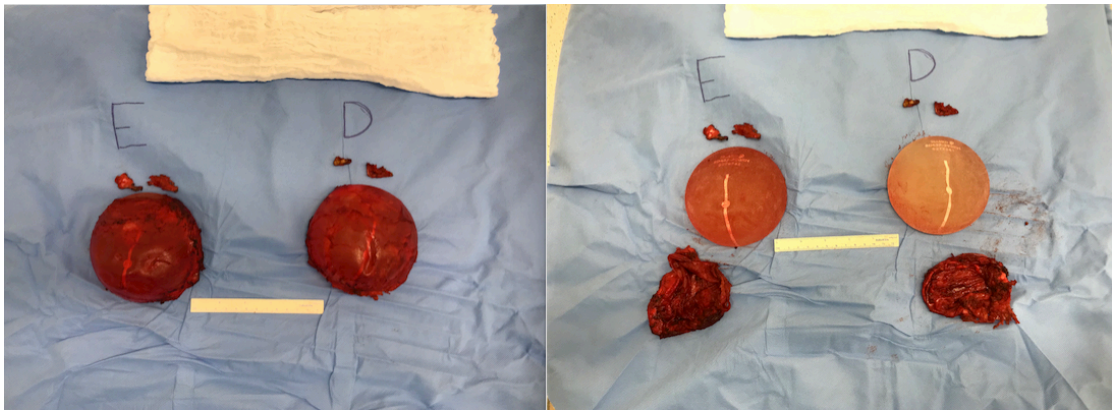
Plastic surgeons should inform their patients that explantation alone may not provide permanent relief of symptoms. The removal of the implant may also have implications, such as changes in breast esthetics and additional scarring, in addition to the complications that attend any type of surgery (19).

When the implant is underneath the pectoralis major muscle, the capsule may have adhered to the ribs, making it difficult or impossible to perform *en bloc* explantation. But every effort should be made to achieve total capsulectomy; thus, even when the implants and capsules cannot be removed in one piece, the capsules adhering to the muscles and ribs can usually still be completely removed (Figure 4).

However, in rare cases the capsule may adhere to the ribs in such a manner that it cannot be entirely removed. The surgeon will then remove what is possible and cauterize the remainder to avoid complications like bleeding and pneumothorax.

In addition, in patients with submuscular implants, the muscle may need to be repaired and reinserted in its original position.

Figure 4: Explantation of submuscular implants. Left: Implants and capsules in one piece. Right: implants with separate capsules. Note the capsule fragments in both images.



Source: the author

Preoperative stage

It is important to be well prepared for your first appointment with the plastic surgeon. Write down questions you might want to ask, and always check if the professional is a board-certified plastic surgeon.

Below are some suggestions on how to prepare for your appointment.

1. Is the professional a properly trained specialist and a board-certified plastic surgeon?

Verify the surgeon's credentials and curriculum.

2. Is the surgeon experienced in *en bloc* explantation?

The surgeon should be familiar with the procedure. Check the surgeon's references.

3. What lab tests will be performed on the capsule or fluid removed during explantation?

The capsule is usually sent to a pathologist for evaluation. Fluid or suspected lymphoma should be submitted to immunohistochemistry for CD30 detection and bacterial and fungal culture.

4. How long will the surgery take, what type of anesthesia will be used, and what incisions will be made? How long is the hospital stay, and when can I return to work and daily physical activities?

Surgery takes from 2 to 4 hours under general anesthesia. Incisions may coincide with earlier breast scars, or new incisions may be made along the edge of the areola or in inverted T. The hospital stay is 12-24 hours, but patients cannot go back to work for 15-30 days.

5. What are the postoperative risks?

Risks may be related to allergic reactions to anesthetics or to surgical complications, including hematoma, infection, wound rupture, and thrombosis.

6. Is it possible to photograph the explanted implants with and without the capsules attached?

Yes, if previously agreed with the plastic surgeon.

7. Is the patient allowed to keep the explanted implants?

Yes, as long as the hospital's safety guidelines are complied with.

Postoperative stage

Postoperative care depends on the type of surgery performed. For example, *en bloc* explantation may be performed alone or in combination with a modality of breast lift, such as mastopexy.

When *en bloc* explantation is performed without mastopexy, the patient should rest for 15 days and avoid driving, working, raising the arms or lifting objects. After this 15-day period, the patient can get back to routine, but light physical exercise will have to wait until after 30 days.

When *en bloc* explantation is combined with mastopexy, the resting period is 30 days, after which the patient can get back to her routine. No heavy physical exercise should be done until after 60 days.

In the first postoperative week the patient will be prescribed antibiotics, pain killers and other medications.

A drain may be necessary, with removal after 5-7 days.

A post-surgical bra should be worn for 60 days, and anti-thrombotic compression stockings should be worn for 10 days. In some cases, the plastic surgeon may prescribe drainage.

Usually, patients return to the office at 1 week, 1 month and 3 months to monitor the healing process and photograph the breasts.

Surgical risks

Every procedure is associated with risks, but these can be minimized if proper care is taken. Risks fall into two categories: anesthesia and surgery.

The first type is related to allergic reactions to the anesthetics administered.

The second type include infection, hematoma, seroma, areola necrosis, wound rupture, deep-vein thrombosis and thrombo-embolism. When the implant is underneath the muscle, there is a small risk of pneumothorax (air trapped between the lung and the chest wall).

Risks can be minimized through adequate preoperative evaluations, asepsis and antisepsis, compression stockings and sufficient rest.

Breast implant illness

Introduction

Breast implant illness (BII) should not be confused with ASIA (22). BII is a constellation of symptoms reported by implant recipients (fatigue, hair loss, anxiety, depression, light sensitivity, insomnia) which are not backed up by lab tests or imaging exams (23, 24, 25).

BII is known under several names, including adjuvant-induced autoimmune syndrome, adjuvant-induced autoimmune/ inflammatory syndrome, and silicone implant incompatibility syndrome (26).

The disease is not formally recognized by the medical community. It may occur regardless of the manufacturer and type of prosthesis, from 3 days to 30 years after implantation (27).

Fear of symptoms and complications associated with silicone implants has increased the demand for explantation. Since 2017, the demand for explantation has risen by 34.4% while the demand for implantation has decreased by 14.9% in the US (28). In 2019, about 33 thousand explantations were performed in the US alone (29).

Illnesses and symptoms associated with breast implants were first described in 1980. Due to these concerns, the FDA took silicone protheses off the market in 1992. Subsequent studies have tried to establish associations between breast implants and autoimmune or rheumatic disease, but the results have been inconclusive (30).

One review of the literature found a slightly increased risk of breast implant patients developing Sjögren syndrome and rheumatoid arthritis, but the study's authors acknowledged further evidence was required to confirm their findings (31).

Since the association between breast implants and systemic disease could not be proven, silicone prostheses were allowed back

on the market in 2006, with the manufacturers pledging to conduct long-term studies to determine their safety profile (30).

A growing number of patients and sympathizers are advocating for the recognition of BII as a medical entity. The movement is supported by well-organized social media groups, but it has also had the effect of aggravating anxiety over common and unspecific symptoms that may or may not be related to BII (32, 33, 34)

Mechanisms of breast implant illness

Many theories have been proposed to explain how silicone might induce systemic disease, but the exact mechanism remains unclear. Current theories point to mechanisms of inflammation, bacterial contamination, the alleged toxicity of certain implant components, and the activation of the autoimmune system (30, 35).

Below are some of the most well-known theories regarding the mechanism of BII.

- Autoimmune syndrome: First reported by Japanese researchers in 1964, the theory posits an excessive autoimmune response in genetically predisposed patients when exposed to a foreign body. The autoimmune response triggers chronic inflammation, resulting in enhanced allergic symptoms, immunodeficiency and autoimmune disease (36).
- Biofilm: Bacterial colonies firmly attached to the surface of human tissues or implants of different materials, causing chronic local inflammation, which may be responsible for capsule contracture and breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). The most commonly associated bacterial species is *Propionobacterium acnes*, also known as *Cutibacterium acnes*, an organism normally found on skin (26).
- Silicone toxicity: Silicone particles may leak from the implant and spread to other organs, especially the axillary lymph nodes. This could lead to inflammation and even cell death in such organs. Heavy metals employed in the manufacture of silicone implants can also spread to and damage other organs (9, 37, 38).
- Psychosomatic illness: BII symptoms may be a psychosomatic entity which amplifies common symptoms, distress, and disability, without an identifiable biological cause.
- Social media phenomenon: Information shared by online communities can increase anxiety and fear of wearing a silicone implant, leading some women to self-diagnose with BII.

BII has also been compared to chronic fatigue syndrome, repeated strain injury, fibromyalgia and sarcoidosis (an autoimmune disease triggered by foreign bodies) (39).

Controversies

BII is a hotly debated topic in the medical community, but more research is needed to prove the connection between silicone implants and the systemic symptoms patients report.

Many patients seem to be more willing to listen to friends and online communities than to specialists. There can be several reasons for this lack of trust in the specialists. Some patients become frustrated because they find no explanation for their symptoms, let alone a treatment (40, 41).

Disappointment in specialists of different areas may have led such patients to lose interest in conventional medicine and physicians. For them, the social media serve as a community for the exchange of experience and support of a kind not found in the doctor's office.

The medical community should seize the opportunity to improve communication with patients and to clearly present the benefits and risks associated with all relevant surgical procedures (42).

Curiously, the symptoms of BII are not observed in patients with silicone implants in body parts other than the breasts. The patients also display the psychological traits and symptoms of conditions like fibromyalgia and chronic fatigue syndrome. These symptoms are attributed to somatization or fixed beliefs about a foreign body (28, 43).

The blood of patients with breast implants has not been found to contain raised levels of heavy metals, failing another hypothesis for the etiology of BII (9).

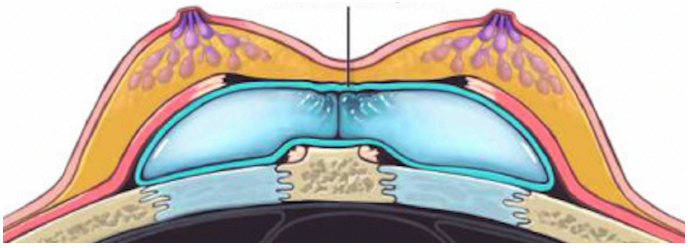
Moreover, the prevalence of BII is not significantly higher among patients with ruptured implants (heightened exposure to silicone) than among patients with intact implants. In other words, the integrity of the implant does not appear to have much effect on the development of clinical symptoms (9).

Another heated controversy is centered on whether the capsule must necessarily be removed at the time of explantation (29).

There is little evidence to justify total or *en bloc* capsulectomy in BII patients. But capsulectomy is beneficial in patients with severe contracture as it reduces the risk of seroma, of the capsules being palpable, or identifiable on imaging, and of silicone retention in the capsules (44, 45, 46, 47).

Capsulectomy is potentially contraindicated when the capsules are very thin, adherent to the ribs or submuscular, and in cases of symmastia (Figure 5) (27, 48, 49, 50, 51, 52).

Figure 5: Symmastia is the confluence of the breast tissue, giving the impression that the breasts are not separated.



Source: Guillier et al., 2020

One systematic review concluded that the primary indication for total capsulectomy is severe capsular contracture. No evidence was found to support total capsulectomy as a way of reducing the risk of BIA-ALCL or BII symptoms. *En bloc* explantation is formally indicated in confirmed or suspected cases of BIA-ALCL (48).

Diagnosis

Patients who self-diagnose with BII often forget that symptoms may be multifactor or related to other autoimmune or rheumatic diseases (Table 3) (53).

One should keep in mind the possibility of somatization disorders, which reflect a disproportionate anxiety over symptoms, even in the absence of medical evidence of disease (54, 55, 56).

Table 3: Differences between ASIA and BII

	Diagnosis	Specific test	Formally recognized	Mechanism	Exclusively silicone-related
ASIA	Defined criteria	No	Yes	Autoimmune	No
BII	Varied symptoms	No	No	Unknown	Yes

Symptoms

The BII symptoms most commonly reported are fatigue, cognitive problems such as memory loss, headache, muscle and joint pain, hair loss, recurrent infection, skin spots, lymph node swelling, and thyroid and adrenal dysfunction.

BII can only be diagnosed by ruling out all other diseases with similar symptoms. Therefore, BII patients should be examined not only by the plastic surgeon but by specialists in several areas. In fact, a multidisciplinary evaluation is highly recommended (Table 4) (57).

Table 4: Symptoms according to the specialists treating them.

Symptom	**Specialist**
Fatigue	Cardiologist, hematologist
Cognitive problems	Neurologist, psychiatrist
Anxiety	Psychiatrist
Muscle and joint pain	Rheumatologist, orthopedist
Hair loss	Dermatologist

Some websites providing support for implant recipients claim the the genes HLA B27, HLA DR52 and HLA DR53 are associated with a greater likelihood of BII symptoms (58, 59).

Many studies describe how BII symptoms subside over time, following explantation (9, 44). In one study, symptoms partially resolved in 74% of cases and completely disappeared in 23% (30).

Other researchers have reported improvement of symptoms in 50-75% of patients. However, it is important to stress that all studies show that a certain percentage of the patients do not improve by being submitted to explantation (10, 19, 60, 61).

A parameter which seems to improve in nearly all patients, even immediately after surgery, is breathing quality. Patients report breathing more comfortably after explantation. The benefit may be subjective, and no study has so far proved that implant removal improves lung function (62), but it may also be explained by the reduction of the weight on top of the chest, as observed in patients receiving breast reduction surgery (63).

FDA recommendations

In September 2020, as a result of years of activism on part of women involved the fight for the recognition of BII, the FDA ordered breast implant manufacturers to add a warning to their products listing potential negative effects (64).

FDA recommends that a boxed warning generally inform patients that:

- Breast implants are not considered lifetime devices;
- The chance of developing complications increases over time;
- Some complications 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);
- BIA-ALCL occurs more commonly in patients with textured breast implants than smooth implants, and deaths have occurred from BIA-ALCL; and
- Breast implants have been associated with systemic symptoms.

In addition, the 'gel bleed' theory posits that small silicone particles leak from the envelope of the prosthesis and end up accumulating in other organs. The prosthesis contains residues of heavy metals and toxic substances used in the manufacture (59).

In September 2022, the FDA announced that a review of the literature identified fewer than 20 cases of squamous cell carcinoma and fewer than 30 cases of lymphoma in implant capsules. The FDA concluded that patients should be informed of the risk, though rare, of developing squamous cell carcinoma or lymphoma in breast implant capsules.

The FDA recommends following up breast implant recipients with magnetic resonance imaging at intervals of 2-3 years, starting 5-

6 years after implantation. Breast ultrasound scanning is an acceptable alternative in asymptomatic patients (64).

On the other hand, there are studies showing an improvement of symptoms following explantation. It is difficult to say whether this is due to the removal of the object of somatization and anxiety, a placebo effect, or to a mechanism of chronic inflammation and autoimmunity (44). Improvement may be partial or temporary, and follow-up by a multiprofessional team is advisable (65).

Treatment

Treatment of BII should be tailored to the patient, and diagnosis should be differential. A thorough multidisciplinary investigation is necessary to rule out other diseases with similar symptoms. Following this investigation, the plastic surgeon should explain to the patient that *en bloc* explantation may or may not relieve symptoms (66).

Surgery may have several outcomes: a significant long-term improvement of all symptoms, a significant long-term improvement of some of the symptoms, temporary improvement of symptoms followed by relapse, and no improvement of symptoms at any time. Improvement of symptoms tends to happen within 6-12 months of the surgery, after which the chance of improvement is small (67).

Why remove the capsule around the implant?

Breast capsules contain cells called myofibroblasts, which are responsible for capsular contracture. Silicone particles from the implant are found in the capsule, inside or outside specialized cells such as histiocytes and giant cells (68).

Capsules may be thin, thick, nodular, calcified, or double. The synovial metaplasia observed in biopsies is formed as the breast tissue adapts to the movement of the implant. In cases of severe contracture, capsules should be removed to avoid seroma and palpability (69, 70).

The removed capsule should be examined by a pathologist. The incidence of BIA-ALCL is from 0.03% to 0.05% in patients with textured implants, and other tumors may be diagnosed, such as invasive carcinoma (0.16%), ductal carcinoma *in situ* (0.16%) and lobular carcinoma *in situ* (0.04%) (71).

The commensal bacterial genus most often found in biofilm is *Propionibacterium* (72, 73, 74).

Anaplastic large cell lymphoma

Introduction

Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) was first described over two decades ago, but has been receiving more attention from physicians and the media since 2016 (75).

BIA-ALCL is a T-cell non-Hodgkin's lymphoma. T cells are important components of our immune system. The incidence of BIA-ALCL is estimated to be 1 in 30,000 recipients of textured implants. Up until 2020, the FDA had received reports of 733 cases of BIA-ALCL, with 36 deaths around the world (76, 77).

The condition was first described by Keech and Creech in 1997, but only in 2011 did the FDA issue a warning about its association with silicone implants. In July 2019, the FDA asked manufacturers of Allergan breast implants to voluntarily stop marketing textured prostheses due to the risk of BIA-ALCL (78).

Considered a rare tumor, BIA-ALCL usually presents as a collection of fluid around the implant or capsule. In one study, the incidence is estimated to be 1 case in 500,000 breast implant recipients. The age of BIA-ALCL patients varies from 34 to 59 years (average 46 years). The tumor is most likely to develop 3-7 years after implantation (79).

The tumor has only been observed in patients with textured implants ('textured' means the surface is rough). No case has been associated with smooth prostheses (80).

Symptoms

The main symptom of BIA-ALCL is the sudden and spontaneous appearance of fluid around the implant or capsule, on average 8-10 years after surgery (81).

Less frequent symptoms include skin rash, hardening of the breasts due to capsular contracture, and the presence of nodules in the body due to swollen lymph nodes (82).

The presence of fluid in the breasts (known as seroma) is a very important symptom. Any seroma appearing after 1 year of implantation is suspected of ALCL. If the seroma manifests before 1 year of implantation, other causes such as trauma and infection should be considered (83).

Symptoms may present in two different ways. One is through late seroma, the other through the development of a tumor around the implant. The second form is associated with more severe disease (76).

Diagnosis

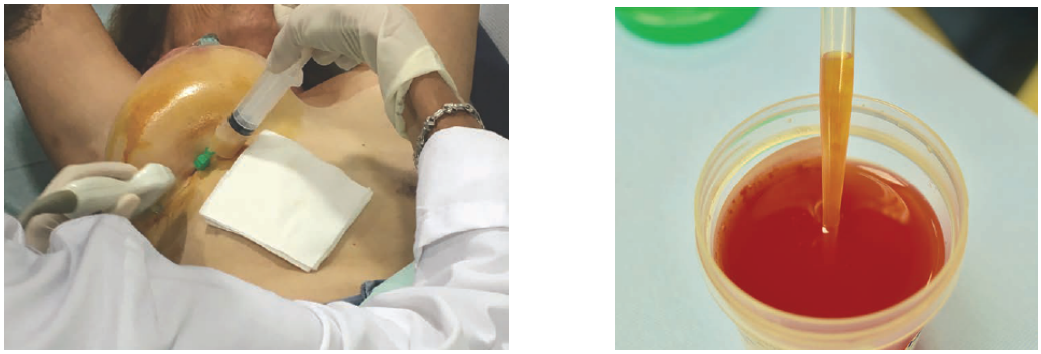
Diagnostic tests are used to detect the presence of fluid around the implant and breast tumors. In the first case, ultrasound is an adequate method, but magnetic nuclear resonance imaging is better to evaluate the implant itself and visualize breast tumors (84).

The fluid around the implant should be aspired through ultrasound-assisted puncture at a clinic or laboratory. In case of breast tumor formation, palpable lymph nodes or grade IV capsule contracture, the collected material should be submitted to pathology, cytology (detection of anaplastic large cells), immunohistochemistry (CD30 and ALK), and bacterial culture (85).

If the tests confirm the presence of atypical (anaplastic) cells and the immunohistochemical analysis is positive for CD30 and negative for ALK, the patient should undergo a PET scan (positron emission tomography) to verify the existence of tumors in other parts of the body (76, 85).

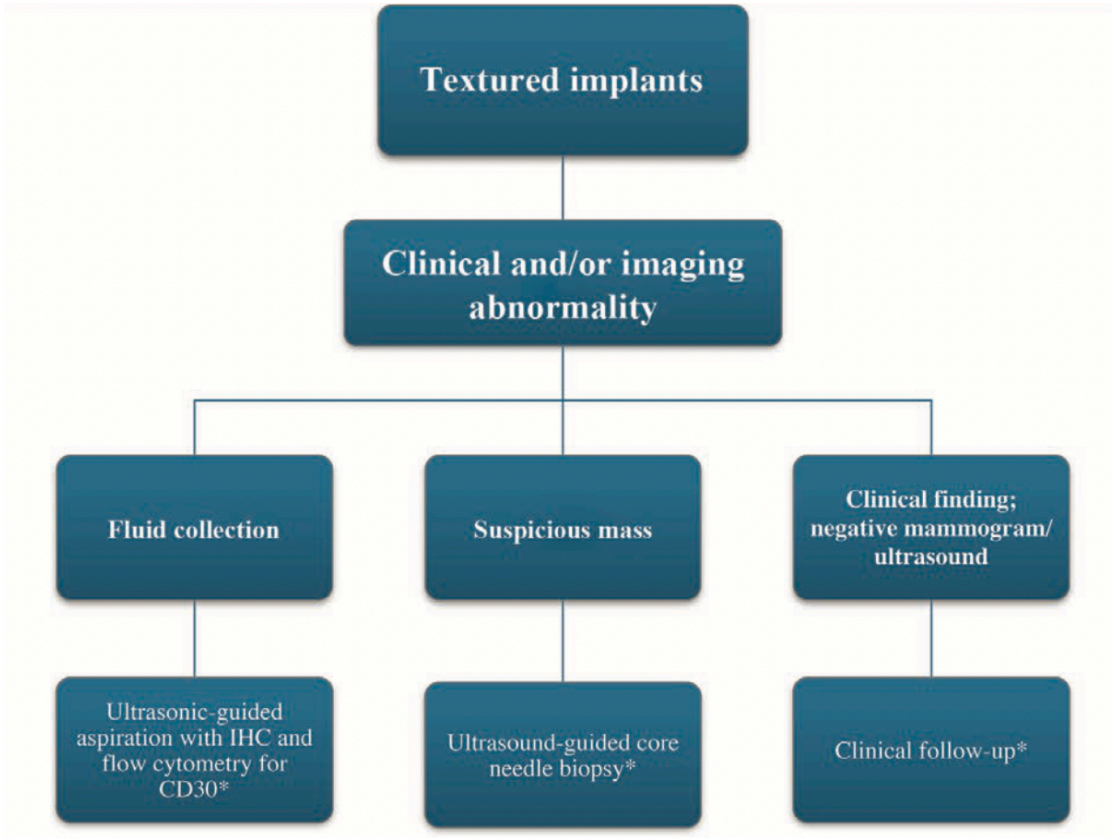
The aspired fluid is yellowish and bloody, as shown in Figure 6. Specific protocols are followed in the investigation of BIA-ALCL (Figure 7) (80, 86).

Figure 6: Left: Aspiration of breast fluid assisted by ultrasound. Right: Appearance of aspired fluid.



Source: Gidengil CA et al., 2015.

Figure 7: Protocol for evaluation of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL).



Source: Colwell A.S., 2021

Disease mechanism

A number of studies and theories have been put forward to explain the relationship between textured breast implants and lymphoma (87).

The most widely accepted theory is that the implant triggers a process of chronic inflammation which leads to the proliferation of specific cells (T cells) and the development of tumors in genetically predisposed patients (88).

Preoperative stage

Following confirmation, the patient should see the oncologist and, in some cases, the oncological surgeon. Other lab tests or scans may be necessary to define the tumor or rule out tumors in other body regions. In most cases, the tumor is limited to the capsule.

Treatment

Surgery is usually enough to treat the lymphoma. The procedure consists of removing the implant, the entire capsule and any tumor adhering to the capsule. The manifestion is bimodal, meaning that the tumor is either restricted to the capsule (most cases) or disseminated to other organs (76)

The ideal option is *en bloc* explantation, that is, removing the implant and the entire capsule in one piece. In some cases, especially when the implant is underneath the muscle, the entire capsule is removed but the procedure is not *en bloc*. Lymph nodes and tumors adhering to the capsule should be removed as well.

In early-stage lymphoma (stages I and II), breast reconstruction can be performed immediately after *en bloc* explantation, but in advanced lymphoma (stages III and IV), it should be postponed by 5 years (85).

The presence of lymphoma in one breast increases the risk of lymphoma in the other. Removal of the implant and capsule from the unaffected breast should therefore be considered.

Tumors are graded from I to IV according to severity. Stages I and II are considered less severe and easier to treat, while stages III and IV and considered advanced and severe.

Primary and less severe BIA-ALCL (stages I and II) respond well to surgical treatment, and disease-free survival rates are high. When the diagnosis is established early and the prosthesis and the entire capsule are removed *en bloc*, the cure rate is above 90% (90, 91).

Patients with advanced BIA-ALCL (stages III and IV) and lymph node metastases need both surgery and chemo/radiotherapy (89).

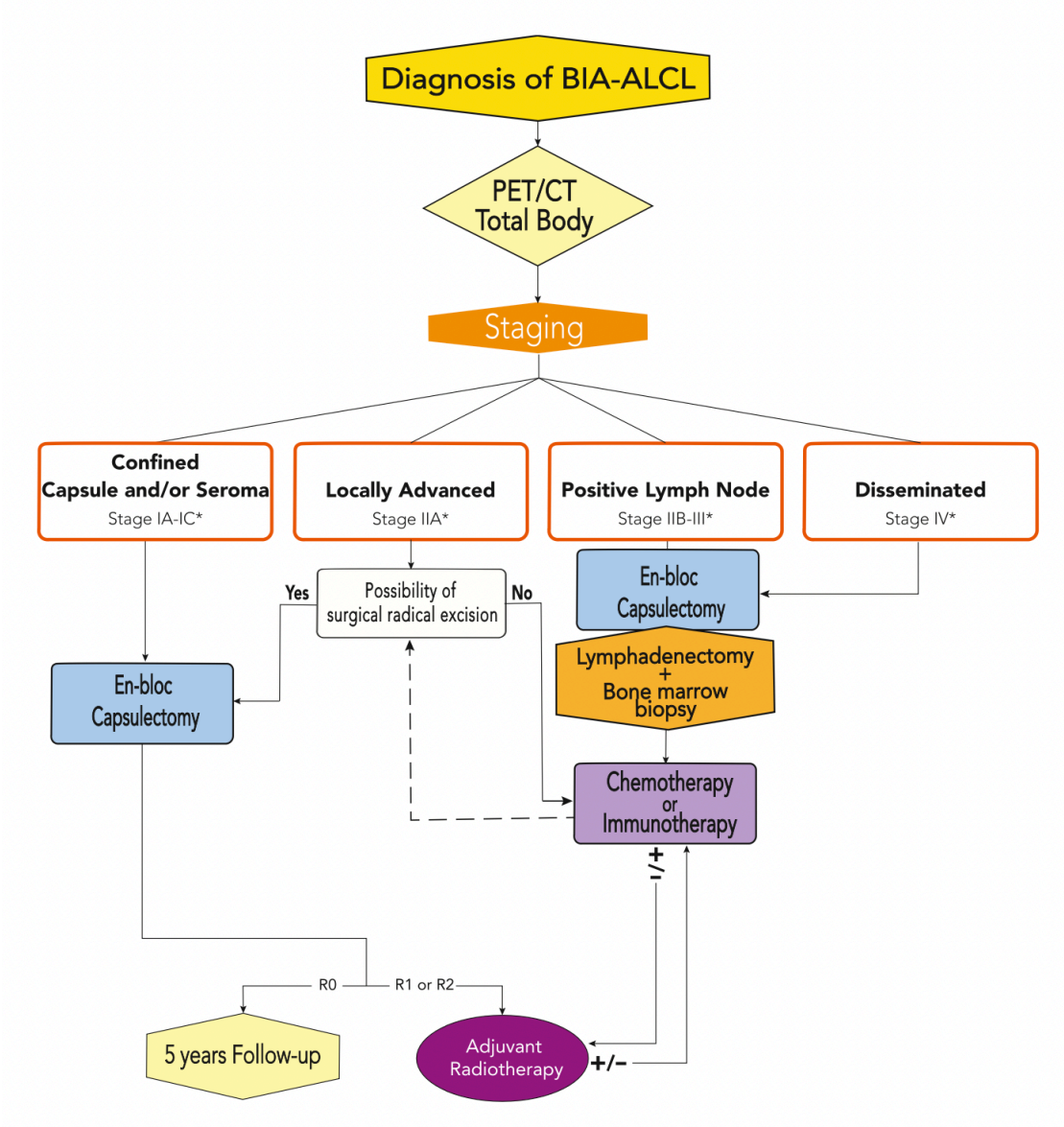
The standard treatment for stage I BIA-ALCL is *en bloc* explantation. If the pathologist concludes that the tumor has been completely removed, with tumor-free margins, the patient is considered cured (Figure 8).

Stage II BIA-ALCL is also treated with *en bloc* explantation, in addition to the removal of the tumor adjacent to the capsule and potentially involved lymph nodes (lymphadenectomy). If the excised lymph nodes are found to be compromised, postoperative chemotherapy and/or immunotherapy is prescribed.

Treatment of stage III and IV BIA-ALCL requires planning by a multidisciplinary team (oncologist, chest surgeon, plastic surgeon, oncological surgeon). The procedure includes *en bloc* explantation, removal of distant tumors, lymphadenectomy, bone marrow biopsy, chemotherapy, immunotherapy and/or radiotherapy (85).

Regardless of the stage, patients should be followed up with imaging every 3-6 months in the first 2 years, then annually until completing 5 years.

Figure 8: Treatment of BIA-ALCL according to stage.



Source: Longo B. et al, 2022

Postoperative stage

Following surgery, the patient should rest for 2-4 weeks, wear a surgical bra for 2 months, and maintain a follow-up schedule with the plastic surgeon.

This follow-up should be accompanied by an oncologist to detect a possible recurrence of the tumor. The patient should return to the doctor's office every 6 months for 2 years, then once a year for at least 5 years.

Mechanical complications in breast implants

Mechanical complications are the main reason why women wish to replace or remove prostheses and capsules. They can happen any time after implantation, but are more likely to occur 10-15 years after surgery. The prosthesis is not for lifelong use but has a useful life of around 15 years (92, 93).

After 15 years, 50% of implant recipients will need revision surgery to deal with pain, esthetic issues, or mechanical complications such as capsular contracture or rupture (94).

Contracture

The formation of a capsule around the prosthesis is an expected reaction when the organism is exposed to a foreign body triggering chronic inflammation. The inflammatory process leads to the migration of cells which deposit collagen and other substances, thereby forming a capsule isolating the prosthesis from the organism (81).

Some of the cells involved in building the capsule acquire muscle cell functions which allow them to contract. Over the years, these modified cells cause the capsule to contract, producing the phenomenon known as capsular contracture (95).

The incidence of capsular contracture ranges from 2.8% to 18.9% in the first 5-10 years. When patients receive a replacement implant, capsular contracture may recur in 18.1 to 39.7%. Placing the new implant underneath the muscles and using an acellular dermal matrix can reduce the incidence of capsular contracture (96).

The capsule is an inflammatory response to a foreign body. Under normal circumstances it helps keep the prosthesis in position, but it can become painful when the fibrous formation is excessive, leading to severe contracture (97).

Potential risk factors for severe contracture include radiotherapy, extended time of use, textured materials, postoperative hematoma and infection (98).

Capsular contracture is graded according to severity. The Baker classification system, using a scale from I to IV, is the most widely adopted (Table 5) (99).

Table 5: Baker's classification of capsular contracture.

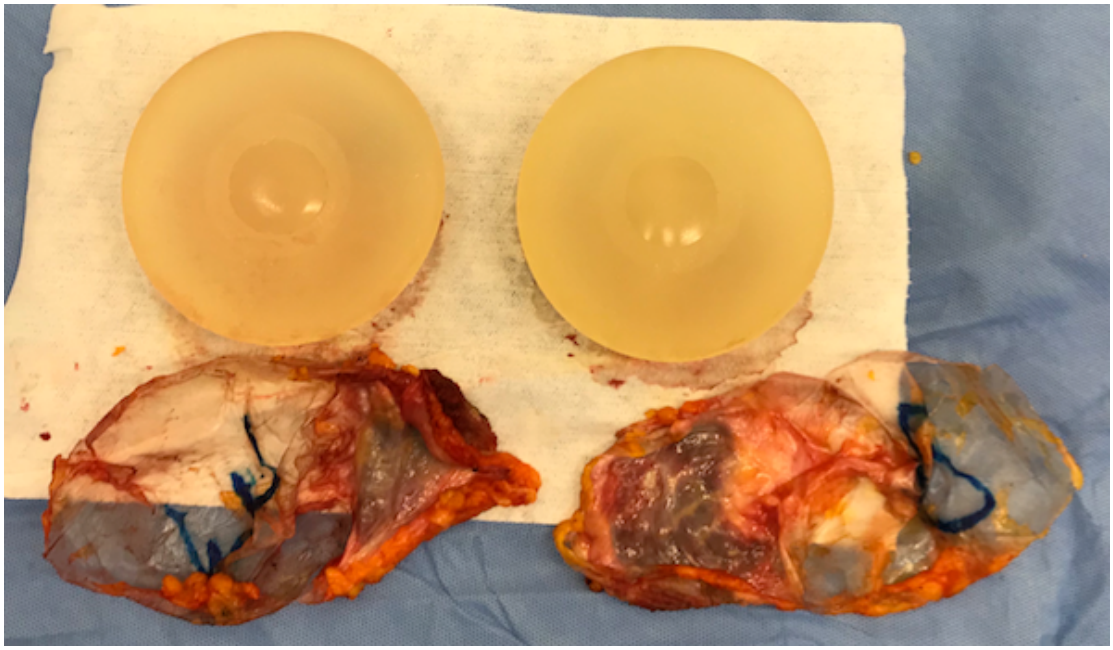
Grade	Contracture	Palpation of breast
I	None	Similar to an unoperated breast
II	Mild	Hardened compared to a normal breast, prosthesis palpable but not visible
III	Moderate	Moderately hardened, prosthesis easily palpable, distortion visible
IV	Severe	Severely hardened and painful, significant distortion of breast anatomy

Source: Rotatori DS et al., 1991.

Grade I and II contracture (Figure 9) does not require treatment, but grade III and IV contracture (Figure 10) should be treated with *en bloc* explantation or total capsulectomy. The need for mastopexy depends on the level of breast flaccidity.

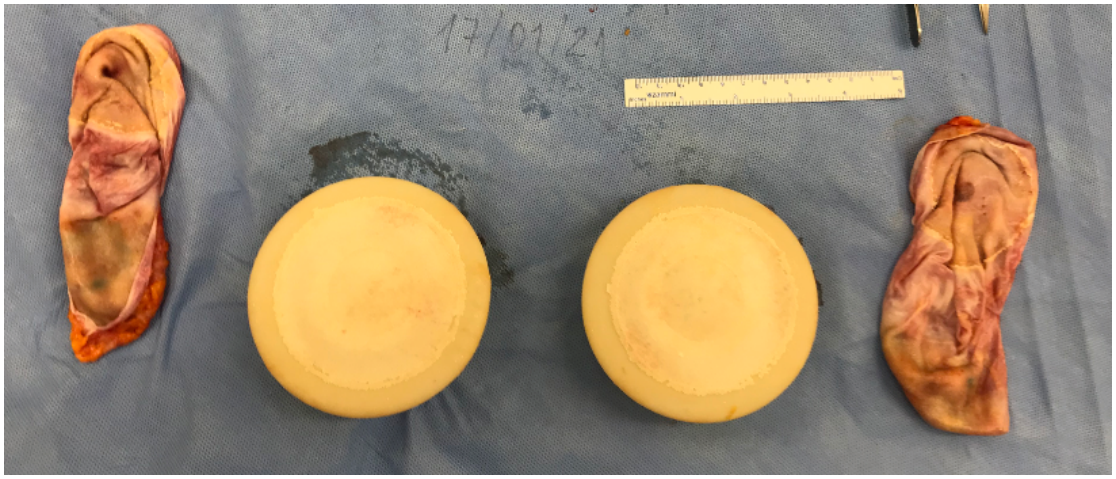
The bacteria in the biofilm of the prosthesis play an important role in the development of the contracture. The most common species are *Staphylococcus epidermidis*, *Cutibacteria acnes* and coagulase-negative staphylococci. The bacterial culture in the biofilm is by some experts believed to exacerbate the existing inflammatory response, causing contracture. The prosthesis may be contaminated with bacteria on occasion of the surgery. The biofilm is a layer of bacteria lodged in an extracellular polymer matrix on the surface (100, 101, 102, 103).

Figure 9: Grade I contracture. Thin capsules.



Source: the author

Figure 10: Grade IV contrature. Thick capsules and prostheses lined with polyurethane.



Source: the author

In addition to surgical treatment for grade III and IV contracture, some preventive non-surgical measures are available, such as pre- and intraoperative administration of antibiotics, washing of the prosthesis with antibiotics, washing of the surgical gloves. and the use of devices to implant the posthesis without skin contact (for example, Keller Funnel®, Figure 11). Mild contracture can be relieved with anti-inflammatory drugs, corticoids, and other medications such as montelukast (94).

Figure 11: Device for the implantation of breast prostheses.

Source: www.kellerfunnel.com

Rupture

The older the implant, the higher the risk of rupture due to degradation of the outer envelope (Figure 12) or, less commonly, breast trauma. Rupture can cause pain or changes in breast consistency but may also be asymptomatic.

Magnetic resonance is usually the best method of diagnosis (Figure 13), but small ruptures are occasionally found during surgery in patients with negative imaging findings.

The content of the ruptured implant may be contained by the capsule (intracapsular rupture) or may leak through it (extracapsular rupture). A leaked rupture can lead to silicone-induced mastitis and foreign-body granuloma.

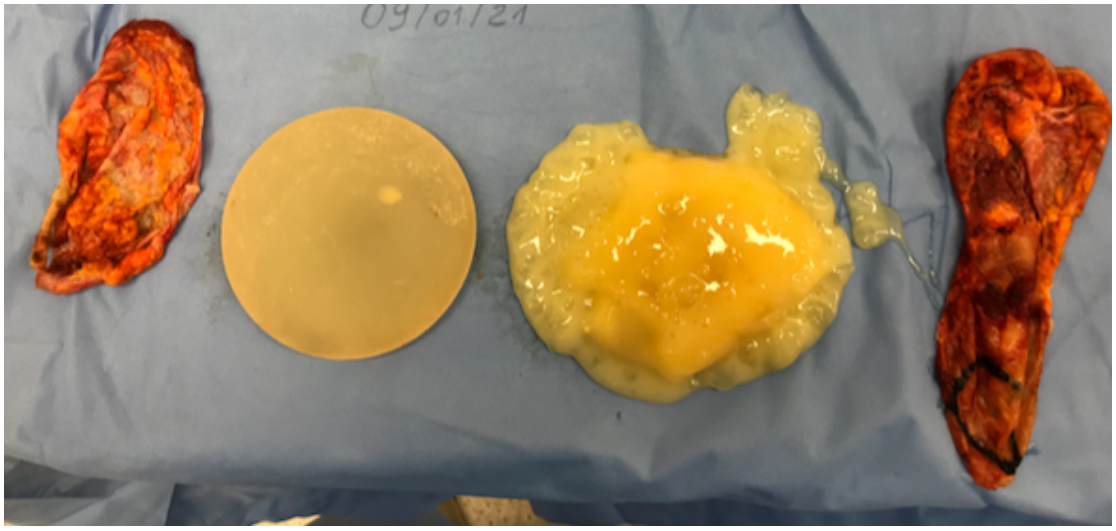
Rupture is treated by removing the prosthesis and capsule, if possible, by total intact capsulectomy to prevent the silicone from coming into contact with the breast tissue.

Rupture may be clinically evident upon physical examination or may require imaging to identify. Physically, it may be suspected from changes in breast shape, consistency and volume, pain, loss of sensitivity and greater hardening in case of contracture. Most cases of rupture require imaging to be diagnosed.

The causes of rupture include iatrogenesis (damage inflicted by medical treatment), time of use, chest trauma during mammography, and severe capsular contracture.

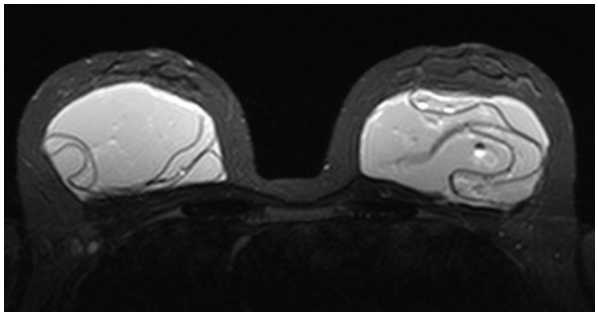
A study using nuclear magnetic resonance found the incidence of breast implant rupture after 8 years to be 12.2% (104).

Figure 12: Rupture of the right prosthesis, with advanced deterioration of the envelope.



Source: the author.

Figure 13: Nuclear magnetic resonance image showing bilaterally ruptured breast prostheses.



Source: eradiology.com

Seroma

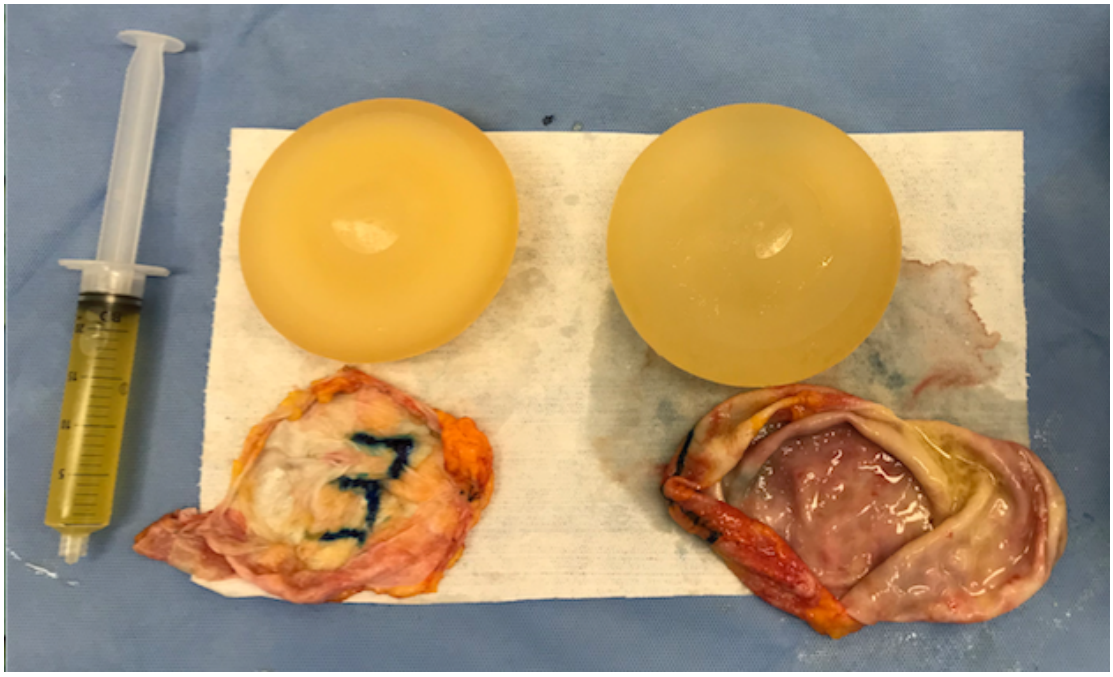
A seroma is a collection of yellowish fluid that may appear in the breast a few days after surgery or years later (Figure 14). In most cases, it is benign and not related to tumors.

When the seroma appears late, it usually results from the detachment of the capsule from the surface of the implant. When the seroma is large and spontaneous, the fluid should be investigated to rule out ALCL. Some studies have described seromas following coronavirus infection, but little is known about this possibility (105).

At an incidence of 1%, late seroma is a rare complication in breast implant recipients. It is defined as fluid collection appearing over 12 months after implantation. It is most often associated with light breast trauma or subclinical infection, such as biofilm or mycobacteria. According to one hypothesis, late seroma is caused by friction between the prosthesis and the capsule (106, 107).

In cases with large or recurrent late seroma, the implant and capsule should be completely removed and the collected fluid should be submitted to lab analysis (108).

Figure 14: Seroma in the left breast prosthesis.



Source: the author.

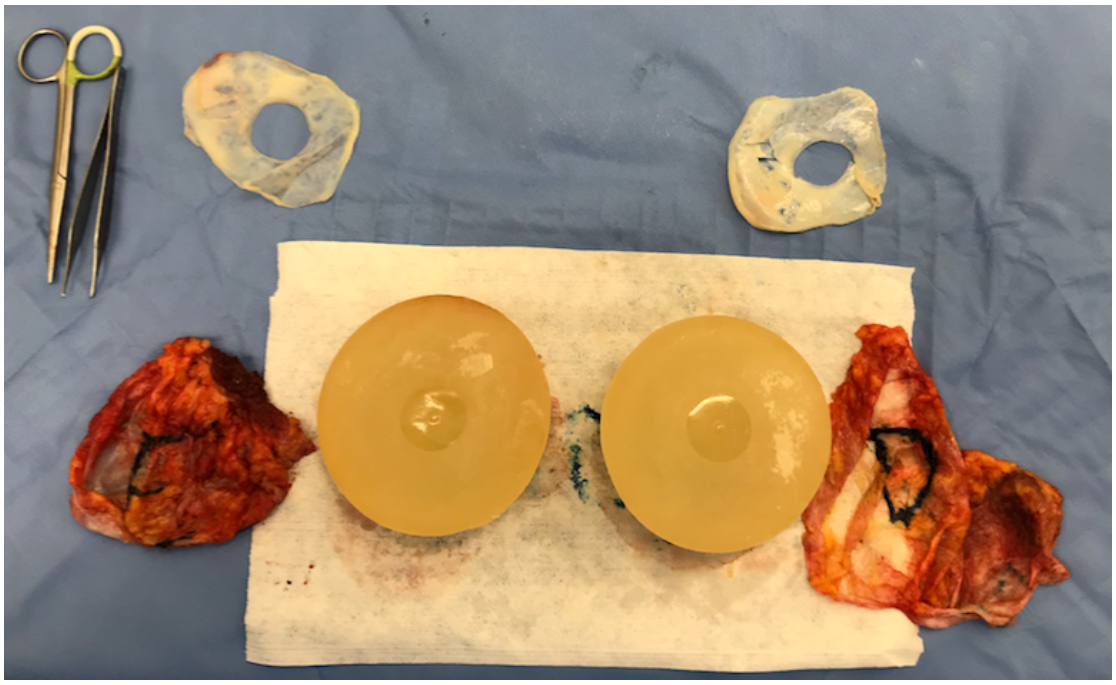
Double capsule

Double capsule was first described in 2002. The phenomenon occurs when the original capsule detaches from the surface of the implant and a seroma is created. Once the seroma is reabsorbed, a second capsule is formed on the surface of the capsule (109).

A double capsule may be partial (Figure 15) or complete (when the two capsules envelop the prosthesis entirely). According to one theory, insufficient adherence of the original capsule to the prosthesis is the cause of the phenomenon (110, 111).

Another theory holds that small traumas cause the capsule to detach, thereby creating a space where fluid can collect. It is most likely to happen with textured prostheses which have a rough surface (112).

Figure 15: Breast prostheses with double capsules.

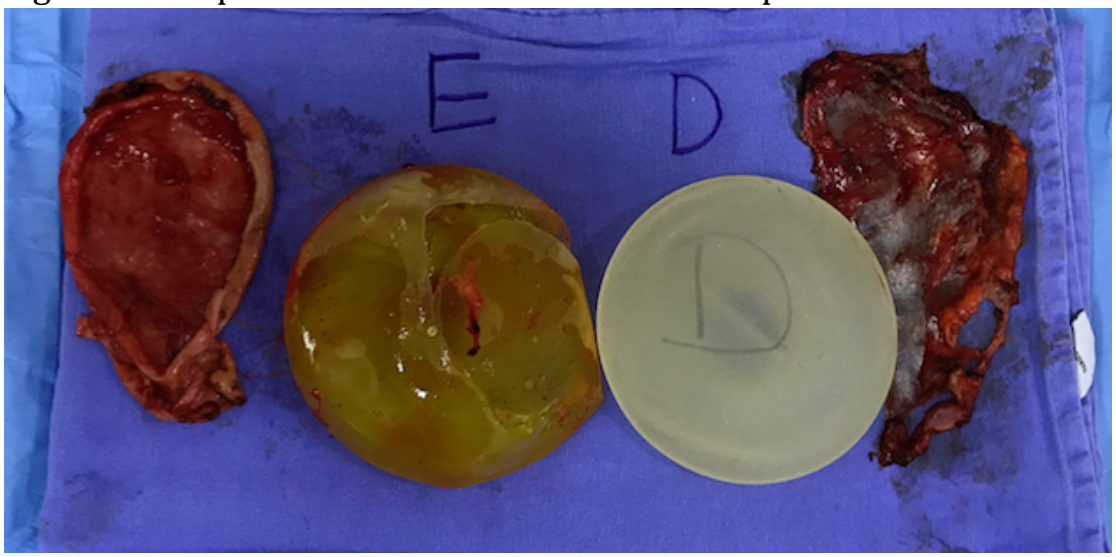


Source: the author.

Silicone-induced granuloma

The body may react to the presence of a foreign body by forming a granuloma. In the case of gel bleed (silicone leaking from the prosthetic envelope), a silicone-induced granuloma may arise. The leak occurs due to changes in the permeability of the envelope over time. Figure 16 shows the yellowish coloring of a ruptured prosthesis. In comparison, the right prosthesis is intact.

Figure 16: Rupture and deterioration of the left prosthesis.



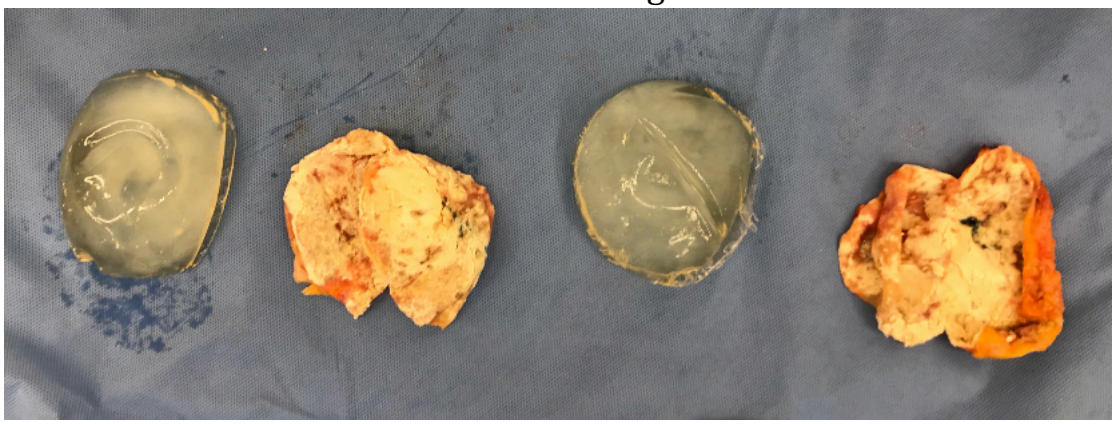
Source: the author.

The medical term for this condition is 'silicone-induced granuloma in breast implant capsule' (SIG-BIC). Figure 17 shows capsules with granulomas inside.

SIG-BIC should be distinguished from ALCL by differential diagnosis. On nuclear magnetic resonance imaging the two conditions can look very similar.

The granuloma develops as an inflammatory response to the gel bleed. When silicone is in direct contact with the capsule, inflammation ensues and the immune cells start producing tumors and/or thickening the capsule (113).

Figure 17: Breast implant capsule with grade IV contracture, showing foci of calcification and silicone-induced granulomas.



Source: the author.

Some believe SIG-BIC and ALCL are different aspects of the same condition, or different pathologies triggered by the exact same factors (114).

Clinically, both conditions may present with breast swelling caused by seromas and changes in consistency.

SIG-BIC should be treated with total intact capsulectomy, also called *en bloc* explantation, meaning the capsule and the granuloma are removed in one piece. No postoperative treatment is required (90, 115).

Breast reconstruction following explantation

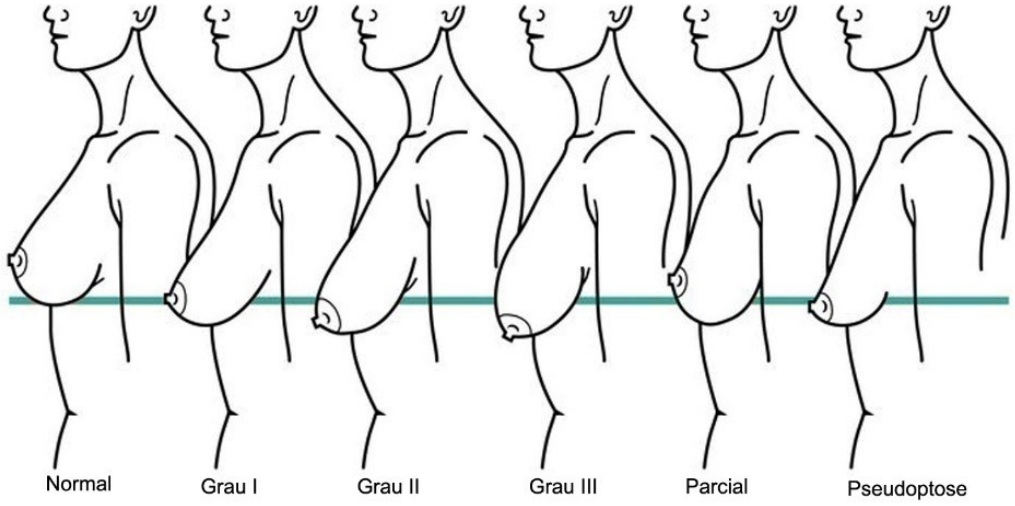
The possibilities of reconstructing the breasts after implant removal should be discussed by the surgeon and the patient. The decision will depend on the level of sagging (breast ptosis) and the breast volume without the prosthesis. Ptosis is measured based on the height of the areola relative to the breast fold. As shown in Table 6 and Figure 18, ptosis may be mild, moderate or severe (116).

Table 6: Classification of breast ptosis

Grade	Position of areola
I	The areola is at the height of the breast fold
II	The areola is below the height of the breast fold
III	The areola is the lowest part of the breast

Source: Regnault P, 1976

Figure 18: Classification of breast ptosis.



Source: enhancemyself.com

Following explantation, the need for breast reconstruction should be discussed. Breasts with adequate volume and without flaccidity do not need reconstruction, but flaccid breasts need mastopexy (surgical breast lift) while breasts with small volume and no flaccidity may be treated with a fat graft (117).

After many years of silicone implant wear, the volume of the breasts may have decreased or increased, whether from atrophy or weight gain.

In some cases of submuscular implant, the pectoral muscle needs to be reconstructed. It may also be necessary to remake the breast fold, or 'inframammary fold' as physicians call it. In such cases, stitches are made in the fold to provide support, much like an internal bra.

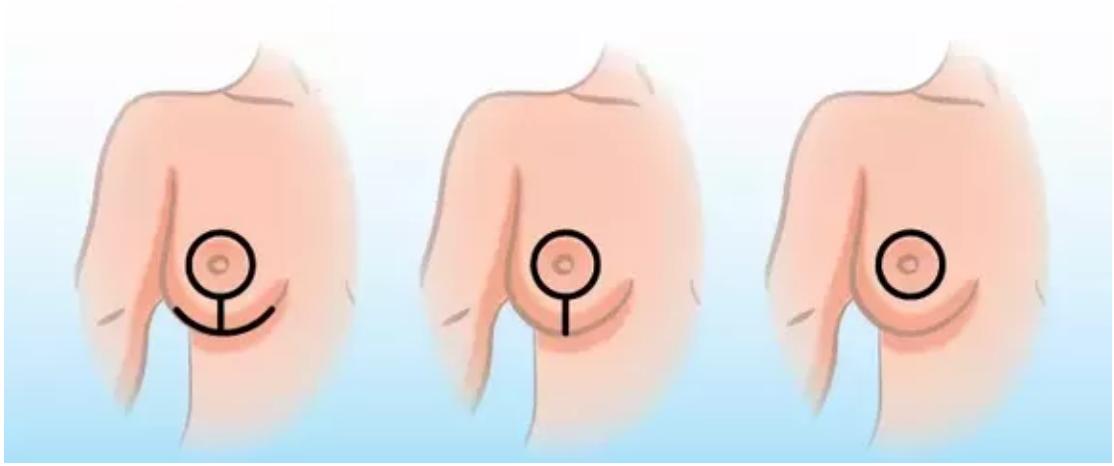
The following procedures are performed to correct sagging and loss of volume:

***En bloc* explantation only**: Uses the previous incision. Reserved for patients with little or no breast flaccidity.

***En bloc* explantation plus fat grafting:** Indicated for patients who can supply enough fat for grafting. The graft increases the breast volume though not as much as an implant. Moreover, part of the fat is reabsorbed, making more than one graft often necessary.

***En bloc* explantation plus mastopexy, with or without fat grafting:** Indicated for patients with moderate to severe breast flaccidity. The incision may be around the areola, at the breast fold or in inverted T, if the flaccidity is severe (Figura 19). The procedure may be combined with fat grafting to slightly increase the breast volume (118).

Figure 19: Options of incisions for mastopexy.



Source: enhancemyself.com

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