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Understanding Breast Implant Illness

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KEYWORDS
• Breast implants • Breast implant illness • Silicone • Silicone toxicity • Capsulectomy
• Autoimmune/inflammatory syndrome

KEY POINTS
- Review of breast implant illness symptoms and systemic complications.
- History of breast implants and the associated adverse events.
- The impact of certain breast implant-related chemicals like silicone on the body.
- Explantation of the breast implant and capsule reduces systemic symptoms in all populations.
- Saline and silicone, smooth, and textured all come with risks of cancer.
- Identifying the patients' need for explant based on the clinical symptoms and imaging studies.

UNDERSTANDING BREAST IMPLANT ILLNESS

The goal of this article is to provide you with a better understanding of breast implants and their impact on health. Studies have shown that removal of the implants leads to improved health in most patients [1–3]. Breast implants have been associated with autoimmunity and other systemic symptoms for over 60 years. The terms for the symptoms have been labeled many things and only recently have they been referred to as breast implant illness (BII). BII remains a poorly defined and controversial complication. First described in the early 1960s as a human adjuvant disease and recently coined as BII, breast implant illness syndrome is a constellation of symptoms which begins after the placement of breast implants. These symptoms may include, but are not limited to, fatigue, arthralgia, myalgia, cognitive impairment, dry eyes and mouth, alopecia, skin lesions, and Raynaud's syndrome [4–7]. Some publications suggest that BII may be an autoimmune condition and/or an inflammatory reaction that occurs in response to a stimulating agent (breast implant) and presents as a wide range of symptoms with similarities to connective tissue disease [8–10].

More recent reports have suggested that, for a subset of women experiencing systemic symptoms consistent with BII, removal of the breast implants and associated capsules significantly reduces their symptoms [1–3]. Although the mechanism of BII remains unknown, multiple theories suggest an inflammatory process triggered by the introduction of silicone [8].

Multiple names for the same disease process.
- Autoimmune/inflammatory syndrome induced by adjuvants (ASIA)
- Human adjuvant disease
- Silicone implant incompatibility syndrome (SIIS)
- Silicone toxicity
- Siliconosis
- Silicone autoimmune induced syndrome
- Silicone induce immune dysfunction syndrome

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- Silicone implant disease
- Silicone immune toxicity syndrome
- BII
- Generalized/unexplained illness
- Unexplained systemic symptoms

Breast implants are made of many chemicals from the shell to the internal composition. The Food and Drug Administration (FDA) states that these chemicals are used in the production of making breast implants.

The potential toxicity of the chemicals and metals listed in Tables 1 and 2 have been evaluated with both toxicity testing and risk assessments to assess the exposure. The testing methods used were based on the manufacturer Summary of Safety and Effective Data Sheet (SSED). The manufacturer created an environment to defined extractables and volatiles in serum at 37°C for 90 days. What they found are listed in the following charts. Everyone's response to these chemicals may be different and responses to chemicals may vary, and all reactions cannot be predicted [11].

Saline-filled breast implants have a silicone rubber shell made of polysiloxane(s), such as polydimethylsiloxane and polydiphenylsiloxane, and are filled with sterile saline solution. Silicone gel-filled breast implants has a silicone rubber shell made of polysiloxane(s), such as polydimethylsiloxane and polydiphenylsiloxane, which is filled with a fixed amount of silicone gel [12]. It is understood that the shell surface, shape, thickness, degradation, and permeability qualities may influence the immune system's response.

There are multiple chemicals used to manufacture the breast implants and some of these chemicals may have a collective and chronic impact on the body [12]. Siloxanes are the most studied chemical in the breast implants, but data are still lacking. Having a complete understanding of these chemicals and their impact on the body regarding the biodegradation, biotransference, and bio-integrity of siloxanes may be a piece of the puzzle toward understanding BII [8].

Historically, it has been difficult to understand how many women may be affected by breast implants because there is no database that tells us how many implants have been placed, nor is there a way to track and/or follow these implanted devices. Breast implants as we know them have been around since the 1960s; it is estimated that over 13 million breast implants have been sold. On average, 350 thousand breast implants are being sold per year in the United States. The American Society of Plastic Surgeons (ASPS) states that 4.9% of the women have breast implants; with these numbers, we are looking at a significant health need for a currently ill-defined health issue [13–20].

Over the past 60 years, there have been a range of systemic issues reported to the FDA Manufacture and User facility Device Experience (MAUDE) database. Some of the systemic issues are multiple types of cancers such as, but not limited to, breast implant associated anaplastic large cell lymphoma (BIA-ALCL), squamous cell carcinoma (SCC), and other lymphomas. In a literature search, we see case studies also associating breast implants to adenocarcinoma, stromal carcinoma, invasive cribriform carcinoma, follicular carcinoma, cutaneous T-cell lymphoma, fibrosarcoma, inflammatory breast cancer, lymphoplasmacytic lymphoma, invasive micropapillary carcinoma, melanoma, angiosarcoma, neuroendocrine carcinoma, intravascular large B-cell carcinoma, invasive ductal cell carcinoma, secondary lung cancers, multiple myeloma, and so forth [21–50].

As of April 1, 2022, FDA is aware of 1130 Global cases of BIA-ALCL and 59 deaths, worldwide, related to BIA-ALCL. BIA-ALCL is the first of the well-known man-made cancers and this was first identified in 1997. https://www.plasticsurgery.org/for-medical-professionals/health-policy/bia-alcl-physician-resources In 2011, the FDA announced that there were a growing number of cases (34 at that time), the numbers have steadily increased as more people become aware, get tested, placed in the Patient Registry and Outcomes for Breast Implants and Anaplastic Large Cell Lymphoma Etiology and Epidemiology (PROFILE) database. To note that the peak of BIA-ALCL may not be known until 2026 and after [21,49,50].

On September 8, 2022, the FDA released a safety communication about SCC and various lymphomas that form in the scar tissue capsule those forms around breast implants. These cancers have been reported with both textured and smooth breast implants and for both saline and silicone breast implants. The lymphomas are different from previously reported BIA-ALCL. This is an emerging issue, and the FDA is asking health care providers and people with breast implants to report cases of SCC, lymphomas, or any other cancers around the breast implant to the FDA.

The ASPS issued a statement in September 2022 alerting society members that breast implant associated SCC is an aggressive cancer that does not respond to chemotherapy and radiation. The average onset of BIA SCC is 22.74 years, with 80% of patients presenting with extracapsular spread, whereas BIA-ALCL has only 28% extracapsular spread. The mortality rate for BIA SCC is 43.8% at 6 months from diagnosis and BIA-

TABLE 1
Chemicals Released by Breast Implants

Volatiles		Extractables	
Compound	**Whole Device (ppm)**	**Compound**	**Whole Device (ppm)**
D_3 Siloxane	0.18	D_3 Siloxane	0.5
D_4 Siloxane	0.46	D_4 Siloxane	<2.5
D_5 Siloxane	1.47	D_5 Siloxane	<4.8
Methoxytrimethylsilane	0.43	D_6 Siloxane	<8.4
Dimethoxydimethylsilane	0.03	D_7 Siloxane	<8.4
Methoxytriethoxysilane	ND	D_8 Siloxane	<8.3
Tetramethyldiethyldisiloxane	0.04	D_9 Siloxane	<10.92
Acetone	0.18	D_{10} Siloxane	<21.86
Isopropanol	0.26	D_{11} Siloxane	32.92
2-Pentanone	ND	D_{12} Siloxane	47.85
Methyl butanoate	0.01	D_{13} Siloxane	113.11
Ethylbenzene	ND	D_{14} Siloxane	172.4
m- and p-xylene	0.08	D_{15} Siloxane	203.8
4-Methyl-3-penten-2-one	0.01	D_{16} Siloxane	584.9
o-Xylene	ND	D_{17} Siloxane	533.0
Alpha-pinene	ND	D_{18} Siloxane	429.4
Cyclohexanone	ND	D_{19} Siloxane	609.9
1-Ethyl-2-methylbenzene	0.01	D_{20} Siloxane	775.5
Decane	0.01	o-Xylene	<0.4
Benzaldehyde	0.01	Siloxane	3.9
1,3,5-Trimethylbenzene	0.35	Di(Ethylhexyl) Phthalate	ND
Limonene	0.01	*Total Extractables (μg/g*	*<4086.7*
Undecane	0.07		
Acetophenone			
Dodecane			
Total Volatiles	*3.67*		

Data preceded with a "<" symbol means that the level of the individual component, if present, was below the method detection limit indicated. Volatiles: Chemicals that are released by breast implants as a gas. Extractables: Chemicals that are released by breast implants following soaking in water and/or organic solvent (liquid).

Abbreviations: ND, not detected; ppm, parts per million.

From US Food and Drug Administration (FDA). Breast Implants - Certain Labeling Recommendations to Improve Patient Communication. September 2020. Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/breast-implants-certain-labeling-recommendations-improve-patient-communication.

TABLE 2
Heavy Metals Found in Breast Implants

Heavy Metals	
Metal	**Concentration (ppm)**
Antimony	0.014
Arsenic	0.123
Barium	0.001
Beryllium	0.006
Cadmium	0.002
Chromium	0.028
Cobalt	0.052
Copper	0.025
Lead	0.011
Magnesium	0.391
Mercury	0.004
Molybdenum	0.001
Nickel	0.050
Platinum	0.299
Selenium	0.069
Silver	0.001
Tin	0.004
Titanium	0.033
Vanadium	0.310
Zinc	0.034

From US Food and Drug Administration (FDA). Breast Implants - Certain Labeling Recommendations to Improve Patient Communication. September 2020. Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/breast-implants-certain-labeling-recommendations-improve-patient-communication.

ALCL mortality rate is 2.8% at 1 year from diagnosis. The full impact is not yet known; therefore, awareness and reporting will be key to help diagnose and treat this patient population.

Also reported are variety of systemic symptoms that have recently been defined as BII. According to Breast Implant Reporting Trends [21], breast implants are the 6th most reported device as the inception of the FDAs adverse event (AE) reporting system called MAUDE in 1994. Of the 186,009 breast implant medical device reports (MDRs) to the FDA, 75,364 reports were from physicians (an increase of 15,879 since last year—2021), 2612 were from nurses, and 3454 reports were from other health care providers. There were an additional 450,843 alternative summary reports disclosed by the FDA in June 2019 covering the years of 1997–2019 (Table 3).

TABLE 3
A Breakdown of Medical Device Reports and Alternative Summary Reports Through September 2022

Implant Type	Injury Reports	Death Reports	Lymphoma, ALCL, or Carcinoma
Saline-filled	377,395	66	1237
Silicone-filled	241,597	128	1781
Tissue expanders	7034	4	95

The FDA recently acknowledged cases of Breast Implant Associated Carcinoma and Lymphoma (non-ALCL). Each report must be analyzed to determine if the type of cancer was verified but a keyword search on all three terms is illustrated in Fig. 1.

It is important that every physician understand the reporting structure, guidelines, and where to go to enter the data.

1. MDR: This is the acronym used for the form that manufacturers are required to file with the FDA within 5 or 30 days of their awareness date. This report goes by other names including MedWatch Form, 3500A Form, or AE report; however, the use of the term AE report is not specific enough to describe what form it takes when it is submitted to the FDA. MDRs are searchable in MAUDE for the last 10 years. This is the FDAs definition of an MDR-reportable event.
2. To learn more about how to report medical device AEs please visit deviceevents.com, fda.gov

To show how important reporting is, the MAUDE database allowed the FDA to conclude that the Allergan textured implants were six times more likely to cause ALCL than other textured implants. BII and breast implant related cancers are an emerging issue, our understanding is evolving, and more research is needed. In effort to obtain information and follow-up data, in 2019, the National Breast Implant Registry (NBIR) was implemented.

Breast implants are Class III medical devices that are approved through the FDA 510(k) process. The 510k pathway allows a device to be approved if it is "substantially equivalent" to another device already on the market, even if that device has been recalled. Unlike a premarket approval agreement (PMA), which requires rigorous clinical and laboratory studies and a detailed

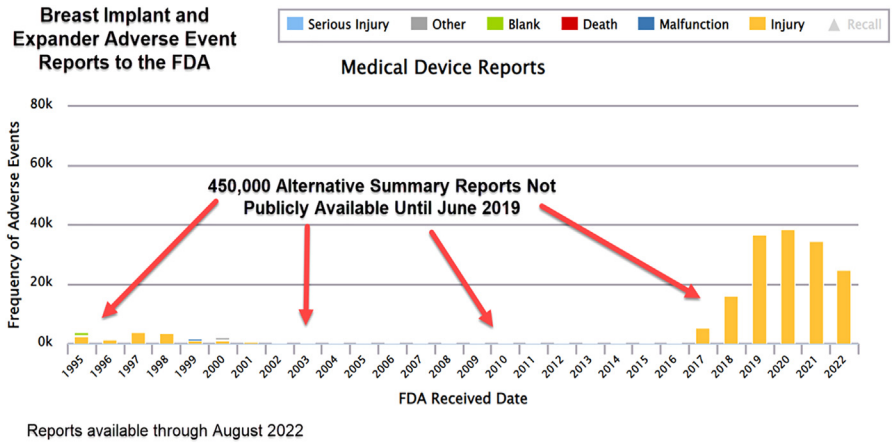

FIG. 1 Breast implant reporting trends out of all medical device reports.

process to determine safety and effectiveness, the 510(k) allows manufacturers to forego clinical trials and testing. Essentially, when the FDA clears a device through the 510(k), it is not analyzing safety and effectiveness, it is approving the device based on a manufacturer's claim that the device is like one that is already on the market. This process is designed to save time and money when getting a device approved to the market.

In the 1990s, the FDA issued a moratorium on all silicone breast implants due to health concerns and lack of long-term safety data. The FDA concluded that there was inefficient safety and effectiveness information, and silicone breast implants were removed from the market except for use in breast cancer reconstruction and patients enrolled in clinical trials. The moratorium was lifted in 2006 and the FDA-approved Mentor and Allergan silicone implants, with strict conditions of approval including: (1) perform a core post-approval study, (2) conduct a large post-approval study, (3) study device failure modes, (4) conduct a focus group study, (5) terminate adjunct clinical studies from the moratorium period, and (6) include informed consent documentation. In addition, the FDA required that each manufacturer's device labeling include a recommendation for patients to undergo an MRI at 3 years and every 2 years thereafter and in 2020 the screening change to obtain an MRI at 5 years post-implant and every 2 to 3 years after. Consider the rupture rates as described in the Safety and Effectiveness Data Sheet (SSED) per each manufacturer's SSED one can observe that the rupture rates begin to occur at the 3- and 4-year mark [51–56].

It is important for each physician to familiarize themselves with the rupture and deflation rates that each company has submitted to the FDA with their clinical trial data and PMA application. The clinical studies as shown in Fig. 2 are not to be used as a comparison between manufactures but to examine the main AE rates including rupture of each manufacturer's highest cohort.

Emerging evidence shows that free silicone (rupture, injectable, gel bleed) in the body can have a negative impact. Initially, it was believed that health complications were only caused by ruptured breast implants. However, there are studies that show that non-ruptured silicone implants and saline implants have also led to systemic symptoms. Spiera and colleagues [57] have stated that silicone and siloxanes are not biologically inert and have proven capable of eliciting inflammatory and fibroproliferative responses.

Literature also shows that when free silicone is injected, tissue degradation and systemic symptoms can be present. In 2017, the FDA cautioned to never get injectable silicone and that silicone injections can lead to long-term pain, infections, and serious injuries, such scarring, permanent disfigurement, embolism, stroke, and death. The FDA also stated that silicone is unlike other fillers it does not break down and is not absorbed by the body. Gel bleed is another way that silicone can be released into the body. When one looks at the SSED, we can see that each manufacture reports on their gel bleed rate. In studies for gel bleed, they used a 90-day trial of an implant at 37 °C in serum. This testing yielded a list of extractables and volatiles that exit from an intact shell and enter the serum, this is what the companies referred to gel bleed [51–56].

In 2018, MD Anderson reported on a summary of data on two breast implant manufacturers; they found

	SIENTRA[b]	MENTOR MEMORYGEL[c]	MENTOR MEMORYSHAPE[c]	ALLERGAN NATRELLE[d]	MCGHAN SALINE[e]	MENTOR SALINE[f]	IDEAL SALINE[a]
Overall Adverse Events	44.6%	50.1%	67.7%	57.2%	--	--	61%
Reoperation	56.7%	50.7%	59.7%	71.5%	38.7%	40.1%	42.6%
Rupture, leaking, deflation of implant	16.5%	43.9%	18.9%	35.4%	9.1%	22.6%	19.4%
Capsular Contracture III/IV	15.8%	36.9%	16.4%	28.7%	47.7%	30%	10.4%
Breast pain	4.5%	5.2%	3.7%	11.7%	15.6%	17.2%	1.1%
Inability to breast feed	11.4%	1.6%	NR	30.0%	NR	NR	1.6%
Implant removal	39.0%	24.1%	25.9%	32.4%	22.5%	26.8%	22.6%

FIG. 2 Breast implant adverse events. [+]The clinical studies from these manufacturers are not designed to be compared head-to head. Each individual company's own individual and published rates werw presented Stevens WG, Calobrace MB, Alizadeh A, Zeidler KR, Harrington JL, d'Incelli RC. Ten-year core study data for Sientra's food drug Administration approved round and shaped breast implants with cohesive silicone gel. Plast Reconstr Surg. 2018;141(4s):7s-19s. [++]Values presented are the highest percentage (cohort) per manucaturer. [a] Ideal Implant Patient Decision Checklist https://idealimplant.com/wp-content/uploads/2021/11/IDEAL-IMPLANT-Checklist.pdf. [b]Sientra patient decision checklist https://sientra.com/app/uploads/2021/10/MDC-0748-R2-Patient-Decision-Checklist-AUG-v1.pdf. [c]Mentor worldwide LLC. Patient Decision Checklist: MemoryShape &Memory Gel: https://www.breatimplantsbymentor.com/MENTOR-implant-safety-information. [d]Allergan Sales, LLC. Patient Decision Checklist: https://www.natrellesurgeon.com/Content/PDF/Augmentation_Consent_Form.pdf. Accessed December 2021. [e]Mentor Saline SSED https://www.accessdata.fda.gov/cdrh_docs/pdf/P990075b.pdf. [f]Mcghan Saline SSED https://www.accessdata.fda.gov/cdrh_docs/pdf/P990074b.pdf.

higher rates of Sjogren's syndrome, rheumatoid arthritis, scleroderma, melanoma, dermatomyositis, and anaplastic large cell carcinoma, reported higher rate of stillbirth, preterm birth, and neonatal intensive. Clemens stated that "these two areas merit additional research to fully understand the underlying issue." To further investigate the safety of silicone, in 2021, the FDA partnered with Emergency Care Research Institute to investigate silicone in breast implants and the concern level was raised to a moderate concern level [8,58–62].

Although initially it was thought that polydimethylsiloxane (silicone) was biologically inert, we now know that silicone can be inflammatory and lead to a foreign body host response. Under the right conditions, silicone can cause monocytes to secrete pro-inflammatory cytokines, interleukins, TNF (Tumor Necrosis Factor) alpha, and reactive oxygen species which can have a direct impact on T cells and the IgG response, which is an antibody response. Low molecular weight silicone has been shown to cause cell death and decrease natural killer cells [8,59,63–65]. Recent data with Glicksman and colleagues show certain interleukins being present in those with BII. In short, we can say that there is a measurable immune response directed against siloxane. The Glicksman and colleagues study was the first level 1 study and it showed statistically significant IL (Interleukin)17a, IL22, and IL13 even when the majority of the BII cohort was 64% saline. Additional research shows that breast implants cause inflammation and can create an environment where granulomas can form, and overgrowth of regular bacteria, biofilm, and other microbes can prosper [66–68]. An objective sign of silicone-induced granulomas can be seen on a breast MRI. Dr Eduardo Fleury has several publications studying the granulomas within the breast implant capsule and states that it is due to the gel bleed of particles crossing the intact shell [67,69]. With the evolving data around free silicone, well-designed studies are needed to take a closer look at the associated risk of free silicone from breast implants. Several other case studies show migration of silicone particles exiting through the skin in the form of skin lesions, whereas other publications look at silicone as the key ingredient to creating the environment for things like biofilm [9,67,68,70].

Literature defined factors for BII.

- Breast implants causing: Silicone and chemical disruption (bio-incompatibility, carcinogenicity, immunotoxicity, teratogenicity, toxicokinetics, biodegradation)
- Breast implants causing: Immune system response and dysregulation (FBR - foreign body reaction)
- Genetic disposition
- Breast implants causing: Tissue damage
- Breast implants causing: Inflammation
- Breast implants causing: Hypoxia

- Antigens and neo-antigens
- Infections
- Tribology: Friction
- Granuloma to cancer via the dysregulation of the immune system

Colaris and colleagues [8], a review article, stated "In previous studies, it has been postulated that implant rupture and/or aging can be important factors for eliciting an inflammatory response or triggering the immune system on silicone particles migrating throughout the body. The phenomenon of gel bleed is known for all types of silicone breast implant (SBI) [72–74]. The migration of the silicone gel particles throughout the body is accompanied by lymph node and thoracic silicone infiltration, with giant-cell granulomas and small silicone vacuoles found in lymph node biopsies [71,75]. Droplets and plaques containing silicone are found in tissue samples of different parts of the brain as well as in the spinal cord [74] https://link.springer.com/article/10.1007/s00266-021-02762-x. Silicon-containing particles are transported to the regional lymph nodes, possibly resulting in an adjuvant effect [6,76–78]. The amount and size of the silicone molecules may determine the induction of the apoptotic processes by silicones, known as "silicon toxicity." Exposure of cultured human Jurkat cells, a human T lymphoblast non-adhering cell line, to low molecular weight methylcyclosiloxanes, the smallest cyclic silicone oligomer octamethylcyclotetrasiloxane (D4), and the decamethylcyclopentasiloxane (D5), can induce cell death by apoptotic processes such as cleavage of caspase substrates and DNA fragmentation [59].

In 1964, human adjuvant disease was described by Miyoshi who reported a series of patients with diverse symptoms after receiving treatment with silicone or paraffin fillers. Since then, the literature has been flooded with case reports and case series of granulomatous and systemic autoimmune disorders related to vaccines, infection, or other adjuvants such as silicone and other biomaterials [7,67,79]. Yasuo Kumagai MD, in 1979, presents a publication about Scleroderma After Cosmetic Surgery [80]. Human adjuvant disease may be caused by prolonged hypersensitization activated by the injected foreign materials which act as an adjuvant. Schoenfeld further describes ASIA and Frank Vasey specified chronic fatigue differences between those with and without implants [80]. In 2004, Dr Borenstein [81,82] presented siliconosis, and Dr Tervaert in 2013 [5] discusses SIIS. Dr Tervaert states "despite changes in the principal constituents of the silicone implants during the past fifty years, silicone remains an adjuvant that may 'bleed' and subsequently may be a chronic stimulus to the immune system resulting in similar clinical manifestations as observed in the Maastricht cohort, the Baylor College cohort, and 18 other large cohorts of patients. We therefore conclude that silicone-related disease has not changed during the last 30 years."

According to Dr Tervaert [83], when diagnosing BII, we should look for an exposure to an external stimulus: implantable devices, infection, and silicone before clinical manifestations. Some of the clinical manifestations are myalgia, myositis, or muscle weakness arthralgia and/or arthritis, chronic fatigue, un-refreshing sleep, or sleep disturbances, neurological manifestations (especially associated with demyelination), cognitive impairment, memory loss, pyrexia, dry mouth, removal of inciting agent induces improvement. Per Dr Tervaert, patients with silicone breast implants who have ASIA type symptoms have a calculated risk to develop chronic illness of 45%. When the symptoms progress and become a formal diagnosis, it is hard to achieve optimal health and as such reaching these people early is imperative [84,85]. Regardless of the name one wants to give this condition, there are a significant number of publications, peaking in the 1990s and resurging again in the mid-2000s regarding silicone/siloxane and its impact on the body.

As stated above we know that explantation provides symptom relief. In the 1990s, Weinzweig and colleagues [86] were among the first to identify that capsular tissue silicon (different than silicone) levels were significantly greater than breast tissue levels. This finding may indicate that the capsule serves as a barrier to the distribution of silicone from the implant into adjacent breast tissue. Multiple studies prove that when the stimulus (breast implant and capsule) is removed the patient improves. A peer-reviewed published literature has surfaced with new investigators, showing that removal of capsule and implant improve symptoms [1,3,69,87]. Rohrich and colleagues [88] published an article in 2000 showing that patients who had undergone explantation showed a temporary decrease in musculoskeletal symptoms and body pain as well as an increase in vitality, mental health, and body area satisfaction. We can conclude from this study that we must listen to our patients, and if they want their silicone implants removed, it is their choice if the operation can be performed safely. Earlier studies do not provide details about the type of capsule removed. However, recent studies [1,2,89] show a higher percentage of improvement in symptoms when a known total/complete capsulectomy is performed in

comparison to the earlier studies when partial capsulectomy or capsulotomy may have been performed.

Feng's study [89] published in 2021 showed objective evidence that in patients presenting with symptoms of pulmonary complaints had improvement in forced vital capacity, forced expiratory volume, and peak inspiratory flow rate after implant removal and complete/total capsulectomy [89]. Dr Buinewicz [2] also published a study in 2021 outcomes of implant removal and capsulectomy for BII in 248 patients. They reported that capsular inflammation is significantly associated with silicone and textured implants. Implant removal with capsulectomy can be safely performed in patients with BII with a low complication rate and high patient satisfaction. This study also showed that silicone was present in the capsule and demonstrated that silicone can migrate regarding saline and silicone implants. In 2021 and 2022, Glicksman and colleagues [3] study showed that patients who self-report BII demonstrated a statistically significant improvement in their symptoms after explantation, despite the type of capsulectomy performed. Long-term data are needed to further define the necessity of complete capsule removal and our understanding of this disease process. When removing the breast implant, it is also crucial to consider that various forms of cancer are known to develop within the breast implant capsules. It has been shown that complete and total capsulectomy can be performed safely and effectively, and as physicians, it is important to be sure that we understand the impact of leaving the capsule in the body and its potential to cause further symptoms and/or malignancy.

Onset of symptoms may begin slowly and increase to more severe symptoms in rate and in number. It is known that chronic inflammation in the body can present with many different symptoms and these symptoms can be vague like symptoms with BII (Table 4).

BII is a diagnosis of exclusion in which the explantation of the implant and capsules has shown to successfully improve symptoms. It is the author's clinical experience that complete capsulectomy improves the patients' symptoms; however, for some the improvement is not always curative, and the patient may need further interventions to optimize their health. This condition (BII) being described seems to suggest a link between breast implants. The plastic surgery community is beginning to identify explantation as a supportive intervention for those with clinical signs and symptoms. Further research is required to establish guidelines for diagnosis and ensure evidence-based treatment, and that patients and clinicians have a more refined understanding of the potential risks of silicone and saline breast implant use. More long-term studies large cohorts, decisive explantation measures, and longer follow-up greater than 1-year studies are needed to learn more about this explanted population. Studies on free silicone, silicone migration, and its impact on the body are needed. Publications from Dr Yoshida and colleagues and Teuber and colleagues [86,90], Dr Rita Kappel, Dr Eduardo Fleury, and Dr Brain Buinewicz are foundational and can guide future studies to investigate the migration patterns and the potential impact on the immune system. A registry collecting the explant data from pre-imaging to the type of capsulectomy, the constitution of the breast implant on removal, and tissue samples for malignancy, cytokines, microorganisms, and so forth and how explant relates to symptom resolution may help us better understand the disease process and help navigate these patients toward optimal health.

TABLE 4
Most Common Systemic Signs or Symptoms

Symptoms	Percentage of MDRs (*N* = 7467)
Fatigue	43.6%
Joint pain	29.0%
"Brain fog"	23.6%
Anxiety	22.7%
Hair loss	20.3%
Depression	17.2%
Autoimmune diseases	16.6%
Rash	15.6%
Headache	15.3%
Inflammation	14.7%

CLINICS CARE POINTS

- In the literature reviewed for this article, we have identified the lack of properly designed studies, from chemical testing (degradation, biocompatibility, bioreference, and so forth) to foreign body reactions and acute and chronic impact on the body. Studies are needed with larger populations and long-term follow-up.

- Plastic surgeons would benefit from an implant and an explant database so we can best track and follow the events that surround the impact of breast implants.
- What we can do as plastic surgeons:
  - Pre-implant:
    - Identify if the patient is at-risk for systemic symptoms and autoimmunity.
    - Review patient checklist including cancer risk with each patient considering implants.
  - *Patient with implants*: Once the patient has implants, make sure that they are aware of cancer and autoimmune risk and symptoms associated with them and make sure that the patient is aware of the MRI imaging schedule set forth by the FDA.
    - File information into NBIR
  - *Identifying the need for explant*: clinical symptoms and imaging studies. Issues to further define.
    - Enbloc/total capsulectomy
    - Type of testing at explant
    - Capsule Testing
    - File any confirmed diagnosis into PROFILE registry.
  - Post-explant need:
    - Ultrasound post-explant to identify seroma.
    - Patients may need support post-explant and as a community, we can learn how to optimize health post-explant (HOPE clinical trial).

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