

## Review Article

# Evidences on Silicone Breast Implants Safety and Relation with Systemic Diseases: A Mini-Review

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Breast implant based surgery is one of the most commonly performed procedures in plastic surgery. In the implants manufacture the highly cohesive silicone maintains its shape within the body in the presence of physiologic forces, minimizes implant-related complications and optimizes aesthetic outcomes. FDA's report supports the safety and effectiveness of these implants. The aim of this study is to provide some evidences on silicone breast implants safety and their relation with systemic diseases. By querying the search engines PubMed, Scopus, Medscape and Embassy, we found 22 papers, and only 12 of them fully satisfied our inclusion criteria. Five of the reviewed papers investigate the association with breast-feeding. Two of them talk about the possible linkage with breast cancer, four explore the connection with Anaplastic Large-Cell Lymphoma (ALCL) and finally two papers are case-reports about the association with Sjogren's syndrome and chronic silicone embolism syndrome. To date, there is no evidence that silicone breast implants can be of any health hazards for the patients. However, no study has been large enough or lasted long enough to definitely confirm or exclude these complications.

**Keywords:** Breast implants; Silicone gel prostheses; Safety; Systematic reviews**Introduction**

Breast implant based surgery is one of the most commonly performed procedures in plastic surgery. The modern silicone breast implants have been available since 1963 and have gone through an evolution [1]. Silicone gel-filled breast implants are FDA approved for breast augmentation in women older than 22 years and for breast reconstruction in women of any age [2]. These implants are available in different sizes, shape and surface; they have a more natural feel than saline-filled implants and can be positioned through a periareolar, inframammary and transaxillary approach. Several generations of silicone implants have been introduced in the clinical practice. The first one (1962-1970) was characterized by a dense and viscous silicone gel, surrounded by a thick, smooth shell. The second prostheses generation (1970-1982) was rounder, with less cross-linked gels (less viscous) and covered by a smooth, thinner and slightly permeable shell. The third generation implants (1982-1992) had a more viscous gel and a thicker envelope, either smooth or textured.

In the fourth-generation devices (1993) texturing of implant surface was due to the experience with Poly Urethane (PU) - coated foam implants [3]. In the implants manufacture the shell is currently made still of an outer layer of a mix of dimethyl siloxane and amorphous silica with an inner barrier coat of diphenyl siloxane to minimize silicone gel bleed [1]. The highly cohesive silicone maintains its shape within the body in the presence of physiologic forces, minimizes implant-related complications and optimizes aesthetic outcomes [4,5]. As well as in the Plastic Surgery, silicone has been widely used in many areas of medicine demonstrating its biosafety and biocompatibility [6,7]. FDA's report continues to support the safety and effectiveness of these implants, but states that

women should understand the risks before considering getting them: breast implants are not lifetime devices. The longer a woman has them, the more likely she is to have complications and needs to have the implants removed or replaced. Women with breast implants will need to monitor their breasts for the rest of their lives [8]. The aim of this study is to provide some evidences on silicone breast implants safety and their relation with systemic diseases.

**Literature Review and Study Selection**

We interrogated the search engines PubMed, Scopus, Medscape and Embassy by using the following keywords: silicone breast implant, silicone implants and cancer, breast implants and breastfeeding, breast implant lymphoma, breast implant complications. We analysed the abstracts of the resulting papers, published between January 2007 and September 2016. Only articles addressing breast implant safety and the relationship with systemic disease were retrieved in full text. We skipped letters and papers investigating other complications.

With these criteria we selected 22 papers.

**Results**

Only 12 articles full satisfied our inclusion criteria. Among them 11 were original research articles and one was a literature review Table 1. Among the 12 articles reviewed, five [1,9-12] investigate the association with breast-feeding, two [1,13] talk about the possible linkage with breast cancer, four [14-17] explore the connection with Anaplastic Large-Cell Lymphoma (ALCL) and two articles are case-reports about the association with Sjogren's syndrome [18] and chronic silicone embolism syndrome [19].

Although implants can cause local symptoms, such as hematoma,

**Table 1:** Characteristics of the included studies.

AUTHOR	LOCATION	YEAR	STUDY POPULATION	OUTCOMES
Brody G. S. [1]	USA	2015		Lactation insufficiency could be related either to congenital glandular inadequacy or with periareolar access surgery.
Zoccali G. et al. [8]	Italy	2008	30 women near term pregnancy	Antibodies in all groups were compared and the difference was not significant. Silicon in maternal blood was more concentrated in the group A but the difference was not significant. No correlation between mammary implants and silicone values in the milk was found.
Michalopoulos K. [10]	UK	2007		Women with periareolar breast incisions are five times more likely to suffer from lactation insufficiency compared with women without surgery.
Lund H.G. et al. [11]	USA	2016	4927 subjects	Incidence of lactation issues was similar to that reported in postpartum women who did not have breast implants.
Seaman A. M. [12]	USA	2015		Breast implants could be linked to a decreased risk of breast and endometrial cancers.
Moling O. et al. [13]	Italy	2016	1 case-report	The genetic background of the patient with silicone breast implants might have predisposed her to three rare syndromes: macrophage activation syndrome, autoimmune/inflammatory syndrome induced by adjuvants, and intravascular large B-cell lymphoma.
Clemens M. W. Et al. [14]	USA	2015	87 patients	Timely diagnosis and complete surgical excision of lymphoma, implants, and the surrounding fibrous capsule is the optimal approach for the management of patients with BI-ALCL.
Clemens M. W. Et al. [15]	USA	2016	940 breast implants	Breast implant-associated ALCL should be included during preoperative counseling on the risks of breast implantation.
Hu H. et al. [16]	USA	2016	88 patients	The finding of bacterial biofilm and a distinct microbiome in breast implant-associated ALCL samples points to a possible infectious contributing cause.
Akyol et al. [17]	Turkey	2015	1 case-report	The possibility of an association between breast implantation and Sjögren's syndrome should be considered when a patient with silicone implants is admitted to the hospital for treatment of Sjögren's syndrome.
Gopinath et al. [18]	UK	2015	1 case-report	The diagnosis of a chronic pulmonary disease related to silicone leakage is an important one for patients awaiting explantation or those being monitored for implant-related symptoms.

seroma, infection, rupture, silicone leakage, changes in mammary sensitivity, chronic pain, poor positioning, wrinkling skin, and capsular contracture, the researchers are interested in possible links between silicone gel breast implants and cancers, connective tissue diseases, immune system disorders, breastfeeding and reproductive issues. We have found numerous case-reports suggesting a possible association among silicone breast implant and systemic diseases, but no study is large enough or lasted long enough to definitely establish or exclude a relationship. Furthermore, regarding the silicone leakage from intact implants, infinitesimal amounts of silicone have been found in the breast and surrounding subcutaneous tissue during post-mortem examinations of women with implants who died of unrelated trauma, but no silicone was found in the major organs. Presumably, if it occurs, the quantities are too small to be measured [1].

## Silicone Breast Implants and Breastfeeding

The association of silicone implants with breastfeeding is one of the most commonly investigated issues. At the University of L'Aquila (Italy), [9] performed a haematochemical study on a group of patients with term pregnancies and silicone gel breast implants (group A) compared with a control group without implants (B). They evaluated antibody (TRIM) and silicone concentrations in patient's blood, maternal milk and in neonate. Antibodies in the two groups were compared and the difference was not significant. Silicon in maternal blood was more concentrated in the group A but the difference with the group B was not statistically significant. No correlation between mammary implants and silicone values in the milk was found. In a systematic review dated 2014 [10], suggested that breast augmentation is associated with 40% decrease in the possibility of exclusive breastfeeding. However, this finding was based on only three relatively small and heterogeneous studies, and therefore its validity is limited. Reduced likelihood of exclusive breastfeeding may be attributed directly or indirectly to the augmentation surgery. Breast implantation surgery can cause damage to ducts, glandular tissue, or innervation of the breast. Alternatively,

breast implants may place pressure on the breast tissue, which can damage the tissue or block lactiferous ducts. Another possible explanation of these findings is the pre-surgical condition of breast hypoplasia. In agreement with this hypothesis, Garry S Brody in his study [1] suggested that lactation insufficiency could be related either to congenital glandular inadequacy, usually associated with smaller breasts, or with periareolar access surgery that damages the ductal system. In addition, Kostas Michalopoulos [11] stated that women with periareolar breast incisions are five times more likely to suffer from lactation insufficiency compared with women without surgery. These women have an altered nipple sensation, which leads to a loss of the suckling reflex and then to a decrease or inability to produce milk. A careful incision, be it periareolar, transaxillary or inframammary, combined with a careful subcutaneous approach to the breast pocket can help minimise both nerve and glandular tissue damage [12]. Considered instead that incidence of lactation issues was similar to that reported in postpartum women who did not have breast implants.

## Silicone Breast Implants and Carcinoma

Another important issue is the question of whether breast implants are associated with breast cancer, and why. To date, no evidence exists that the silicone used in breast implants is carcinogenic in humans [1]. Moreover, there was a suggestion that breast implants are linked to a decreased risk of breast and endometrial cancers [13]. Perhaps the most significant concern regarding breast implants is the possibility of delayed detection of breast cancer. The implant itself is radio-opaque and depending on the degree of contracture can compress the breast tissues. Anyway no cases have been documented in the medical literature in which a diagnosis of breast cancer was delayed by the presence of an implant [20,21]. The Society for Breast Imaging, the American Society of Plastic and Reconstructive Surgeons (ASPRS), and the American Cancer Society agree that a woman with breast implants should be on the same schedule of routine mammography as other women [22-24].

## Silicone Breast Implants and Connective Tissue Diseases

With regard to rheumatologic disorders, since these are rare diseases, they require large-scale epidemiologic studies to determine if a relationship is present. We reviewed an article by [18] which states that a cause-effect relationship between breast implantation and Sjögren's syndrome cannot be established. However, the possibility of such an association should be considered when a patient with silicone implants is admitted to the hospital for treatment of Sjögren's syndrome.

### Silicone Breast Implants and ALCL

Breast implant-associated Anaplastic Large Cell Lymphoma (ALCL) is a rare T-cell lymphoma arising around breast implants. Although it has demonstrated a good prognosis, public awareness has increased following a communication warning by the U.S. Food and Drug Administration in 2011. Suggest that breast implant-associated ALCL should be included during preoperative counselling on the risks of breast implantation when obtaining informed consent [16]. Furthermore, in another article, [15] show that complete surgical excision of lymphoma, implants, and the surrounding fibrous capsule is the optimal approach for the management of patients with BI-ALCL. In fact, patients who underwent a surgical excision had better overall survival and event-free survival than did patients who received partial capsulectomy, systemic chemotherapy, or radiation therapy. Have noted a linear correlation between the number of activated lymphocytes and the number of bacteria around breast implants [17]. They postulate that chronic bacterial biofilm infection is an inflammatory trigger producing chronic lymphocyte activation, hyperplasia, and potential transformation into breast implant-associated ALCL. We have also found an article in which [14] reported a case of a patient with silicone breast implants whose genetic background might have predisposed her to three rare syndromes: macrophage activation syndrome, autoimmune/inflammatory syndrome induced by adjuvants, and intravascular large B-cell lymphoma.

### Silicone Embolism

Have found a new clinical entity which suggests the association with chronic silicone embolism [19]. They described a case of a 41-year-old woman who has undergone a breast augmentation surgery ten years before. She presented with a 4-year history of progressive dyspnoea. The patient underwent a transbronchial biopsy, which showed interstitial inflammation with no established fibrosis and no specific features. Four months later a video assisted thoracoscopic surgical right lung biopsy was performed. The main observed pathology was the presence of variably sized, clear, non-birefringent globules, mainly within the alveolar capillaries, but with focal involvement of the interstitium and alveolar spaces. The morphology of the globules closely resembled silicone globules, seen in silicone mastitis and lymphadenitis resulting from leakage or rupture of silicone breast prostheses. This appearance, similar to that seen in the acute silicone embolism syndrome, together with the history of breast augmentation with silicone implants, led to a diagnosis of chronic silicone embolism. Both implants were removed and rupture of the left implant was confirmed.

## Conclusion

This article reviewed the literature evaluating the possible associations among silicone breast implants and systemic diseases, leaving aside all the most common local complications. Although it is appropriate to keep in mind that breast implants are not lifetime devices and that women with breast implants will need to monitor their breasts for the rest of their lives, currently it is sufficiently established that implants are safe and can be used for breast reconstruction and aesthetic augmentation. There is no evidence that silicone breast implants can be of any health hazards for the patients [25]. Studies do not indicate that silicone breast implants cause breast cancer, fertility problems, or connective tissue disease. However, no study has been large enough or lasted long enough to completely confirm or exclude these and other rare complications [26].

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