

Silicone Lymphadenopathy After Breast Augmentation: Case Reports, Review of the Literature, and Current Thoughts

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Abstract

Background Silicone lymphadenopathy after implantation of silicone breast implants is a foreign body reaction due to the release or migration of silicone into the tissues surrounding the breast implant.

Methods For the study, 14 cases of silicone lymphadenopathy were identified from the authors' files. Four patients had been implanted before 2000 and had various types of implants. The remaining 10 patients all were implanted between 2006 and 2009, and all had Poly Implant Prothèse (PIP) implants. In addition to an analysis of the authors' own cases, a thorough bibliographic search was initiated to identify all reports of lymphadenopathy related to silicone breast implants.

Results The implant age of the four patients implanted before 2000 was 12–34 years (mean, 17.25 years). The implant age of the 10 patients implanted after 2000 was 2–6 years (mean 3.45 years). The literature search identified 29 papers with case reports of silicone lymphadenopathy published between 1978 and 2012, with a total of 175 cases. Usable data were extracted from 164 of the 175 cases. Of these patients, 159 were implanted before (and including) the year 2000 and had a mean age of 11 years at presentation or explantation, and 5 of these patients were implanted after the year 2000 and had a mean age of 4.6 years at presentation or explantation. After inclusion of the authors' own cases, the mean age of the implants at presentation or explantation was 10.56 years in a total of

178 cases. Of these patients, 163 were implanted before (and including) the year 2000 and had a mean age of 11.16 years at presentation or explantation, and 15 of these patients were implanted after the year 2000 and had a mean age of 4.06 years at presentation or explantation.

Conclusions Current breast implant technology has minimized the release of silicone gel due to rupture or bleeding of silicone and its migration into the surrounding tissues, thus reducing the rate of silicone lymphadenopathy in the last 10 years. The PIP implant scandal highlights the fact that disregard for the implant manufacturing technologies and standards in favor of higher profits increased rupture rates and gel diffusion, leading to increased local complication rates. Silicone lymphadenopathy is a foreign body reaction that does not warrant treatment unless it is symptomatic or interferes with breast cancer detection.

Level of Evidence III This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Silicone breast implants · Lymphadenopathy · Granuloma · PIP implants

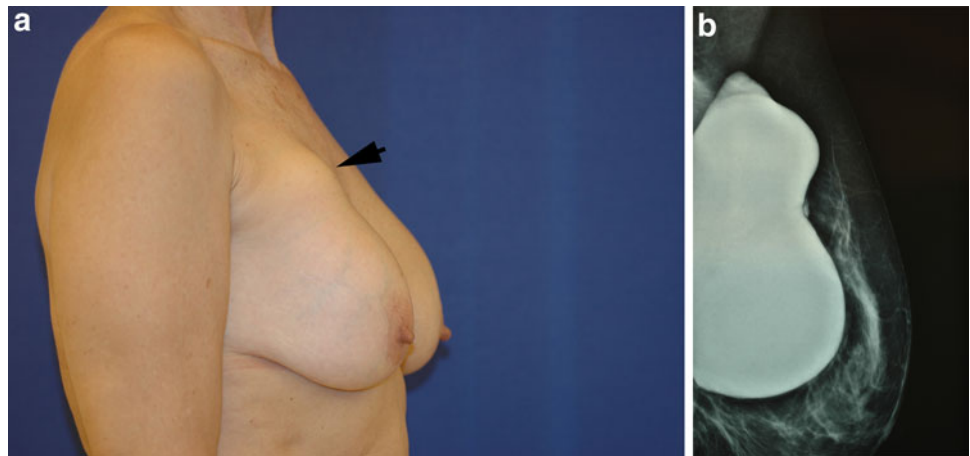
Introduction

Cronin and Gerow developed the first silicone breast prosthesis in 1961 and performed the first breast augmentation in 1962 [1, 2]. In terms of basic design, silicone breast implants are silicone rubber shells filled with silicone gel of various consistencies [3]. Medical grade silicone is a specific polymer called poly(dimethylsiloxane)

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Fig. 1 Patient 1 (V.A.). **a** Large palpable lump on the *upper pole* of the *right breast*. **b** Mammogram of the right breast showing rupture of the implant extending to the *upper pole* of the breast



(PDMS), and the more units in its formation, the more solid the silicone polymer becomes [3].

Low-molecular-weight silicone polymers are oils (fluids), whereas higher-molecular-weight silicones are more viscous. The silicone gel used in breast implants contains both low- and high-molecular-weight polymers mixed together in various ratios. The low-molecular-weight silicone fluid is not chemically attached to the main gel and can move or be extracted the same as water in a sponge [3].

The implant shell can be single or double, smooth or textured, or covered with polyurethane foam. The shell is a rubber-like membrane made of silicone elastomer [2]. Shells vary in the composition and characteristics of the elastomer, the type of coating, the number of layers, and the type of barrier layer used [4]. Barrier layers are specifically constructed to lessen the diffusion of low-molecular-weight silicone fluids into the surrounding tissues (gel bleed). Despite these barrier layers, Yu et al. [5] measured the silicone gel fluid diffusion of various implant models at about 300 mg per year, with considerable variation depending on implant age and manufacturer.

The initial breast implants designed by Cronin and Garrow and produced by Dow Corning had a thick smooth shell and a thick silicone gel roughly consisting of 50 % low-molecular-weight silicone fluid and 50 % high-molecular-weight silicone gel. The second-generation implants had thinner shells and softer gels (80 % low-molecular-weight silicone fluids and 20 % high-molecular-weight silicone gel) to give a more natural feel, but it soon became clear that gel bleed and rupture rates were increased. The third-generation implants introduced barrier layers and increased the cohesiveness of the gels to reduce gel bleed. Fourth-generation implants introduced shell texturing to reduce capsular contracture and increased gel cohesiveness to improve the feel and performance of the implants. Finally, fifth-generation

implants have a form-stable design with increased gel cohesiveness and an anatomic shape [6, 7].

The life span of silicone implants was initially presumed to be unlimited, but it was later demonstrated that the silicone elastomer has a finite life span and that silicone implants age and eventually fail [8]. Rohrich et al. [8] reported implant failure rates of 4–71 % depending on the definition of implant failure, the population base, and the diagnostic method used. According to the Inamed and Mentor Silicone Breast Implant Core Studies published in 2007, the overall implant rupture rate was 3.5 % at 6 years for Inamed implants [9] and 0.9 % at 3 years for Mentor implants [10].

Release or migration of silicone into the surrounding tissues invokes a straightforward, nonspecific foreign body reaction, resulting in typical macrophage invasion, giant cell formation, and eventual scarring [3, 11–13]. Silicone lymphadenopathy is simply a deposition of silicone in one or more lymph nodes due to lymphatic migration of silicone [14] and represents a normal physiologic response to the presence of foreign material [15]. Silicone seems to be phagocytosed by multinucleated giant cells that have uniformly distributed nuclei with abundant eosinophilic cytoplasm and prominent vacuoles partly containing silicone gel [13, 16].

When it occurs, silicone lymphadenopathy typically is a rather late finding. It has been reported 6–10 years after breast implantation [15].

According to published statistics, the women with breast implants number more than 3,500,000 in the United States alone [16, 17]. Given the magnitude of these numbers, it can easily be understood that silicone lymphadenopathy, secondary to placement of silicone breast implants, can be the cause of considerable morbidity and anxiety, taking into account the stress caused by the identification of enlarged axillary lymph nodes in female patients.

Table 1 Patients

	Patient	Year of implantation	Make & type of implant	Age of implant (years)	Onset of symptoms	Symptom findings & interventions	U/S, mammography, MRI	Year of explantation	Intraoperative findings	Histology/cytology
1	V.A.	1976	Unknown	34	Unknown 2010	Capsular contracture (closed capsulotomy) Bilateral axillary lymphadenopathy	Bilateral axillary lymphadenopathy Ruptured implants bilaterally	2010	Ruptured implants (totally destroyed) Bilateral lymphadenopathy (not removed)	Siliconomas (FNA)
2	V.M.	1982	CUI SGR double lumen	10	1990 1992 1992 1994	Capsular contracture on R breast (closed capsulotomy) Capsular contracture bilaterally Palpable lump on L breast (unknown histology) Four enlarged lymph nodes of R axilla	Rupture of L implant Four suspicious lymph nodes of R axilla	1992 1994	Ruptured implants bilaterally Capsulectomy & replacement of implants (CUI) Four suspicious nodules of R axilla Level 3 axillary clearance	Siliconomas
3	V.K.	1997	CUI MLP textured	13	2002 2007 2010	Pain in L breast Pain in L breast L axillary lymphadenopathy	No pathology No pathology L axillary lymphadenopathy	2010	Intact implants Capsulectomy (replacement of implants Allergan Inspira TSF) Excision of enlarged lymph node of L axilla	Siliconoma Periprosthetic fluid & capsule –ve for malignancy
4	A.F.	1999	Mentor Siltex textured	12	2010	Bilateral axillary lymphadenopathy (FNA) Palpable lump in R breast	Bilateral axillary lymphadenopathy	2011	Intact implants Nodule in upper pole of R breast Bilateral axillary lymphadenopathy	Siliconomas Periprosthetic fluid & capsule –ve for malignancy
5	F.T.	2006	PIP IMGHC	6	2012	No symptoms, presented for checkup Palpable lump of L axilla	Inhomogeneity inside the implant + silicone in lymph node on L side	2012	Totally destroyed implant in L breast Suspicious lymph node of L axilla	Siliconoma Periprosthetic fluid & capsule –ve for malignancy
6	S.Z.E	2007	PIP IMGHC	5	2012	Palpable lump of R axilla	Silicone traces outside shell R breast Silicone trace in lymph node of R axilla	2012	Rupture implant in R breast Suspicious lymph node of R axilla	Siliconoma Periprosthetic fluid & capsule –ve for malignancy
7	G.Z.S	2008	PIP IMGHC	4	N/A	No symptoms recalled	Silicone trace in lymph node on R side + inhomogeneity inside the implant on L side	2012	Leakage on R side Lymph node not removed	N/A
8	M.J.	2008	PIP IMGHC	4	N/A	No symptoms, self-presented for checkup Palpable lump of R axilla	Silicone trace outside the shell & in lymph node on R side	2012	Ruptured implants bilaterally Lymph node of R axilla	Siliconoma
9	H.R.	2008	PIP IMGHC	4	N/A	No symptoms recalled	Silicone trace outside the shell & in lymph node on R side	2012	Destroyed implant on R side Lymph node of R axilla not removed	N/A

Table 1 continued

	Patient	Year of implantation	Make & type of implant	Age of implant (years)	Onset of symptoms	Symptom findings & interventions	U/S, mammography, MRI	Year of explantation	Intraoperative findings	Histology/cytology
10	V.F.	2008	PIP IMGHC	4	2012	No symptoms Recalled palpable lump of R axilla	Silicone trace outside the shell & in lymph node on R side + silicone granuloma next to implant in R breast	2012	Ruptured implants bilaterally Suspicious lymph node of R axilla	Siliconoma Periprosthetic fluid & capsule –ve for malignancy
11	P.B.	2008	PIP IMGHC	4	2012	No symptoms Routine check Palpable lump of R axilla	Silicone trace outside shell & in lymph node on R side	2012	Totally destroyed implant in R breast Three suspicious lymph nodes of R axilla	Siliconoma Periprosthetic fluid & capsule –ve for malignancy
12	B.T.	2008	PIP IMGHC	3	2011	No symptoms Routine check Palpable lump of L axilla	Silicone in lymph node of L axilla	2011	Intact implants Severe bleeding	Siliconoma
13	L.L.I.	2009	PIP IMGHC	2	2011	No symptoms Routine check Palpable lump of R axilla	Silicone in lymph node of R axilla	2011	Totally destroyed implant in R breast Suspicious lymph node of R axilla	Siliconoma Periprosthetic fluid & capsule –ve for malignancy
14	M.N.	2009	PIP IMGHC	2	2011	No symptoms Routine check Palpable lump of L axilla	Silicone in lymph node of L axilla	2011	Totally destroyed implant in L breast Suspicious lymph node of L axilla	Siliconoma Periprosthetic fluid & capsule –ve for malignancy

U/S ultrasonography, MRI magnetic resonance imaging, FNA fine-needle aspiration, CUI Cox Uphoff International, R right, L left, SGR, MLP, –ve negative, TSF, PIP Poly Implant Prothèse, IMGHC, N/A not applicable

Patients and Methods

For this study, 14 cases of silicone lymphadenopathy were identified from our files (Table 1). Four patients in these cases were implanted before 2000 (patients 1–4) and had an implant age of 12 to 34 years (mean, 17.25 years) at explantation.

Patient 1 (V.A.) presented in 2010 with a large palpable lump on the upper pole of her right breast. She had been implanted in 1976 with silicone breast implants of unknown origin. Mammography showed rupture of the right breast implant extending to the upper pole of the breast (Fig. 1a, b). Histology of the enlarged axillary nodes was confirmed preoperatively with fine-needle aspiration (FNA), and the axillary lymph nodes were not removed during the explantation.

Patient 2 (V.M.) presented in 1992 with a palpable lump on the upper lateral quadrant of her left breast and bilateral Baker 3 capsular contracture. She had undergone breast augmentation with Cox Uphoff International (CUI) Saline Gel Round (SGR) double-lumen breast implants in 1982 and bilateral closed capsulotomy in 1990. Mammography and ultrasonography showed rupture of the left implant and identified

four suspicious lymph nodes in the right axilla. Both implants were found ruptured and were replaced during surgery. A level 3 axillary clearance was performed on the right side. All four lymph nodes were identified as siliconomas.

Patient 3 (V.K.) initially presented with pain in the left breast, but repeated clinical examination and breast imaging failed to identify any pathology for nearly 8 years. She had been implanted in 1997 with CUI MLP textured implants. She finally presented, 13 years after implantation with clinically palpable left axillary lymphadenopathy confirmed by mammography (Fig. 2a). Histology identified this lesion as a siliconoma (Fig. 2b–c).

Patient 4 (A.F.) presented with bilateral axillary lymphadenopathy and a palpable lump on the upper pole of her right breast. She had been implanted in 1999 with Mentor Siltex textured implants. Preoperative mammography confirmed the enlarged axillary nodes (Fig. 3a, b). Another lymph node was identified intraoperatively at the site of the palpable lump in the right breast (Fig. 3c–e). Histology confirmed all these lesions as siliconomas. Notably, the implants were found intact during surgery.

The remaining 10 patients (patients 5–14) all were implanted between 2006 and 2009 and all had Poly Implant

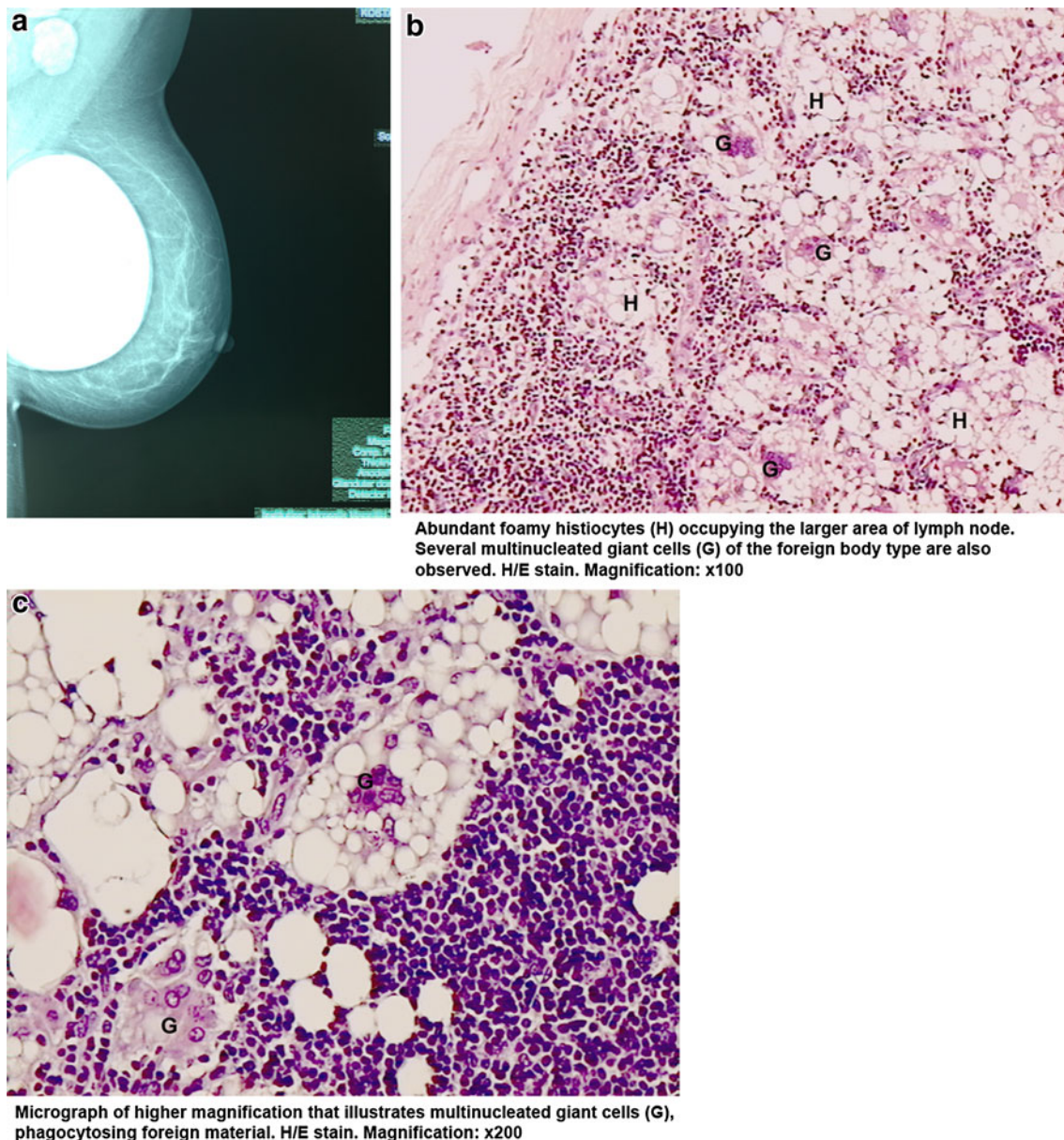


Fig. 2 Patient 3 (V.K.). **a** Mammogram of the left breast showing left axillary lymphadenopathy. **b** Histology of the lymph node showing abundant foamy histiocytes (H) occupying the larger area of lymph node. Several multinucleated giant cells (G) of the foreign body

reaction type also are observed (hematoxylin and eosin [H&E] stain; magnification, $\times 100$). **c** Micrograph of higher magnification illustrating multinucleated giant cells (G) phagocytosing foreign material (H&E stain; magnification, $\times 200$)

Prothèse (PIP) implants. The age of the PIP implants at explantation was 2–6 years (mean, 3.45 years). The time that the implants had been in situ was significantly less than with that of the initial four patients, but due to the small number of patients, conclusions cannot be safely drawn.

All the cases but one had ruptured or leaking implants (Fig. 4a–c). The diagnosis was either clinical (palpable lump in the axilla or the breast itself) (8 cases) or incidental during ultrasonography or mammography (2 cases) (Fig. 5a, b). All suspect lymph nodes, which caused complaints, in the PIP patients were removed at the time of explantation (Fig. 6b).

The histology of the lymph nodes removed was identical in all cases and referred to as “siliconoma”. The cytology of the periprosthetic fluid was negative for malignancy in all eight cases.

The results of our study showed that most problems were related to silicone implants used before 2000, except for the PIP implants, for which all the problems started after 2006. This of course could easily be attributed to a biased cohort due to the small number of patients included. On the other hand, this finding prompted us to review the available literature to identify cases of silicone-related

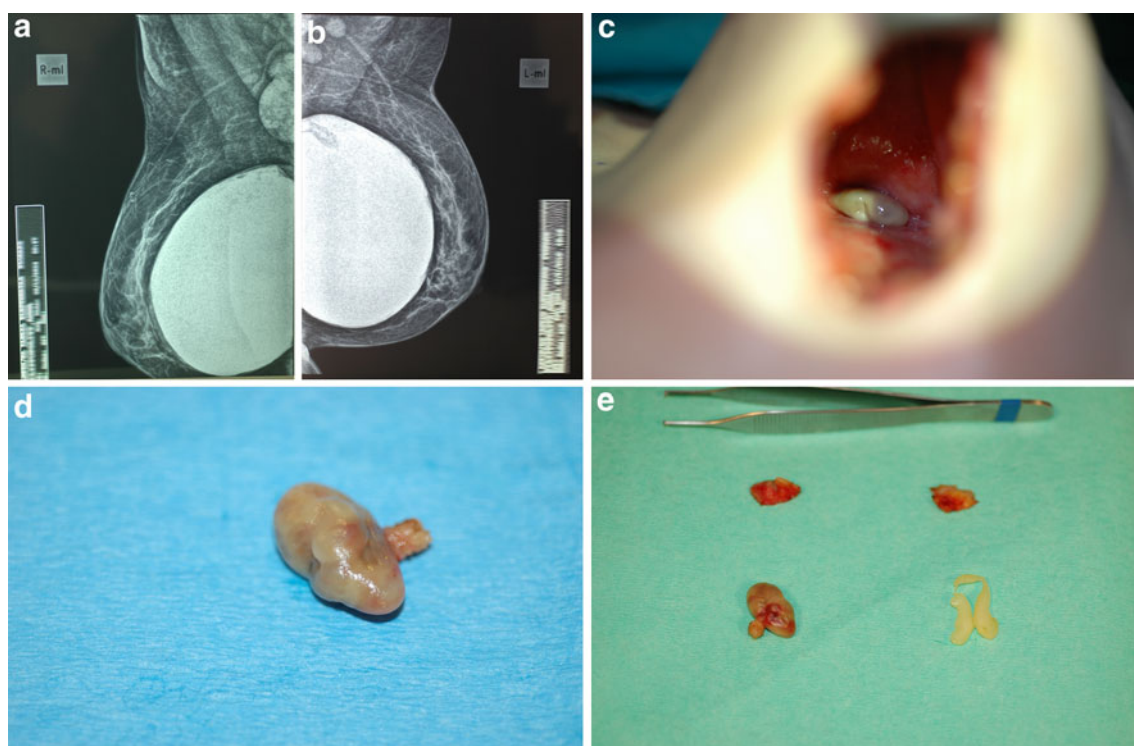


Fig. 3 Patient 4 (A.F.). **a, b** Mammogram showing bilateral axillary lymphadenopathy. **c** Intraoperative view of the lymph node in the upper pole of the right breast. **d, e** Two lymph nodes were

removed from the right axilla (**e** upper right and left) and one large lymph node from the upper pole of the right breast in two pieces (**d, e** lower right and left)

lymphadenopathy and to investigate the relation of implant manufacturer and year of implantation to the incidence of lymphadenopathy.

A thorough bibliographic search was initiated to identify all reports of lymphadenopathy related to silicone breast implants in the English literature. The search was performed through Medline using the following search terms in various combinations: “breast,” “mammary,” “lymphadenopathy,” “silicone,” “implant(s),” “prosthesis/es,” “mammoplasty,” “mammaplasty,” “augmentation,” “axilla,” “axillary,” “migration,” “granuloma(s),” “lymph node(s),” and “siliconoma(s).” A forward search also was performed from the references of all the articles identified in the aforementioned search to locate additional primary papers of interest.

Results

Using the described criteria, we identified 29 papers with case reports of silicone lymphadenopathy published between 1978 and 2012, for a total of 175 cases (Table 2) [11, 14, 16, 18–43]. Every effort was made to identify the exact type of implant and the date of implantation in these papers. Where possible, the authors were contacted to establish the identity of the implants and the time of implantation when this information was not clear from the

text. Where we did not get a response or where we could not contact the authors, we calculated the estimated latest time that the implantation could have taken place by using the date of submission for publication as a starting date and moving backward using the data published in each paper.

We were able to extract accurate implant age data in 19 cases [11, 20, 23, 26, 31–34, 37, 43]. Approximate implant age data (as described earlier) were extracted in 12 cases [19, 22, 24, 27–30, 35, 36, 41]. Mean implant age data were already available in four papers, for a total of 133 cases (Table 3) [16, 25, 38, 42]. Implant age data were insufficient in 11 cases [14, 18, 21, 43]. Altogether, we were able to extract usable data in 164 of the 175 cases (12 of which were approximate calculations using the assumptions described earlier) (Table 4).

The minimum age of the implants at presentation or explantation was 1–31 years. The mean age of the implants at presentation or explantation was 10.8 years for a total of 164 patients. Of these patients, 159 had been implanted before (and including) the year 2000, and their implants had a mean age of 11 years at presentation or explantation. The remaining 5 patients had been implanted after the year 2000, and the mean age of their implants at presentation or explantation was 4.6 years. Of these five patients, two had PIP implants and two had implants of unknown origin.

When we added the data from our own cases, the results changed as follows. The mean age of the implants at

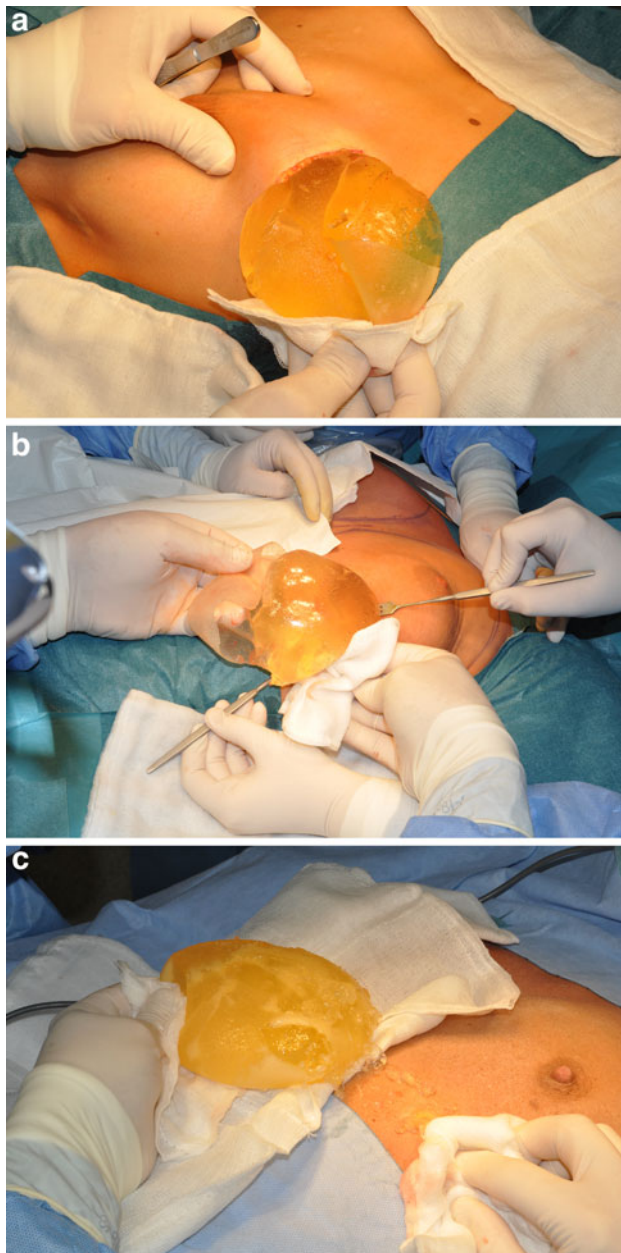


Fig. 4 Ruptured Poly Implant Prothèse (PIP) implants at explantation. **a** Patient 10. Ruptured right implant. **b** Patient 11. Ruptured right implant. **c** Patient 14. Ruptured left implant

presentation or explantation was 10.56 years in a total of 178 cases. Of these patients, 163 had been implanted before (and including) the year 2000, and their implants had a mean age of 11.16 years at presentation or explantation. The remaining 15 of these patients were implanted after the year 2000, and their implants had a mean age at presentation or explantation of 4.06 years. With our own cases included, 12 of the 15 cases implanted after (and including) the year 2000 and presenting with lymphadenopathy had PIP implants.

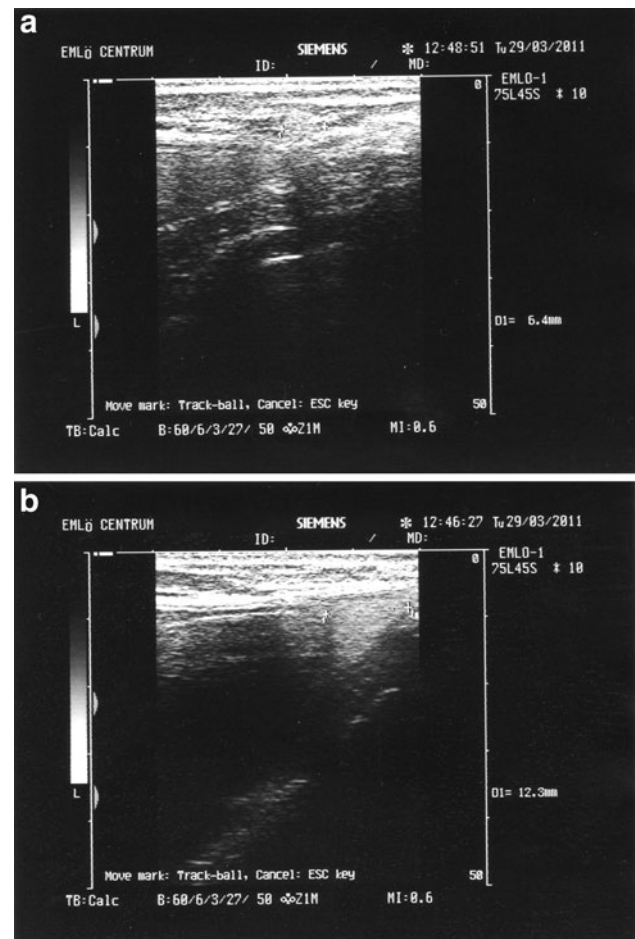


Fig. 5 Ultrasonographic evidence of silicone traces inside one or more lymph nodes in one of the axillae. **a** Patient 14 (M.N.). Silicone in the lymph node of the *left axilla*. **b** Patient 8 (M.J.). Silicone in the lymph node of the *right axilla*

Discussion

Since the introduction of the first silicone breast implant, more than 240 different types and 8,300 models of breast implants and expanders have been manufactured in the United States alone, with a substantial number of individual characteristics differentiating them. Some of these characteristics or “features” have had important influences on the biologic responses and complications of the implantation process [3]. The basic design shared by all implants is a silicone rubber shell either factory filled with silicone gel of various consistency or filled at surgery with normal saline.

Complications such as rupture and silicone migration may vary with implants from different manufacturers based on factors that are not precisely identified including different shells, different gel consistencies and diffusion characteristics, different gel chemical compositions, different siloxane molecular weights, different shapes, and so forth [44].

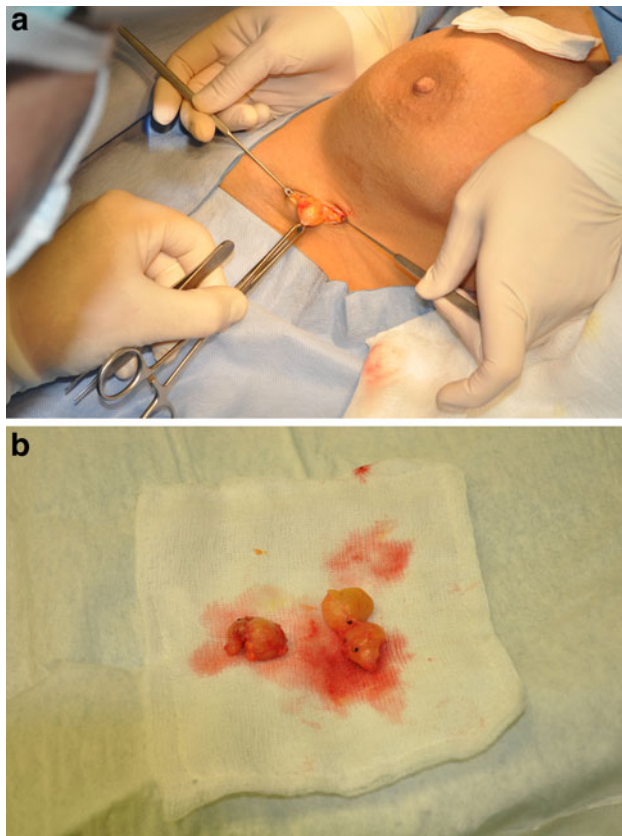


Fig. 6 Excision of suspect lymph nodes. **a** Patient 10 (V.F.). Excision of enlarged lymph node from the right axilla. **(b)** Patient 11 (P.B.). Three enlarged lymph nodes excised from the *right axilla*

Texturing and coating have been designed to reduce capsular contracture by promoting tissue ingrowth into the interstices of projections or pores, prolonging chronic inflammation, disorienting collagen fibrils, and weakening their contractile forces [3, 45, 46]. Barrier shells, on the other hand, have been designed to reduce the diffusion of low-molecular-weight silicone fluids through the intact elastomer shell, a process called “gel bleed” [3, 5, 7, 47].

Dow Corning incorporated a thin fluorosilicone layer (barrier shell) on the interior surface of the implant shell in 1981 to reduce diffusion [3]. McGhan (Allergan Inc, Irvine CA, USA) introduced two outer barrier layers named Natrashiel and Natrashiel II in 1977, an Ultra High Performance decreased-bleed shell in 1978, and its currently used dimethyl diphenyl siloxane barrier layer (Intrashiel) in 1979. Mentor introduced barrier shells on gel-filled models in the late 1970 s, and acquired McGhan’s licensed barrier technology in 1990 [3]. Cox Uphoff International (CUI) introduced the diffusion rate inhibiting envelope (DRIE) low-bleed shell in 1984, which still is used currently, although CUI was acquired by Inamed (McGhan) in 1989 and currently is owned by Allergan.

The PIP implants were introduced in France in 1991 and managed to obtain the CE Marking in 1997 [48]. In their

current form, they have been available since 2001. Initially, the implant shell contained a barrier layer, and the gel used for filling was the standard medical grade Nusil Med3-6300 (Nusil Technology LLC, Carpinteria, CA) [6]. In 2010, several laboratory studies on retrieved PIP breast implants conducted by the French Health Authorities (AFSSAPS) showed that the marketed PIP implants have not been produced according to the documented procedures provided to obtain the CE mark. The barrier layer was removed from the shell in 2007, and the medical grade Nusil gel was replaced by two types of inferior industrial grade gels, PIP1 (used before 2008) and PIP2 (used after 2008) [6]. The PIP silicone gels contained significant levels of silicones with low molecular weight, which increased diffusion through the implant shell. In addition, the PIP1 and PIP2 gels were much less stable than the Nusil gel and demonstrated an irritant potential not found with the silicone gels from other prostheses nor with the Nusil gel. This latter finding indicates an increased potential for local tissue reactions [6].

The 1976 Medical Device Amendments Act of the U.S. Congress gave the Food and Drug Administration (FDA) the power to regulate medical devices including silicone breast implants. All breast implants in use before that date were “grandfathered” and accepted “as is.”

In 1988, about the time when the manufacturers started to produce “good” devices, the FDA classified breast implants as class 3 medical devices, which required that they be subject to a stringent safety and effectiveness control standard. This gave the FDA the authority to demand information about the devices and eventually led to the FDA’s moratorium on the use of silicone breast implants in 1992 [49]. McGhan (subsequently known as Inamed and now owned by Allergan) and the Mentor Corporation, the only two companies that stayed in business, were forced to conduct large prospective multicenter studies to prove the safety and efficacy of their implants [50] before being allowed back into the market for augmentation mammoplasty by the FDA in 2006 [51].

We managed to identify 189 published cases of silicone lymphadenopathy in the English literature, of which 178 cases (including ours) had usable data. The mean age of the implants at explantation was 10.56 years. When we broke down the cases into those before and including 2000 and those after 2000, the mean age at explantation of the devices implanted before 2000 was 11.16 years, and that of the devices implanted after 2000 was 4.06 years. This difference reflects the large numbers of PIP implants used after 2000 that failed.

Ironically, the PIP implant “scandal” highlights the fact that current technologies implemented in breast implant design and manufacturing are safe and effective. It was when PIP chose to disregard these technologies and

Table 2 Papers with case reports of axillary silicone lymphadenopathy

No.	Reference	Year of publication	No. of cases	Types of implants ^a	Year of implantation	Age of implants at explantation (years)
1	Wintsch et al. [18]	1978	1	Unknown	<1978	Unknown
2	Hausner et al. [11]	1978	1	Unknown	1967	11
3	Hausner et al. [19]	1981	1	Unknown	<1973	>8
4	Truong et al. [20]	1988	4 ^b	Unknown	<1970–1980	8–18
5	Tabatowski et al. [21]	1990	1	Unknown	<1990	Unknown
6	Lin et al. [22]	1993	1	MEME	<1990	>3
7	Ahn and Shaw [23]	1994	4	Snyder	1985	9
				Unknown	1973	21
				Unknown	1981	13
				Unknown	1979	15
8	Rivero et al. [24]	1994	1	Unknown	<1982	>12
9	Kulber et al. [25]	1995	23 ^c	Unknown	<1990–1993	1–22
10	Vaamonde et al. [26]	1997	2	Unknown	1990	6
					1992	4
11	Kao et al. [27]	1997	1	Mentor Becker	<1995	>2
12	Barnard JJ et al. [14]	1997	8	Unknown	<1993	>4
13	Santos-Briz Jr et al. [28]	1999	1	Unknown	<1993	>6
14	Shaaban et al. [29]	2003	1	Allergan	<2001	>2
15	Katzin et al. [16]	2005	87	Dow Corning	<1974–2003	2–31
				Heyer-Schulte		
				Mentor		
				McGhan		
				Aesthetech		
				Cox-Uphoff		
				Medical Engineering Corporation/Surgitek		
				Bristol-Myers Squibb		
16	Lahiri and Waters [30]	2006	1	PIP	<1997	>9
17	Shipchandler et al. [31]	2007	1	Unknown	1985	22
18	Khan [32]	2008	1	PIP	2005	3
19	Ganau et al. [33]	2008	1	Mentor Becker	1994	14
20	Accurso et al. [34]	2008	1	PIP	1999	9
21	Tehrani et al. [35]	2008	1	Unknown	<2003	>5
22	Kaufman et al. [36]	2009	1	R PIP	<2005	>4
				L McGhan 410		
23	Gil et al. [37]	2009	1	Mentor Becker 25	2000	9
				(replaced by)	2001	8
				Mentor Siltex HP	2002	7
				(replaced by)		
				Mentor Becker 35		
24	Dragu et al. [38]	2009	5	Unknown	<1988	>10
25	Adams et al. [39]	2009	1	Unknown	<2001	>8
26	Takenaka et al. [40]	2009	1	Unknown	<1980	>29
27	Dragoumis et al. [41]	2010	1	Nagor ^d	<2000	>10
28	Bauer et al. [42]	2011	18	Unknown	1998–2008	7–13

Table 2 continued

No.	Reference	Year of publication	No. of cases	Types of implants ^a	Year of implantation	Age of implants at explantation (years)
29	Grubstein et al. [43]	2011	4	Unknown	1991	20
				Unknown	Unknown	Unknown
				Unknown	2002	9
				(replaced due to leakage with other unknown)	2008	3
				Unknown	1998	13
			Total cases	175		

R right, L left

^a Types of implants and year of implantation: where possible, all authors were contacted to establish the identity of the implants and the time of implantation. Where we did not get a response or where we could not contact the authors, we calculated the estimated latest time that the implantation could have taken place by using the date of submission for publication as a starting date and moving backward using the data published in each paper. These cases can be identified in the table by the < sign before the date(s), which means that the implantation was performed before the date presented in the table. In the last column (“Age of implants at explantation”), we tried to calculate the age of the implants at explantation using the same method. Where we could not calculate the age exactly, the sign > was used, meaning that in these cases, the age of the implants was at least the number of years shown

^b Truong et al. [20] presented 9 cases of silicone lymphadenopathy, but 4 of these were related to injection of liquid silicone and not breast implants. One case was bilateral, and this was considered as two separate cases in the original paper

^c Kulber et al. [25] studied 15 patients after breast augmentation who had a mean time for presentation of symptoms after implantation of 6 years (range, 1–12 years) and 8 patients after breast reconstruction who had a mean time for presentation of symptoms after implantation of 5 years (range, 1–22 years)

^d Dragoumis et al. [41] refer to Mentor Siltex round textured implants, 220 ml in size. Because no 220-ml Mentor implant is available, we contacted the senior author to determine whether there has been an error in the paper. The senior author confirmed that the implants were indeed not Mentor but Nagor implants and that a typographic error was made in the original published paper

Table 3 Papers with available mean/median data of implant age at presentation or explantation

Reference	No. of cases	Mean age of implants at explantation (years)	Age of implants at explantation years (range)
Kulber et al. [25]	15	6	1–12
	8	5	1–22
Katzin et al. [16]	87	12.2	1–30
Dragu et al. [38]	5	18	N/A
Bauer [42]	18	9.4 ^a	N/A

N/A not available

^a Bauer et al. [42] chose to report the median age of the implants at presentation or explantation (107 months; range, 82–156 months, or 8.9 years; range, 6.8–13 years). We used the formula devised by Hozo et al. [55] to estimate the mean age from these values. This formula uses the values of the median (m) and the low and high end of the range (a and b, respectively). According to this formula, mean = (a + 2 m + b)/4. In our case, mean = (82 + 2 × 107 + 156)/4 = 113 months or 9.4 years

standards in favor of increased profits that rupture rates and gel diffusion started rising, leading to increased local complication rates. The PIP “scandal” was a giant step backward in silicone breast implant history, but at the same time, it gave us the opportunity to confirm that the currently available devices approved by the FDA actually are “good” devices.

The extremely lengthy and expensive pre- and post marketing studies required for any change in breast implant design and manufacturing or for the introduction of new devices means that any developments in breast implant

technology will require a considerable investment, both in time and money. In our opinion, and in view of the fact that the current devices are considered “safe” and “effective,” significant advances in breast implant design are not to be expected for several years.

With regard to patient management, there are two separate yet closely linked subgroups of patients: those who have failed or ruptured implants with silicone lymphadenopathy diagnosed radiologically and those with clinically and radiologically intact implants that nonetheless present with clinically or radiologically identified silicone lymphadenopathy.

Table 4 Mean age of implants at presentation or explantation^a

Total (literature)	Years 10.8
Before 2000 (literature)	11.0
After 2000 (literature)	4.6
Total (all cases)	10.56
Before 2000 (all cases)	11.16
After 2000 (all cases)	4.06

^a Data are from the literature search or total cases including data from the literature search and our own cases

The management of implant rupture has been extensively discussed in the literature and is not the scope of the current study. The clinical significance of silicone lymphadenopathy, however, warrants discussion. Its incidence and prevalence in the total population of women with breast implants are largely unknown, and no publications have discussed this issue directly [15].

For breast cancer patients who have undergone breast reconstruction with the use of silicone breast implants or expanders, the clinical differential diagnosis of regional lymph node enlargement should include both silicone lymphadenopathy and metastatic breast cancer [16]. It is therefore important to identify and confirm the nature of the enlarged lymph nodes in these patients by radiology, FNA, or open biopsy, and excision of these lesions should be carefully considered.

In patients with silicone breast implants for breast augmentation, silicone lymphadenopathy, once it has been properly diagnosed, must be treated for what it is. It is not a disease process but rather a type of foreign body reaction. It simply is a deposition of silicone in one or more lymph nodes and represents a normal physiologic response to the presence of foreign material [12, 15]. Interestingly, both the FDA and the Department of Health in the United Kingdom pay little attention to silicone lymphadenopathy in their documents regarding the safety and complications of silicone breast implants [52–54]. Patients typically present with a small palpable mass in their axilla. Once the diagnosis has been established, removal is not considered necessary unless the lesions are clinically symptomatic or painful or unless they mimic breast cancer [12, 15].

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