Safety & imaging of modern silicone breast implants

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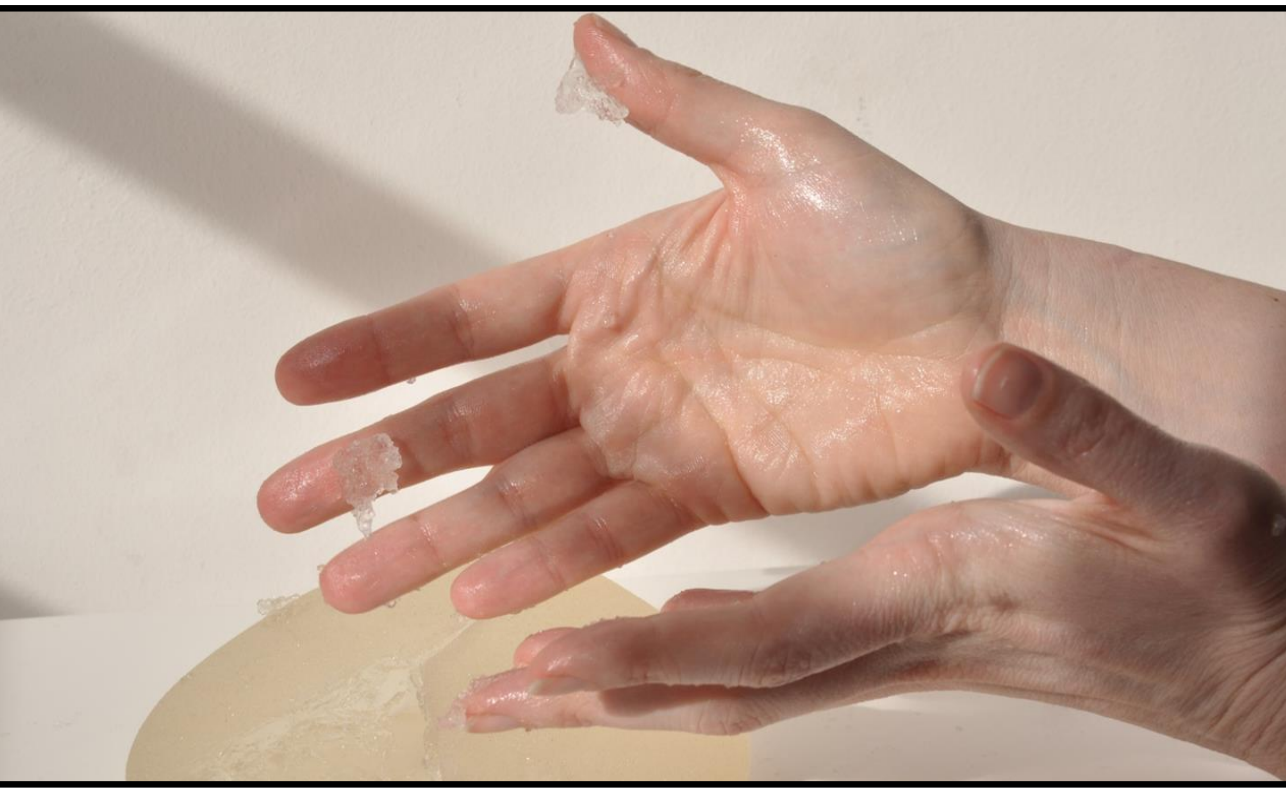
CHAPTER 5

Clinical & Diagnostic Consequences of Poly Implant Prothèse Silicone Breast Implants Recalled from the European market in 2010



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CHAPTER 5

ABSTRACT

BACKGROUND: Recently, Poly Implant Prothèse silicone breast implants were recalled from the European market. The authors studied 112 women and previously published data on rupture prevalence. Women are presenting with symptoms they feel may be a result of ruptured implants. The authors' aim was to study the clinical consequences of Poly Implant Prothèse implants.

METHODS: One hundred twelve women with 224 proven Poly Implant Prothèse implants after 10 years of implantation were enrolled in this study. All women underwent physical examination and magnetic resonance imaging and were interviewed regarding symptoms. Details of the explantations of 35 women with at least one ruptured implant were documented. Tissue from 10 women was sent for pathologic investigation.

RESULTS: Of 112 women, 34 (30.4 percent) had symptoms attributable to their implants. Physical examination showed that 12 of the 112 women (10.7%) had findings suggestive of rupture, most commonly pain. Three had lymphadenopathy that seemed to correlate with implant rupture or excessive "gel bleed". Pathologic findings showed no malignancies. Eight women who underwent explantation had no implant rupture. Excessive gel bleed was documented in half of them.

CONCLUSIONS: Clinical consequences of women with Poly Implant Prothèse implants are comparable to those reported in the literature of other manufacturers. Neither complaints nor findings at physical examination had a significant correlation with implant rupture at explantation. Magnetic resonance imaging still is the preferred method compared with physical examination for diagnosing rupture. The low specificity was probably caused by the difficulty to differentiating between rupture and excessive gel bleed in these implants.

BACKGROUND

Recently silicone breast implants from the French manufacturer Poly Implant Prothèse have been the subject of debate and public unrest in women with silicone breast implants. An inspection in 2009 by the French health watchdog Agence Française de Sécurité sanitaire des Produits de Santé, found that the silicone gel used in these implants was unauthorized for medical use but approved instead for use in mattresses and cushions.[1] This came to light after case reports of unexpectedly high rupture rates in this brand were reported in medical literature[2] and resulted in the recall of all Poly Implant Prothèse implants in 2010.

In December 2011, Poly Implant Prothèse implants were in the news again when the French authorities stated the possible health dangers, including a possible increased risk of breast cancer involved with these implants. They advised all Poly Implant Prothèse implants to be removed, regardless of whether they had ruptured or not.[3] In response, Scientific Committee of the European Commission attempted to examine the health consequences of these Poly Implant Prothèse implants to the patient. They stated that in Poly Implant Prothèse implants the shell is weaker than in other available implants and that an in vivo test for irritancy is positive, although the material is not cytotoxic or genotoxic to women. Unfortunately, because of limited clinical data and the absence of epidemiologic data on Poly Implant Prothèse silicone breast implants, they could only conclude that any health effect could not be ruled out.[4]

Since then, increasing numbers of women have come forward with symptoms they feel may be a result of ruptured Poly Implant Prothèse implants. In the early 1990s, there was similar press coverage and public alarm when silicone implants were banned from the U.S. market. Many epidemiological studies have since shown that there is no association between silicone breast implants and increased risk of any rheumatic diseases, breast cancer[5] and other cancers,[6] fibromyalgia, typical or atypical connective tissue diseases[7,8] or effects on pregnancy and future children.[9] Eventually, the FU.S. Food and Drug Administration decided, after supporting evidence about the safety of silicone implants, to reintroduce the use of silicone breast implants to the U.S. market.[10]

We acknowledge the concerns that this Poly Implant Prothèse debacle has raised among women with Poly Implant Prothèse implants. However, no study so far has documented the exact symptoms women experience with Poly Implant Prothèse implants. The aim of this study is to document the clinical consequences in women with Poly Implant Prothèse implants and to find out whether these complaints are related to implant rupture. As the diagnosis of rupture is difficult, we compared physical examination by a plastic surgeon and magnetic resonance imaging screening. We also report on the explantation results and, where available, pathology reports.

PATIENTS AND METHODS

In early 2011, the Jan van Goyen Clinic (Amsterdam, The Netherlands) recalled patients who underwent augmentation with Poly Implant Prothèse implants, which were the most frequently used breast implant for cosmetic augmentation at the clinic in the years 2000 and 2001. All women (*n* = 474) were informed by letter about the concerns of the quality of their implants. They were requested to come for follow-up. Medical records were used to trace manufacturer and implantation specifics.

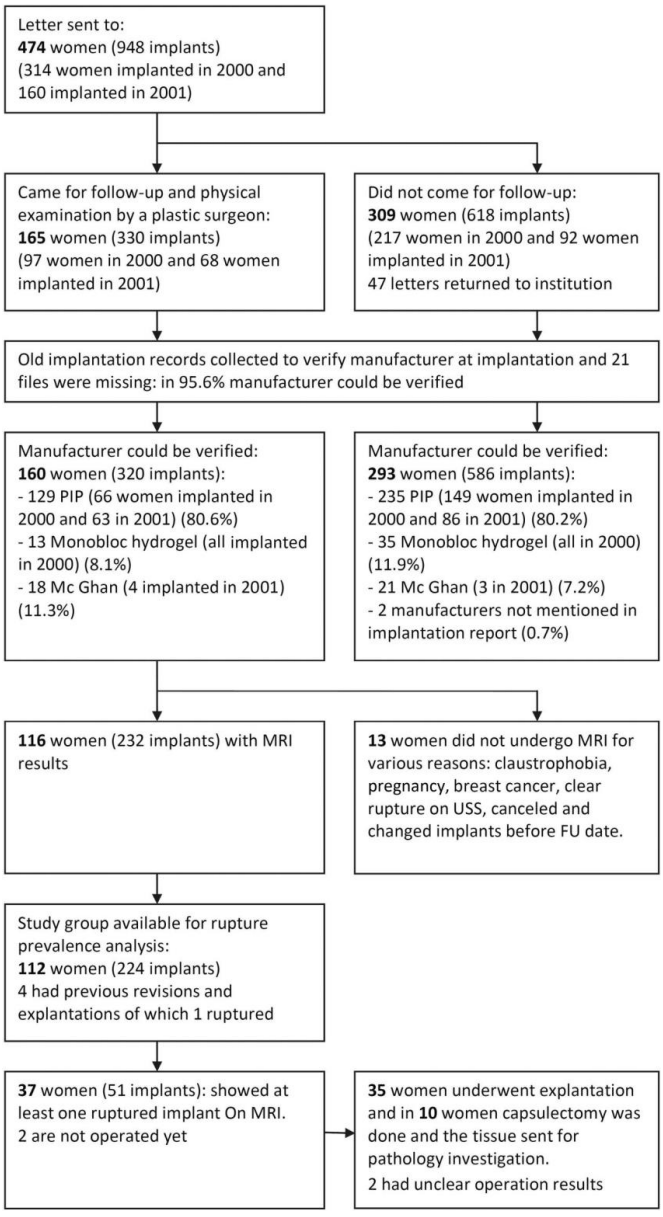

Figure 1. Study flowchart. PIP= Poly Implant Prothèse ; USS= ultrasonography; FU= follow-up; MRI= magnetic resonance imaging.

Of the 475 letters sent, 165 patients came for a follow-up visit. During first enrollment, some women were found ineligible for the study for reasons such as having a different implant manufacturer (13 had Monobloc hydrogel, 18 had McGhan, five were unknown), an implantation date outside of the range, or a contraindication for magnetic resonance imaging (*n* = 13; pregnant, breastfeeding, claustrophobia, breast cancer, clear rupture on ultrasound, cancelled and changed implants before follow-up date), or when no medical record could be found. An additional four women had previous revisions, excluding these and the above noted women, and 112 unselected women with 224 proven Poly Implant Prothèse implants were enrolled in the study (see Figure 1 for study flowchart.)

All women were interviewed and underwent a standardized clinical examination by a plastic surgeon, which included inspection and palpation. The following abnormal findings were documented: changed form, consistency and/or size, and palpable masses in breasts or axilla. Capsular contractures were documented according to Baker classification.[11]

All women were referred for a single magnetic resonance imaging facility to conduct (silent) rupture screening according to an established protocol. All subjects completed magnetic resonance imaging screening within 6 weeks of the physical examination and 85 (76 percent) completed screening within 2 weeks. We obtained magnetic resonance images using a 1.5-T unit (Siemens Magnetom Symphony, Siemens Medical Solutions, Erlangen, Germany.) Open CP Breast array coils were used for imaging both breasts of each patient. Short T1 inversion recovery T2-weighted axial images were obtained in all cases with an echo times of 70 msec. Short T1 inversion recovery T2-weighted axial and sagittal images with spectral suppression of silicone were obtained with an echo time of 84 msec. Short T1 inversion recover T2-weighted axial and sagittal images were obtained with spectral suppression of water with an echo time of 84 msec. All had repetition times of 2120 msec, Inversion recovery of 140 msec, slice thickness of 4mm, 256 x 128 matrix and field of view of 320 x 320 mm. The images were evaluated by an experienced radiologist as either evidence for rupture or evidence for extracapsular leakage.

Only women who were shown to have at least one ruptured implant and were offered explantation and replacement of both implants. Two delayed their operation date and in two operations results were not clearly documented. In 10 women, capsulectomy was performed and the tissue sent for pathologic investigation.

In all analysis, the unit of observation was both the implant as the woman. The data was analyzed using SPSS 17.0. (SPSS, Inc., Chicago, Ill.). Quantitative standard statistical significance was used in Pearson chi-square tests of the data tables. The critical level of statistical significance chosen was $p < 0.05$.

RESULTS

The mean age of the 112 enrolled women at the time of their implantation was 33.5 years. The 224 proven Poly Implant Prothèse implants had a mean implant age of 122 months (range, 111 to 133 months) at the time of physical examination. All implants were round, textured Poly Implant Prothèse silicone breast implants. The most frequently implanted size was 330ml. Of the 112 women 93 had subglandular placement of their implants. Table 1 summarizes all characteristics of our study group.

In our study group of 112 women with 224 Poly Implant Prothèse implants, 34 women (30.4 percent) mentioned any preexisting complaints in 53 implants (33.7 percent). Complaints mentioned were pain or a burning sensation by 20 women, and changed size, form and/or

consistency by nine women. Four women mentioned a palpable mass in their breast or axilla. These symptoms were not a reason for them to come to the clinic independently for follow-up.

Twelve women showed physical signs of rupture; changed form, size or consistency in nine women and a palpable lymph node in an axilla in three women. Fifteen implants (6.7 percent) could be classified as Baker grade III and only could be classified as Baker grade IV.

Of the 171 implants in which women reported no preexisting complaints, in 40 implants (23.4 percent) a rupture was found by magnetic resonance imaging, compared to 14 (26.4 percent) in the symptomatic group (Table 2). We found no significant correlation between reported complaints by women with Poly Implant Prothèse breast implants and their rupture rate. Except for one woman with some rheumatic complaints, none have mentioned having developed any medical conditions during their 10-year follow-up.

Table 1. Characteristics of study group of 112 women with PIP implants

	n	%
Age at implantation		
< 20 years	6	5.4
20-24 years	13	11.6
25-29 years	17	15.2
30-34 years	28	25.0
35-39 years	22	19.6
> 40 years	26	23.2
Implantation year		
2000	55	49.1
2001	57	50.9
Position of implant		
Subglandular	93	83.0
Subpectoral	19	17.0
Volume of implant		
< 200 ml	2	1.8
200-250 ml	13	11.6
250-300 ml	33	29.5
300-350 ml	40	35.7
350-400 ml	20	17.8
400-450 ml	4	3.6

PIP= manufacturer Poly Implant Prothèse; n= number; All women have 2 implants

Of 112 women assessed by physical examination, 12 showed physical signs of rupture, six of which (50 percent) were confirmed ruptured by magnetic resonance imaging results (Table 3). Of the 206 implants in which no signs of rupture were found by physical examination, 45 (21.8 percent) showed rupture on magnetic resonance imaging

Table 2. Pre-existing complaints in 112 women with 224 PIP implants in relation to results at Magnetic Resonance Imaging and explantation

	Women		Implants				Explanted Implants			
				Ruptured on MRI				Ruptured at Expl.		
All	(n=112)		(n=224)	(n = 54) 24.1%			(n=70)	(n = 39) 55.7%		
Self-referred complaints	n	%	n	n	%		n	n	%	
No symptoms	78	69.6	171	40	23.4		52	32	61.5	
Pain or burning sensation	20	17.9	30	8	26.7		9	3	33.3	
Changed size, form or consistence	9	8	16	3	18.8		5	2	40.0	
Mass in mamma or axilla	4	3.6	6	3	50.0		4	2	50.0	
Loss of sensation	1	0.9	1	0	0.0		0	0	0.0	
Total self-referred complaints	34	30.4	53	14	26.4	*p=0.57*	18	7	38.9	*p=0.41*

PIP= manufacturer Poly Implant Prothèse; n= number; All women have 2 implants; % = percentage of implants ruptured with a specific complaint. MRI= Magnetic Resonance Imaging; Not all women got explanted, only the women with at least one ruptured implant on MRI, Expl.= Explantation

Table 3. Findings at physical examination, suggestive of implant rupture in 112 women with 224 PIP implants in relation to results at magnetic resonance imaging and explantation

Women			All Implants				Explanted Implants			
				Ruptured on MRI				*Ruptured on Expl.*		
All	(n=112)		(n=224)	(n=54) 24.1%			(n=70)	(n=39) 55.7%		
Findings at physical examination	n	%	n	n	%		n	n	%	
No findings	100	89.3	206	45	21.8		62	35	56.5	
Changed size, form or consistence	9	8.0	15	7	46.7		6	3	50.0	
Palpable lymph node in axilla	3	2.7	3	2	66.7		2	1	50.0	
Total findings	12	10.7	18	9	50.0	*p=0.02*	8	4	50.0	*p=0.93*

PIP= manufacturer Poly Implant Prothèse; n= number; All women have 2 implants; % = percentage of implants ruptured with a specific complaint. MRI= Magnetic Resonance Imaging; Not all women got explanted, only the women with at least one ruptured implant on MRI, Expl.= Explantation

screening. In the 18 implants with signs suggestive of rupture, nine (50 percent) appeared to be ruptured on magnetic resonance imaging. Although physical signs judged by a plastic surgeon increased the likelihood of rupture found on magnetic resonance screening, we found no significant correlation with the rupture rate seen at actual explantation. In the majority of women in our study group we saw no severe capsular contracture. At magnetic resonance imaging screening, an increase in likelihood of rupture with the increase of Baker score was seen. In the explantation results, however, just one of the 16 implants with Baker III and IV was ruptured.

Of the 51 implants that showed rupture on magnetic resonance imaging, 35 (68.6 percent) were ruptured at explantation (16 false-positives) (Table 4). Of the 19 intact implants that were explanted, because the contralateral implant showed rupture on magnetic resonance imaging, four implants (21 percent) were ruptured on explantation (false-negatives). In total, eight of the 35 women with a positive magnetic resonance imaging result, showed no rupture of implants. Excessive "gelbleed" was documented in half of these. A series of photographs (Figure 2) illustrates one of our patients and the results at explantation; the milky colored fluid seen in Figure 2, *center, left* was also seen at times in intact implants and documented as excessive gel bleed. Besides this gel bleed, a change in consistency and color of the silicone gel was noticed when the shell was ruptured (Figure 2, *below right*).

Table 4. Explantation results of 70 PIP implants correlated to Magnetic Resonance Imaging screening

			Result at explantation						
	All implants		**Intact**		**Ruptured**		**Unknown**		***p***
	n	%	n	%	n	%	n	%	
At MRI:									
Intact	19	27.1	14	73.4	4	21.1	1	5.3	
Ruptured	51	72.9	13	25.5	35	68.6	3	5.9	*0.001*

PIP= manufacturer Poly Implant Prostheses; No= number; All women have 2 implants; MRI= Magnetic Resonance Imaging; Not all women got explanted, only the women with at least one ruptured implant on MRI

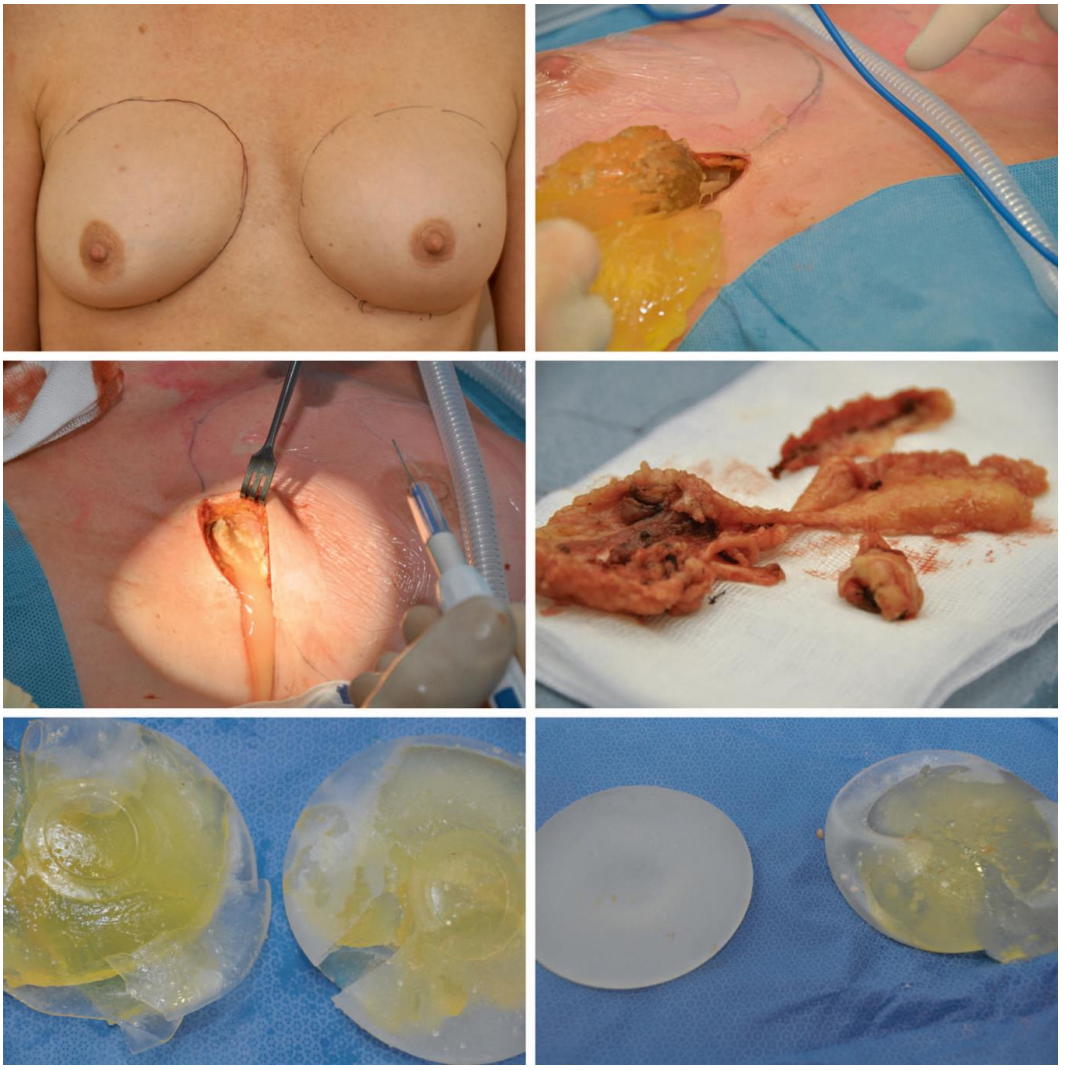

Figure 2. (*Above*, *left*) Patient with 305-ml Poly Implant Prothèse implants with subglandular implantation in the year 2001 reported no preexisting complaints, and at physical examination a change in form and asymmetry was found. (*Above*, *right*) Magnetic resonance imaging screening showed both implants to be ruptured, and explantation was performed. (*Center*, *left*) The milky liquid "bleed" seen in this patient was at times also seen in patients with intact implants. (*Center*, *right*) Capsulectomy was performed on both sides. (*Below*, *left*) Both Poly Implant Prothèse implants were found to be ruptured at explantation. (*Below*, *right*) A patient with Poly Implant Prothèse implants, of **which** one is intact and one is ruptured at explantation. One can notice the difference in structure, consistency, and even color of the silicone gel once the shell is torn and the silicone gel is exposed to the patient's own tissue

Thirty-seven women, with at least one ruptured implant on magnetic resonance imaging screening were offered an explantation at our clinic. Two women delayed their explantation, and one underwent explantation in another hospital; information regarding details of the procedure has been requested for this study. Of two explantations, the rupture status of the implants is unknown. Capsulotomy had to be performed bilaterally in 24 patients and unilaterally in two women. Of 10 women in whom capsulectomy was performed, the tissue was sent for pathologic

research. There were cultures obtained at the first few explantations, but they never showed any bacterial growth. Pathology findings of the excised tissue showed fibroadipose tissue with histiocytic reaction, silicone depositions, and in one case giant cells; none had signs of malignancy.

DISCUSSION

After being banned from the European market in 2010, Poly Implant Prothèse implants have been the subject of debate regarding international medical device regulation, policies and responsibilities.[12,13] After the French media announced health concerns regarding this specific brand, increasing numbers of women have come forward in the European media with concerns related to their Poly Implant Prothèse silicone breast implants. This study shows that in 112 women with 224 Poly Implant Prothèse implants, no relationship was found between rupture and complaints. Most women (69.6 percent) were asymptomatic.

It is important to note that these patients were recalled and interviewed from January to April of 2011 and therefore the complaints raised were not biased by the media attention this brand received after December of 2011. Pain or a burning sensation is the most frequently mentioned symptom (17.9 percent). This has also been described earlier in two explantation studies of silicone breast implants[14,15] that showed rates of 20 and 24.3 percent respectively. Like these studies, we found no correlation of breast pain and implant rupture at both magnetic resonance imaging screening and explantation, whereas other research has found breast pain to be a predictor to implant rupture.[16] This last study is more recent and, like other studies on modern silicone implants, reported a lower percentage of implants associated with breast pain of 8.2 to 10 percent after 2- to 6-year follow-up.[16-18]

The Scientific Committee of the European Commission suggested that Poly Implant Prothèse implants might be more prone to cause painful and/or enlarged local lymph nodes or sensation in the breast because of the positive irritancy test. Four women presented with a mass in axilla and/or breast, and in three (2.7 percent) of them a palpable lymph node was identified at physical examination. All three women had their implants explanted, and two showed a ruptured implant on the ipsilateral side. One implant that appeared intact on magnetic resonance imaging screening, showed excessive gel bleed during operation. Our 2.7 percent of lymphadenopathy is lower than the prevalence of 8 and 16.7 percent reported by two studies that compared women after “non silicone involve” cosmetic surgery with women with silicone implants.[19,20] Enlarged lymph nodes in the nearest axilla have been described in case reports with silicone implant rupture[21] and in cases of gel bleed.[22] A recent study found no association between enlarged lymph node and implant rupture.[16] They did not perform explantation on all women and might have missed gel bleed, as we saw in our study.

Except for lymphadenopathy, we found no significant correlation between complaints and implant rupture. This is in line with a study from Denmark in 2003 in which no association between silicone implant rupture and specific diseases or symptoms were found.[23] Most authors believe that

asymptomatic rupture does not imply a health risk to the patient. One study even left ruptured implants in situ and prospectively followed women with untreated implant ruptures, and concluded that implant rupture is a relatively harmless condition, which only rarely progresses and gives rise to notable symptoms (i.e., change in breast shape and size and breast pain).[24]

Severe capsular contraction was found in 16 implants (7.1 percent), which is lower than the 9.8 to 14.8 percent rate mentioned for other modern implants such as Allergan (Irvine, Calif.), Inamed (Santa Barbara, Calif.),[17,18,25] but higher than the 5.6 percent rate for Inamed Style 410 implants.[26] In our study, severe capsular contracture was not significantly correlated to rupture rate at magnetic imaging screening or explantation. In literature, some studies also found no association between capsular contraction and implant rupture,[27] whereas others do.[14]

When there is no correlation between pre-existing complaints and implant rupture, what is our best tool in diagnosing implant rupture in Poly Implant Prothèse implants? The original advice of European authorities to perform physical examination was in contradiction with literature that found that neither the sensitivity nor the specificity is acceptable.[16] Recently the advice has been changed to perform explantation of all Poly Implant Prothèse implants regardless of any diagnostic evidence for rupture.

Signs at physical examination that have been described to predict implant rupture in the literature are changed (especially softened) breast consistency or palpable nodules or mass.[16,21,22] In our study, only 10.7 percent of plastic surgeons found any findings suggestive of implant rupture. In our study, physical examination seemed significantly correlated with findings at magnetic resonance screening but not with the explantation results. The sensitivity of physical examination in our study is 10.3 percent and the specificity is 87 percent when compared with explantation results. This is in line with other studies that found sensitivity of clinical examination of 12.5 to 30 percent and specificity of 84.2 to 88 percent.[16,28]

There is international agreement that magnetic resonance imaging screening is the most accurate method to detect implant rupture.[29-32] A meta-analysis in 2001 has estimated the overall sensitivity to be 78% and the overall specificity 91%.[33] Also in our study magnetic resonance imaging is the best tool to diagnose implant rupture. We found a sensitivity of 89.7 percent and a specificity of 51.9 percent due to many false positive results. If we compare our specificity to other studies it is quite low, although some other authors also find lower specificity of 63 percent and 77 percent,[31,32] most find a higher specificity of 97 percent.[29,30] The accuracy of magnetic resonance imaging diagnosis of rupture has been studied in first- to third-generation implants but not yet in highly cohesive implants of the last two generations. In half of the false-positives we found extensive gel bleed, which might explain why on magnetic resonance imaging screening these implants are judged to be ruptured. Management-wise, the consequences of this extensive “silicone bleed” are the same, as these implants still need to be explanted just like ruptured implants.

"Silent" rupture is a well-described phenomenon in modern silicone implants, and some claim high cohesive silicone gel to less likely escape from a ruptured implant shell.[34] Our observation at explantation, however, is that the Poly Implant Prothèse non-medical cohesive silicone gel changes consistency and color in vivo when the gel is exposed to the surrounding tissue through shell rupture (Figure 2, *below, right*). This feature could explain why in these ruptured Poly Implant Prothèse implants the silicone gel seems less viscous and therefore more prone to escape through its shell. In our study, not all implants were explanted- only 33 women, who had one of their implants ruptured on magnetic resonance imaging screening underwent explantation. As this treatment advice changed recently in the Netherlands all other implants will be explanted, which should give better insight into possible false-negatives in our future studies.

CONCLUSIONS

The recent health concerns about Poly Implant Prothèse silicone breast implants caused fear and unrest in women, some of whom have presented with various symptoms they feel may be related to ruptured Poly Implant Prothèse implants. The Scientific Committee of the European Commission required more clinical and epidemiological data to determine what the health consequences of Poly Implant Prothèse implants were. We acknowledge the fact that long-term effects of the unauthorized silicone gel used in these Poly Implant Prothèse implants are still uncertain, but the aim of our study was objectify the recent worries in the media about clinical consequences of ruptured Poly Implant Prothèse implants. The percentages of complaints and the pathology results in our study are, however, comparable to the clinical consequences of silicone breast implants of other manufacturers. In this study, no correlation has been found between symptoms, rupture at magnetic resonance imaging screening, and explantation. Still we would advise that all Poly Implant Prothèse implants be explanted, as their shell quality is poor and their silicone content unauthorized. Although magnetic resonance imaging screening in our study had a good sensitivity of 89.7%, but a low specificity of 51.9%, it remains the preferred method to diagnosing rupture compared with physical examination. We believe that the excessive gel bleed often seen at explantation of Poly Implant Prothèse implants caused more false-positives observed on magnetic imaging screening.

CHAPTER 5

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