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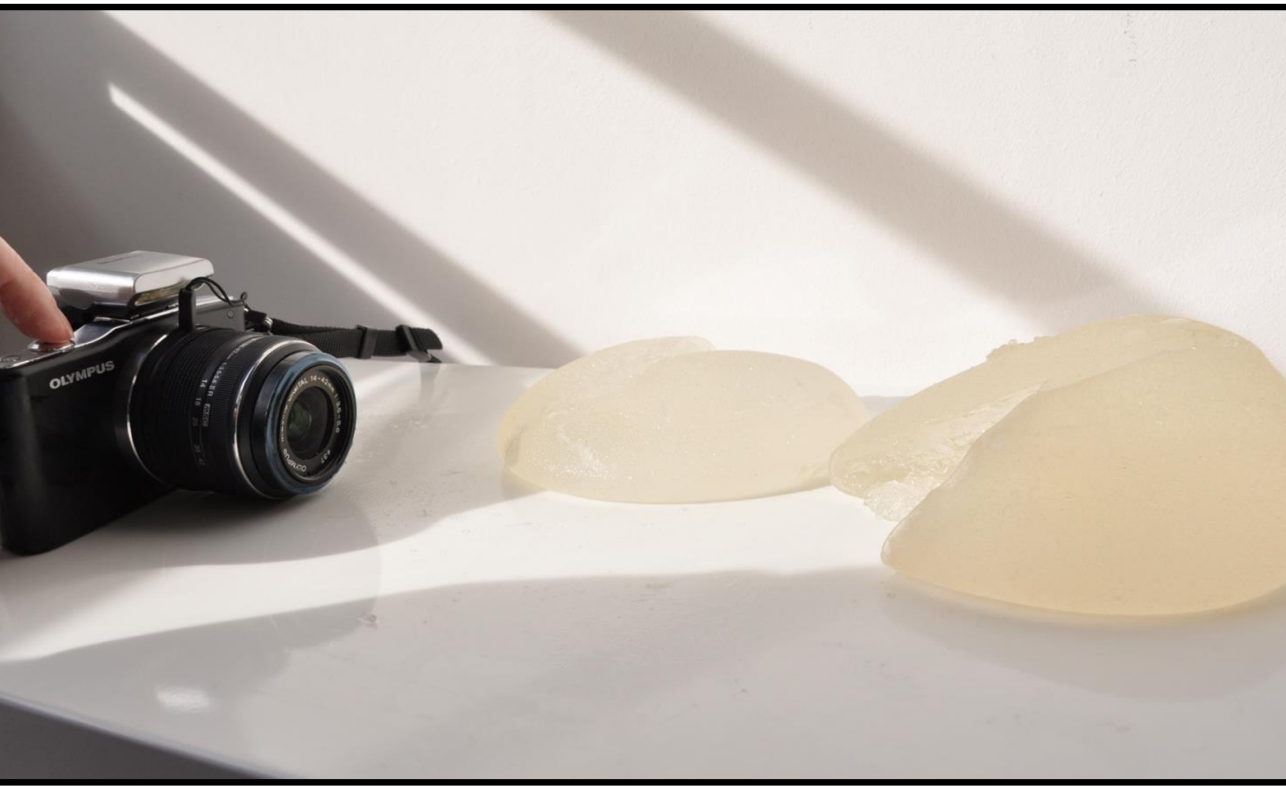
CHAPTER 6

MRI Screening Results Compared with Explantation Results in Poly Implant Prothèse Silicone Breast Implants Recalled from the European Market in 2010



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CHAPTER 6

ABSTRACT

BACKGROUND: In a prospective cohort study, the authors followed 112 women whose Poly Implant Prothèse silicone breast implants were recalled. Magnetic resonance imaging results and clinical consequences were previously published. The authors compared magnetic resonance imaging screening with explantation results to study the diagnostic value of magnetic resonance imaging in this unique unselected and nonbiased group.

METHODS: One hundred twelve women with 224 proven Poly Implant Prothèse implants after a mean implantation time of 10 years were enrolled in 2011. All women underwent magnetic resonance imaging screening and were offered explantation. The explantation details of 107 women could be compared with magnetic resonance imaging results.

RESULTS: Of 107 women, 29 (27 percent) had at least one ruptured implant at explantation, and 44 of 214 explanted implants (21 percent) were ruptured. The magnetic resonance imaging results correctly diagnosed 154 intact and 35 ruptured implants. Sensitivity and specificity were 80 percent and 91 percent. The positive predictive value was 69 percent, and the negative predictive value was 95 percent.

CONCLUSIONS: The accuracy of magnetic resonance imaging is comparable to previously published data from other manufacturers of modern silicone implants but lower than of some recent validation studies in selected symptomatic women. The authors believe that this study is representative of the common daily practice as they followed normal day-to-day magnetic resonance imaging protocol without using multiple independent readers. The authors hope that this study will contribute to the ongoing discussion to screen asymptomatic women with modern silicone breast implants.

BACKGROUND

Silicone breast implants from the French manufacturer Poly Implant Prothèse were recalled from the European market in 2010 because unauthorized industrial-grade silicone gel and allegedly fraudulent, substandard manufacturing processes were used.[1] An example of one of these implants in the original packaging is shown in Figure 1. In a prospective cohort study, we followed 112 women with 224 Poly Implant Prothèse silicone breast implants since 2011 and previously published magnetic resonance imaging results and clinical consequences.[2,3] In Europe, the advice of health authorities regarding Poly Implant Prothèse implants changed in 2012 from explantation of ruptured implants only to explantation of all Poly Implant Prothèse implants of all fabrication years.[4] Therefore all women in our cohort study, regardless of their magnetic resonance imaging results and symptoms, have been offered explantation, and, at present, 96 percent of the women in our cohort underwent an explantation.

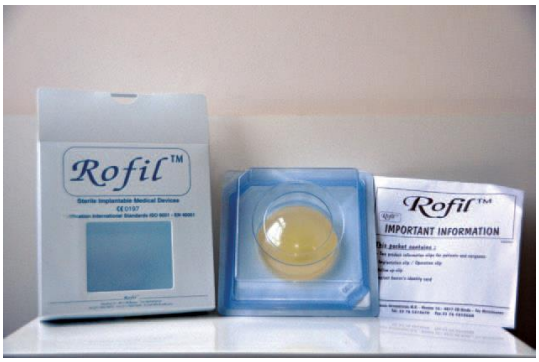

Figure 1. An example of a Poly Implant Prothèse silicone breast implant in its original packaging

Although magnetic resonance imaging has been considered to be the preferred method of diagnosing implant rupture in silicone breast implants,[5-8] some researchers have questioned its value in silicone breast implants of the past two generations.[9-11] Other researchers have argued that (high-resolution) ultrasonography is an equally valuable and more economical tool in diagnosing implant rupture,[10,12,13] and in Poly Implant Prothèse implants specifically.[14] In addition, a somewhat disappointing accuracy of magnetic resonance imaging screening was found in our previous studies.[3] Sensitivity and specificity of 90 and 52 percent, respectively, were based on explantation results of 33 women in whom one implant showed rupture at magnetic resonance imaging screening.[3]

Most previous large explantation and magnetic resonance imaging studies have been criticized for including not only different generations, types and manufacturers, but also symptomatic women only.[15] magnetic resonance imaging screening studies of asymptomatic women with silicone breast implants[8,11] have reported lower sensitivity and specificity than those in symptomatic patients.[7,16-19] Thus far, there has been no published magnetic resonance imaging study in which almost all of the asymptomatic women in their cohort had the implants explanted. The value of magnetic resonance imaging as a screening modality has recently been under debate, despite the Food and Drug Administration's advice to regularly screen asymptomatic women with breast implants with magnetic resonance imaging.[20] The nature of the recent recall offered us a unique opportunity to study a group of unselected, mostly asymptomatic women who were implanted with Poly Implant Prothèse implants 10 years earlier.

This study aimed to present the explantation results of 214 silicone breast implants to determine the prevalence of rupture and to evaluate magnetic resonance imaging screening as a diagnostic tool for silicone implant rupture in Poly Implant Prothèse implants. Results of this study might provide valuable information about magnetic resonance imaging as a screening modality in modern silicone breast implants in asymptomatic women in a common clinical setting.

PATIENTS AND METHODS

In early 2011, the Jan van Goyen clinic, in Amsterdam, the Netherlands, recalled Poly Implant Prothèse that were implanted in women 10 years previously. The women were informed by postal mail about quality concerns regarding their implants and were requested to visit the clinic for follow-up. Medical records were used to trace manufacturer and implantation specifics. Implantation details of the 112 unselected women with 224 proven Poly Implant Prothèse implants who were enrolled in our study cohort and the study flow chart were previously published.[2,3]

All women were referred to a single magnetic resonance imaging facility to conduct rupture screening according to an established protocol. We obtained magnetic resonance images using a 1.5-T unit (Siemens Magnetom Symphony, Siemens Medical Solutions, Erlanger, Germany). A dedicated CP breast array coil (Siemens) was used for imaging both breasts of each patient. Short-tau inversion recovery T2-weighted axial images were obtained in all cases, with echo times of 70 msec. Both short-tau inversion recovery T2-weightd axial and sagittal images with spectral suppression of silicone and water were obtained, with echo times of 84 msec. The other parameters were as follows: repetition times of 2120 msec, inversion time of 140 msec, slice thickness of 4mm, 256 x 128 matrix, and field of view of 320 x 320 mm.

In our previous studies, three experienced radiologists individually interpreted the images. Findings were described in common clinical magnetic resonance imaging reports as used in the daily practice of the MRI Centre Amsterdam. In the reports, a plastic surgeon had classified whether the implants were ruptured and whether there was proof of extracapsular silicone leakage. This was done to establish data on the prevalence of rupture in Poly Implant Prothèse implants and the diagnostic value of magnetic resonance imaging screening. For the recent study one radiologist re-evaluated the interpretation of all magnetic resonance imaging reports and classified all implants as ruptured or not. This was done to verify that the interpretation of the plastic surgeon was not different from the intended conclusion of the radiologist.

All women were offered explantation and replacement of both implants at the clinic's expenses. Information on explantation results and perioperative procedure was collected from the operation report at the Jan van Goyen clinic. In most women, one of five plastic surgeons did the explantation procedure at the Jan van Goyen clinic by one out of a team of five plastic surgeons. Of the 10 women who chose to be explanted elsewhere, the operation records were requested from colleagues. We obtained written operation records of eight women, and because another

private clinic had closed, we asked two women to recall the specifics of the explantation. Explantation data of 107 women with 214 implants were compared with the magnetic resonance imaging screening results.

In all analysis, the unit of observation was both the implant and the woman. Data were analyzed using SPSS 20.0 software (IBM Corp., Armonk, N.Y.). 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 characteristics of our cohort of 112 women with 224 proven Poly Implant Prothèse implants were published in 2012 and are summarized in Table 1. The mean age at the time of 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 time of their first recall visit. All were round, textured Poly Implant Prothèse silicone breast implants. The most frequently implanted size was 330 ml. A majority of 83 percent had their implants placed in the subglandular position. Most women were asymptomatic (70 percent), and when symptoms were mentioned, they did not lead to a request for medical attention before their recall. These symptoms or complaints have been described in detail in a previous publication.[3]

Table 1. Characteristics of MRI screening study cohort of 112 women with 224 PIP implants

	All women	
	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
Symptomatic		
Asymptomatic	78	69.6
Symptomatic	34	30.4
Explantation		
Already explanted	107	95.5
Explantation	5	4.5

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

Five women were not explanted: Two did not wish to be explanted because they felt secure enough without any complaints; two were still waiting for explantation, which was postponed because of a serious cardiovascular condition and prednisone usage for an auto-immune disease; and one patient will be operated in the coming months in another private clinic. The specifics of the explantation of 214 Poly Implant Prothèse implants in 107 women are summarized in Table 2. In 97 women (91 percent), the explantation procedure was done at the Jan van Goyen clinic. We obtained all key information about the explantation and implant status from the 10 women who were explanted at another facility. Explantation took place after a

mean period of 10 months after magnetic resonance imaging screening (range, 1 to 22 months.)

Of 107 women, 29 (27 percent) had at least one ruptured implant at explantation. Of the 214 explanted implants, 44 (21 percent) were ruptured. “Gel bleed” was seen in 30 implants (14 percent), and in 17 implants the surgeon described this as “excessive gel bleed” (8 percent). A total or partial capsulectomy was done bilaterally in 16 women (15 percent) and unilaterally in nine (8 percent). A capsulotomy was done bilaterally in 75 women (73 percent) and unilaterally in four. Seven women (8 percent) chose not to have their implants replaced by new silicone breast implants; they were offered explantation and lifting. In all other women, new implants were placed; in most cases (81 percent), the implant manufacturer was Allergan, although four women had their Poly Implant Prothèse implants replaced with Mentor (Santa Barbara, Calif.) implants and two received Eurosilicone (Eurosilicone S.A.S., Apt, France). In 14 women, the position of their implants was changed from subglandular to submuscular position.

The original interpretations of the magnetic resonance imaging screening results were compared with the explantation results in order to

Table 2. Explantation specifics of 214 PIP implants in 107 women

	All women	
	n	**%**
Explantation clinic		
Jan van Goyen	97	90.7
Other private clinic	4	3.7
Other general hospital	6	5.6
Position		
Changed to submuscular	14	13.1
Unchanged	93	86.9
New Implants		
None	7	6.5
Allergan Natrelle Inspira	78	72.9
Allergan Natrelle ST410	9	8.4
Mc Ghan CUI	5	4.7
Mentor	4	3.7
Eurosilicone	2	1.9
Unknown	2	1.9
Rupture status per woman		
At least one of implants ruptured	29	27.1
Both intact	78	72.9
	All implants	
	n	**%**
Capsulotomy		
Yes	154	72.0
No	60	28.0
Partial or total Capsulectomy		
Yes	41	19.2
No	173	80.8
Implant integrity		
Intact	170	79.4
Ruptured	44	20.6
Signs of "gelbleed"		
None	184	86.0
Some	13	6.1
Excessive	17	7.9

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

Table 3. Explantation results of all 214 PIP implants correlated to Magnetic Resonance Imaging screening and the diagnostic value of MRI

	Explantation result		
	Intact	Ruptured	Total
MRI result	*n*	*n*	*n*
Intact	154	9	163
Ruptured	16	35	51
Total	170	44	214

Sensitivity	*0.80*
Specificity	*0.91*
Positive Predictive Value	*0.69*
Negative Predictive Value	*0.95*

PIP= manufacturer Poly Implant Prothèse; n= number; All women have 2 implants; MRI= Magnetic Resonance Imaging

validate it as a screening modality for implant rupture. One independent radiologist re-evaluated the conclusions of all original clinical magnetic resonance imaging reports and found that the plastic and reconstructive surgeon correctly interpreted all but one implant. When compared with the explantation results, the original magnetic resonance imaging screening results correctly diagnosed 154 intact implants and 35 ruptured ones. There were 16 false-positive and nine false-negative diagnoses of rupture. Sensitivity was calculated to be 80 percent and specificity to be 91 percent. The positive predictive value was 69 percent, and the negative predictive value 95 percent (Table 3).

DISCUSSION

This cohort study evaluated explantation results of 214 round, textured modern Poly Implant Prothèse silicone breast implants and presents a prevalence of rupture of 20.6 percent per implant after a mean implantation time of 122 months. This prevalence found by explantation is in coherence with the prevalence of rupture we previously reported of 24 percent per implant after 10-year implantation period, on the basis of magnetic resonance imaging screening.[2] This is in line with the prevalence of 15.9 to 33.8 percent found by Berry and Stanek after a follow-up period of 5 to 9 years.[21] On the basis of this last study and other reports from the manufacturer and clinics in the United Kingdom, the National Health Service has estimated the prevalence of rupture in these implants to be around 15 to 30 percent after 10 years, compared with 10 to 14 percent after 10 years in other brands of modern implants.[22]

We had the unusual opportunity, as a result of the recall, to study a single type and manufacturer of modern silicone breast implant and compare explantation with magnetic resonance imaging screening results. Rupture prevalence studies of single type and manufacturer of modern silicone breast implants have been based on studies sponsored by manufacturer's themselves.[23,24] They often suffer from large failure to follow up on their originally enrolled study population. As a result of advice of health care authorities in a number of European countries to explant all Poly Implant Prothèse implants regardless of their clinical and radiological status, we obtained explantation results from 107 of the 112 women (96 percent) in our magnetic resonance imaging screening cohort.

Most large explantation studies[25-27] have been based on self-referred women with complaints or signs of rupture previous to their explantation and might very well report a higher prevalence of rupture than one would in asymptomatic women. Most women (70 percent) in this study were asymptomatic and had no reason to see a clinician before their recall their recall. The prevalence found is therefore a reliable estimate of the real prevalence of implant rupture in Poly Implant Prothèse implants after 10 years. A review in 1990 of 8000 mainly second-generation silicone breast implants found a failure rate (including gel bleed) of 50 percent at 10 years.[19] The prevalence of rupture in Poly Implant Prothèse implants would therefore be as incomparable to the prevalence of rupture in second-generation implants as to modern ones. Recent literature on

third- and fourth-generation implants report much lower frequencies of rupture in their cohorts of 0.3 to 11.8 percent after a follow-up of 3 to 13 years, respectively.[11,28-30]

As Poly Implant Prothèse implants obtained European Community marketing approval in 1997 and became available in their current form in 2000, according to their fabrication year, they should be classified as fourth- or fifth-generation silicone breast implants. Although these implants were advertised by their manufacturer as modern, high-cohesive silicone gel implants, their rupture prevalence after 10 years suggests otherwise. Chemical studies have very recently demonstrated fewer cross-linking sites in silicone gel in a Poly Implant Prothèse implant compared with silicone gel of another modern implant and a lack of impermeability of its elastomer shell.[31] Figure 2 shows a sliced-open virgin Poly Implant Prothèse implant. We previously reported that the silicone gel of even intact implants at explantation had a more liquid feel than expected from other highly cohesive silicone implant brands.[3] This finding can be explained by the exchange found in an intact Poly Implant Prothèse implant of not only low-molecule-weight silicone from the implant to the surrounding breast tissue but also of solvent, soluble, lipophilic tissue-derived components such as cholesterol from the surrounding breast tissue into the intact implant.[31]

Figure 2. A sliced-open virgin Poly Implant Prothèse silicone breast implant

The result of the lack of impermeability of the elastomer shell of Poly Implant Prothèse implants, combined with the fact that the silicone gel has less cross-linking and becomes more liquid over time, could explain the high percentage (14 percent) of gel bleed we found at explantation in Poly Implant Prothèse implants compared with what one would expect from modern, highly cohesive silicone breast implants. In 17 implants (8 percent) in the present study, the surgeon even described the gel bleed as being excessive. In a case series of Poly Implant Prothèse implants compared with other modern implants, the more easy migration of the Poly Implant Prothèse silicone gel might have caused an increase of silicone lymphadenopathy.[32] Gel bleed is, however, a phenomenon that is difficult to objectify. The only true proof that the fluid often seen subcapsular around the implant at explantation is gel bleed is if silicone is found by histologic research, and this was not done in the present study.

We used explantation results to evaluate magnetic resonance imaging screening as a diagnostic tool for silicone implant rupture in Poly Implant Prothèse implants. The 20.6 percent actual rupture found at explantation does not vary much from the prevalence of 24 percent rupture previously predicted by magnetic resonance imaging screening, which does suggest a good accuracy. Accuracy further improved after all women were explanted. The sensitivity and

specificity of magnetic resonance imaging screening in Poly Implant Prothèse silicone breast implants found of 80 percent and 91 percent, respectively, are in line with a meta-analysis in 2001 that estimated overall sensitivity to be 78 percent and overall specificity to be 91 percent.[33] Although the sensitivity improved in our study, it is still lower than the 97 percent found by Hölmich et al.[6] Validation studies often use multiple readers who come to a consensus about implant status; this is not the same in the day-to-day clinical setting, where different radiologists are subject to inherent intraobserver and interobserver variations of interpretation. When magnetic resonance imaging screening of silicone breast implants in a common clinical setting such as ours results in a lower sensitivity, one needs to keep in mind the potential morbidity of unnecessary surgery associated with false-positive magnetic resonance imaging results. This is true even more when a broad consensus on the surgical treatment of intracapsular rupture of modern, highly cohesive silicone breast implants is not yet in sight.

Since the reintroduction of silicone gel-filled implants in 2006, the Food and Drug Administration advises offering magnetic resonance imaging screening 3 years after implantation and every 2 years thereafter.[34] However magnetic resonance imaging is the most expensive imaging modality for the evaluation of silicone breast implants. Researchers have questioned whether magnetic resonance imaging to be the best cost-effective screening method in asymptomatic women, because its accuracy in the setting of asymptomatic and unselected women might be lower than in most validation studies,[20] which is an argument our results support. Screening with ultrasound followed by magnetic resonance imaging in asymptomatic women and screening with ultrasound in symptomatic women are suggested alternatives.[35] Ultrasonography is operator dependent, and accuracy will vary according to the experience and skill of the radiologist.[36] However, there is also a learning curve for interpreting magnetic resonance images. When the accuracy of magnetic resonance imaging screening in Poly Implant Prothèse implants is in line with previously reported accuracy in other manufacturers' implants, magnetic resonance imaging screening would be an equal effective or ineffective tool to diagnose implant rupture. Nonetheless, to avoid unnecessary costs, all Poly Implant Prothèse implants will at the time of writing be explanted without previous magnetic resonance imaging screening.

CONCLUSIONS

The prevalence of rupture in 214 round, textured Poly Implant Prothèse implants at explantation found after 10 years is 20.6 percent in a group of unselected, non-biased, mostly asymptomatic women. This prevalence is as comparable to the literature on silicone breast implants of the second generation as on modern generations. The fact that the unauthorized non-medical silicone gel has shown to eventually be more fluid over time and therefore more easily "bleeds" through its more permeable shell makes these implants incomparable to modern implants of the fourth and fifth generation. In the present prospective cohort study the sensitivity of magnetic resonance imaging screening was 80 percent, and the specificity was 91 percent.

Data from our study is useful in the light of the recent debate on the regular magnetic resonance imaging screening as advised by the Food and Drug Administration because offers good insight into the sensitivity and specificity of magnetic resonance imaging in asymptomatic women in a day-to-day clinical setting. Sensitivity and specificity could be further improved with multiple readings by experienced readers or with a more structured and uniform way of reporting magnetic resonance imaging findings on implant status.

CHAPTER 6

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