Safety & imaging of modern silicone breast implants

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CHAPTER 8

MRI Screening for Silicone Breast Implant Rupture: Accuracy, Inter- and Intraobserver Variability using Explantation results as reference standard

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CHAPTER 8

ABSTRACT

BACKGROUND: The recall of Poly Implant Prothèse (PIP) silicone breast implants in 2010 resulted in large numbers of asymptomatic women with implants who underwent magnetic resonance imaging (MRI) screening. This study's aim was to assess the accuracy and interobserver variability of MRI screening in the detection of rupture and extracapsular silicone leakage.

METHODS: A prospective study included 107 women with 214 PIP implants who underwent explantation preceded by MRI. In 2013, two radiologists blinded for previous MRI findings or outcome at surgery, independently re-evaluated all MRI examinations. A structured protocol described the MRI findings. The ex vivo findings served as reference standard.

RESULTS: In 208 of the 214 explanted prostheses, radiologists agreed independently about the condition of the implants. In five of the six cases they disagreed (2.6%), but subsequently reached consensus. A sensitivity of 93%, specificity of 93%, positive predictive value of 77% and negative predictive value of 98% was found. The interobserver agreement was excellent (kappa value of 0.92).

CONCLUSIONS: MRI has a high accuracy in diagnosing rupture in silicone breast implants. Considering the high kappa value of interobserver agreement, MRI appears to be a consistent diagnostic test. A simple, uniform classification, may improve communication between radiologist and plastic surgeon.

BACKGROUND

Silicone breast implants have been used over the last 5 decades for breast augmentation in more than 4 million women in the US alone.[1] In 2011, 307.180 American women underwent cosmetic breast augmentation with silicone implants and 96.277 women underwent reconstruction with silicone implants after mastectomy for cancer.[1] Since the reintroduction of silicone breast implants in 2006,[2] breast augmentation has become the most common cosmetic surgical procedure. Implant rupture and "gel bleed" are known complications and might indicate revision surgery.[3] As physical examination has been found to be unreliable to diagnose implant rupture in most modern high cohesive silicone implants,[4] magnetic resonance imaging (MRI) is presently considered to be the most accurate imaging modality to examine women with silicone breast implants.[5-7]

In 2010, silicone breast implants of the French manufacturer Poly Implant Prothèse (PIP) have been recalled from the European market because an unauthorized industrial grade silicone gel and substandard manufacturing processes were used.[8] This recall had huge implications on financial and medical resources in Europe and caused unrest in women with silicone breast implants.[9,10] In The Netherlands the Dutch Health Care Inspectorate (IGZ) requested all institutions that had used PIP implants in the past to recall their patients to diagnose a possible implant rupture and remove or replace the ruptured implants. In the medical center Jan van Goyen (JvG) in Amsterdam it was decided from the start of the recall process early 2011 to offer all patients a MRI of the breasts on expenses of the clinic, to ensure the best possible accuracy to diagnose implant rupture. During the course of our research the advice of the IGZ changed to a recommendation of explantation of all PIP silicone breast implants, regardless of their condition. This explains why all women included in our study eventually underwent explantation regardless of the results of the clinical examination or the reported findings on MRI.

Radiologists all over Europe are nowadays confronted with the same task to diagnose rupture of silicone breast implants[11] In the US at the time of the reintroduction of silicone breast implants to the market in 2006, the FDA recommended that all silicone breast implants recipients should undergo screening with MRI 3 years after implantation and every 2 years thereafter.[12] Nevertheless, the justification of this FDA advice has been much debated and has not become a widely accepted practice.[13,14]

The accuracy of MRI has been investigated mainly in cohort studies of symptomatic women, but not yet in a large cohort of women unselected on symptomatology who all underwent explantation, even when MRI showed no signs of rupture.[6,15-17]

The aim of this study was to assess the consistency of accuracy and interobserver variability of MRI screening of women with modern silicone breast implants. Due to the PIP implants recall and the fact that all women underwent explantation, we were able to use the findings at surgery as a reference standard.

PATIENTS AND METHODS

Patients and Silicone Breast Implants

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

In early 2011, the medical center Jan van Goyen recalled all women who underwent breast augmentation with PIP implants, performed in this clinic. All were informed by letter about the concerns regarding the quality of their implants and were invited for follow-up. Medical records were used to trace manufacturer and implantation specifics. Characteristics and details of the 112 unselected women with 224 proven PIP implants, who were enrolled in our study cohort as well as the study flow-chart can be found in our previous publications[17,18] and in Table 1.

The present study is based on MRI examinations of 214 PIP silicone breast implants in 107 women who underwent explantation of both prostheses. The implant is the unit of observation. The mean age of the implants was 122 months (range, 111-133 months) at their preoperative visit. All were round shaped textured PIP silicone breast implants. Most of them had a volume of 330ml (range, 185-430ml). A majority of 70% of women was asymptomatic. When symptoms were mentioned, they had not led to a request for medical consultation before their recall. These symptoms in 30.4% of the women have been described in detail in a previous publication.[18]

Examination protocol and reporting of the first round of MRI screening in 2011

All examinations were performed in a single MRI facility (MRI Centre, Amsterdam) with a 1.5-T MRI unit (Siemens Magnetom Symphony, Siemens Medical Solutions, Erlangen, Germany). Open CP Breast array coils were used for imaging both breasts of each patient. The examination protocol consisted of the following sequences: STIR T2-weighted axial images, STIR T2-weighted axial and sagittal images with spectral suppression of silicone and STIR T2-weighted axial and sagittal images with spectral suppression of water. All image acquisitions had repetition times of 2120 msec, IR of 140 msec, slice thickness of 4 mm, 256 x 128 matrixes and a field of view of 320 x 320 mm. The TE was 70 msec for the STIR acquisitions without suppression and 84 msec for those with suppression of water and silicone.

The MRI images were stored and viewed in the Picture Archiving and Communication System (PACS) of the MRI Centrum (Centricity PACS-IW GE Healthcare, Allendale, NY, USA). Each examination was interpreted and reported by a single one out of a group of three experienced radiologists in a usual clinical setting.[19] The ID data of the women and the reports were stored in the Radiology Information System (RIS) of the MRI Centrum (Lotus Notes 7; IBM, Amonk, NY, USA). The average time interval between the MRI examinations and explantation was 10 months (range, 1-22 months).

Second round of interpretation and reporting MRI in 2013

An average of 22 months after the primary reporting, all MRI examinations of the 214 explanted PIP prostheses were again interpreted and reported by two of the three radiologists, independently and without knowledge of the first MRI report or the state of the prostheses at explantation. The two radiologists had respectively 15 and 8 years of experience in breast MRI.

The criteria used to diagnose implant rupture or signs of extracapsular leakage of silicone are summarised in Table 2 (Figs. 1, 2, 3, and 4). Reporting of the condition of the implant was performed according to a structured protocol and scoring system, that was inspired by the Breast Imaging Reporting and Data System (BI-RADS) classification.[20-22] We named it Silicone Implants Reporting and Data System (SI-RADS), Table 3.

Table 2. Diagnostic criteria used to identify implant rupture in a study of 214 PIP silicone breast implants

- Collapsed implant elastomer shell surrounded by silicone gel (fig. 1)
- Silicone gel layer between the shell and fibrous capsule (fig. 2)
- Interruption of the continuity of elastomer shell documented on serial adjacent slices
- Recognition of several visual patterns of collapsed and folded elastomer shell that is floating in gel: “linguine”, “keyhole”, “teardrop”, “inverted teardrop”, “noose” signs which depict silicone visible both inside and outside a radial fold (fig. 3)
- Visible free silicone as foci outside the implant capsule with the same signal characteristics as the silicone implant (high s.i. on plain STIR and STIR with suppression of water and low s.i. on STIR with suppression of silicone) (fig. 4).

Table 3. Silicone Implant Reporting and Data System (SI-RADS)

A. Integrity of the implant

Category	Description	Clinical*
0	Incomplete**	Ad imaging**
1	Intact	None
2	Probably intact	None
3	Probably ruptured	Referral
4	Ruptured	Referral

B. Extracapsular leakage of silicone

Category	Description	Clinical
0	Incomplete**	Ad imaging**
1	No EL***	None
2	Probably no EL***	None
3	Probably EL***	Referral
4	Extracapsular leakage	Referral

Clinical Management; **the MRI is inconclusive, either additional imaging or second opinion from colleague radiologist should be sought; * extracapsular leakage*

Statistical analysis

The sensitivity, specificity, negative predictive value and positive predictive value of MRI review were calculated. The interobserver and intraobserver variation was assessed by calculating the Kappa value according to Landis and Koch[23] using SPSS version 20.0 (SPSS, Chicago, IL, USA). By this method agreement is rated as poor (0.0- 0.20), fair (0.21- 0.40), moderate (0.41- 0.60), good (0.61-0.80) or excellent (0.81- 1.00).[23] For calculation of the sensitivity and specificity "probably ruptured implants" were categorised as ruptured and "probably intact implants" as intact.

RESULTS

Accuracy of radiological interpretation and reporting in 2011

Data from the 2011 examination and reporting round has only been used for the estimation of the intraobserver agreement of the two radiologists who each examined all implants in 2013 and only a part of them in 2011. The accuracy in a day to day clinical setting in 2011 without the use of the SI-RADS protocol are reported in a previous publication (in press).[19]

Accuracy of radiological interpretation and reporting in 2013

From the 214 explanted silicone prostheses, 44 have been found by the surgeons to be ruptured and 170 intact. In 208 of the 214 implants, both radiologists agreed about their state and independently diagnosed 160 as intact and 48 as ruptured. They disagreed with each other on six implants (2.6%) (Fig. 5). For these cases they attempted to reach a non-forced consensus by examining the images together. In five of the six implants they reached a consensus. These five consensual diagnoses were added to the cases independently agreed upon for the calculation of the sensitivity, specificity and of the positive and negative predictive values. A complete overview of these values is shown in Table 4.

Table 4. Explantation results of 214 PIP implants correlated to Magnetic Resonance Imaging screening evaluation in 2013, a consensus of 2 radiologists

	Explantation result		
	Intact	**Ruptured**	**Total**
	n	*n*	*n*
MRI result			
Intact	158	3	161
Ruptured	12	40	52
Total	170	43	213*

Sensitivity	*0.93*
Specificity	*0.93*
Positive Predictive Value	*0.77*
Negative Predictive Value	*0.98*

*PIP= manufacturer Poly Implant Prothèse; n= number; All women have 2 implants; MRI= Magnetic Resonance Imaging; * about one implant the 2 radiologists could not come to a consensus; for the calculation of the sensitivity and specificity e.g. "probably intact" group was included in the "intact" group, this was only applicable to 5 implants.*

Interobserver agreement on diagnosis of rupture

Table 6. Interobserver variability of 214 PIP implants on the diagnosis of implant rupture diagnosed at MRI review

	Radiologist B		
	Intact*	Ruptured**	Total
Radiologist A	*n*	*n*	*n*
Intact*	160	4	164
Ruptured*	2	48	50
Total	162	52	214

kappa coefficient	*0.92*

*PIP= manufacturer Poly Implant Prothèse; n= number; All women have 2 implants; MRI= Magnetic Resonance Imaging; * Intact or probably intact; ** Ruptured or probably ruptured. For the calculation of the sensitivity and specificity e.g. "probably intact" group was included in the "intact" group, this was only necessary for 5 implants*

The individual sensitivity, specificity, positive and negative predictive value of each radiologist before a consensus was reached is presented in Table 5. Their diagnoses differed for six implants (2.6%). Three implants were diagnosed by radiologist B as most likely ruptured and by radiologist A as intact. One implant which radiologist B diagnosed as ruptured, was considered intact by radiologist A and two more implants were diagnosed by radiologist A as ruptured and by radiologist B as intact. The calculation of interobserver variability resulted in a Kappa coefficient of 0.92 (Table 6).

Table 5. Explantation results of 214 PIP implants correlated to Magnetic Resonance Imaging screening and the diagnostic value of MRI by radiologist A and B

	Review by radiologist A			Review by radiologist B		
	Explantation result			Explantation result		
	Intact	Ruptured	Total	Intact	Ruptured	Total
MRI	*n*	*n*	*n*	*n*	*n*	*n*
Intact	161	3	164	158	4	162
Ruptured	9	41	50	12	40	52
Total	170	44	214	170	44	214

Sensitivity	*0.93*	*Sensitivity*	*0.91*
Specificity	*0.95*	*Specificity*	*0.93*
Positive Predictive Value	*0.82*	*Positive Predictive Value*	*0.77*
Negative Predictive Value	*0.98*	*Negative Predictive Value*	*0.98*

PIP= manufacturer Poly Implant Prothèse; n= number; All women have 2 implants; MRI= Magnetic Resonance Imaging.
For the calculation of the sensitivity and specificity e.g. "probably intact" group was included in the "intact" group, this was only necessary

Intraobserver agreement on diagnosis of rupture

The two radiologists involved in the present study examined 44 (radiologist A) and 62 (radiologist B) implants in the 2011 round, respectively. At the 2011 reading of 44 implants, all diagnoses of the radiologist A were the same as the surgical findings at explantation, so sensitivity and specificity were both 100%. At the second reading of these same 44 implants in 2013, he gave 43 correct and one false-positive result. The kappa coefficient of his intraobserver variability was 0.94.

Radiologist B gave 59 correct diagnoses at the first reading, 1 false positive and 2 false negatives. At the second reading in 2013, he gave 60 correct diagnoses, 1 false positive and 1 false negative, but differed in more than one implant in his diagnosis of the 2013 round compared with the 2011 round. The kappa coefficient of his intraobserver variability was 0,57.

Interobserver agreement on diagnosis of extracapsular leakage of silicone

In the second category of our questionnaire, i.e. extracapsular leakage of silicone, both radiologists agreed with each other in 197 implants there was no extracapsular silicone leakage, in 10 implants that there was extracapsular silicone leakage and in 7 implants they disagreed. The kappa coefficient was 0.74 (Table 7). In three implants, radiologist B considered that there was extracapsular leakage and radiologist A held an opposite opinion, whereas in the other four implants it was the other way around.

Table 7. Interobserver variability of 214 PIP implants on the diagnosis of extracapsular leakage of silicone at MRI review

	Radiologist B		
	No ES*	**ES***	**Total**
Radiologist A	*n*	*n*	*n*
No ES*	197	3	200
ES*	4	10	14
Total	201	13	214
	kappa coefficient		*0.74*

*PIP= manufacturer Poly Implant Prothèse; n= number; All women have 2 implants; MRI= Magnetic Resonance Imaging; * ES= Signs of Extracapsular Silicone leakage. Probably no or probably yes were categorized in respectively no or yes ES, which was necessary for 38 implants*

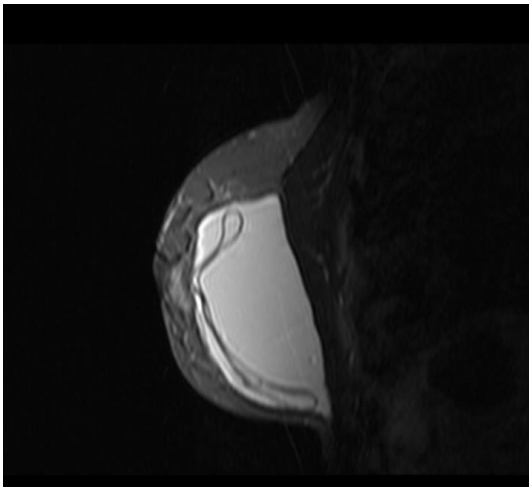

Figure 1. STIR with spectral suppression of water. Collapsed ruptured elastomere shell surrounded by silicone gel.

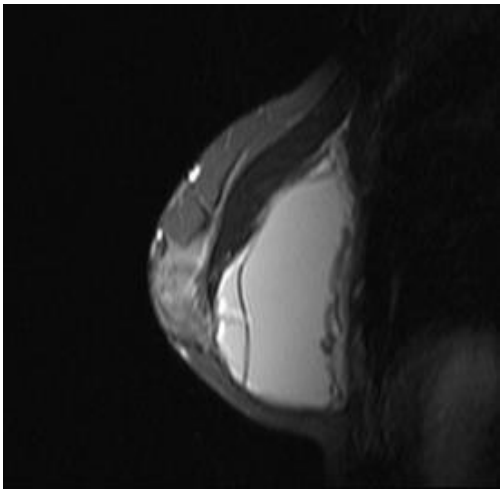

Figure 2. STIR with spectral suppression of water. Silicone gel layer between ruptured elastomere shell and fibrous capsule

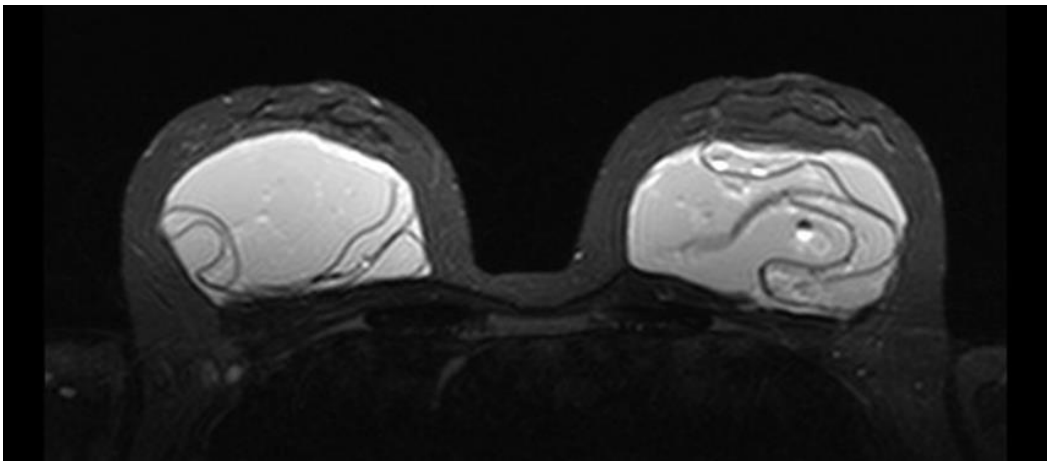

Figure 3. STIR with spectral suppression of water. Both implants are ruptured. “Pince-nez” sign in right breast. “Linguine” sign in the left breast

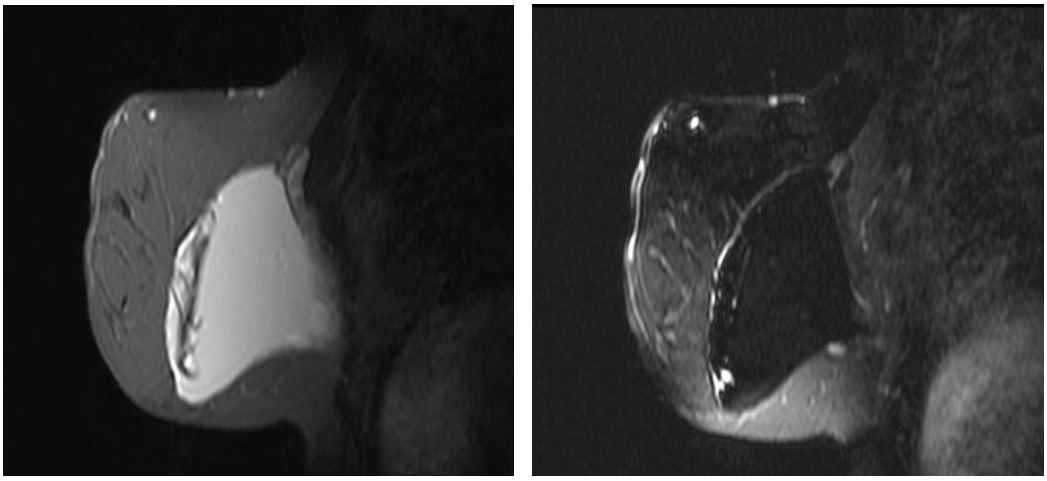

Figure 4. (A = left and B= right) Ruptured and almost completely collapsed elastomere shell. Silicone gel between fibrous capsule and pectoralis major. 4A: Intermediately high signal intensity on water suppressed STIR and 4B: low signal intensity on silicone suppressed STIR.

DISCUSSION

MRI is widely regarded as the most accurate imaging modality to diagnose rupture of silicone breast implants.[6,15,24] Ultrasound is the only available alternative, but this modality has the limitation of being too operator dependent.[25] Neither is MRI free of observer variability. A learning curve in interpreting MR images of silicone breast implants has been reported by radiologists, who scored a higher accuracy as they gained experience.[26] An important advantage of MRI is that the generation and the interpretation of the images are two independent processes. Thus, once

obtained and archived, a set of images can be repeatedly examined by an unlimited number of readers. This advantage was used in the present study, which was aimed as a solely radiologic re-evaluation. We acknowledge the fact that this setting is different from the usual clinical situation.

A strong point of our study is that in all implants the radiologic diagnoses were verified by the best conceivable reference standard, thus excluding any verification bias.[27] A recent Italian study found a sensitivity of 96% and specificity of 77% in detecting implant rupture, but only included women with a clinical suspicion of rupture.[28] The higher sensitivity and lower specificity can be explained by selection bias, as more than 75% of the implants in this study of symptomatic women were ruptured.[27] As the women in our study were not selected on symptomatology and most of them were in fact asymptomatic, we also have no "spectrum bias" or "selection bias". This may be of relevance because the sensitivity and specificity in MRI studies based on a symptomatic sample has been shown to be higher in comparison with studies using an asymptomatic sample.[27,29,30]

A meta-analysis in 2001 found an overall sensitivity of 78% (95% CI, 71%-83%) and specificity of 91% (95% CI, 86%-94%).[31] The sensitivity and specificity of 93% found in our study is within this range. A more recent study found a higher accuracy with a sensitivity of 89% and a specificity of 97%.[32] Concerning the false-negative results we cannot exclude the possibility of implant rupture in the interval between MRI examination and explantation or the rupture at the time of operation, e.g. "disease progression bias."[27]

Accuracy and interobserver variability of MRI screening of ruptured silicone breast implants in asymptomatic women has been studied, but not yet in a single generation, single manufacturer and single type of modern silicone breast implant.[7,26] One MRI validation study has been published about a single, textured, third-generation implant type, but only 21 out of the 149 included women had the MRI diagnosis verified by explantation.[25] The fact that only women with modern moderate cohesive silicone breast implants of the manufacturer PIP were included is both strength and a limitation of the study. A very recent report from the European Commission concluded that despite the flaws in manufacturing processes, the physical and mechanical tests suggest that the properties of PIP shells were comparable to those of other implants and met the requirements of international standards.[33] We therefore believe that our results can benefit all radiologists involved in evaluating modern silicone breast implants, including other manufacturers than PIP.

We assume that our accuracy descriptors are also valid for other types of silicone implants but we have no definite proof of this. It is conceivable, but not yet comparatively investigated, that the likelihood of infoldings to mimic rupture or of the shell to undergo small ruptures which are not visible on MRI may vary depending on the physical properties of the elastomeric shell of different manufacturers.

In our study the interobserver agreement on the diagnosis of implant condition was excellent. We found a kappa coefficient of 0.92 for the diagnosis of implant rupture, showing a strong agreement between the two radiologists. Interobserver agreement was only evaluated in a few

earlier studies and never in a cohort of women with silicone breast implants who had all undergone explantation. A weighted kappa value between 0.89 and 0.91 was found between three radiologists evaluating MR images of different types and generations silicone breast implants in a cohort of asymptomatic women in the USA.[34] A Finish study reported a low-to-moderate interobserver variability, but did not report a calculated kappa value.[35] An example of MR imaging with poor inter and intra observer agreement in given in Figure 5.

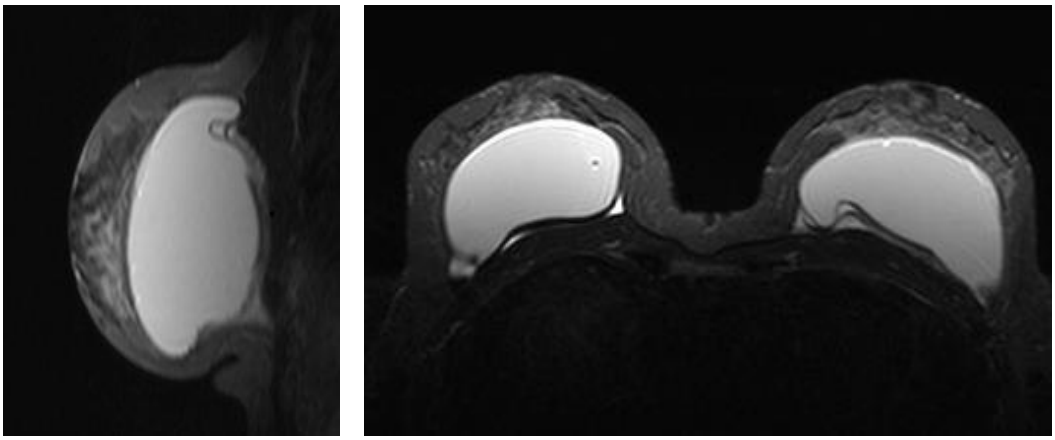

Figure 5. (A = left and B= right) 5A: sagittal left breast and 5B: axial both breasts. Example of a case of exzitant diagnosis and lack of inter- and intraobserver agreement. There is pull-in of the shell, subcapsular double contour and silicone-equivalent signal within the folds in the osterosuperior part of the left breast. Intact prosthesis in the right breast. The surgeon found a profuse gel bleed and an intact prosthesis.

To our knowledge, there are no published data concerning the intraobserver agreement in the MRI diagnosis of implant rupture. Both the intraobserver and interobserver variability gives us insight in the consistency of accuracy of MRI screening in modern silicone breast implants. Due to the fact that some examinations of this study were reported 2 years earlier by the same radiologists, we had the possibility to confront the diagnoses and calculate the K-coefficient.

We would like to underline the fact that the circumstances of interpretation of the MRI images for this study were different from the regular reporting conducted 2 years earlier. The examinations for this study were interpreted according to a strict protocol in dedicated time slots free of any other task assignments in the institution and without any exterior interference. The primary examinations in 2011 were reported within the regular work schedule among other examinations, sometimes interrupted by various other activities. As in a normal radiological practice, the radiologists asked for the opinions of colleagues in certain doubtful cases.

Despite these differences, we found a consistent intraobserver agreement. The two radiologists, who both had at least 8 years of experience in the MRI of breast, showed no obvious improvement after 2 years. One radiologist disagreed with himself in one out of 44 and the other in 4 out of 62 implants. Intraobserver agreement was high for one radiologist (κ=0.94) and moderate for the

other (κ= 0.56) and resulted in a slightly improved sensitivity of one radiologist and a slightly diminished specificity for the other. A limitation of our evaluation of intraobserver agreement is that we could not use the whole cohort for the calculation. Nevertheless, we believe that our results are of sufficient importance, since there is a lack of other data available in the literature.

As yet there is no in vivo reference standard better than MRI to diagnose the extracapsular leakage of silicone.[15] As such we have no possibility to define the accuracy of our findings in terms of sensitivity. Concerning the specificity we would like to mention that we recorded no diagnoses of extracapsular leakage among the women whose implants were found intact at surgery. The interobserver agreement concerning the leakage was less than for implant rupture but enough for a kappa coefficient of 0.74. We hold the opinion that the appearance of leakage is less well-defined than that of rupture, at least on the MRI examinations with the pulse sequences of the protocol employed by us. This is in line with a previous study where it was found that radiologists disagreed more on the presence of extracapsular leakage than on rupture. Without the use of a structured protocol, they even found kappa values as low as 0.5-0.65.[15]

Both consensus by more independent readers and the use of a structured protocol are known methods to improve the accuracy of MRI screening of asymptomatic women with silicone breast implants.[35] The importance of good communication between radiologists and plastic surgeons and the need to simplify the radiologists' jargon in MRI reports has been previously underlined.[36] This inspired the authors to develop a SI-RADS methodology with simple and uniform reporting of the condition of silicone breast implants. This tool was used in the review of the MRI of 214 PIP implants by two independent radiologists. Both groups of radiologists and plastic surgeons who participated in this study agree that this classification improved communication and provided the surgeons with clear information on which they may base the decision to operate or not. Furthermore, we believe it is easily implemented in the daily routine of a general hospital or clinic.

CONCLUSIONS

In conclusion, we found a high accuracy of MRI in diagnosing rupture of silicone breast implants. Considering the excellent kappa value of interobserver agreement and good-to-excellent intraobserver agreement, MRI appears to be a consistent diagnostic test. A simple, uniform reporting protocol, may improve communication between radiologist and plastic surgeon.

CHAPTER 8

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