Silicone Gel Breast Implant Rupture, Extracapsular Silicone, and Health Status in a Population of Women

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ABSTRACT. ***Objective.*** To assess whether breast implant rupture or extracapsular silicone are associated with selected symptoms of self-reported physician-diagnosed connective tissue disease (CTD).

Methods. Women with silicone gel breast implants responded to a questionnaire that included questions on health status, satisfaction with implants, symptoms of CTD, and physician-diagnosed disease. These women then had magnetic resonance imaging (MRI) of their breasts to determine the status of the implants with respect to rupture and extracapsular silicone.

Results. Women with breast implant rupture diagnosed by MRI were no more likely to report a diagnosis of selected CTD than those with intact implants or those with implants of indeterminate status. Women with extracapsular silicone (silicone gel outside of the fibrous scar that forms around breast implants) were more likely to report having fibromyalgia (FM, $p = 0.004$) or other CTD, which included dermatomyositis, polymyositis, Hashimoto's thyroiditis, mixed CTD, pulmonary fibrosis, eosinophilic fasciitis, and polymyalgia ($p = 0.008$) than other women in the study. The association with FM remained statistically significant when adjusted for multiple comparisons (7 diagnoses) and implant age, implant location, or implant manufacturer ($p < 0.05$ in all cases), but became of borderline statistical significance when adjusted for multiple comparisons and self-perceived health status ($p = 0.094$) or self-perceived rupture status ($p = 0.051$). The association with other CTD remained statistically significant when adjusted for multiple comparisons and implant location or implant manufacturer, but became borderline or insignificant when adjusted for multiple comparisons and for implant age ($p = 0.051$), self-perceived health status ($p = 0.434$), or self-perceived rupture status ($p = 0.145$). Logistic regression was used to compute odds ratios of self-reported diagnoses comparing women with and without extracapsular silicone. The odds ratios were 2.8 (95% CI 1.2 to 6.3) for FM, and 2.6 (95% CI 0.8 to 8.5) for other CTD after adjustment for implant age, implant location, implant manufacturer, implant type, self-perceived health, self-perceived rupture status, and site of surgery practice.

Conclusion. These data suggest an association between extracapsular silicone from ruptured silicone breast implants and FM. If this association persists in other studies, women with silicone gel breast implants should be informed of the potential risk of developing fibromyalgia if their breast implants rupture and the silicone gel escapes the fibrous scar capsule. (J Rheumatol 2001;28:996–1003)

Key Indexing Terms:
BREAST IMPLANTS BREAST PROSTHESES SILICONE
FIBROMYALGIA ADVERSE EVENTS

Silicone gel breast implants have been available in the United States since 1963. In 1976, with the passage of the Medical Device Amendments, implants became regulated products. After manufacturers of silicone gel breast implants failed to provide adequate scientific evidence of the safety and effectiveness of their products in 1991 and because of emerging health concerns, the US Food and Drug Administration (FDA) imposed a short voluntary

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moratorium on their sale and implantation in 1992. After a second panel meeting in 1992, the FDA agreed with the General and Plastic Surgery Devices Advisory Panel that there was a public health need for silicone gel breast implants to remain on the market for use only by women requiring implants for reconstruction after breast cancer or for other medical indications while manufacturers performed safety and efficacy studies[1]. Women desiring breast implants for reconstruction were required to receive silicone gel implants in an adjunct study to ensure that they gave informed consent prior to implantation. Unanswered questions about the prevalence of breast implant rupture and the potential link, if any, between implants and immune-related disorders were cited as important factors in the FDA's decision[2].

Recent studies have ruled out a large increased risk of connective tissue disease (CTD) overall for women with breast implants[3-5], but they have not ruled out small increases in specific rare CTDs. Neither have these studies ruled out the possibility that women with breast implants may have a complex of symptoms or a syndrome that is not typical of diagnosed CTD. A genetic predisposition for developing symptoms has been investigated and may be a factor in the development of symptoms in women with breast implants[6]. Another factor that has not been studied is the potential role of exposure to silicone gel from ruptured implants.

In our study, a population of women with silicone breast implants underwent MR imaging examinations to determine the status of their silicone gel breast implants. These women were invited to participate in the MR imaging examination without regard to health status or self-reported symptoms or diagnoses. Our study reports on the health status of women with ruptured implants.

MATERIALS AND METHODS

Patients. Participating women were from 2 plastic surgery practices in Birmingham, Alabama, included in a National Cancer Institute (NCI) study to examine whether implants were associated with cancer or connective tissue disease. A cohort of women having their first augmentation mammoplasty prior to 1988[7] were identified in the medical records from the implanting plastic surgeon and information was abstracted from the record on the surgery and the implant. Women were subsequently located, contacted by mail, and asked to complete a questionnaire. The protocol for the current study was reviewed and approved by 5 institutional review boards and a Certificate of Confidentiality was obtained from the Department of Health and Human Services. Women who had responded to the questionnaire in the NCI study and still lived in Alabama at the time of that questionnaire were eligible for the current cohort.

Of 1247 eligible women, 907 responded to a computer assisted telephone interview that focused on past surgeries in which implants were removed or replaced (the results of this study have been submitted elsewhere). Women were also asked questions regarding their current health status including whether they had certain symptoms or disease diagnosed by their doctors. Of these 907 women, 837 reported still having implants and of those, 654 reported having either single or double lumen silicone gel breast implants. Women were invited to undergo an MRI to determine the status of their implants after completing the telephone interview providing there were no contraindications for undergoing an MRI (metal implant or battery activated stimulator, pregnancy, tattoos, body weight exceeding 300 pounds, or a history of metal fragments in the eye). The order in which women were called and invited to participate in the study was random in that the order in which women were interviewed was random. The study had funding for up to 400 MRI examinations and was also constrained by the contract period the FDA had with the MRI facility. Women were invited to participate in the examination until all possible appointments were filled. Initially, only women within a 50 mile radius of the clinic were invited to participate. As the study progressed, women outside of the area were called back and invited, as were subsequent contacts. Of the 445 women invited to participate in the study, 359 (80.7%) accepted during the allotted time period. Fourteen with saline breast implants and one woman with no implants in either breast were excluded. The remaining 344 women with silicone gel breast implants comprised our study population. A comparison between the women accepting and undergoing the examination and other women has been described[8]. Women gave informed consent prior to receiving an MRI. The telephone interviews were completed between December 1, 1997 and May 20, 1998 and the MRI were completed between January 6 and May 26, 1998.

Radiological assessment. Three radiologists independently assessed the MR images for evidence of breast implant rupture. Implants were rated as having no evidence of rupture (intact), indeterminate (suspicious for rupture, but not certain), or ruptured. The agreement between radiologists was almost perfect[9] as has been reported[8]. Radiologists also assessed the images of the breasts for the presence of extracapsular silicone that had migrated out of the fibrous scar capsule that forms around the implant. The agreement between radiologists for extracapsular silicone was moderate to substantial[8,9].

Analyses. Women with ruptured implants were compared to all others (intact or indeterminate) and women with extracapsular silicone were compared to all others. Rupture and extracapsular silicone were examined for association with increases in self-reported symptoms or physician-diagnosed diseases. The associations were measured with exact p values based on the Fisher-Freeman-Halton test for 2 by C tables, which generalizes Fisher's exact test for 2 by 2 tables. Significant associations were reassessed by stratifying the data on a number of covariates. The possible covariates were implant satisfaction, participant age, implant age (from time of mammoplasty), current problems with implants, perceived rupture, implant manufacturer (Surgitek, Cox-Uphoff International, Dow Corning, Mentor or Heyer-Schulte, and McGhan or 3M/McGhan), implant type (single or double lumen), and implant location (subglandular or submuscular). After stratifying on a covariate, homogeneity of stratum-specific odds ratios (OR) was tested with Zelen's test. If this hypothesis was not rejected, then a common OR across strata was assumed and was tested against a value of one by the uniformly most powerful (UMP) test based on the conditional distribution given by Gart. The p value of the test was computed by the horizontal line method of summing all probabilities of data sets with probability less than or equal to the probability of the data set observed. An exact maximum likelihood estimate of the common OR was computed with respect to the conditional distribution. An approximate 95% CI was computed by inverting the UMP test by the method of Cox and using the mid p value adjustment to compute upper and lower bounds. All of these calculations were made in StatExact[10].

Logistic regression was used to compute OR simultaneously adjusted for multiple covariates. In addition to the covariates mentioned above, the logistic models included site of surgery practice and interactions between covariates.

P values were adjusted for multiple comparisons by computing an upper bound on the smallest familywise significance level at which the comparison would still be significant, where familywise significance level is the probability of a falsely significant result among any of the comparisons in the family. The upper bound was based on Sidek's inequality and is $1 - (1 - p)^k$, where p is the unadjusted p value and k is the number of comparisons in the family[11].

RESULTS

The mean age for the 344 women at the time of their first mammoplasty was 34.1 ± 7.9 years and their mean age at the time of the MRI was 51.4 ± 8.4 years. Women received their first implant between 1970 and 1988 and the mean implant age was 16.5 ± 3.4 years. As reported[8], the radiologists found that 236 (68.6%) women had at least one ruptured implant. While a majority of women had a ruptured implant, 73 (21.2%) had extracapsular silicone gel that had migrated outside of the fibrous scar capsule that forms around the implant. Of the 265 women with either a ruptured or indeterminate implant, 72 (27.2%) had extracapsular silicone gel. One woman had extracapsular silicone but no evidence of implant rupture or self-reported explantation of a previous implant. Overall 378 (55.0%) of 687 implants had ruptured and 85 (12.4%) had extracapsular silicone gel.

Table 1 shows the distribution of women with ruptured implants or with extracapsular silicone according to satisfaction with implants, self-perceived health, participant age, and report of current local complication with implants, including self-perceived rupture of implants(s). Women with ruptured implants did not differ from other women (with intact or indeterminate implants) with respect to satisfaction with their implant(s), self-perceived health, age, or report of current implant problems. Women with ruptured implants were also no more likely than other women to report that they suspected that their implants were ruptured. Women with extracapsular silicone did not differ from other women with respect to satisfaction with implants or report of current problems with implants, but were more likely to report poor health status. Women with extracapsular silicone depicted by MRI were also more likely to suspect that their implant(s) were ruptured.

Table 2 shows the prevalence of women with ruptured implants or with extracapsular silicone according to implant type, implant location, implant age, and implant manufacturer. The prevalence of rupture differed significantly among manufacturers, implant age groups, and locations of

Table 1. Satisfaction with implant, self-perceived health, age group, current problem with implant, and self-perceived rupture by implant status among 344 women with silicone gel breast implants (column percents).

	Ruptured*				Extracapsular Silicone*			
	No (n = 108)		Yes (n = 236)		No (n = 271)		Yes (n = 73)	
	n	%**	n	%**	n	%**	n	%**
Implant satisfaction								
Very satisfied	47	43.5	109	46.2	121	44.6	35	47.9
Somewhat satisfied	30	27.8	59	25.0	76	28.0	13	17.8
Neither satisfied nor dissatisfied	5	4.6	19	8.0	19	7.0	5	6.8
Somewhat dissatisfied	7	6.5	26	11.0	25	9.2	8	11.0
Very dissatisfied	19	17.6	22	9.3	29	10.7	12	16.4
		p = 0.130				p = 0.345		
Self-perceived health**								
Excellent	38	35.2	71	30.1	84	31.0	25	34.2
Very good	25	23.1	71	30.1	81	29.9	15	20.5
Good	24	22.2	60	25.4	66	24.4	18	24.7
Fair	15	13.9	20	8.5	30	11.1	5	6.9
Poor	6	5.6	13	5.5	10	3.7	9	12.3
		p = 0.363				p = 0.044		
Participant Age, yrs								
< 40	8	5.6	19	8.1	17	6.3	8	11.0
40–44	16	14.8	42	17.8	48	17.7	10	13.7
45–49	29	26.9	48	20.3	59	21.8	18	24.7
50–54	26	24.1	47	19.9	61	22.5	12	16.4
55–59	17	15.7	38	16.1	41	15.1	14	19.2
60+	14	13.0	42	17.8	45	16.6	11	15.1
		p = 0.556				p = 0.521		
Current problems with implants (compared to No)								
Yes	30	27.8	55	23.3	67	24.7	18	24.6
		p = 0.419				p = 1.000		
Ruptured (perceived)								
Yes	9	8.3	22	9.3	19	7.0	12	16.4
		p = 0.842				p = 0.020		

*Consensus reading for either implant, left or right.

**Column percentages may not add up to 100% because of refusals or missing answers.

For 2 × 2 tables, the Fisher exact test (SAS) was used; for 2 × C tables, the Fisher-Freeman-Halton test (2 sided) was used (StatExact).

Table 2. Implant location, implant type, and implant manufacturer by implant status.

Characteristic	Ruptured*				Extracapsular Silicone*			
	No		Yes		No		Yes	
	n	%**	n	%**	n	%**	n	%**
Implant location								
Subglandular (n = 137)	65	47.4	72	52.6	112	81.7	25	18.2
Submuscular (n = 202)	41	20.9	161	79.7	154	76.2	48	23.8
		p = 0.0000				p = 0.281		
Implant type***								
Single lumen (n = 284)	88	31.0	196	69.0	220	77.5	64	22.5
Standard double lumen (n = 57)	17	29.8	40	70.2	48	84.2	9	15.8
		p = 1.000				p = 0.293		
Implant manufacturer***								
CUI (n = 12)	5	41.7	7	58.3	10	83.3	2	16.7
Dow Corning (n = 29)	16	55.2	13	44.8	27	93.1	2	6.9
Mentor H/S (n = 45)	8	17.8	37	44.8	36	80.0	9	20.0
McGhan/3M (n = 9)	9	100.0	0	0.0	8	88.9	1	11.1
Surgitek (Medical Engineering Corp) (n = 238)	62	26.1	176	76.9	180	75.6	58	24.3
		p = 0.0000				p = 0.198		
Implant age, yrs***								
6–10	13	52.0	12	48.0	22	88.0	3	12.0
11–15	25	20.5	97	79.5	94	77.0	28	23.0
16–20	45	28.3	114	71.7	119	74.8	40	25.2
21–25	17	65.4	9	34.6	24	92.3	2	7.7
26+	1	33.3	2	66.7	3	100	0	0
		p = 0.0000				p = 0.191		

*Consensus reading for either implant, left or right.
**Row percentages.
***When characteristic is the same for left and right breast implant.
For 2 × 2 tables the Fisher exact test (SAS) was used; for 2 × C tables the Fisher-Freeman-Halton test (2 sided) was used (StatExact).

the implant (submuscular or subglandular). The prevalence of extracapsular silicone did not differ significantly among the levels of any variable.

During the interview, women were asked whether they currently had any of 5 symptoms. Neither rupture nor extracapsular silicone was associated with an increase in the report of any symptom by women (Table 3) nor were they associated with the number of symptoms reported (latter results not shown). Women were also asked whether they currently had each of 7 physician-diagnosed conditions (Table 4). While rupture was not associated with an increase in any of these diagnoses, extracapsular silicone was significantly associated with fibromyalgia (FM, p = 0.004) and other connective tissue disease (p = 0.008), which included dermatomyositis, polymyositis, Hashimoto's thyroiditis, mixed connective tissue disease, pulmonary fibrosis, eosinophilic fasciitis, and polymyalgia. Extracapsular silicone was also borderline significantly associated with

Table 3. Persistent symptoms reported by implant status.

	Implant Status*					
	Ruptured (%)			Extracapsular Silicone (%)		
	Yes (n = 236)	No (n = 108)	p**	Yes (n = 73)	No (n = 271)	p**
Persistent Symptom						
Joint pain, swelling, or stiffness	41.4	38.9	0.724	46.6	38.7	0.230
Rash on breast or chest	5.5	9.3	0.224	8.2	4.9	0.598
Cognitive disorder	28.4	30.6	0.702	28.8	29.1	1.000
Fatigue	18.2	25.9	0.115	21.9	20.3	0.747
Hair loss	16.1	13.0	0.518	13.7	15.5	0.854

*Status of implant determined by MRI, consensus reading.
**Fisher's exact test (2-tail) computed in SAS.

Table 4. Self-reported physician diagnosis by implant status.

Reported Diagnosis	Implant Status* Ruptured (%) Yes (n = 236)	No (n = 108)	p**	Extracapsular Silicone (%) Yes (n = 73)	No (n = 271)	p**
Scleroderma, Systemic Sclerosis, Sclerodactyly, CREST syndrome	1.3	0.0	0.555	0.0	1.1	1.000
Systemic lupus erythematosus	3.0	0.9	0.443	1.4	2.6	1.000
Sjögren's Syndrome or Sicca Syndrome	0.9	0.9	1.000	1.4	0.7	0.512
Raynaud's	3.8	4.6	0.771	8.2	2.9	0.086
Fibrositis FM	13.1	14.8	0.736	24.7	10.7	0.004
Chronic fatigue syndrome	8.5	10.2	0.685	9.8	8.9	0.820
Other CTD***	6.4	3.7	0.447	12.3	3.7	0.008

*Status of implant determined by MRI, consensus reading.
**Fisher exact test (2 sided) computed in SAS.
***Listed such as dermatomyositis, polymyositis, Hashimoto's thyroiditis, mixed connective tissue disease, pulmonary fibrosis, eosinophilic fascitis, polymyalgia.

Raynaud's phenomenon (p = 0.086). Adjustments for multiple comparisons had little impact on the conclusions. Multiplicity adjusted p values based on applying Sidek's inequality to the family of 7 diagnoses tested for association with extracapsular silicone were 0.028 for FM, 0.055 for other connective tissue disease, and 0.467 for Raynaud's (Table 4). A logistic regression was used to calculate the odds ratio that at least one of a woman's implants had extracapsular silicone for each of the symptoms and diagnoses in Tables 3 and 4. The OR was 2.7 (95% CI = 1.4 to 5.2) for FM, indicating that the odds of self-reported FM were 2.7 times greater for women with extracapsular silicone than women without extracapsular silicone. The OR was 2.9 (95% CI = 1.0 to 8.7) for Raynaud's, and 3.7 (95% CI = 1.4 to 9.4) for other CTD. Statistically significant or borderline associations of extracapsular silicone with diagnosis were reassessed by stratifying by the participant's age group at time of MRI, self-perceived implant status, and self-perceived health, (Table 5) and by implant age group, implant location, and implant manufacturer (Table 6). Stratification variables were considered one variable at a time. For each diagnosis, stratum-specific OR were not significantly different for each variable, according to Zelen's exact test, the smallest p value being 0.135 for FM stratified on implant age. We therefore assumed a common OR across strata and tested the hypothesis that the common OR is one. Under this assumption, associations with extracapsular silicone that were borderline before stratification (Raynaud's) remained borderline or became statistically significant. Associations with extracapsular silicone that were statistically significant (FM and other CTD) continued to be statistically significant except in the case of other CTD

Table 5. Raynaud's phenomenon, FM, and other CTD by extracapsular silicone stratified on participant age, self-perceived health and self-perceived implant rupture.

Diagnosis	Participant Age Common OR and 95% CI	p* p**	Self-Perceived Health Common OR and 95% CI	p* p**	Self-Perceived Implant Rupture Common OR and 95% CI	p* p**
Raynaud's	2.6	0.100	2.1	0.208	2.5	0.114
	(0.8, 8.1)	0.521	(0.6, 6.8)	0.804	(0.8, 7.7)	0.570
Fibrositis/FM	2.9	0.003	2.5	0.014	2.5	0.007
	(1.5, 5.6)	0.021	(1.2, 5.2)	0.094	(1.3, 4.9)	0.051
Other CTD	3.7	0.009	2.81	0.078	3.2	0.022
	(1.4, 10.0)	0.061	(1.0, 7.9)	0.434	(1.2, 8.4)	0.145

*Exact p value is the value for testing for the common odds ratio (OR) of 1. $p \leq 0.05$ indicates that the common OR is not equal to 1.
**The Sidek p value is an adjustment to the exact p value for multiple comparisons[11]. The comparisons were the associations of extracapsular silicone with 7 diagnoses.
The confidence interval (CI) is approximate and is calculated by the mid p correction method[10].

stratified on self-perceived health, which was borderline (p = 0.078). P values were adjusted for multiple comparisons within the family of 7 diagnoses considered by applying Sidek's inequality. Borderline associations (Raynaud's) became insignificant and statistically significant associations (FM and other CTD) remained significant except for other CTD stratified on implant age, which just missed being significant (p = 0.051).

Logistic regression was used to compute OR of diagnoses, comparing women with and without extracapsular silicone, that were adjusted simultaneously for multiple covariates. The logistic models included the variables listed in Tables 5 and 6, except for patient age, which was not a significant predictor of extracapsular silicone. The models also included implant type, site of surgery practice, implant manufacturer by implant age interaction, and implant manufacturer by site interaction. These extra 4 variables were significant predictors of women with ruptured implants or ruptured or indeterminate implants as explained elsewhere[8]. Implant age was modeled as a continuous variable with a linear effect on the log scale rather than as a categorical variable as in Tables 2 and 6. The OR were 4.2 (95% CI 1.1–16.0, p = 0.037) for Raynaud's, 2.8 (95% CI 1.2–6.3, p = 0.013) for FM, and 2.7 (95% CI = 0.8–8.5, p = 0.102) for other CTD.

DISCUSSION

Extracapsular silicone was associated with an increase in self-reported physician-diagnosed fibromyalgia and other connective tissue disease in women with silicone gel breast implants. These associations remained statistically significant after separately controlling for the woman's age, implant age, location, and manufacturer. After an adjustment for multiple comparisons, the association with FM remained significant. Breast implant rupture alone was not associated with self-reported physician-diagnosed FM or other CTD. The natural history of breast implant rupture is not completely understood but it is believed in some cases that rupture with intracapsular containment of silicone gel may progress to extracapsular silicone gel.

In a report on 29 patients with ruptured silicone gel implants diagnosed during open capsulotomy, 17.2% tested positive for antinuclear antibody (ANA), which was not significantly different than control subjects[12]. Whether the implant rupture was extracapsular was not stated in this study. A positive test for ANA may be seen in undifferentiated connective tissue disease but it is not a hallmark of FM. Another study reported the presence of positive ANA in women with breast implants referred by rheumatologists to be 18/24 (75%) of patients, but there was no comparison or control group[13]. The authors of this study also reported that a history of trauma to the breast, which was presumed to cause implant rupture, accelerated the onset of CTD. However, no evidence of the rupture status, either by imaging or explantation, was provided. Epidemiologic studies have ruled out a large increase in CTD associated with breast implants[3-5,14,15] but the status of implants with respect to rupture or extracapsular silicone in these studies was unknown.

American College of Rheumatology criteria for FM include a history of widespread pain and tenderness at specified tender points[16] and it has been estimated that FM occurs with a prevalence of 2% in the US and 3.4% for women[17]. Symptoms reported by women with silicone gel breast implants are common in patients diagnosed with FM, suggesting that the atypical syndrome in women with breast implants reported by rheumatologists[18-21] may be FM[22]. In one study, the most common diagnosis for women with breast implants referred for evaluation was FM (27/70, 38.6%) but the status of their implants with respect to rupture or extracapsular silicone was not known[23]. In another study of patients with breast implants referred to a

Table 6. Raynaud's phenomenon, FM, and other CTD by extracapsular silicone stratified on implant location, implant age, or implant manufacturer.

Diagnosis	Implant Location		Implant Age		Implant Manufacturer	
	Common OR and 95% CI	p* p**	Common OR and 95% CI	p* p**	Common OR and 95% CI	p* p**
Raynaud's	3.2	0.042	3.4	0.038	3.9	0.024
	(1.0, 9.9)	0.259	(1.0, 10.9)	0.236	(1.2, 13.6)	0.159
Fibrositis/FM	2.9	0.003	2.8	0.003	2.9	0.004
	(1.4, 5.6)	0.021	(1.4, 5.6)	0.021	(1.4, 5.8)	0.028
Other CTD	3.8	0.007	3.9	0.007	4.0	0.007
	(1.4, 10.0)	0.048	(1.4, 10.7)	0.051	(1.4, 11.2)	0.050

*Exact p value is the value for testing for the common odds ratio (OR) of 1. $p \leq 0.05$ indicates that the common OR is not equal to 1.

**The Sidek p value is an adjustment to the exact p value for multiple comparisons[11]. The comparisons were the associations of extracapsular silicone with 7 diagnoses.

The confidence interval (CI) is approximate and is calculated by the mid p correction method[10].

rheumatology practice, 124/300 (41.3%) met the criteria for a diagnosis of FM[24]. In a study of women having their implants removed, 10/100 (10%) patients had FM[25]. While it was reported that 57% of the implants in that study had ruptured, any association between ruptured implants or extracapsular silicone and FM was not reported. Peters, *et al* did report that although there was an initial improvement after removal of implants in women with FM, symptoms of FM recurred within the next 6 to 12 months[25].

Not all clinicians regard the diagnosis of FM as definitive, and some consider FM and other syndromes whose diagnoses rely on subjective symptoms as functional somatic syndromes, implying that the pathogenesis is psychosomatic or related to litigation[26]. Others describe the pathophysiology of this syndrome in terms of pain amplification due to biochemical imbalances in the nervous or immune system[27]. Women in our study were more likely to think that their implants were ruptured when extracapsular silicone was present (Table 1). However, after adjusting for self-perceived rupture status, the association between self-reported physician-diagnosed FM and extracapsular silicone remained significant.

Women in our study were also asked whether a physician had diagnosed them with other CTD such as dermatomyositis, polymyositis, Hashimoto's thyroiditis, mixed connective tissue disease, pulmonary fibrosis, eosinophilic fasciitis, or polymyalgia. Women with extracapsular silicone gel were more likely to report that they had other CTD than were other women in the study. It is not possible to determine whether any of these disorders predominated. Our category of other CTD is artificial and therefore those results are difficult to interpret.

Raynaud's phenomenon may occur in isolation or be present in association with CTD such as scleroderma. We found the association between extracapsular silicone and Raynaud's syndrome had borderline statistical significance while there was no significant association observed for scleroderma and extracapsular silicone. The 3 cases of scleroderma reported to us were by women whose implants had ruptured but who did not have extracapsular silicone.

The principle limitation of our study was its small size It would not be possible to rule out rare diseases (such as scleroderma) in association with ruptured implants, ruptured or indeterminate implants, or extracapsular silicone. Our study is cross-sectional in that we only have information on current implant status and current self-reported symptoms and diseases. We were unable to determine whether symptoms or disease occurred before or after the development of extracapsular silicone or whether it was before or after the implant was surgically implanted. Also, the results from this study were based on self-report of physician-diagnosed disease and therefore have the weaknesses attributed to self-reported disease. However, since the women did not know the status of their implants with respect to rupture, any error in disease misclassification would be expected to dilute the association of disease with rupture. We cannot know what effect the media or litigation had on participation in this study: anecdotal evidence suggests that some litigants were encouraged to participate in the NCI study and others were discouraged by their attorney(s) or others. Despite these limitations, the results of this study are valuable because it is the first study in which the implant status has been evaluated for all women. The women for the MRI study were invited to participate from a larger population of women with breast implants from Alabama without regard to their health status or knowledge of their implant status. While not definitive, our study does raise the question of whether implant status, especially implant rupture with extracapsular spread of silicone gel, may have a bearing on the health status of implanted women.

It should be noted that we did not compare women with implants to those without. It is possible that there may be an increased prevalence of disease or symptoms in women with breast implant rupture compared to women without implants but we could not make this comparison.

Our results indicate that women with extracapsular silicone gel may be at an increased risk for FM. If future studies confirm our findings, consideration as to whether women with silicone gel breast implants should be screened for implant rupture should be considered. Clearly, if the risk of rupture and subsequent extracapsular silicone increases the risk of fibromyalgia, women considering augmentation or reconstruction mammoplasty with silicone gel breast implants should be informed.

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