Association between Enlarged Axillary Lymph Nodes and Silicone Breast Implant Ruptures seen on Magnetic Resonance Imaging

Eyal Klang MD[1,2], Michal M. Amitai MD[1,2], Stephen Raskin MD[1,2], Noa Rozendorn[2], Nicholas Keddel MD[3], Jana Pickovsky MD[1,2] and Miri Sklair-Levy MD[1,2]

[1]Department of Diagnostic Imaging, Sheba Medical Center, Tel Hashomer, Israel
[2]Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
[3]St George's University of London, London, Israel

ABSTRACT: **Background:** Silicone breast augmentation is a common cosmetic surgery. Previous case reports demonstrated lymphadenopathy in the presence of implant ruptures.

Objectives: To investigate the association between enlarged axillary lymph nodes and silicone implant ruptures as seen on breast magnetic resonance imaging (MRI).

Methods: Two groups were derived retrospectively from breast MRI reports in our institution for the period December 2011–May 2014. We conducted a search of our hospital records for "silicone" and "lymph node" (group A) to evaluate the relationship between the presence of enlarged nodes and ruptures. The prevalence of ruptures in the presence of nodes was calculated and the association between MRI imaging features and ruptures evaluated. We then searched for "silicone" and "implant rupture" (group B) and, as for group A, evaluated the relationship between the presence of ruptures and nodes and calculated the prevalence of enlarged nodes in the presence of ruptures.

Results: Group A comprised 45 women with enlarged nodes. Intracapsular ruptures were associated with nodes ($P = 0.005$), while extracapsular ruptures showed a trend of association with nodes ($P = 0.08$). The prevalence of ruptures in the presence of nodes was 31.4%. Nodes associated with ruptures showed a strong silicone signal ($P = 0.008$) and absent enhancement ($P = 0.005$). Group B comprised 73 women with ruptures. Enlarged nodes were associated with both intra- and extracapsular ruptures ($P < 0.001$ and $P = 0.002$ respectively). The prevalence of nodes in the presence of ruptures was 22.2%.

Conclusions: Enlarged axillary nodes were associated with ruptures in two groups of patients. This finding can guide clinical decisions when either enlarged nodes or ruptures are encountered in patients with silicone implants. The association between silicone lymphadenopathy and implant rupture raises concerns regarding the role of rupture in silicone-induced systemic disease.

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Breast augmentation continues to be one of the most popular cosmetic surgeries, and the most common material used in implants is silicone [1]. Implant rupture is an extremely serious complication of silicone implants. In most implants a fibrous capsule forms around the implant [2]; these ruptures can be either intra- or extracapsular. Ruptures usually do not produce a change in volume and are not clinically evident [3]. Magnetic resonance imaging (MRI) examination is the gold standard for diagnosing implant ruptures [4]. Several case studies and series have shown lymphadenopathy in association with silicone implant ruptures [5-10]. Zambacos et al. [6] presented a case series of 14 patients with silicone lymphadenopathy and conducted a literature search that identified 29 case reports of silicone lymphadenopathy.

Silicone implants have been linked to autoimmune diseases such as lupus, scleroderma, and others [11-14]. A recently described syndrome, "autoimmune/inflammatory syndrome induced by adjuvants" (ASIA), has also been linked to silicone implants [11,12,15,16]. A recent case series presented four women who developed systemic disorders following rupture of silicone breast implants that resulted in lymph node and thoracic silicone infiltration [12].

Silicone implants have been linked to lymphoma, in particular anaplastic large cell lymphoma (ALCL), a rare type of T cell lymphoma [17-19]. A recent literature review concluded that implants pose a small risk of lymphoma development, and since the behavior of ALCL in these cases was indolent it could suggest an abnormal reactive process [19].

The purpose of the present study was to investigate the association between enlarged axillary lymph nodes and silicone implant ruptures as seen on breast MRI. This association should prompt a search for ruptures when nodes are encountered, and a search for nodes when ruptures are encountered. This association also raises concerns regarding the possible connection between implant rupture and systemic disease.

PATIENTS AND METHODS

Institutional review board approval was obtained for a retrospective review of breast MRIs.

BREAST MRI PROTOCOL

MRIs were performed on 1.5 Tesla (Signa Excite HDX, GE Healthcare, USA) with a dedicated double breast coil (8 channels) and a standard dynamic and implant bilateral breast MRI protocol. A dynamic contrast-enhanced T1-weighted 3D axial vibrant multiphase with the following parameters was used: TR/TE 5.4/2.6, flip angle 15, bandwidth 83.3 khz, matrix 512 x 364, field of vision (FOV) 340 mm, section thickness 2 mm, no intersection gap.

MRIs were interpreted by a breast radiologist with 15 years of experience reading breast MRIs (M.S.). A second reading was performed by a board-certified radiologist (E.K.). Of the 116 revision MRIs, node measurements were made in consensus in 15 (12.9%).

STUDY PROTOCOL

Two groups of women were investigated in this study.

GROUP A

Interpretations of 4356 consecutive breast MRIs performed in our institution from December 2011 to December 2013 were searched using the combined terms "silicone" and "lymph node." Included were only those examinations with enlarged axillary lymph nodes, defined as nodes with a short axis > 10 mm, with a round shape, a cortical thickening and without a fatty hilum [20]. Exclusion criteria in group A were nodes in sites other than the axilla, repeat examinations, cases with missing data, and cases with silicone injections.

Data collected on each patient included patient's age, indication for breast augmentation (post-mastectomy versus cosmetic breast enlargement), age of implant, presence and side of breast cancer, presence and side of intra- and extracapsular ruptures, and presence and side of enlarged nodes. The largest enlarged node in each axilla was measured in the short and long axis.

Analysis of the MRI imaging features of the nodes was conducted as follows:

- The nodes were categorized into four different types of gross appearance: (i) widened smooth cortex nodes, (ii) widened lobulated cortex nodes, (iii) absent hilum with smooth cortex, and (iv) absent hilum with lobulated cortex
- The signal intensity of the nodes in the MRI silicone sequence (water and fat suppressed) was categorized as being absent, mild, or strong
- The post-contrast sequence was evaluated to categorize nodes as either enhancing or not enhancing.

Statistical analysis in group A evaluated the association between:

- The presence of enlarged nodes and the presence of ruptures, allowing also a calculation of the prevalence of ruptures in the presence of enlarged nodes
- The short and long axis diameters of enlarged nodes and the presence of ruptures
- Age of implant and the presence of enlarged nodes
- Age of implant and the presence of ruptures
- A history of breast carcinoma and the presence of enlarged ipsilateral axillary nodes
- Association between MRI imaging features of the enlarged nodes and implant ruptures.

GROUP B

Interpretations of 5302 consecutive breast MRI examinations performed in our institution between December 2011 and May 2014 were searched using the terms "silicone" and "implant rupture." Exclusion criteria in group B were repeat examinations.

Data collected on each patient included patient's age, indication for surgery (post-mastectomy versus cosmetic breast enlargement), age of implant, presence and side of breast cancer, presence and side of intra- and extracapsular implant rupture, and presence and side of enlarged axillary lymph nodes. The largest enlarged node in each axilla was measured in the short and long axis.

Statistical analysis in group B evaluated the association between the presence of enlarged nodes and the presence of ruptures, allowing also a calculation of the prevalence of enlarged nodes in the presence of ruptures.

STATISTICAL ANALYSIS

Statistical analysis was performed using IBM SPSS statistic (Version 20.0) (Armonk, NY, USA). Chi-square test or Fisher's exact test was used for categorical variables, and *t*-test was used for continuous variables. A P value < 0.05 was considered significantly different.

RESULTS

GROUP A

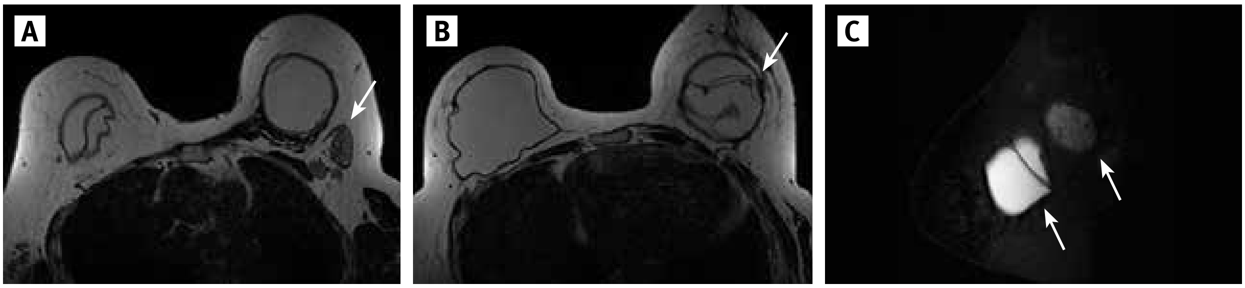
We identified 702 breast MRIs using the search term "silicone," and 109 of these (15.5%) were identified using the search term "lymph node." Of these 109 examinations, 64 were excluded: 51 exhibited internal mammary or retropectoral lymph nodes (the vast majority of these had a short axis < 10 mm) but not enlarged axillary nodes, 9 were repeat examinations, 3 had incomplete data and one patient had silicone injections.

Group A included 45 examinations that exhibited enlarged nodes: 31 in the right axilla and 23 in the left axilla. Nine patients had bilateral enlarged nodes. Thus, group A comprised 90 axillae (45 x 2); of these, 54 (60.0%) showed enlarged nodes. There were 87 breast implants in group A since three patients had a unilateral implant. The demographics of group A are presented in Table 1.

Table 1. Demographic data on group A (n=45) and group B (n=73)

	Group A	Group B
Patients' age, yrs ± SD (range)	50 ± 11.4 (24–68)	47.9 ± 11.9 (22–72)
Implant age, yrs ± SD (range)	6.6 ± 5.9 (0–25)	11 ± 7.3 (1–35)
Implant due to cosmetic breast augmentation, n (%)	17 (37.8%)	56 (76.7%)
Implant related to cancer treatment, n (%)	24 (53.3%) breast carcinoma 4 (8.9%) protective mastectomy	15 (20.5%) breast carcinoma 2 (2.7%) protective mastectomy

Figure 1. A 62 year old women with extensive left intracapsular rupture

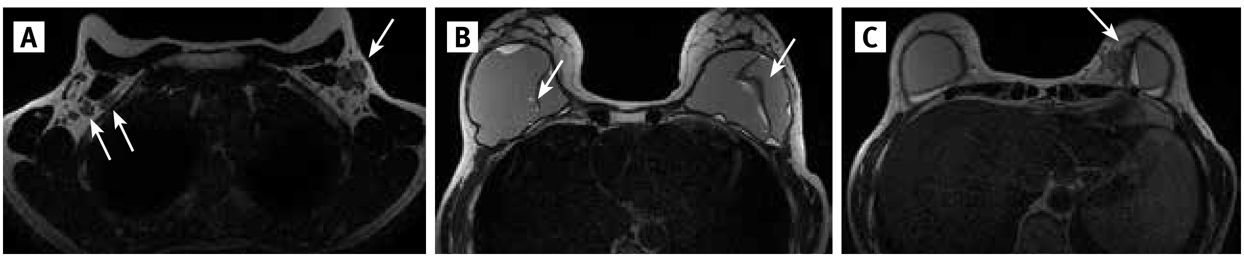


[A] Axial T2 fast spin echo (FSE). Arrow points to extensive left axillary lymphadenopathy. Nodes have absent hilum and smooth cortex

[B] Axial T2 fast spin echo. Arrow points to marked left intracapsular rupture

[C] Sagittal short tau inversion recovery (STIR) in water-saturated silicone sequence. Long arrow points to the breast implant, short arrow points to an axillary lymph node with a strong silicone signal

Figure 2. A 59 year old women with right intracapsular and left intra- and extracapsular ruptures



[A] Axial T2 fast spin echo. Long arrow points to left axillary lymphadenopathy. Short arrows point to right axillary lymphadenopathy

[B] Axial T2 fast spin echo. Long arrow points to left intracapsular rupture. Short arrow points to right intracapsular rupture

[C] Axial T2 fast spin echo. Long arrow points to extracapsular rupture

Overall, 19 of 87 implants (21.8%) showed intracapsular rupture (right 11, left 8), and 6 (6.9%) showed extracapsular rupture (right 4, left 2). As expected, all extracapsular ruptures showed a concurrent intracapsular rupture. Figure 1 shows an intracapsular rupture and unilateral lymphadenopathy. Figure 2 shows bilateral intracapsular ruptures and left extracapsular rupture with bilateral lymphadenopathy.

A statistical association was demonstrated between enlarged nodes and intracapsular ruptures, with 17/19 (89.5%) intracapsular ruptures associated with enlarged nodes, compared to 37/68 axillae (54.4%) without ipsilateral intracapsular rupture showing nodes ($P = 0.005$). This association was maintained after exclusion of the cases of combined intra- and extracapsular ruptures, with 11/13 (84.6%) only-intracapsular ruptures associated with enlarged nodes, compared to 37/68 (54.4%) axillae without ipsilateral intracapsular rupture showing enlarged nodes ($P = 0.042$).

All 6 cases (100%) of extracapsular ruptures showed associated nodes, compared with 48/81 axillae (59.3%) without ipsilateral extracapsular rupture showing enlarged nodes ($P = 0.08$). The prevalence of rupture in the presence of enlarged nodes was 17/54 (31.4%) [95% confidence interval (95%CI) 18.7–44.3%]. No statistical association was found between node diameter and rupture (short axis: nodes with rupture 12.1 ± 4.0 mm vs. nodes without rupture 11.5 ± 2.2 mm, $P = 0.6$; long axis: nodes with rupture 18.9 ± 6.3 mm vs. nodes without rupture 16.0 ± 4.5 mm, $P = 0.1$). No association was found between age of implant and presence of enlarged nodes

Table 2. Associations between MRI imaging features and implant ruptures for group A (n=52 MRI examinations with 52 enlarged lymph nodes)

	Widened smooth cortex	Widened lobulated cortex	Absent hilum smooth cortex	Absent hilum lobulated cortex	Mild silicone signal	Strong silicone signal	Enhancement
Intracapsular rupture	P = 0.706 OR = 1.3	P = 0.443 OR = 0.6	P = 0.557 OR = 1.4	P = 1.0 OR = 0.5	P = 0.507 OR = 1.6	P = 0.008 OR = 8.8	P = 0.005 OR = 0.1
Extracapsular rupture	P = 0.270 OR = 2.8	P = 0.081 OR = 0.1	P = 0.675 OR = 1.6	P = 1.0 OR = 1.4	P = 1.0 OR = 0.5	P = 0.026 OR = 10.5	P = 0.040 OR = 0.1

OR = odds ratio

(average age without nodes 5.5 ± 4.7 years vs. average age with nodes 6.7 ± 6.0 years, P = 0.3). No association was found between implant age and rupture (average age without rupture 6.8 ± 5.9 vs. average age with rupture 4.2 ± 3.2, P = 0.08). No association was found between a history of breast cancer and presence of enlarged nodes (P = 0.9).

Evaluation of the associations between MRI imaging features and implant rupture is presented in Table 2. Analysis of the imaging features was conducted for 52 nodes since 2 of the 54 MRIs with nodes did not have the silicone sequence. As can be seen in Table 2 there was no significant association between the gross appearance of the nodes (widened cortex or absent hilum, smooth or lobulated cortex) and implant ruptures. There was a significant association between the presence of a strong signal in the silicone sequence and both intra- and extracapsular ruptures (P = 0.008 and P = 0.026, respectively), as well as the absence of enhancement (P = 0.005 and P = 0.040, respectively).

GROUP B

Using the search term “silicone” we identified 851 breast MRIs; of these, 84 (9.9%) were identified using the search term “implant rupture.” Eleven repeat examinations were excluded. Thus, group B comprised 73 examinations, which included 51 intracapsular ruptures on the right side, 7 with a concurrent extracapsular rupture, and 39 intracapsular ruptures on the left side, 5 with a concurrent extracapsular rupture. In 17 cases, both sides showed intracapsular rupture.

Thus, group B consisted of 146 axillae (73 x 2) and 142 breast implants (four patients had a unilateral implant). Of these 142 implants, 90 (63.4%) exhibited implant rupture. The demographics of group B are presented in Table 1.

The average short axis diameter of lymph nodes in group B was 12.2 ± 4.1 mm, and the average long axis diameter 18.9 ± 7.3 mm. The study results showed a statistically significant association between enlarged axillary lymph nodes and intracapsular ruptures, with 20/90 (22.2%) enlarged nodes associated with intracapsular rupture, compared to no enlarged nodes (0/52, 0%) in axillae without ipsilateral intracapsular rupture (P < 0.001). This association was maintained after exclusion of cases of combined intra- and extracapsular ruptures, with 14/78 (17.9%) enlarged nodes associated with only-intracapsular rupture, compared to no enlarged nodes (0/52, 0%) in axillae without ipsilateral intracapsular rupture (P = 0.001). There was also an association between enlarged nodes and extracapsular rupture, with 6/12 cases (50%) of enlarged nodes associated with extracapsular rupture, compared to 14/130 (10.8%) nodes in axilla without ipsilateral extracapsular rupture (P = 0.002). The prevalence of enlarged nodes in the presence of implant rupture was 20/90 (22.2%) (95%CI 13.5–30.0%).

DISCUSSION

This study investigated the association between intra- and extracapsular silicone breast implant ruptures and enlarged axillary lymph nodes. The study population was divided into two groups: group A where the independent variable was node enlargement, and group B where the independent variable was rupture. The study showed a significant association between rupture and node enlargement in both groups.

In group A, comprising 87 implants, intracapsular rupture was found to be associated with enlarged nodes (P = 0.005). Extracapsular rupture showed a trend of association with enlarged nodes (P = 0.08); the small number of extracapsular ruptures in group A may have precluded statistical significance.

In group B, comprising 142 implants, enlarged nodes were also associated with intra- and extracapsular rupture (P < 0.001, P = 0.002, respectively). The prevalence of ruptures in the presence of nodes was 31.4%, and the prevalence of nodes in the presence of ruptures was 22.2%.

Although several case reports and case series have shown enlarged nodes in relation to ruptures [5-10], to the best of our knowledge our study is the first to statistically prove this association and provide the incidence of associations. We found only two studies that investigated the association between rupture and clinically enlarged nodes [21,22]. In the 2005 study by Holmich et al. [21], clinical examination was compared with the appearance of rupture on MRI in 55 women. In contrast to our study, their findings did not show an association between enlarged nodes and rupture, but that study used clinical node enlargement as the parameter of investigation, whereas our study used node enlargement and node appearance on MRI as the parameters of investigation. In a study by Maijers and colleagues [22] in 120 patients with

Poly Implant Prothèse silicone implants, 3 patients (2.7%) exhibited a palpable node at physical examination; of these, two showed a ruptured implant on the ipsilateral side on MRI, and one implant that appeared intact on MRI showed excessive gel bleed during surgery.

Our study showed no association between the nodes' short and long axis diameters and rupture ($P = 0.6$ and $P = 0.1$, respectively). No association was found between implant age and the presence of enlarged nodes ($P = 0.3$) or between implant age and rupture ($P = 0.08$). This finding was in contrast with previous studies that showed a frequency of 0.2%–4% for asymptomatic ruptures that increases with the age of the implant [23], and rupture-free survival that is estimated to be 98% at 5 years and 83–85% at 10 years [24]. We suspect that this result is due to a bias in our study, with cases of clinically suspected rupture sent for MRI investigation, compared to several cases with long lasting intact implants (up to 25 years in group A).

When analyzing the MRI imaging features of the nodes [Table 2], we found that although nodes associated with rupture did not exhibit a specific gross appearance (widened cortex or absent hilum, smooth or lobulated cortex), these nodes were significantly associated with the presence of a strong signal in the silicone sequence, and absence of enhancement. Most probably the absence of enhancement is due to replacement of the normal lymph structure by the silicone substance.

The results of our study have several clinical implications:

- When encountering enlarged axillary lymph nodes in patients with silicone implants, either in imaging studies (ultrasound, mammography, computed tomography, MRI) or physical examination, we suggest searching for implant rupture since 31% of nodes are associated with rupture. Preferably the search should be with MRI, which is the gold standard for diagnosing implant rupture [4]. This is important because a rupture usually does not produce a change in volume and the patient is generally asymptomatic [3].
- When encountering a silicone implant rupture, we suggest searching for axillary lymph nodes for documentation, either by ultrasound or MRI, as 22% of ruptures are associated with enlarged lymph nodes and these lymph nodes may later be confused with malignancy. We suggest further evaluation of the nodes using ultrasound to search for the typical snowstorm silicone sign [4].
- Since lymphadenopathy represents an inflammatory response, questions are raised regarding the possible connection between rupture and systemic disorders such as autoimmune diseases [11-13] and anaplastic large cell lymphoma (ALCL) [17-19], and further research is warranted.

The limitations of this study include its retrospective nature and the relatively small number of extracapsular ruptures. Moreover, because of the limited number of enlarged intramammary lymph nodes, the study included only enlarged axillary lymph nodes.

In conclusion, our findings verified an association between enlarged axillary lymph nodes and silicone implant rupture, using nodes and rupture separately as independent variables. The prevalence of rupture in the presence of nodes was 31.4%, and the prevalence of nodes in the presence of rupture 22.2%. This association has several clinical implications for the management of patients with silicone breast implants who present with either enlarged nodes or rupture, and also raises concerns regarding the possible connection between rupture and systemic disease.

Correspondence
Dr. E. Klang
Dept. of Diagnostic Imaging, Sheba Medical Center, Tel Hashomer 5265601, Israel
Fax: (972-3) 5357315
email: eyalkla@hotmail.com

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