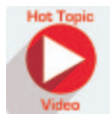


U.S. Epidemiology of Breast Implant–Associated Anaplastic Large Cell Lymphoma

Erin L. Doren, M.D.
Roberto N. Miranda, M.D.
Jesse C. Selber, M.D.,
M.P.H.
Patrick B. Garvey, M.D.
Jun Liu, M.D.
L. Jeffrey Medeiros, M.D.
Charles E. Butler, M.D.
Mark W. Clemens, M.D.

Milwaukee, Wis., and Houston, Texas



Background: Breast implant–associated anaplastic large cell lymphoma (ALCL) is a distinctive type of T-cell lymphoma that arises around breast implants. Although rare, all cases with adequate history have involved a textured breast implant. The objective of this study was to determine the U.S. incidence and lifetime prevalence of breast implant–associated ALCL in women with textured breast implants.

Methods: This is a retrospective review of documented cases of breast implant–associated ALCL in the United States from 1996 to 2015. The incidence and prevalence were determined based on a literature and institutional database review of breast implant–associated ALCL cases and textured breast implant sales figures from implant manufacturers’ annualized data.

Results: One hundred pathologically confirmed breast implant–associated ALCL cases were identified in the United States. Mean age at diagnosis was 53.2 ± 12.3 years. Mean interval from implant placement to diagnosis was 10.7 ± 4.6 years. Forty-nine patients had breast implants placed for cosmetic reasons, 44 for mastectomy reconstruction, and seven for unknown reasons. Assuming that breast implant–associated ALCL occurs only in textured breast implants, the incidence rate is 2.03 per 1 million person-years (203 per 100 million person-years), which is 67.6 times higher than that of primary ALCL of the breast in the general population (three per 100 million per year; $p < 0.001$). Lifetime prevalence was 33 per 1 million persons with textured breast implants.

Conclusions: This study demonstrates a statistically significant association between textured breast implants and breast implant–associated ALCL. Although women with a textured breast implant have a low risk of developing breast implant–associated ALCL, the current U.S. incidence is significantly higher than that of primary ALCL of the breast in the general population. (*Plast. Reconstr. Surg.* 139: 1042, 2017.)

There are an estimated 10 million women worldwide with breast implants.¹ In the United States, breast augmentation is the number one cosmetic procedure performed, with a recent estimate of over 550,000 implants placed per year.² Breast implant–associated anaplastic large cell lymphoma (ALCL) is a distinctive type of T-cell lymphoma that arises around breast implants.¹ Although rare, it has been documented worldwide, with the sentinel case reported in 1997.³ Since that time, over 170 cases have been documented.⁴ Most cases have been diagnosed during revision surgery for a delayed or persistent seroma, associated with

breast pain or swelling, occurring on average 9 years after implantation.^{5,6} All reported cases of breast implant–associated ALCL with adequate surgical history have involved a textured breast implant.^{4,6,7} There have been only two reports in the literature indicating that breast implant–associated ALCL may have occurred in association with a smooth silicone gel implant.^{8,9} However, these reports are questionable, as the clinical history given in both case reports reveals that the implant surface was unknown or the implant had been replaced

Disclosure: *The authors have no financial interest to declare in relation to the content of this article.*

A “Hot Topic Video” by Editor-in-Chief Rod J. Rohrich, M.D., accompanies this article. Go to PRSJournal.com and click on “Plastic Surgery Hot Topics” in the “Digital Media” tab to watch. On the iPad, tap on the Hot Topics icon.

From the Department of Plastic Surgery, Medical College of Wisconsin, Tosa Center; and the Departments of Hematopathology and Plastic Surgery, The University of Texas M. D. Anderson Cancer Center.

Received for publication August 16, 2016; accepted November 4, 2016.

Copyright © 2017 by the American Society of Plastic Surgeons

DOI: 10.1097/PRS.0000000000003282

multiple times with other types of implants that were incompletely documented.

Because of the rarity and sporadic reporting of breast implant–associated ALCL, accurate estimations of its incidence and prevalence have been difficult to determine. A 2008 Dutch study found a positive association between breast implants and the development of ALCL, with an odds ratio of 18.2 (95 percent CI, 2.1 to 156.8), meaning that patients with implants were 18 times more likely to develop ALCL than patients without breast implants.¹⁰ The authors reported the incidence to vary between 0.1 and 0.3 per 100,000 women with prostheses per year, based on five cases in a relatively small study population.¹⁰

In 2011, the U.S. Food and Drug Administration (FDA) published a safety communication stating, “Women with breast implants may have a very small but increased risk of developing ALCL in the scar capsule adjacent to an implant.”¹¹ The FDA based this safety communication on published reports of the first 34 published cases of breast implant–associated ALCL known at that time. Without any additional epidemiologic data in the literature, they estimated the incidence of primary ALCL of the breast to be approximately three in 100 million women per year in the United States, based on data from the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute.¹¹ This reported incidence, however, is not specific to breast implant–related ALCL, but instead represents any ALCL of the breast in the general population. In 2016, the FDA subsequently updated their safety communication to reflect that their Manufacturer and User Facility Device Experience database had received approximately 258 adverse event reports of ALCL in women with breast implants as of September of 2015. The purpose of this study was to more accurately determine the U.S. incidence and lifetime prevalence of breast implant–associated ALCL in women with textured breast implants.

PATIENTS AND METHODS

Study Design

We performed a retrospective review of the U.S. literature of documented cases of breast implant–associated ALCL from 1996 to 2015, with the first known case documented in 1996. Corresponding authors of all published cases were contacted to request clinical information, pathology slides, and treatment and follow-up data. All slides were centralized to our institution and were reviewed at The University of Texas

M. D. Anderson Cancer Center and pathologically confirmed by the following criteria. Breast implant–associated ALCL was defined as a T-cell lymphoma that was in continuity with a breast implant or scar capsule, composed of large, pleomorphic cells that uniformly expressed CD30 and lacked anaplastic lymphoma kinase expression or genetic abnormalities involving anaplastic lymphoma kinase at chromosome 2q23. Unpublished cases diagnosed at our institution and the cases we were able to pathologically confirm from the literature created our institutional registry of confirmed U.S. cases of breast implant–associated ALCL. We included only those cases that had been pathologically confirmed by strict criteria as breast implant–associated ALCL and had clinical, therapeutic, and follow-up data, including age at diagnosis; date of first breast implant placement; date of diagnosis; surgical history; treatment; and follow-up indicating whether the patient was disease-free, alive, or dead. We recorded additional patient clinical data, including breast implant procedures, reason for breast implantation, implant manufacturer, and device texturing. We determined the incidence and lifetime prevalence of breast implant–associated ALCL among women with textured breast implants on the basis of U.S. textured breast implant sales figures publicly available or provided by the implant manufacturers, Allergan (Allergan, Inc., Irvine, Calif.) and Mentor (Mentor Worldwide LLC, Santa Barbara, Calif.) (Fig. 1). Allergan Corporation performs a salt-loss technique for shell texturization, and Mentor Corporation performs a negative-imprint stamping technique for texturization.

Statistical Analysis

Because all confirmed cases to date of breast implant–associated ALCL with adequate clinical history are documented to have occurred in patients with a textured breast implant, we estimated the incidence rates by assuming that all cases had textured breast implants. We determined the U.S. incidence of breast implant–associated ALCL per year and overall from 1996 to 2015. The incidence was determined using the number of newly diagnosed cases per year and the number of textured breast implants in the U.S. population for the same year and provided an exact Poisson 95 percent confidence interval. We estimated the number of textured breast implants in the population assuming a 0.7 percent breast implant removal rate per year (Fig. 2). This

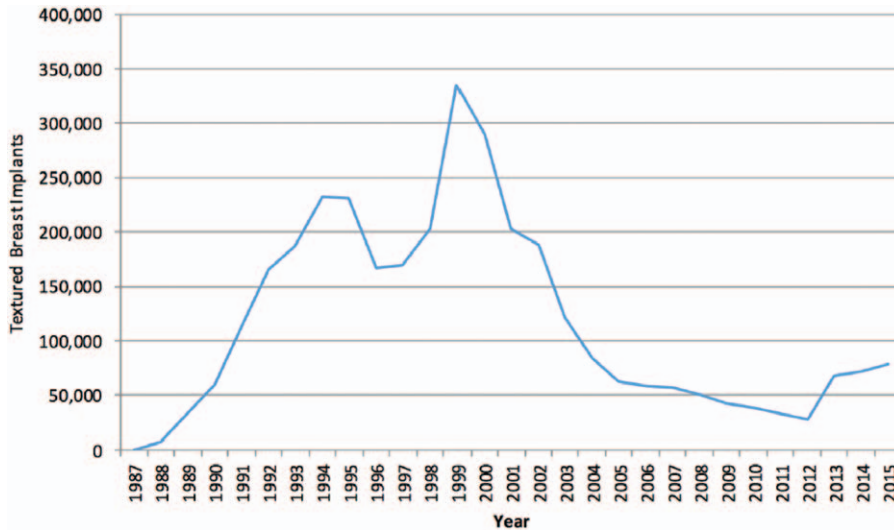


Fig. 1. U.S. textured breast implant sales figures, including manufacturers Allergan and Mentor, from 1987 to 2015.

was based on data from the Natrelle 410 implant study reporting an average implant removal rate of 6.7 percent at 10 years.¹² A binomial test compared the overall breast implant-associated ALCL incidence rate to the previously reported U.S. primary breast ALCL incidence rate of three in 100 million.¹¹ Values of $p < 0.05$ were considered significant.

Because breast implant-associated ALCL is a curable disease in most patients, with median overall survival rates of 93 percent and 89 percent at 3 and 5 years, respectively, we used lifetime prevalence as our statistical measure.⁷

Lifetime prevalence reflects the number of individuals in a population that at some point in their life experienced the disease in question. Because the study period was from 1996 to 2015, we considered this rate as the 20-year prevalence. We calculated the lifetime prevalence from the number of cumulative cases up to the time of assessment divided by the number of women having textured breast implants at the time of the assessment. These analyses were performed using SAS 9.3 (SAS Institute, Inc., Cary, N.C.) and R (The R Foundation for Statistical Computing, Vienna, Austria).

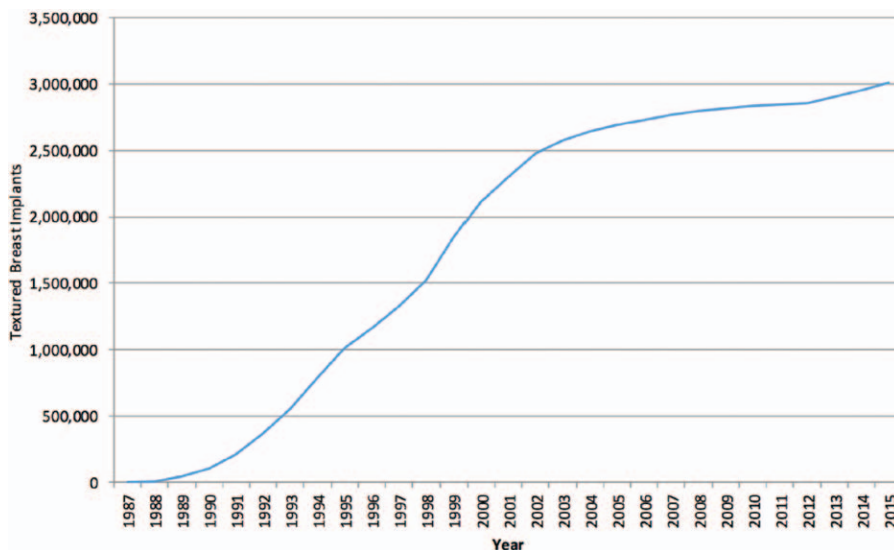


Fig. 2. Number of implanted textured breast implants in the U.S. population per year.

RESULTS

Patient Characteristics

Table 1 summarizes the patients’ demographic and clinical characteristics. We identified and pathologically confirmed a total of 100 breast implant–associated ALCL cases in the United States from 1996 to 2015. Figure 3 demonstrates the cases documented geographically across the United States during that period. The mean age at the time of diagnosis was 53.2 ± 12.3 years. The

mean interval from breast implantation to diagnosis of disease was 10.7 ± 4.6 years (Fig. 4). Forty-nine percent of patients received breast implants for cosmetic augmentation and 44 percent received implants for postmastectomy breast reconstruction; 7 percent received implants for unknown reasons. Among the 100 cases, 51 patients had a confirmed history of textured breast implants, no patients reported smooth implants, and the implant texturing status was unknown for 49 patients.

Table 1. Patient Demographics and Implant Characteristics

Variable	Frequency (%)
No.	100
Mean age \pm SD, yr	53.2 ± 12.3
Mean interval from implant to diagnosis of BIA-ALCL \pm SD	10.7 ± 4.6
Reason for implant	
Cosmetic	49 (49)
Mastectomy	44 (44)
Unknown	7 (7)
Texturing of implant	
Textured	51 (51)
Smooth	0 (0)
Unknown	49 (49)
Manufacture type	
Salt-loss	43 (43)
Negative-imprint stamp	5 (5)
Both	3 (3)
Unknown	49 (49)
Incidence years	
Before 2000	7 (7)
2000–2013	70 (70)
After 2013	23 (23)

Incidence of Breast Implant–Associated ALCL

Figure 5 illustrates the number of newly diagnosed cases of breast implant–associated ALCL by year and per implant manufacturer. The incidence of cases in textured breast implants was 2.03 per 1 million person-years (i.e., 203 cases of breast implant–associated ALCL per 100 million person-years), which was 67.6 times higher than the incidence of primary ALCL in the breast, based on Surveillance, Epidemiology, and End Results data reporting an incidence rate of 3 per 100 million per year ($p < 0.0001$).¹¹ Figure 6 demonstrates the incidence rates by year from 1996 to 2015. Incidence rates ranged from one to three per 1 million person-years over time until an increase in 2011, potentially because of an increase in awareness and reporting.

We then evaluated the incidence of breast implant–associated ALCL by implant manufacturer (Fig. 5). The overall incidence rate for

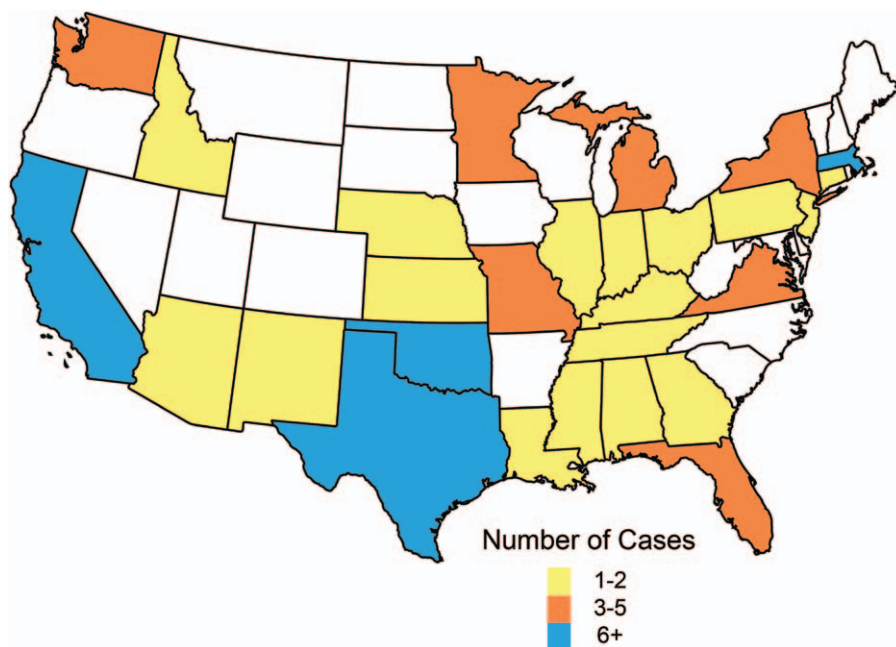


Fig. 3. Geographic distribution of the 100 U.S. cases of breast implant–associated ALCL.

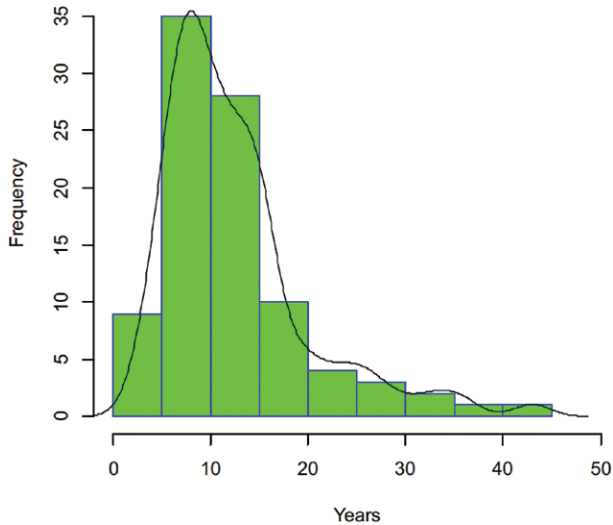


Fig. 4. Time intervals from breast implant placement to diagnosis of breast implant-associated ALCL.

salt-loss implants during this period was 1.87 per 1 million person-years. The overall incidence rate of breast implant-associated ALCL for negative-imprint stamping implants during this period was 0.33 per 1 million person-years. Compared to the salt-loss implants, the negative-imprint stamping implants were associated with a significantly lower incidence rate ($p < 0.001$). Pure cases representing exclusively each texturing technique were

reported in the data set for both types of texturing surface studied.

Lifetime Prevalence of Breast Implant-Associated ALCL

Based on annualized sales data, we estimated there were approximately 3 million women with textured breast implants in the United States by 2015 (Fig. 2). From 1996 to 2015, in total, 100 women were diagnosed with breast implant-associated ALCL. Therefore, the lifetime prevalence of the disease was 33 per 1 million women with a textured breast implant, or 1 per 30,000 women with a textured breast implant.

DISCUSSION

This is the first U.S. report demonstrating that the absolute risk of developing breast implant-associated ALCL around a textured breast implant appears to be significantly higher than the risk of developing primary breast ALCL in the general population. This study strengthens previous reports of an *association* but does not address *causation*, an important distinction that is outside the scope of this article. The disease appears to develop just over 10 years from the time of implant placement. Our reported incidence of 2.03 per 1 million person-years means that one case of breast

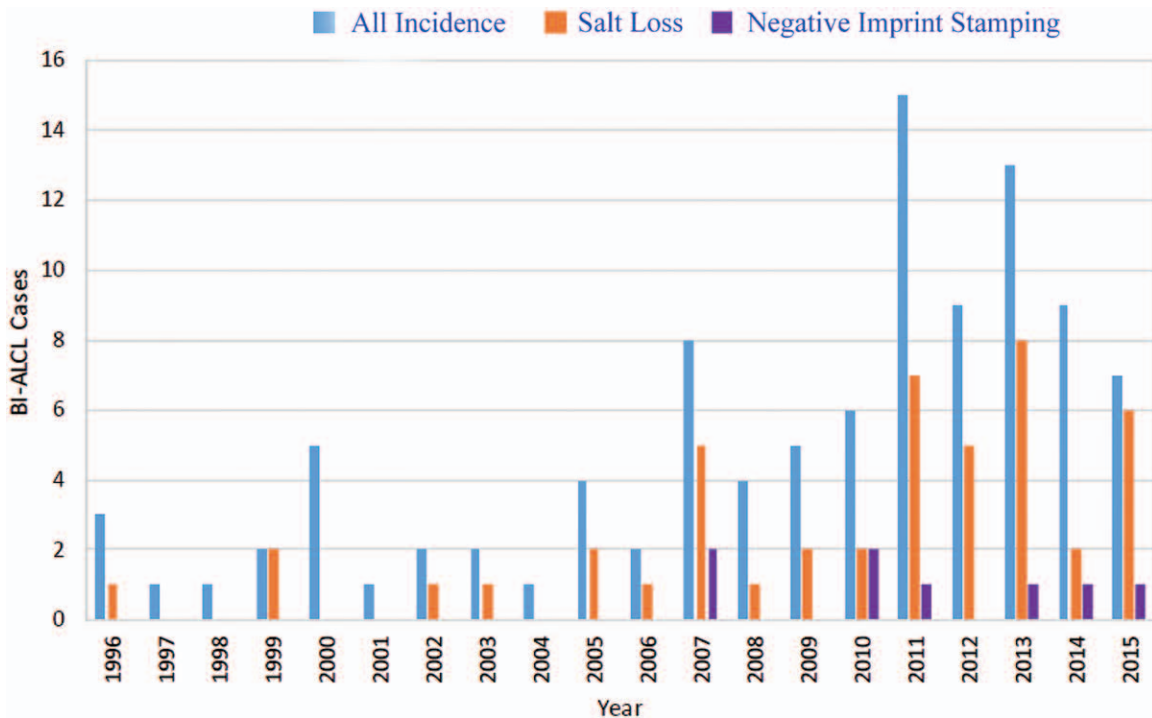


Fig. 5. Number of U.S. breast implant-associated ALCL cases by year and implant manufacturer. BI-ALCL, breast implant-associated ALCL.

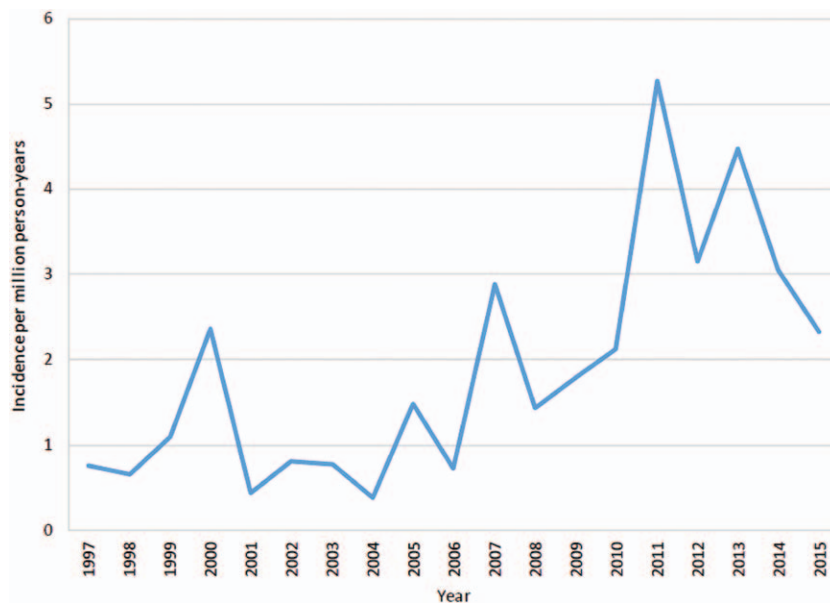


Fig. 6. U.S. incidence rates of breast implant–associated ALCL per 1 million person-years per year.

implant–associated ALCL will be observed when 50,000 patients with textured breast implants are followed for 10 years. Our reported lifetime prevalence is one in 30,000 women with textured breast implants. A limitation of the study is that these rates assume the disease predominantly or exclusively occurs in association with textured breast implants.

Accurate epidemiologic data on the incidence and prevalence of breast implant–associated ALCL have been lacking because of small study populations, inaccurate and unconfirmed reporting, and inclusion of both smooth and textured breast implant sales figures. Previously published U.S. epidemiologic studies among patients with breast implants have concluded that there was no association between implant devices and lymphoma.^{8,13–20} However, these studies were limited by sample size and short follow-up. Surveillance, Epidemiology, and End Results data report a relatively low U.S. incidence of primary breast ALCL, three in 100 million women per year.¹¹ However, our study not only suggests a statistically significant association between textured breast implants and breast implant–associated ALCL but also finds the incidence to be approximately 66 times higher than that of primary breast ALCL in the general population.

Previous literature supports our study findings of an association between breast implants and the development of ALCL, but with several limitations. The 2008 study from The Netherlands¹⁰ reporting five cases of breast implant–associated

ALCL and an estimated incidence of 0.1 to 0.3 per 100,000 women with breast implants per year was limited by a small sample size ($n = 5$), documented “uncertain data” of sales figures for number of breast implants, and inclusion of all implants, both smooth and textured. In 2011, Largent et al.⁸ reported on observed cases of ALCL in Allergan-sponsored breast implant clinical studies. They reported three cases of ALCL per 204,682 person-years, yielding a “crude incidence of 1.46 per 100,000 person-years.”⁸ More recently, in 2015, Wang et al.²¹ reported an association between breast implants and ALCL. They performed a prospective cohort study of a population of 123,392 women, 2990 of whom had breast implants. The population was followed for 20 years, and two cases of breast implant–associated ALCL developed in women with breast implants, resulting in a statistically significant association and an increased risk of 10.9-fold for ALCL in women with breast implants.²¹ Like study from The Netherlands, these studies were also limited by a small number of cases, the inclusion of both smooth and textured devices, questionable diagnostic criteria, and a short mean duration of follow-up.^{8,10,21} Recently, McGuire and colleagues reported on the long-term follow-up of 17,656 women receiving 31,985 salt-loss textured implants and found four breast implant–associated ALCL cases at a mean follow-up of 3.4 years.²² While not intended to be an epidemiology study, this represents the largest series ever reported for any type of textured implant.

In comparison with these previous reports, our study's reported incidence is strengthened by verified annualized sales figures of textured implants by the major implant manufacturers in the United States during the study period. This allowed for a stable denominator to facilitate calculating the incidence and prevalence of breast implant-associated ALCL. In addition, our study looks specifically at the population of women with textured breast implants, as no cases of breast implant-associated ALCL with a complete implant history have been described in patients with purely smooth implant devices to date worldwide. A limitation of our study methodology is that we assumed that breast implant-associated ALCL occurred only in textured breast implants. However, the available worldwide experience over two decades with breast implant-associated ALCL supports this assumption. Of the 100 reported U.S. cases of breast implant-associated ALCL, zero reported purely smooth breast implants, 51 reported textured implants, and 49 did not report the type of implant. Furthermore, previous literature supports that breast implant-associated ALCL has only been confirmed in patients with textured breast implants when a complete implant history was known. In 2011, Largent et al.⁸ reported three cases of the disease, one of which was associated with a smooth breast prosthesis. However, in the documented cancer history, they state that it was unknown whether the original breast implant was textured, and it was followed by multiple subsequent implant exchanges.⁸ Similarly, a case report by Lazzeri et al.⁹ in 2011 reported a diagnosis of breast implant-associated ALCL 19 years after a McGhan smooth silicone gel implant was placed; however, the authors acknowledged that the patient had an implant exchange with an unknown device in the interim. In 2015, Brody et al.⁴ published a review of referral cases plus that of the world literature that included 173 cases. For all cases that reported an implant history, the patient was known to have had at least one textured device.⁴ In 2016, Clemens et al.⁷ reported on 87 documented and pathologically confirmed U.S. cases of breast implant-associated ALCL treated with surgical resection. All of the patients for whom a complete surgical history was available had a textured breast implant.⁷ Based on these data, we believe that our study makes a reasonable assumption that all cases of the disease have occurred with textured breast implants, as no cases have ever been confirmed in patients who received only smooth implants. One cannot say that there definitely are not or will never be any purely smooth implant cases, and based on our best understanding of possible causes, a few rare

smooth cases may be reported in the years to come. Hypothetically, even if a few rare smooth cases were reported in the future, it remains statistically significant that this is predominantly if not exclusively a textured association. Therefore, the purpose of this study to give a best evidence estimate of the current incidence and prevalence remains sound, and the data would still not shift measurably.

Another potential limitation of this study is its retrospective design. Because of the rare nature of this disease and the medical community's relative unfamiliarity with its symptoms, it is very reasonable to assume that there were cases of breast implant-associated ALCL during this review period that were either not documented or not diagnosed. Given this assumption, our reported incidence rate likely underestimates the actual incidence of the disease. In addition, we have reported the incidence rate per textured breast implant. If one assumes that most cosmetic augmentation patients have two breast implants and breast reconstructive patients have one or two implants, the incidence rate per person-years would again be higher. This study could have been strengthened by the use of a matched control group or a prospective cohort study. However, this would have been impossible, as the entire population of women receiving textured implants would have had to have been followed for more than 10 years, as the time from breast implantation to diagnosis of disease has been reported to range from 8 to 20 years.^{7,21} Most cohort studies involving tens of thousands of patients are underpowered, and may capture only one or a few patients. A national breast implant registry may have accomplished this goal but at present remains unavailable.

In our study, 43 percent of patients with breast implant-associated ALCL had a salt-loss implant, only 5 percent had a negative-imprint stamping technique implant, and 3 percent had a history of both. Without knowing the manufacturer for 49 percent of the study population, it was impossible to determine the true incidence of the disease by implant manufacturer. We estimated the incidence rates using the known salt-loss and negative-imprint stamping cases. With this assumption, the overall incidence rate for salt-loss was 1.87 per 1 million person-years, whereas the incidence rate for negative-imprint stamping was 0.33 per 1 million person-years. This observed difference in manufacturer incidence rates may be important, as the method of implant texturing differs by manufacturer, resulting in different microscopic properties of the textured silicone surface that may be associated with the development of breast implant-associated ALCL. However, limited and incomplete

data with significant confounders such as reporting bias, brand identifier labeling differences over time, and surgical technique variation may significantly skew conclusions about the frequency of events associated with a particular device. Although negative-imprint stamping products were associated with a significantly lower incidence rate ($p < 0.001$) in this study, an important conclusion from our findings is that breast implant–associated ALCL has occurred in patients with all types of textured implants and does not appear to be solely associated with a specific method of implant texturing. Furthermore, cases have been reported worldwide with a number of different textured implant manufacturers not included in this national study.²³ It is important to note that recently the Australian Therapeutic Goods Administration released an update on breast implant–associated ALCL, and based on internal calculations of 46 national cases, came to an estimated disease risk of 1 in 1000 to 1 in 10,000 women with textured implants.²⁴ This discrepancy in risk between Australia and our U.S. data may be due to geographic predisposition or physician reporting and requires further study.

Although we report here an association between textured breast implants and the development of breast implant–associated ALCL, the epidemiologic data from our study do not address mechanisms of causation. There are many theories surrounding development of the disease. Some theories implicate the immune system response to chronic inflammation, likely induced by silicone particulate, modified silicone, or bacterial antigen in a genetically susceptible patient, much like the link between *Helicobacter pylori* infection and gastric lymphoma.²⁵ In a recent study, Hu et al. compared the implant capsules of patients with breast implant–associated ALCL to those of patients with normal capsular contracture, finding a high bacterial load and significantly different microbiome in the breast implant–associated ALCL specimens.²⁶ They propose this finding as a potential explanation for the differing rates of breast implant–associated ALCL throughout the world.²⁶ Previous work comparing the capsules of textured and smooth implants in pigs showed that there are increased lymphocytes on textured breast implants, with a T-cell predominance, further supporting the association between textured implants and breast implant–associated ALCL.^{27–30} Further research into pathogenesis, genetic drivers, and geographic distributions will help elucidate the shortcomings of this study.

The goal of this study was to try to quantify the relative risk of breast implant–associated

ALCL in patients with textured implants to facilitate more informed discussions with our patients. The FDA maintains that all breast implants, textured and smooth, have a reasonable assurance of safety and efficacy and that ALCL remains a very rare disease. The FDA assures us that physicians do not need to make any changes to their current practice because of the risk of breast implant–associated ALCL, and should continue to provide routine care and support to asymptomatic patients. We believe that breast implant–associated ALCL disclosure should occur during the informed consent process for all breast implant procedures.³¹ We recommend informing patients that, although very rare, the risk of developing ALCL around a textured breast implant is higher than the risk of developing ALCL in the general population. Screening or prophylactic breast implant removal in patients without symptoms or other abnormality is not recommended. Diagnosis and management of breast implant–associated ALCL should follow standardized guidelines recently released from the National Comprehensive Cancer Network.³² Efforts need to be made to increase public awareness and health care provider education on this topic.

CONCLUSIONS

This study represents the first U.S. population-based report demonstrating that the absolute risk of developing breast implant–associated ALCL around a textured breast implant is much higher than the risk of developing breast ALCL in the general population. Although patients with a textured breast implant have a very low risk of breast implant–associated ALCL, the current incidence of the disease is greater than that previously reported. In light of this, we believe that a discussion of the risk of breast implant–associated ALCL should be a standard part of the informed consent process before placement of a breast implant. Furthermore, improved global registry mechanisms are needed to elucidate predisposing factors and genetic susceptibility to this rare condition. Future studies are required to determine whether geographic, genetic, or surgical technique variability affects risk.

Mark W. Clemens, M.D.
 Department of Plastic Surgery
 The University of Texas M. D. Anderson Cancer Center
 P.O. Box 301402
 1400 Pressler, Unit 1488
 Houston, Texas 77230-1402
 mwclemens@mdanderson.org

REFERENCES

1. U.S. Food and Drug Administration. Anaplastic large cell lymphoma (ALCL) in women with breast implants: Preliminary FDA findings and analyses. Available at: <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/BreastImplants/ucm239996.htm>. Accessed March 1, 2016.
2. American Society of Plastic Surgeons. 2015 plastic surgery statistics report. <http://www.plasticsurgery.org/Documents/news-resources/statistics/2015-statistics/cosmetic-procedure-trends-2015.pdf>. Accessed March 1, 2016.
3. Keech JA Jr, Creech BJ. Anaplastic T-cell lymphoma in proximity to a saline-filled breast implant. *Plast Reconstr Surg*. 1997;100:554–555.
4. Brody GS, Deapen D, Taylor CR, et al. Anaplastic large cell lymphoma occurring in women with breast implants: Analysis of 173 cases. *Plast Reconstr Surg*. 2015;135:695–705.
5. Clemens MW, Miranda RN. Coming of age: Breast implant-associated anaplastic large cell lymphoma after 18 years of investigation. *Clin Plast Surg*. 2015;42:605–613.
6. Miranda RN, Aladily TN, Prince HM, et al. Breast implant-associated anaplastic large-cell lymphoma: Long-term follow-up of 60 patients. *J Clin Oncol*. 2014;32:114–120.
7. Clemens MW, Medeiros LJ, Butler CE, et al. Complete surgical excision is essential for the management of patients with breast implant-associated anaplastic large-cell lymphoma. *J Clin Oncol*. 2016;34:160–168.
8. Largent J, Oefelein M, Kaplan HM, Okerson T, Boyle P. Risk of lymphoma in women with breast implants: Analysis of clinical studies. *Eur J Cancer Prev*. 2012;21:274–280.
9. Lazzeri D, Agostini T, Giannotti G, et al. Null-type anaplastic lymphoma kinase-negative anaplastic large cell lymphoma arising in a silicone breast implant capsule. *Plast Reconstr Surg*. 2011;127:159e–162e.
10. de Jong D, Vasmel WL, de Boer JP, et al. Anaplastic large-cell lymphoma in women with breast implants. *JAMA* 2008;300:2030–2035.
11. Altekruse SF, Kosary CL, Krapcho M, et al. *SEER Cancer Statistics Review, 1975–2007*. Bethesda, Md: National Cancer Institute; 2010. Available at: http://seer.cancer.gov/csr/1975_2007/, Table 19.28, based on November 2009 SEER data submission, posted to the SEER web site, 2010. Accessed March 1, 2016.
12. Maxwell GP, Van Natta BW, Bengtson BP, Murphy DK. Ten-year results from the Natrelle 410 anatomical form-stable silicone breast implant core study. *Aesthet Surg J*. 2015;35:145–155.
13. Vase MØ, Friis S, Bautz A, Bendix K, Sørensen HT, d'Amore F. Breast implants and anaplastic large-cell lymphoma: A Danish population-based cohort study. *Cancer Epidemiol Biomarkers Prev*. 2013;22:2126–2129.
14. Brinton LA, Lubin JH, Burich MC, Colton T, Brown SL, Hoover RN. Cancer risk at sites other than the breast following augmentation mammoplasty. *Ann Epidemiol*. 2001;11:248–256.
15. Brisson J, Holowaty EJ, Villeneuve PJ, et al. Cancer incidence in a cohort of Ontario and Quebec women having bilateral breast augmentation. *Int J Cancer* 2006;118:2854–2862.
16. Deapen DM, Hirsch EM, Brody GS. Cancer risk among Los Angeles women with cosmetic breast implants. *Plast Reconstr Surg*. 2007;119:1987–1992.
17. Friis S, Hölmich LR, McLaughlin JK, et al. Cancer risk among Danish women with cosmetic breast implants. *Int J Cancer* 2006;118:998–1003.
18. Lipworth L, Tarone RE, Friis S, et al. Cancer among Scandinavian women with cosmetic breast implants: A pooled long-term follow-up study. *Int J Cancer* 2009;124:490–493.
19. Mellekjaer L, Kjølner K, Friis S, et al. Cancer occurrence after cosmetic breast implantation in Denmark. *Int J Cancer* 2000;88:301–306.
20. McLaughlin JK, Lipworth L, Fryzek JP, Ye W, Tarone RE, Nyren O. Long-term cancer risk among Swedish women with cosmetic breast implants: An update of a nationwide study. *J Natl Cancer Inst*. 2006;98:557–560.
21. Wang SS, Deapen D, Voutsinas J, et al. Breast implants and anaplastic large cell lymphomas among females in the California Teachers Study cohort. *Br J Haematol*. 2016;174:480–483.
22. McGuire P, Reisman NR, Murphy DK. Risk factor analysis for capsular contracture, malposition, and late seroma in subjects receiving Natrelle 410 form-stable silicone breast implants. *Plast Reconstr Surg*. 2017;139:1–9.
23. Knight R, Loch Wilkinson A, Wessels W, et al. Epidemiology and risk factors for breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) in Australia and New Zealand. *Plast Reconstr Surg Global Open* 2016;4:82–83.
24. Australian Therapeutic Goods Administration. Breast implants: Update on TGA monitoring of anaplastic large cell lymphoma. Available at: <https://www.tga.gov.au/alert/breast-implants>. Accessed December 20, 2016.
25. Bizjak M, Selmi C, Praprotnik S, et al. Silicone implants and lymphoma: The role of inflammation. *J Autoimmun*. 2015;65:64–73.
26. Hu H, Johani K, Almatroudi A, et al. Bacterial biofilm infection detected in breast implant-associated anaplastic large-cell lymphoma. *Plast Reconstr Surg*. 2016;137:1659–1669.
27. Hu H, Jacombs A, Vickery K, Merten SL, Pennington DG, Deva AK. Chronic biofilm infection in breast implants is associated with an increased T-cell lymphocytic infiltrate: Implications for breast implant-associated lymphoma. *Plast Reconstr Surg*. 2015;135:319–329.
28. Kadin ME, Deva A, Xu H, et al. Biomarkers provide clues to early events in the pathogenesis of breast implant-associated anaplastic large cell lymphoma. *Aesthet Surg J*. 2016;36:773–781.
29. Deva AK, Adams WP Jr, Vickery K. The role of bacterial biofilms in device-associated infection. *Plast Reconstr Surg*. 2013;132:1319–1328.
30. Jacombs A, Tahir S, Hu H, et al. In vitro and in vivo investigation of the influence of implant surface on the formation of bacterial biofilm in mammary implants. *Plast Reconstr Surg*. 2014;133:471e–480e.
31. Clemens MW, Miranda RN, Butler CE. Breast implant informed consent should include the risk of anaplastic large cell lymphoma. *Plast Reconstr Surg*. 2016;137:1117–1122.
32. Clemens MW, Horwitz SM. NCCN consensus guidelines for the diagnosis and management of breast implant-associated anaplastic large cell lymphoma. *Aesthet Surg J*. 2017;37:285–289.