Textured Silicone Breast Implant Use in Primary Augmentation: Core Data Update and Review

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Summary: Evolution of silicone breast implant design has focused primarily on advances in implant fill, surface texture, and shape. Fifth-generation, shaped, form-stable, silicone breast implants from all three major implant manufacturers are now approved for use by the U.S. Food and Drug Administration in the United States. As part of this approval, the U.S. Food and Drug Administration mandated Core Study follow-up of silicone implants for 10 years after premarket approval. An updated and comprehensive collection of Core data from all three manufacturers is presented in this review. In addition, cause and rates of capsular contracture, seroma, rippling, and malposition are discussed. New concepts such as tissue friction coefficient are discussed that may influence outcome after primary breast augmentation. The theoretical advantages and disadvantages of the various textured surfaces ranging from microtexturing to macrotexturing are presented in relation to breast tissue incorporation. (*Plast. Reconstr. Surg.* 135: 113, 2015.)

Statistics from the American Society of Plastic Surgeons indicate that 290,000 breast augmentations were performed in the United States in 2013.[1] Implant selection for primary augmentation has evolved away from use of smooth round saline implants, toward increasing use of round textured silicone implants and shaped devices. Since shaped devices were approved for use in 2013, surgeons who have been accustomed to smooth round implants are using textured devices often as practice patterns have changed. This article describes the differences between the textured implants and provides a summary of the long-term Core data from manufacturer and clinical studies. The concept of microtexturing and macrotexturing is described in detail with scanning electron microscopy of the different manufacturers' implant surfaces (Fig. 1). Furthermore, the Core data are summarized in a single reference with respect to evidence-based outcome data.

Cronin and Gerow introduced the first silicone breast implant in 1964 (Dow-Corning Corp., Midland, Mich.).[2] The silicone breast implant evolved over subsequent decades (Table 1), yet despite these advances, adverse outcomes such as capsular contracture led to a U.S. Food and Drug Administration moratorium on silicone breast implant use in the United States in 1992, other than for investigational purposes. The moratorium was lifted in 2006, permitting the use of silicone implants for primary breast augmentation.

As a condition of approval, the U.S. Food and Drug Administration mandated follow-up of silicone device performance through Core Studies.[3–9] The goals of the Core Gel Studies are to provide evidence-based results over 10 years from evaluation of patients with silicone breast implants from different manufacturers. Three- to 10-year follow-up is now available from the three major implant manufacturers.

The most common complications following primary breast augmentation include capsular contracture, implant malposition, rippling, and seroma. Because reports of capsular contracture rates range from 2 to 45 percent of patients, there is often lack of clarity in complication rate reporting in the literature.[10–15] The data are also confounded by multiple variables, including cohorts ranging from single-surgeon series to meta-analyses, different techniques incorporating

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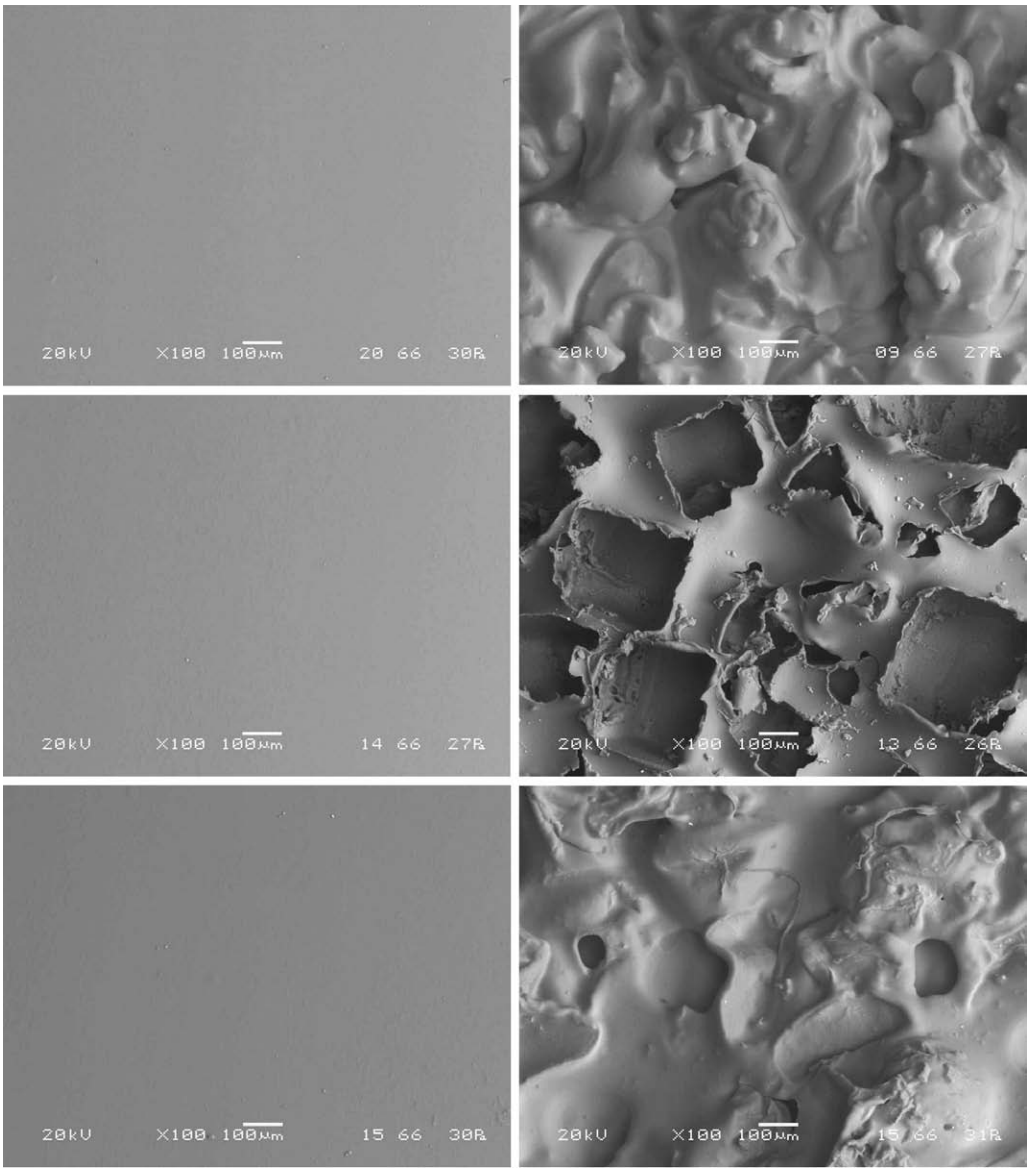


Fig. 1. Scanning electron microscopic images of smooth and textured implant surfaces. Mentor, Allergan, and Sientra smooth implant surfaces are represented by *left, above, center, and below*, respectively (original magnification, × 100). Mentor Siltex, Allergan Biocell, and Sientra TRUE Texture surfaces are represented in *right, above, center, and below*, respectively (original magnification, × 100). (Images provided by Mentor Corp.)

Table 1. Generational Differences in Silicone Breast Implants

Generation	Years	Shell Thickness (mm)	Gel	Internal Barrier Lining	Shaped
First	1963–1972	0.75	Thick	No	No
Second	1972–1980	0.13	Thin	No	No
Third	1981 onward	0.28–0.30	Thick	Yes	No
Fourth	1993 onward	0.5	More cohesive, form-stable	Yes	No
Fifth	1993 onward	0.075–0.75	Highly cohesive, form-stable	Yes	Yes

subglandular versus submuscular placement, and different implant texturing methods from different manufacturers.

To provide more objective evaluation of capsular contracture, Baker and Gylbert et al. developed capsular contracture grading systems[16,17]

(Table 2). Gylbert's Breast Augmentation Classification system is comparable to the Baker scale, but the opinion of the patient is not included.[18] Although the causes of capsular contracture are multifactorial, the leading theory points toward subclinical implant infection with *Staphylococcus epidermidis* from mammary ducts.[19–23] Biofilm formation and blood in the breast pocket, contributing iron as a source of bacterial nutrient, have also been described.[24,25] Results of a higher incidence of capsular contracture with smooth implant surface in the subglandular position have been reproducible in several studies, suggesting that implant physical properties such as surface may also contribute to capsular contracture.[26,27] Textured implants, particularly in the submuscular position, have been associated with the lowest rates of capsular contracture.[28,29]

Current implant textured surfaces use a number of different techniques to create microscopic pores in the surface of silicone implants. Theoretically, this leads to physical disruption of surrounding capsular tissue. The efficacy of surface texturing in reducing capsules may derive from interruption of parallel collagen fiber orientation during capsular formation around a breast implant.[30–33] This has been repeatedly studied in clinical series, randomized controlled trials, Core Gel Studies, and meta-analyses.[26,27,34–42]

Allergan (Allergan, Inc., Irvine, Calif.), Mentor (Mentor Corp., Santa Barbara, Calif.), and Sientra (Sientra, Inc., Santa Barbara, Calif.) have all received approval from the U.S. Food and Drug Administration for clinical use of textured breast implants. Since these companies use markedly different techniques for the formation of their respective textured implant surfaces, the purpose of this article is to summarize these differences and the long-term outcome data reported by the manufacturers and individual clinical studies to provide a single summary of the complication rates.

This article compiles the three major manufacturers' data for capsular contracture, malposition, seroma, and rippling for silicone implants from the Core Studies. Although rippling rates have been reported to be higher in a single surgeon's series of textured implants, this has not been substantiated in studies with higher levels of evidence with multiple surgeons and increased numbers of patients.[12,13] Double capsules and late seromas have also been reported.[43–45] A discussion of manufacturer differences in textured implant surfaces, form-stable implants, and the impact on complications is presented. New concepts, including tissue friction coefficient, that may influence malposition after primary breast augmentation, are also presented.

Table 2. Comparing Baker and Breast Augmentation Classification Grading Systems for Capsular Contracture*

Grade	Baker	BAC
I	Breast feels normal; neither surgeon nor patient with complaint	Breast feels normal to surgeon
II	Minimal contracture; surgeon feels capsule but patient does not	Breast capsule feels slightly thickened to surgeon; none to slight distortion
III	Moderate contracture; surgeon and patient feel capsule	Breast capsule feels firm to hard to surgeon; none to slight distortion
IV	Severe contracture; breast distortion noticeable with naked eye	Breast capsule feels hard to surgeon; severe distortion

BAC, Breast Augmentation Classification.
*Data from Barnsley GP, Sigurdson LJ, Barnsley SE. Textured surface breast implants in the prevention of capsular contracture among breast augmentation patients: A meta-analysis of randomized controlled trials. *Plast Reconstr Surg.* 2006;117:2182–2190.

PATIENTS AND METHODS

A literature search of PubMed and the Cochrane Library was performed to obtain the most updated data from silicone breast implant Core data studies. The following key words were used for the literature search: core, silicone implant, augmentation mammaplasty, capsule, capsular contracture, breast, complication, texture, seroma, and rippling. Authoritative Web sites were also reviewed for Core data retrieval.[46] Data were extracted; entered into a Microsoft (Microsoft Corp., Redmond, Wash.) Excel spreadsheet; and separated for Mentor, Allergan, and Sientra. Bar graph figures were generated to demonstrate Core Study complication rates over a 10-year period following primary breast augmentation with silicone implants. Only verifiable data from each manufacturer were included (Figs. 2 through 7) for a side-by-side trend comparison of different manufacturer Core data.

RESULTS

Table 3 demonstrates Core complication profiles for silicone breast implants from the three major manufacturers. Mentor and Allergan data were recorded separately for round and shaped implant models. These two manufacturers

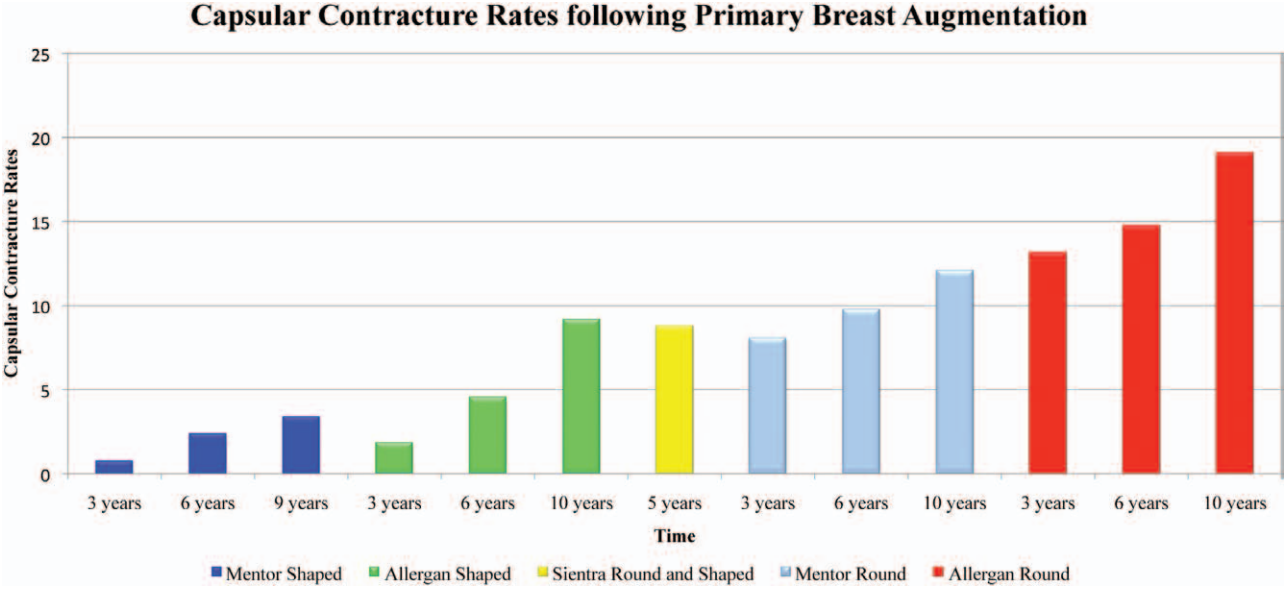


Fig. 2. Primary breast augmentation capsular contracture rates, expressed as percentage of patients, from the three major silicone implant manufacturers.

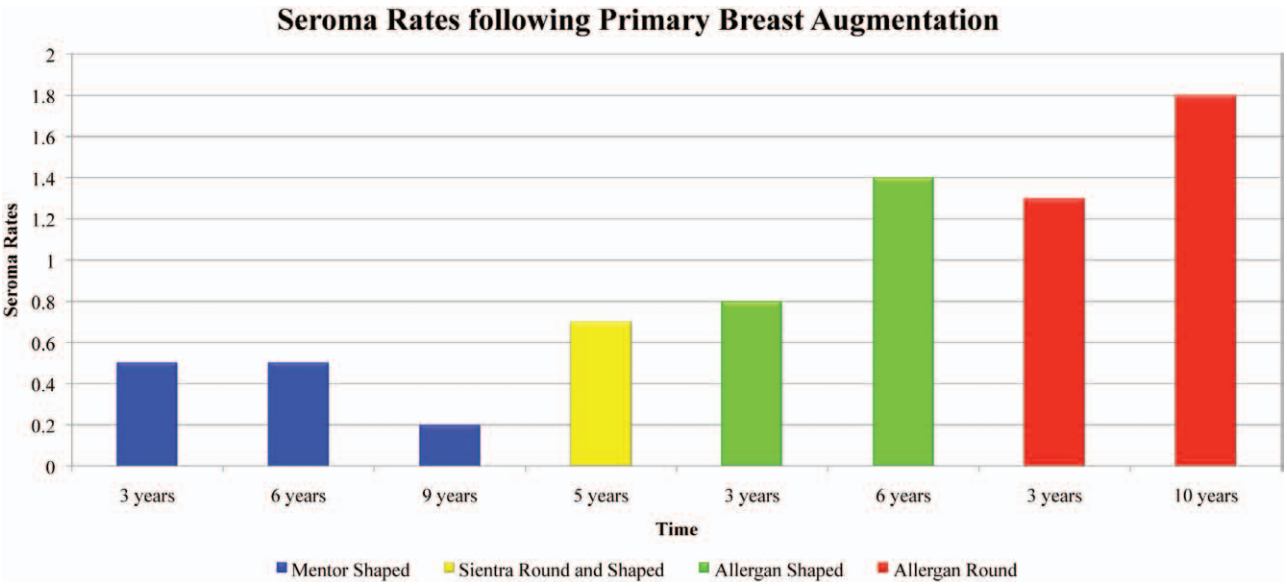


Fig. 3. Primary breast augmentation seroma rates, expressed as percentage of patients, from the three major silicone implant manufacturers.

underwent separate U.S. Food and Drug Administration approval processes for their round and shaped silicone implants. Sientra received U.S. Food and Drug Administration approval for their round and shaped breast implants through a single application process, and therefore their data are combined. Figures 2 through 5 demonstrate key complication rates over a 10-year period following primary breast augmentation. Figure 2 demonstrates an increased trend in capsular contracture rates over time for both round and shaped implants. Because of the reporting differences in the Core data among manufacturers, capsular contracture rates cannot be directly compared. Furthermore, the Core study design also limited the extent of seroma results reported in Figure 3. Figure 4 summarizes the differences in manufacturer-specific rippling rates. Figure 5 demonstrates a tendency toward reduced malposition with the use of textured, shaped Allergan implants compared with round implants by the same manufacturer. This measure of malposition

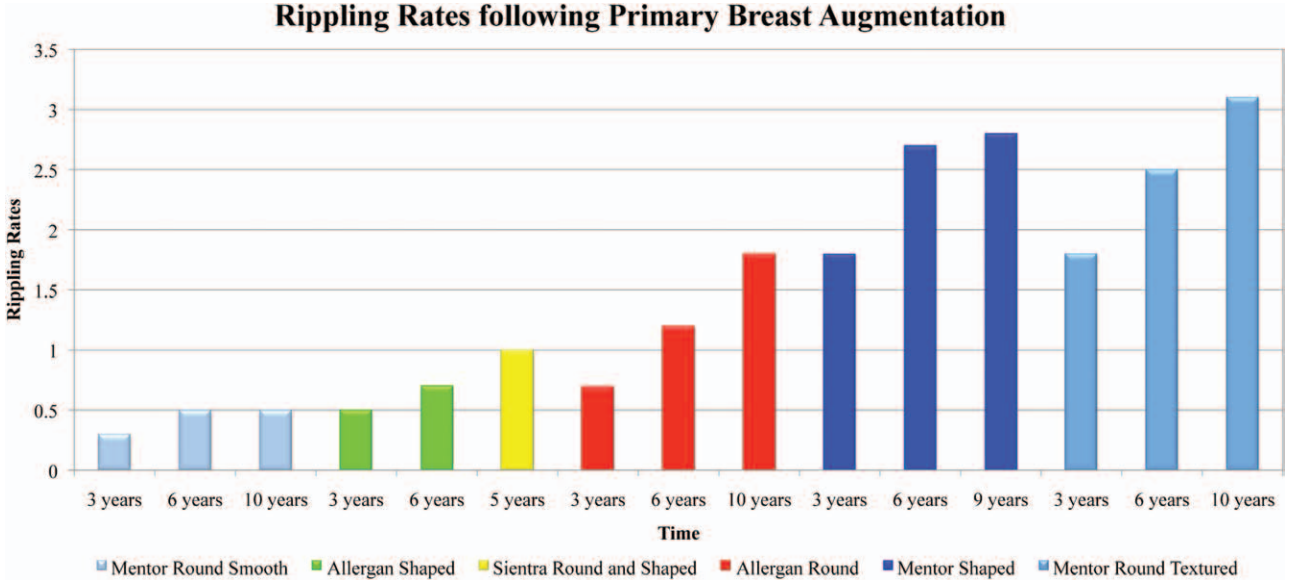


Fig. 4. Primary breast augmentation rippling rates, expressed as percentage of patients, from the three major silicone implant manufacturers.

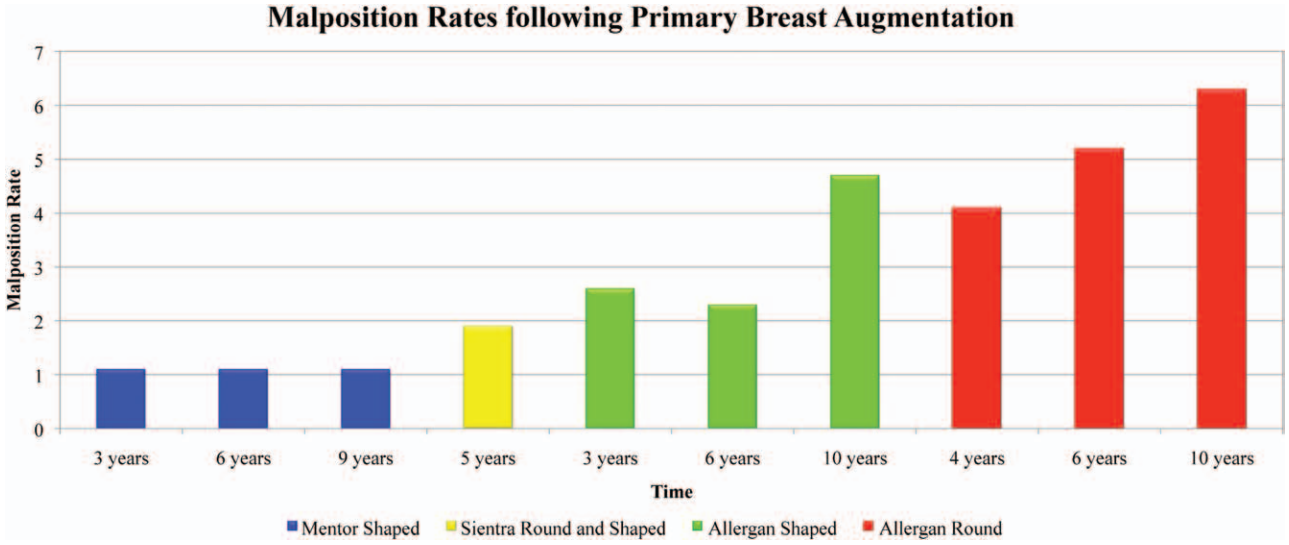


Fig. 5. Primary breast augmentation implant malposition rates, expressed as percentage of patients, from the three major silicone implant manufacturers.

does not include malrotation of shaped devices. Similar trends cannot be studied for Mentor or Sientra either because of a lack of data acquisition in Core studies, or the combined inclusion of smooth, round, and shaped device data in their cohorts. Therefore, statistical comparison between manufacturers was not possible because of the variability in manufacturer-specific Core study design.

DISCUSSION

A summary of the three U.S. manufacturers' Core Studies of complication profiles for silicone implants, up to 10 years following primary breast augmentation, has been provided. Different implant textures were compared using the following complication rates: capsular contracture, malposition, seroma, and rippling. Although direct comparisons cannot be made, this article serves as a source summary of the largest cohort of long-term data. The advantages and disadvantages of manufacturer-specific texturing processes were correlated with the recently described phenomena of double capsules and late seromas. Lastly, the concept of tissue friction coefficient as it relates to breast implant surgery is discussed.

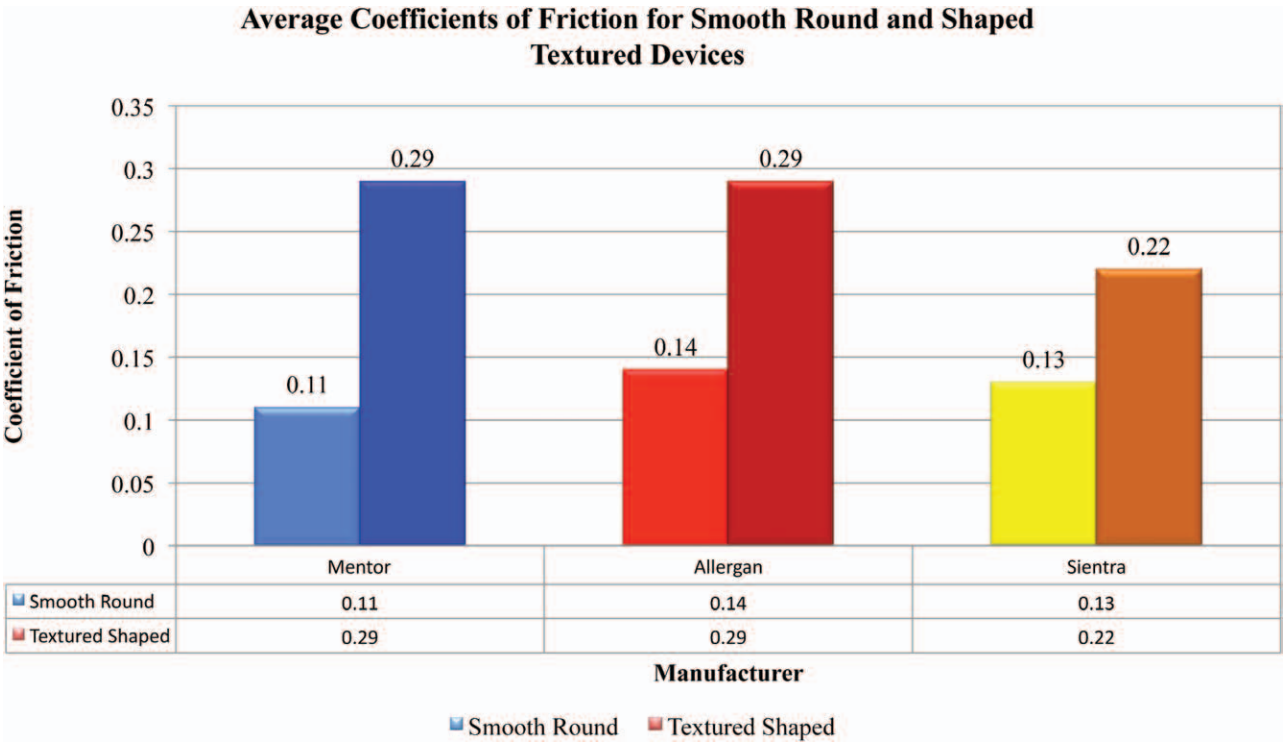


Fig. 6. Average coefficient of friction for Mentor, Allergan, and Sientra smooth and shaped breast implants. (Data from Rowe S. Ethicon AS&T Laboratories Protocol No. CP526. *Determination of Coefficient of Friction for Sientra, Allergan, and Mentor Anatomically Shaped, Gel-Filled Mammary Implants*. October 2013, Santa Barbara, Calif. October 31, 2013.)

Histology of Capsular Contracture

Histologic tissue responses to textured and smooth silicone implant device surfaces contrast with clinical outcomes.[31,47] Textured implants result in thicker and more inflammatory capsular tissue formation than smooth-surfaced implants, yet despite these findings, clinical comparisons suggest reduced capsular contracture rates with textured implant use.[26,27,34,39,40,47]

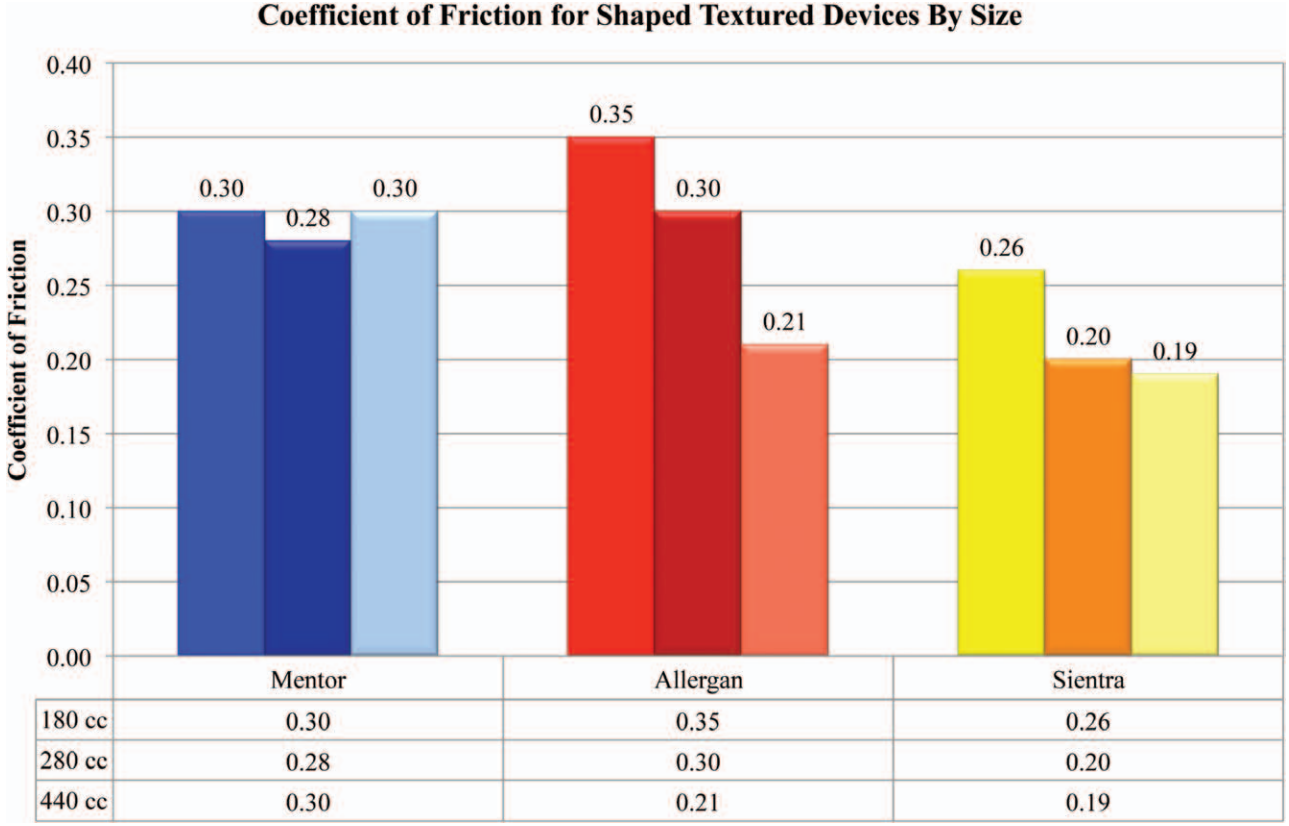
Force vectors around an implant contribute to capsular contracture.[31] Myofibroblasts may contribute to this force production.[30,48] These cell populations peak during the first week of wound healing in breast capsular tissue and have demonstrated responsiveness to agonists and antagonists of smooth muscle contractility.[30] Because the inflammatory mediator leukotriene triggers smooth muscle contraction in bronchioles, use of antileukotriene agents has been reported to reduce progression of early stages of capsular contracture.[49]

In summary, despite histologic findings of thicker and more inflamed capsular tissue around textured implants, textured implants demonstrate reduced capsular contracture rates compared with smooth implants in primary breast augmentation. Capsulotomy has been theorized to be clinically effective because of unloading of myofibroblast tension, resulting in apoptosis and cell death, with improvement in capsular contracture.[50]

Manufacturer-Specific Texturing Processes

Each manufacturer uses a proprietary texturing process, resulting in differences in texture pore density, diameter, depth, and distribution on the implant surface. All implants undergo an initial process of silicone shell manufacture followed by company-specific processes for surface texturing.[51] Allergan uses a "salt-loss technique" for Biocell macrotexturing. Mentor uses negative-contact polyurethane foam imprinting to produce Siltex microtexturing.[31] Sientra claims proprietary confidentiality for their TRUE Texture technique.

Detailed assessment of textured breast implant surface histology has been performed.[52] Biocell pores demonstrate diameters of 600 to 800 μm, with depths of 150 to 200 μm that are distributed irregularly across the implant's surface. Siltex pores are five times smaller, with a 70- to 150-μm diameter and 40- to 100-μm height. Siltex texturing is more evenly distributed over the surface of the implant. Round Siltex breast implants have 100 pores per inch, whereas shaped Siltex implants have 65 pores per inch. Microscopic



	Mentor	Allergan	Sientra
180 cc	0.30	0.35	0.26
280 cc	0.28	0.30	0.20
440 cc	0.30	0.21	0.19

Fig. 7. Average coefficients of friction, according to implant size, for Mentor, Allergan and Sientra shaped breast implants. (Data from Rowe S. Ethicon AS&T Laboratories Protocol No. CP526. *Determination of Coefficient of Friction for Sientra, Allergan, and Mentor Anatomically Shaped, Gel-Filled Mammary Implants*. October 2013, Santa Barbara, Calif. October 31, 2013.)

architectural description of Sientra's TRUE Texture implant surface has not been released by the manufacturer. Figure 1 demonstrates scanning electron microscopic architectural differences between smooth and textured implant surfaces from the three major manufacturers.

Danino et al. were among the first to examine corresponding capsular architecture surrounding textured surface implants. Biocell's 600- to 800-μm diameter surface pores allowed for mirror-image capsular ingrowth, whereas Siltex's 70- to 150-μm diameter surface pore microtexturing resulted in linear fibrosis of corresponding capsular tissue.[52] Microtexturing and macrotexturing parameters are likely to be more formally defined as implant manufacture evolves and the contribution to surgical outcomes of proprietary processes are better appreciated through more rigorous comparative study.

Improved understanding of pore density, depth, and diameter of microtexturing versus macrotexturing may assist in the appropriate selection of breast implants for use in primary breast augmentation. This concept, combined with the suspected multifactorial causes of capsular contracture, is an important component of an evolving pool of evidence-based medicine.[30,31,48,53,54]

Cause of Capsular Contracture and Textured Implants

Subclinical implant infection with *Staphylococcus epidermidis* is a leading cause of capsular contracture.[20,21,23] Bacteria can bind to an implant regardless of smooth or textured surface characteristics.[55] Once exposed to an implant, bacteria may form a biofilm through established stages: reversible attachment, irreversible attachment, growth, differentiation, and dissemination.[56] Several studies name bacterial biofilm as a potential cause of breast implant capsular contracture.[19,25,57] Other causes of contracture that support the multifactorial hypothesis have been considered: silicone versus saline fill,[58] hematoma,[12,59] implant pocket location,[27,28] use of antiseptic irrigation,[20,23,60] incision location,[61,62] and implant surface morphology.[26,27,29,40]

Seven randomized controlled trials evaluating the impact of surface texture on capsular

Table 3. Kaplan-Meier Estimated Cumulative Incidence Rates for Key Complications up to 10 Years after Primary Breast Augmentation for Mentor Implants*

Follow-Up (yr)	Implant Texture	Total No. of Patients	Augmentation Patients	Contracture Rate (III/IV) (%)	Seroma Rate (%)	Rippling Rate (%)	Malposition Rate (%)
3	Smooth and Siltex round	1008	552	8.1	N/A	Smooth, 0.3; textured, 1.8	N/A
6	Smooth and Siltex round	1008	552	9.8	N/A	Smooth, 0.5; textured, 2.5	N/A
10	Smooth and Siltex round	1008	552	12.1%	N/A	Smooth, 0.5; textured, 3.1	
3	Siltex shaped	955	572	0.8	0.5	1.8	1.1
6	Siltex shaped	955	572	2.4	0.5	2.7	1.1
9	Siltex shaped	955	572	3.4	0.2	2.8	1.1

N/A, not available.
*Sources: 10-Year Core Gel Clinical Study Final Report. Santa Barbara, Calif: Mentor Worldwide, LLC; April of 2013; and 9-Year MemoryShape (formerly Contour Profile Gel) Clinical Study Annual Report. Santa Barbara, Calif: Mentor Worldwide, LLC; November of 2013.

Table 4. Kaplan-Meier Estimated Cumulative Incidence Rates for Key Complications up to 10 Years after Primary Breast Augmentation for Allergan Implants*

Follow-Up (yr)	Implant Texture	Total No. of Patients	Augmentation Patients	Contracture Rate (III/IV) (%)	Seroma Rate (%)	Rippling Rate (%)	Malposition Rate (%)
4	Smooth and Biocell round	715	455	13.2	1.3	0.7	4.1
6	Smooth and Biocell round	715	455	14.8	N/A	1.2	5.2
10	Smooth and Biocell round	715	455	19.1	1.8	1.8	6.3
3	Biocell shaped	941	492	1.9	0.8	0.5	2.6
6	Biocell shaped	941	492	4.6	1.4	0.7	2.3
10	Biocell shaped	941	492	9.2	N/A	N/A	4.7

N/A, not available.
*Sources: Health Canada. Summary basis of decision for Natrelle silicone-filled breast implants-smooth and textured shell. September 25, 2012. Available at: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/md-im/sbd_smd_2012_natrelleround_61865_60524-eng.php. Accessed February of 2014; Health Canada. Summary basis of decision for NATRELLE highly cohesive silicone-filled breast implants. January 17, 2014. Available at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/md-im/sbd_smd_2013_natrellecohesive_88573-eng.php. Accessed February of 2014; and U.S. Food and Drug Administration summary of safety and effectiveness data for Inamed silicone-filled breast implants. November 17, 2006. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf2/P020056b.pdf. Accessed March of 2014.

Table 5. Kaplan-Meier Estimated Cumulative Incidence Rates for Key Complications up to 10 Years after Primary Breast Augmentation for Sientra Implants*

Follow-Up	Implant Texture	Total No. of Patients	Augmentation Patients	Contracture Rate (III/IV) (%)	Seroma Rate (%)	Rippling Rate (%)	Malposition Rate (%)
5 yr	Smooth round TRUE Texture round TRUE Texture shaped	1788	1116	8.8	0.7	1.0	1.9

*Source: Stevens WG, Harrington J, Alizadeh K, et al. Five-year follow-up data from the U.S. clinical trial for Sientra's U.S. Food and Drug Administration-approved Silimed brand round and shaped implants with high-strength silicone gel. *Plast Reconstr Surg.* 2012;130:973–981.

contracture are summarized in the meta-analysis by Barnsley et al.[26] Pooled data yielded an odds ratio of 0.19 (95 percent CI, 0.07 to 0.52), supporting capsular contracture reduction associated with surface textured implants. Capsular contracture occurred five times more frequently with smooth surface implants in the subglandular plane. Data for submuscular subgroup analysis were derived from a single, underpowered comparative study.[36] Nonrandomized studies support the claim of reduced capsular contracture when implants are placed in the submuscular position.[6,28,29] The systematic review by Wong et al. included six studies (all included in Barnsley's meta-analysis) demonstrating reduced capsular contracture rates at 1, 3, and 7 years postoperatively with textured devices used in breast augmentation.[27]

Although the former studies focused on review of data collected before 2000, Stevens and colleagues offered a more contemporary analysis.[28] Sientra TRUE Texture implants were used for subglandular and submuscular primary breast

augmentation. The 5-year Kaplan-Meier overall device rate for capsular contracture was 7.6 percent. Textured implants demonstrated the lowest contracture rates: 2.1 percent for submuscular and 4.9 percent for subglandular placement. Smooth-surfaced submuscular and subglandular implants demonstrated less favorable capsular contracture rates of 5.1 and 21.0 percent, respectively. Multivariate analysis revealed that smooth implants and subglandular placement increased the risk of developing capsular contracture by 4.7 and 4.6 times, respectively. Therefore, smooth silicone implants should be avoided in the subglandular position.

Fifth-generation, form-stable, highly cohesive, shaped breast implants have reduced rates of capsular contracture in comparison with earlier generation implants.[4,6–9,63–66] Hypothetically, the highly cohesive gel exerts counterpressure, expanding the surrounding breast tissue, thereby improving shell incorporation and minimizing capsular contracture formation.[8,66] Figure 2 demonstrates potential reduced capsular contracture with shaped implant use compared with round implant use in primary breast augmentation. A more natural feel has been described with shaped implants because the implant, breast, and capsule move and feel like a natural breast.[8,66] This is often in contrast to the feel of smooth-surfaced implants that move separately within the pocket from the breast tissue.

Malposition and Shaped Textured Implants

Textured shaped devices minimize the risk of malrotation within the pocket resulting from friction between the implant and the tissue. The concept of "friction coefficient" mentioned by Bengtson in his report of style 410 Core Study results at 3 years is an important concept, as textured implants have a higher tissue friction coefficient than smooth implants.[8] Friction (f) equals the coefficient of friction (μ) multiplied by force (n) pressing two objects together ($f = \mu N$).[67] The coefficient of friction (μ) is dependent on the materials used (i.e., glass on ice has a low coefficient of friction, and rubber on cement has a high coefficient of friction).[67] Industry-directed study has determined the coefficient of friction for all three major manufacturers' smooth and shaped implant surfaces (Figs. 6 and 7).[68] All manufacturers' textured implants demonstrated statistically greater friction coefficients compared with their smooth surface counterparts. Mentor and Allergan demonstrated statistically significant differences in average coefficients of friction for their textured implant surfaces compared with Sientra's textured surface, but not when compared with each other (Fig. 6). The implant shells of larger Allergan and Sientra shaped implants have reduced coefficients of friction compared with smaller implants from the same manufacturers (Fig. 7). This is likely because of a reduction in pore density over a larger surface area in the larger implants. This size-dependent phenomenon was not demonstrated between smaller and larger Mentor microtextured devices. Considered together, the results from Figures 5 through 7 are suggestive of the relationship between microtexturing, macrotexturing, and the tissue friction coefficient that may reduce the incidence of malposition. Despite comparable coefficients of friction for Mentor and Allergan shaped devices, microtextured devices demonstrated reduced malposition rates compared with macrotextured devices (Fig. 5). Precise pocket development to optimize contact between implant surface and surrounding tissue likely contributes to a reduced risk of implant malposition.

Seromas and Textured Implants

Despite the reduction in capsular contracture that textured devices provide, macrotexturing may be responsible for late seroma formation and double capsules.[43] "Late seroma" is generally believed to occur more than 1 year after surgery.[63] Spear et al. demonstrated late seroma occurrence at a mean of 4.7 years after surgery.[44] Late seromas have drawn recent attention given the ongoing investigation into their possible relationship with anaplastic large-cell lymphoma.[69–71] Hall-Findlay identified a subset of primary breast augmentation patients who developed late seroma formation and double capsules.[43] Fourteen patients with double capsules were identified, all of whom had macrotextured implants. The cause of the problem was suggested to be mechanical, secondary to forceful separation between aggressively textured implants and their capsule. Microtextured surfaces have also been demonstrated to result in seroma but may have received less attention because of lack of literature support regarding microtextured surface seroma formation and symptomatic double capsules.[72] Guidelines for management of late seroma after breast implant placement are available to rule out anaplastic large-cell lymphoma.[45] Both the seroma fluid and capsule tissue should be sent for malignant cytologic and immunohistochemical stains, including CD30 and cytokeratin.[45]

Rippling and Textured Implants

Limited reports suggest that rippling may occur more frequently with the use of textured implants.[12,13] Appropriate patient selection, accounting for adequate soft-tissue coverage through tissue pinch and calculation of body mass index, may minimize this risk. Rippling correlates strongly with body mass index less than 18.5 in primary breast augmentation. Underweight patients demonstrate statistically more frequent rippling with smooth saline implants compared with smooth silicone implants in the subglandular position.[73]

Earlier generation silicone implants have less silicone cross-linking and, therefore, less form-stability. To be truly form-stable, an implant must maintain its shape, regardless of position. An implant's form-stability may affect how well its superior pole maintains shape and avoids rippling when subjected to gravity in the upright position.

Texture-type also seems to correlate with rippling. Handel et al. noted a significant difference in frequency of skin rippling among breast augmentation cohorts with Biocell (10 percent) compared with Siltex (2.2 percent) textured implants.[12] These results complement the understanding that Siltex microtexturing results in a weakly adherent capsule, contrary to the strong adherence and tissue incorporation of Biocell macrotexturing.[43,54] In cases of revision surgery for capsular contracture after Siltex implant use, Malata et al. found capsules lined with synovial-like fluid.[34] The weakly adherent capsule associated with Siltex devices may be secondary to synovial metaplasia. Synovial metaplasia has not been shown to occur with Biocell implants.[74]

STUDY LIMITATIONS

With the exception of rippling rates for Mentor round implants, Allergan and Mentor Core data did not report complication rates separately for each surface subtype. This prevented extraction of round, textured implant–specific complication rates for the majority of complications reported in this review, along with valid statistical comparison of these rates among manufacturers. Only complication rate *trends* were reported in this article. The intention of the article was to offer a consolidated resource referencing 10 years of published Core data. Reported data should be considered in the context of the studies from which they were derived. Manufacturer studies were not set up similarly, and reported results are incomplete, or not specific to textured devices, as shown in Table 3. Future comparative, randomized trials may validate use of one textured implant over another to minimize complications focused on in this review. Other limitations, inherent in a retrospective review of primary breast augmentation outcomes, include the confounding variables of surgical technique, implant location, and differences in manufacturer texturing processes. Furthermore, this study was primarily limited by reviews of single-surgeon series, a limited number of meta-analyses/systematic reviews, and Core manufacturer reports.

CONCLUSIONS

This review article describes the fundamental differences in the microscopic surface textures of silicone breast implants with respect to size, depth, and surface area distribution in addition to the techniques used to manufacture the three different surfaces. A summary of the 10-year Core data is presented for ease of comparison. Although no conclusions can be drawn with respect to direct comparison between groups because of the inherent differences in the design of the Core Gel Studies, the incidences of three large cohorts are presented side-by-side in a single reference demonstrating rates of capsular contracture, seroma, and malposition in the largest series available in the literature. These data, despite the limitations, are very important for beginning to recognize potential differences in outcomes and complications based on microtexturing and macrotexturing.

Furthermore, the concept of a textured implant surface's tissue friction coefficient is presented. The coefficient of friction produced by macrotexturing and microtexturing objectively quantifies the level of adherence between the implant and surrounding breast tissue. The clinical relevance relates to differences in tissue and implant adherence by ingrowth, distinct from the friction produced without tissue ingrowth. Potential advantages include reduction in capsular contracture and rotation. Potential disadvantages include surface fragmentation, rippling, and double capsules.[52] Future implant studies should focus on the clinical outcomes associated with implant surface microtexturing compared with macrotexturing used in breast augmentation.

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INCISIONS & INSIGHTS

Mastopexy and MENTOR® MemoryShape® Breast Implants: A Perfect Fit

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ABSTRACT

Novel breast implant options continue to enter the US marketplace adding flexibility as well as complexity to surgical decision making. However, the basic concepts of round vs. shaped, and textured vs. smooth implants remain key elements within the treatment algorithm. This white paper looks at two significantly different Mastopexy-Augmentation patient populations (pseudo-ptosis and glandular ptosis after weight loss) with the intention of enabling surgeons to better understand the versatility and unique properties of shaped implants and how they can deliver practice-differentiating results.

INTRODUCTION

From 2014 to 2015 primary breast augmentation cases declined 2% while mastopexy procedures increased by 7%.[1] Two of the more challenging scenarios breast surgeons commonly face are the augmentation of breasts with pseudo-ptosis as well as those with glandular ptosis in patients who have experienced significant weight loss. Various techniques have been described to correct these deformities. They often involve a variety of mastopexy procedures aimed at reducing and/or tightening the skin envelope to help reposition the breast tissue on the chest wall in combination with the placement of a breast implant. Although round gel implants may prove effective, there are many cases in which a textured shaped device may provide a superior and longer lasting result.

In our practices, we have found that shaped implants alone can often adequately address mild ptosis eliminating the need for a mastopexy altogether. Additionally, shaped implants are helpful in treating patients with more significant ptosis who do also require a mastopexy. Having had an opportunity to use MENTOR® MemoryShape® Breast Implants (known as CPG outside of the US) over the past 17 years we have become acutely aware of the virtues of form stability and MENTOR® SILTEX® Texture. The combination of this highly cohesive gel and micro-texture allows these devices to "define the shape of the breast", rather than allowing the external soft tissue forces to define the shape of the implant. These features make MemoryShape Implants a very powerful tool.

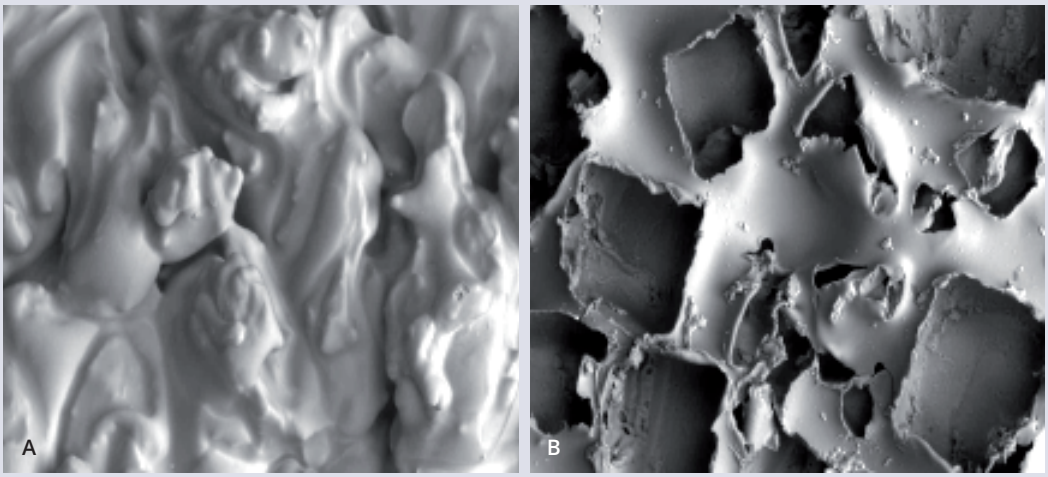
In mildly ptotic patients the inherent shape of the implant, with higher volume distribution in the lower pole, stretches the overlying tissues and forces them to conform to the more anatomical shape of the implant. This provides a gentle upper pole slope with maximal projection extending from the nipple down towards the IMF. As a result, they can very effectively correct the ptotic appearance of the breast while providing the requested volume increase. In some patients, with somewhat greater degrees of ptosis, placing a submuscular MemoryShape Implant through an IMF incision, and then performing a periareolar mastopexy, can produce exceptional results. Or in patients whose areolar diameter allows for an adequately sized incision the implant placement and the purse string mastopexy may be performed through the same periareolar incision.

A key technical point is the manner in which the pocket is created. Although round gel devices may be used effectively in pockets that exceed the dimensions of the chosen implant this is not the case with shaped implants. These require a pocket that provides a hand-in-glove relationship with the implant to hold it in its desired position. The SILTEX Texture provides the needed coefficient of friction and MemoryShape Implants impart a very youthful feel to the augmented breast and are more likely to hold their position and not drop over time. This is in direct contrast with smooth round devices which are more likely to drop or move in an undesired direction in these patients. The question becomes what degree of texturing is necessary to achieve this end?

In order to minimize the chance of implant rotation, all shaped implants require some degree of texturing. This creates the necessary shear force, or frictional effect, to hold the implant in place. SILTEX Texture has not been shown to promote tissue ingrowth (as this is not necessary to stabilize the implant's position) and its unique surface characteristics limit many of the problems more commonly associated with macro-texturing. It does, however, provide an appropriate amount of rotational resistance so that, in a properly crafted pocket, rotation is extremely unlikely to occur.

Through the following cases we hope to showcase the type of results that can be achieved using MemoryShape Implants in a range of patients with breast shape issues ranging from pseudo-ptosis to severe ptosis.

TEXTURE IS DIFFERENT



Scanning Electron Microscopy (SEM) at 100X

Figure 1
(A) MENTOR® SILTEX® imprinted texture, (B) Salt-loss macro-texturing

CASE 1: Augmentation with Ptosis Camouflage

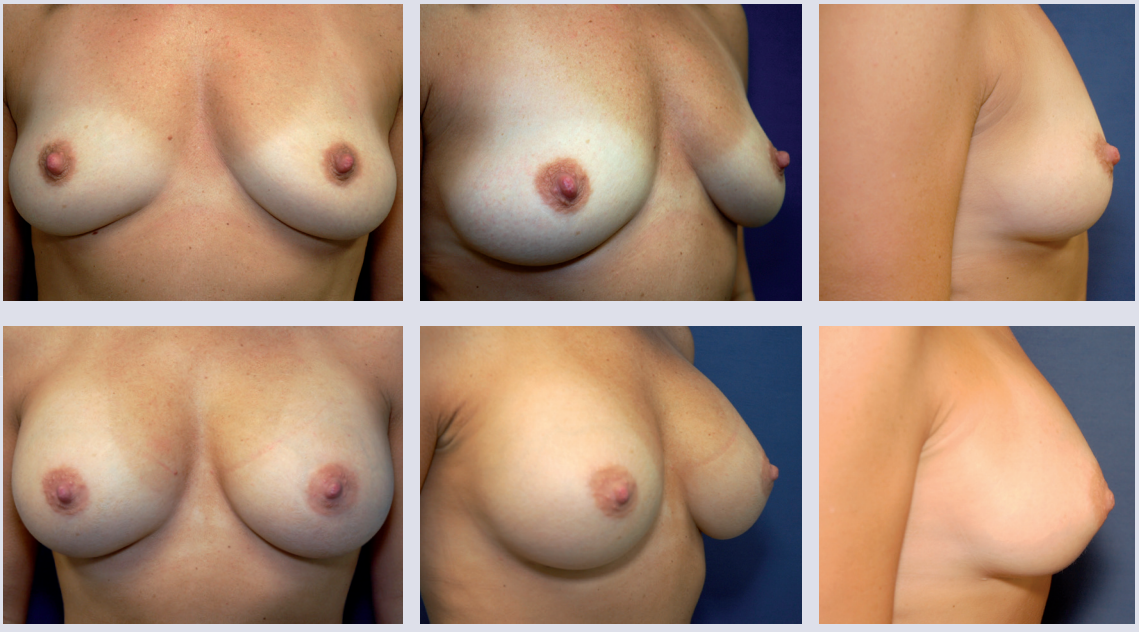
This 48 y/o woman presented with glandular ptosis and volume deficiency. As is often the case she requested that both elements be corrected in one procedure with the minimum amount of scarring possible.

Her pre-op measurements were as follows: Suprasternal Notch to Nipple: 21cm; Width: 12cm
IMF to Nipple (Under stretch): 8.5cm (Left) 9cm (Right).

SURGICAL TECHNIQUE:

After a standard prep and drape, nipple shields were placed and through a midline inframammary approach dissection was carried down to and through Scarpa's fascia and the submuscular plane was entered. The muscle was released only to the 5 o'clock and 7 o'clock positions. The pocket dissection was limited to allow the placement of a smooth, shaped sizer with the above described hand-in-glove relationship between the implant and the pocket.

Preliminary implant style and size selection had been made based on preoperative breast dimensions and patient preference. Desired breast width was the most important factor in this selection process. If the smooth-shelled sizer fits the pocket properly the textured shaped implant will fit even more tightly in the pocket. Great care was taken to not overdissect the pocket. After a final check for hemostasis, copious evidence-based antibiotic irrigation was performed. The breast was re-prepped with Betadine and an Ioban sheet was used to cover the entire breast. The Ioban film was incised and a 350cc TM+ MemoryShape Implant was placed with a limited-touch technique. In this case a dual plane I partial submuscular implant placement was utilized. After positioning the chosen MemoryShape Implant (utilizing the orientation marks on the device), and assuring that it was completely unfolded and lying smoothly on the chest wall, 3-0 Vicryl sutures were used for the deep closure taking solid bites of Scarpa's fascia on the undersurface of the superior skin flap and incorporating a bite of the thoracic fascia and Scarpa's facia along the lower edge of the incision. The remainder of the closure was performed with 4-0 Vicryl and a running 4-0 Monocryl. Five (5) year post-op results are shown.



CASE 1:
MENTOR® MemoryShape®
Breast Implant TM+, 350cc

Pre-op

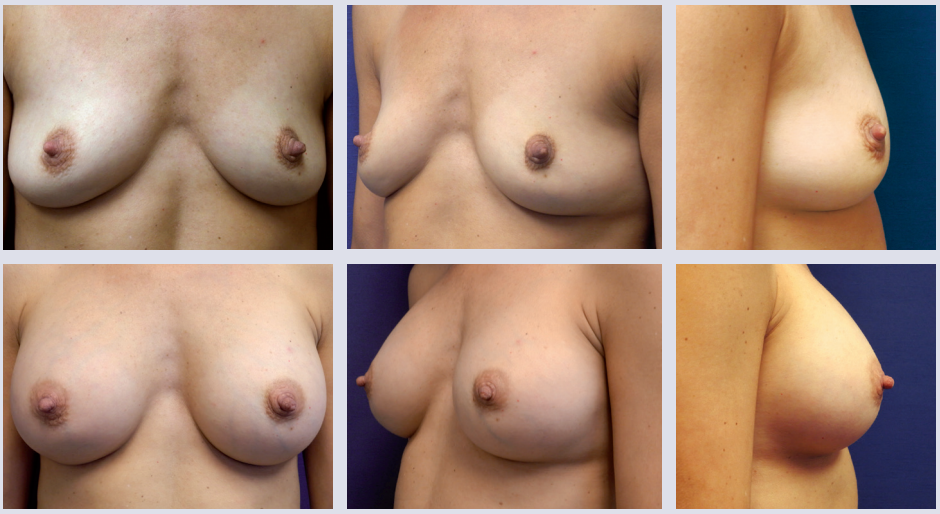
Five years post-op
David A. Caplin, MD

CASE 2: Augmentation with Glandular Ptosis Correction

This 45 y/o woman presented with glandular ptosis and involutional changes in her breasts following several pregnancies.

Her pre-op measurements were as follows: Suprasternal Notch to Nipple: 19.5cm; Width: 12cm; IMF to Nipple (Under stretch): 7.5cm

External sizers were utilized during the consultation and based on this the patient chose an implant in the 300cc range. Her breast width of 12cm made her an ideal candidate for a 295cc MM+ Memory Shape Implant. Her stretched Nipple to IMF distance of 7.5cm allowed the incision to be placed directly in the native inframammary fold. The implant placement and closure were as described in Case #1. Five (5) year post-op results are shown.



CASE 2:
MENTOR® MemoryShape®
Breast Implant MM+, 295cc

Pre-op

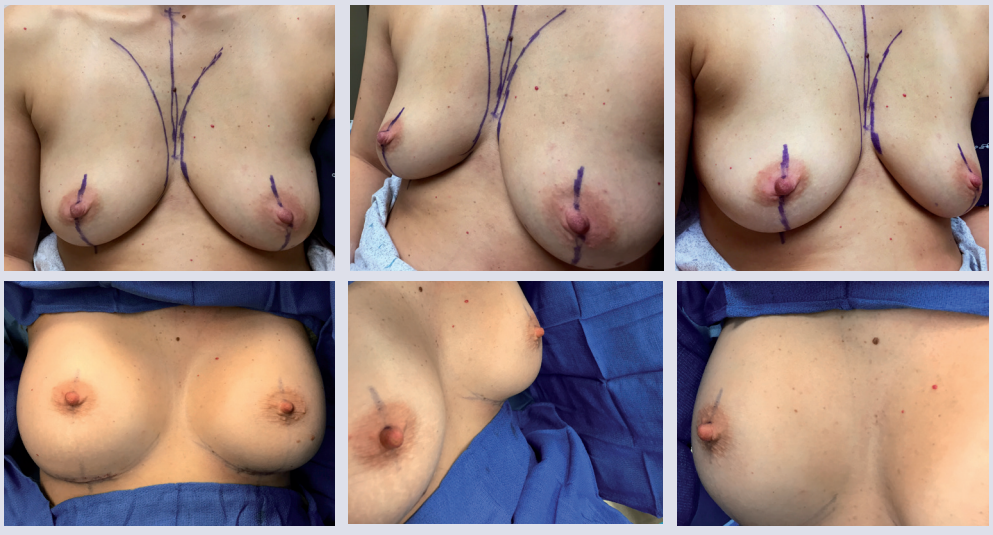
Five years post-op
David A. Caplin, MD

CASE 3: Pre- and Intra-Operative Ptosis

This 49 y/o requested a volume increase as well as correction of the involutional changes in the upper pole of her breasts. She stated that after breast feeding her breasts became "droopy" and decreased in size.

Her pre-operative measurements were as follows: Suprasternal Notch to Nipple: 19.5cm (Right) 20cm (Left); Width: 12.5cm IMF to Nipple (Under stretch): 8.5cm

Following the surgical technique described above a 295cc MM+ MemoryShape Implant was placed bilaterally. The pre-op and intra-operative photographs show the immediate correction of this patient's glandular ptosis.



CASE 3:
MENTOR® MemoryShape®
Breast Implant MM, 395cc

Pre-op

Intra-operative
(at completion
of procedure)
David A. Caplin, MD

CASE 4: Massive Weight Loss Augmentation Mastopexy

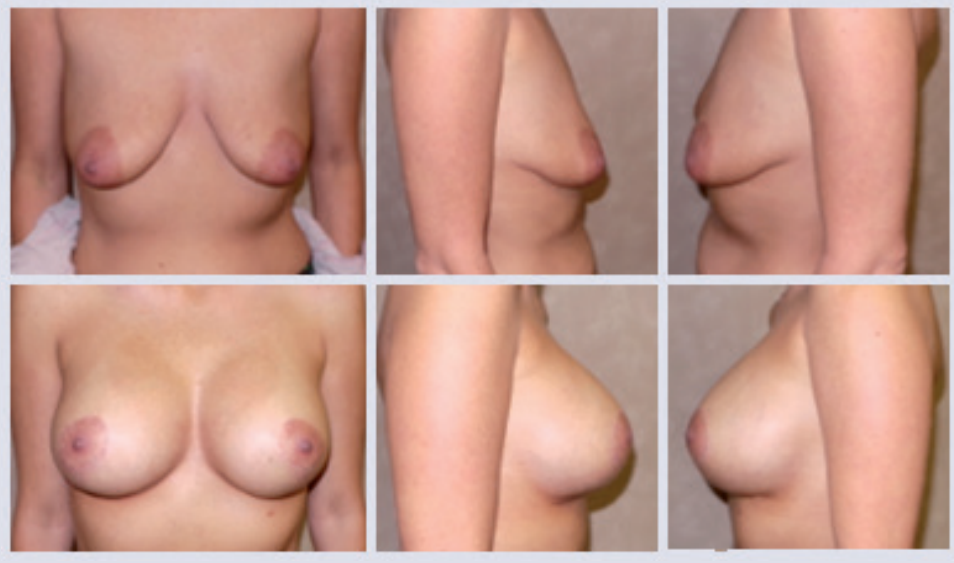
This 43 y/o woman presented for breast augmentation following a 95 pound weight loss. She was noted to have thin breast tissue with ptosis.

Her measurements were as follows: Sternal Notch to Nipple: 27cm (Right) 27cm (Left)
Width: 14.5cm and 13.5cm; IMF to Nipple (At rest) 8.5cm and 11.5cm (Under stretch), Ptosis 4cm

Her situation was addressed using a combination of breast augmentation with mastopexy. The ability of MemoryShape Implants to predictably maintain position was seen as advantageous in this situation, given that massive weight loss patients frequently face challenges supporting the weight of a breast implant.

SURGICAL TECHNIQUE:

In single-stage augmentation mastopexy, the implant can be placed using an inframammary approach followed in sequence by the breast lift. Alternatively, the lift incisions can be used for access for device placement which was the approach used in this patient. The nipple areolar complex was demarcated, deepithelialized, and transposed to the planned location. Through the space created, access was gained directly down through breast tissue to the lateral border of the pectoralis major muscle. Following copious irrigation with evidence-based antibiotic solution, the subpectoral space was entered and a dual plane I partial subpectoral pocket was created in a preliminary fashion. This preliminary pocket is ALWAYS smaller than the dimensions of the anticipated ultimate implant. The ideal width of the patient's breast and potential optimal width of the tissue pocket were assessed and measured. This led to the selection of the 475cc MM+ MemoryShape Implant. The dimensions of the implant pocket were then modified to precisely match the height and width dimensions of the device chosen. The pocket was irrigated with antibiotic solution, following which the device was placed with correct orientation using an insertion sleeve. The correct orientation of the device was confirmed. The anterior and posterior surfaces of the device were confirmed to smoothly conform to the ribcage posteriorly and muscle/breast tissue anteriorly without folds or wrinkles. 10 Fr Blake drains were placed along the IMF with low posterior exit sites, separate from access incisions. A vertical mastopexy was then performed using a tailor tack approach, creating a profound tightening of her thin tissue onto the form-stable implant. After completing an identical procedure on the contralateral side, tissue was excised within the tailor tack markings and closed using 2-0 Vicryl in the deep Scarpa's fascial layer, followed by 2-0 vicryl and 3-0 PDS in the deep and more superficial dermal layers. BIOPATCH® Protective Disk with CHG devices with occlusive dressings were placed over the drain sites, followed by a pressure dressing. It is important to note that this approach depends upon liberal use of evidence-based antibiotic irrigation to the breast tissue and pocket to decrease exposure of the device to breast tissue bacterial flora during placement. 18 Month post-op results are shown.



CASE 4:
MENTOR® MemoryShape®
Breast Implant MM+, 445cc

Pre-op

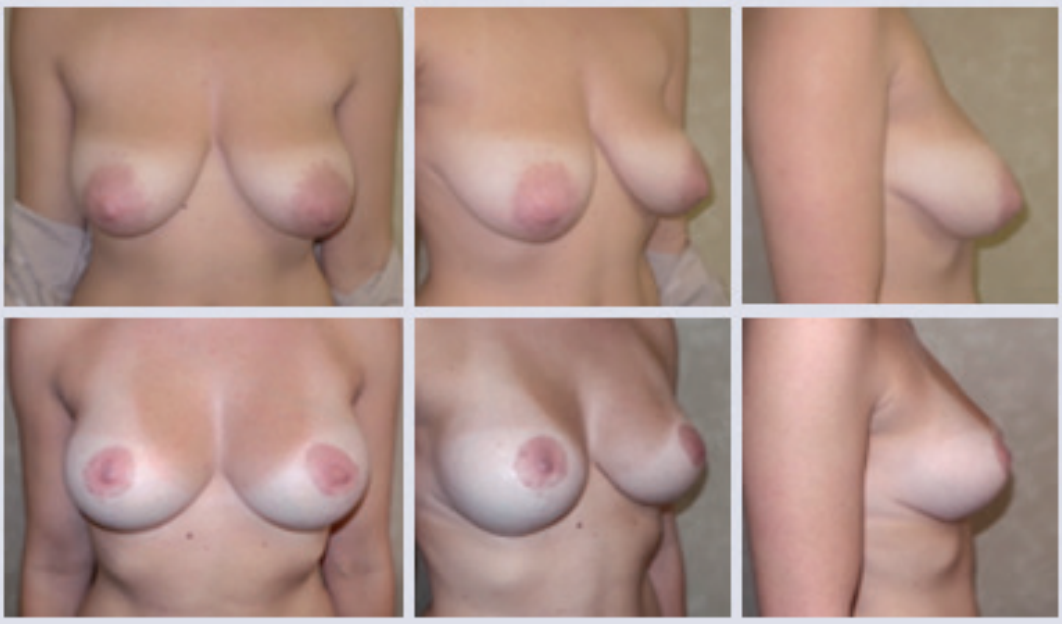
18 Months post-op
Louis L. Strock, MD

CASE 5: Postpartum, Weight Loss Augmentation Mastopexy

This patient is a 30 y/o woman who presented for breast enhancement. She had one child with a long course of breast feeding and a postpartum 25 pound weight loss. She requested a larger volume with improved shape. Her exam showed low and loose tissue with significant ptosis.

Her measurements were as follows: Sternal Notch to Nipple: 27cm (Right) and 27.5cm (Left) Width: 14.5cm and 14cm; IMF to Nipple: 11cm (Rest) and 15cm (Under stretch), Ptosis 5cm

Her situation was addressed with a combination augmentation mastopexy. A MemoryShape Implant was chosen to lessen unwanted device movement and provide a form-stable device onto which her tissue could be lifted and shaped. She requested a conservative approach to device size selection, leading to use of the 245cc Medium height, Moderate projection, Style MM MemoryShape Implant. As shown with the preceding case, the approach selected utilized the lift incisions for access for device placement and closures were as described in Case #4. 32 Month post-op results are shown.



CASE 5:
MENTOR® MemoryShape® Breast Implant MM, 245cc

Pre-op

32 Months post-op
Louis L. Strock, MD

CONCLUSION

With the introduction of MENTOR® MemoryShape® Breast Implants a powerful new tool has been added to our surgical armamentarium. These implants have wide application in primary and revisional cosmetic and reconstructive breast procedures. They offer a unique combination of features which provide a low incidence of capsular contracture, an impressive ability to “shape” the overlying soft tissues and, as these cases demonstrate, are very effective at dealing with varying degrees of breast ptosis delivering results that last.

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DISCLAIMER:

This white paper has not been subject to independent peer review. This white paper includes a demonstration of the use of a surgical device; it is not intended to be used as a surgical training guide. Other surgeons may employ different techniques. The steps demonstrated may not be the complete steps of the procedure. Individual surgeon preference and experience, as well as patient needs, may dictate variation in procedure steps. Before using any medical device, including those demonstrated or referenced in this white paper, review all relevant package inserts, with particular attention to the indications, contraindications, warnings and precautions, and steps for use of the device.

IMPORTANT SAFETY INFORMATION:

MENTOR® MemoryGel® Breast Implants, MENTOR® MemoryShape® Breast Implants, and MENTOR® Saline-filled Breast Implants are indicated for breast augmentation in women (at least 22 years old for MemoryGel® Implants and MemoryShape® Implants, and 18 years old for Saline Implants) or for breast reconstruction. Breast implant surgery should not be performed in women with active infection anywhere in their body, with existing cancer or pre-cancer of their breast who have not received adequate treatment for those conditions, or who are currently pregnant
or nursing.

Breast implants are not lifetime devices and breast implantation may not be a one-time surgery.

The most common complications for breast augmentation and reconstruction with MemoryGel® Implants include any reoperation, capsular contracture, and implant removal with or without replacement. The most common complications with MemoryShape® Implants for breast augmentation include reoperation for any reason, implant removal with or without replacement, and ptosis. The most common complications with MemoryShape® Implants for breast reconstruction include reoperation for any reason, implant removal with or without replacement, and capsular contracture. A lower risk of complication is rupture. The health consequences of a ruptured silicone gel breast implant have not been fully established. MRI screenings are recommended three years after initial implant surgery and then every two years after to detect silent rupture.

The most common complications with MENTOR® Saline-filled Implants include reoperation, implant removal, capsular contracture, breast pain, and implant deflation.

For MemoryGel® Implants, patients should receive a copy of *Important Information for Augmentation Patients about MENTOR® MemoryGel® Breast Implants* or *Important Information for Reconstruction Patients about MENTOR® MemoryGel® Breast Implants*. For MemoryShape® Implants, patients should receive a copy of *Patient Educational Brochure – Breast Augmentation with MENTOR® MemoryShape® Breast Implants* or *Patient Educational Brochure – Breast Reconstruction with MENTOR® MemoryShape® Breast Implants*, and a copy of *Quick Facts about Breast Augmentation & Reconstruction with MENTOR® MemoryShape® Breast Implants*. For MENTOR® Saline-filled Implants, patients should receive a copy of *Saline-Filled Breast Implants: Making an Informed Decision*. Your patient needs to read and understand the information regarding the risks and benefits of breast implants, with an opportunity to consult with you prior to deciding on surgery.

The ARTOURA™ Breast Tissue Expander or CONTOUR PROFILE® Breast Tissue Expander can be utilized for breast reconstruction after mastectomy, correction of an underdeveloped breast, scar revision, and tissue defect procedures. The expander is intended for temporary subcutaneous or submuscular implantation and is not intended for use beyond six months. Do not use the ARTOURATM Tissue Expander nor CONTOUR PROFILE® Tissue Expander in patients where an MRI may be needed. The device could be moved by the MRI causing pain or displacement, potentially resulting in a revision surgery. The incidence of extrusion of the expander has been shown to increase when the expander has been placed in injured areas.

For detailed indications, contraindications, warnings, and precautions associated with the use of all MENTOR® Implantable Devices, which include MENTOR® Saline-filled Implants, MemoryGel® Implants, MemoryShape® Implants, ARTOURA™ Expanders, and CONTOUR PROFILE® Expanders, please refer to the Product Insert Data Sheet provided with each product or visit www.mentorwwllc.com.

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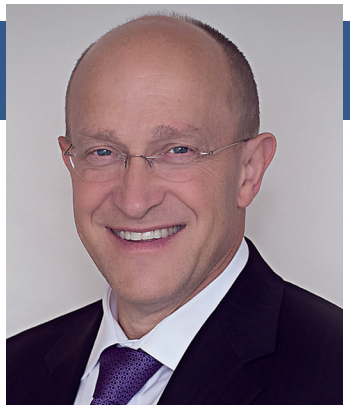
INCISIONS & INSIGHTS

The MENTOR® MemoryGel® Xtra Breast Implant in Aesthetic and Reconstructive Breast Surgery



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INTRODUCTION

Breast implant design has now come full circle with the recent development of the MENTOR® MemoryGel® Xtra Breast Implant. To understand the significance of this device it is helpful to review breast implant design over the years. The very first implant designs from the mid to late 1960's incorporated a smooth walled, anatomically shaped device that featured textured patches made of Dacron adhered onto the back of the implant. *(Figure 1 A,B)*

Figure 1 A, B: Appearance of one of the first mid 1960's implant designs featuring an anatomic shape, smooth surface, and Dacron patches adhered to the back to hold the asymmetrically constructed device in position.

The tissue incorporation created by these patches was a very important design feature as it was realized early on that an anatomically shaped implant must maintain its orientation to effectively shape the breast, and any element of postoperative rotation would variably compromise the aesthetics of the result. These patches stimulated a very aggressive ingrowth of soft tissue and thus, very solidly held the devices in the proper orientation.

Unfortunately, likely because of faulty silicone materials, these devices were associated with a very high rate of complications with capsular contracture being a particularly severe problem, and soon fell into disfavor. Moving forward, it was demonstrated that "round" implants, meaning implants that were symmetrically designed with regards to the base width and the height of the device, provided very satisfying results in breast surgery.[4] Different design modifications including different fill materials, shell constructions, and dimensions dominated the attention of the plastic surgery community for many years. The topic of implant fill material merits specific mention as the physics of the different fill materials require different strategies for fill volume. When an

implant shell is filled with a less cohesive silicone gel, the tendency for the gel to variably flow allows the implant to be underfilled relative to its maximal fill volume. This creates an implant that has a very soft feel as the implant variably collapses under the effect of external pressure or gravity, and assumes a shape partially dictated by the forces applied to it *(Figure 2 A,B).* The deleterious effect of this partial shell collapse is folding and wrinkling of the implant shell which places stress points that ultimately, over time, can lead to shell failure *(Figure 3 A,B)*.

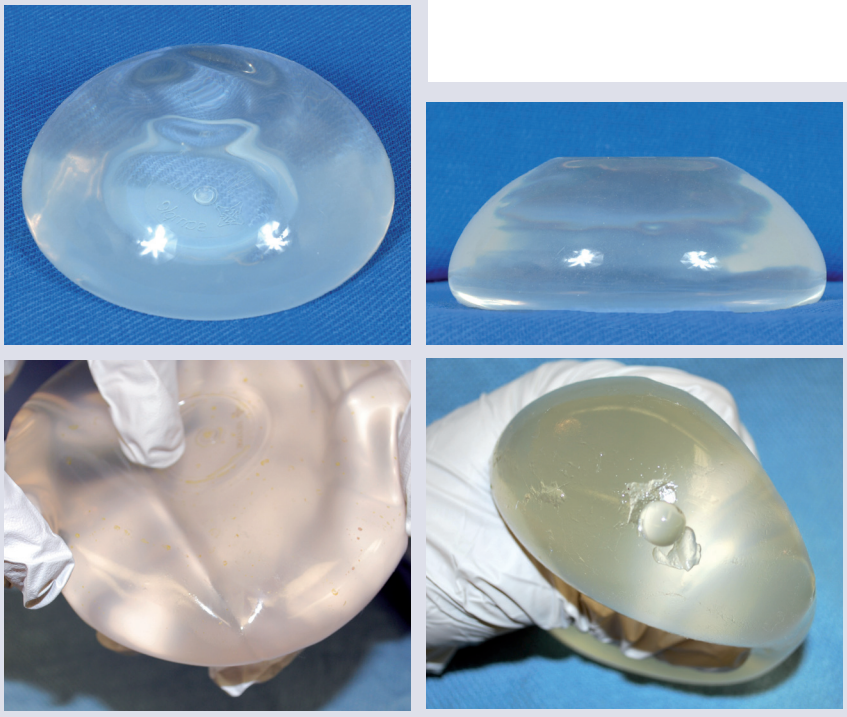


Figure 2 A, B: The traditional MemoryGel® Implant demonstrates mild collapse in the apex of the device when lying flat due to the underfilled nature of the implant.

Figure 3 A, B: Wrinkling in an implant shell can create stress points that can lead to shell fracture.

To counteract this tendency for the shell to wrinkle, and although off-label, overfilling implant shells with saline became a popular strategy as the collapse of the device when placed upright could be minimized. While effective in many patients, this strategy tended to create a firmer feeling breast with rounded distortion in the upper pole.

To maximize shape and limit the saline "water balloon" feel effect, anatomically shaped, highly cohesive gel filled implants were then developed. By incorporating a firmer, more cohesive gel in an anatomically molded shell, an array of desired shapes could be created using a gel that resisted collapse of the upper pole of the device *(Figure 4 A,B)* .

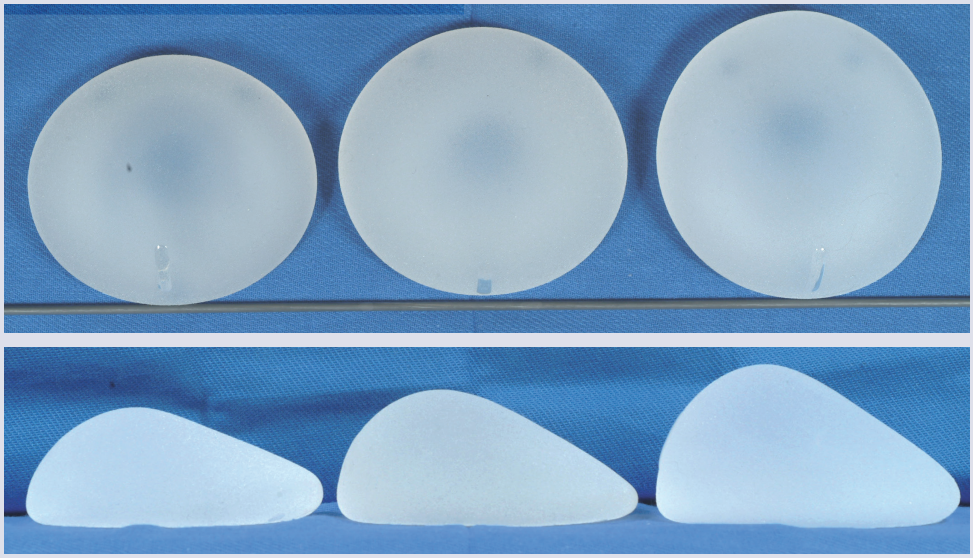


Figure 4 A, B: The MENTOR® MemoryShape® Breast Implants feature a textured anatomically shaped shell filled with a cohesive gel that allow the surgeon to directly shape the breast with the implant.

Theoretically, it was expected that these devices would limit folding and wrinkling in the implant shell resulting in greater longevity and improved aesthetic results. This is exactly what has been noted in several publications to date.[1-3] Despite these advantages, acceptance of the shaped implant concept has been less than universal. Namely, complications related to implant rotation and a firm feel to the breast have been noted. The result of this progression of engineering and design advances has been that the "perfect" breast implant has yet to be fully realized and continuing efforts to improve the performance of these devices is warranted.

It is with this history in mind that the most recent development of the MENTOR® MemoryGel® Xtra Breast Implant becomes important. During the original approval granted by the FDA to the MemoryGel® line of breast implants, a range of fill volume was allowed for each individual device. Up until now, the fill volume used for these devices was chosen to be on the lower end of what was allowable. As such, these devices are somewhat underfilled, resulting in a soft, malleable implant that conforms to the pressures of the overlying soft tissue. In essence, it is the soft tissue that shapes the implant. While this implant design has provided excellent clinical results for years[4], the utility for a less malleable and more projecting[5] implant was realized by many. This need has been met by offering a line of implants using the same MemoryGel® Implant construction, but now one that is filled more toward the high end of the allowable fill volume stipulated by the FDA *(Figure 5 A,B).*

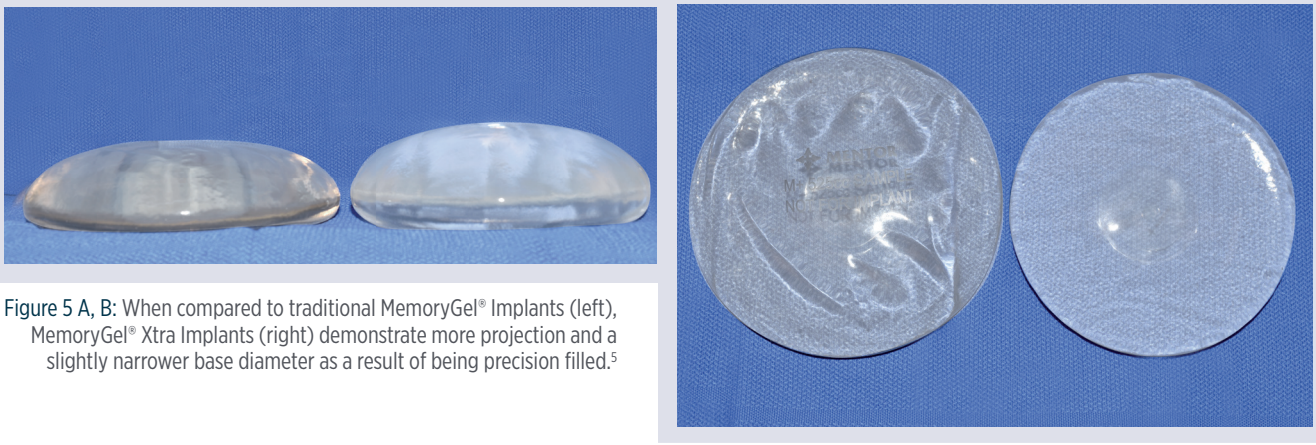


Figure 5 A, B: When compared to traditional MemoryGel® Implants (left), MemoryGel® Xtra Implants (right) demonstrate more projection and a slightly narrower base diameter as a result of being precision filled.[5]

With the alteration of precision filling each specific SKU in design, come some very interesting advantages. Because the implant is more closely situated towards a maximal fill volume relationship, less pressure on the device is required to meet resistance to deformation. In other words, the implant maintains back to front projection in the presence of a force applied to the apex of the device such as happens when the implant is placed under the breast. In fact, MemoryGel® Xtra Breast Implants provide comparable firmness to Natrelle Inspira Breast Implants based on bench top testing.[6]* However, due to the shell construction and the use of a less cohesive gel, when the implant is compressed from side to side, it maintains a very soft feel. In a blinded comparison, 9 out of 10 consumers chose MemoryGel® Breast Xtra implants as feeling more like natural (or real) breasts than Inspira Responsive and Inspira Cohesive breast implants.[7]**

While these parameters can be measured, there are some theoretical advantages that may be observed as well. Due to the maximal fill volume relationship of the shell and the gel, wrinkling is likely to be less of a problem. This may provide an advantage in patients with a thin soft tissue envelope where visible wrinkling in the implant could become problematic, thus compromising the quality of the aesthetic result. As well, if wrinkling were less common, the implant rupture rate might be reduced as one would expect that the shell over time would experience less stress. Long term study will be required to document the validity of these potential advantages.

* Head-to-head compression benchtop testing between MemoryGel® Xtra (n=4) and Natrelle Inspira (n=3).

** Head-to-head blinded in-person tabletop product comparison (MemoryGel Xtra vs. Inspira Responsive vs. Inspira Cohesive) with 452 respondents.

CLINICAL CONSIDERATIONS

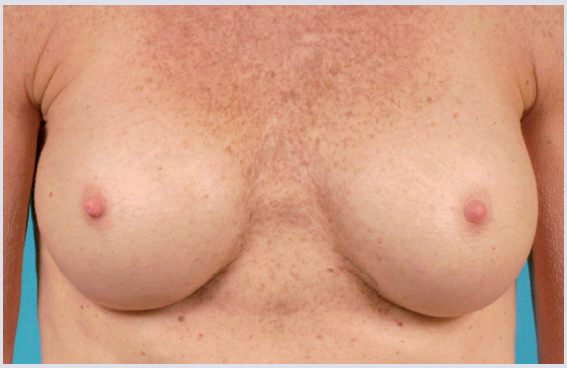
In my clinical experience, the advantages afforded by the MemoryGel® Xtra Breast Implant design can be most effectively realized in patients who present with thin skin envelopes, those who require a narrower base diameter for a given volume, and in those patients seeking additional projection.

CLINICAL CASES

CASE 1: Revision Augmentation

This 36-year-old woman presented with a history of undergoing a previous capsulectomy with placement of a 300 cc high profile smooth round implant as primary treatment for capsular contracture. She remained soft and demonstrated an aesthetic result, however, after several years presented requesting an increase in breast size *(Fig 6 A,B).*

Due to her thin soft tissue framework and her narrow breast base diameter, a MemoryGel® Xtra implant was chosen as the implant of choice for her revision. Preoperative evaluation focused on using a 450 cc implant for her revision. Despite this significant increase in implant volume, a modest increase in base diameter from 11.1 to 11.9 cm was required to accommodate this new implant *(Fig 6C)*. Her postoperative result demonstrated an aesthetic breast shape with the desired amount of upper pole fullness *(Fig 6 D,E,F)*.



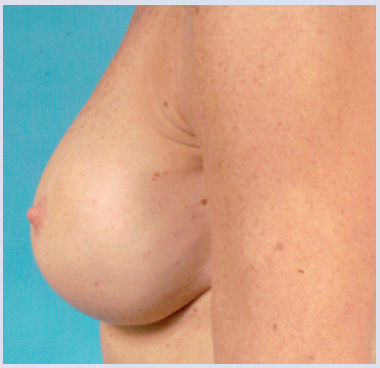


Figure 6 A, B: Preoperative appearance of a 36-year-old woman after capsulectomy and placement of a 300 cc high profile smooth round MemoryGel® Implant. The patient desires an increase in implant size.

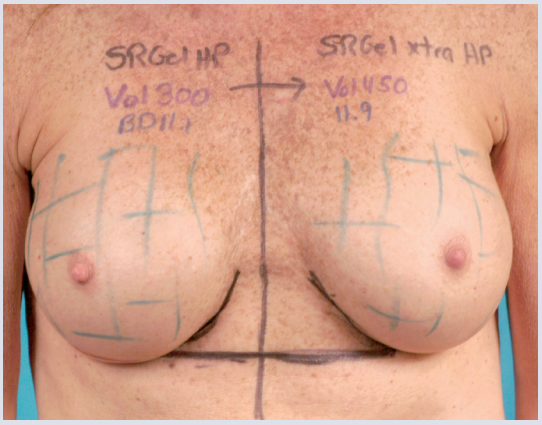
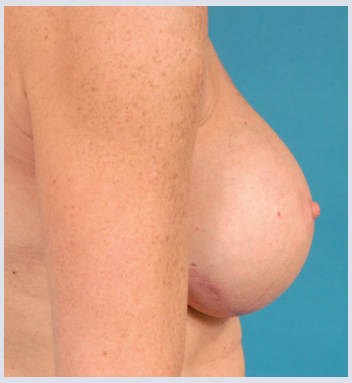
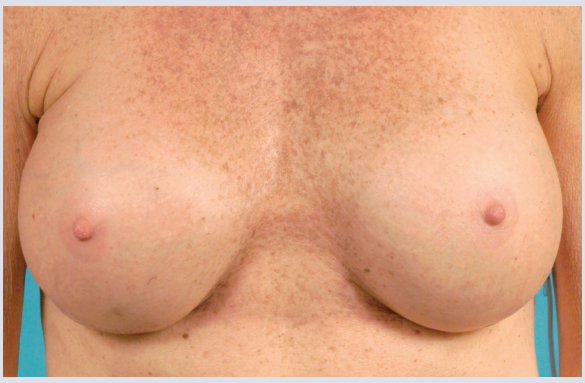
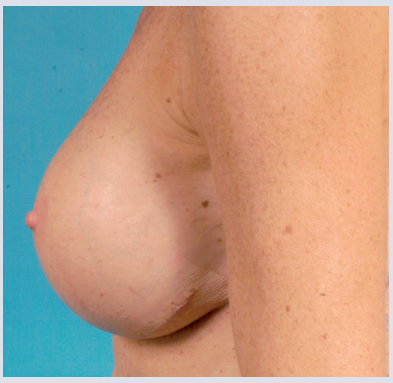


Figure 6 C: Preoperative marks demonstrating a planned implant size increase from 300 cc to a 450 cc high profile MemoryGel® Xtra Implant with a minimal 8 mm increase in implant base diameter from 11.1 cm to 11.9 cm.

Figure 6 D, E, F: Postoperative 6 week result demonstrating an aesthetic breast shape with no excess upper pole fullness despite the increase in implant volume.







CASE 2: Primary Reconstruction

This 36-year-old woman presented with a strong family history of breast cancer along with positive at risk gene testing. She opted to proceed with bilateral nipple sparing mastectomy and immediate tissue expander and ADM breast reconstruction *(Fig 7 A,B)*. After complete filling of her 13 cm expanders to 520 cc, she presented for second stage reconstruction. She desired a full augmented appearance to her breasts, therefore, a high profile smooth round MemoryGel® Xtra Implant with a 595 cc fill volume and a 13.1 cm base diameter was utilized as her implant of choice to complete her reconstruction *(Fig 7 C)*. Her result demonstrates an aesthetic breast contour and the desired full rounded appearance to the breast *(Fig 7 D,E)*.

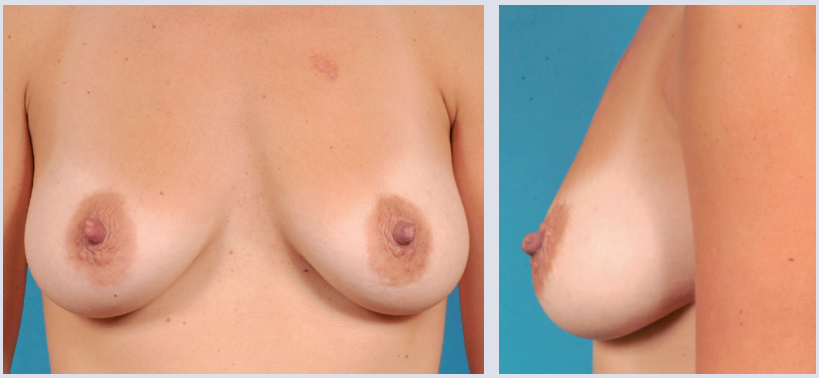


Figure 7 A, B: Preoperative appearance of a 36-year-old woman in preparation for bilateral prophylactic mastectomy with immediate tissue expander and ADM breast reconstruction.

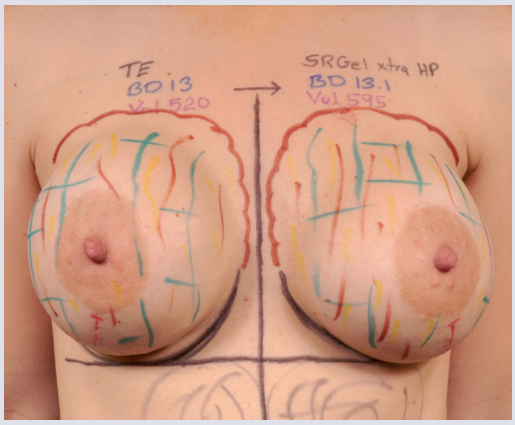


Figure 7 C: Each 13.0 cm base diameter expander has been filled to 520 cc. The patient desires a full rounded breast; therefore, the preoperative plan includes tissue expander replacement with a high profile smooth round MemoryGel® Xtra Implant with a 595 cc fill volume and a 13.1 cm base diameter.

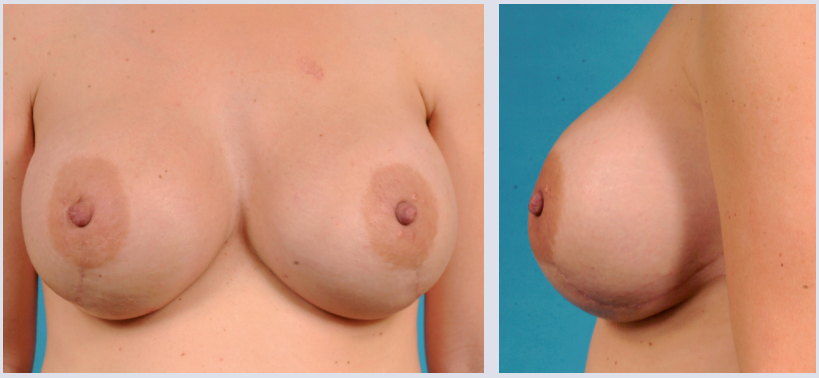


Figure 7 D, E: Postoperative appearance demonstrating an aesthetic breast shape with excellent projection and increased fullness.

SUMMARY

By precision filling MemoryGel® Xtra Breast Implants, a device that provides greater projection retention than the traditional MemoryGel® line, while maintaining a soft, pliable feel is created without dramatically changing the overall design and engineering of the device. This implant can be particularly useful in patients with thin soft tissue envelopes, patients who present with a narrow breast base diameter, and in those patients seeking extra projection. Theoretical advantages of decreased implant wrinkling and an improvement in the overall rupture rate may be realized, although long term study is necessary to document these potential advantages.

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IMPORTANT SAFETY INFORMATION:

MENTOR® MemoryGel® Breast Implants are indicated for breast augmentation in women at least 22 years old or for breast reconstruction. Breast implant surgery should not be performed in women with active infection anywhere in their body with existing cancer or pre-cancer of their breast who have not received adequate treatment for those conditions or are pregnant or nursing.

Breast implants are not lifetime devices and breast implantation is not necessarily a one-time surgery. The most common complications with the MemoryGel® Breast Implants include reoperation, capsular contracture, asymmetry, and breast pain. A lower risk of complication is rupture. The health consequences of a ruptured silicone gel-filled breast implant have not been fully established. MRI screenings are recommended three years after initial implant surgery and then every two years after to detect silent rupture.

Patients should receive a copy of Important Information for Augmentation Patients about MENTOR® MemoryGel® Silicone Gel-Filled Breast Implants or Important Information for Reconstruction Patients about MENTOR® MemoryGel® Silicone Gel-Filled Breast Implants. Your patient needs to read and understand the information regarding the risks and benefits of breast implants, with an opportunity to consult with you prior to deciding on surgery.

For detailed indications, contraindications, warning and precautions associated with the use of MemoryGel® Breast Implants. Please refer to the Instructions for Use (IFU) provided with each product, or online at www.mentorwwllc.com.

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The Functional Influence of Breast Implant Outer Shell Morphology on Bacterial Attachment and Growth

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Background: The introduction of texture to the outer shell of breast implants was aimed at increasing tissue incorporation and reducing capsular contracture. It has also been shown that textured surfaces promote a higher growth of bacteria and are linked to the development of breast implant–associated anaplastic large cell lymphoma.
Methods: The authors aimed to measure the surface area and surface roughness of 11 available implants. In addition, the authors aimed to subject these implant shells to an in vitro bacterial attachment assay with four bacterial pathogens (*Staphylococcus epidermidis*, *S. aureus*, *Pseudomonas aeruginosa*, and *Ralstonia pickettii*) and study the relationship among surface area, surface roughness, and bacterial growth.
Results: Surface area measurement showed grouping of implants into high, intermediate, low, and minimal. Surface roughness showed a correlation with surface area. The in vitro assay showed a significant linear relationship between surface area and bacterial attachment/growth. The high surface area/roughness implant texture grew significantly more bacteria at 24 hours, whereas the minimal surface area/roughness implant textures grew significantly fewer bacteria of all types at 24 hours. For implants with intermediate and low surface areas, some species differences were observed, indicating possible affinity of specific bacterial species to surface morphology.
Conclusions: Implant shells should be reclassified using surface area/roughness into four categories (high, intermediate, low, and minimal). This classification is superior to the use of descriptive terms such as macrotexture, microtexture, and nanotexture, which are not well correlated with objective measurement and/or functional outcomes. (*Plast. Reconstr. Surg.* 142: 837, 2018.)

The texturization of the outer shell of breast implants was first introduced in 1968 with the "natural Y" implant, which incorporated a 1.2- to 2-mm polyurethane foam coating on its outer surface.[1] It was proposed that this surface prevented organized alignment of myofibroblasts, reducing the risk of capsular contracture.[1] In 1991, a specific association between polyurethane and the carcinogen 2,4-toluenediamine was reported.[2,3] This led to a voluntary withdrawal of polyurethane-coated silicone implants in the United States, which is still in place. Alternative surface technologies to modify the outer silicone

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shell were introduced in an attempt to mimic the polyurethane surface. There are four processes for generating surface texture on the external silicone shell: salt loss, vulcanisation, imprinting techniques,[4] and a more recently released surface that claims a novel "nano" texture that remains proprietary.[5]

The benefits of textured implants in reducing capsular contracture remain controversial. Systematic reviews of comparative clinical studies concluded that texturization may reduce the incidence of early capsular contracture in subglandular augmentation.[6,7] Many published reports lack adequate description of implant type, surgical technique, and outcome assessment. Smaller comparative or split breast studies are evenly divided as to the benefit of texturization.[8–18]

Previous published data have confirmed that textured implants are able to support higher rates of bacterial growth in vitro.[19] Furthermore, there is a correlation between higher bacterial contamination and host response in vivo, which suggests a threshold phenomenon where bacterial load triggers a host inflammatory response.[20] More recently, bacterial infection has been proposed as one of four factors that may play a role in the genesis of breast implant–associated anaplastic large cell lymphoma (ALCL).[21] This study aimed to look at textures of varying morphology to study the relationship among surface area, roughness, and capacity for bacterial attachment and growth in vitro.

MATERIALS AND METHODS

Implant Surfaces Tested

Eleven implant surface types were subjected to testing: Silimed polyurethane (Sientra, Dallas, Texas); Polytech POLYtxt (Polytech Health and Aesthetics, Dieburg, Germany); Mentor Siltex and Mentor Smooth (Mentor Worldwide LLC, Irvine, Calif.); Motiva SilkSurface and Motiva VelvetSurface (Motiva Alajuela, Costa Rica); Allergan Biocell (Allergan, Dublin, Ireland); Allergan Natrelle Smooth (Allergan); Nagor Nagotex (Nagor Ltd, Glasgow, UK); Sientra Smooth (Santa Barbara, Calif.); and Eurosilicone textured (Eurosilicone, Apt Cedex, France). Table 1 lists the manufacturing types for the various textured surfaces.

Table 1. Manufacturing Process for Textured Implants

Manufacturing Type	Implant Type
Polyurethane bonded foam	Silimed polyurethane
Salt loss	Allergan Biocell
	Eurosilicone texture
	Nagor Nagotex
Vulcanisation (ammonium carbonate)	Polytech POLYtxt
Imprinting	Mentor Siltex
Unknown	Motiva VelvetSurface
	Motiva SilkSurface

Implant Surface Imaging

Scanning Electron Microscopy

Following fixation in 3% glutaraldehyde, samples (up to 1 cm^2) were dehydrated in ethanol and immersed in hexamethyldisilazane (Polysciences, Inc., Warrington, Pa.) for 3 minutes, and the hexamethyldisilazane was allowed to evaporate overnight. Samples were mounted onto aluminium stubs (ProSciTech, Thuringowa, Queensland, Australia) and sputter-coated with 20-nm gold film in the Emitech K550 gold coater (Emitech, West Sussex, United Kingdom). The gold-coated breast implant samples were visualized using a JEOL 6480LA scanning electron microscope (JEOL Ltd., Tokyo, Japan).

Micro–Computed Tomographic Scan

The specimens were mounted horizontally on a metal pin with adhesive before loading into a pin vice holder. These were then scanned in a Zeiss Xradia MicroXCT-400 system operating in absorption mode with a peak source energy of 50 kV and a beam current of 200 μA (Carl Zeiss, Oberkochen, Germany). The projections were collected every 0.25 degree over a total rotation of 180 degrees, with an exposure time of 3 seconds and saved as 16-bit images in a proprietary file format.

The projections were reconstructed using XMReconstructor v7.0.2817 (Zeiss Xradia) with consistent reconstruction parameters, resulting in 2.2-μm isotropic voxels. Surface area and roughness measurements were taken from this model to calculate the various required material properties. Analysis was performed with Avizo 9.3 (FEI Visualization Sciences Group, Bordeaux, France) and Fiji,[22] where a binarized model of the sample was produced by thresholding after noise-reduction filtering of the reconstructed slices.

Surface Area Determination

The three-dimensional–to–two-dimensional sample size surface area ratio was calculated by first measuring the surface area of the interface between the binarized sample and air (SA_{3D}) and then comparing it to the x-y dimensions of the sample itself (SA_{2D}). (**See Figure, Supplemental**

Digital Content 1, which shows the algorithm for calculation of the three-dimensional–to–two-dimensional area ratio, ***http://links.lww.com/PRS/C956***.). All ratios were normalized to smooth implants.

Surface Roughness Determination

To measure the roughness of the surface of each sample, it was necessary to first wrap the sample to avoid overhangs and cavities. To simplify things, a new surface was created by effectively dropping an thin probe toward the surface at each point. At the point of contact with the sample, the new surface was defined. The arithmetic mean deviation of the assessed profile (S_a) was calculated over this approximated surface by means of the following:

$$S_a = \frac{1}{kn}\sum_{j=1}^{k}\sum_{i=1}^{n}\left|y_{ij} - \bar{y}\right|$$

where i and j represent column and row positions, y_{ij} is the surface height at ij, and $\bar{y}$ is the mean surface height across the surface. The roughness was expressed as a multiple of the value for smooth implants.

In Vitro Bacterial Attachment Assay

In vitro analysis was conducted on nine types of implants of varying morphology, against four bacterial types: *Staphylococcus epidermidis*, *S. aureus*, *Pseudomonas aeruginosa*, and *Ralstonia pickettii*. The implants were prepared by cutting a strip of implant shell from the whole implant and scraping away any residual silicone from the inner surface with the blunt edge of a knife. Sections of the implant shell were obtained using a 5-mm punch biopsy tool. The implants sections were placed outside surface down in a glass petri dish and sterilized under dry heat conditions at 115°C for 39 hours. After sterilization, sterile water was added to each petri dish and the implants were pressed into the water and the air was expelled. Then, 10% tryptone soy broth containing 10^5 cells/ml of *S. epidermidis*, *S. aureus*, and *R. pickettii* or 10^4 cells/ml of *P. aeruginosa* was added to the petri dish and the implants were incubated at 37°C for up to 24 hours.

Implant samples were removed at 2, 6, and 24 hours for *S. epidermidis* and at 24 hours for *S. aureus*, *P. aeruginosa*, and *R. pickettii* for colony-forming unit determination. The implant samples were washed three times in phosphate-buffered saline. Four implant disks were placed in 0.5 ml of phosphate-buffered saline and subjected to sonication for 20 minutes followed by 1 minute of vortexing as described previously.[19] Quantitative numbers of bacteria attached to the implant outer surface were determined by serial 10-fold dilutions and standard plate culture. Each condition was tested five times.

Statistical Analysis

Statistical analysis was conducted using the statistical package Sigma Plot 13 (Systat Software, Inc., San Jose, Calif.). For comparing different implant surfaces and bacterial attachment, the data were transformed and a one-way repeated measures analysis of variance was applied, and all pairwise multiple comparison procedures were performed using the Holm-Sidak method. If data were not distributed normally, the Kruskal-Wallis one-way analysis of variance on ranks test was performed, and all pairwise multiple comparison procedures were conducted using the Dunn method. The relationship between implant three-dimensional–to–two dimensional surface area ratio and number of attached bacteria at 24 hours was tested using Pearson correlation if distributed normally or Spearman rank order correlation if distributed nonnormally. A value of $p < 0.05$ was set as significantly different.

RESULTS

Scanning Electron Microscopy

Figure 1 demonstrates the surface morphology of some of the implants studied, demonstrating a range of appearance from highly complex with many hidden surfaces to relatively featureless.

Surface Area Determination

Analysis using fine-cut computed tomographic scans and confocal microscopy allowed visualization and calculation of surface area for each of the implant shells. Table 2 summarizes the findings. Figure 2 shows three-dimensional surface area images, which were used for calculating the three-dimensional–to–two-dimensional ratios for three of the implant surfaces. (**See Figure, Supplemental Digital Content 2**, which shows the polyurethane three-dimensional extraction, ***http://links.lww.com/PRS/C957***. **See Figure, Supplemental Digital Content 3**, which shows the polyurethane three-dimensional gray-scale reconstruction, ***http://links.lww.com/PRS/C958***. **See Figure, Supplemental Digital**

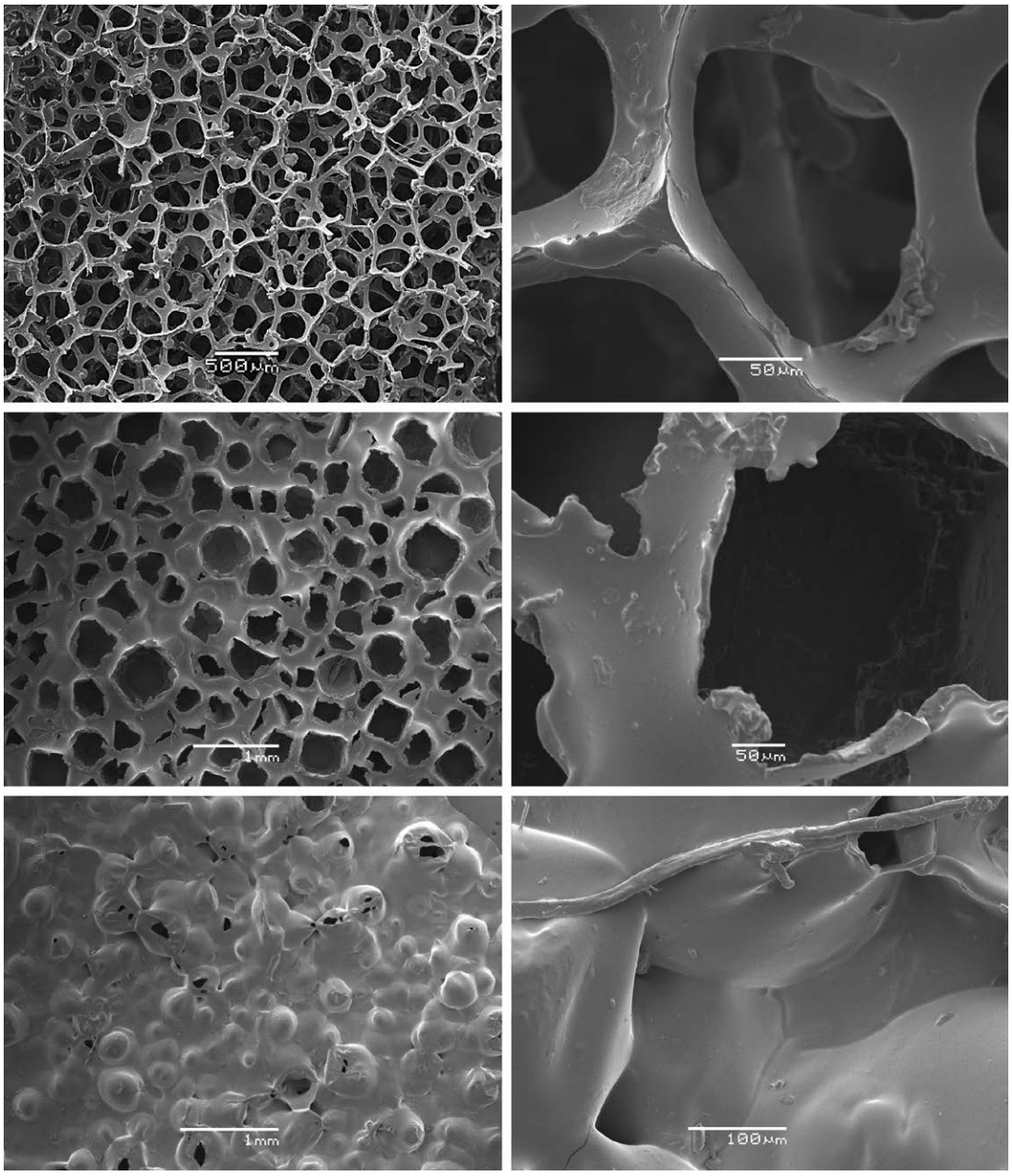


Fig. 1. Scanning electron micrographs of the surface morphology of implants studied at 25× and 400× magnification. (*Above*) Silimed polyurethane. (*Center*) Eurosilicone. (*Below*) Polytech POLYtxt.

Content 4, which shows the Polytech POLYtxt three-dimensional extraction, ***http://links.lww.com/PRS/C959***. **See Figure, Supplemental Digital Content 5**, which shows the Polytech POLYtxt three-dimensional gray-scale reconstruction, ***http://links.lww.com/PRS/C960***.) Figure 3 is a graphic representation of three-dimensional–to–two-dimensional surface area ratio.

There were four groupings for surface area measurements according to three-dimensional–to–two-dimensional surface area ratio. These were as follows: (1) high (>5), (2) intermediate (between 3 and 5), (3) low (between 2 and 3), and (4) minimal (<2).

These categories corresponded generally to implant shell manufacturing processes, with polyurethane open pore having the highest surface area; some salt-loss type and vulcanisation as intermediate; other salt-loss and imprinting type textures as low; and smooth and "nano" labeled surfaces as minimal. Salt-loss textures may vary in surface area dependent on the size of the crystals selected in the process. Interestingly, although the Polytech POLYtxt had a high surface area

Table 2. Raw Surface Area Calculation and Three-Dimensional–to–Two-Dimensional Surface Area Ratio for Each Implant Type

Implant Type	3D Surface Area (from 1.4 × 1.4-mm square) (mm^2)	3D-to-2D Surface Area Ratio*
Silimed polyurethane	79	20.8
Eurosilicone textured	15	3.9
Allergan Biocell	12	3.2
Polytech POLYtxt†	12	3.2
Nagor Nagotex	10	2.8
Mentor Siltex	8.1	2.2
Motiva VelvetSurface	4.3	1.2
Sientra Smooth	4.1	1.1
Motiva SilkSurface	3.9	1.1
Allergan Smooth	3.9	1.0
Mentor Smooth	3.8	1.0

3D, three-dimensional; 2D, two-dimensional.
*Normalized to Mentor Smooth.
†Represents available surface area after exclusion of internal cavities.

reading on first analysis, many of these surfaces were contained within the structure of the silicone outer shell and had no direct communication to the outer surface. An analysis of the choke zones (variation between 1 and 10 μm and hidden "caves" of sequestered internal surfaces) allowed an available surface area to be determined using subtractive analysis. The three-dimensional–to–two-dimensional surface area ratio for Polytech POLYtxt was calculated assuming a mean choke size of 5 μm. [**See Figure, Supplemental Digital Content 6**, which shows the demonstration of caves (sequestered surface area) for Polytech POLYtxt colored red on three-dimensional reconstruction, ***http://links.lww.com/PRS/C961***. **See Video, Supplemental Digital Content 7**, which shows real-time demonstration of caves (sequestered surface area) for Polytech POLYtxt colored red on three-dimensional reconstruction, ***http://links.lww.com/PRS/C962***.]

Surface Roughness Determination

There were four groupings for surface roughness measurements. These were as follows: (1) high (>150), (2) intermediate (between 75 and 150), (3) low (between 25 and 75), and (4) minimal (<25). Table 3 and Figure 4 summarize surface roughness findings.

In Vitro Bacterial Attachment Assay

S. epidermidis

Figure 5 shows the number of *S. epidermidis* attached to different types of implant outer shells at 2, 6, and 24 hours. Even by the 2-hour time point, the high surface area of textured Silimed polyurethane implants had a significantly larger number of bacteria attached to them than less textured implants with lower surface areas such as Mentor Siltex, smooth (i.e., Mentor, Sientra, and Allergan), Motiva VelvetSurface, and Motiva SilkSurface ($p < 0.001$). By 24 hours, implants with high or intermediate three-dimensional–to–two-dimensional surface area ratios had significantly more bacteria attached to them than implants with low or minimal three-dimensional–to–two-dimensional surface area ratios ($p < 0.001$), and although Silimed polyurethane implants had more bacteria attached to them, this was not significantly different from implants with intermediate profiles (Fig. 6, *above*). Within the salt-loss–produced implants, roughly double the number of *S. epidermidis* attached to Nagor Nagotex implants ($p < 0.4$). At 24 hours, the number of bacteria attached to the smooth implant shell was no different from the number attached to implants with a low or minimal profile ($p > 0.07$); however, it was significantly less than the number of bacteria attached to implants with intermediate to high profiles ($p < 0.001$). Over time, the number of bacteria attached to implants was positively correlated with the three-dimensional–to–two-dimensional surface area ratio; the higher the three-dimensional–to–two-dimensional surface area ratio, the more bacteria that were attached ($R = 0.64$; $p < 0.001$).

S. aureus

Figure 6, *below*, shows the number of *S. aureus* attached to different types of silicone implant outer shells at 24 hours. Silimed polyurethane implants had significantly more bacteria attached to them than any other implant ($p < 0.05$), whereas smooth implants (i.e., Mentor, Sientra, and Allergan) had significantly fewer bacteria attached to them than any other implant ($p < 0.001$) except Mentor Siltex ($p = 0.4$). There was no significant difference in the number of bacteria that attached to the three salt-loss implants. The number of bacteria attached to implants was positively correlated with the three-dimensional–to–two-dimensional surface area ratio; the higher the three-dimensional–to–two-dimensional surface area ratio, the more bacteria that were attached ($R = 0.75$; $p < 0.001$).

P. aeruginosa

Figure 7, *above*, shows the number of *P. aeruginosa* attached to differing implant shells at 24 hours. The maximum number of bacteria attached to Silimed polyurethane implants, followed by Polytech POLYtxt, and the Biocell implant produced by salt loss. The other two salt-loss implants, Eurosilicone textured and Nagor Nagotex, had

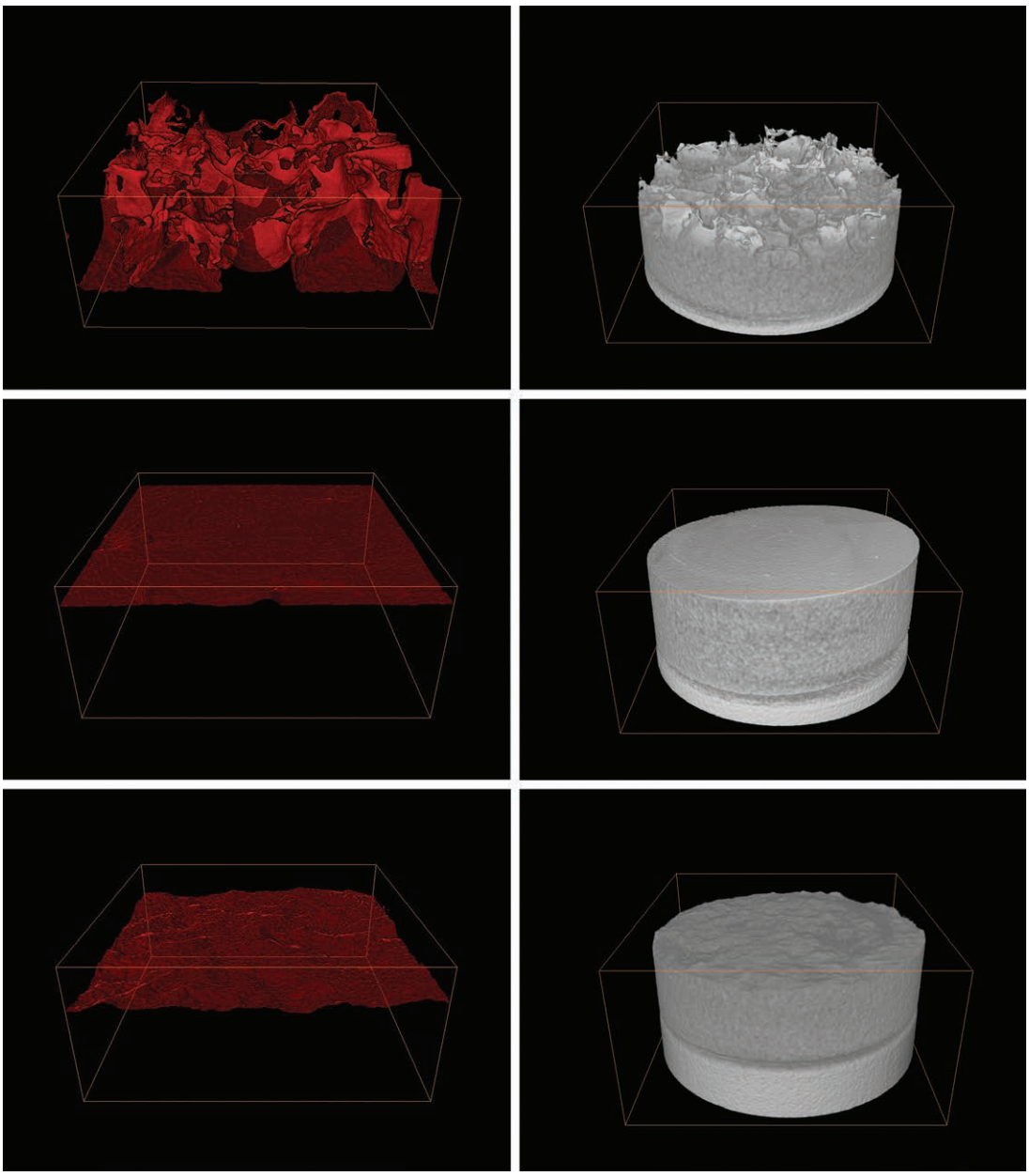


Fig. 2. Samples of three-dimensional cross-sections: extraction (*left*), and gray-scale reconstruction (*right*) from micro–computed tomographic analysis used for measurement of surface area/roughness. (*Above*) Allergan Biocell. (*Center*) Mentor Smooth. (*Below*) Motiva VelvetSurface.

less bacteria attached at 24 hours, but this was not significantly different from the numbers attached to the Biocell implant ($p > 0.09$). The number of bacteria attached to implants was positively correlated with the three-dimensional–to–two-dimensional surface area ratio; the higher the three-dimensional–to–two-dimensional surface area ratio, the more bacteria that were attached ($R = 0.81$; $p < 0.001$). Significantly fewer bacteria grew on smooth implants compared with all other implants ($p < 0.001$). In contrast to the findings for staphylococcal species, significantly fewer bacteria attached to Motiva VelvetSurface implants compared with Motiva SilkSurface implants ($p = 0.008$); the number was significantly less than for all of the other implants ($p < 0.001$).

R. pickettii

Figure 7, *below*, shows the number of *R. pickettii* attached to the different types of silicone outer shell at 24 hours. Only Silimed polyurethane, Biocell, and Nagor Nagotex had significantly more bacteria attached than smooth implants

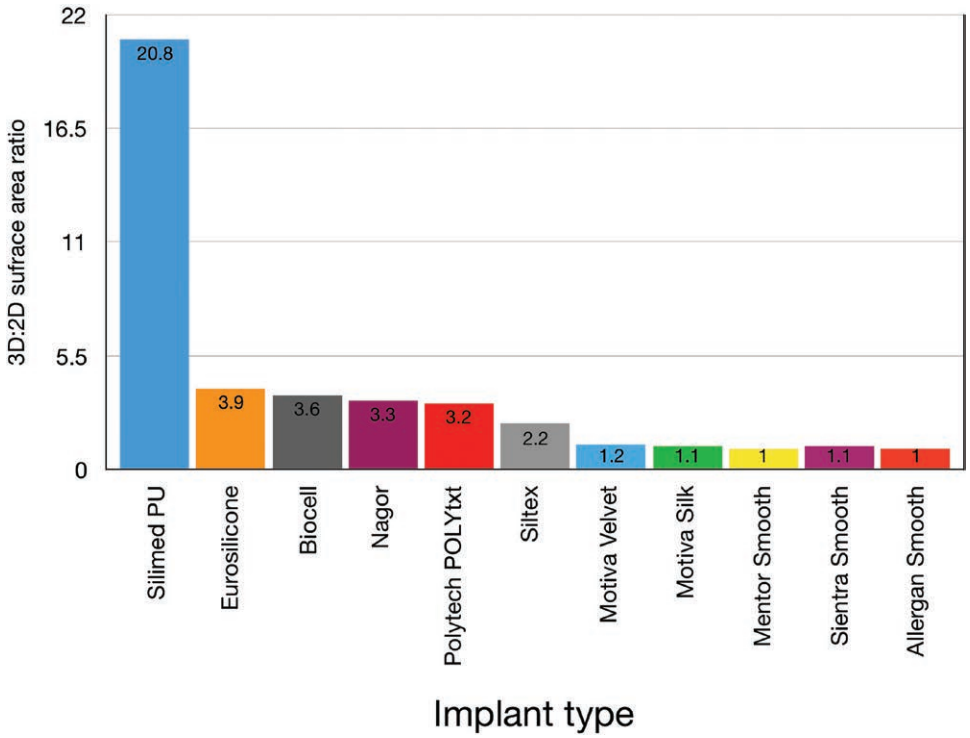
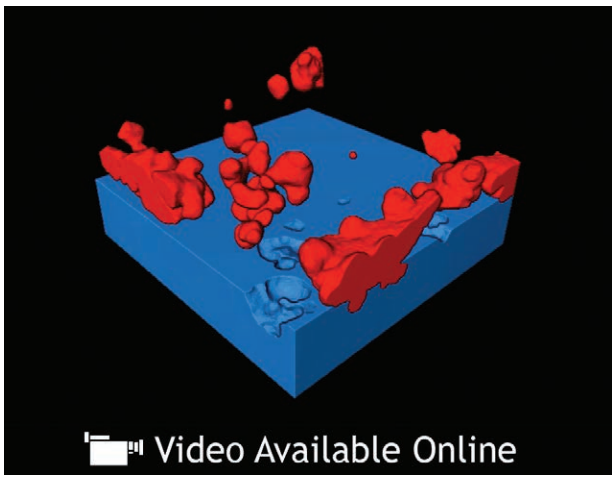


Fig. 3. Three-dimensional–to–two-dimensional surface area ratios (*3D:2D*) for various implant types studied. *PU*, polyurethane.

($p < 0.001$). There was no significant difference in the number of bacteria attached to the three salt-loss–produced implants. The number of bacteria attached to implants was positively correlated with the three-dimensional–to–two-dimensional surface area ratio; the higher the three-dimensional–to–two-dimensional surface area ratio, the more bacteria that were attached ($R = 0.87$; $p < 0.001$).



Video. Supplemental Digital Content 7 shows real-time demonstration of caves (sequestered surface area) for Polytech POLYtxt colored red on three-dimensional reconstruction, ***http://links.lww.com/PRS/C962***.

Combined Categories

Figure 8 summarizes the proposed surface classification based on combining surface area with surface roughness. The surface grade can then be combined with a nomenclature to define fill, surface, shape, and size of the implant. Table 4 summarizes the proposed classification. A Cohesive Gel 410 Allergan Biocell Anatomic 330-cc implant, for example, would be classified as GF4A330.

DISCUSSION

These findings support the use of a new classification system for implant outer shells based on measurable parameters of surface area and

Table 3. Surface Roughness for Each Implant Type

Implant Type	Surface Roughness	SD
Silimed polyurethane	277.6	32.5
Eurosilicone textured	111.7	24.9
Allergan Biocell	91.7	13.9
Nagor Nagotex	60.9	12.3
Polytech POLYtxt	58.8	19.2
Mentor Siltex	51.4	12.1
Motiva VelvetSurface	12.9	1.7
Motiva SilkSurface	20.1	0.3
Allergan Smooth	8.5	1.4
Sientra Smooth	8.1	0.8
Mentor Smooth	2.1	0.9

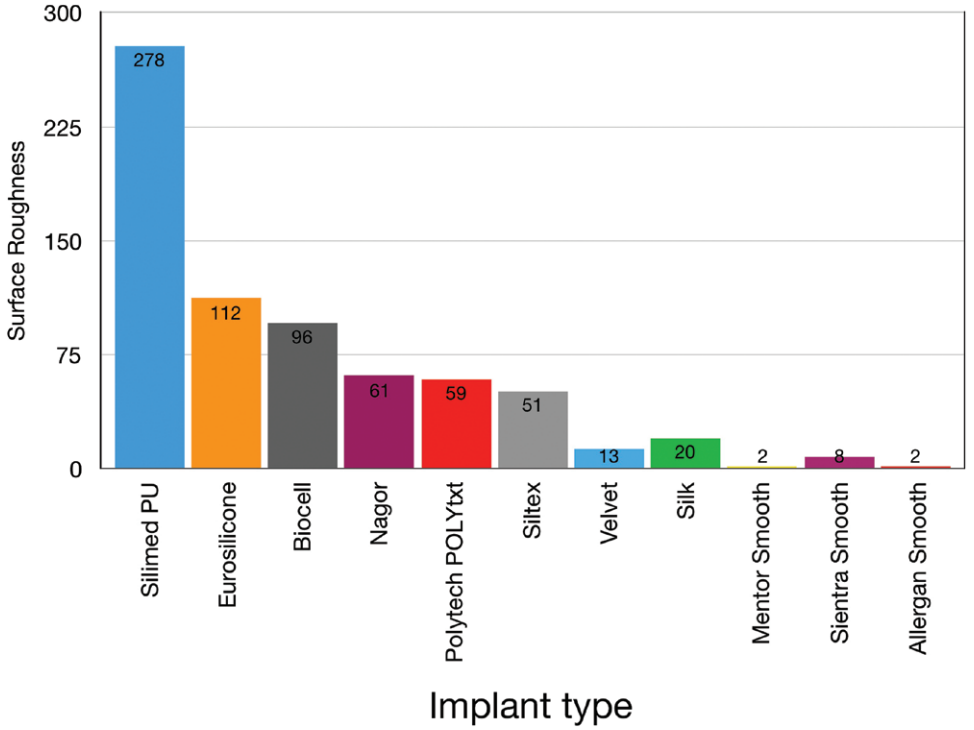


Fig. 4. Surface roughness for various implants studied. *PU*, polyurethane; *error bars* = SD.

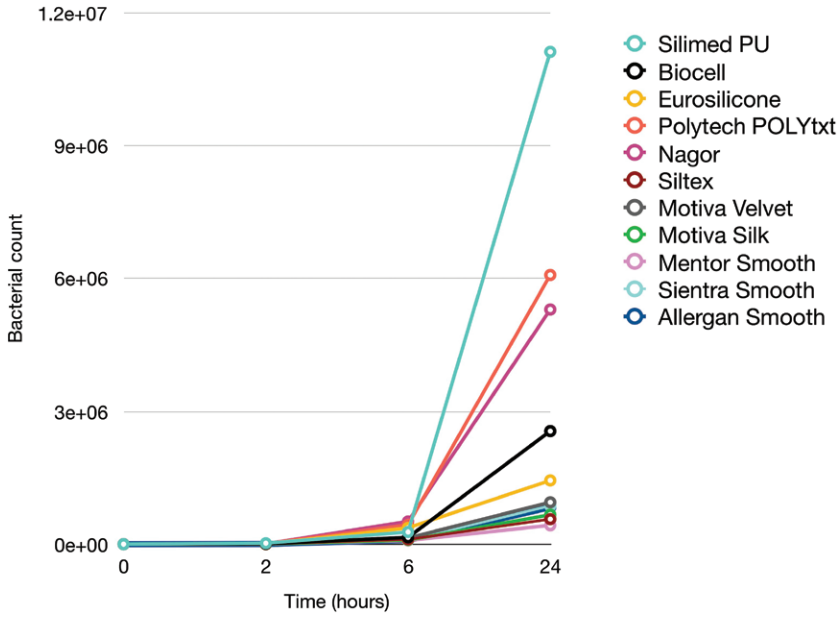


Fig. 5. *S. epidermidis* attachment and growth on various implants shells measured at 0, 2, 6, and 24 hours.

roughness that correlate with bacterial growth. We now propose a classification of implant surfaces into four grades (high, intermediate, low, and minimal) based on the direct measurement of their surface area and roughness.

Analysis of bacterial growth over varying implant surfaces showed a significant correlation, with the three-dimensional–to–two-dimensional surface area ratio demonstrating a linear relationship of bacterial attachment and growth as the surface area ratio increased. Figure 5 confirms the exponential growth rates for higher surface area textured implants for *S. epidermidis* we have reported previously.[19] The Silimed polyurethane

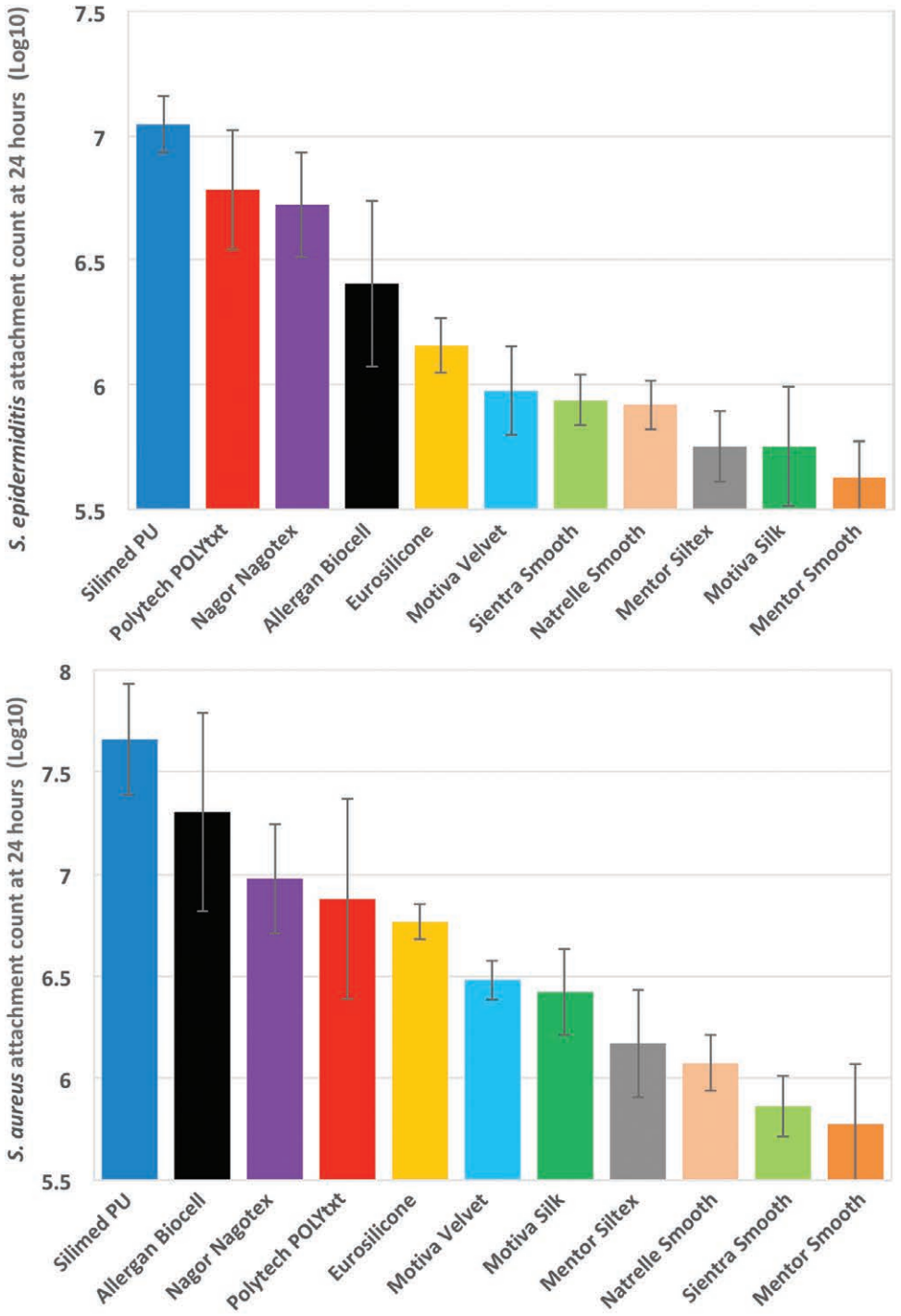


Fig. 6. Twenty-four–hour attachment and growth of bacteria on various implant shells. (*Above*) *S. epidermidis* attachment and growth on various implant shells measured at 24 hours. (*Below*) *S. aureus* attachment and growth on various implant shells measured at 24 hours. *PU*, polyurethane.

texture grew significantly higher numbers of bacteria for all species at 24 hours. Interestingly, the intermediate-surface-area implants showed good correlation and were no different from the high-surface-area implants for *S. epidermidis* and *P. aeruginosa*. These prolific biofilm formers may well overwhelm the surface area available and reach maximal growth capacity earlier than other species. These species and surface differences for intermediate/low texture require further investigation and may relate to the available surface area, specific bacterial cell size, motility, and capacity to

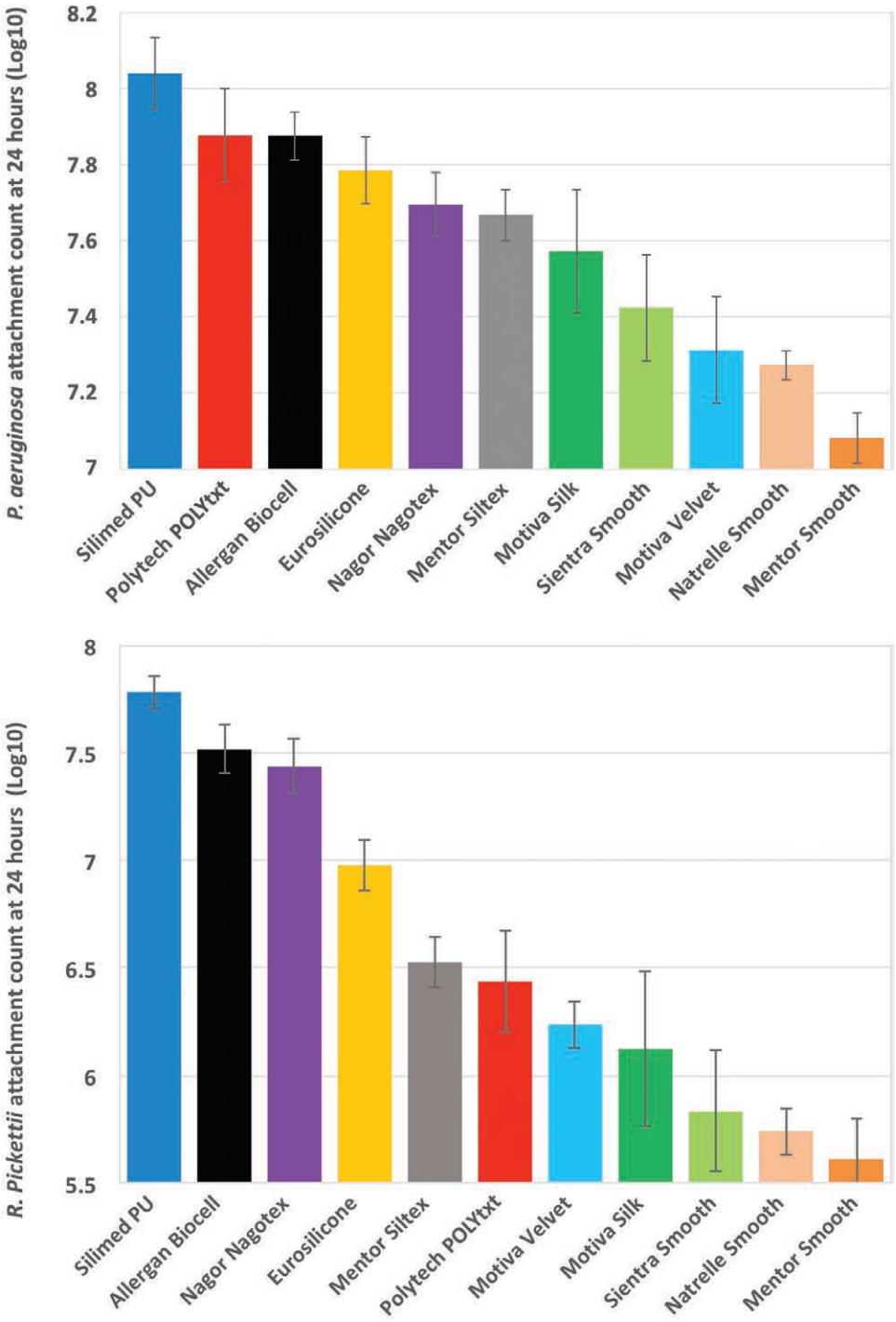


Fig. 7. Twenty-four–hour attachment and growth of bacteria on various implant shells. (*Above*) *P. aeruginosa* attachment and growth on various implant shells measured at 24 hours. (*Below*) *R. pickettii* attachment and growth on various implant shells measured at 24 hours. *PU*, polyurethane.

form biofilm together with environmental factors and availability of nutrition.

The Polytech POLYtxt surface showed a high proportion of hidden surface area (caves) within the substance of the texture. These were either walled off entirely from the external environment or had very narrow choke zones to reduce the passage of bacteria and/or host cells. This may also explain higher growth for some species for this texture. Atlan et al.[23] have used similar measurement techniques and demonstrated variation in texture morphology on different sites of the same

Process	Polyurethane foam	Salt Loss (Biocell/ Eurosilicone)	Vulcanisation	Salt Loss (Nagotex)	Imprinting	Smooth/Nano
Surface Area	High	Intermediate	Intermediate	Low	Low	Minimal
Roughness	High	Intermediate	Low	Low	Low	Minimal
SURFACE TYPE	4	3	3	2	2	1

Fig. 8. Implant surface classification relating manufacturing method, surface area, and surface roughness.

implant. This was beyond the scope of this study but will be the subject of future bacterial attachment analysis.

Previously published morphologic analyses of breast implant outer shells have used confocal microscopy,[24–26] scanning electron microscopy,[25] and/or light microscopy[26] and wettability[25] to classify implant surfaces. We have previously used these techniques[21] but found significant errors when examining higher thickness implant textures with loss of resolution in deeper zones. The use of the micro–computed tomography method has allowed a more accurate morphologic assessment of the entire implant shell. These authors have also used fibroblast adhesion and/or macrophage activation as surrogate markers for predictors of tissue incorporation and reduction in capsular contracture.[25] Although these in vitro factors may be important, they have yet to translate into proven clinical benefit; thus, their functional significance will need to be validated by clinical studies.

Table 4. Proposed Generic Breast Implant Classification Based on Fill, Surface, Shape, and Size

Characteristic	Definition
Fill	
GF	Gel filled
S	Saline filled
A	Part air filled
Surface area	
4	High
3	Intermediate
2	Low
1	Minimal
Shape	
A	Anatomical
R	Round
Size	In cubic centimeters (cc)

The presence of bacteria, by contrast, on the surface of implants has been shown to be a significant potentiator for the formation of capsular contracture in clinical and laboratory studies.[19,27,28] Clinical correlation has confirmed a significant correlation of bacterial contamination with increasing grade of capsular contracture.[29] In patients with high-grade capsular contracture, polyurethane texture was also shown to support a significantly higher load of bacteria compared with other textured implants.[20] Furthermore, translational research has now supported the use of antibacterial mitigation to reduce capsular contracture, thus linking the surface area/bacterial growth relationship directly to a functional clinical outcome.[30,31]

We are not claiming that textured implants cause more contracture, as is often suggested in commentaries critiquing our previous findings. Surface texture provides a dual opportunity for

better host tissue incorporation but also, unfortunately, for bacterial growth and proliferation. In the event that bacterial contamination is kept low, the advantages of a textured surface may well promote better long-term results. High-quality clinical comparative studies are still required to confirm this finding. It is also likely that factors other than implant texture alone have a suppressive effect on the development of biofilm and subsequent capsular contracture, including antibacterial pocket irrigation, prophylactic antibiotic use, avoidance of contamination, anatomical pocket location, and careful atraumatic dissection of the breast pocket.[27,32] Strategies to prevent contamination of the implant as it is placed help to reduce the numbers of bacteria and keep the contamination below threshold.[33] This underscores the importance of overall bacterial load on breast implants that ultimately drives the clinical outcome.

More recently, an antigen driver for breast implant–associated ALCL has been proposed. This along with surface texture, patient genetics, and time form the unifying hypothesis that explains both observed biology and epidemiology of breast implant–associated ALCL.[21] The propensity for high- and intermediate-surface-area textured implants to cause breast implant–associated ALCL is 10 times higher than for low-surface-area texture and is consistent with these data.[21] The need for a biological antigen to drive carcinogenesis indicates that it is likely that bacterial proteins rather than inert silicone particles initiate the stimulation and transformation of T cells.[34] The pathway from bacterial antigen stimulation to lymphoma has been proven for *Helicobacter pylori*, gastric mucosa-associated lymphoid tissue lymphoma, and gastric cancer.[35] Understanding the interaction among genes, the microbiome, and immunity may well provide new approaches to both the treatment and prevention of cancer.

CONCLUSIONS

We support the use of a novel and functional classification of implant outer shells based on objective measurement into four degrees of surface texture: high, intermediate, low, and minimal. The correlation of surface area/roughness with propensity for bacterial growth links this classification to a functional outcome and strengthens its validity as a tool to help surgeons to select the optimal implant surface for both breast augmentation and reconstruction.

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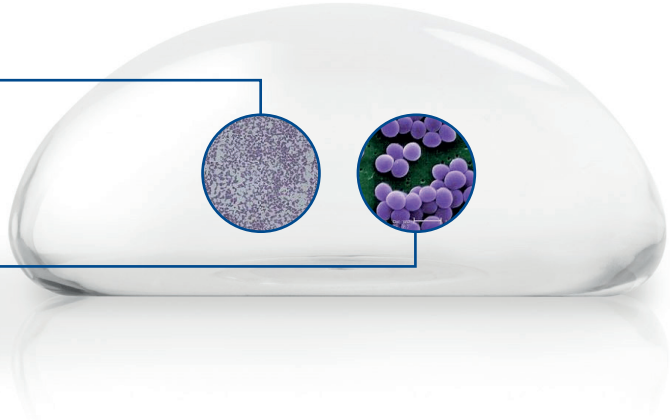
Neuere klinische Studien haben hinsichtlich der Verwendung von glatten Brustimplantaten eine signifikante Korrelation zwischen bakterieller Kontamination und höheren Kapselkontrakturraten aufgezeigt.[1]

Staphylococcus epidermidis ist die primäre Ursache einer Kapselkontraktur[3]

Staphylococcus aureus ist eine der häufigsten Infektionsursachen[3]



Nicht alle glatten Implantate sind gleich![1*]

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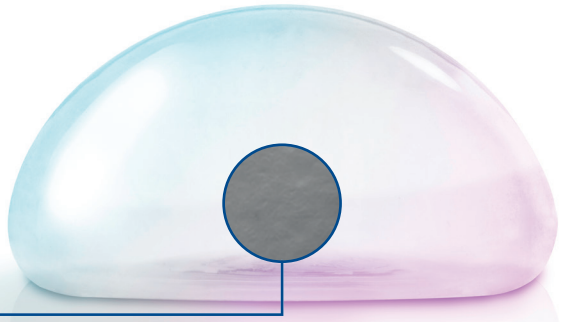
Mentor® MemoryGel™ Xtra

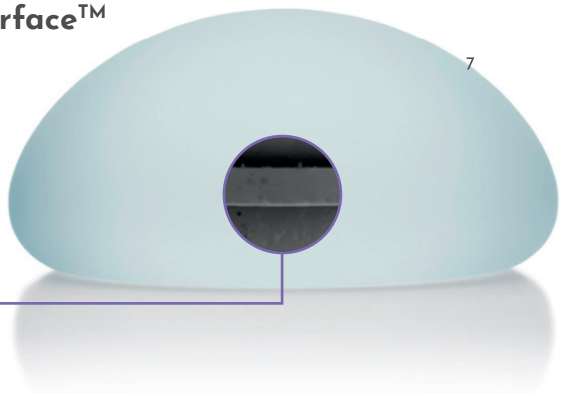
- Weniger Bakterienwachstum[1**]
- Geringe Oberflächenstruktur und Rauheit[1**]
- 1 % Fehlpositionierung nach 10 Jahren[¥5]
- Niedrigstes mit Staphylococcus epidermidis assoziiertes Komplikationsrisiko[2**]
- Herstellung der Implantathülle im automatisierten Dipping-Verfahren[8]



Motiva®

Motiva Implants® SilkSurface™

- Höheres Bakterienwachstum als mit Mentor® Smooth[1]
- 5,6 % Fehlpositionierung nach 1 Jahr[6]
- Keine veröffentlichten klinischen Langzeitdaten
- Herstellung der Implantathülle im manuellen Dipping-Verfahren



¥ Kaplan-Meier-Schätzung: Risiko für erstes Eintreten. MemoryGel™ Kernstudien
* Untersuchte Bakterien: S. epidermidis, S. aureus, P. aeruginosa, R. pickettii. Versus Silimed mit Polyurethan-Beschichtung, Eurosilicone™ texturiert, Allergan® Biocell®, Nagor™ Nagotex®, Polytech POLYtxt®, Mentor® Siltex™, Motiva Implants® VelvetSurface™, Motiva Implants® SilkSurface®, Allergan® glatt, Sientra® glatt, Mentor® glatt.
** Versus Silimed Polyurethan, Eurosilicone™ texturiert, Allergan® Biocell®, Nagor™ Nagotex®, Polytech POLYtxt®, Mentor® Siltex™, Motiva Implants® VelvetSurface™, Motiva Implants® SilkSurface®, Sientra® glatt, Mentor® glatt.

Mentor® Implantaten können Sie vertrauen, Wie sieht es mit den Mitbewerberprodukten aus?

Mentor, nachweislich zuverlässig mit erstklassigen klinischen Langzeitergebnissen:

10 *Jahre*

NIEDRIGSTE RATE DER HÄUFIGSTEN KOMPLIKATIONEN[5]

Niedrigste 10-Jahres-Rate der häufigsten Komplikationen[5]

MITTELS **MRT** DIAGNOSTIZIERTE IMPLANTATRUPTUR

MEHR ALS **1.000** PATIENTINNEN

Unabhängige Multicenter-Kernstudie der Evidenzstufe 2 mit mehr als 1.000 Patientinnen

5.2% KAPSEL-FIBROSERATE NACH **10 *Jahren***

Kapselfibroserate von 5,2 % nach 10 Jahren, untersucht wurden 614 Patientinnen mit glatten Implantaten und submuskulärer primärer Brustaugmentation

Literatur

1. Jones P, et al. The Functional Influence of Breast Implant Outer Shell Morphology on Bacterial Attachment and Growth. Plast. Reconstr. Surg. 142: 837, 2018.
2. Agnello, M, et al. Association of Microbial Growth on Silicone Breast Implants with Capsular Contracture: A Systematic Review. Journal of Aesthetic & Reconstruction Surgery. ISSN 2472-1905, 2015. Jones P, et al. The Functional Influence of Breast Implant Outer Shell Morphology on Bacterial Attachment and Growth. Plast. Reconstr. Surg. 142: 837, 2018.
3. Tony Y.C, Steven, et al. Staphylococcus aureus Infections: Epidemiology, Pathophysiology, Clinical Manifestations, and Management. American Society for Microbiology. 2015; 10.1128/CMR.00134-14.
4. Mentor Worldwide LLC. MemoryGel™ Clinical Study Final Report, April 2013
5. Not a head to head clinical study. Based on a comparison of 10 year core clinical study data for Primary Augmentation, Revision Augmentation, and Primary Reconstruction for MENTOR® MemoryGel® Breast Implants and NATRELLE™ Round TruForm1 Gel Breast Implants. a) Spear, Scott, et all. Natrelle Round Silicone Breast Implants: Core Study Results at 10 Years. Plas. Reconstr. Surg. 2014;133(6):1354-1361 b) Health Canada: Summary Basis of Decision (SBD) for Natrelle™ Highly Cohesive Silicone Filled Breast Implants. Application No. 88573. License No.72262. Date Issued: 2014/01/17. c) Health Canada: Summary Basis of Decision (SBD) for Natrelle™ Silicone Filled Breast Implants Smooth Shell With Barrier and Natrelle(TM) Silicone Filled Breast Implants Textured Shell with Barrier Layer. Application No. 61865 and 60524 License No License No 72264 and 72263. Date Issued: 2012/09/25.
6. Huemer G, et al. Motiva Ergonomix Round SilkSurface Silicone Breast Impants: Outcome Analysis of 100 Primary Breast Augmentations over 3 Years and Technical Considerations. Plast. Reconstr. Surg. 141:831e, 2018.
7. Atlan M, et al. Breast Implant Surface Texture Impacts Host Tissue Response. Journal of the Mechanical Behavior of Biomedical Materials, 88: 377-388, 2018.
8. Mentor Worldwide LLC. TX820_130420_01

Wichtige Sicherheitsinformationen: MENTOR® Brustimplantate sind für Brustvergrößerungen bei Frauen ab 18 Jahren und für Brustrekonstruktionen bestimmt. Bei Frauen mit einer aktiven Infektion im Körper, mit Brustkrebs oder einer Vorstufe davon, die diesbezüglich noch keine adäquate Behandlung erhalten haben, sowie bei schwangeren und stillenden Frauen sollte keine Brustimplantat-OP durchgeführt werden. Es bestehen Risiken im Zusammenhang mit einer Brustimplantat-OP. Brustimplantate haben eine begrenzte Lebensdauer und eine Brustimplantat-OP umfasst möglicherweise mehrere Eingriffe. Zu den häufigsten Komplikationen im Zusammenhang mit den MENTOR® MemoryGel® Brustimplantaten zählen Revisionseingriffe, die Implantatentfernung, eine Kapselkontraktur, Asymmetrie und Brustschmerzen. Eine seltenere Komplikation stellt die Implantatruptur dar, die häufig unauffällig verläuft. Welche gesundheitlichen Folgen die Ruptur eines mit Silikongel gefüllten Brustimplantats hat, wurde noch nicht vollständig untersucht. Es wird empfohlen, nach dem Implantationseingriff regelmäßig eine bildgebende Untersuchung wie etwa Mammographie, MRT oder Ultraschall durchzuführen, um eine mögliche Implantatruptur feststellen zu können. Ihre Patientin muss über die Risiken und den Nutzen von Brustimplantaten informiert werden und diese verstehen, und sie muss die Möglichkeit erhalten, ein Beratungsgespräch mit Ihnen zu führen, bevor sie eine Entscheidung bezüglich der Operation trifft. Ausführliche Indikationen, Kontraindikationen, Warnhinweise und Vorsichtsmaßnahmen im Zusammenhang mit der Verwendung sämtlicher MENTOR® Implantate finden Sie im jeweiligen Produktdatenblatt, das mit jedem Produkt mitgeliefert wird, und in den wichtigen Sicherheitsinformationen, die Sie auf der Seite www.mentorwwllc.eu finden. Zu den häufigsten Komplikationen im Zusammenhang mit der Brustvergrößerung mit MemoryGel™ Implantaten zählen Revisionseingriffe, eine Kapselkontraktur, verminderte oder erhöhtes Empfindungsvermögen in der Brustwarze, die Implantatentfernung mit oder ohne Erneuerung. Zu den häufigsten Komplikationen im Zusammenhang mit einer Brutsvergrößerung mit CPG™ Implantaten zählen Revisionseingriffe, die Implantatentfernung mit oder ohne Erneuerung und Ptosis. Eine seltenere Komplikation stellt die Implantatruptur dar. Welche gesundheitlichen Folgen die Ruptur eines mit Silikongel gefüllten Brustimplantats hat, wurde noch nicht vollständig untersucht. Die gesundheitlichen Folgen nach Ruptur eines gelgefüllten Silikon-Brustimplantats sind nicht vollständig bekannt. Es wird empfohlen, 3 Jahre nach dem Implantationseingriff und danach alle zwei Jahre eine MRT-Untersuchung durchzuführen, um eine mögliche Implantatruptur feststellen zu können.

www.mentorwwllc.de
Dieses Dokument ist nicht zur Verteilung in Ländern außerhalb der Region EMEA bestimmt.

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Evidenzbasierte Einschätzung zu Rupturen

Die Ruptur ist eine seit langem bekannte Komplikation von Brustimplantaten, und ihr Risiko nimmt zu, je länger die Implantation zurückliegt.[1] In der Kernstudie zu MemoryGel® Brustimplantaten betrug die mittels Kaplan-Meier-Schätzer ermittelte kumulative Rate der bestätigen Rupturen in der MRT-Kohorte mit Primäraugmentation nach 10 Jahren 9,8 %.[2] Die 10-jährige Kernstudie belegt die Sicherheit und Wirksamkeit der MemoryGel® Brustimplantate. Ebenfalls nennenswert ist, dass im Fall einer Ruptur, MemoryGel Brustimplantate durch eine lebenslange Austauschpolitik abgedeckt sind.[3]

Auszug aus der FDA Executive Summary von 2019: Brustimplantate – Sonderthemen

Es wurden die Rupturdaten aus den 10-jährigen Kernstudien zu Silikonimplantaten von Allergan, Mentor und Sientra analysiert. Aufgrund der Unterschiede bei den Methoden, mit denen die Rupturen festgestellt und bestätigt wurden, der Art der erhobenen Daten, der Dauer und Häufigkeit der Nachbeobachtung der Patientinnen sowie den Methoden der Analyse und Darstellung der Daten sind Vergleiche zwischen den Herstellern nur sehr begrenzt möglich.

Den Ergebnissen der abgeschlossenen Kernstudien von Allergan und Mentor zufolge wurde in den MRT- und den Nicht-MRT-Kohorten eine ähnliche Anzahl von stummen und symptomatischen Rupturen festgestellt. Aufgrund des Designs der Sientra-Studie war es nicht möglich, eine zum Vergleich geeignete Zahl stummer und symptomatischer Rupturen in den MRT- und Nicht-MRT-Kohorten zu bestimmen.[4]

Rupturdaten aus der Kernstudie zu MemoryGel® Brustimplantaten nach Patientin

9,8%

Mittels Kaplan-Meier-Schätzer ermittelte Rate bestätigter Rupturen nach 10 Jahren*[2]

* 11 bestätigte Rupturen, unter insgesamt 202 Patientinnen in der MRT-Kohorte der Studiensubgruppe mit Primäraugmentation.[5,6]
Bestätigte Rupturen wurden durch Untersuchungen des Implantats bei Patientinnen, die das Implantat entfernen ließen, abgesichert.

Interpretation von Schätzungen nach Kaplan-Meier

Schätzungen nach Kaplan-Meier (KM) werden zwar in vielen Studien angegeben, allerdings kann die Genauigkeit von Kaplan-Meier-Analysen durch mehrere statistische Faktoren beeinflusst werden. Die kumulative Inzidenz der Rupturen nimmt im Lauf der Zeit zu; daher muss jede aussagekräftige Berechnung die Dauer der Nachbeobachtung berücksichtigen. In der klinischen Kernstudie zu MENTOR® MemoryGel® beispielsweise wurden 202 Patientinnen mit Primäraugmentation (PA) in die MRT-Kohorte aufgenommen, und die Nachbeobachtungsrate betrug 46 %.
Die mittels Kaplan-Meier-Schätzer ermittelte Rate bestätigter Rupturen von 9,8 % ist eine zuverlässigere Angabe als die mittels Kaplan-Meier-Schätzer ermittelte Rate vermuteter oder bestätigter Rupturen von 24,2 % bei Primäraugmentations-Patientinnen, da bestätigte Rupturen durch physische Untersuchung des Implantats nach der Explantation als Rupturen gesichert sind.[1,5]

Klinische Kernstudie zu MemoryGel®: Vermutete vs. bestätigte Ruptur		
	24.2%*	9.8%†
Kaplan-Meier	✓	✓
Pro Patientin	✓	✓
MRT-Kohorte	✓	✓
Primäraugmentation	✓	✓
46 % nachbeobachtet	✓	✓
	Vermutet und bestätigt	Nur bestätigt

* 25 vermutete oder bestätigte Rupturen, nach Patientin, unter insgesamt 202 Patientinnen[5]
† 11 vermutete oder bestätigte Rupturen, nach Patientin, unter insgesamt 202 Patientinnen[5,6]
Vermutete Rupturen sind solche, die im MRT als mögliche Rupturen erkannt wurden, jedoch nicht durch physische Untersuchung der explantierten Implantate bestätigt wurden, da sich die Patientinnen häufig dafür entschieden, diese Implantate nicht entfernen zu lassen.
Bestätigte Rupturen wurden durch Untersuchung des Implantats bei Patientinnen, die das Implantat entfernen ließen, abgesichert.

Fazit

Es gibt mehrere Methoden zur Berechnung von Langzeit-Rupturraten, und bei der Bewertung eines Produkts müssen die verschiedenen Methoden berücksichtigt werden. Wie unsere klinischen Langzeitdaten belegen, haben sich MemoryGel® Brustimplantate als sichere und zuverlässige Wahl für Millionen von Frauen erwiesen.

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3. MentorPromise Protection Plan Terms & Conditions 2017.
4. FDA Executive Summary: Breast Implant Special Topics. Advisory Panel March 25 & 26, 2019.
5. Mentor Worldwide LLC. MemoryGel® Breast Implants Mentor Worldwide LLC. 10-Year Core Gel Clinical Study Final Report. April 2013.
6. Mentor MemoryGel Rupture Stats Confirmed and Iatrogenic, Reported January 2020.

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Evidenzbasierte Perspektive
BRUSTIMPLANTAT-ASSOZIIERTES ANAPLASTISCHES GROSSZELLIGES LYMPHOM

Hintergrund im Überblick

- BIA-ALCL ist ein seltenes T-Zell-Lymphom mit ALCL-Zellen (CD30+ / ALK-), die in der Seromflüssigkeit oder der fibrösen Kapsel um das Brustimplantat gefunden werden[1]
- Zeigt sich meist (ca. 80 %) als Spätstadium-Serom (Erguss) etwa 8–10 Jahre nach der Implantation; in ca. 30 % der Fälle zeigt sich ein Geschwulst neben einem Implantat[1]
- Im Allgemeinen gute Prognose bei frühzeitiger Diagnose, wenn die gesamte Kapsel und das Implantat entfernt werden[1]
- Nur bei Patientinnen mit einer Vorgeschichte von texturierten Implantaten gab es bislang Fälle von BIA-ALCL. Das Risiko ist je nach Art der Textur unterschiedlich[2]
- Bis November 2019 wurden keine Fälle gemeldet, die mit MENTOR® SILTEX® Brustgewebe-Expandern in Zusammenhang gebracht wurden.
- Weitere Informationen zu Diagnose und Behandlung finden Sie in den "2020 NCCN Consensus Guidelines on the Diagnosis and Treatment of BIA-ALCL"[3]
- In der neueren Literatur wird die Entnahme von 12 Biopsien/Kapsel empfohlen, um das Vorhandensein eines BIA-ALCL mit über 95-%iger Sicherheit auszuschließen.[4]
- Es wird dringend empfohlen, alle vermuteten und bestätigten Fälle von BIA-ALCL in das PROFILE Registry, beim Hersteller und bei den Gesundheitsbehörden zu melden[5]

Bekannt ist, dass BIA-ALCL auf T-Zellen zurückzuführen ist, jedoch ist die Ätiologie nach wie vor ungeklärt[6]

Die derzeitigen Hypothesen umfassen:

- Implantat-Oberfläche[7]
- Genetische Veranlagung[8]
- Chronische Entzündung durch gramnegative Biofilme[9]
- Stimulation des Aryl-Hydrocarbon-Rezeptors (AhR)[10]
- Chronische Irritation im Laufe der Zeit[11]
- Partikel in der Brustimplantatkapsel[12]

Obwohl MENTOR® Brustimplantate eine geringe BIA-ALCL-Quote aufweisen, nehmen wir das Problem ernst. Wir arbeiten mit Branchengruppen, Medizinern, Wissenschaftlern und Gesundheitsbehörden zusammen, um die entsprechenden Risiken und Ursachen dieser Art von Lymphomen besser zu verstehen. Bitte zögern Sie nicht, einen Fall von BIA-ALCL in Zusammenhang mit Mentor-Brustimplantaten auch bei uns zu melden und die Explantate, nach der Untersuchung in der Pathologie, an uns weiterzuleiten.

Wie häufig ist BIA-ALCL?

Stand: 24.April 2020
→ 322 vermutete oder bestätigte BIA-ALCL-Fälle in den Vereinigten Staaten und 903 BIA-ALCL-Fälle weltweit bei allen Herstellern.[13]

Zum Vergleich: Weltweit erhalten jedes Jahr schätzungsweise 1,5 Millionen Patientinnen Brustimplantate.[14]

Dem BfArM liegen zurzeit 30 gemeldete Fälle von Brustimplantat-assoziiertem anaplastischem großzelligem Lymphom (BIA-ALCL) aus Deutschland vor.[25]

Das Risiko von BIA-ALCL für 4 Implantattypen, basierend auf Verkaufsdaten und Einzelimplantatexposition. Dargestellt sind Mittelwert und 95%-Konfidenzintervalle.[18]

Implantat		Mittelwert der Implantatverkäufe pro Einzelfall von BIA-ALCL (95% KI)		Rate pro 10.000 Implantatjahren (95% KI)
Silimed PU	95% CI	2596	(1486-5024)	**0.59** (0.30-1.02)
Biocell	95% CI	3194	(2387-4379)	**0.38** (0.27-0.50)
Nagor	95% CI	6024	(2768-16417)	**0.22** (0.08-0.47)
Siltex	95% CI	36730	(12568-178107)	**0.050** (0.010-0.147)

Unterschiede bei der Implantat-Texturierung:

- Die Implantat-Texturierungsverfahren sind von Hersteller zu Hersteller verschieden, was zu unterschiedlichen klinischen Ergebnissen in Bezug auf Gewebeanhaftung, Stabilität in der Brusttasche und Inzidenz von BIA-ALCL führt[15]
- Mehrere Studien haben gezeigt, dass die Zahl der BIA-ALCL-Fälle im Zusammenhang mit MENTOR® Brustimplantaten gegenüber anderen Herstellern[12], durchgehend niedrig ist[16-20]

Oberflächen-Charakterisierung:

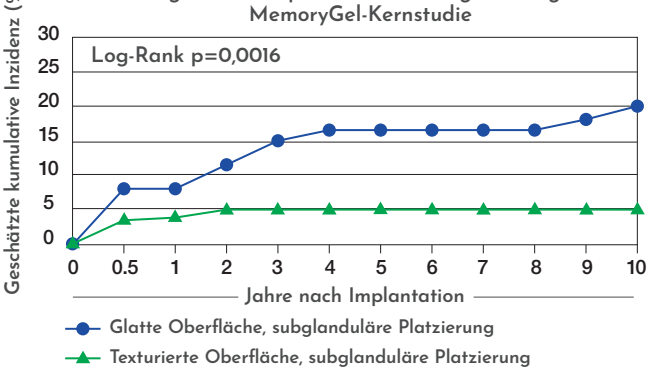
- Wie in einer neueren Studie[21] festgestellt wurde: „Obwohl die genaue Ätiologie des BIA-ALCL nach wie vor unbekannt und wahrscheinlich multifaktoriell bedingt ist, haben einige vorgeschlagen, dass das BIA-ALCL-Risiko nur auf der Grundlage verschiedener vorgeschlagener Klassifikationssysteme für die Oberflächentextur stratifiziert werden könne. Angesichts der unsicheren Ätiologie sind jedoch die bei weitem zuverlässigsten derzeit verfügbaren Informationen zum BIA-ALCL-Risiko die Langzeitdaten, die für bestimmte Implantate verfügbar sind, und nicht ein unterstelltes Risiko, das den verschiedenen, klinisch erst noch zu validierenden Klassifikationssystemen zugeordnet wird, in denen Implantate mit und ohne solche langfristigen Ergebnisinformationen zusammengefasst sind."
- Millionen von Frauen weltweit haben sich seit über 30 Jahren für Mentor Brustimplantate entschieden.
- Zusätzlich zu der oben erwähnten australischen Langzeitstudie sprechen für MENTOR® Brustimplantate langfristige klinische Daten, darunter drei prospektive klinische Studien, bei denen Patientinnen 10 Jahre lang beobachtet wurden*

* Summary of the Safety and Effectiveness of Mentor's MemoryGel® Silicone Gel-Filled Implants in Patients who are Undergoing Primary Breast Augmentation, Primary Breast Reconstruction, or Revision. 10-Year Core Gel Final Clinical Study Report. April 2013. Mentor Worldwide, LLC. MemoryShape™ Post-Approval Cohort Study (formerly Contour Profile Gel Core Study) Final Clinical Study Report. 02. Juni 2015. Bielefeld, B. A Prospective Clinical Study of Mentor Corporation Saline-filled Mammary Prosthesis, Siltex® Saline-filled Mammary Prosthesis, and Siltex® Saline-filled Postoperatively Adjustable Mammary Prosthesis (Spectrum™) for Augmentation Mammoplasty and Reconstruction Mammoplasty. 10. Nov. 1999.

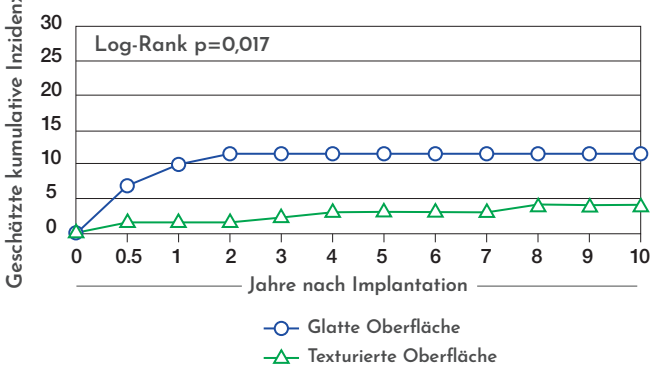
Vorteile texturierter Implantate:

- Die Vorteile von SILTEX® hinsichtlich einer Risikominderung im Vergleich zu glatten Implantaten wurden in der MemoryGel 10-Jahres-Kernstudie nachgewiesen[24]
  - o Bei Patientinnen, die sich einer subglandulären primären Brustvergrößerung unterzogen, war die Inzidenz von Kapselkontrakturen, die Revisionseingriffe erforderten, geringer (4,21 % ggü. 19,84 %; p= 0,0016)
  - o Bei Patientinnen, die sich einer primären Brustrekonstruktion unterzogen, war die Inzidenz von Asymmetrien, die Revisionseingriffe erforderten, geringer (3,88 % ggü. 11,10 %; p= 0,017)

Nach Kaplan-Meier geschätztes kumulatives Risiko einer Kapselkontraktur (Baker III/IV) mit Reoperation bei Patientinnen mit subglandulärer primärer Brustvergrößerung in der MemoryGel-Kernstudie



Nach Kaplan-Meier geschätztes kumulatives Risiko einer Asymmetrie mit Reoperation bei Patientinnen mit primärer Brustrekonstruktion in der MemoryGel-Kernstudie



Wo finde ich Quellen zu BIA-ALCL, Diagnose und Behandlung?

Quelle	Website
Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)	https://www.bfarm.de/SharedDocs/Risikoinformationen/Medizinprodukte/DE/Brustimplantate_ALCL_FDA.html
BfArM Formular – Meldung zum Brustimplantat-assoziierten anaplastischen großzelligen Lymphom	https://www.bfarm.de/SharedDocs/Formulare/DE/Medizinprodukte/BIA-ALCL-Meldung.pdf?__blob=publicationFile&v=3
Deutsche Gesellschaft der Plastischen, Rekonstruktiven und Ästhetischen Chirurgen (DGPRÄC)	https://www.dgpraec.de/patienten/sonderthemen/alcl/
Gesellschaft für Ästhetische Chirurgie Deutschland (GÄCD)	https://www.gacd.de/blog/details/wie-sicher-sind-brustimplantate-heute
Deutsche Gesellschaft für Ästhetisch-Plastische Chirurgie (DGÄPC)	https://www.dgaepc.de/bia-alcl/
Food & Drug Administration (FDA)	https://www.fda.gov/medical-devices/breast-implants/medical-device-reports-breast-implant-associated-anaplastic-large-cell-lymphoma
Vereinigung der Deutschen Ästhetisch-Plastischen Chirurgen (VDÄPC)	https://www.vdaepc.de/wp-content/uploads/2019/09/vdaepc-checkliste-brustimplantate.pdf

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1. HClemens, M.W., et al., Finding Consensus After Two Decades of Breast Implant-Associated Anaplastic Large Cell Lymphoma. Semin Plast Surg, 2019. 33(4): p. 270-278.
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Breast implant surface texture impacts host tissue response

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Highlights

- Surface texture characteristics of 12 breast implants differed qualitatively.
- The depth and complexity of textures allowed for groupings based on similarities.
- Similarity in surface area between textures resulted in similar capsular response.
- Classifying implants based on surface area features may help in implant choice.

Abstract

Background

Surface texture of a breast implant influences tissue response and ultimately device performance. Characterizing differences among available surface textures is important for predicting and optimizing performance.

Methods

Scanning electron microscopy (SEM) and X-ray computed tomography (CT)-imaging were used to characterize the topography and surface area of 12 unique breast implant surface textures from seven different manufacturers. Samples of these surface textures were implanted in rats, and tissue response was analyzed histologically. In separate experiments, the force required to separate host tissue from the implant surface texture was used as a measure of tissue adherence.

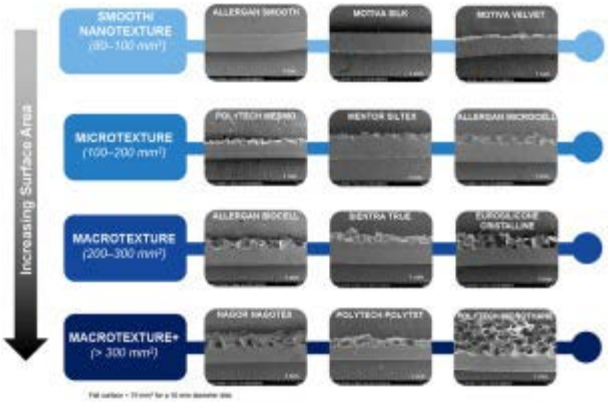
Results

SEM imaging of the top and cross section of the implant shells showed that the textures differed qualitatively in evenness of the surface, presence of pores, size and openness of the pores, and the depth of texturing. X-ray CT imaging reflected these differences, with the texture surface area of the anterior of the shells ranging from 85 to 551 mm^2, which was 8–602% greater than that of a flat surface. General similarities based on the physical structure of the surfaces were noted among groups of textures. In the rat models, with increasing surface texture complexity, there was increased capsule disorganization, tissue ingrowth, and tissue adherence.

Conclusions

Surface area and topography of breast implant textures are important factors contributing to tissue ingrowth and adherence. Based on surface area characteristics and measurements, it is possible to group the textures into four classifications: smooth/nanotexture (80–100 mm^2), microtexture (100–200 mm^2), macrotexture (200–300 mm^2), and macrotexture-plus (> 300 mm^2).

Graphical abstract



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Keywords

Breast implants; X-ray computed tomography; Scanning electron microscopy; Surface texture; Tissue adherence

1. Introduction

Breast implants are widely used for cosmetic augmentation and post-mastectomy breast reconstruction. Many types of breast implants are available that differ across a range of physical characteristics, such as shape, size, gel material, and surface texture (Atlan et al., 2016, Maxwell et al., 2014) and also differ in the chemical composition of implant components, such as the elastomer shell (Kappel et al., 2014). Selecting the appropriate implant among the many options depends on personal preferences of the physician and patient, and the desired aesthetic outcome. However, the physical characteristics of an implant may influence clinical performance and should be considered during the selection process. This is particularly true for implant surface texture, which plays a key role in shaping breast tissue response (Harvey et al., 2013).

Following implantation, the host tissue recognizes the breast

implant device as a foreign body and initiates an immune response that can result in formation of a collagen fiber capsule around the implant (Efanov et al., 2017, Sheikh et al., 2015). Capsule formation is a normal tissue response but can become problematic when the capsule contracts around the implant, making the breast hard and deformed, a complication known as capsular contracture (Hakelius and Ohlsen, 1992). It is thought that collagen fiber alignment plays a key role in capsular contracture, and that disruption of such fiber alignment may lead to reductions in the incidence and severity of capsular contracture (Bui et al., 2015). The surface texture of the breast implant can impact capsule formation, specifically the organization of the capsule's collagen fibers and adherence of the tissue to the device (Barr et al., 2009, Harvey et al., 2013, Valencia-Lazcano et al., 2013). A smooth silicone implant leads to formation of a nonadherent dense capsule with highly aligned and organized collagen fibers (Brohim et al., 1992, Danino et al., 2018). However, when a device with a textured surface is implanted, tissue ingrowth into the texture surface can disrupt the alignment of the surrounding capsule, which has been associated with lower rates of clinically significant capsular contracture and malposition compared with smooth surface implants (Barnsley et al., 2006, Brohim et al., 1992, Clugston et al., 1994, Derby and Codner, 2015, Hakelius and Ohlsen, 1992, Hakelius and Ohlsen, 1997, Headon et al., 2015). Deeper and more complex textures promote increased tissue ingrowth (Brohim et al., 1992, Danino et al., 2001, Minami et al., 2006). As a result, the force required to break the interface between the capsule and implant is greater than less complex textures, which may reduce the risk of device rotation (del Rosario et al., 1995, Maxwell et al., 2014). Greater tissue ingrowth has also been correlated with reduced synovial-like metaplasia in human breast capsules due to the reduction in movement between the implant and surrounding stroma (Yeoh et al., 1996).

Breast implant manufacturers continue to develop new implant surface textures using varying methodologies in an effort to stabilize the implant in the pocket through increased coefficient of friction or enhanced integration of the device with breast tissue (Derby and Codner, 2015, Harvey et al., 2013). Herein, we describe the use of scanning electron microscopy (SEM) and X-

ray computed tomography (CT) imaging to characterize the topography and surface area of 12 unique breast implant surface textures from 7 different manufacturers and evaluate how surface texture influences capsule formation and tissue adherence in rats.

2. Materials and methods

2.1. Breast implants

The surface texture of shells from 12 different breast implant devices were evaluated (Table 1). Each of these implants are silicone coated except for Polytech Microthane, which is polyurethane coated to create an irregular sponge-like surface. The processes for creating surface texture on the silicone implants differ across manufacturers. For example, the Microcell, Biocell, Nagotex, and Cristalline textures are created using different lost-salt techniques, in which a layer of fine granular salt is applied to the silicone shell before curing, and then removed by rinsing with water after curing. The lost-salt technique used to prepare Allergan Biocell was designed to produce overhangs at the opening of the pores to promote greater tissue adherence. In comparison, the Mentor Siltex texture is generated by a pressure imprint-stamping technique, and the Sientra True texture is produced by an undisclosed technique that does not involve use of salt or pressure stamping (Barr et al., 2017, Chao et al., 2016, Maxwell and Gabriel, 2017).

Table 1. Manufacturer and surface texture of breast implant devices.

Manufacturer	Implant type
Allergan plc (Dublin, Ireland)	Smooth texture
	Microcell texture
	Biocell texture
Eurosilicone S.A.S. (Apt, France)	Cristalline texture
Mentor (Irvine, CA, USA)	Siltex texture
Motiva/Establishment Labs (Alajuela, Costa Rica)	SilkSurface texture
	VelvetSurface texture

Nagor (Glasgow, Scotland)	Nagotex texture
Polytech Health & Aesthetics (Dieburg, Germany)	MESMOsensitive texture
	POLYtxt texture
	Microthane texture
Sientra (Santa Barbara, CA, USA)	True texture

2.2. Breast implant surface imaging

SEM was used to image the surface of the breast implant textures using a single shell per implant type (Atlan et al., 2016, Barr et al., 2017). One 10-mm diameter disk was cut from the anterior of the shell of each breast implant device and used to capture a top and cross-sectional view of the surface texture. Samples were secured to a specimen mount with carbon adhesive, sputter coated with gold at 25 mA for 2 min, and imaged with a Hitachi S-3400N Tungsten Filament Scanning Electron Microscope using an electron beam accelerating voltage of 5 kV and aperture of 0. Images were captured at 40× and 100× magnification for the top view and 40× magnification for the cross section.

In a separate experiment designed to explore additional methods of pore characterization, SEM images were taken of 2 similar pore textures of different surface areas (i.e., Allergan Microcell and Allergan Biocell) to quantify pore density, pore opening area, surface openness, and texture depth. Details of the methods used in this experiment can be found in the Supplementary material.

X-ray CT was used to determine the surface area of the breast implant textures. Eight 10-mm diameter disks were cut from the shell of each breast implant device, four from the anterior and four from the posterior of the shell. The entire geometry of each disk was acquired by taking a series of 2-dimensional X-ray images (slices) while the implant disk was concentrically rotated 360° in the X-ray beam. These slices containing information about the implant disk's position (with 15 µm voxel resolution) and density (gray scale) were used as the basis for digital 3-dimensional reconstruction of the sample's volume data (Fig. 1a)

(ASTM International, 2011, Landis and Keane, 2010). All internal and external surfaces of the implant sample were extracted from this CT volume data. The spatial precision of the CT projection data was checked by a certified CT test standard (ruby bar with a length of 4.0432 ± 0.0020 mm; GE Sensing & Inspection Technologies, GmbH, Wunstorf, Germany).

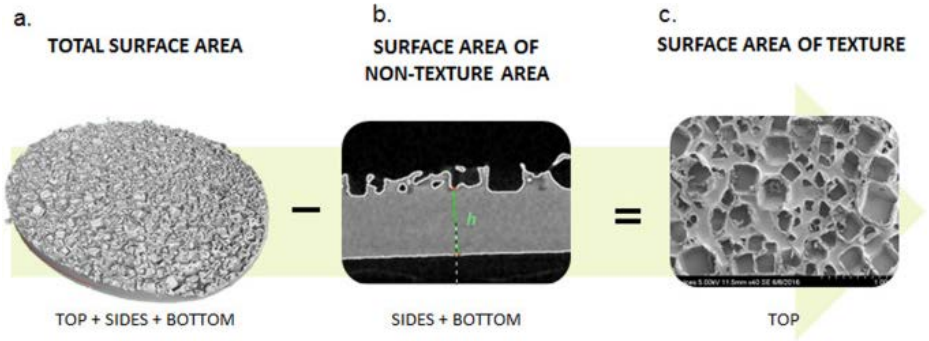

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Fig. 1. Method for calculating surface area of the textured surface of a 10-mm diameter disk taken from the shell of a breast implant. (a) The implant shell disk was imaged using X-ray CT, and with the CT software, a threshold applied to distinguish between material and air was used to produce a value for total surface area of the disk. (b) The thickness of the non-textured portion of the shell was measured and used to calculate the surface area of the non-textured area ($A = 2\pi rh + 2\pi r^2$, where A is surface area, r is radius, and h is height.). (c) The surface area of texture was calculated by subtracting the surface area of the non-textured area from the total surface area based on the assumption that the bottom of the disk was a flat surface.

A vertical cross section of the X-ray CT image was used to measure the thickness of the non-textured area, which was defined as the location starting from the bottom of the disk to the flat area near the top of the disk or the lowest point of any protrusions present on the surface (Fig. 1b). The thickness of the non-textured area was measured in three areas of the cross section and averaged. The average thickness of the non-textured area was used to calculate the surface area of the non-textured area (sides and bottom of disk) according to the formula for the area of a cylinder based on the assumption that the bottom of the disk was a flat surface. The resulting surface area of the non-textured surface was subtracted from the total surface area of

the disk (obtained using CT software) to produce a surface area measurement for the textured surface (top of disk) (Fig. 1c). The surface area of the textured surface was calculated in terms of mm^2 as well as the percentage higher than that of a flat surface. The textured surface of the disk can be seen as the top circle of a cylinder; therefore, the surface area of a flat surface texture would be the surface area of a circle with a 5 mm radius (i.e., 79 mm^2).

2.3. Capsule formation

The protocols used in the animal studies were approved by the Institutional Animal Care and Use Committee. This study is conducted in compliance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and Allergan, plc standard operating procedures. Capsule formation following subcutaneous implantation of disks cut from the shells of the different breast implants was evaluated in male Sprague -Dawley rats (Charles River Laboratories; Wilmington, MA). A total of six 30-mm disks (3 each from the anterior and posterior of the implant shell) were evaluated for each implant surface texture. The implantation scheme comprises three disks per rat in one of four locations along the torso (right cranial, right caudal, left cranial, and left caudal). The disks were implanted under anesthesia with 4% isoflurane in 2 L/min oxygen, with the textured surface of the disk facing the muscle. Six weeks later, the disk and surrounding tissue were explanted, and the tissue in contact with the textured surface of the disk was excised. Tissue samples were fixed in 10% neutral-buffered formalin, then processed and embedded in paraffin. Sections were cut at 5 µm and stained with hematoxylin and eosin (H&E) to qualitatively visualize the gross morphology of the tissue-implant surface interface, including the arrangement of collagen fibers of the capsule. Stained slides were imaged using bright-field microscopy.

2.4. Tissue adherence

The strength of the interaction between the breast implant shell and fibrous capsule was evaluated by peel test in male Sprague-Dawley rats. Strips of the anterior of the implant shells measuring 1 cm in width and 4 cm in length were implanted under

anesthesia with 4% isoflurane in 2 L/min oxygen. Each rat received two subcutaneous implants along the dorsal surface, one on the right side and the other on the left side, with the texture surface of the implant facing toward the muscle (n = 8 per implant surface texture). Six weeks later the strip and surrounding tissue capsule were explanted.

The strength of tissue adherence to the implant surface texture was measured by the peak force that was required to separate the surrounding tissue from the shell material. Testing was performed using an ADMET 5601 Universal Testing Machine (ADMET; Norwood, MA) with a 22 lb load cell. The excised tissue capsule and attached implant strip were each fastened into separate grips on the mechanical tester and pulled apart at a rate of 2 mm/s. Testing continued until the tissue was completely separated from the implant strip. Peak force, or maximum value on the force-displacement curve was recorded.

2.5. Statistical analyses

The surface area of the implant textures determined by X-ray CT was evaluated using descriptive statistics. Comparisons between the texture surface area of the anterior versus posterior of the implant shell were performed using a 2-sample *t*-test, with significance achieved at a $P \leq 0.05$. Differences in tissue adherence force were evaluated using an analysis of variance model with Tukey's correction.

3. Results

3.1. Breast implant surface imaging

SEM imaging revealed the implant textures differed visually in evenness of the surface, presence of pores, size and openness of the pores, and the depth of texturing. Nonetheless, general similarities were noted among groups of textures. Allergan Smooth, Motiva SilkSurface, and Motiva VelvetSurface textures appeared relatively flat, with little or no depth in the texturing, but differed in the unevenness of the surface (Fig. 2; SEM panels). Polytech MESMOsensitive, Mentor Siltex, and Allergan Microcell all exhibited pores or nodules and showed increased complexity compared with Allergan Smooth, Motiva SilkSurface, and Motiva VelvetSurface textures (Fig. 3; SEM panels). The remaining

textures, in turn, showed increasing surface unevenness and depth of texture that could be grouped according to similarities in appearance (Fig. 4, Fig. 5; SEM panels).

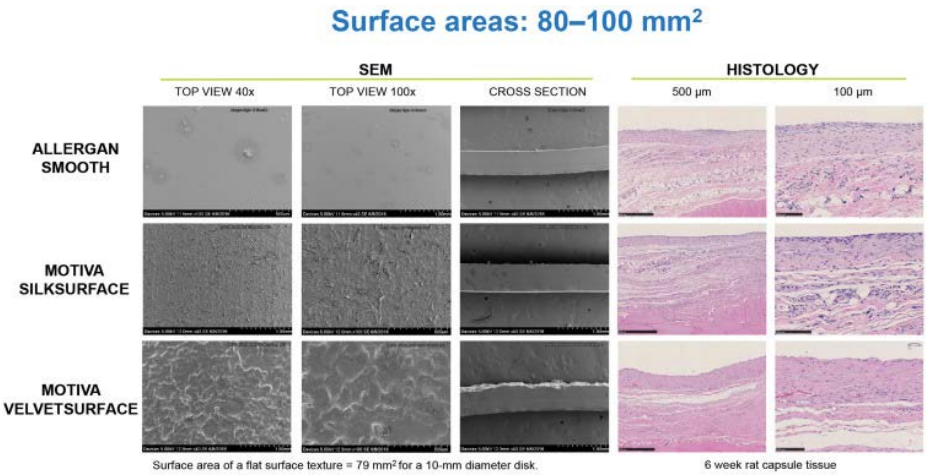

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Fig. 2. Left panels show SEM images of the top view (40× and 100×) and cross section of Allergan Smooth, Motiva SilkSurface, and Motiva VelvetSurface textures. Surface areas range from 80 to 100 mm^2. Right panels show representative H&E-stained slides of the capsule at the tissue-implant interface at 6 weeks after subcutaneous implantation of 30-mm disks of each surface texture into Sprague-Dawley rats. The scale bars at the bottom of the histology figures represent 500 µm and 100 µm, respectively.

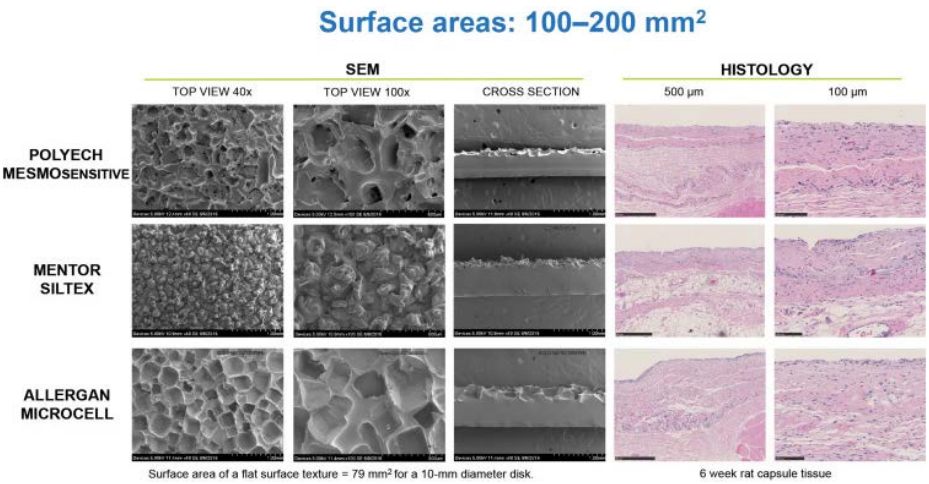

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Fig. 3. Left panels show SEM images of the top view (40× and 100×) and cross section of Polytech MESMOsensitive, Mentor Siltex, and

Allergan Microcell textures. Surface areas range from 100 to 200 mm^2. Right panels show representative H&E-stained slides of the capsule at the tissue-implant interface at 6 weeks after subcutaneous implantation of 30-mm disks of each surface texture into Sprague-Dawley rats. The scale bars at the bottom of the histology figures represent 500 µm and 100 µm, respectively.

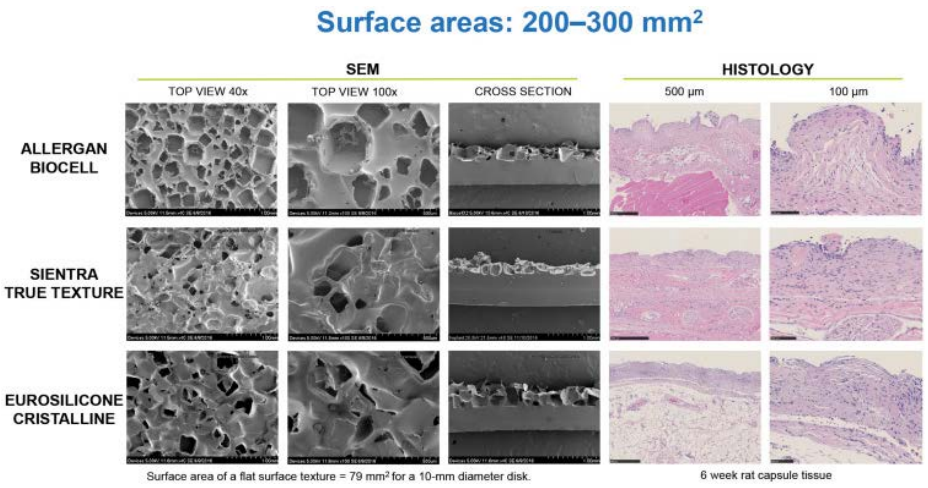

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Fig. 4. Left panels show SEM images of the top view (40× and 100×) and cross section of Allergan Biocell, Sientra True, and Eurosilicone Cristalline textures. Surface areas range from 200 to 300 mm^2. Right panels show representative H&E-stained slides of the capsule at the tissue-implant interface at 6 weeks after subcutaneous implantation of 30-mm disks of each surface texture into Sprague-Dawley rats. The scale bars at the bottom of the histology figures represent 500 µm and 100 µm, respectively.

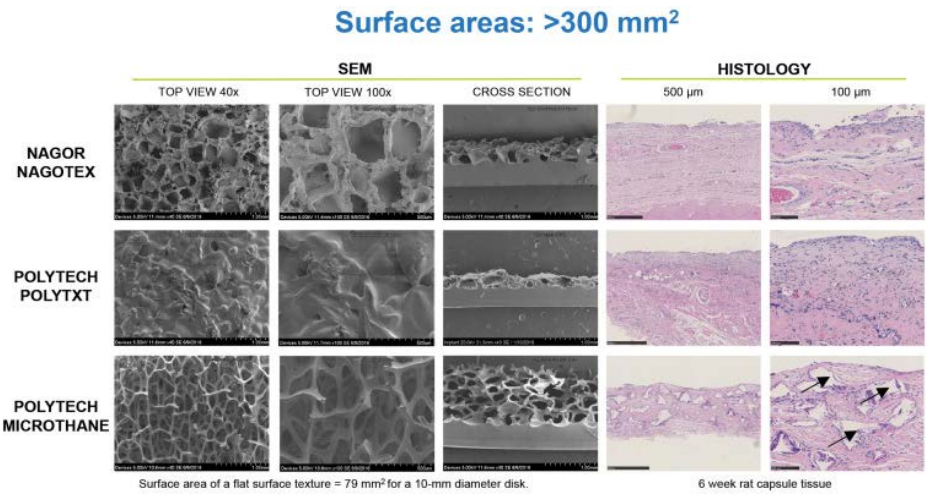

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Fig. 5. Left panels show SEM images of the top view (40× and 100×) and cross section of Nagor Nagotex, Polytech POLYtxt, and Polytech Microthane textures. Surface areas were > 300 mm^2. Right panels show representative H&E-stained slides of the capsule at the tissue-implant interface at 6 weeks after subcutaneous implantation of 30-mm disks of each surface texture into Sprague-Dawley rats. The scale bars at the bottom of the histology figures represent 500 µm and 100 µm, respectively. In the H&E stained slides for Polytech Microthane, the clear material identified by the arrows represent texture material.

To quantify differences across the implant textures, X-ray CT was used to measure the surface area of the texture. The texture surface area of a 10-mm diameter disk from the anterior of the shell from the 12 breast implant devices ranged from 85 to 551 mm^2, and correspondingly, their surface texture was 8–602% greater than that of a flat surface (79 mm^2) (Table 2). The texture surface area did not differ significantly between the anterior and posterior for most implant devices, except for Mentor Siltex (125 vs 143 mm^2; $P = 0.02$), Allergan Biocell (213 vs 248 mm^2; $P < 0.01$), and Polytech POLYtxt (347 vs 431 mm^2; $P = 0.01$) which had more texture surface area on the posterior of the shell, and Nagor Nagotex (337 vs 278 mm^2; $P < 0.01$), which had more texture surface area on the anterior of the shell.

Table 2. Texture surface area from anterior and posterior of the shell of each breast implant surface texture determined by X-ray computed tomography.

	Mean (SD) texture surface area (mm^2)		Mean % greater texture surface area than flat surface[a]
Implant texture	**Anterior**	**Posterior**	**Anterior**
Allergan Smooth[b]	85 (4)	85 (4)	9
Motiva SilkSurface	85 (1)	85 (2)	8
Motiva VelvetSurface	90 (2)	89 (2)	14

Polytech MESMOsensitive	115 (7)	119 (5)	47
Mentor Siltex	125 (4)	143 (8)	60
Allergan Microcell	145 (4)	132 (12)	85
Allergan Biocell	213 (10)	248 (7)	171
Sientra True	218 (6)	244 (16)	178
Eurosilicone Cristalline	293 (8)	307 (17)	273
Nagor Nagotex	337 (9)	278 (12)	329
Polytech POLYtxt	347 (16)	431 (37)	341
Polytech Microthane	551 (21)	585 (46)	602

SD, standard deviation.

a Surface area of a flat surface texture is 79 mm^2 for a 10-mm diameter disk.

b The inside of the shell is not flat and contributes to the overall surface area.

Results of the experiment designed to compare the shell surface features of implants based on calculations of pore density, pore opening area, surface openness, and texture depth showed that these features can be used to distinguish implant surface textures. Details of the results of this experiment can be found in the Supplementary material.

3.2. Capsule formation

Capsule formation in response to the implant surface texture was qualitatively evaluated 6 weeks after subcutaneous implantation of 30-mm disks cut from the shell of each implant device. Representative H&E-stained sections illustrating the gross morphology of the tissue-implant interface are shown in Fig. 2,

Fig. 3, Fig. 4, Fig. 5 (histology panels).

Overall, the morphology of the capsule tissue aligned with the topography of the implant surface regardless of whether the disks were from the anterior or posterior of the implant shell. Capsule morphology was similar across groups of surface textures with the larger surface area textures showing disorganized alignment of collagen fibers. The tissue along the implant-tissue interface for the textures with the smallest surface area (Allergan Smooth, Motiva SilkSurface, and Motiva VelvetSurface) was mostly flat, with the collagen fibers of the capsule aligned parallel to the surface. Polytech MESMO, Mentor Siltex, and Allergan Microcell had small tissue projections scattered along the interface adding a small degree of disorganization to the collagen fiber alignment. Allergan Biocell, Sientra True, Eurosilicone Cristalline, Nagor Nagotex, Polytech Polytxt, and Polytech Microthane showed larger, more prominent tissue projections, resulting in irregular arrangement of collagen fibers and creating a more disorganized capsule morphology. The capsule morphology of Polytech Microthane contained fragments of texture material (see clear material in Fig. 5) embedded throughout the capsule tissue; this was not observed with any other implants.

3.3. Tissue adherence

The peak force required for separation of the surrounding tissue capsule from the different surface textures was assessed using a peel test at 6 weeks following implantation. As shown in Fig. 6, the peak force required for tissue-implant separation generally increased with increasing complexity of surface texture. The peak force was approximately 0.3 N for Allergan Smooth and Motiva VelvetSurface, 0.5–0.6 N for Allergan Microcell and Mentor Siltex, and 0.9–1.9 N for Sientra True and Allergan Biocell. The peak force for surfaces with the greatest area was variable (0.5 N for Polytech POLYtxt, 1.7 N for Nagor Nagotex, and 4.6 N for Polytech Microthane). The adherence force required for separation was significantly greater for the Polytech Microthane than for the other textures ($P < 0.05$). The adherence force for the Allergan Biocell and Nagor Nagotex textures differed significantly (all $P < 0.05$) from the textures with lower surface area (Allergan Smooth, Motiva VelvetSurface, Allergan

Microcell, and Mentor Siltex), with Biocell also significantly different compared with Mentor Siltex ($P < 0.05$).

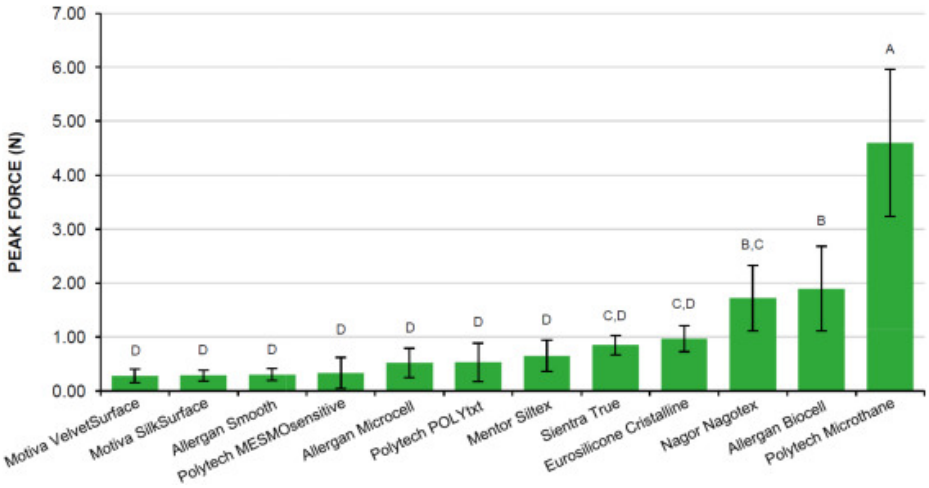

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Fig. 6. Mean ± SD adherence force required to separate the tissue capsule from the implant surface assessed 6 weeks after implantation of the different surface textures in Sprague-Dawley rats. N = 8 for each texture. Means that do not share a letter are significantly different ($P \leq 0.05$).

4. Discussion

Our study is unique in that it connects the physical properties of an implant to in vivo physical performance and tissue morphology. The histological observations help to provide the biological context for the quantitative measurements and the foundation for a better understanding of the role of implant surface texture features in the clinical setting. Other studies have included imaging analyses and in vitro assessment of fibroblast, macrophage, or bacterial adhesion to the shell surface, but have not related these factors to in vivo data (Barr et al., 2009, Barr et al., 2017, Jones et al., 2018, Valencia-Lazcano et al., 2013). Characterizing the physical properties of implant surfaces is key to understanding how a surface texture may impact tissue response to a breast implant. The topography and surface area of 12 implant surface textures from seven different manufacturers were characterized using SEM and X-ray CT imaging. The differences in surface texture may reflect differences in the manufacturing process for each implant (Chao

et al., 2016). For example, the Allergan Microcell, Allergan Biocell, Nagor Nagotex, and Eurosilicone Cristalline textures are made by exposing the silicone shell to salt before curing. Although they have similar open pore-like structures, they differ in surface roughness and pore depth, because the salt is removed in a different manner during the manufacturing of each texture. In comparison, the Mentor Siltex surface texture is created using a pressure stamping technique (Chao et al., 2016). The Polytech Microthane texture is made of polyurethane and is manufactured using a different process compared with all other implants in this study. As a result, its appearance is dissimilar to the other textures, with a thin interconnected skeletal framework that creates a much deeper texture. It is important to recognize that all of the surface textures are very different from one another, and the use of texture surface area is just one way to compare them. Other evaluations of the implant surface, such as roughness, are still to be made and will allow for more comprehensive comparisons. This is especially true for smoother-textured surfaces where subtle differences in the evenness of the surface texture may not be fully discernible by the X-ray CT due to the resolution setting of the machine (15 μm) (ASTM International, 2011). This study did not examine the potential role of the differences in chemical composition of the implant surfaces and thus no conclusions can be drawn regarding impact of these differences on the results.

SEM imaging shows that, while the surface characteristics of the textures varied (i.e., pore size, pore number), the depth and complexity of textures allow for groupings based on similarities in texture appearance and depth. The groupings also reflect ranges of the surface texture area as determined by X-ray CT. Consequently, we propose four classifications of textures (smooth/nanotexture, microtexture, macrotexture, and macro-plus texture) based on similarities in visual observations and surface area measurements, with the surface area and degree of texturing and depth increasing with each classification (Fig. 7). The smooth/nanotexture grouping reflects the similarity of the texture depth among members of this classification, although surface roughness may be somewhat greater for a nanotexture compared with a smooth surface texture. This grouping includes

devices with a texture surface area of 80–100 mm and consists of Allergan Smooth, Motiva SilkSurface, and Motiva VelvetSurface; microtexture includes devices with a texture surface area of 100–200 mm^2 and consists of Polytech MESMOsensitive, Mentor Siltex, and Allergan Microcell; macrotexture includes devices with a texture surface area of 200–300 mm^2 and consists of Allergan Biocell, Sientra True, and Eurosilicone Cristalline; and macrotexture-plus includes devices with a texture surface area more than 300 mm^2 and consists of Nagor Nagotex, Polytech POLYtxt and Polytech Microthane.

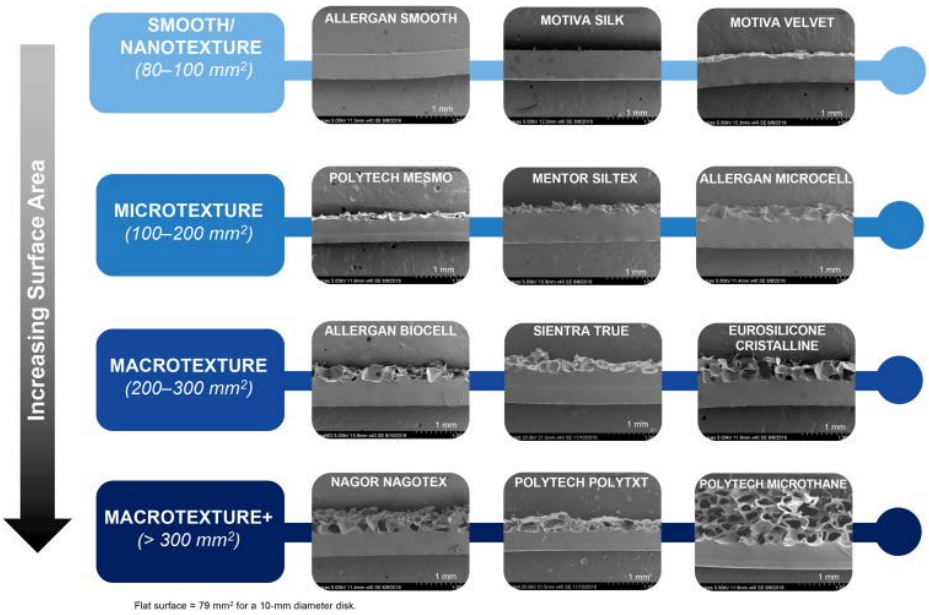

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Fig. 7. Classification of implant textures based on texture surface area. SEM images of the cross section of each implant texture are organized into categories according to the magnitude of the texture surface area measured from the anterior of the shell by X-ray computed tomography.

Using SEM and laser confocal imaging, Barr and colleagues classified 13 commercially available textures based on surface roughness into four main groupings, which they termed nano, meso, micro, and macro textures (Barr et al., 2017). The presence of an overhang associated with pores was used to subclassify the microtexture and macrotexture classifications. The classification system described herein does not correspond directly with that reported by Barr et al., likely reflecting differences in implant surfaces examined, methodology, and

parameters used to characterize surface texture. Information obtained on topographical evaluation of textured breast implants depends on the methodology used, with a recent study suggesting that white light interferometry may serve as an alternative to laser confocal imaging (Garabedian et al., 2017). Nonetheless, the classifications proposed in the current study and in Barr et al. provide a conceptual framework around the variety of available implants to assist with communication between surgeons and researchers, and to potentially assist surgeons in choosing the right implant to meet patient needs.

In addition to helping classify the implant surface textures, the surface area results of the current study also address questions regarding the variability of the texture across a single implant. Within a single implant, low variability in texture surface area was seen among the multiple samples taken from the anterior of the shell, and separately, among the multiple samples taken from the posterior of the shell. Statistically significant differences in texture surface area between the anterior and posterior of the shell were seen for four of the implants (Mentor Siltex, Allergan Biocell, Nagor Nagotex, and Polytech POLYtxt) with the greatest difference observed with the Polytech POLYtxt implant shells. These differences may not be clinically relevant in that the tissue adherence data show that large disparities in texture surface area between implants do not always result in a statistical difference in tissue adherence (e.g., tissue adherence for the more complex Sientra TRUE texture is not significantly greater than the tissue adherence for the less complex Mentor Siltex texture). The variability in implant textures between the anterior and posterior of the shell is most likely due to the processes used to manufacture the different implant textures. Even though there were differences in texture surface area between the anterior and posterior, the classification of each surface texture remained the same, except for the Nagor Nagotex and Eurosilicone Cristalline. Nagor Nagotex was classified as macrotexture-plus based on the anterior measurement, but would have been classified as macrotexture based on the posterior measurement. The opposite was seen for Eurosilicone Cristalline.

The histology results of this study provide visualization of the

tissue integration and show that textures within a given surface area classification had similar capsule morphology, supporting the proposed groupings. The fibrous capsule reflected the surface texture, with an organized fiber structure parallel to the surface of the smooth/nanotexture implants and a disrupted, more disorganized structure found with the macrotexture and macrotexture-plus implants. Specifically, tissue ingrowth increased with increasing complexity of surface texture from smooth/nanotexture to macrotexture-plus. In those implants tested, the peak force required for tissue-implant separation generally increased with surface-texture classification from smooth/nanotexture to microtexture to macrotexture. Two of three surface textures in the macrotexture-plus classification also required high peak force to separate the implant from the tissue. However, the Polytech POLYtxt was an outlier, in that it was classified as macrotexture-plus on the basis of surface area but exhibited tissue adherence similar to that for members of the microtexture classification. On SEM, a cross section of the surface texture of POLYtxt showed large, almost fully enclosed pores in the texture whereas a view of the top surface showed an undulating surface with little to no depth (which was similar to that of a smooth/nanotexture surface). Although the enclosed pores contributed to measurement of the overall surface area of the texture, the lack of depth and openness on the texture surface likely accounted for the minimal tissue adherence.

Previous studies have shown that the tissue capsule forming around an implant mirrors the surface texture pores with which it comes into contact (Nicholson et al., 2007). The macrotexture and macrotexture-plus surfaces have the deepest pores and largest pores based on visual observation, and consequently allow more tissue integration (with the exception of POLYtxt), as reflected by the larger tissue projection along the capsule-implant interface and the greater force required to separate the tissue from the shell material. Smooth/nanotexture implants have a smooth and irregular microstructure with no pores, which limits the number of sites for tissue ingrowth and consequently reduces the opportunity for tissue adherence to the implant. These observations lend substantiation to pore characteristics being the feature of implant surface texture that most impacts tissue adherence. This hypothesis is supported by the comparison of

the pores found in the Allergan Microcell and Allergan Biocell textures using quantitative assessments (details provided in Supplementary material). The manufacturing process used for the Biocell texture is designed to create deeper pores than found in the Microcell texture, but the overhang on the surface of Biocell creates a lip over the pore. As a result, surface openness is reduced which allows the tissue to anchor itself into the deeper pores (Barr et al., 2017), resulting in greater tissue adherence with the Biocell texture than the Microcell texture. The greatest tissue adherence was demonstrated by Polytech Microthane, a polyurethane-coated implant, which also exhibited a unique capsule morphology that differed from the other implants in the macrotexture-plus classification. Although the chemical composition of this implant may contribute to these observations, further research would be required to distinguish the relative contributions of surface texture topography and chemical composition. While strong tissue adherence and a unique pattern of tissue integration could be clinically desirable, the polyurethane coating on currently available implants has been shown to degrade over time (Castel et al., 2015). The development of an implant with a similar open pore structure that retains its structural integrity and provides the desired biological and clinical performance could be a focus for future implant design. A new subcategory of implants defined by their unique pore structure might result from the availability of such an implant.

5. Conclusions

The data from this study show that variations in implant surface texture directly affected capsule structure and morphology, and in turn, influenced capsule adherence to the implant. Increasing complexity of the surface texture can markedly alter the pathophysiology of the foreign body response, leading to more tissue ingrowth, which disrupts capsule fiber organization and increases tissue adherence. Surface area is, therefore, an important factor contributing to tissue ingrowth and adherence. These findings provide a better understanding of the landscape with respect to the surface texture properties of breast implants, thus enabling the classification of the implants evaluated in this study into groups based on their surface characteristics.

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Author disclosures

Michael Atlan is a consultant for workshops and has developed educational presentations for Allergan.

Gina Nuti is an employee of Allergan plc.

Hongpeng Wang is an employee of Allergan plc.

Sherri Decker is an employee of Allergan plc.

TracyAnn Perry was an employee of Allergan at the time of study conduct and manuscript preparation.

Appendix A. Supplementary material

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Supplementary material

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Designation: E1441–11

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Angeborene Fehlbildungen der weiblichen Brust

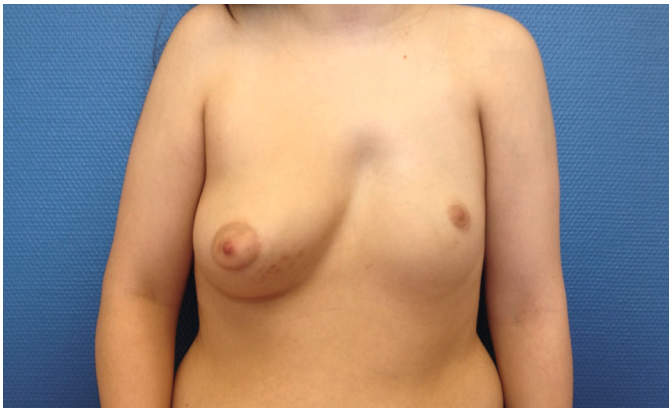

Abb. 1
19 -jährige Patientin mit Poland-Syndrom li. mit Fehlen des M. pectoralis major und Mammahypotrophie

Einleitung

Die Akzeptanz des eigenen Körpers ist eine wesentliche Voraussetzung für ein gesundes Selbstwertgefühl und letztendlich prägend für die eigene Identität. Kommt es im Verlauf der Pubertät und der Adoleszenz zu einem asymmetrischen Wachstum der weiblichen Brust oder zu einer dauerhaft abweichenden Form, können bei betroffenen Frauen häufig schon frühzeitig Verhaltensauffälligkeiten erkennbar werden, die sich z. B. in einem reduzierten Selbstwertgefühl und einer depressiven Symptomatik äußern können.

Brustentwicklung

Die Entwicklung der Brustdrüse wird u. a. durch den Einfluss von Östrogen, Gestagen, Prolaktin und Insulin gesteuert. Etwa ab der 4. Woche der Embryonalphase bilden sich die paarigen Milchleisten aus. Die Milchleisten entwickeln sich bis zur siebten Schwangerschaftswoche in die sogenannten Milchhügel zurück, aus denen bis zum fünften Schwangerschaftsmonat die eigentlichen Brustdrüsenanlagen (Epithelknospen) in Höhe der IV. Rippe entstehen. Die während der Schwangerschaft über die Plazenta zum Feten gelangten Östrogene können postpartal durch die noch unreife Leber des Neugeborenen nicht adäquat verstoffwechselt werden. Dies kann zu einer beidseitigen oder einseitigen Brustdrüsenschwellung führen, die sich in der Regel bis zum 6. Lebensmonat zurückbildet. Mit Einsetzen der endokrinen Ovarialfunktion kommt es zur Knospung der Brust (Thelarche), als erstes sichtbares Zeichen der beginnenden Pubertät (9. bis 13. Lebensjahr) - noch vor der Pubarche (Entwicklung der Schambehaarung) und der Menarche (erste Menstruationsblutung). Die weitere physiologische Entwicklung der Brust wurde von Tanner in fünf Stadien beschrieben, die zwischen dem 16. und 18. Lebensjahr in den meisten Fällen abgeschlossen ist. Die Brustbasis bildet sich auf dem M. pectoralis major zwischen der zweiten bis sechsten Rippe aus und wird durch eine Faszie vom M. pectoralis major getrennt. Ein komplexes Band- (Cooper-Ligamente) und Fasziensystem (Fascia superficialis „Scarpa-Faszie)" durchzieht in allen räumlichen Dimensionen die Brust und verleiht dem Gewebe so Form und Stabilität.

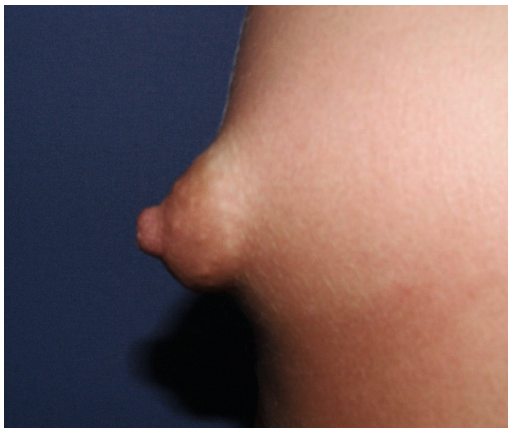

Abb. 2
Tuberöse/tubuläre Brustform mit schmaler Brustbasis, hochgezogener Brustfalte und Areola"hernie".

Einteilung der angeborenen Fehlbildungen

Fehlbildungen der weiblichen Brust umfassen Fehlbildungen der Brustwand und der Brust, wobei letztere wesentlicher häufiger auftreten. Zu den Fehlbildungen der Brustwand gehören u. a. Pectus excavatum (Trichterbrust), Pectus carinatum (Kiel- oder Hühnerbrust), Poland-Syndrom und Anomalien des Sternums (Brustbein).

Angeborene Fehlbildungen der Brust umfassen ein breites Spektrum:

- **Asymmetrie oder Anisomastie**
  Ungleiche Brüste in Form, Größe und Position
- **Poland-Syndrom**
  Fehlen des Musculus pectoralis major, Anlagestörung der gleichseitigen Brust, muskuläre und skelettale Deformitäten der gleichseitigen Thoraxwand und der oberen Extremität
- **Tuberöse oder Tubuläre Brust**
  Knollen- oder Rüsselbrust, snoopy-nose-deformity
- **Symmastie**
  Fehlender definierter medialer Brustrand durch vermehrtes Fett- und Drüsengewebe, das beide Brüste über dem Sternum verbindet
- **Mammahypo- und hypertrophie**
  Ungewöhnlich kleine oder große Brust.
- **Amastie und Athelie**
  Fehlen der Brustanlage/MAK
  Fehlen des Mamillen-Areola-Komplexes (MAK),
- **Polymastie und Polythelie**
  zusätzliche Brustanlage mit MAK
  zusätzliche Brustwarze

Aufklärung

Für die vornehmlichen jungen Frauen (< 30 Jahre) bedeutet die operative Korrektur der Fehlbildung die lang ersehnte Akzeptanz des eigenen Körpers, eine dadurch bedingte

Prof. Dr. med. Andree Faridi

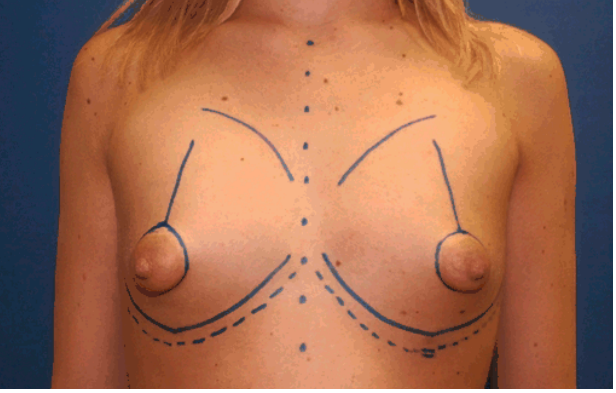

Abb. 3a 24-jährige Patientin mit symmetrischer tuberöser Brustfehlbildung bds.

Steigerung des Selbstwertgefühls und eine deutliche Verminderung der körperlichen Probleme (Rücken- und Nackenschmerzen, einschnürende BH-Träger). Liegen angeborene, insbesondere deutlich sichtbare Fehlbildungen vor, kann ein qualifiziertes fachärztliches Gutachten zur Vorlage bei der Krankenkasse zu einem Leistungsanspruch führen (SGB V). Dem Wunsch nach operativer Korrektur ist zumeist ein längeres Leiden und ein längerfristiger Entscheidungsprozess vorausgegangen, sodass die Frauen für diese Operation hoch motiviert sind. Die daraus resultierende positive Einstellung zu der geplanten Operation verlangt vom Operateur eine ebenso wohl überlegte Planung wie Durchführung des Eingriffs, um ein optimales Ergebnis zu erreichen. Unverzichtbarer, integraler Bestandteil der Behandlungsplanung ist die ausführliche und individualisierte Aufklärung vor und nach der Operation (Risiko- und Sicherheitsaufklärung). In diesem Zusammenhang müssen die Patientinnen auf die Möglichkeit der Einholung einer Zweitmeinung hingewiesen werden. Die Aufklärung über das operative Vorgehen sollte nicht am Tag vor der Operation, sondern möglichst einige Tage oder wenige Wochen zuvor erfolgen, um den jungen Frauen die notwendige Bedenkzeit einräumen zu können. Da es sich fast ausnahmslos um einen Wahleingriff handelt, muss in einem ausführlichen Aufklärungsgespräch, unabhängig von der Häufigkeit des Auftretens, auf die möglichen typischen Komplikationen der gewählten Operationsmethode eingegangen werden. Die Patientin muss nach der Aufklärung die Erfolgs- und Heilungschancen, die Behandlungsalternativen sowie Vor- und Nachteile der Operationsmethoden kennen und entscheiden können, welche Risiken, Folgen und Komplikationen sie auf sich nehmen will (Risikoaufklärung). Zur Sicherung eines optimalen Heilerfolgs sollten entsprechende Hinweise, Empfehlungen oder Warnungen für die Zeit nach der Operation besprochen werden (Sicherheitsaufklärung oder therapeutische Aufklärung). Das Aufklärungsgespräch und die Aufklärungsinhalte sollten z. B. in einem Aufklärungsvordruck schriftlich fixiert und mit Unterschriften von Arzt und Patient (bei Minderjährigen dem Erziehungsberichtigten) dokumentiert werden.

Planung und Anzeichnung

Die präoperative Planung und Anzeichnung sind die wesentlichen Voraussetzungen für eine erfolgreiche operative Korrektur der Brustfehlbildung. Die Festlegung der Umschneidungsfigur verlangt vom Operateur die Kenntnis der annähernden „Idealmaße" einer weiblichen Brust, die in Abhängigkeit von den Körperproportionen sowie der Brust- und Körpergröße und den Wünschen der Frauen individuell angepasst werden müssen. Das Einzeichnen der Umschneidungsfigur erfolgt an der stehenden Patientin entweder am Vorabend der Operation oder am Morgen des Operationstages. Im Wesentlichen kommen Freihandanzeichnungen zur Anwendung, die u.a. auf eine präoperative exakte Festlegung der Brustwarzenposition verzichten und Raum für intraoperative Anpassungen lassen. Die notwendige Fotodokumentation kann mit oder ohne Anzeichnungsfigur erfolgen.

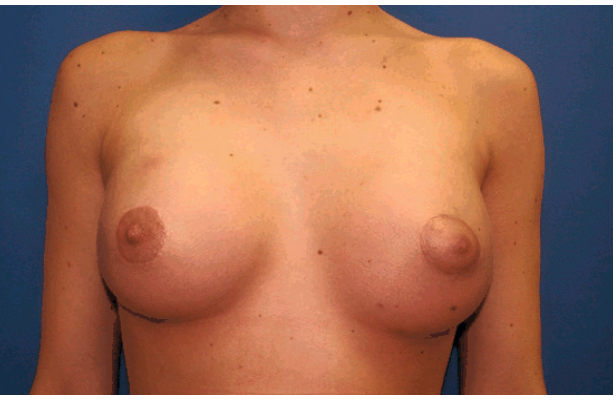

Abb. 3b Korrektur der Brust- und Areolaform sowie Einlage von anatomischen texturierten Implantaten (MENTOR® CPG™ 321, 245 cc)

Implantatauswahl

Implantate können da eingesetzt werden, wo ein zusätzliches Volumen entweder medizinisch empfohlen oder aber von Seiten der Patientin gewünscht wird. Grundsätzlich stehen runde und anatomisch geformte Implantate unterschiedlicher Basisbreite, Höhe und Projektion mit verschiedenen Oberflächenstrukturen zur Verfügung (glatt oder mikro-texturiert in verschiedenen Variationen; siehe Abb. 4). Manche Operateure bevorzugen bei der reinen Augmentation glattwandige runde Implantate, während z. B. bei der tubulären Brust eher anatomisch geformte Implantate eingesetzt werden, die eine bessere Volumenauffüllung im Bereich der unteren Quadranten ermöglichen sollen. Eine weitere Entscheidung bei der operativen Planung ist die Lage des Implantats, unter oder auf dem Muskel (subpectoral oder präpectoral). Die aktuellen Daten sprechen mehrheitlich für die präpektorale Einlage, selbst wenn der Unterhautfettmantel eher dünn ist, denn die subpektorale Lage zeigt in der Langzeitbeobachtung zwei wesentliche Nachteile:

1. Die wulstartige Rückverlagerung des Muskels über das Implantat in Richtung Brustansatz.
2. Das Risiko der willkürlichen Bewegung des Muskels (Animation) mit dem kosmetisch unbefriedigenden Effekt der springenden Implantate (jumping breast).

Operation

Grundsätzlich müssen weder Konserven gekreuzt noch Eigenblutspenden vorgehalten werden. Bei den überwiegend jungen Frauen kann eine Mammasonographie zur Beurteilung des Brustdrüsenkörpers durchgeführt werden, bei Frauen über 40 Jahre empfiehlt sich eine Mammographie. Perioperativ sollte eine Antibiotikaprophylaxe erfolgen. Auf dem Operationstisch wird die Patientin mit leicht angehobenem Oberkörper gelagert, einige Operateure bevorzugen dabei die Anlagerung der Arme an den Oberkörper, was die stehende Position am besten imitiert. Ein Blasenverweilkatheter ist bei einer Opera-

Abb. 4
Runde und anatomisch geformte Implantate werden mit auffüllbarer Kochsalzlösung oder Silikongel (MemoryGel®) angeboten. Gelimplantate stehen dem Operateur mit glatter oder texturierter Oberfläche (SILTEX®) zur Verfügung. Alle Gelimplantate verwenden ein Silikon, das kohäsiv, sicher und ästhetisch zuverlässig ist.

tionszeit von unter 180 Minuten in der Regel nicht notwendig. Die Verwendung von Drainagen hat sich bewährt, ist aber nicht zwingend erforderlich.

Operationstechniken

Aufgrund der verschiedenen Formen der Brustfehlbildungen kommen unterschiedliche Operationstechniken zum Einsatz. Neben der sub- oder präpectoralen Implantateinlage können alle Reduktions- oder Mastopexietechniken sowie Lipofilling (Eigenfett) und andere autologe Gewebetransfers zur Anwendung kommen. Die Eigenfettmethode wird ergänzend zum Brustaufbau mit Silikonimplantaten eingesetzt, wenn das Unterhautfettgewebe der Patientin nicht ausreicht.

Anisomastie/Asymmetrie

Eine Korrektur im Sinne einer Wiederherstellung der perfekten Symmetrie kann geplant aber selten erreicht werden, wohl aber eine deutliche Verbesserung. Bei einer Ungleichheit der Brüste muss grundsätzlich entschieden werden, ob die größere Brust über eine Reduktionsplastik/Mastopexie an die kleinere Brust oder die kleinere Brust über eine Augmentation mit Implantat und/oder Lipofilling an die größere Brust angeglichen wird. Hier bedarf es einer ausführlichen Aufklärung über die weitere Formentwicklung der Brust.

Amastie, Poland-Syndrom und Mammahypotrophie

Bei diesen Anomalien der Brust kann eine akzeptable Brustform in den meisten Fällen durch ein geeignetes Implantat oder ein Lipofilling bzw. anderweitiges autologes Gewebe rekonstruiert werden. Bei der Eigenfetttransplantation muss berücksichtigt werden, dass häufig mehr als eine Operation notwendig sein wird, um das gewünschte Volumen zu erreichen. In Abhängigkeit von der Ausprägung des Poland-Syndroms kann sich die Notwendigkeit ergeben, eine Implantateinlage mit einer Eigenfetttransplantation zu kombinieren, insbesondere bei vollständigem Fehlen des großen Brustmuskels (Abb. 1).

Tuberöse oder Tubuläre Brust

Die tuberöse Brustfehlbildung ist eine angeborene, einseitig oder beidseitig auftretende Abweichung der „normalen" Form, Kontur und Projektion der Brust, die mehrheitlich mit einer Asymmetrie verbunden ist. Die Inzidenz ist wahrscheinlich höher als vermutet, da viele Formen der tubulären Brust nicht erkannt und als Mammahypertrophie oder Asymmetrie klassifiziert werden. Die wesentlichen Merkmale dieser Anomalie sind (Abb. 2):

- Konzentrische verschmälerte Brustbasis mit hochgezogener Brustfalte,
- Vorwölbung des Drüsenkörpers in die hernienartig veränderte, vergrößerte Areola,
- häufig kombiniert mit einer Asymmetrie und/oder Hypoplasie.

Die wichtigsten Ziele der operativen Strategie sind die Verbreiterung der Brustbasis, die Verkleinerung der häufig vergrößerten Areola mit gleichzeitiger Beseitigung der Hernie und die Volumenauffüllung der defizienten Quadranten der Brust. Der Zugang erfolgt über eine Schnittführung um die Areola oder von der Brustfalte aus, wenn die Areola keiner operativen Korrektur bedarf. Zum Volumenausgleich in den unteren Quadranten kann der Brustdrüsenkörper entweder radiär eingeschnitten werden und/oder ein gestielter Brustdrüsenlappen (unfurling flap) wird in die Defektregion eingeschwenkt. Aufgrund langjähriger eigener Erfahrung sollte intraoperativ eine digitale Dehnung des subkutanen Gewebes/der Haut vorgenommen werden, um den bindegewebigen Ring zu sprengen (Abb. 3a/b).

Symmastie

Bei der Symmastie scheinen die Brüste in der Mitte (über dem Brustbein) zusammengewachsen zu sein. Das Gewebe zwischen den Brüsten besteht aus Drüsengewebe, subkutanem Fett und fibrösen Septen. Die operative Korrektur besteht in der Entfernung des überschüssigen Gewebes und der Fixierung durch Einzelknopfnähte der subkutanen Faszie medial oder über der Mittellinie des Sternums, um so ein ansprechendes Dekolleté zu schaffen.

Mammahypertrophie

Die überschießende Brustentwicklung in der Adoleszenz stellt ein besonderes Problem dar, da häufig die erheblichen psychischen (Anstarren, auf die Brust reduziert zu werden, Einschränkungen in den sozialen Kontakten) und körperlichen (Schnürfurchen im Bereich der BH Träger, rezidivierenden Ekzeme in den Brustfalten, Körperhaltung) Beschwerden auch seitens der beratenden Ärzte nicht entsprechend gewürdigt werden. Grundsätzlich kann eine Verkleinerung der Brüste (Reduktionsplastik) nach dem abgeschlossenen Brustwachstum (17. Lj.) durchgeführt werden, in Einzelfällen ergibt sich allerdings auch deutlich vorher (12.-16. Lj.) eine klare medizinische Indikation.

Bei jungen Frauen sollte, wenn möglich, eine Stielung der Brustwarze gewählt werden, bei der grundsätzlich die Stillfähigkeit erhalten bleibt.

Postoperative Versorgung

Die Drainagen werden üblicherweise am 1. bis 4. postoperativen Tag entfernt. Ab dem 2. postoperativen Tag kann ein individuell angepasster fester Büstenhalter oder ein Sport-BH für mindestens 4 bis 6 Wochen getragen werden. Eine Entlassung ist bereits ab dem 1. postoperativen Tag (ggf. auch am Operationstag) möglich und muss im Einzelfall mit der Patientin besprochen werden. Da die meisten Operateure heute resorbierbares Nahtmaterial verwenden, entfällt das für die Patientinnen oft schmerzhafte Entfernen der Fäden. Eine spezielle Nachsorge ist nicht vorgesehen, allerdings empfiehlt sich die Wiedervorstellung mit Fotodokumentation 6-8 Wochen nach der Operation.

Fazit

Jede Fehlbildung bedarf einer individuellen Planung der Operation und einer für die Bedürfnisse speziell ausgewählten Operationstechnik. Häufig müssen verschiedene Operationstechniken kombiniert werden, um ein akzeptables ästhetisches und funktionelles Ergebnis zu erreichen. Es gelingt nicht immer komplexe Fehlbildungen in einer Operation angemessen zu korrigieren, manchmal kann nur durch einen zweiten oder weiteren operativen Eingriff das gewünschte Ergebnis erzielt werden. Alle aktuellen Studien weisen für die jungen Frauen einen deutlichen psychosozialen Benefit, ein gesteigertes Selbstwertgefühl und eine signifikant verbesserte Akzeptanz des eigenen Körpers nach.

Informationen

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Mentor Contour Profile Gel Implants: Clinical Outcomes at 10 Years

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Background: Contour Profile Gel/MemoryShape breast implants consist of a textured silicone elastomer shell filled with silicone gel. The objective of this clinical study was to assess the safety and effectiveness of Contour Profile Gel/MemoryShape breast implants in women who were undergoing primary breast augmentation, primary breast reconstruction, or revision surgery (revision-augmentation or revision-reconstruction).

Methods: This was a prospective, open-label, multicenter clinical study involving Contour Profile Gel/MemoryShape breast implants in 955 female subjects, including 572 primary augmentation, 124 revision-augmentation, 190 primary reconstruction, and 69 revision-reconstruction subjects. Safety was assessed based on the incidence, severity, and method of resolution of all complications. Endpoints were examined on both a per-subject and a per-implant basis.

Results: For the primary augmentation, revision-augmentation, primary reconstruction, and revision-reconstruction cohorts, the Kaplan-Meier estimated 10-year cumulative incidence rates for the key complications at the subject level were as follows: Baker grade III/IV capsular contracture, 3.6 (primary augmentation), 15.5 (revision-augmentation), 14.3 (primary reconstruction), and 16.4 (revision-reconstruction) percent; infection, 0.7 (primary augmentation), 1.9 (revision-augmentation), 1.6 (primary reconstruction), and 2.9 (revision-reconstruction) percent; explantation with or without replacement, 9.2 (primary augmentation), 25.9 (revision-augmentation), 34.1 (primary reconstruction), and 49.0 (revision-reconstruction) percent; explantation with replacement with study device, 4.0 (primary augmentation), 10.8 (revision-augmentation), 16.7 (primary reconstruction), and 27.9 (revision-reconstruction) percent; and any reoperation, 22.3 (primary augmentation), 35.0 (revision-augmentation), 52.7 (primary reconstruction), and 59.7 (revision-reconstruction) percent.

Conclusion: The results of this study demonstrate that Contour Profile Gel/MemoryShape breast implants are safe and effective for primary and revision breast augmentation and reconstruction for women at least 22 years old. (*Plast. Reconstr. Surg.* 140: 1142, 2017.)

Anatomically shaped silicone gel breast implants were introduced to improve the safety profile associated with silicone gel breast implants and enhance aesthetic results. Mentor's Contour Profile Gel implant (Mentor Worldwide LLC, Irvine, Calif.), known as the MemoryShape breast implant in the United States, is a device filled with a more cohesive gel than round devices, and which concentrates

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This trial is registered under the name "Mentor Siltex® Contour Profile Gel Mammary Prosthesis Clinical Trial (CPG)," ClinicalTrials.gov identification number NCT00812097 (https://clinicaltrials.gov/ct2/show/NCT00812097).

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the fill volume in the lower pole with a tapered upper pole. The firmer gel allows the implant to resist deformation and is intended to shape the breast rather than the breast shaping the implant, as is the case with round devices. Thus, by using a properly chosen implant, the Contour Profile Gel/MemoryShape device is designed to fit synergistically with the patient's soft tissue. The Contour Profile Gel/MemoryShape breast implant is textured using microtexture (Siltex; Mentor) designed to reduce the rate of capsular contracture and to providing sufficient friction between the implant and the capsule to retain proper orientation. This 10-year, open-label, multicenter, prospective study was designed to collect safety and efficacy data on the Contour Profile Gel/MemoryShape breast implant. These findings extend the previously reported 2-, 6-, and 9-year results.[1–3]

PATIENTS AND METHODS

Study Design

The current study was conducted in accordance with U.S. Food and Drug Administration Breast Implant Guidance.[4] Inclusion and exclusion criteria, along with study endpoints and schedule of visits, were described previously.[2] The medium-height, moderate-profile breast implant was used in this study. Informed consent was obtained from patients before study enrollment in compliance with the principles of the International Conference on Harmonization and Good Clinical Practice according to the Declaration of Helsinki. The supplemental material provides details on (1) the Contour Profile Gel/MemoryShape Post Approval Continued Access Study and (2) the Contour Profile Gel/MemoryShape Styles Study, both initiated after enrollment into the Core Study was completed. (**See Document, Supplemental Digital Content 1**, which shows Methods and Results from the Contour Profile Gel/MemoryShape PostApproval Continued Access Study and the Contour Profile Gel/MemoryShape Styles Study, ***http://links.lww.com/PRS/C438***.)

Supplemental digital content is available for this article. A direct URL citation appears in the text; simply type the URL address into any Web browser to access this content. A clickable link to the material is provided in the HTML text of this article on the *Journal*'s website (www.PRSJournal.com).

Statistical Analysis

Demographic variables and baseline and operative characteristics were summarized by cohort using descriptive statistics for continuous variables and frequency counts and percentages for categorical variables. Safety analyses were based on events having an onset date calculated to be within 120 months of the initial implant surgery. The cumulative incidences of complications and reoperations through each of the scheduled follow-up visits were estimated using the Kaplan-Meier method. Subjects were censored as of the date of their last office visit, the 120-month time point, or the date of explantation of all initial study devices, whichever was earliest. A subject was counted only once regardless of whether the subject had bilateral or unilateral implants. In addition, if a subject or implant experienced more than one event of the same type over the course of the study, only the first event was considered in the analyses.

Kaplan-Meier survival analyses of time to rupture was calculated as the number of days from surgery to the earliest of the following dates: (1) the investigator-reported onset date, (2) the nominal date of the earliest scheduled magnetic resonance imaging at which the rupture was detected, and (3) the actual date of the earliest interim magnetic resonance imaging at which the rupture was detected. These analyses were conducted using only subjects who underwent magnetic resonance imaging evaluation. Verification of rupture, identified either directly by study investigator or through magnetic resonance imaging screening, also included visual examination of explanted and retrieved devices by Mentor Product Evaluation, whenever possible. The overall mean in circumferential chest and bra cup size change from the preoperative assessment was calculated. The Wilcoxon signed rank test was performed to test whether the overall mean change equals 0.

Percentages were tabulated and reported according to responses for global subject satisfaction ("Would subject make the same decision to have this breast surgery?"), investigator satisfaction ("Are you satisfied with implant results?"), and the Breast Evaluation Questionnaire ("How satisfied with the general appearance of your breasts are you?"). Response options were very satisfied, somewhat satisfied, neither satisfied nor dissatisfied, somewhat dissatisfied, or very dissatisfied.

RESULTS

Patient Demographic and Surgical Characteristics

A total of 1831 devices (Contour Profile Gel/MemoryShape textured, medium-height,

moderate-profile) were implanted in 955 study patients including 572 primary augmentation, 124 revision-augmentation, 190 primary reconstruction, and 69 revision-reconstruction patients between February of 2002 and September of 2004. Demographic and operative characteristics were previously published (note: one patient was reclassified from primary to revision-reconstruction, and although we acknowledge there is a clear difference between submuscular and subpectoral implant placement, through further investigation, we discovered these terms were used interchangeably among physicians and therefore have combined them into one category).[3]

Overall, 63 percent of patients completed follow-up at 10 years after implantation (equivalent to 95.5 percent follow-up each year of patients from the prior year). Follow-up rates at 10 years were 60 (primary augmentation), 63 (revision-augmentation), 67 (primary reconstruction), and 74 (revision-reconstruction) percent. The primary reasons for discontinuation were subject noncompliance (31.1 percent), subject lost to follow-up (29.9 percent), and explantation without study device reimplantation (21.4 percent).

Safety Outcomes

The vast majority (93.9 percent) of postoperative complications among all cohorts were considered mild (e.g., breast sensation changes) or moderate (e.g., infection) in severity, with only 5.8 percent of complications categorized as severe (e.g., Baker grade IV capsular contracture; 0.3 percent of data were missing). Per cohort, 4.6 (primary augmentation), 5.3 (revision-augmentation), 7.7 (primary reconstruction), and 10.5 (revision-reconstruction) percent of complications were categorized as severe at the event level (Table 1).

Reoperation was required in 22.3 (primary augmentation), 35.0 (revision-augmentation), 52.7 (primary reconstruction), and 59.7 (revision-reconstruction) percent of patients (Fig. 1). The most commonly reported reasons for reoperation included breast mass/cyst, asymmetry, lack of projection, size change, wrinkling, and Baker grade III capsular contracture (Fig. 2). Although breast masses/cysts requiring biopsy count toward reoperations in the present study, it is important to note that women with implants continue to undergo routine breast cancer surveillance including biopsy of any suspicious masses.

The rates of explantation among patients, with or without replacement of study device, were 9.2 (primary augmentation), 25.9 (revision-augmentation), 34.1 (primary reconstruction), and 49.0 (revision-reconstruction) percent (Fig. 3). The rates of explantation among patients with replacement of the study device were 4.0 (primary augmentation), 10.8 (revision-augmentation), 16.7 (primary reconstruction), and 27.9 (revision-reconstruction) percent. Patients without replacement of study devices underwent implantation with a Mentor nonstudy device (i.e., MemoryGel), Mentor saline device, other gel device, other saline device, or did not undergo reimplantation with any device. The most common reasons for implant removal included size change, lack of projection, asymmetry, wrinkling, and position dissatisfaction (Fig. 4).

Postoperative Complications

The Kaplan-Meier estimated 10-year cumulative incidence rates of Baker grade III/IV capsular contracture, at the subject level, were 3.6 (primary augmentation), 15.5 (revision-augmentation), 14.3 (primary reconstruction), and 16.4 (revision-reconstruction) percent (Fig. 5). Capsular contracture was measured by the investigator at 10 weeks and annually until 10-year follow-up and was graded in severity on a scale of I to IV according to the Baker classification. Capsular contracture among primary augmentation patients at 10 years for patients with subglandular placement (7.7 percent) compared to those with submuscular/subpectoral placement (3.05 percent) was not significantly different ($p = 0.0625$, log-rank test). To further test this finding, a proportional hazards

Table 1. Postoperative Complications through 10 Years after Implantation by Severity (Event Level)*

	Severity			
Subject Cohort	**Mild (%)**	**Moderate (%)**	**Severe (%)**	**Missing (%)**
Primary augmentation	1089 (71.4)	362 (23.7)	70 (4.6)	5 (0.3)
Revision-augmentation	286 (65.7)	125 (28.7)	23 (5.3)	1 (0.2)
Primary reconstruction	353 (62.0)	170 (29.9)	44 (7.7)	2 (0.4)
Revision-reconstruction	119 (59.5)	60 (30.0)	21 (10.5)	0 (0.0)
Overall accounting	1847/2730	717/2730	158/2730	8/2730

*Adverse events that were noticed by the subject were mild, those noted by both the subject and/or doctor were moderate, and those requiring treatment/intervention were severe.

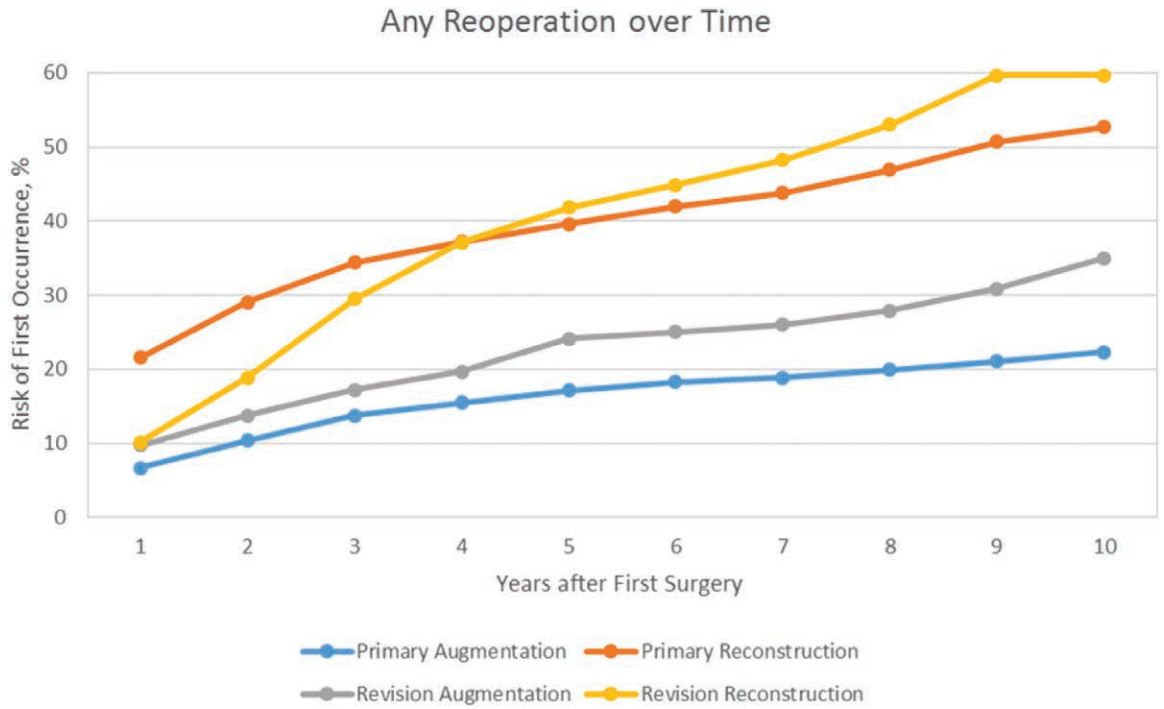

Fig. 1. Kaplan-Meier estimated cumulative incidence of any reoperation at the subject level.

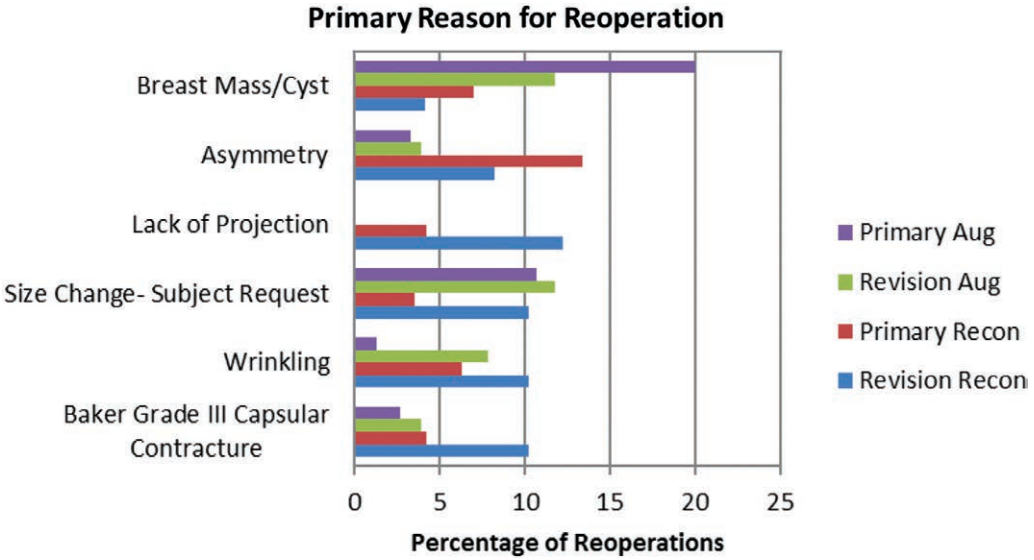

Fig. 2. Reasons for reoperation (includes only those that occurred at a rate ≥10 percent in each cohort).

regression model was fit to compare device placement while controlling for surgical approach, prior occurrence of a hematoma or seroma, and clinical site. Sites with fewer than 10 patients were pooled and included as a random effect. The proportional hazards assumption was satisfied. After controlling for these effects, the capsular contracture rate associated with subglandular device placement was significantly higher (hazard ratio, 3.1; 95 percent CI, 1.0 to 9.8; $p = 0.0358$).

The Kaplan-Meier estimated 10-year cumulative incidence rates of implant rotation were 1.3 (primary augmentation), 3.6 (revision-augmentation), 6.3 (primary reconstruction), and 5.7 (revision-reconstruction) percent. The cumulative rate of moderate and severe wrinkling among primary augmentation patients at 10 years was 2.82 percent overall, 5.37 percent for subglandular placement, and 2.46 percent for submuscular/subpectoral placement. This difference by

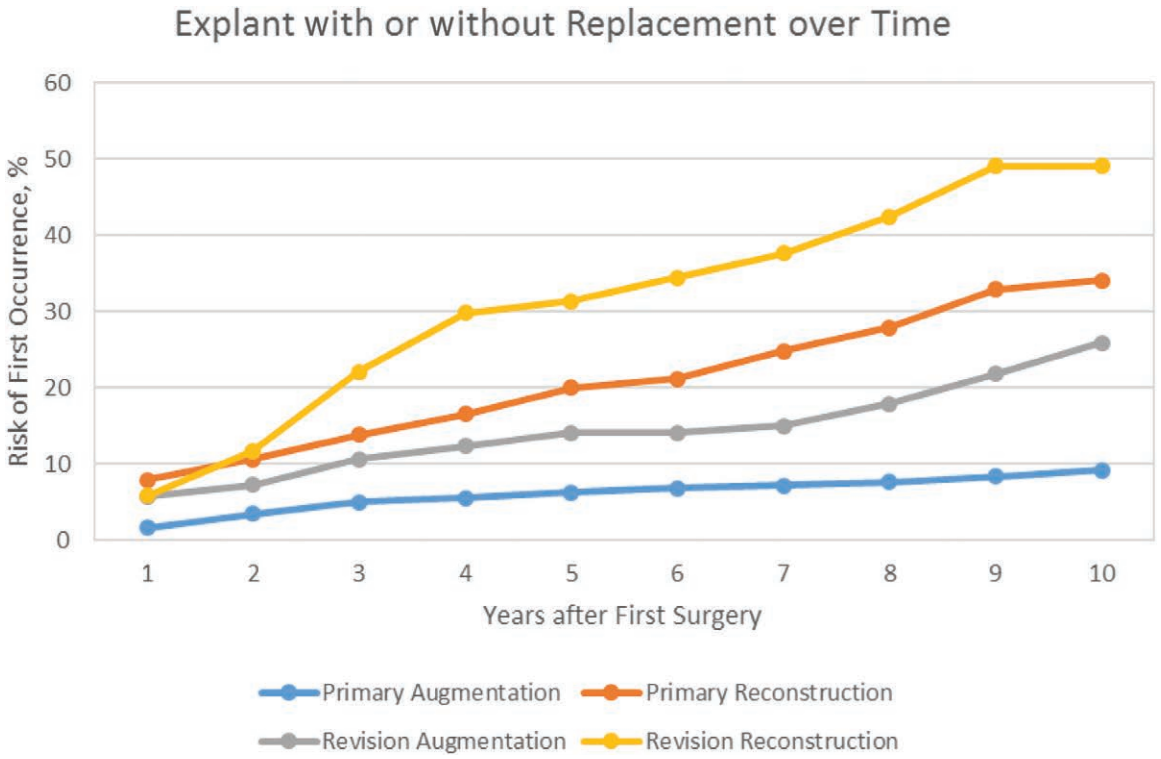

Fig. 3. Kaplan-Meier estimated cumulative incidence of explantation with or without replacement at the subject level.

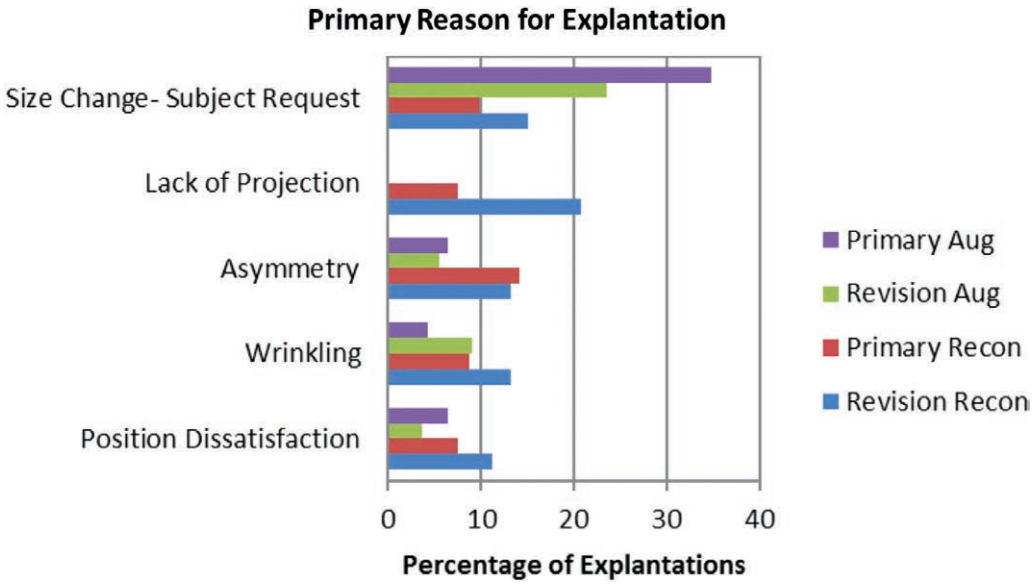

Fig. 4. Reasons for explantation (reasons include only those that occurred at a rate ≥10 percent in each cohort).

device placement was not statistically significant ($p = 0.1136$, log-rank test). Again, to further test this finding, a proportional hazards regression model was fit to compare device placement while controlling for surgical approach, prior occurrence of a hematoma or seroma, and clinical site. Sites with fewer than 10 patients were pooled and included as a random effect. The proportional hazards assumption was satisfied. Significant variation was observed between sites. Various sensitivity models were also performed to investigate the significant site effect. One site was identified as

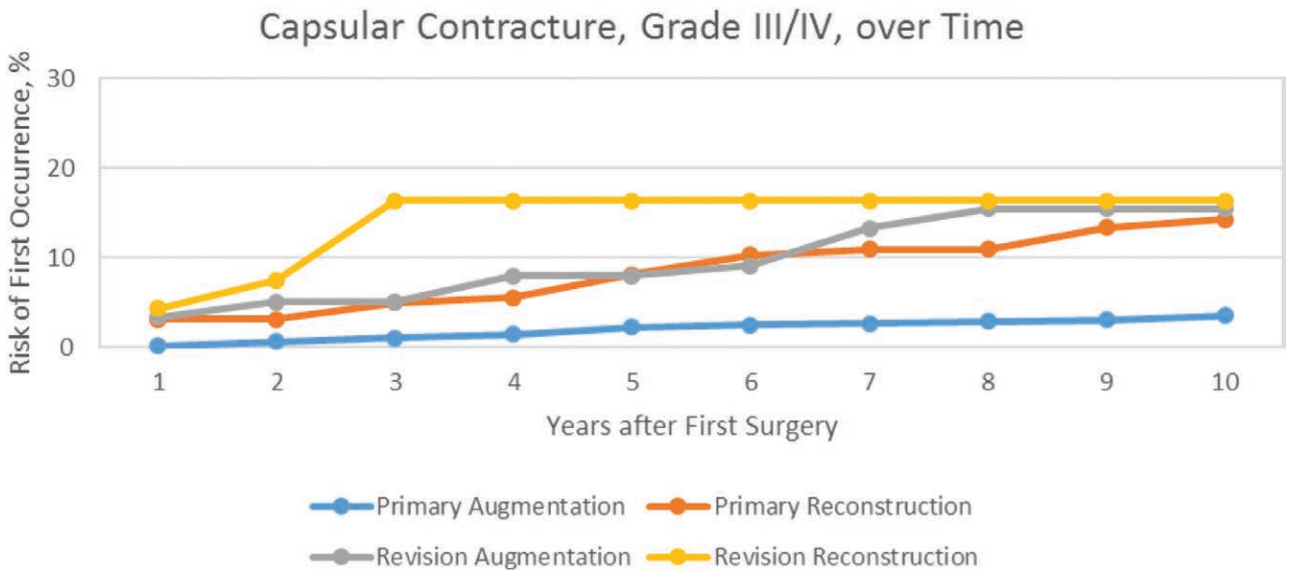

Fig. 5. Kaplan-Meier estimated cumulative incidence of Baker grade III/IV capsular contracture at the subject level.

having higher than anticipated rates of wrinkling compared with all other sites. The outlying site had high rates of wrinkling within both device placement options. When this site was removed, the cumulative rate of wrinkling was 2.17 percent at 10 years, and there was still no significant difference in wrinkling rates by device placement observed (hazard ratio, 1.66; 95 percent CI, 0.35 to 7.82; $p = 0.5219$), controlling for site variation.

Four hundred patients were initially enrolled in the magnetic resonance imaging portion of the study, as that was determined to be an adequate number to detect a silent rupture rate of 5 percent. In 2010, the protocol was modified and magnetic resonance imaging screening was implemented for all study patients. At 1, 2, 4, 6, 8, and 10 years, the respective overall follow-up rates of all patients who passed the follow-up anniversary minus deaths and discontinuations because of explantation for the magnetic resonance imaging cohort were 71, 86, 72, 63, 56, and 45 percent, respectively. Figure 6 presents the estimated rupture rates through 1, 2, 4, 6, 8, and 10 years. Overall, there were 17 suspected or confirmed reports of implant rupture for 17 patients in the original magnetic resonance imaging cohort and

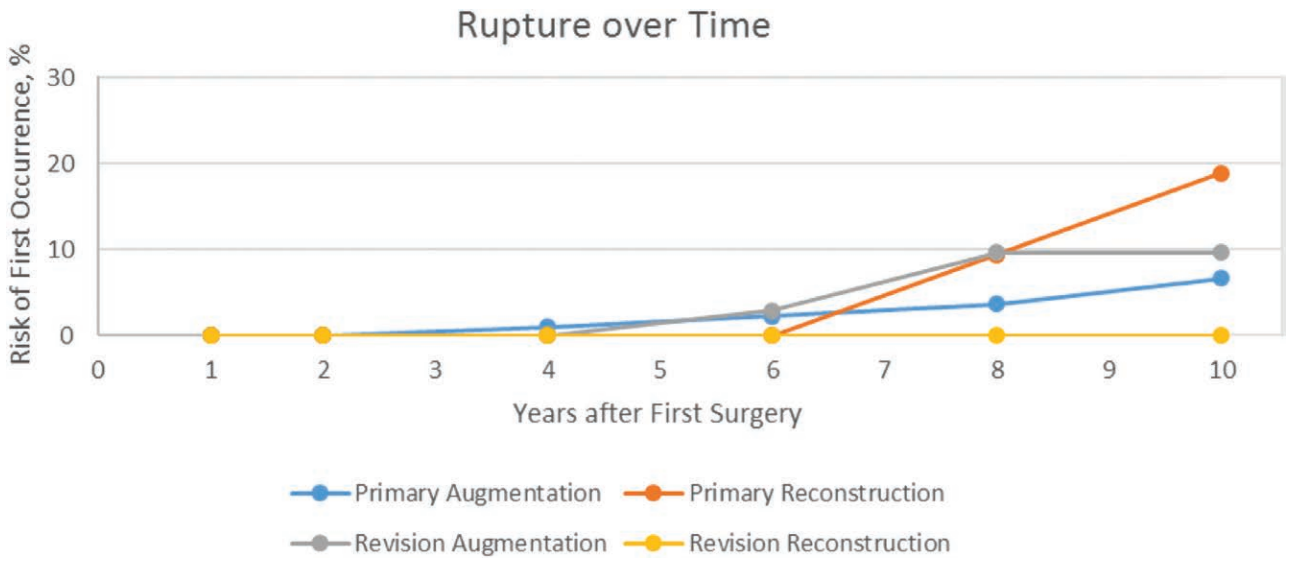

Fig. 6. Kaplan-Meier estimated cumulative incidence rates for rupture for magnetic resonance imaging substudy patients at the subject level.

20 suspected or confirmed reports of implant rupture for 18 patients in the original cohort of patients who did not undergo scheduled magnetic resonance imaging screening before 2010. A suspected rupture was identified by investigator adverse event report or magnetic resonance imaging finding. Of the 37 suspected or confirmed ruptured implants in the overall study, four cases showed definite extracapsular silicone by magnetic resonance imaging and four cases were indeterminate for extracapsular silicone. Kaplan-Meier estimated cumulative incidence rates of suspected or confirmed rupture for the magnetic resonance imaging substudy subjects at 10 years (on an implant level) were 3.3 (primary augmentation), 4.7 (revision-augmentation), 11.2 (primary reconstruction), and 0 (revision-reconstruction) percent. At the subject level, 10-year rates of suspected or confirmed rupture were 6.6 (primary augmentation), 9.6 (revision-augmentation), 18.9 (primary reconstruction), and 0 (revision-reconstruction) percent.

Through 10 years after implantation, six patients (1.0 percent) in the primary augmentation cohort had seven new diagnoses of breast cancer and one patient (0.8 percent) in the revision-augmentation cohort had one new diagnosis of breast cancer. There were no new cases of breast cancer in the primary reconstruction and revision-reconstruction cohorts. There were four incidences of late seroma at 10-year follow-up, one in the primary augmentation cohort, two in the primary reconstruction cohort, and one in the revision-reconstruction cohort. No subject was diagnosed with anaplastic large cell lymphoma (ALCL).

Efficacy Outcomes

For the primary augmentation cohort, the overall mean change in circumferential chest size through 10 years was 2.1 inches, with a mean increase of 2.2 cup sizes from baseline ($p < 0.0001$). At the 10-year follow-up visit, 96.9 percent of patients who responded to the global satisfaction question (total respondents: $n = 322$ primary augmentation patients, $n = 87$ primary reconstruction patients, $n = 66$ revision-augmentation patients, and $n = 34$ revision-reconstruction patients) indicated they would make the same decision to undergo breast implant surgery. Similarly, when asked about satisfaction with breast appearance, 86.2 percent (total respondents: $n = 299$ primary augmentation patients, $n = 93$ primary reconstruction patients, $n = 60$ revision-augmentation patients, and $n = 33$ revision-reconstruction patients) of patients indicated they were very satisfied or somewhat satisfied at 10 years, compared with only 20.7 percent at baseline (total respondents: $n = 569$ primary augmentation patients, $n = 187$ primary reconstruction patients, $n = 124$ revision-augmentation patients, and $n = 68$ revision-reconstruction patients). Investigator satisfaction was 97.6 percent ($n = 1728$).

DISCUSSION

When evaluating the results of this study, two important aspects merit emphasis: the documented safety profile and the quality of the aesthetic results as evidenced by patient satisfaction. When viewed alongside results associated with round implants[3] and even other types of anatomical implants,[5] not only do shaped implants have a superior safety profile, but the results of this study demonstrate an encouraging performance history that translates into effective results. To place the results of this study into context, it is helpful to reemphasize why shaped implants were initially developed. A typical, round, silicone gel implant merges with the overlying soft-tissue framework to create the external three-dimensional result the human eye evaluates aesthetically. When the patient is upright, the gel in a round implant can settle to the bottom of the device, causing a variable, irregular folding in the shell.[6] The result is a trend toward a teardrop shape, with the now underfilled upper pole shell variably folding and wrinkling. If there is enough soft tissue to mask these contour irregularities, this is an aesthetically tolerable event. However, the long-term sequelae of such sharply defined stress points along the fold may result in weakening of the shell, ultimately leading to fold flaw failure and rupture.[7] In cases where a proportionately higher volume round implant provides most of the volume to a smaller breast, the round implant can tend to overfill the upper pole, creating a distracting and, in many instances, undesirable amount of upper pole breast fullness.[8] The design of the Contour Profile Gel/MemoryShape device was strategically developed to address both concerns. By creating the teardrop shape initially with the anatomically shaped shell, and then filling this shell with a firmer, more cohesive gel, a stable shape is created directly by the device. Rather than the breast shaping the implant, now with the Contour Profile Gel/MemoryShape device, it is most decidedly the implant that is shaping the breast. Because the shape of the implant is stable secondary to

the presence of a more cohesive gel, the tendency for the shell to fold is reduced, leading to fewer creases in the implant, less chance for fold flaw failure, and, theoretically, a reduced rupture rate (Fig. 7). This becomes important, as long-term rupture is a common complication associated with silicone breast implants. The 10-year data reported here show a favorable rupture rate in the primary augmentation cohort, which lends support to the initial premise that limiting the propensity of the shell to fold will translate into improved long-term device performance. The reported rupture rates for the other cohorts are higher, possibly because of the more challenging surgical environments posed by revision or reconstructive procedures, where the incidence of capsular contracture and shell folding might occur more frequently. It is also important to note that there were no cases of breast implant-associated ALCL in the current study. Although, to date, all patients with breast implant-associated ALCL have had prolonged exposure to textured implants, a recent study suggests that the implant-specific risk of developing breast implant-associated ALCL per 10,000 implant years is 1:60,631 with Siltex texturing.[9]

The data confirm that the Contour Profile Gel/MemoryShape device is associated with a relatively low rate of capsular contracture that compares very favorably with reported rates for other devices.[3,5] Siltex texture is created by pressing a sheet of foam into an uncured sheet of silicone and then bonding this thin sheet to the surface of the implant, thereby creating a microtextured relief on the outer implant shell. This roughed surface then assists in maintaining the orientation of the implant because of the friction that is subsequently present between the implant surface and capsule. More importantly, this texture has been noted to reduce the rate of capsular contracture in textured versus smooth implants.[10] The precise mechanism of action for the reduction in the rate of capsular contracture with shaped implants remains poorly understood.[10] Another but perhaps small contribution to observed differences relates to these implants being firmer and more resistant to shape change than a traditional round device; therefore, a mild amount of capsular contracture can develop without any appreciable change in the overall feel or shape of the breast.

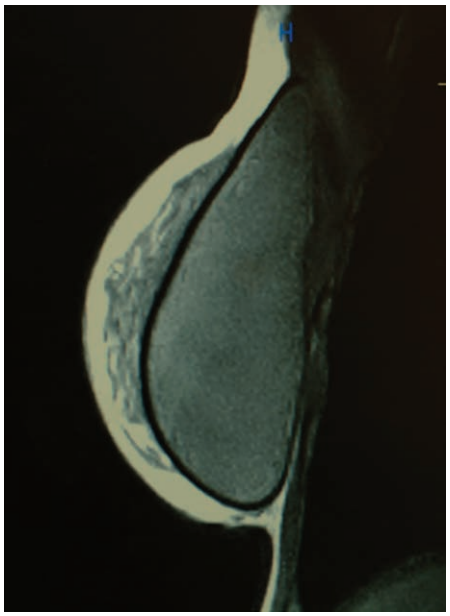

Fig. 7. Upright magnetic resonance imaging scan of a MemoryShape implant.

This study also supports the overall effectiveness of the implant. Both patient and surgeon satisfaction rates are high, implying overall aesthetic success with the device. It is difficult to assess the aesthetic performance of the implant more definitively than what has been reported because of patient body type, breast size, implant size, implant location, and varying aesthetic goals. Based on the personal experience of the surgeon authors of this article, Contour Profile Gel/MemoryShape implants offer aesthetic advantages related to control of the upper pole contour and the creation of an overall pleasing shape to the breast.

Although this study has documented both safety and effectiveness associated with the use of Contour Profile Gel/MemoryShape devices, certain modifications in technique must be incorporated into the overall surgical plan for the implants to function effectively. Perhaps the most important concern associated with the use of anatomical devices relates to the risk of postoperative rotation with distortion of the breast shape. The incidence of rotation in this study ranged from 1.3 percent in the primary augmentation cohort to 6.3 percent in the primary reconstruction cohort. Contributing to these low rotation rates are the technical modifications relating to pocket development that are required to limit the potential for rotation. Specifically, the dimensions of the pocket should closely match the dimensions of the chosen implant. In this fashion, the soft-tissue–supporting framework along with the textured surface can reliably combine to hold the implant in position until the pocket stabilizes. In any surgical situation where the implant pocket and the base diameter of the pocket exceed those of the chosen implant, the risk for rotation increases.

Therefore, in cases of total capsulectomy, or implant-based reconstruction after mastectomy, it may be difficult to control pocket base diameter, and Contour Profile Gel/MemoryShape implants should be used only with great care in such cases. It should be pointed out to the patient that the breast will have a firmer palpability because of the more highly cohesive gel, and if this feature of the operative strategy is deemed to be problematic, a more traditional, round, less cohesive implant could avoid this potential problem.

Although the present study has many strengths, limitations included the open-label nature, lack of a control group, and lower than desired follow-up rate to optimally minimize potential bias. Also, the sample size determined to prove acceptable precision in the estimation of commonly occurring complications following breast implantation does not allow for the detection of rare events.

CONCLUSION

Given appropriate surgical technique, the results from this study suggest that Contour Profile Gel/MemoryShape implants provide for safe and effective use in a variety of clinical situations.

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OPEN

MemoryGel Breast Implants: Final Safety and Efficacy Results after 10 Years of Follow-Up

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PATIENT SAFETY

Background: Mentor MemoryGel Breast Implants were approved by the U.S. Food and Drug Administration in November of 2006. Patients in the Core clinical study supporting this approval were followed for 10 years.
Methods: This prospective, multicenter, clinical study included primary augmentation, revision augmentation, primary reconstruction, and revision reconstruction patients implanted with smooth or Siltex Texture MemoryGel Implants. Incidence, severity, and method of resolution for all postoperative complications were assessed on per-patient and per-implant bases. The primary effectiveness endpoints were overall mean change in chest circumference and bra cup size following the implantation procedure.
Results: Primary augmentation (n = 552), revision augmentation (n = 145), primary reconstruction (n = 251), and revision reconstruction (n = 60) patients were enrolled in the study. Kaplan-Meier estimated 10-year cumulative incidence rates for key complications at the subject level for Baker grade III/IV capsular contracture were as follows: primary augmentation, 12.1 percent; revision augmentation, 24.4 percent; primary reconstruction, 20.5 percent; and revision reconstruction, 36.9 percent. For infection, rates were as follows: primary augmentation, 1.6 percent; revision augmentation, 1.4 percent; primary reconstruction, 6.2 percent; and revision reconstruction, 0 percent. For explantation with or without replacement, rates were as follows: primary augmentation, 11.6 percent; revision augmentation, 24.1 percent; primary reconstruction, 33.4 percent; and revision reconstruction; 37.8 percent. For rupture, rates were as follows: primary augmentation, 24.2 percent; revision augmentation, 23.7 percent; primary reconstruction, 32.7 percent; and revision reconstruction, 38.7 percent. For any reoperation, rates were as follows: primary augmentation, 25.5 percent; revision augmentation, 43.6 percent; primary reconstruction, 49.0 percent; and revision reconstruction, 50.7 percent.
Conclusion: The results of this study demonstrate that MemoryGel Implants are safe and effective for use in women undergoing breast augmentation or reconstruction. (*Plast. Reconstr. Surg.* 147: 556, 2021.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

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MemoryGel Breast Implants (Mentor Worldwide LLC, Irvine, Calif.), approved by the U.S. Food and Drug Administration in 2006 for breast augmentation in women aged 22 years and older and for breast reconstruction in women of any age, consist of a single-lumen, round silicone elastomer shell, with a patch on the posterior side, and filled with a cohesive silicone gel. The 10-year prospective clinical study, initiated in September of 2000, was designed to assess the safety and effectiveness of MemoryGel Implants in women undergoing primary breast augmentation, primary breast reconstruction, or revision surgery. These findings extend the previously reported 3- and 6-year results,[1,2] which demonstrated that MemoryGel Implants were safe and effective. In this article, we present final safety and effectiveness data from the MemoryGel Core Study with 10 years of follow-up.

PATIENTS AND METHODS

Study Design

The study was designed and conducted in accordance with the U.S. Food and Drug Administration's then-current draft of "Guidance for Saline, Silicone Gel, and Alternative Breast Implants: Final Guidance for Industry and Food and Drug Administration Staff" (final version dated February 11, 2003), and safety analyses were conducted in accordance with the November 17, 2006 "Saline, Silicone Gel, and Alternative Breast Implants: Guidance for Industry and FDA Staff" that superseded the 2003 document (*https://www.fda.gov/media/71081/download*). The study evaluation schedule summary, measures of patient satisfaction, assessments of quality of life, protocol for magnetic resonance imaging substudy, and statistical analyses have been described elsewhere.[1] Briefly, at each scheduled follow-up visit through 10 years, the following procedures and evaluations were performed: nipple and breast sensitivity assessment, breast measurements, capsular contracture assessment, concomitant medications, quality-of-life questionnaires (at 1-, 2-, 3-, 4-, 6-, 8-, and 10-year visits), adverse event evaluation, magnetic resonance imaging scan on subset of patients (1-, 2-, 4-, 6-, 8-, and 10-year visits), and Rheumatic Disease Diagnosis Questionnaire (if investigator believed, in his or her medical opinion, that the patient's symptoms warranted a rheumatologic examination, rheumatologic confirmation was to be performed).

Patients

Eligible patients were women who were candidates for primary breast augmentation, primary breast reconstruction, or revision surgery. Although the study presented here enrolled augmentation patients who were aged 18 years or older, primary augmentation with MemoryGel Implants is currently indicated for women aged 22 years or older in the United States. Each patient provided written informed consent, and the study was approved by the institutional review board at each site. Women who were pregnant, had nursed a child within 3 months of study enrollment, were previously implanted with any silicone implant other than breast implants, had a confirmed diagnosis of rheumatic disease, currently had a condition that could compromise or complicate wound healing (except reconstruction patients), had a diagnosis of active cancer (only augmentation patients), had an infection or abscess, demonstrated tissue characteristics incompatible with implant placement (e.g., tissue damage resulting from radiation therapy, inadequate tissue, or compromised vascularity), had a premalignant breast disease without a subcutaneous mastectomy, had an untreated or inappropriately treated breast malignancy, without mastectomy, or who had any condition that would make magnetic resonance imaging prohibitive were excluded from this study.

Safety Analyses

All patients undergoing implantation with a study device were included in the safety analysis. If a study device was explanted, data up to and including the date of the explantation were included in all analyses. As a condition of the 2006 U.S. Food and Drug Administration approval, patients who underwent explantation continued to be followed for safety through 10 years, even if a study device was not reimplanted.

Incidence of postoperative complications were analyzed using the Kaplan-Meier method. All event rates presented here are at the subject level, unless otherwise specified. The severity, resolution, treatment required, and causality of the complications were assessed in addition to reoperations and explantations.

Magnetic Resonance Imaging Substudy

A subset of randomly selected patients underwent magnetic resonance imaging at the 1-, 2-, 4-, 6-, 8-, and 10-year visits after implantation in an attempt to estimate the overall rupture rate (magnetic resonance imaging cohort A). However,

beginning in November of 2006, as a condition of U.S. Food and Drug Administration approval, all patients enrolled in the study from this point onward were required to undergo magnetic resonance imaging evaluation at the same times as magnetic resonance imaging cohort A (i.e., 6, 8, and 10 years after surgery; magnetic resonance imaging cohort B). An implant was considered to be ruptured if the investigator reported rupture as an adverse event, the most recent magnetic resonance imaging evaluation indicated that on implant evaluation there was rupture or indeterminate rupture, or on soft-tissue evaluation there was a judgment of definite extracapsular silicone or indeterminate extracapsular silicone. If the implant was explanted and returned to and physically examined by Mentor and determined not to be ruptured, it was not counted as a rupture. Kaplan-Meier survival analyses of time to rupture were performed to estimate the cumulative incidence of rupture.

Effectiveness Analyses

The primary effectiveness endpoints were the overall mean change in chest circumference and the overall mean increase in bra cup size, to be assessed principally in the primary augmentation cohort. The overall mean changes and standard deviation from the preoperative assessment were calculated for circumferential chest size and cup size increase. The Wilcoxon signed rank test was performed to test for statistical significance.

Secondary effectiveness was based on changes in quality of life. Each quality-of-life endpoint was summarized using descriptive statistics (mean, median, standard deviation, and minimum and maximum). Global patient satisfaction, assessed by asking the patient whether she would make the same decision to undergo breast implant surgery, was an additional effectiveness endpoint. Frequency counts, percentages, and 95 percent confidence intervals for the proportion of patients who would make the same decision to undergo surgery were tabulated for each follow-up visit. Immediate postmastectomy patients were excluded from these analyses for the primary reconstruction cohort and the overall patient population.

RESULTS

Patient Demographics

A total of 1008 patients (receiving 1898 implants) across 48 sites in the United States were included in four cohorts: primary augmentation ($n = 552$ patients), revision augmentation ($n = 145$), primary reconstruction ($n = 251$), and revision reconstruction ($n = 60$). The overall 10-year follow-up rate across all cohorts was 62 percent, equivalent to approximately 95.3 percent patient retention from each year prior (primary augmentation, 57 percent; revision augmentation, 64 percent; primary reconstruction, 73 percent; and revision reconstruction, 67 percent). Demographic characteristics are summarized in Table 1.

Effectiveness

For patients in the primary augmentation cohort and in the other three cohorts, the overall mean changes over the course of the study in circumferential chest size were positive and highly statistically significant (overall mean change of all cohorts was 6.1 cm; $p < 0.001$). For the primary augmentation cohort, there was a statistically significant mean increase of 1.8 bra cup sizes from baseline ($p < 0.0001$).

At the 10-year follow-up visit, 97.6 percent of patients who answered the question (523 of 536) indicated that they would make the same decision to undergo breast implant surgery (primary augmentation, 97.1 percent; revision augmentation, 98.8 percent; primary reconstruction, 99.1 percent; and revision reconstruction, 94.4 percent). Similarly, at 10-year follow-up, among patients who had any type of reoperation, 98.2 percent indicated that they would make the same decision to undergo breast implant surgery.

Postoperative Complications and Resolution

The 10-year Kaplan-Meier estimated cumulative incidence rates for key postoperative complications are shown in Table 2 and Figure 1. In the overall patient population, 48.3 percent of reported complications (excluding rupture/indeterminate rupture) did not receive any treatment, 36.9 percent were treated by a secondary procedure, and 14.3 percent were treated with medication. Only 0.8 percent of the complications resulted in hospitalization.

Reoperations

The 10-year estimated cumulative incidence rates for any reoperation and implant-related complications (including only reoperations because of capsular contracture, rippling, infection, hematoma/seroma, and rupture) are listed in Table 2. The primary reasons for reoperation that occurred at a rate of greater than or equal to 10 percent in at least one patient cohort were

Table 1. Demographic Characteristics*

Characteristic	Augmentation		Reconstruction	
	Primary (*n* = 552)	Revision (*n* = 145)	Primary (*n* = 251)	Revision (*n* = 60)
Median age, yr	34	43	46	51
Age range, yr	18–65	20–63	18–79	29–72
Race				
Caucasian	483 (87.5)	134 (92.4)	231 (92.0)	56 (93.3)
Asian	17 (3.1)	2 (1.4)	3 (1.2)	1 (1.7)
African American	11 (2.0)	2 (1.4)	7 (2.8)	2 (3.3)
Other	41 (7.4)	7 (4.8)	10 (4.0)	1 (1.7)
Marital status				
Married	313 (56.7)	86 (59.3)	173 (68.9)	40 (66.7)
Never married	135 (24.5)	25 (17.2)	35 (13.9)	5 (8.3)
Divorced	81 (14.7)	26 (17.9)	30 (12.0)	13 (21.7)
Separated	17 (3.1)	3 (2.1)	5 (2.0)	1 (1.7)
Widowed	6 (1.1)	5 (3.4)	8 (3.2)	1 (1.7)
Education				
<12 yr	7 (1.3)	0 (0)	3 (1.2)	2 (3.3)
High school graduate	74 (13.4)	26 (17.9)	42 (16.7)	9 (15.0)
Some college	215 (38.9)	56 (38.6)	66 (26.3)	20 (33.3)
College graduate	189 (34.2)	45 (31.0)	85 (33.9)	16 (26.7)
Postgraduate	60 (10.9)	17 (11.7)	47 (18.7)	9 (15.0)
Missing	7 (1.3)	1 (0.7)	8 (3.2)	4 (6.7)
Previous breast surgery (excluding mastectomy)				
No	535 (96.9)	89 (61.4)	180 (71.7)	22 (36.7)
Yes	17 (3.1)	55 (37.9)	71 (28.3)	38 (63.3)
Missing	0 (0)	1 (0.7)	0 (0)	0 (0)
Smoking history				
Never smoked	328 (59.4)	79 (54.5)	151 (60.2)	29 (48.3)
Currently smoker	107 (19.4)	25 (17.2)	21 (8.4)	8 (13.3)
Former smoker	117 (21.2)	41 (28.3)	79 (31.5)	23 (38.3)

*Values are No. (%) unless otherwise stated.

capsular contracture (Baker grade II, III, or IV), breast mass, rupture, and asymmetry (Fig. 2). The number of reoperations and additional operations are listed in Table 3. Types of additional surgical procedures through 10 years that occurred at a rate of greater than or equal to 10 percent in at least one patient cohort are listed in Table 4.

Explantation

The most commonly reported reasons for explantation that occurred at a rate of greater than or equal to 10 percent in at least one patient cohort through 10 years were size change, capsular contracture (Baker grade II, III, or IV), rupture, and asymmetry (Fig. 3). Of the 189 patients whose devices were explanted, 108 (57.1 percent) were reimplanted with a study device.

Rupture

Patient accounting for both the original magnetic resonance imaging substudy cohort (magnetic resonance imaging cohort A) and the non–magnetic resonance imaging cohort who underwent magnetic resonance imaging evaluation starting in 2006 as a condition of approval (magnetic resonance imaging cohort B) is presented in Figure 4. For the 420 patients enrolled in magnetic resonance imaging cohort A (primary augmentation, $n = 202$; revision augmentation, $n = 56$; primary reconstruction, $n = 134$; and revision reconstruction, $n = 28$), the overall 10-year follow-up rate was 53 percent (primary augmentation, 46 percent; revision augmentation, 48 percent; primary reconstruction, 68 percent; and revision reconstruction, 58 percent). The overall Kaplan-Meier estimated cumulative rupture rates (suspected or confirmed) for patients and implants are presented in Table 2 and Figure 5. There were 77 suspected or confirmed ruptured implants (primary augmentation, $n = 31$; revision augmentation, $n = 11$; primary reconstruction, $n = 29$; and revision reconstruction, $n = 6$) among 64 patients (primary augmentation, $n = 25$; revision augmentation, $n = 8$; primary reconstruction, $n = 25$; and revision reconstruction, $n = 6$) in magnetic resonance imaging cohort A. Of these 77 implants in 64 patients, at 6-year follow-up, rupture was detected in 20 implants in 17 patients, and at 8-year follow-up, rupture was detected in 40 implants in 33 patients. Mean time to rupture for the 77 implants was 7.9 years. Seventy-five of the 77 implants were considered silent ruptures. The overall Kaplan-Meier estimated cumulative silent rupture rates at 10 years were 27.3 percent and 18.1 percent for patients and implants, respectively. The overall Kaplan-Meier estimated

Table 2. Ten-Year Kaplan-Meier Estimated Cumulative Incidence Rates of Occurrence of Key Complications

	Augmentation				Reconstruction			
	Primary (n = 552)		Revision (n = 145)		Primary (n = 251)		Revision (n = 60)	
Complications	**%**	**95% CI**	**%**	**95% CI**	**%**	**95% CI**	**%**	**95% CI**
Key complications								
Any reoperation	25.5	21.9–29.5	43.7	35.8–52.4	49.0	42.6–55.7	50.7	38.7–64.0
Implant-related reoperation*	11.94	9.39–15.13	21.03	15.09–28.89	23.00	17.60–29.73	28.41	18.07–42.91
Capsular contracture Baker grade III/IV	12.1	9.6–15.2	24.4	18.1–32.5	20.5	15.5–26.7	36.9	25.0–52.2
Explantation with or without replacement	11.6	9.1–14.8	24.1	17.7–32.3	33.4	27.6–40.1	37.8	26.7–51.7
Explantation with replacement with study device	7.4	5.4–10.2	13.6	8.6–21.1	19.8	14.9–25.9	24.8	15.0–39.2
Rupture rates for MRI cohort A patients (suspected or confirmed)	24.2	17.0–33.9	23.7	12.3–42.8	32.7	23.2–44.8	38.8	19.1–67.9
Rupture rates for MRI cohort A implants (suspected or confirmed)	14.9	10.7–20.6	16.5	9.3–28.3	24.3	17.4–33.3	25.8	12.1–49.8
Rupture rates for MRI cohort B patients (suspected or confirmed)	21.4	15.3–29.5	7.5	2.5–21.6	36.1	24.3–51.4	43.9	22.3–73.5
Rupture rates for MRI cohort B implants (suspected or confirmed)	12.5	9.1–17.2	6.3	2.7–14.6	28.1	19.2–40.0	44.4	24.8–70.1
Infection	1.6	0.9–3.1	1.4	0.4–5.5	6.2	3.8–10.1	0	
Other complications ≥5% in at least one cohort								
Nipple sensation changes†	12.8	10.2–16.0	13.6	8.9–20.4	2.1	0.9–5.0	4.0	1.0–15.2
Breast mass	5.6	3.9–7.9	6.0	3.0–11.6	8.6	5.5–13.4	5.2	1.7–15.1
Breast pain†	2.9	1.8–4.8	3.2	1.2–8.2	5.2	2.9–9.2	5.2	1.7–15.2
Patient dissatisfaction	0.4	0.1–1.5	3.6	1.5–8.5	4.8	2.5–9.2	9.0	3.4–23.0
Granuloma	0.2	0.0–1.3	2.3	0.8–7.1	0		5.0	1.6–14.7
Implant malposition/displacement†	1.0	0.4–2.5	2.3	0.7–7.0	2.3	1.0–5.5	6.7	2.6–16.9
Metastatic disease	0		0		6.9	4.2–11.2	3.8	1.0–14.6
Lack of projection	0		0		1.0	0.2–3.8	5.5	1.8–16.3
Symmastia	0.2	0.0–1.7	0		0		5.0	1.6–14.7

MRI, magnetic resonance imaging.
*Implant-related complications included capsular contracture, rippling, infection, hematoma/seroma, and rupture.
†Mild occurrences excluded.

cumulative symptomatic rupture rates based on the magnetic resonance imaging cohort at 10 years were 0.6 percent and 0.3 percent for patients and implants, respectively. The cumulative incidence rate of confirmed rupture in magnetic resonance imaging cohort A on a patient and implant level is reported in Table 5.

For the remainder of patients enrolled in magnetic resonance imaging cohort B, the overall 10-year follow-up rate was 41 percent (primary augmentation, 37 percent; revision augmentation, 45 percent; primary reconstruction, 55 percent; and revision reconstruction, 44 percent). The overall Kaplan-Meier estimated cumulative rupture rates at 10 years are listed in Table 2. There were 68 suspected or confirmed ruptured implants (primary augmentation, n = 34; revision augmentation, n = 5; primary reconstruction, n = 21; and revision reconstruction, n = 8) among 56 patients (primary augmentation, n = 29; revision augmentation, n = 3; primary reconstruction, n = 18; and revision reconstruction, n = 6). Of these 68 implants in 56 rupture patients, at 6-year-follow up, rupture was detected in 15 implants in 13 patients, and at 8-year follow-up, rupture was detected in 35 implants in 30 patients. Mean time to rupture for the 68 implants was 8.3 years. Sixty-five of the 68 implants were considered silent ruptures. The overall Kaplan-Meier estimated cumulative silent and symptomatic rupture rates at 10 years were 22.8 percent and 0.6 percent for patients, and 14.7 percent and 0.5 percent for implants, respectively. The cumulative incidence rate of confirmed rupture in magnetic resonance imaging cohort B on a patient and implant level is reported in Table 5.

In total (including magnetic resonance imaging cohorts A and B), 81 confirmed ruptured implants were removed, seven suspected ruptured implants (including one not ruptured at explantation) were removed, and 41 suspected ruptured implants were not removed (unknown, two confirmed ruptures and 14 suspected ruptures). Rupture was reported as the reason for implant removal in 45 implants (primary augmentation, n = 14; revision augmentation, n = 7; primary reconstruction, n = 21; and revision reconstruction, n = 2) in 38 patients. Four additional implants (primary augmentation, n = 2; revision augmentation, n = 1; primary reconstruction, n = 0; and revision reconstruction, n = 0) in four patients

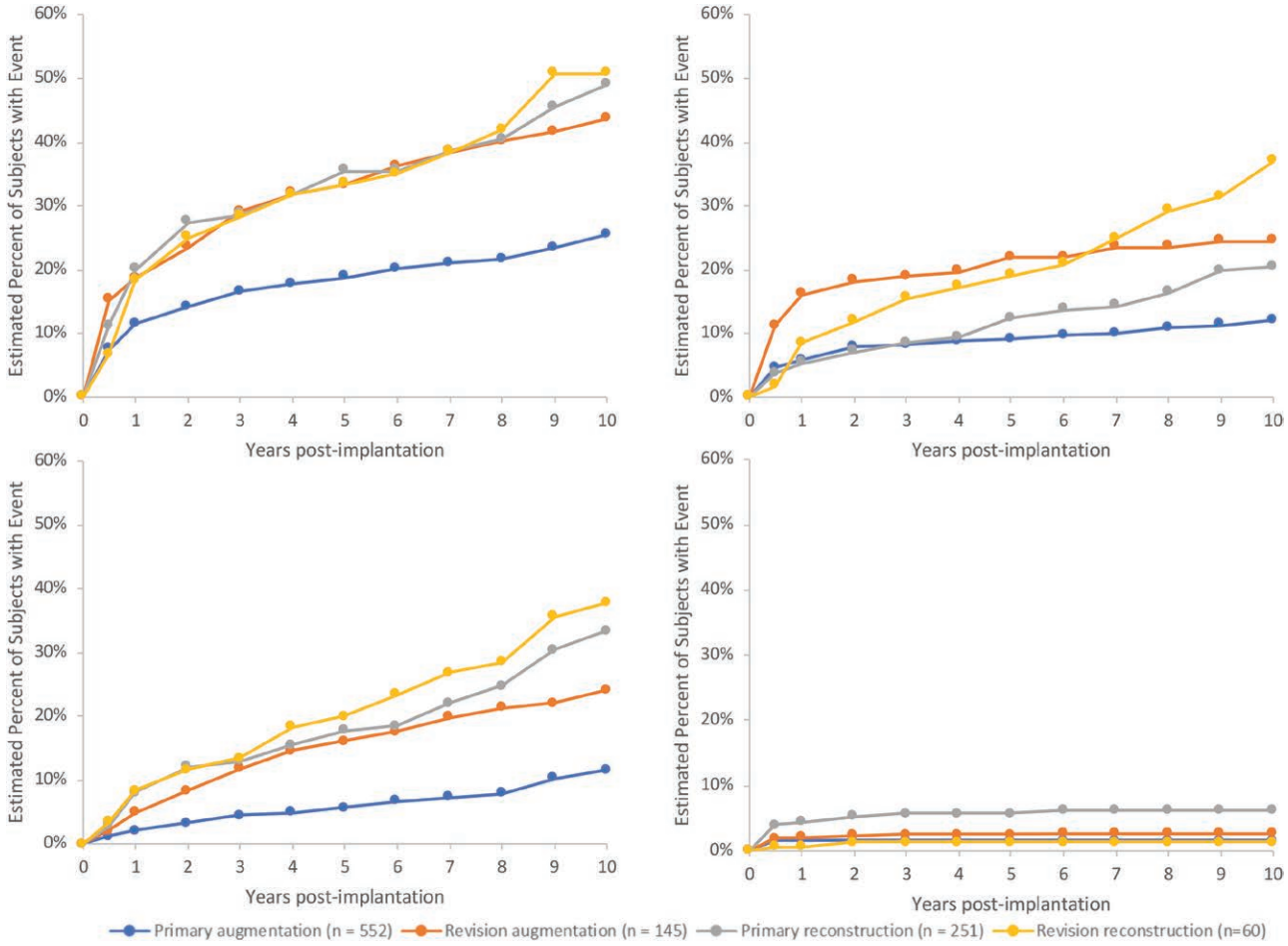

Fig. 1. Kaplan-Meier estimated cumulative incidence rates of (*above*, *left*) reoperation, (*above*, *right*) capsular contracture Baker grade III and IV, (*below*, *left*) explantation with or without replacement, and (*below*, *right*) infection.

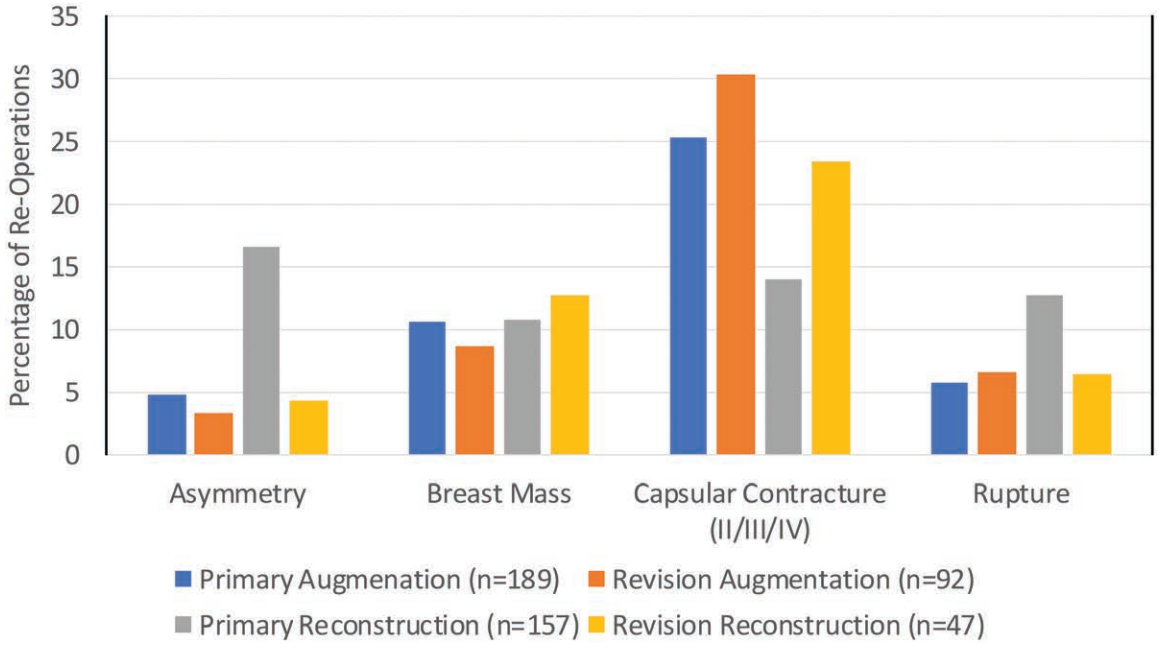

Fig. 2. Primary reason for reoperation through 10 years (frequency ≥10 percent in at least one cohort).

Table 3. Numbers of Reoperations and Additional Surgical Procedures through 10 Years

	Augmentation		Reconstruction	
	Primary	Revision	Primary	Revision
No.	552	145	251	60
No. of patients who had reoperations	133	61	115	30
No. of reoperations	189	92	157	47
Additional surgical procedures	329	172	320	94

Table 4. Types of Additional Surgical Procedures through 10 Years*

	Primary Augmentation	Revision Augmentation	Primary Reconstruction	Revision Reconstruction
No.	329	172	320	94
Explantation	105	61	116	31
Explantation with replacement with study device	61	31	62	19
Explantation without replacement with study device	44	30	54	12
Capsulectomy	55	29	25	10
Capsulotomy	31	23	39	5
Biopsy	29	13	23	13

*Greater than or equal to 10% in at least one cohort.

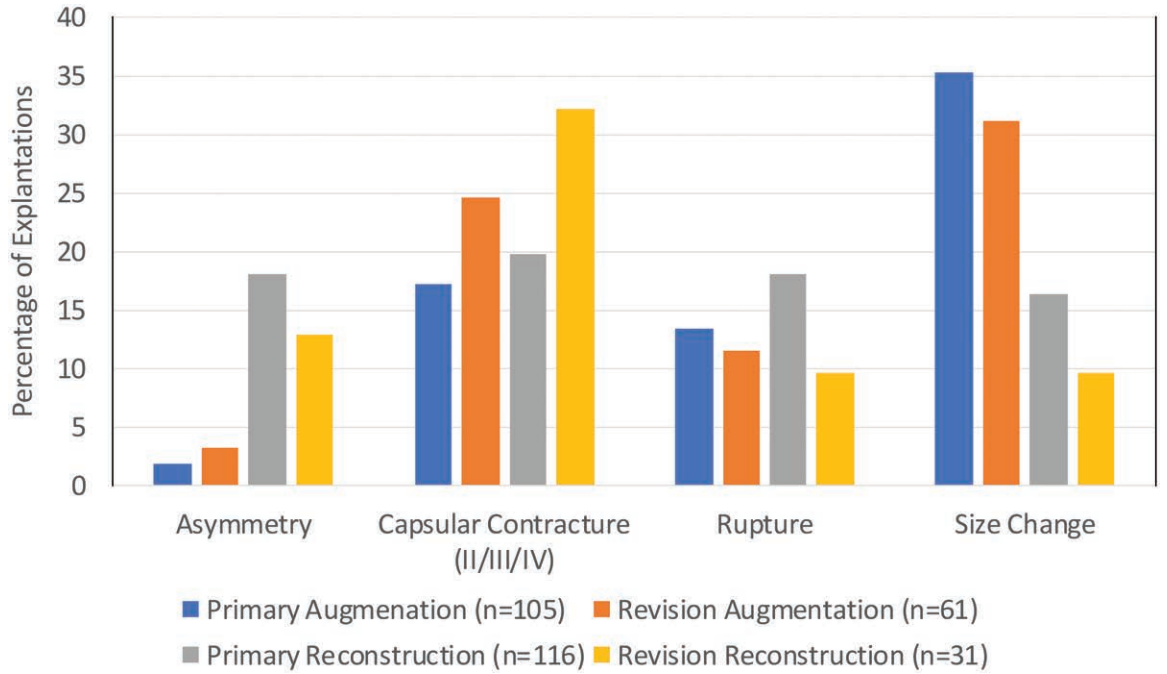

Fig. 3. Primary reason for explantation through 10 years (frequency ≥10 percent in at least one cohort).

were removed because of suspected rupture. Two implants (revision augmentation, $n = 1$; and primary reconstruction, $n = 1$) in two patients were removed because of suspected rupture, but the implants were intact on explantation. Fifty-four suspected ruptures were not removed.

Deaths

Overall, 28 deaths occurred through 10-year follow-up: two in the primary augmentation cohort (lung cancer, $n = 1$; and acute alcohol intoxication, $n = 1$), two in the revision augmentation cohort (suicide, $n = 1$; and primary brain carcinoma, $n = 1$), 23 in the primary reconstruction cohort (cancer, $n = 21$; hypertrophic cardiomyopathy, $n = 1$; and unknown but according to the site "probably cancer," $n = 1$), and one in the revision reconstruction cohort (metastatic breast cancer).

Stillbirth

Among study participants, there was one incidence of stillbirth of 291 pregnancies.

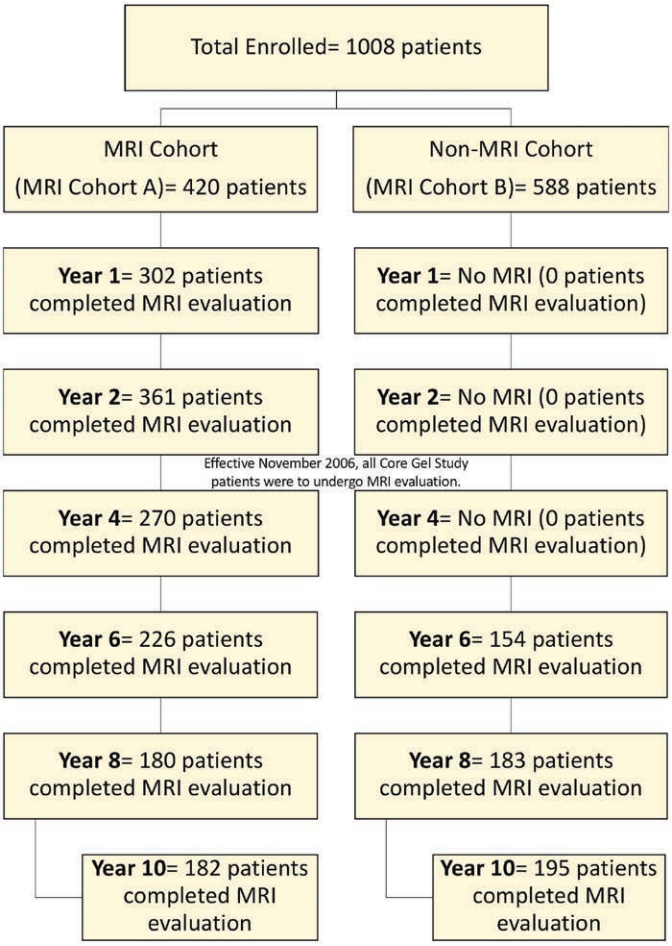

Fig. 4. Patients in magnetic resonance imaging (*MRI*) cohorts A and B who completed magnetic resonance imaging evaluation by year.

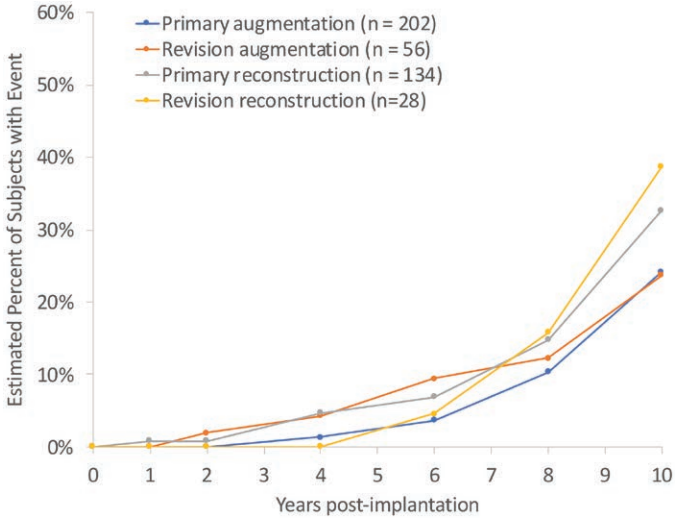

Fig. 5. Kaplan-Meier estimated cumulative incidence of rupture by patient.

Table 5. Cumulative Incidence Rate of Confirmed Rupture in Magnetic Resonance Imaging Cohorts A and B

	Augmentation				Reconstruction			
	Primary		Revision		Primary		Revision	
	%	95% CI	%	95% CI	%	95% CI	%	95% CI
MRI cohort A								
Implant level	7.36	4.53–11.84	9.85	4.71–20.01	18.98	12.91–27.41	12.26	3.87–35.14
Patient level	9.81	5.49–17.21	13.85	5.83–30.92	23.04	15.02–34.39	17.65	5.83–30.92
MRI cohort B								
Implant level	4.63	2.64–8.06	7.90	5.68–10.93	21.29	13.50–32.65	25.56	10.35–54.95
Patient level	7.61	4.14–13.76	2.63	0.37–17.25	27.70	17.29–42.54	23.64	8.20–57.27

MRI, magnetic resonance imaging.

Breast Cancer

During the 10-year follow-up, 10 new diagnoses of breast cancer in eight patients were reported (primary augmentation, $n = 3$; revision augmentation, $n = 2$; primary reconstruction, $n = 1$; and revision reconstruction, $n = 2$).

Connective Tissue, Autoimmune, and Rheumatic Disease

Twenty-three patients had 29 newly confirmed diagnoses of connective tissue, autoimmune, or rheumatic disease during the 10-year follow-up period. These included fibromyalgia ($n = 6$), rheumatoid arthritis ($n = 4$), Sjögren syndrome ($n = 3$), systemic lupus erythematosus ($n = 3$), other inflammatory arthritis ($n = 2$), Raynaud syndrome ($n = 2$), carpal tunnel syndrome ($n = 1$), chronic fatigue syndrome ($n = 1$), Hashimoto thyroiditis ($n = 1$), other connective disorder ($n = 1$), pyoderma gangrenosum ($n = 1$), sarcoidosis ($n = 1$), scleroderma ($n = 1$), spondyloarthropathies ($n = 1$), and an unknown type of arthritis ($n = 1$).

DISCUSSION

For the primary augmentation cohort, the 10-year cumulative estimated risk rates for key complications were as follows: any reoperation, 25.5 percent; suspected or confirmed rupture, 24.2 percent (magnetic resonance imaging cohort A); capsular contracture (Baker grade III and IV), 12.1 percent; explantation, 11.6 percent; and infection, 1.6 percent. As to be expected, and consistent with the literature,[3–5] the incidence rates of key complications, including reoperations, were higher in the revision than in the primary cohorts for augmentation and reconstruction procedures, and higher in the reconstruction than in the augmentation cohorts for primary and revision procedures. Notably, there was a relatively low rate of malposition observed across cohorts, with only a 1.0 percent cumulative incidence rate in primary augmentation patients.

Often, aesthetic concerns, not medical complications, are the driving force for reoperation. These elective revisions that are cosmetic in nature can elevate the reoperation rate without distinguishing between medically necessary and elective reoperation.[6] As suggested by Tebbetts[7] and Spear,[6] we have also presented an implant-specific reoperation rate that included reoperations attributable to capsular contracture, rippling, infection, hematoma/seroma, and rupture, as it has been suggested that the implant-specific reoperation can be more informative when interpreting breast implant safety and efficacy outcomes.[8]

The overall Kaplan-Meier estimated rupture rates (suspected or confirmed) for magnetic resonance imaging cohorts A and B are presented in Table 2. It should be noted that these rates may be overestimates because of the strict definition of rupture used in this study: indeterminate ruptures were considered to be ruptures; and disagreement between a local and a central reviewer, who reviewed all magnetic resonance imaging scans, was considered as a rupture. The rates presented in Table 2 include both suspected (based on magnetic resonance imaging evaluation alone) and confirmed (based on surgical removal of the implant) ruptures. This study also used the most rigorous calculation method to determine the rupture rate using data for patients up until the time of their last magnetic resonance imaging examination (or removal of the device). Follow-up for subjects without a rupture was censored at the date of their last magnetic resonance imaging scan. Ruptures are most often silent; therefore, using an office visit rather than magnetic resonance imaging as a screening method may result in missing silent ruptures and a falsely low estimated rupture incidence.[9] If the calculation method took into account the last office visit, the estimated rupture rate decreased to 19.3 percent for primary augmentation patients. The precision of the 24.2 percent (95 percent CI, 17.0 to 33.9 percent) Kaplan-Meier estimated cumulative rupture rate

(suspected or confirmed) for primary augmentation patients at 10 years is also influenced by the relatively lower follow-up rate, which decreases the precision of the calculation, leading to relatively wide confidence intervals. Understanding the limitations of imaging in determining rupture, we also present the Kaplan-Meier estimated cumulative rupture rates of only those ruptures that were confirmed on explantation of 9.81 percent on a patient level and 7.36 percent on an implant level for the primary augmentation cohort (Table 5). The crude rupture rates (obtained by dividing the number of ruptures by the total number of patients enrolled in the study) in those patients who had primary breast augmentation (magnetic resonance imaging cohorts A and B) were 9.8 percent (54 of 552) by patient and 5.8 percent (65 of 1130) by implant. These rates may be potentially underestimated because of the relatively lower follow-up of 46 percent. Conversely, the Kaplan-Meier formula looks at longitudinal occurrence of discrete events using censored observations (e.g., incomplete data such as individuals lost to follow-up, discontinuation of the study), leading to a presumably more accurate, less biased estimated risk of confirmed and unconfirmed rupture, most of which were silent ruptures. The prevalence of silent ruptures compared to symptomatic ruptures likely contributes to the low U.S. rupture complaint rate between November of 2006 and December of 2019 of 0.7 percent for more than 2 million MemoryGel Breast Implants. It is important to note that silent ruptures do not manifest clinically significant symptoms and, therefore, although these patients are given the choice of surgery or observation, approximately one-third in our study did not undergo device removal. Other studies have shown that most patients do not undergo additional reoperations.[9] One study focused on addressing the health implications resulting from an untreated silicone breast implant rupture demonstrated that, of the women with intracapsular rupture (n = 77), 90 percent (n = 69) showed no changes over a 2-year period between the first and second magnetic resonance imaging evaluations.[10] This suggests that, often, explantation of the implant is not required, as no specific significant risk was associated with intracapsular ruptured implants. Along these lines, rupture accounted for a low number of reoperations across cohorts. When comparing across studies, it is critical to note the timing of when the magnetic resonance imaging scans were obtained and which methods were used to collect and calculate the rupture rates, as these can significantly impact the reported outcome.[9] Furthermore, rupture is a time-related complication. and rupture rates tend to increase notably around 6 to 10 years after implantation.[9] For example, the 6-year cumulative incidence by Kaplan-Meier of rupture (suspected or confirmed) of MemoryGel breast implants was 1.1 percent for primary augmentation, 11.6 percent for revision augmentation, 3.8 percent for primary reconstruction, and 5.9 percent for revision reconstruction,[2] similar to the 1 percent rupture rate reported in a retrospective analysis comparing postoperative outcomes between patients implanted with Allergan (Allergan, Inc., Dublin, Ireland) versus Mentor implants after 6.8 years' follow-up.[11] In the present study, approximately half of the observed implant ruptures were identified at the 10-year follow-up.

Separate analyses examining the differences in complication and reoperation rates for smooth and textured devices were included in the original statistical analysis plan and have been reported elsewhere and highlight the risk-reduction benefits of textured implants.[12] Briefly, the incidence of capsular contracture leading to reoperation in subglandular primary augmentation patients was significantly lower in patients implanted with textured (4.21 percent; 95 percent CI, 1.60 to 10.85 percent) versus smooth devices (19.84 percent; 95 percent CI, 12.52 to 30.63 percent; $p = 0.0016$). In primary reconstruction patients, the incidence of asymmetry with reoperation was significantly lower in those patients implanted with textured (3.88 percent; 95 percent CI, 1.63 to 9.13 percent) versus smooth implants (11.10 percent; 95 percent CI, 6.29 to 19.19 percent; $p = 0.0169$).

Importantly, no patients in this Core study were diagnosed with breast implant-associated anaplastic large cell lymphoma ($n = 701$ textured-surface implants included in the study). Although this study was not designed to statistically evaluate potential cause-and-effect associations, which would require well-designed, controlled, epidemiologic studies, there was no evidence of an association between the study device and incidence (or recurrence) of breast cancer or connective tissue/autoimmune/rheumatic disease. Twenty-nine confirmed new diagnoses of connective tissue, autoimmune, or rheumatic disease were reported in 23 patients during the 10-year follow-up period. With a total of 8469 person-years of follow-up across all four cohorts, this represents an annual incidence rate of 3.4 new diagnoses per 1000 person-years. Four confirmed new diagnoses of rheumatoid arthritis were reported during the 10-year follow-up period. This represents

an annual incidence rate of 0.5 per 1000 person-years. By comparison, among the plastic surgery control patients in the study by Brinton et al., there were 49 cases of rheumatoid arthritis observed in 23,724 person-years of follow-up, corresponding to an annual incidence rate of 2.1 per 1000.[13] Ten new diagnoses of breast cancer in eight patients were reported during the 10-year follow-up period, representing an annual incidence rate of 1.2 per 1000 person-years. In a separate study by Brinton et al., there were 136 cases of breast cancer observed in 96,675 person-years of follow-up, corresponding to an annual incidence rate of 1.4 per 1000.[14] The study event rate of stillbirths was one of 291 pregnancies (0.34 percent), as compared to 6.05 per 1000 deliveries in 2012 in a study using data from the U.S. National Statistics System.[15] Thus, in this study, there is no evidence of an association between MemoryGel Implants and incidence of connective tissue/autoimmune/rheumatic disease or breast cancer. This is consistent with other epidemiologic studies, which found no association between silicone breast implants and breast cancer or rheumatoid arthritis.[16–19]

CONCLUSION

The 10-year follow-up results from this study demonstrate that MemoryGel Implants are safe and effective for use in adult patients undergoing breast augmentation or breast reconstruction.

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This trial is registered under the name "Core Gel Study of the Safety and Effectiveness of Mentor Round Low Bleed Silicone Gel-filled Mammary Prostheses," ClinicalTrials.gov identification no. NCT00753922 (https://www.clinicaltrials.gov/ct2/show/NCT00753922).

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Breast Surgery

Transitioning From Conventional Textured to Nanotextured Breast Implants: Our Early Experience and Modifications for Optimal Breast Augmentation Outcomes

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Abstract

Background: Nanotextured breast implants were hailed as an innovation that may address capsular contracture and breast implant-associated anaplastic large cell lymphoma and may provide the sweet spot between smooth and conventional textured implants.

Objectives: This study aimed to evaluate the introduction of nanotextured implants alongside conventional textured implants and to compare early complications.

Methods: Patients who underwent breast augmentation from the introduction of nanotextured implants in the author's practice with at least 1 year of follow-up were included. They were divided into nanotextured and conventional textured implant groups and then into 3 chronological subgroups. Patient characteristics, implant specifications, operative factors, and complication rates were compared.

Results: A total 415 cases with a mean follow-up of 26.9 months were identified, of which 38.8% utilized nanotextured implants and 61.2% conventional textured implants. Utilization of nanotextured implants increased from 26.9% in period 1 to 54.5% in period 3. Complication rates for the conventional textured group were 0.8% at 1 year and 3.5% on overall follow-up, with mostly capsular contractures; for the nanotextured group, complication rates were 6.8% and 8.7%, respectively, and "bottoming out" was most common. When analyzed across chronological subgroups, complication rates decreased for nanotextured implants by period 3.

Conclusions: A learning curve and associated complications are expected for early adopters of new implants. In our series, nanotextured implants were associated with higher complication rates at 1 year and on overall follow-up. Modifications in patient selection, intraoperative techniques, and postoperative care reduced complications in the later period.

Level of Evidence: 4

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Since the first-generation devices of the 1960s, breast implants and implantation techniques have evolved substantially over the past 6 decades. Implant-based breast augmentation has weathered through different seasons of gloom and concern. These include the historical ban of silicone gel implants by the US Food and Drug Administration in 1992,[1] the emerging risk of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL),[2,3] and most

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recently the evolving recognition of breast implant illness.[4-6] Despite these challenges, advances in implant technology and understanding of tissue-implant interactions have contributed to the state of the art today. Nonetheless, the risk of capsular contracture, implant rupture, malposition, and BIA-ALCL has not been completely eliminated.

The advent of "nanotextured" implant shell surface has been hailed as an innovation that may address both the risks of capsular contracture and BIA-ALCL. Surface texturization was previously purported to reduce the risk of capsular contracture by avoiding the parallel alignment of collagen fibers.[7,8] However, more recent studies have challenged the notion, and "macrotextured" shell surfaces are now being implicated for late seroma, double capsule formation, increased risk of biofilm formation, and subsequent development of BIA-ALCL.[8] The new generation of Motiva breast implants with "nanotextured" shell surface (Establishment Labs, Alajuela, Costa Rica) was marketed as a sweet spot between smooth and conventional textured implants. Plastic surgeons previously utilizing smooth or conventional textured implants were therefore intrigued by these new devices. Of note, the latest ISO 14607:2018 definition classifies the SilkSurface shell surface as "smooth." Early adopters might be thwarted by the initial learning curve and be frustrated by a global lack of experience with its peculiarities and long-term outcomes. Importantly, the limited literature reports the outcome of these "nanotextured" implants without direct comparison with other surface types and the prevailing complication rate at the surgeons' practice.[9-11] In this study, we aimed to evaluate our early experience when introducing the utilization of "nanotextured" implants alongside conventional textured implants. Through the review of our experience, we sought to discern the complication rate and potential pitfalls with "nanotextured" implants compared with conventional textured implants. In addition, we discussed the modifications in patient selection, surgical techniques, and postoperative care that we have adopted with this new generation of implants.

METHODS

Patients and Database Management

A clinical database of primary breast augmentations performed by the first author (P.M.) between July 2016 and March 2019 was utilized for retrospective chart review. Patient characteristics, implant specifications, operative factors, and complications were routinely recorded for the purpose of clinical audit. Patients from the date on which nanotextured implants were introduced into our practice were included. Patients with less than 1 year of follow-up were excluded. The dataset was rendered anonymous by an institutional trusted third party and organized into 2 main implant groups (ie, conventional textured and nanotextured). The groups were further organized chronologically into 3 period subgroups for analysis of period effect. Patient characteristics included age, body mass index, smoking status, parity, and preoperative cup size. Implant specifications such as height, projection, and volume, and operative factors such as incision, plane of implant placement, and date of surgery were recorded. Presence of complication was recorded as binary endpoints at 1 year and at start of analysis, which is employed to derive the complication rate at 1-year follow-up and overall complication rate, respectively. The type of complication (ie, rotation, Baker grade III/IV capsular contracture, malposition, infection, double-bubble deformity, double capsule formation, seroma, implant rupture) and time to complication were recorded. Statistical analysis and modeling were performed utilizing STATA/IC 15.1 (StataCorp LLC, College Station, TX). Informed consent was waived because the study is non-interventional and an anonymous database without identifiers was analyzed by the authors. All aspects of this study were conducted in accordance with the Declaration of Helsinki and the subsequent revisions.

Preoperative Consultation and Planning

All patients underwent a standardized preoperative assessment and counseling by the first author (P.M.) and trained nurse clinicians before surgery. Preoperative planning and marking were performed utilizing the AK method,[12] and the exact implants were decided based on patient's desires and tissue characteristics. Conventional textured implants included both round and anatomic implants from Mentor (CPG Gel with SILTEX surface; Mentor Worldwide LLC, Irvine, CA), Polytech (Replicon with MESMO sensitive surface; Polytech Health & Aesthetics GmbH, Dieburg, Germany), and Allergan (Natrelle 410 or INSPIRA with Biocell surface, Allergan, Dublin, Ireland). Nanotextured implants utilized were Motiva Round or Ergonomix silicone gel implants with SilkSurface (Establishment Labs, Alajuela, Costa Rica).

Surgical Technique

The inframammary fold incision was utilized in all cases. A no-touch technique utilizing electrostatic mitigation, antibiotic wash, nipple shields, pre-insertion glove change, and insertion sleeve (Keller funnel, Allergan) were routine in all cases. No drain or postoperative antibiotics were utilized. The inframammary fold was fixed and the incision was closed utilizing barbed sutures as previously described in the "4-layered closure technique."[13]

Table 1. Patient Demographics, Breast Characteristics, Implant Volume, and Plane of Implantation

	Conventional textured group	Nanotextured group
No. of patients	254 (61.2%)	161 (38.8%)
Mean follow-up, mo (SD)	28.6 (9.26)	24.3 (8.17)
Mean age, y (range)	33.5 (18-60)	30.8 (18-62)
Mean BMI, kg/m^2 (SD)	20.92 (1.912)	20.36 (1.691)
Mean parity (SD)	1.35 (1.179)	0.93 (1.189)
Number of tobacco users (%)	18 (7.1%)	15 (9.3%)
Preoperative cup size, count (%)		
A	165 (65.0%)	118 (73.3%)
B	81 (31.9%)	35 (21.7%)
C	8 (3.1%)	8 (5.0%)
Mean volume of implant, mL (SD)	322.0 (59.56)	341.82 (69.32)
Dual plane type, count (%)		
1	0 (0%)	0 (0%)
2	128 (50.4%)	120 (74.5%)
3	107 (42.1%)	28 (17.4%)
Subglandular	19 (7.5%)	13 (8.1%)

BMI, body mass index; SD, standard deviation.

Postoperative Care and Follow-up

Postoperatively, the patients were started on a specialized support brasserie immediately after surgery and continued to wear it day and night for up to 3 months. They are discharged on the same day and allowed to resume light exercises after 3 weeks (ie, no chest exercise and running). They were reviewed at 1 week, 6 months, and 1 year by the operating surgeon. Follow-up review at the end of the first year was encouraged by the waiver of fees for any related revisional surgery within the first year. Any patient noted to have a complication was additionally evaluated by the operating surgeon when needed.

RESULTS

A total 415 cases of primary breast augmentation with a mean follow-up of 26.9 months (range, 12.2-45.3 months) were identified based on the inclusion and exclusion criteria. Of these, 254 cases (61.2%) aged a mean of 33.5 years (range, 18-60 years) utilized conventional textured implants, and 161 cases (38.8%) aged a mean of 30.8 years (range, 18-62 years) utilized nanotextured implants. All patients were female. The patient characteristics of the conventional textured and nanotextured groups were largely comparable (Table 1). When divided into 3 chronological subgroups, the utilization of nanotextured implants demonstrated a steady increase from 26.9% of implants in period 1 to 54.5% of implants employed in period 3 (Table 2). In period 3, the number of patients receiving either implant type was comparable.

Table 2. Subgroups by Chronological Periods

	Conventional textured group	Nanotextured group
No. of patients	254	161
Period 1	136 (73.1%)	50 (26.9%)
Period 2	67 (57.3%)	50 (42.7%)
Period 3	51 (45.5%)	61 (54.5%)

The complication rate at the 1-year follow-up was 0.8% (2 cases) for the conventional textured group with 1 case of rotation and 1 case of seroma. For the nanotextured group at 1-year follow-up, 6.8% (11 cases) of patients experienced complications with all recorded as "bottoming out." Of these, most occurred in period 1 (7 cases). The higher complication rate with nanotextured implants at 1-year follow-up is statistically significant ($P < 0.01$). The overall complication rate for the conventional textured group was 3.5% (n = 9) with 4 cases of Baker III/IV capsular contracture, 3 cases of rotation, and 2 cases of seroma at a mean follow-up of 28.6 months (range, 12.2-45.3 months). The overall complication rate was 8.7% (n = 14) for the nanotextured group, with 12 cases of bottoming out and 2 cases of Baker III/IV capsular contracture at a mean follow-up of 24.3 months (range, 12.3-45.3 months). The higher complication rate with nanotextured implants in overall follow-up was also statistically significant ($P < 0.05$).

When the period subgroups were compared, a statistically significant decline in complication rate at 1-year follow-up was seen in the nanotextured group over time (ie, from 14.0% to 1.6%, $P < 0.05$; Table 3). No significant difference in complication rates was noted for the conventional textured group over time ($P > 0.05$; Table 3). Logistic regression demonstrated the utilization of conventional textured implants was associated with lower risk of complications at 1-year follow-up (odds ratio: 0.108; 95% confidence interval [CI]: 0.024-0.495) and at overall follow-up (odds ratio: 0.386; 95% CI: 0.163-0.913) when compared to nanotextured implants (Table 4). When age, chronological subgroup, body mass index, parity, and volume of implants were considered, conventional textured implants were significantly associated with lower risk of early complication

Table 3. Complication Rates at 1-Year and Overall Follow-up

	Conventional textured group	Nanotextured group	*P* value
Complications at 1-year follow-up			
Period 1	1 (0.7%)	7 (14.0%)	<0.01
Period 2	0 (0%)	3 (6.0%)	NS
Period 3	1 (2.0%)	1 (1.6%)	NS
Total	2 (0.8%)	11 (6.8%)	<0.01
Overall complications			
Period 1	5 (3.7%)	8 (16.0%)	<0.01
Period 2	1 (1.5%)	3 (6.0%)	NS
Period 3	3 (5.9%)	3 (4.9%)	NS
Total	9 (3.5%)	14 (8.7%)	<0.05

NS, not significant.

(adjusted odds ratio: 0.140; 95% CI: 0.028-0.710) when compared to nanotextured implants. Utilizing stepwise logistic regression modeling, implants ≥400 cc (adjusted odds ratio: 5.15; 95% CI: 1.32-20.2) were also identified as a predictor of complication at 1-year follow-up.

Representative results of breasts augmented with nanotextured implants and with conventional textured implants are shown in Figures 1 and 2, respectively.

DISCUSSION

Early Complication Rates With Nanotextured and Conventional Textured Implants

Interestingly, with the new generation of nanotextured implants, the type of complication and time of presentation differed from our experience with the conventional textured implants. We observed a high occurrence of bottoming out (n = 11) as the prime complication as early as in the first year of follow-up. This was not seen in the conventional textured group, which presented mainly with complications after the first year including seroma, capsular contracture, and implant rotation. The higher rate of bottoming out in the nanotextured group may be explained by the thinner capsules that we have observed during the explant or exchange of these implants and its performance being similar to smooth implants. Further studies may be needed to confirm the causality and examine the quality of the capsule formed with nanotextured shell surface. Capsular contractures were noted in both conventional textured and nanotextured implants. The overall complication rates are ostensibly higher in the nanotextured group, but higher rates in the earlier period of introduction likely skewed this. The short duration of follow-up precludes any conclusion on the occurrence rate of capsular contracture over a longer time period. No BIA-ALCLs were noted in the overall follow-up period of our study.

Learning Curve When Transitioning to Nanotextured Implants

As with any transition to a new surgical technique or medical device, a learning curve was observed in our study. The utilization of preoperative planning methods, surgical techniques, and postoperative care employed with conventional textured implants resulted in a higher complication rate with nanotextured implants (ie, 14.0%) in period 1. The complication rate decreased over the study period to match the conventional textured implant group by period 3. We noted that this coincided with the restriction in patient selection and modifications in surgical techniques devised by the authors to address the early occurrence of bottoming out. However, for surgeons from a predominantly smooth implant practice, the learning curve may be different or less steep. This is because the required approach in patient selection and surgical technique may be similar with that taken in the utilization of smooth implants. Nonetheless, whether the behavior of nanotextured implants is identical to that of smooth implants is still undetermined. Future basic and clinical studies that compare the capsule characteristics and long-term outcomes may provide answers.

Modifications in Planning, Surgical Technique, and Postoperative Care for Nanotextured Implants

The observation of a higher rate of bottoming out on early follow-up prompted the authors to modify planning, surgical technique, and postoperative care that may prevent its occurrence. By period 3, the authors began to use the nanotextured implants only in patients with good soft tissue elasticity (small and firm breasts) and lower intended implant volume (<350 cc) due to the observation of higher complications among patients not satisfying these criteria. The main modification in surgical technique is the dissection of a very tight pocket to minimize inferior and lateral migration. In patient postoperative care, the authors reinforced the advice to utilize a support brasserie for up to 3 months by period 2. Patients were also strongly advised to resume strenuous activities only after 3 months with the strict utilization of a sport brassiere. The authors opined

Table 4. Odds Ratios for Complication Demonstrated Lower Risk With Utilization of Conventional Textured Implants

	Odds ratio for complication (95% CI)		Adjusted odds ratio[a] for complication (95% CI)	
	1-year follow-up	Overall	1-year follow-up	Overall
Use of conventional textured implants[b]	0.108 (0.0237-0.495)	0.386 (0.163-0.913)	0.110 (0.0226-0.539)	0.393 (0.154-1.01)

BMI, body mass index; CI, confidence interval. [a]When adjusted for age, chronological subgroup, BMI, parity, implant >400 cc. [b]When compared to nanotextured implant as the reference category for logistic regression computation.

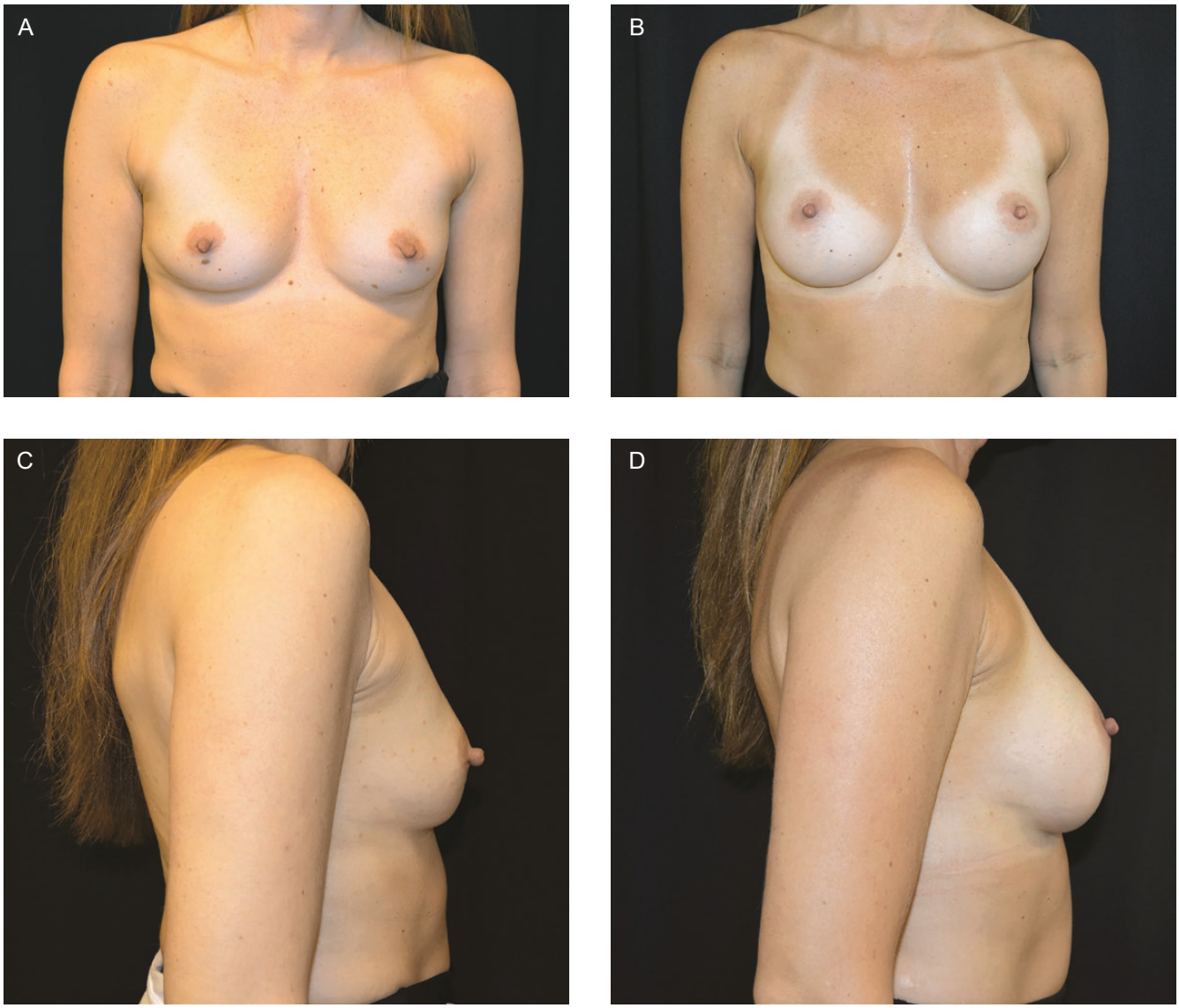

Figure 1. (A, C) Preoperative photos of this 38-year-old woman who underwent primary breast augmentation with 230-cc nanotextured implants. (B, D) Appearance at 13 months postoperatively.

that nanotextured implants should be treated similarly as smooth surface implants in decision-making and choice of surgical technique. As a result, a steady decrease in usage of nanotextured implants was seen (19% of all implants; unpublished data) beyond period 3 of this study (from April 2019 to February 2020) in our practice due to the stricter patient selection criteria and concern for the higher early complications observed in this review.

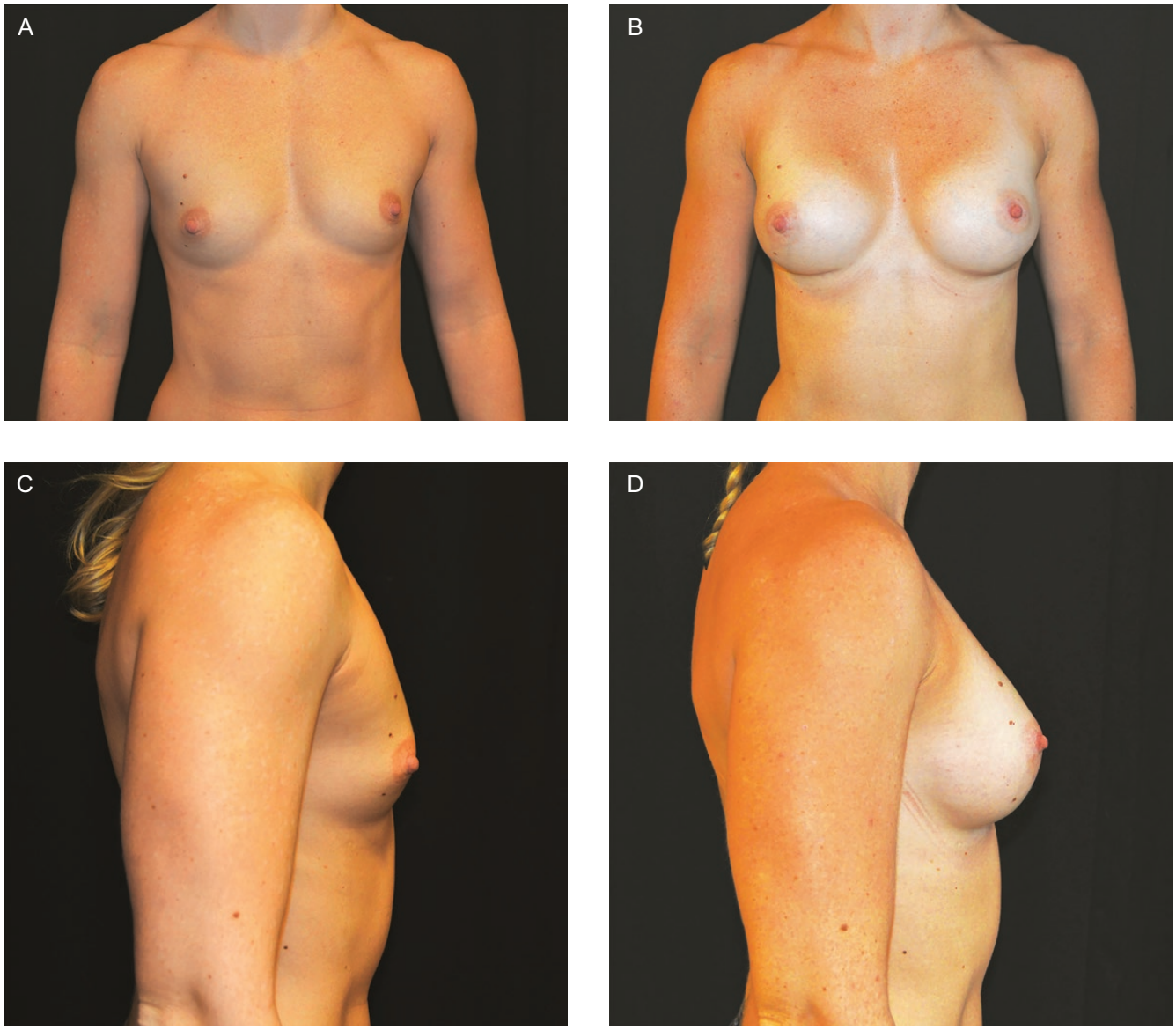

Figure 2. (A, C) Preoperative photos of this 30-year-old woman who underwent primary breast augmentation with 240 cc conventional textured implants. (B, D) Appearance at 14 months postoperatively.

Limitations

One of the limitations of this study is the retrospective approach without randomization and blinding. The possibility of observer bias or under-detection of complications should be acknowledged. However, as an unsponsored study it provides early data that compares the utilization of nanotextured implants with the ongoing employment of conventional textured implants. Importantly, a considerable sample size is utilized with good follow-up for early complications at 1 year. Despite the absence of blinding, Baker grade III/IV capsular contractures were detected in both groups through routine clinical care. This provides a missing perspective not previously reported in literature, to our knowledge. This study is informative to readers amid the paucity of clinical literature on outcomes with this new generation of implants.

We acknowledge that the gradual change in patient selection, surgical technique, postoperative care, and increase in experience with the nanotextured implants may have confounded the comparison over the study period. Therefore, in addition to the broad comparison of the 2 implant types, we have attempted to analyze the data in chronological subgroups. The period subgroups comparison detected the period effect and illuminated the learning curve.

Another limitation is the comparison of nanotextured implants against all other textured implants with no

breakdown according to manufacturer or subtype. However, it was not statistically sound to further reduce the group size. Therefore, we could only draw conclusions of nanotextured implants against a backdrop of existing practice with various textured implants.

The single-center and single-surgeon nature of the study may limit generalizability of our results to other centers. However, it also provides consistency in surgical techniques and experience to illuminate the effect of learning curve and implant type on complication rate.

Lastly, the short follow-up period may only describe the early complications observed with these implants. It may not capture incidence of late complications like capsular contracture, implant rupture, late seroma, and BIA-ALCL. However, the 1-year timepoint was reliable in our setting with the notably good follow-up that was attributed to the 1-year revision fee waiver at our clinic. Further randomized controlled trials and longer term studies may be useful in confirming our conclusion and elucidating late complication rates.

CONCLUSIONS

The perfect breast implant does not exist. However, with each new and innovative generation of implant, the armamentarium of the plastic surgeon is enriched to address the varying needs of the patients. In our series, compared with conventional textured implants, nanotextured breast implants were associated with a higher number of complications, especially on initial introduction. Nonetheless, restriction in patient selection, modifications of surgical technique, and reinforcement of aftercare were effective in reducing the incidence of these complications, as shown in the later period. The aesthetic plastic surgeon needs to remain impartial and choose the appropriate implant and surgical technique for the patient.

Disclosure

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Canadian breast implant cohort: Extended follow-up of cancer incidence

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Cosmetic breast implants are not associated with increased breast cancer incidence, but variations of risk according to implant characteristics are still poorly understood. As well, the assessment of cancer risk for sites other than breast needs to be clarified. The purpose of this study was to fill these research gaps. This study presents an extended analysis of 10 more years of follow-up of a large Canadian cohort of women who received either cosmetic breast implants (n = 24,558) or other cosmetic surgery (15,893). Over 70% of the implant cohort was followed for over 20 years. Cancer incidence among implant women was compared to those of controls using multivariate Poisson models and the general female population using the standardized incidence ratios (SIRs). Women with breast implants had reduced rates of breast and endometrial cancers compared to other surgery women. Subglandular implants were associated to a reduced rate of breast cancer compared to submuscular implants [incidence rate ratio (IRR) = 0.78, 95% confidence interval (CI) = 0.63–0.96] and this reduction persisted over time. We observed a sevenfold increased rate (IRR = 7.36, 95% CI = 1.86–29.12) of breast cancer in the first 5 years after the date of surgery for polyurethane-coated subglandular implant women but this IRR decreased progressively over time (p value for trend = 0.02). We also observed no increased risk of rarer forms of cancer among augmented women. A reduction in breast cancer incidence was observed for women with subglandular implants relative to women with submuscular implants. Possible increase of breast cancer incidence shortly after breast augmentation with polyurethane implants needs to be verified.

Epidemiology

Cosmetic breast implants have been the subject of numerous investigations of the long-term risk of mortality and cancer incidence.[1–3] Early concerns focused on their potential carcinogenic effect, especially for breast cancer, because of the possible link between silicone and such disease.[4] Consequently, silicone gel-filled breast implant (SGFIs) were removed from the market in the United-States and Canada in the early 1990s, but were reapproved for general cosmetic use in both countries in 2006 because later studies showed no carcinogenic effect of silicone.[1–3,5] Indeed, a recent report from the U.S. Food and Drug Administration concluded that cosmetic breast implants are not associated with increased breast cancer incidence.[3] However, examining long-term health risks associated with these devices remains important as adverse health effects may occur only after a long latency period.

More recently, breast implants have been studied in an attempt to evaluate variations of breast cancer risk according to specific implant characteristics. Results across epidemiological studies that collected information on implant characteristics have been inconclusive.[6–11] Common implant characteristics include the type of implant [saline or silicone gel-filled implants (SGFIs)], the placement of the implant (submuscular or subglandular), the implant fill volume and the implant envelope (polyurethane coated or not). Polyurethane foam-covered breast implants were withdrawn from the market in 1991, both in the United-States and Canada, when a report showed that polyurethane could degrade into significant quantities of 2,4-diaminotoluene (2,4-toluene diamine) (TDA) which has been recognized as an animal carcinogen and potential human carcinogen.[12] However, polyurethane implants are still used in Europe and South America. Little is known to date about the long-term health effects in humans of such implants. Evaluation of the potential cancer risk associated with these devices, especially in the subglandular

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position because of proximity to breast tissue, is important. Furthermore, the concern raised in our earlier study of a possible twofold increased risk of breast cancer for women with polyurethane implants in the subglandular position needs to be clarified over a longer period of follow-up.[7]

A number of epidemiological investigations have evaluated the relationship between breast implants and the incidence of nonbreast cancers.[1,6,7,13–18] The findings from these studies have been largely negative when women with implants were compared to women who had other cosmetic surgeries[6,7,17] or with women from the general population.[6,7,14,16] However, some studies reported an increased risk for some types of cancer when compared to general population estimates including the brain,[19] lung,[13,15,19,20] vulva[14] and cervix.[18] Additionally, a recent report by the FDA as well as review articles recommended that the risk of hematopoietic malignancies among women who have cosmetic breast implants be further investigated.[18,21,22] Taken as a whole, the epidemiological evidence for risk of cancer at body sites other than the breast, especially for hematopoietic malignancies, needs to be further clarified.

In this updated analysis, 10 more years of follow-up have been added to the largest cohort study carried-out to date on cosmetic breast implants. The considerable number of additional incident breast cancer cases provides opportunities to evaluate breast cancer risk according to implant characteristics over a much longer period of time. Additionally, the assessment of nonbreast cancer risk will confirm or verify several of the associations that were observed in our previous analyses. Finally, this analysis provides some comparisons of current results with those of our previous publication of cancer incidence among augmented women.[7]

Material and Methods

Study design, study population and selection criteria

The study population was described in detail in our previous publication.[7] The cohort consisted of women, 18 years of age or older, who were residents of the province of Ontario or Quebec, in Canada, and who underwent bilateral cosmetic breast augmentation (implant group) or received other common elective cosmetic surgeries (controls/comparison group) in their province of residence between January 1, 1974 and December 31, 1989. Other cosmetic surgeries included the following: chemical peel or dermabrasion, coronal brow lift (eyebrow and forehead lift), otoplasty (ear surgery), rhinoplasty (nose surgery), rhytidectomy (face-lift) or blepharoplasty (eyelid surgery). Implant women were frequency matched to other plastic surgery patients by year of entry into the cohort, province of residence and by surgeon. Frequency of women excluded for various reasons is documented in our earlier paper.[7]

In total, the cohort consisted of 40,451 women: 24,558 received cosmetic breast implants (7,153 women from Ontario and 17,405 from Quebec) and 15,893 women (4,418 from Ontario and 11,475 from Quebec) received other common elective cosmetic surgeries. Information on year of surgery, age at surgery, personal identifying information (used only for linkage purposes) and verification of eligibility criteria for both the implant subjects and the controls and information on implant characteristics such as the type of implant, implant envelope, fill volume and site of implantation, was collected by review of medical (hospital or private clinic) records of all women (implant and control) in the cohort.

The implant and control cohorts were compared to the general population of women. General female population rates of cancer incidence and mortality for the provinces of Ontario and Quebec were obtained from provincial vital and cancer registries (unpublished mortality and cancer tabulations, Chronic Diseases Surveillance and Monitoring Division, Public Health Agency of Canada, Ottawa, 2011).

Ethics approval for the study was granted by the University of Toronto's Office of Research Ethics, the ethics committee of the Centre Hospitalier Affilié universitaire de Québec's (CHA) Saint-Sacrement Hospital and the Ethics Committee for Clinical Research of Laval University.

Ascertainment of outcomes

Incident cases of cancer and deaths that occurred from the date of surgery until December 31, 2006 (Quebec) or December 31, 2007 (Ontario) were identified by linking personal identifying information (surname, given and maiden names, mother's name, father's name, birth date, residential address and health insurance number) of the cohort members to national and provincial cancer and mortality registries. Specifically, in our previous follow-up,[7] cohort members were linked to the Canadian Cancer Registry (CCR)[23] and the Canadian Mortality Database (CMDB)[24] until December 31, 1997. These national registries are managed by Statistics Canada through collaboration with provincial and territorial cancer registries and capture all cancer cases and deaths that occur in Canada and in ~20 states in the United-States. The cohort was also linked to cancer incidence data before the index date of surgery, the earliest being 1969. This enabled us to exclude women diagnosed with cancer before their index cosmetic surgeries. Second, for this extended follow-up, incident cases of cancer who were diagnosed between January 1, 1998 and December 31, 2006 (Quebec) or December 31, 2007 (Ontario) were identified by linking to provincial registries, namely the Ontario Cancer Registry (OCR)[25] for the Ontario cohort and the Quebec Tumor Registry (QTR) for the Quebec cohort.[26] These provincial cancer registries collect information on cancer cases diagnosed in the province corresponding to the cancer registry. The cohort was also linked to provincial mortality databases to identify mortality cases for the period between January 1, 1998 and December 31, 2006 for the Quebec cohort using the mortality file of Quebec held by the Quebec Institute of Statistics and between January 1, 1998 and December 31, 2007 for the Ontario cohort with the use of the Ontario Mortality Database (OMDB) provided by the Registrar General of Ontario. Linkage of the Quebec cohort to the QTR and mortality file were

conducted using a deterministic approach whereas the linkage of the OCR and OMDB to the Ontario cohort were conducted using a probabilistic record linkage system.[27] Where no link was found and each patient was assumed to be cancer-free and alive at the end of follow-up.

Statistical analysis

Person-years of follow-up were calculated for each woman in the breast implant and other cosmetic surgery cohorts from 1 year after the date of surgery until the earliest of date of death, date of cancer diagnosis, December 31, 2006 (Quebec cohort) or December 31, 2007 (Ontario cohort). The first year of follow-up was excluded from analysis, consistent with other investigations,[17,18] to reduce the influence that preclinically detectable cancers at the time of index cosmetic surgery may have had on our comparisons. The numbers of person-years and incident cases of cancer were tabulated across strata defined by study group (implant or surgical control group), province of residence at the time of index cosmetic surgery (Quebec or Ontario), attained age (18–24, 25–29, 30–34, . . . , 75–79, $\geq$ 80 years), calendar period of follow-up (1974–1977, 1978–1981, . . . , 1994–1997, 1998–2001, 2002–2007), period of surgery (1974–1979, 1980–1984, 1985–1989), age at surgery (18–<30, 30–<40, $\geq$ 40 years) and time since surgery (1-<5, 5-<10, 10-<15, 15-<20, 20-<25, $\geq$25 years). Attained age, follow-up interval and time since surgery were time-dependent variables because women would contribute person-years to different categories within these variables as they were followed over time. In contrast, women would contribute person-years to only one level of the classification variables period of surgery and age at surgery. The DATAB module in the Epicure software program was used to calculate person-years of follow-up.[28]

The expected numbers of incident cancers in the cohort and the other cosmetic surgeries group were estimated by multiplying the tabulated person-years of follow-up by the corresponding overall and site-specific cancer rate observed in the general population according to province (Ontario or Quebec), age (by 5-year age intervals), and calendar period of follow-up (1974–1977, 1978–1981, . . . , 1994–1997, 1998–2001, 2002–2007). Differences in cancer incidence rates between the implant and surgical control cohorts relative to the general population were evaluated by calculating the standardized incidence ratio (SIR), which is the ratio of the observed-to-expected number of incident cancers.[29] For the comparison with general population estimates, person-years contributed for the period after 1998 were reduced by an interprovincial migration rate according to province, attained age and calendar period of follow-up on the basis of migration rates observed through active follow-up of the Canadian population.[30] This was done to account for interprovincial mobility. This approach has been previously applied to reduce the impact of losses to follow-up in a cohort study.[31] The 95% confidence intervals (CIs) were calculated for the SIR by assuming that the observed number of incident cancers followed a Poisson distribution, using formulae detailed elsewhere.[29] All the p values reported are two sided.

Comparisons of site-specific incident cancer rates between the implant recipients and the other plastic surgery patients, rather than the general population, were done using multivariate Poisson regression models using incidence rate ratios (IRR) as the measure of association.[32] We used Cox proportional hazards regression models to evaluate cumulative incidence of breast cancer over the follow-up period.[33] The potential confounding influence of the following factors were evaluated: linear and quadratic attained age components, province of residence, calendar period of follow-up, age at surgery, year of surgery and time since surgery. Confounding was examined by a backward deletion approach.[34] Specifically, we first adjusted for all potential confounders and then removed one by one in a stepwise manner the least significant confounding variables until the total proportional change in IRR estimates compared to those of the fully adjusted model was less than 10%. Covariates that were not confounders, but increased the precision of the estimates were kept in the final model. To evaluate whether the IRR differed by province, a test of homogeneity was conducted by including in the Poisson regression model a first-order interaction term of province and implant status. The two provinces were deemed to have different risk estimates if the interaction term was found to be statistically significant based on a two-tailed alpha of <5%. p values for trend of IRR over time since surgery were computed, where applicable, using the median time since surgery value for each category as a continuous variable. We included in the regression model a first-order interaction term of this continuous time since surgery variable and the main exposure variable of interest. There was a trend of increasing (or decreasing) IRR if the interaction term was found to be statistically significant based on a two-tailed alpha of <5%. For instance, if the main exposure variable is study group (implant *vs.* controls), a positive and statistically significant interaction term indicates that the IRR comparing implant women to controls increases with time since surgery.

Analyses including only women who received breast implants were performed using multivariate Poisson regression models to assess associations of implant characteristics to breast cancer incidence. The following implant characteristics were evaluated: type of implant (SGFIs), envelope (polyurethane-coated or not), subglandular or submuscular placement, and fill volume. For implant fill volume, women were categorized based on the quartiles of the observed frequency distribution of the mean value of the right and left implants (<175, 175–<200, 200–<225 and $\geq$ 225 cc).[7] Confounding, trend and interaction were assessed with the same approaches mentioned earlier. Analyses were done with SAS, version 9.2.[35]

Results

A total of 581,331 and 374,996 person-years of follow-up were accrued in the breast implant (n = 24,558) and the other cosmetic surgery (n = 15,893) cohorts, respectively

Table 1. Frequency distribution for selected characteristics of women who received breast implants and women who received other cosmetic surgeries, Canadian Breast Implant Cohort Study

Characteristics	Implant patients	Control patients
Length of follow-up (years), *N* (%)		
<1	28 (0.1)	21 (0.1)
1 to <5	173 (0.7)	138 (0.8)
5 to <10	267 (1.1)	227 (1.4)
10 to <15	400 (1.6)	342 (2.2)
15 to <20	5,356 (21.8)	3,016 (19.0)
20 to <25	8,359 (34.0)	5,834 (36.7)
≥25	9,975 (40.6)	6,315 (39.7)
Year of surgery, *N* (%)		
1974–1977	4,726 (19.2)	3,011 (19.0)
1978–1981	5,750 (23.4)	3,766 (23.7)
1982–1985	6,685 (27.2)	4,706 (29.6)
1986–1989	7,397 (30.1)	4,410 (27.7)
Age at surgery (years), *N* (%)		
18 to <25	3,665 (14.9)	3,481 (21.9)
25 to <30	5,961 (24.3)	3,064 (19.3)
30 to <35	6,868 (28.0)	2,828 (17.8)
35 to <40	4,195 (17.1)	2,357 (14.8)
40 to <45	2,068 (8.4)	1,562 (9.8)
≥45	1,801 (7.3)	2,601 (16.4)
Mean age at surgery (SD), years	32.2 (7.8)	33.5 (10.4)
Mean duration of follow up (range), years	23.7 (0.1–34.0)	23.6 (0.0–33.9)
Total person-years of follow up[1]	581,331	374,996
Total number of women	24,558	15,893

[1]Person-years were accrued from the date of surgery until the earliest date of cancer diagnosis, death, December 31, 2006 (Quebec) or December 31, 2007 (Ontario).

(Table 1). The total amount of person-years accrued when the interprovincial migration correction was applied reached 577,257 and 372,532, respectively, for the implant group and the other plastic surgery patients (data not shown). The mean duration of follow-up was about the same in the two study groups; 23.7 years for the implant cohort and 23.6 years for the control cohort. Specifically, more than 70% of the women in both the breast implant and other cosmetic surgery cohort were followed for at least 20 years. As reported in our previous publication, most of women in the breast implant cohort (65.6%) received implants filled with silicone gel.[7] The site of implantation was more frequently submuscular (56%) than subglandular (32.6%).[7] Few recipients received implants with a polyurethane foam covered envelope (10.5%); of those who did, most came from the province of Quebec.[7]

A total of 1,521 and 1,220 incident cancers were identified among implant women and other cosmetic surgery women, respectively (Table 2). Comparisons with general female population estimates showed that the observed number for cancers of all sites was significantly lower than the expected number in both the implant cohort (SIR = 0.71, 95% CI = 0.67–0.75) and other cosmetic surgery cohort (SIR = 0.79, 95% CI = 0.74–0.83). Statistically significant reductions in rate of breast cancer were observed in both the implant women (SIR = 0.54, 95% CI = 0.49–0.59) and the control group (SIR = 0.88, 95% CI = 0.80–0.96). As well, significantly lower than expected rates for stomach, colorectal, endometrial, ovary, lymphohematopoietic cancers and all other cancer sites combined were observed among implant women compared to the general female population. There were also reduced risks of colorectal, endometrial, lymphohematopoietic cancers and all other cancer sites combined for the other cosmetic surgery cohort relative to general female population estimates.

Internal comparisons revealed that compared to other cosmetic surgery women, those with breast implants had significantly reduced rates for cancers of all sites (IRR = 0.88, 95% CI = 0.82–0.95), breast (IRR = 0.60, 95% CI= 0.53–0.69), overall genital (IRR = 0.77, 95% CI = 0.63–0.95) and endometrial (IRR = 0.55, 95% CI= 0.38–0.78) cancers (Table 3). However, when removing breast and endometrial cancers from all sites combined, there were little or no differences between implant women and other cosmetic surgery women for overall cancer incidence (IRR = 1.08, 95% CI = 0.94–1.23) (data not shown). As well, when removing endometrial cancers from overall genital cancers, little or no differences were seen between implant women and those with other cosmetic surgeries for overall genital cancer incidence (IRR = 0.92, 95% CI = 0.70–1.20) (data not shown). Breast cancer cumulative incidence is shown in Figure 1. After 30 years of follow-up, breast cancer risk for the implant patients reached 2.3% compared to 3.7% for other plastic surgery women. Moreover, IRRs for different lengths of follow-up remained steadily around 0.60 (p value for trend in IRR over time since surgery = 0.95) (data shown in footnote of Fig. 1).

Table 4 presents breast cancer incidence among implant women according to specific implant characteristics. Results show that women whose implants were inserted in the subglandular position had a significantly reduced rate of breast cancer compared to those whose implants were inserted submuscularly (IRR = 0.78, 95% CI = 0.63–0.96). As well, women who received polyurethane coated implants had a nonstatistically significant elevated IRR of 1.22 (95% CI = 0.84–1.77) for breast cancer when compared to implant women without such coating. There was no statistically significant difference in breast cancer rates for type of implant and fill volume. Results did not change when we mutually adjusted for implant characteristics in the multivariate models (results not shown).

We further investigated the pattern of breast cancer risk for subglandular implants relative to submuscular implants

Table 2. Standardized incidence ratios (SIRs)[1] for selected cancers based on general population cancer incidence rates (1974–2007) among breast implant and other cosmetic surgery women with comparisons with previous follow up[2]

		Implant patients			Control patients		
Cancer site	ICD-9	Obs. cases	SIR 1974–2007 follow-up interval	SIR 1974–1997 follow-up interval	Obs. cases	SIR 1974–2007 follow-up interval	SIR 1974–1997 follow-up interval
All sites	140–208 (excl. 173)	1,521	0.71[3]	0.75[3]	1,220	0.79[3]	0.81[3]
Stomach	151	12	0.47[3]	0.68	18	0.85	0.79
Colorectal	153–154	151	0.75[3]	0.79	107	0.66[3]	0.61[3]
Pancreas	157	33	0.94	1.22	22	0.74	1.33
Lung	162.2–5, .8, .9	271	1.04	1.09	167	0.85[3]	1.11
Malignant melanoma	172	56	1.08	1.29	28	0.84	0.79
Breast	174	414	0.54[3]	0.57[3]	457	0.88[3]	0.64[3]
Genital	179–184	195	0.64[3]	0.78[3]	173	0.81[3]	0.87[3]
Cervix	180	61	0.83	0.96	40	0.85	0.80[3]
Endometrial	182	52	0.44[3]	0.53[3]	71	0.82	0.91
Ovary	183.0	66	0.76[3]	0.80	49	0.79	0.70
Bladder	188	33	0.86	0.88	18	0.59[3]	0.64
Kidney	189	32	0.72	0.71	30	0.90	0.74
Nervous system	191, 192	27	0.83	0.65	27	1.14	0.88
Brain	191	25	0.73	0.65	26	1.06	0.80
Thyroid	193	61	0.84	0.73	31	0.68[3]	0.42[3]
Lymphohematopoietic	200–208	106	0.75[3]	0.69[3]	79	0.74[3]	0.68[3]
Non-Hodgkin's lymphoma	200, 202	63	0.84	0.75	45	0.81	0.78
Leukemia	204–206, 207.0, .2, .8, 208	27	0.75	0.68	16	0.57[3]	0.66
Other cancer sites not listed above		130	0.75[3]	0.87	63	0.47[3]	0.60[3]

[1]The SIR is the ratio of the observed to expected cases; the expected number of cases was estimated by applying age, period and province (Ontario or Quebec) specific cancer incidence rates to the corresponding number of person-years of follow-up observed in the cohort. [2]Previous follow-up interval standardized incidence ratios (SIRs) for selected cancers based on general population cancer incidence rates (1974–1997). [3]Denotes a statistically significant difference based on a two-tailed alpha of <5%.

over a long period of time since surgery. This analysis revealed IRRs of 0.68 (0.31–1.51) for 1 to <5 years after surgery, 1.03 (0.58–1.83) for 5 to <10 years, 0.64 (0.42–0.98) for 10 to <15 years and 0.80 (0.61–1.06) for over 15 years after surgery (p value for trend in IRR over time since surgery = 0.86). This suggests that the reduction in breast cancer incidence among subglandular implants relative to those with submuscular implants can be observed many years after receiving the surgery.

Further analyses for polyurethane-coated implants in the subglandular position relative to women who received other subglandular implants, by time since surgery, was undertaken (Fig. 2). The results indicate a statistically significant decreasing monotonic trend in the IRR according to time since surgery (p value for trend in IRR over time since surgery = 0.02). Specifically, the IRR of breast cancer incidence among those with subglandular polyurethane-coated implants compared to other women with subglandular implants decreased from 7.36 (95% CI = 1.86–29.12) for 1–5 years after surgery to 0.69 (95% CI = 0.29–1.60) for follow-up of more than 15 years after surgery. An analysis for polyurethane-coated implants in the submuscular position was not possible because only 132 women received such devices and consequently few breast cancer cases were observed among these women.

Discussion

In this extended follow-up of Canadian women with cosmetic breast implants, with at least 20 years of follow-up for more than 70% of cohort members, we observed that breast cancer incidence among implant women continued to be lower than the other plastic surgery cohort over this long period of follow-up. Our extended analysis also allowed us to more confidently report the absence of increased risk of rarer forms of

Table 3. Incidence rate ratios (IRRs)[1] for selected cancers between breast implant and other cosmetic surgery women with comparisons with previous analysis[2]

		Internal comparison 1974–2007 Follow-up interval		Internal comparison 1974–1997 Follow-up interval	
Cancer site	**ICD-9**	**IRR**	**95 % CI**	**IRR**	**95 % CI**
All sites	140–208 (excl. 173)	0.88	0.82–0.95	0.91	0.81–1.02
Stomach	151	0.54	0.26–1.14	0.93	0.34–2.52
Colorectal	153–154	1.14	0.88–1.46	1.22	0.81–1.84
Pancreas	157	1.27	0.73–2.20	0.94	0.45–1.95
Lung	162.2–5, .8, .9	1.18	0.97–1.44	0.93	0.69–1.26
Malignant melanoma	172	1.35	0.85–2.13	1.69	0.88–3.23
Breast	174	0.60	0.53–0.69	0.64	0.53–0.79
Genital	179–184	0.77	0.63–0.95	0.93	0.70–1.24
Cervix	180	0.94	0.63–1.40	1.00	0.62–1.61
Endometrial	182	0.55	0.38–0.78	0.63	0.37–1.09
Ovary	183.0	0.95	0.65–1.38	1.11	0.64–1.91
Bladder	188	1.54	0.86–2.76	1.37	0.56–3.35
Kidney	189	0.79	0.48–1.31	1.02	0.43–2.39
Nervous system	191, 192	0.69	0.40–1.17	0.66	0.28–1.54
Brain	191	0.67	0.38–1.16	0.74	0.31–1.75
Thyroid	193	1.23	0.80–1.90	1.66	0.80–3.46
Lymphohematopoietic	200–208	1.02	0.76–1.36	0.97	0.61–1.54
Non-Hodgkin's lymphoma	200, 202	1.03	0.70–1.52	0.97	0.53–1.76
Leukemia	204–206, 207.0, .2, .8, 208	1.34	0.72–2.51	0.94	0.39–2.25
Other cancer sites not listed above		1.30	0.76–2.22	1.35	0.89–2.04

[1]The IRRs estimates were derived using Poisson multivariate regression model and were adjusted for attained age, calendar period and province of residence. [2]Previous analysis incidence rate ratios (IRRs) for selected cancers (1974–1998).

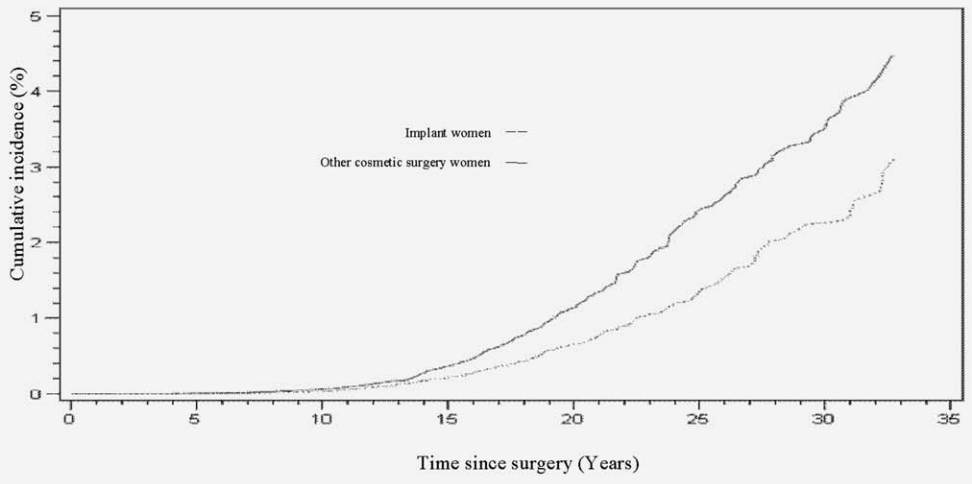

Figure 1. Cumulative breast cancer incidence curves (cumulative incidence curves were adjusted for attained age, calendar period and province of residence using Cox proportional hazards model) for time since index surgery comparing breast implant with other cosmetic surgery women. Incidence rate ratios and respective confidence intervals for different length of follow-up after index date of surgery: 1–5 years, 0.61 (0.38–0.99), 5–10 years, 0.57 (0.41–0.81), 10–15 years, 0.69 (0.52–0.91), 15–20 years, 0.58 (0.44–0.76) and $\geq$20 years, 0.61 (0.48–0.78). p value for trend in IRR over time since surgery = 0.95.

Table 4. Incidence rate ratios (IRRs)[1] and 95% confidence intervals (CIs) of breast cancer for selected breast implant characteristics among implant women

Implant characteristics	Person-years	Cases	IRR	95% CI
Type of fill				
Silicone	356,975	284	1.0	–
Saline	20,489	11	0.74	0.40–1.37
Saline and silicone	100,944	68	0.91	0.66–1.25
Unknown	78,393	51	0.74	0.56–0.96
Polyurethane coating				
No	361,817	260	1.0	–
Yes	45,377	35	1.22	0.84–1.77
Unknown	149,607	119	0.99	0.78–1.24
Fill volume (cc)				
<175	147,957	95	1.0	–
175 to < 200	138,256	108	1.21	0.92–1.59
200 to <225	143,413	121	1.31	1.00–1.72
≥225	123,026	88	1.18	0.88–1.60
Unknown	4,149	2	0.66	0.16–2.68
Site of implantation				
Submuscular	178,446	154	1.0	–
Subglandular	308,488	211	0.78	0.63–0.96
Unknown	66,263	48	0.74	0.54–1.03

[1]Incidence rate ratios estimates were adjusted for attained age, calendar period and province of residence.

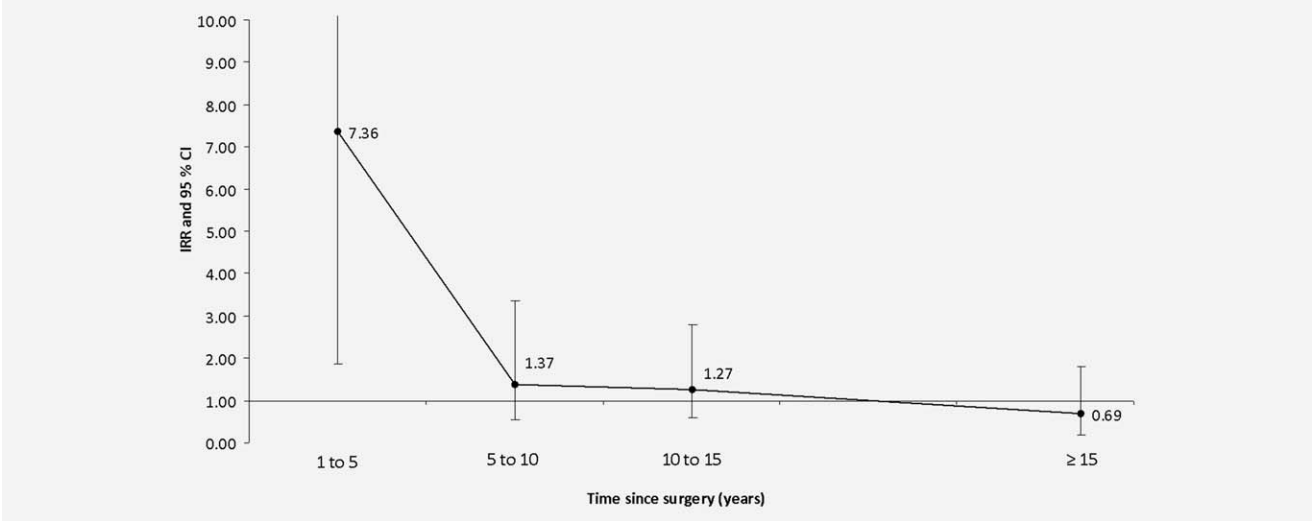

Figure 2. Incidence rate ratios (incidence rate ratios estimates were adjusted for attained age, calendar period and province of residence) and 95% confidence intervals [incidence rate ratios and respective confidence intervals: 7.36 (1.86–29.12), 1.37 (0.55–3.45), 1.27 (0.60–2.67) and 0.69 (0.29–1.60)] to evaluate the trend (p value for trend in IRR over time since surgery = 0.02) in breast cancer risk for women who received subglandular polyurethane coated breast implants relative to other women who received subglandular implants, by time since surgery.

cancer among women with cosmetic breast implants. Moreover, we observed a reduced rate of breast cancer for women with subglandular implants relative to women with submuscular implants that persisted over a long period of follow-up. Finally, we observed a sevenfold increased rate of breast cancer soon after the index date of surgery for women with polyurethane covered subglandular implants that decreased progressively over follow-up.

Findings were somewhat different when the implant cohort was compared to the general female population rather than women with other cosmetic surgeries. The observed reduction in rates for overall cancers in the implant group compared to general female population estimates is consistent with our previous work[7] and previous investigations.[10,16,17,36] However, similar patterns of reduced rates for colorectal, overall genital, lymphohematopoietic cancers and all other cancer sites combined were also seen for the control group compared to women in the general population. Thus, some reductions in rates for site-specific cancers seen in the implant cohort and the other cosmetic surgery women may be because augmented women have different risk factor profile for cancer than the general female population, including the fact that they are more likely to be white and of higher socioeconomic status.[37] Therefore, the observed reductions compared to the general population may be overestimated. This highlights the importance of using a comparable control population, such as women with other cosmetic surgeries who have similarities with breast implant women in terms of sociodemographic and lifestyle characteristics,[38] and not the general population as a reference group for these analyses. Although there is a concern for a possible link between breast implants and anaplastic large T-cell lymphomas of the breast,[21,22] we could not confirm this association because no diagnoses of anaplastic large T-cell lymphomas (ICD-9: 200.6) occurred throughout the follow-up in both the implant subjects and the other cosmetic surgery group (Result not shown).

Women with cosmetic breast implants have lower rates of overall cancers and reduced rates of breast, overall genital and endometrial cancers relative to other cosmetic surgery women. However, the observed reduction in rates for all cancer sites combined and overall genital cancers were explained by the reduced rates of breast and endometrial cancers respectively. Our study confirmed the findings of our previous report and other publications of a reduced rate of breast cancer for implant women compared to other surgery women.[1,7,14] Additionally, we have showed that breast cancer incidence among augmented women remained lower over a long period of time compared to those with other surgeries. Although studies using other cosmetic surgery women as a control group have supported the notion that these patients are a more appropriate comparison group for augmented women,[39] there are still important differences between the two groups. For example, implant patients are more likely than other plastic surgery patients to be white, have earlier age at first birth and be thin.[39] Furthermore, women with a family history of breast cancer may have elected not to receive breast implants, as these devices may interfere with the detection of breast cancer.[40] Therefore, observed differences in breast cancer incidence rates between these two groups may be explained partly by differences in risk factors. In fact, this argument can be supported by the fact that we have found similar patterns of risk for breast and endometrial cancers, two cancers that share many of the same risk factors.[41]

Possible biological mechanisms have been suggested in the literature to explain the reduced breast cancer risk among augmented women. It has been suggested that the presence of breast implants could enhance the immune system, whereby carcinogens and transformed cells would be more easily destroyed.[10] Further, the weight and volume of breast implants may compress the glandular tissue resulting in a decreased blood supply that may reduce the rate of cell proliferation.[10] However, the decreased risk of breast cancer among augmented women might also be due to smaller native breasts (and thus less breast tissue) before augmentation which could make these women less likely to develop breast cancer.[2] Others argue that the exclusion of women with prevalent tumors as a result of the presurgery screening examination may also be a possible mechanism.[15] However, this seems unlikely as we have observed persistently lower breast cancer risk over a long period of time after surgery among augmented women relative to the other surgery group.

Breast implants can be placed in the subglandular position, which is on top of the pectoralis muscle and directly under the breast glands, or in the submuscular position, which is under the pectoralis major muscle.[38] Our analysis according to specific implant characteristics has shown, for the first time, a statistically significant decrease in breast cancer incidence for subglandular breast implants compared to submuscular implants, confirming the nonsignificant pattern we reported in our previous follow-up.[7] As well, the rates of breast cancer incidence for women with subglandular implants remained lower even over a long period of follow-up. This result may be attributable in part to variation in one of our previous explanations of possible effects of breast implants on the immune system and blood flow in the breast gland.[10] This needs to be further studied.

In our previous publication, we had identified the sevenfold increase in breast cancer rate shortly after insertion of subglandular polyurethane coated implants, but the insufficient amount of follow-up time limited the evaluation of a possible trend according to time since surgery.[7] Scientific literature has shown that a polyurethane envelope begins to biodegrade ~2 years after augmentation surgery has been performed.[42] The biodegradation of the polyurethane envelope by body fluids will result in the break-down product TDA[12] which is recognized as an animal carcinogen and a potential human carcinogen.[12] A possible explanation of our finding is that the biodegradation product of polyurethane could act as a tumor promoter. In fact, TDA has been previously shown to stimulate hepatic cellular proliferation and promote mutated cells in rats.[43,44] Therefore, this could explain the sudden increase in breast cancer rate that coincides with the time when the polyurethane envelope biodegrades. In fact, early investigations reported that the polyurethane foam biodegrades rapidly after implantation.[45,46] However, subsequent analyses suggested that polyurethane foam implants biodegrades through a slow process[47] and that large amounts of unbroken polyurethane foam still remains 9 years after implantation.[48] Therefore, we believe further

assessments on the rate of biodegradation of polyurethane among augmented women are needed to clarify our findings. Additionally, to our knowledge, no epidemiological study has been able to provide any confirmation of a tumor promotion effect of TDA. Furthermore, two occupational studies of workers exposed to polyurethane over long periods did not show any increase in cancers of any type.[49,50] Finally, our estimates were based only on a small number of incident cases which increases the possibility that the observed results could be due to chance. However, given the large increase in the IRR observed shortly after implantation and the fact that polyurethane coated implants are still in use, it is critical to pursue investigations to clarify the potential tumor promotion effect of TDA.

Some limitations of our study need to be acknowledged. For instance, no information was available throughout the follow-up if augmented women had their implants removed or if women with other cosmetic surgery had breast implants following their initial procedure. This misclassification bias would only lead to an underestimation of the measures of association. Residential mobility and the resulting loss to follow-up may contribute to lower-than-expected incidence rates among the breast implant and other plastic surgery women when compared to general female population estimates. However, losses to follow-up were minimized with respect to mobility by linking the cohort members to national cancer and mortality databases for the follow-up before 1998. Additionally, we accounted for interprovincial migration for the second phase of this study. In fact, by applying the correction for interprovincial migration, the total amount of person-years for the implant and other surgery women combined went from 956,327 to 949,789. Thus, this correction for interprovincial migration had little impact on expected numbers of cases and the resulting IRR estimates in the comparison of implant cohort to the general population were more conservative. It is possible that some cancers and deaths may have been missed, especially where data were linked to provincial registries because, as time passes, more people are expected to move and be diagnosed in other provinces or other countries. For this reason, we evaluated whether there were differences in completeness of ascertainment of cancer cases and deaths comparing ascertainment using national registries (as in our initial follow-up[7]) to that using provincial registries (as in our extended follow-up). The two approaches could be compared because they were used independently for a common period which extended from 1995 to 1997 for both the Quebec and Ontario cohorts. The assessment of possible differences in completeness of ascertainment revealed that less than 7% of cancer cases identified in the national linkage could not be identified in the provincial linkages and less than 4% of cancer cases were missing in the national linkage compared to the provincial linkages. Similarly, 13% of deaths were missing in the provincial linkage compared to the national linkage. Overall, this results in a net missingness of cancer cases of 3% and a net missingness of deaths of 7%. It should be noted that the comparison of implant and control cohorts should not be materially affected by interprovincial migration or limits in linkages because these factors are expected to be comparable for the two cohorts. Therefore, we know of no reason why incomplete ascertainment would be differential between the implant subjects and other cosmetic surgery women, a condition necessary to bias risk estimates generated from the internal comparison.

Strengths of our study include the largest sample size to date, the cohort design, the long follow-up period, the detailed information on implant characteristics and the fact that we used both other cosmetic surgery women and general female population estimates as the comparison groups. Moreover, we excluded the first year after surgery in the follow-up of this cohort, which is consistent with approaches undertaken by our previous study[7] and other investigations.[39]

In conclusion, this study found significant decreases in incidence rates for breast and endometrial cancers among augmented women compared to other cosmetic surgery women and these reductions persisted for more than 20 years after surgery. No increased incidence of rarer forms of cancers, including hematopoietic cancers, was seen among augmented women. As well, for the first time, a persistent statistically significant reduction in breast cancer incidence was observed for women with subglandular implants. Finally, our study shows that women with subglandular polyurethane covered implants may have an increase in breast cancer rate for the first few years after breast augmentation surgery that decreases with increasing follow-up, suggesting a possible tumor promotion effect on the breast tissue by the biodegradation products of polyurethane. Additional information regarding the possible increase of breast cancer incidence among polyurethane augmented women shortly after surgery is needed.

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Capsular contracture around silicone mini-implants following bacterial contamination: An in-vivo comparative experimental study between smooth, textured and polyurethane implants

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KEYWORDS
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Textured implants;
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Bacteria

Summary *Background:* Capsular contracture remains a problem following breast implant surgery. Although impact of biofilm and implant surface on capsule formation has been demonstrated, interaction of microorganisms with different surface types has not been clarified yet. We aimed to compare the ability of biofilm formation of implants with different surfaces, under standard conditions and to demonstrate its impact on capsular contracture.
Methods: Twenty-four rats were divided into four groups. Mini-implants with three different surfaces (smooth, textured and polyurethane) were placed on the dorsum of each rat. In Group-1, sterile implants were placed in submuscular pockets. In Group-2, implants were incubated in *Staphylococcus epidermidis* medium before implantation. In Group-3, before implantation, implants were immersed in *Rifamycin* solution following bacterial contamination. In Group-4, sterile implants were immersed in *Rifamycin* solution before implantation, and served as the control group. Rats were sacrificed at three months. Clinical, microbiological, histological and immunohistochemical evaluations were performed.

This study is presented at the 40th Congress of the *Turkish Society of Plastic Reconstructive and* Aesthetic Surgeons, October 17-21, 2018, in Antalya, Turkey and the 30th Annual Meeting of the *European Association of Plastic Surgeons*, May 23-25, 2019, in Helsinki, Finland.
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Results: Capsule contracture developed only on infected textured implants. Textured and polyurethane implants showed more biofilm formation than smooth implants. Capsule thickness and inflammatory cell density were higher on textured implants compared to smooth implants ($p = 0.004$). Actin sequence was parallel and concentric on smooth and textured implants; but was in irregular array on polyurethane implants.
Conclusion: In presence of bacterial contamination, textured implants have the most propensity of developing capsular contracture comparing to smooth and polyurethane implants at three months after implantation. Despite high bacterial load and biofilm formation, polyurethane implants are resistant to capsule contracture due to surface characteristics.

Introduction

Background

Although the formation of capsule tissue around the implant materials is a normal result of the body's fibrotic response to the foreign body, occasionally this response can be excessive and caused contracted, distorted, hard, tense and painful capsule tissues. This is an unacceptable outcome for breast augmentation, which is an esthetic procedure and most common cause of revision surgeries.[1-3]

Formation of biofilm layer on the implant surface and subclinical inflammatory process of the biofilm are leading etiological factors for the development of capsular contracture.[4-10] Biofilm formation is also thought to be a trigger in development of breast implant associated anaplastic large cell lymphoma (BIA-ALCL), along with the characteristics of implant surface structure and genetic predisposition.[11,12] Although the effects of biofilm layer and implant surface structure on capsule contracture and BIA-ALCL have been shown in many studies, the interaction of implant surface structure and biofilm formation has not been clarified yet.[13-20]

The core-study results at 10 years have demonstrated that smooth and textured implants displayed different rates of capsular contracture in different settings, such as primary breast augmentations and primary breast reconstructions. The rates were higher in cases of revision augmentation and reconstruction. For Natrelle implants, the capsular contracture rate has been shown to be 18.9% for primary augmentation, 24.6% for reconstruction and 28.7% for revision augmentation cases.[21] Capsular contracture rates for Mentor Contour Profile Gel implants has been demonstrated as 3.6% for primary augmentation, 15.5% for revision-augmentation, 14.3% for primary reconstruction, and 16.4% for revision-reconstruction cases.[22] Comprehensive long-term studies show that capsular contracture rates of micropolyurethane foam implants is 15% lower than that of textured implants and 30% lower than that of smooth implants.[23,24] Recent studies show a reduction in risk not only in primary augmentation, but also in two-stage expander-implant reconstructions, even with radiation.[25] However, there is no single study in the literature, comparing the capsular contracture rates of the three commonly used different breast implant surfaces in a standardized setting. Therefore we planned to conduct a standardized in-vivo animal study to obtain information about the behavior of these surfaces in a standard situation of bacterial contamination and local antibiotic treatment.

Objectives

The main objective of this study is to prove that there is a difference in biofilm formation between different surface implants after bacterial contamination and use of local antibiotics and to demonstrate the impact on capsule contracture. Our hypothesis is that, different implant surfaces should act differently in case of bacterial contamination, therefore biofilm formation and capsule tissue should not be the same on different surface implants, under standard conditions. Additionally, due to surface characteristics, rinsing these implants with antibiotic solution should not result in similar formation of the capsule and the biofilm.

Materials and methods

Ethical statement

Ethical approval was obtained from the Gazi University, Animal Ethics Committee (G.U.ET-17.047).

Experimental animals

This study was conducted on twenty-four Long Evans female rats, weighing approximately 250 gr each.

Study design

The surgical procedure on all animals was performed by the first author (SM). The animals were divided into four groups, 6 animals each, including two experimental and two control groups. In order to minimize the effects of subjective bias, histological and microbiological evaluation was performed by blinded researchers.

Experimental procedures

In this experiment, we used 72 miniature, round, disk-shaped and gel-filled silicone implants, provided by *Polytech Health and Aesthetics, Dieburg, Germany.* The

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Figure 1 Polyurethane coated, smooth and textured silicone mini-implants with 1 × 1 cm/2 ml volume.

implant base was 1 × 1 cm in diameter and the volume was 2 mililiters (Figure 1). All implants contained silicone gel. The implants had three different surface types, such as smooth, textured and polyurethane. The smooth surface is referred as POLYsmooth® and this is the base shell consisting of several layers of silicone including a barrier layer. The textured surface is referred as POLYtxt®, which has a rough surface consisting of pores with average height of 200-300 μm and average diameter of 100-400 μm. During the texturization process, salt-loss technique employing the ammonium carbonate salt is used to avoid sharp edges and loose silicone particles, which is quite different than the sodium chloride salt used in the Biocell® technology. POLYtxt is classified as micro-textured (Ra < 50 μm) according to the specifications of the standard for breast implants, ISO 14607:2018.[26] The polyurethane surface is referred as Microthane®, which is an extra-fine medical grade micropolyurethane foam coat approved for long term implantation. In Microthane® implants, the lower part of a polyurethane foam sheet with a thickness of 2000 μm, is pressed into the 100 to 200 μm thick layer of unvulcanised silicone. During subsequent vulcanization of the silicone, the silicone which engulfed the foam fibers bonds firmly to the shell and the foam is fixed over the implant.

The three different surface implants were placed on the dorsum of each rat under aseptic conditions. In all groups, the location and the surgical plane of the implants were standardized. Smooth implants were placed in the cervical region, textured implants were placed on the right side and polyurethane implants were placed on the left side, into the pockets prepared at a location 1 cm inferior to both scapulae (Figure 2). The implants were placed in a total submuscular plane. Since we did not aim to investigate the capsular contracture rates between implants in the submuscular and subcutaneous planes, we placed all implants in the submuscular plane for standardization purposes. No intraoperative or postoperative systemic antibiotic treatment was needed.

Study groups were designed according to bacterial contamination and local antibiotic treatment.

Group 1 (control group - sterile)

Three implants with different surface types were placed in their designated locations under sterile conditions, without any bacterial inoculation.

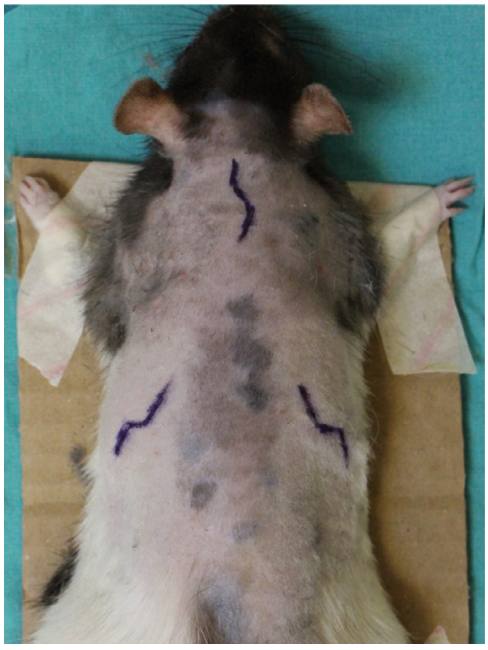

Figure 2 Three different surface implants were placed in the submuscular plane on the dorsum of each rat. Smooth implants were placed in the cervical region, the others were placed into the pockets prepared at the inferior of the both scapulae.

Group 2 (experimental group - infected)

Implants were incubated in *Staphylococcus epidermidis* culture for 24 h prior to insertion in their designated locations. *The Staphylococcus epidermidis* strain was obtained from a breast implant of a patient, who was previously documented to have capsular contracture. The strain was screened for the biofilm formation ability and also documented rifamycin sensitivity. *The Staphylococcus epidermidis* strain was cultured overnight at 37 °C on blood agar plate and bacterial culture diluted to produce specific spectrophotometric transmittance in sterile saline, which yielded a concentration of $1{,}5 \times 10^8$ CFU/ml (0,5 McFarland). The suspension was transferred to fresh brain heart infusion (BHI) medium supplemented with 2% glucose and 2% sucrose at a 1:50 dilution. Different surface implants were transferred into sterile conical vials and the BHI medium inoculated with bacteria was added. Care is taken that the hemisphere of

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Table 1 Description of the groups.

Groups	Implants	Bacteria	Antibiotic
Group 1 (Sterile)	Smooth - Polyurethane - Textured	–	–
Group 2 (Infected)	Smooth - Polyurethane - Textured	*Staphylococcus epidermidis*	–
Group 3 (Infected + Antibiotic)	Smooth - Polyurethane - Textured	*Staphylococcus epidermidis*	Rifamycin
Group 4 (Antibiotic-only)	Smooth - Polyurethane - Textured	–	Rifamycin

the implants was also covered under medium. The vials were sealed and incubated at 37 °C for 24 h on a rocker platform.

Group 3 (experimental group - infected + antibiotic)

Following incubation in the bacterial culture medium for 24 h, implants were immersed in antibiotic solution and eventually were placed in their designated pockets. For local antibiotic treatment, implants were kept in a solution containing 250 mg/3 ml *Rifamycin sodium* for 1 min in related groups.

Group 4 (Control group- antibiotic-only)

Sterile mini-implants were directly immersed in the antibiotic solution mentioned above, without being incubated in bacterial culture medium and placed in the pockets after 1 min. Groups are summarized in Table 1.

Experimental outcomes

Postoperatively, animals were monitored daily in their own cages. We have not observed any bleeding, hematoma or any other complication in any of the animals during or after the surgical procedure. The evaluation period for all groups was determined as 3 months.[27] All implants were evaluated clinically before being explanted and then removed with total capsulectomy. The removed implants were divided into two equal pieces together with the capsule tissues for microbiological evaluation, scanning electron microscopy, histological and immunohistochemical evaluation.

Clinical evaluation

Baker's classification is the most frequently used method in clinical scoring for capsular contrature, where Grade 4 is characterized with visible contracture and the patient describes pain. Since this is difficult to assess in an animal model, we used a modified version of this classification and evaluated the severity of clinical contacture as none, mild, moderate and severe. Two seperate blinded observers have evaluated the animals.

Microbiological evaluation

We used microtiter plate method for the bacterial load measurement from the biofilm layer of half parts of the extracted implants. Optical density (OD) of crystal violet-stained biofilm was determined by using micro ELISA autoreader at wavelength 450 nm.

Scanning electron microscopy (SEM)

Implant surfaces were evaluated under scanning electron microscopy to visualize the biofilm formation to support the microtitration data of the bacterial load. Implant surfaces were fixed with 8% glutaraldehyde buffer and washed with 0.1 M Sorenson phosphate buffer. 1% osmium tetraoxide used for secondary fixation. Specimens were dehydrated with increased alcohol series and acetone. After critical point drying, specimens were coated golden-palladium particles. Specimens were evaluated with Carl Zeiss EVO LS10 (Carl Zeiss Microscopy Ltd., Cambridge, UK).

Histological evaluation

Tissue specimens were fixed with 4% neutral formaldehyde. After routine tissue processing methods tissues were embedded paraffin. 4 μm thickness sections were taken for histochemical and immunohistochemical examinations. Masson's trichrome staining kit (GBL, LOT: A6374) were used for capsule evaluations. Heat induced antigen retrival was made with citrate buffer (pH=6.0) for immunohistochemical evaluations. 3% Hydrogen peroxide incubation was used for inhibiting endogenous peroxidase activity. Sections were incubated with blocking solution (Histostain Plus Broad Spectrum, LOT: 1838146A) for 10 min to prevent nonspecific reaction. Specimens were incubated with primary antibodies for actin (1:400, bs-10196R, LOT:AD080151), CD86 (1:500, bs-1035R, LOT:AH02227980) and CD163 (1:500, bs-2527R, LOT:AG07191275) overnight +4 °C. After secondary antibody and streptavidine peroxidase (Histostain Plus Broad Spectrum, LOT:1838146A) incubation, DAB was used as chromogen. The sections were assessed with DM 4000 Leica Germany Visual Analysis Systems and ImageJ program. Capsule thickness was measured at six different sites (μm). Capsule tissue was evaluated in terms of featuring dense regular connective tissue, loose connective tissue content, inflammatory cell infiltration, distribution of foreign body giant cells on the capsule and synovial membrane-like metaplasia on the surface adjacent to the implant. It was graded from 1 to 4 in terms of the area coated by these histological findings in capsule tissue. CD86/CD163 was evaluated by the ratio of immunopositive cells per area. Percentage of actin positive area to capsule was calculated.

Statistical methods

Analysis of the obtained data was performed by using the package program of IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA). Shapiro Wilk test was used to determine if the distribution of continuous variables was close to normal or not., Levene test was used to examine the homogeneity of the variances. Descriptive statistics were shown as medians (range between the quartiles). Kruskal Wallis test was used to investigate the significance of difference

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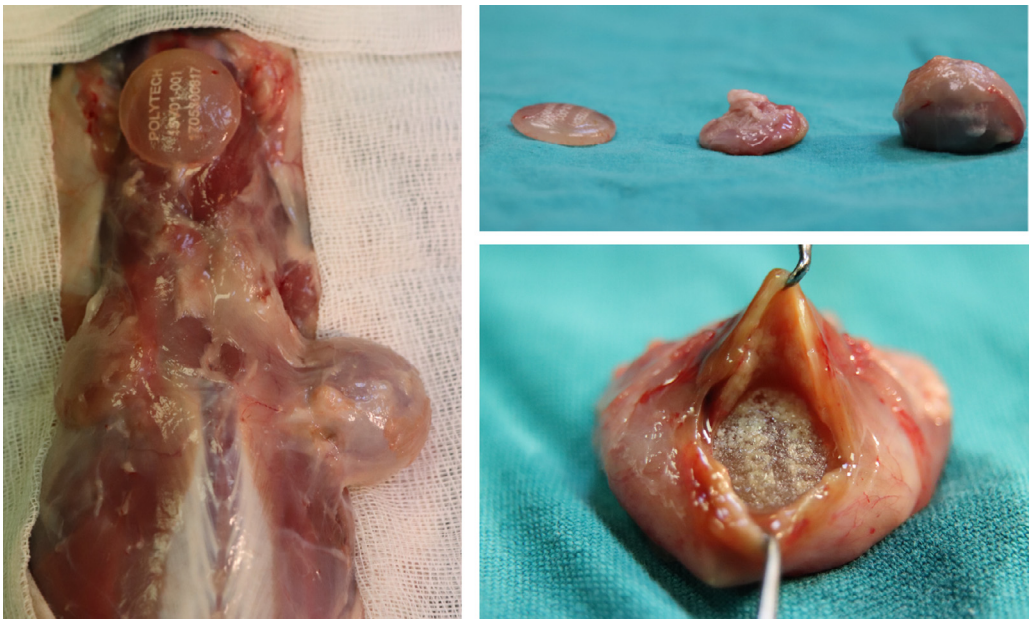

Figure 3 Image of a rat after desepithelization of the skin. Capsular contracture is very prominent around the textured implant on the right side in the infected Group 2 (Left). Capsule formation around smooth, polyurethane and textured implants, respectively (Above right). The capsule around the textured implant was more spherical and thicker (below right).

Table 2 Bacterial load levels by groups and surfaces.

	Smooth	Polyurethane	Textured	p-value
Group 1	0.018 (0.012-0.026)	0.007 (0.000-0.034)	0.001 (0.000-0.018)[A]	0.042
Group 2	0.043 (0.000-0.176)	0.079 (0.028-0.149)	0.052 (0.042-0.146)[A]	0.819
Group 3	0.023 (0.000-0.053)	0.038 (0.019-0.046)	0.040 (0.023-0.057)	0.549
Group 4	0.008 (0.001-0.021)	0.031 (0.017-0.032)	0.030 (0.018-0.034)	0.022
p-value	0.751	0.051	0.003	

Descriptive statistics were shown as medians (range between the quartiles).
[A] The difference between Group 1 and Group 2 is statistically significant (p <0.001).

among the groups in terms of median bacterial load, capsule thickness and histopathology scores when surface types were kept constant. According to the Bonferroni Correction, the results for $p < 0.0167$ were considered statistically significant. When the groups were kept stationary, the significance of difference among the surface types in terms of median bacterial load, capsule thickness, and histopathology scores was examined by the Friedman test. According to Bonferroni Correction, the results for $p<0.0125$ were considered statistically significant. Immunohistochemical results were analyzed with Kruskal Wallis and ANOVA according to data distribution based on Shapiro Wilk test. According to Bonferroni correction $p<0.05$ were considered statistically significant.

Results

Clinical assessment

Modified Baker scoring was used to grade the capsular contracture and no evidence of infection and exposition was observed in any mini-implants. Capsular contracture was detected in all of the six textured implants (6/6) in Group 2 and five of the six textured implants (5/6) in Group 3, following bacterial contamination. Contracture was not observed in the capsule around any of the smooth (0/6) and polyurethane coated implants (0/6) (Figure 3).

Microbiological evaluation

In the assessment of the bacterial load by microtitration plate method; all three surfaces showed an increase in bacterial load following bacterial contamination compared to sterile groups. The increase in bacterial load on textured surfaces was the most prominent amongst the three implants following bacterial contamination and was statistically significant ($p<0.001$) compared to Group 1. Optical densitometric measurement results of the bacterial load is summarized in Table 2.

Scanning electron microscopy

The density of biofilm formation was minimal on smooth surface implants after bacterial contamination. Polyurethane

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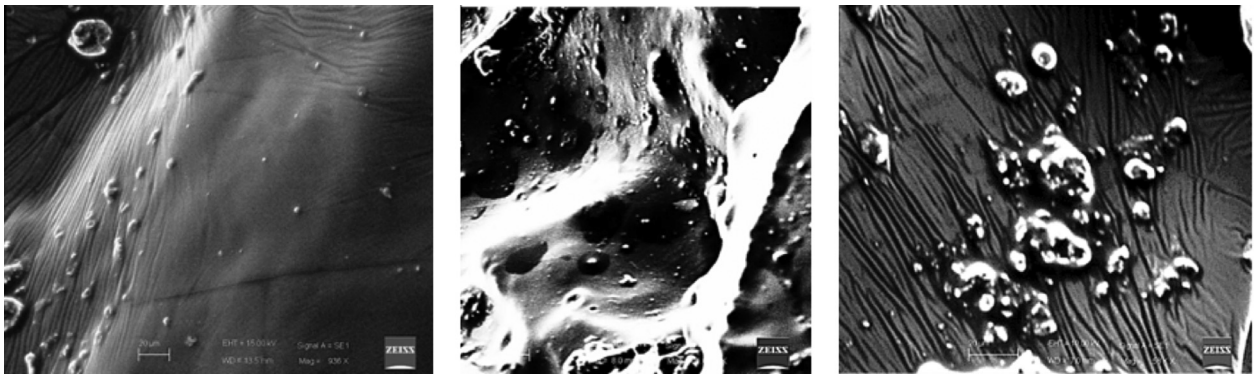

Figure 4 Scanning electron microscopy samples of different surface implants in infected Group 2. The biofilm layer spread along the surface in a circular pattern on smooth (Left), polyurethane (Middle) and textured surface implants (Right) is visualized.

Table 3 Capsule thickness levels by groups and surfaces.

	Smooth	Polyurethane	Textured	p-value
Group 1	124.9 (109.3-335.7)	905.2 (225.9-1019.2)	275.1 (124.9-799.0)	0.717
Group 2	175.7 (155.5-196.6)[A]	387.5 (197.2-443.7)	1300.2 (811.0-1689.1)[A]	0.007
Group 3	134.1 (113.9-181.7)	686.7 (402.0-813.6)	348.0 (264.1-694.8)	0.039
Group 4	118.3 (75.4-163.0)	276.0 (224.2-438.5)	258.1 (104.6-411.4)	0.368
p-value	0.224	0.156	0.028	

Descriptive statistics were shown as medians (range between the quartiles).
[A] The difference between smooth surface and textured surface is statistically significant in Group 2 ($p = 0.004$).

and textured surface implants displayed more intense biofilm formation than smooth implants. However, there was no remarkable difference between polyurethane and textured implants (Figure 4). Following rinsing with local antibiotic solution in Group 3, biofilm formation was found to be decreased on all implant surfaces when compared to Group 2.

Histological evaluation

The thinnest capsule was detected around smooth surface implants among all groups. The thickest capsule was detected around infected textured surface implants in Group 2. In this group, the mean thickness of the smooth capsule was determined as 175.7 μm while the mean thickness of the textured capsule was measured as 1300.2 μm and this was statistically significant ($p = 0.004$). The mean thickness of the polyurethane capsule was determined 387.5 μm. The results of the capsule thickness is summarized in Table 3.

As the histology of the capsule was examined to detect the density of the inflammatory cells; the least amount of inflammation was detected on the smooth surface implants in all groups. The most severe inflammation was detected on textured implants in sterile and infected groups. In Group 2, inflammatory cell density was found to be significantly higher on infected textured surfaces, comparing to smooth surfaces ($p = 0.004$). The inflammation score of polyurethane surfaces, was much higher than the smooth, but less than textured implants in infected groups. The results of the inflammatory cell scores are summarized in Table 4.

Immunohistochemical evaluation

In this evaluation, the sequences and amounts of actin proteins were measured. In the capsule tissues of the smooth surface implants, it was observed that the actin immunopositivity was mild and the arrangement was parallel to the implant surface. In textured surfaces, the actin immunoreactivity was found more severe than smooth surfaces and the arrangement was parallel to implant surface. In the polyurethane coated implants, actin arrangement was in irregular sequence and the intensity of the immunoreactivity was more than smooth surface. The severity of the immunoreactivity was similar to textured surface (Figure 5). While the immunoreactivity was the most intense in the contaminated group, it was observed that this severity decreased with local antibiotic treatment. In the control group, mean actin percentage of the textured implant capsule (32.1) was found to be significantly higher when compared with smooth (19.8) and polyurethane coated implant (19.7) groups ($p = 0.018$, $p = 0.01$, respectively). In Group 2, the increase of actin percentages were not statistically significant (Figure 6).

In the immunohistochemical evaluation of CD86 and CD163, in terms of the polarization of macrophages, CD86 / CD163 ratio was found to be significantly higher in the capsule of the polyurethane coated implants compared to the smooth and textured implants in the contaminated group ($p = 0.006$, $p = 0.009$, respectively). The decrease of CD86/CD 163 ratio in polyurethane surface implants after local antibiotic treatment was statistically significant ($p = 0.023$) (Figure 7).

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Table 4 Inflammatory cell infiltration scores by groups and surfaces.

	Smooth	Polyurethane	Textured	p-value
Group 1	1 (1-1)	1 (1-1)[A,B]	2 (1-3)[A]	0.135
Group 2	1 (1-2.5)[a]	3 (3-3.5)[A,C]	4 (4-4)[A,C,E]	0.011
Group 3	1 (1-1)	2.5 (2-3)[B]	3 (3-3.75)[D]	0.024
Group 4	1 (1-1.75)	2 (1.25-2)[C]	1.5 (1-2)[C,D]	0.368
p-value	0.377	0.006	0.005	

Descriptive statistics were shown as medians (range between the quartiles).
[A] The difference between Group 1 and Group 2 is statistically significant ($p < 0.001$).
[B] The difference between Group 1 and Group 3 is statistically significant ($p < 0.001$).
[C] The difference between Group 2 and Group 4 is statistically significant ($p < 0.001$).
[D] The difference between Group 3 and Group 4 is statistically significant ($p < 0.001$).
[E] The difference between smooth surface and textured surface is statistically significant ($p = 0.004$).

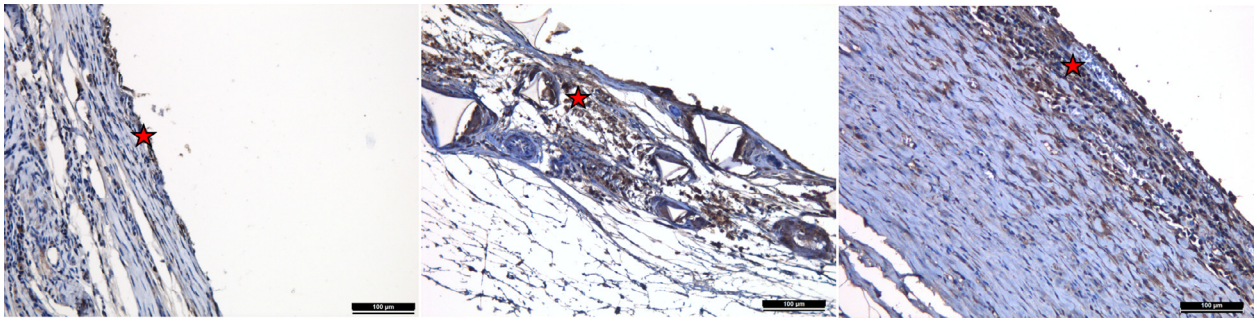

Figure 5 Images of immunohistochemical evaluation with anti-actin antibody. The star-marked regions show the actin protein accumulation in the capsule tissue. Actin alignment is parallel to the implant surface on smooth (left) and textured (right) implants, while irregular alignment in polyurethane implants (middle).

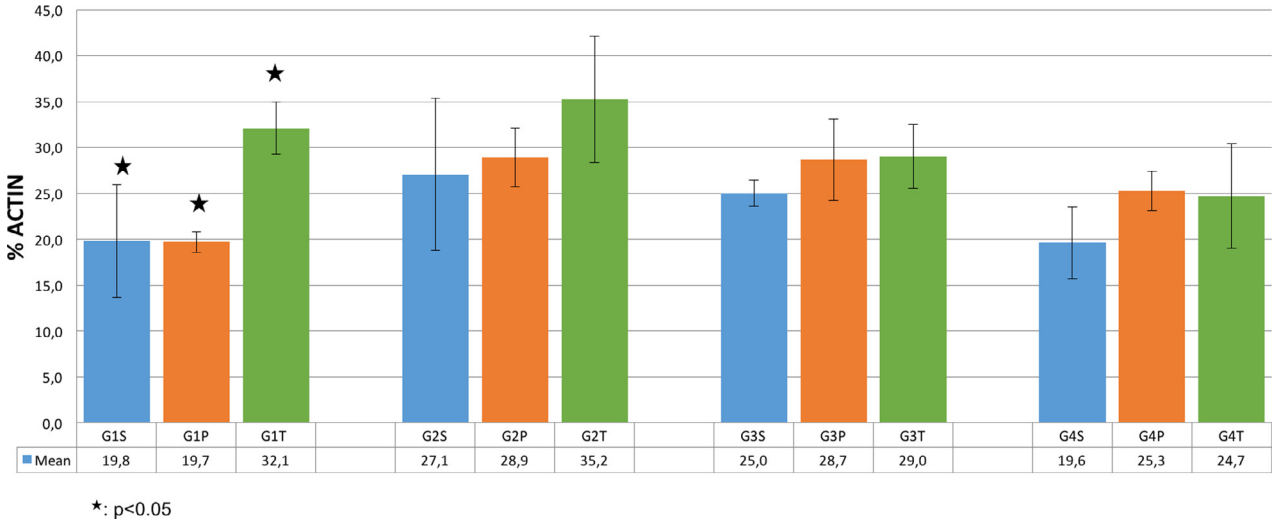

Figure 6 Graph showing percentage of actin according to groups. G: Group, S: Smooth, P: Polyurethane, T: Textured. 1,2,3,4 are group numbers. Mean and standard deviation (SD) values are shown in the graphic.

Outcomes and estimation

In the clinical point of view, it was found that textured implants, those exposed to bacterial contamination, demonstrated significantly more severe capsular contracture, regardless being treated with or without antibiotics (Figure 3). Smooth and polyurethane implants remained capsule-free at postoperative 3 months. Scanning electron microscope showed more intense formation of the biofilm on the surfaces of textured and polyurethane implants; comparing to smooth surfaces. This finding was similar in both antibiotic-treated and non-treated groups.

In the microbiological evaluation, bacterial count in Group 3 (infected+antibiotic-treated group), in which the local antibiotic solution was employed, decreased in all three different-surface implants, comparing to Group 2 (in-

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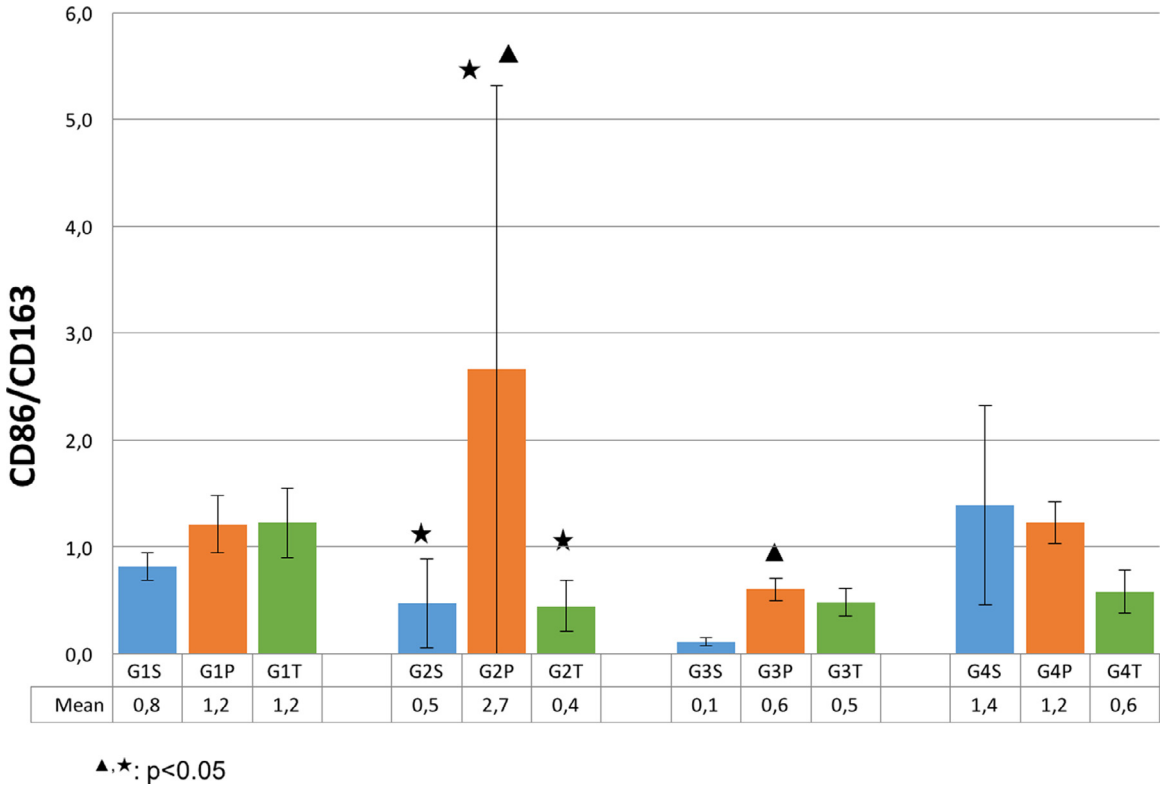

Figure 7 Graph showing mean CD86 / CD163 rate according to groups. G: Group, S: Smooth, P: Polyurethane, T: Textured. 1,2,3,4 are group numbers. Mean and standard deviation (SD) values are shown in the graphic.

fected group). These results were correlated with scanning electron microscopy data. However, the amount of reduction between three surfaces was not statistically significant.

With these results, a significant difference was found in the growth of biofilm and bacterial load between the smooth implants and the textured implants after bacterial contamination in Group 2. As a consequence, capsule thickness and inflammatory cell densities were significantly more complicated in the textured implants.

Adverse events

There were no adverse effects in any of the control and experimental groups.

Discussion

There is an increasing evidence of the role and importance of biofilm layer formation on the implant surface and subclinical infection in the etiology of capsular contracture. However, it is not accurate to say that the only etiologic factor is the biofilm layer. It is a fact that many different factors play a role, such as the surface structure of the implant, the plane in which the implant inserted, history of surgical trauma and hematoma.[4] In this study, implants with three different surfaces were placed in the dorsum of the rats under standard conditions and the differences between biofilm and capsule formations were evaluated following bacterial contamination. To our knowledge, this is the first study in literature, comparing smooth, textured and polyurethane coated implants in a standardized setting in-vivo.

It was determined that bacterial contamination in textured implants resulted in a higher and clinically obvious development of capsular contracture comparing to smooth and polyurethane implants. Considering this situation, this clinical difference between textured and smooth implants may be linked to the difference between the presence of biofilm that is clearly revealed by electron microscopy. The more intense biofilm formation and the more bacterial load on the textured implants compared to the smooth surface implants were revealed by the significant differences in inflammatory cell density and capsule thickness and clearly resulted in capsular contracture. There was no significant difference between polyurethane implants and textured implants in terms of biofilm formation in the electron microscopy. However, polyurethane foam coated implants did not show any evidence of capsular contracture despite dense biofilm formation. This shows that polyurethane-coated implants are more resistant to capsular contracture than textured implants despite the formation of biofilm. This could be explained by the surface characteristics of the polyurethane surface. The three-dimensional matrix surface, that allows collagen fibers wrapping on each other, therefore neutralizing the contractile forces, does not permit parallel alignment. The lack of parallel concentric form of the collagen fibers and actin protein sequences in the capsule tissue was interpreted as protecting the polyurethane surface from contracture development.[27]

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Although different antibiotic regimens such as Gentamicin/Cefuroxime can be used in breast augmentation, in this study we preferred *Rifamycin* for local antibiotic treatment, since it has a wide spectrum of action on the Gram(+) and Gram(-) bacteria and also effective in preventing atypical mycobacterial infections and subclinical inflammatory process. At the same time, due to its orange color, adhesion to the implant surface in local application can be easily detected. The use of *Rifamycin* as a local antibiotic has been shown to reduce biofilm formation on all implant surfaces by electron microscopy. However, this decrease was not statistically significant in bacterial load measurements by microtitration plate method. Although *Rifamycin* was used in Group 3, capsular contracture was observed still in the textured implants. Local *Rifamycin* treatment decreased the bacterial load, however did not prevent the capsule contracture clinically in the textured implants. In addition, hydrophilic features and the spongious structure of the polyurethane foam, enables antibiotic retainment longer than the silicone surface, which may obviously help to reduce the bacterial count on the surface by permitting sufficient contact time for bacterial eradication, compared to smooth and textured surfaces, which do not have the capacity of retaining the fluid thus limits the efficacy of the antibiotic.[28,29]

The biofilm layer is often polymicrobial. *Staphylococcus epidermidis*, a bacterium found on the skin and in the endogenous breast flora, is the most frequently isolated organism from removed implants due to capsule contracture.[7,8,30] Other isolated organisms are *Propionibacterium acnes*, *Staphylococcus aureus*, Streptococcus spp, Bacillus spp, *E.coli*, Mycobacterium spp, Corynebacterium spp, and Lactobacilli.[31-33] In the biofilm, numerous different microenvironments emerge, which vary in pH, oxygen concentration, nutrient availability, and cell density. Therefore, it is difficult to remove the biofilm layer by a single treatment modality.[34-37]

Immunohistochemical evaluation demonstrated that the percentage of actin in the parallel arrangement in the textured implant capsules resulted in capsule contraction following bacterial contamination. Although it was not statistically significant, bacterial contamination increased actin percentage and *Rifamycin* decreased this percentage. The lack of statistically significant differences may be due to the low number of subjects. Increased actin percentage of bacterial contamination is consistent with the literature.[27]

Macrophage polarization is an important process in inflammation. While M1 macrophages (CD86+) are effective in events such as proinflammatory, microbicidal, tissue damage, M2 macrophages (CD163+) are responsible for anti-inflammatory, apoptotic cell clearance, high phagocytic activity and wound healing.[38] In this study, CD86/CD163 ratio in favor of proinflammatory cells suggest that the inflammatory process is predominant in histological evaluations. The decrease in CD86/CD163 ratio with rifamycin suggests that the severity of inflammation is reduced. The CD86/CD163 ratio is higher than the other surface implants in the contaminated polyurethane coated implant group. It has been observed that the contamination of polyurethane coated implants causes more inflammatory macrophage polarization than other implants. However, the fact that the ratio of parallel actin is low due to its surface properties suggested that this inflammation might have less effect on capsular contraction. Although the number of histiocytes was high in polyurethane coated implants, the low percentage of parallel actin was found to be consistent with the literature.[27]

Hydrophilic features and the spongious morphology of the polyurethane foam help to reduce the bacterial load on the surface after local antibiotics use. Therefore, the CD86/CD163 ratio was found to be significantly lower in the polyurethane coated implant capsule in the contaminated plus antibiotic treatment group compare to the infected polyurethane group.

Generalisability/translation

Bacterial biofilms have been implicated not only with capsular contracture but also breast implant-associated anaplastic large-cell lymphoma (BI-ALCL) as well. Due to their increased surface area, implants with highly textured surfaces may harbor greater biofilm loads than those with smooth surfaces. The etiology of BIA-ALCL is multifactorial and is a result of an interaction between tissue, implant texture, microorganisms and genetical predisposition. In our study, we have demonstrated that textured and polyurethane surface implants displayed more bacterial counts than smooth implants in the scenario of bacterial contamination. However, while textured implants suffered capsular contracture, polyurethane implants survived the contracture, probably due to the surface morphology. Furthermore, local antibiotics seemed to be more effective in the polyurethane group, probably as a result of sustained antibiotic efficiency due to the spongious structure of the polyurethane surface. Should this information from the capsular contracture model in rats be translated to the BIA-ALCL, it may help us to understand why BIA-ALCL occurs vastly on implants with highly textured surfaces.[39]

The shortcoming of this paper is the insufficiency of the 3-month period for the evaluation of the capsular contracture. However, incubation of mini-implants in the bacterial culture medium for 24 h, provided sufficient biofilm and inflammatory response that enabled to observe the clinical outcome of capsule contracture around textured mini-implants. It is well known that smooth implants display more, polyurethane implants display less capsular contracture rates comparing to textured implants in clinical settings; and one may anticipate similar results in this experimental study. However, in the standard setting of bacterial contamination and local antibiotic treatment, textured mini-implants demonstrated a rapid onset of inflammation and subsequent capsular contracture; while other mini-implants remained contracture-free. Three months is quite a short period of time to draw a conclusion about the contracture rates around smooth mini-implants in this particular study, and a long term follow-up of at least 1 year is essential in future studies.

Conclusion

There is no single definitive factor in the etiology of capsular contracture and many factors are responsible. The forma-

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tion of biofilm and chronic subclinical infection seems to be the most important etiologic factors. In this study, we have proved that in case of bacterial contamination, the possibility of having capsular contracture around textured implants is much higher than smooth and polyurethane implants in a standardized setting at the early stage, and biofilm formation might have a prominent role in that. Although, the bacterial load is comparable with polyurethane coated implants, PU implants appear to be more resistant to capsular contracture, probably due to the physical characteristics of the three-dimensional matrix surface, which obviously facilitates neutralizing the contractile forces of the unparallel collagen fibers and which augments the efficiency of local antibiotic treatment by the help of its spongious morphology.

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Polyurethane Implants in 2-Stage Breast Reconstruction: 9-Year Clinical Experience

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Abstract

Background: Capsular contracture (CC) is a major complication of breast surgery with smooth and textured implants. Polyurethane (PU) foam–coated breast implants were developed to decrease the incidence of CC.

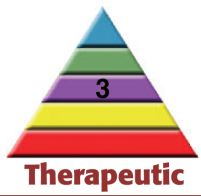
Objectives: The authors determined the incidence of CC following 2-stage breast reconstruction using PU foam–covered implants, with and without radiation therapy.

Methods: The records of 92 patients who received 115 PU implants were retrospectively reviewed. The rates of CC over time were compared for irradiated and nonirradiated groups with a Kaplan-Meier analysis and log-rank test. CC rates also were analyzed with respect to age.

Results: The median follow-up time for patients was 103.3 months. Nine patients experienced unilateral Baker grade III or IV fibrous CC, including 6 patients from the irradiated group and 3 patients from the nonirradiated group. The overall cumulative incidence of CC at 9 years was 8.1%. In the irradiated and nonirradiated groups, the 9-year cumulative incidence was 10.7% and 5.5%, respectively. CC occurred within 3 years in the irradiated group and within 7 years in the nonirradiated group. The incidence of CC appeared to be higher among younger patients.

Conclusions: Radiation therapy increases the risk of high-grade CC with textured or smooth implants. PU implants are associated with a much lower cumulative incidence of CC following 2-stage breast reconstruction, even when radiotherapy is performed.

Level of Evidence: 3



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Since the introduction of breast implants in plastic surgery nearly 50 years ago, capsular contracture (CC) has been the leading cause of morbidity and reoperation, with reported incidences as high as 80%.[1-3] Results of many studies have shown that the incidence of CC is higher for breast reconstruction than for primary cosmetic breast augmentation.[4-10] According to the US Food and Drug Administration, women who received reconstruction with silicone gel implants had a nearly 15% risk of CC (Baker grade III or IV), a 25% risk of implant removal or replacement, and an overall reoperation rate of 40% at the end of 4 years.[11]

Radiation therapy (RT) also appears to increase the risk of CC. In several studies of 2-stage breast reconstruction, the incidence of CC was consistently higher for patients who also underwent RT compared with those who did not receive RT.[12-15] Authors of a long-term prospective analysis of a large cohort of women found that CC of grade III or IV

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occurred in 46.6% of irradiated implants but in only 6.4% of nonirradiated implants.[16]

To decrease the high incidence of CC associated with silicone breast implants, polyurethane (PU) foam–coated implants were introduced (by Ashley[17] in 1970). Many investigators have found that the incidence of CC with PU-coated implants is approximately 2%.[3,5,18-25] However, data are scarce regarding the incidence of CC among women who receive PU foam–coated implants during 2-stage breast reconstruction, particularly when the procedure is combined with RT. We sought to determine the long-term incidence of CC following 2-stage breast reconstruction with PU implants in the presence and absence of RT. The secondary outcome was to examine the association between patient age and occurrence of CC.

METHODS

Study Design

For this retrospective cohort study, we reviewed the medical records of patients (all female) who underwent immediate 2-stage breast reconstruction with PU-coated shaped implants with or without RT from June 2002 through February 2015 (12 years, 8 months) at Sandro Pertini Hospital (Rome, Italy). This study was approved by the ethics review board of the hospital. Exclusion criteria were 1-stage breast reconstruction, delayed reconstruction, secondary breast surgery, and any reconstruction involving round implants, smooth or textured implants, saline implants, acellular dermal matrix, or autologous tissue.

An Excel database was prepared with information for 92 patients (115 breast implants). The following variables were included: diagnosis; patient age; date of mastectomy and placement of tissue expander; date of implantation with the PU device; need for RT; implant type, size, and projection; length of follow-up and dates of follow-up visits; and presence and grade of CC. The original patient database, which included all early and late complications, was refined for this study to only indicate CC occurrence during follow-up.

Surgical Techniques

Consultations and surgical procedures were performed by the senior surgeon (S.P.) or members of his team at Sandro Pertini Hospital. All patients underwent mastectomy with immediate 2-stage breast reconstruction. Round or low-height tissue expanders were positioned subpectorally. One or 2 drains were placed, depending on whether the expander was partially or fully covered by the muscle, respectively. Patients who underwent RT received a mean dose of 50 Gy, over the tissue expander only, between 1 and 6 months (mean, 3 months) after the first surgical session and a mean of 3 months prior to placement of the definitive PU-coated implant. Implant choice was based on the surgeon's recommendation. None of the definitive implants was irradiated. All shaped gel implants were covered with MPS, a micro-PU foam (Microthane, Polytech Health & Aesthetics, Dieburg, Germany).

Determination of CC Incidence

Patients were monitored at follow-up visits attended by at least 4 of the 5 senior team members at 1, 3, and 6 months postoperatively. CC was graded by the Baker scale; cases of grades III and IV CC were evaluated further in this study. Grade III CC corresponds to a hard breast and noticeable implant. Grade IV CC denotes a hard and rigid implant with stretched and tender skin, pain, and distortion of the breast. Capsulectomy, excluding the chest wall, was performed when the overlying tissues were sufficiently thick. For patients with inadequate tissue coverage, partial capsulectomy was performed to promote tissue adhesion to the PU surface of the implant and avoid further depletion of the overlying tissues.

Statistical Analysis

An independent epidemiologist (G.F.) performed data analysis. Because the primary objective of this study was to determine the role of micro-PU foam in the prevention of high-grade CC (Baker III or IV) after primary breast reconstruction, we evaluated individual breast implants rather than individual patients. Breast implants were categorized as irradiated or nonirradiated group. "Time to CC" was defined as the time from the first surgical session to the diagnosis of CC. Patients without a diagnosis of CC were censored at last follow-up or death. Rates of CC, determined for 12-month periods, were estimated with the Kaplan-Meier method, with cumulative incidences and 95% confidence intervals (CI). Cumulative incidence curves, stratified by irradiation status and age, were compared with the log-rank test for equality of survivor functions. A multivariate Cox proportional hazards model was applied to study the association between CC and age while controlling for irradiation status. Statistical significance was defined as $P < .05$. All analyses were performed with Stata 13 statistical software (StataCorp LP, College Station, TX).

RESULTS

Sixty-nine of the 92 patients underwent unilateral mastectomy, and 23 underwent bilateral mastectomy. Of the 115 breasts, 64 underwent skin-sparing mastectomy,

26 received nipple-sparing mastectomy, 17 required radical mastectomy, and 8 underwent skin-reducing mastectomy. Fifty-six breasts (49 patients) were irradiated, and 59 breasts (43 patients) were nonirradiated (Tables 1 and 2). The need for RT could not be predicted in any case.

The patients' mean age was 53 years (standard deviation [SD], 10.2 years; range, 27-76 years), and the median follow-up was 103.3 months (range, 6.2-152.4 months) (Table 1). When the study population was analyzed in terms of individual breast implants, the mean age of implants for the nonirradiated group was 54.6 years (SD, 8.6 years; range, 39-75 years), and the mean age for the irradiated group was 50.8 years (SD, 10.5 years; range, 27-76 years) (Table 2). The median follow-up time was 103.9 months (range, 33.8-152.4 months) for the nonirradiated group and 106.6 months (range, 6.2-151.6 months) for the irradiated group (Table 2).

Fibrous CC (Baker grade III or IV) developed in 9 breast implants (9 patients). Each patient who experienced fibrous CC had undergone unilateral mastectomy. Four cases of CC occurred within the first year following implant placement, additional 3 cases occurred within 3 years, and the remaining 2 cases occurred within 7 years. The cumulative incidence of CC at 9 years was 8.1% (95% CI, 4.3-15.0), as shown in Figure 1. Kaplan-Meier survival curves depicted the likelihood of CC over time, with and without RT (Figure 2). Of the 9 breasts that developed CC, 6 had been irradiated. Four of these breasts developed CC within 1 year, and 2 developed CC within 3 years. The cumulative incidence of CC at 9 years in this group was 10.7% (95% CI, 5.0-22.3). For the 3 nonirradiated breasts that developed CC, this complication was diagnosed 3 to 7 years after implantation. The cumulative incidence of CC at 9 years in this group was

Table 1. Data for Patients

	Irradiated Group (N = 49)	Nonirradiated Group (N = 43)	Total (N = 92)
Age, y			
Mean (SD)	51.0 (11.0)	55.2 (9.0)	53.0 (10.2)
Range	27-76	39-75	27-76
Follow-up time, mo			
Mean (SD)	97.1 (39.5)	105.5 (27.4)	101.6 (34.4)
Median	104.0	102.0	103.3
Range	6.0-151.0	33.0-152.0	6.2-152.4

SD, standard deviation.

Table 2. Data for Breast Implants

	Irradiated Group (N = 56)	Nonirradiated Group (N = 59)	Total (N = 115)
Age, y			
Mean (SD)	50.8 (10.5)	54.6 (8.6)	52.8 (9.7)
Range	27-76	39-75	27-76
Follow-up time, mo			
Mean (SD)	99.0 (38.2)	108.7 (27.9)	104.0 (33.5)
Median	106.6	103.9	104.2
Range	6.2-151.6	33.8-152.4	6.2-152.4

SD, standard deviation.

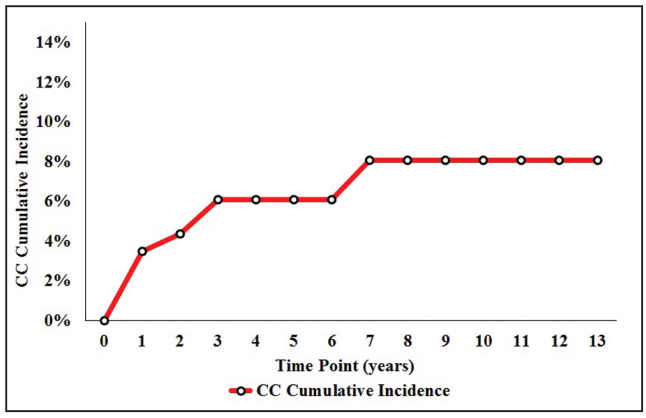

Figure 1. Kaplan-Meier cumulative incidence of capsular contracture (CC) after 2-stage breast reconstruction. The curve depicts the rates of CC over time for the 115 polyurethane (PU) foam–coated breast implants that were analyzed in a retrospective review of hospital records of 92 women. Nine cases of CC (Baker grade III or IV) occurred within 7 years.

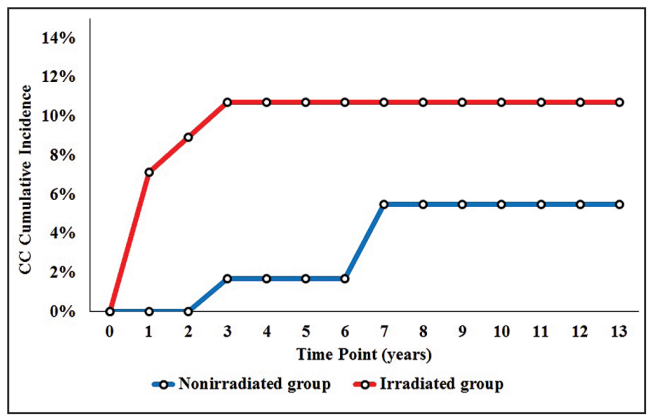

Figure 2. Kaplan-Meier cumulative incidence depicting the rates of capsular contracture (CC) after 2-stage breast reconstruction according to irradiation status. Nonirradiated group, blue curve (n = 59 breast implants). Irradiated group, red curve (n = 56 breast implants). Radiation therapy (RT) was delivered over the tissue expander. Reliable data were available for a median of 9 years of follow-up.

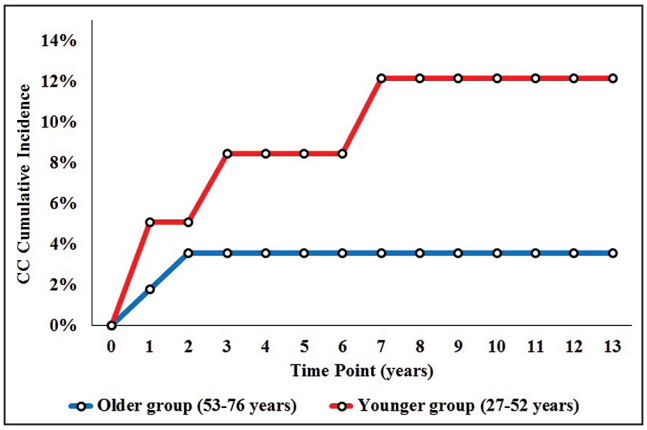

Figure 3. Kaplan-Meier cumulative incidence of capsular contracture (CC) after 2-stage breast reconstruction as a function of age. Older group (27-52 years old), blue curve (n = 56 breast implants). Younger group (53-76 years old), red curve (n = 59 breast implants). The difference between the 2 curves was assessed by the log-rank test (P = .10).

5.5% (95% CI, 1.8-16.1). No statistically significant difference was observed for the cumulative incidence curves for irradiated and nonirradiated groups (log-rank test, P = .23).

To evaluate the role of age in CC occurrence, the PU-coated implants were stratified in two groups using the median age of patients (53 years) as the cut-off value. Fifty-nine breast implants corresponded to patients who were younger (27-52 years old), and 56 breast implants corresponded to patients who were older (53-76 years old). Seven of the 9 breasts with CC, which developed within 7 years, were in the younger group. The remaining 2 breasts with CC, which developed within 2 years, were in the older group (Figure 3). The cumulative incidence of CC at 9 years was 12.2% (95% CI, 6.0-23.9) in the younger group and 3.6% (95% CI, 0.9-13.5) in the older group. The difference between the 2 curves, as determined by the log-rank test, was not statistically significant (P = .10).

Additional epidemiologic analysis was performed to exclude confounding by RT in the association between age and CC. Even after adjustment of the Cox proportional hazards model for RT, the occurrence of CC appeared to be lower among older patients than younger ones (hazard ratio, 0.31; P = .15).

DISCUSSION

Breast augmentation with PU foam–coated implants is associated with a very low risk of CC.[3,5,19,21,22,24-26] In the current study, the 9-year incidence of CC after breast reconstruction with PU implants in nonirradiated breasts was 5.5% (median follow-up, 9 years), which coincides with the results of other investigators.[3,27-29] This rate of CC is among the lowest reported after 2-stage breast reconstruction with textured implants.[16] The results of other studies, in which textured breast implants were monitored for a similar duration, have indicated that a low rate of CC is not guaranteed with these implants. For example, the 10-year incidence of CC associated with Biocell textured implants (Inamed Aesthetics, Santa Barbara, CA) was 14.5% for patients who underwent primary reconstruction, presumably without RT.[30] The CC rate at 9 years for Siltex shaped implants (Mentor, Santa Barbara, CA) was 12.7% for a series of patients who received primary breast reconstruction without specified RT.[31] The CC incidence at 9 years for textured Sientra implants (Sientra, Inc, Santa Barbara, CA) under the same conditions was 14.4%.[32,33]

We found that the incidence of CC following 2-stage breast reconstruction with RT (10.7%; median follow-up, 9 years) reminded the encouraging CC rate for the group that did not receive RT (5.5%; median follow-up, 9 years) (Figure 2). Investigators worldwide have suggested that RT exponentially increases the risk of CC.[14,34-36] Rancati et al[23] recently described a very low incidence of CC after 1-step breast reconstruction with PU-coated implants; however, all 4 cases of Baker grade IV CC observed in that study corresponded to patients who underwent RT. Cordeiro et al[16] examined a large cohort of patients who underwent 2-stage breast reconstruction and found that the most common cause (33%) for implant replacement in the subgroup of patients with RT and textured implants was grade III or IV CC. This complication occurred in 46.6% of irradiated breasts (grade III, 39.7%; grade IV, 6.9%).[16]

In this retrospective analysis, we observed early onset of CC among patients who underwent 2-stage immediate breast reconstruction with adjuvant RT. Specifically, CC occurred within 3 years after breast implantation. In contrast, other investigators have shown that the incidence of CC after breast augmentation or reconstruction with textured or PU-coated implants increases as a function of time for 10 years or more postoperatively.[3,5,24,30,37]

Szycher and Siciliano[38] have noted that the protective effect of PU foam against CC is enduring, and many authors have confirmed the long-term efficacy and safety of PU foam–coated breast implants.[6,22,24,25] PU foam in the capsule degrades very slowly under the influence of inflammatory cell esterases.[39,40] Castel et al[24] noted macroscopic evidence of PU on the surface of implants that were explanted up to 5 years postoperatively. However, these authors performed histologic analyses and found that PU persisted in the capsule for 30 years of monitoring.[24] This observation of persistent microscopic PU and our finding of early onset of CC after 2-stage breast reconstruction with RT strengthen the hypothesis that PU-coated implants are more effective than noncoated implants in decreasing the incidence of CC.

We determined the cumulative incidence of CC in a cohort of women who underwent 2-stage breast reconstruction.

This study may have benefitted from a comparison group of women who received textured implants with or without RT. However, a retrospective comparison of 2 cohorts would have been highly susceptible to bias. We maintain that a descriptive long-term analysis of a cohort and its comparison with similar international cohorts was the optimal design for this study. Moreover, we previously performed a direct comparison between PU implants and textured implants.[20] A randomized controlled trial in which the CC risk associated with PU-coated implants is observed prospectively and compared directly with that of textured implants would provide more definitive results.

Grade II CC was not included in this study design because the international literature generally does not address this grade, even when the rate of CC is the primary objective of the study.[3,5,10,11,16,20,30-33] In addition, grade II CC usually is not painful and does not necessitate intervention. We attempted to account for additional risk factors for CC among patients who underwent 2-stage breast reconstruction (eg, body mass index; age). Patient age tended to influence long-term CC, with the younger group (aged 27-52 years) and the older group (aged 53-76 years) exhibiting 9-year CC incidences of 12.2% and 3.6%, respectively. This difference was not statistically significant, which may be attributed to the small sample size. However, statistical analyses of our data excluded RT as a confounding factor in this potential association. An effect of patient age has been observed in clinical practice for other types of fibrosis. For example, hypertrophic scars generally are more common in younger patients, presumably because younger patients are subject to more physical and hormonal changes.[14,41-43] Further investigation of this finding is warranted.

CONCLUSIONS

The safety of PU foam–coated implants has been demonstrated in clinical practice for more than 4 decades. Compared with textured implants, PU implants are associated with a lower rate of CC, which is the most common complication of breast reconstruction and a frequent reason for reoperation. This attribute of PU implants does not appear to diminish over time and is particularly attractive for patients who undergo RT. The results of this study confirm the low long-term incidence of CC with PU implants and support that these implants are an effective alternative to textured devices, which have failed to attain the benefits of the foam. We advocate recommending PU foam–coated implants as a first choice for patients who undergo 2-stage breast reconstruction with adjuvant RT.

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