A Step Forward Toward the Understanding of the Long-Term Pathogenesis of Double Capsule Formation in Macrotextured Implants: A Prospective Histological Analysis

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Abstract

Background: Although increasingly reported in the literature, most plastic surgeons cannot define the etiology of double capsules. Often an incidental finding at implant exchange, double capsules are frequently associated with macrotextured devices. Several mechanisms have been proposed, including at the forefront that shearing causes a delamination of the periprosthetic capsule into a double capsule.

Objectives: This study was designed to confirm the hypothesis that mechanical forces are involved in formation of double capsules by histological analysis.

Methods: A prospective analysis of consecutive implants with double capsules removed over 2 years was performed. Data collected at the time of surgery included Baker classification, reason for explant, implant manufacturer and style, and any presence of a seroma associated with the capsule. Specimens were sent for analysis by histology utilizing hematoxylin and eosin and alpha-smooth muscle actin staining techniques.

Results: Eight double capsules were collected for specimen analysis. All capsules demonstrated evidence of granulation tissue, alpha-smooth muscle actin positive myofibroblasts, and folds with embedded texture. Fibrosis surrounded weak areas with presence of layering and splitting, creating a potential space that is prone to separation. Tears and folds from granulomatous reaction are also present within the outer layer of the double capsule, which can only be explained by a mechanical shearing force as a pathogenic mechanism.

Conclusions: Understanding the pathogenesis of double capsules may allow plastic surgeons to refine their indications for macrotextured implants while providing guidance to patients on avoidance of activities that produce shear-forces. The findings support the hypothesis that shearing forces delaminate the capsule into 2 separate distinct capsules.

Level of Evidence: 5

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The double capsule phenomenon associated with breast implants, although reported in the literature for more than 20 years,[1,2] continues to be misunderstood by plastic surgeons. Despite several publications asserting its prevalence, there is a paucity of research investigating these complications. Recent estimates reported incidence rates varying from 2% to 13%,[3,4] a proportion that may increase with better recognition and reporting of the entity. Despite the clear connection in the literature between

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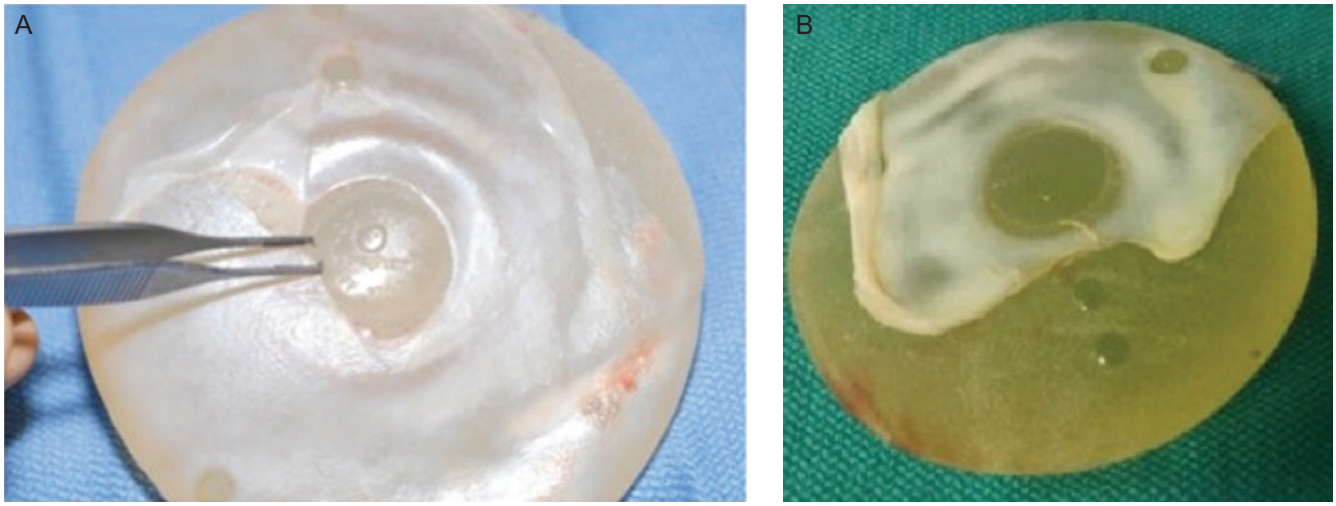

Figure 1. (A) Almost complete double capsule specimen attached to the implant. Note the absence of double capsule over the smooth central patch (patient #2, a 33-year-old woman). (B) Partial double capsule specimen, on the posterior surface only (patient #7, a 32-year-old woman).

macrotextured devices and double capsules, double capsules remain poorly described, perhaps because they are usually inconsequential clinical findings and discovered most often incidentally during implant exchange.

Double capsules consist of 2 distinct capsular layers divided by an intercapsular space.[5] The inner capsule adheres strongly to the surface of the implant, whereas the outer portion of the capsule is adherent to the surrounding soft tissue. Both surfaces facing towards the intercapsular space are white, shiny, and smooth in texture. Double capsules can be found as early as several months after implantation, and not all areas of the implant surface must be covered by an inner capsule. Often there are sections of the implant where a double capsule is and is not present. Partial double capsules have been described in the literature.[4,6]

The clinical relevance of double capsule formation is intertwined with the choice of breast implant and the degree to which the selected device affects the outcome of breast implant surgery. Based on the reported data on double capsules, very few surgeons dispute that macrotextured devices account for the majority of cases.[3,7] The purpose of macrotexturation resides in minimizing intracapsular movement of the implant by encouraging tissue ingrowth and anchoring the device to the chest wall and surrounding soft tissue. Because the outer interface of the outer capsule and the inner interface of the inner capsule are relatively immobile due to the "Velcro effect,"[8] the smooth interfaces of the intercapsular space allow for micro-movements and the occurrence of a dead space.

Understanding the etiology of double capsule formation is fundamental to understanding why one would or would not choose a macrotextured device for certain patients. The objective of this study was to confirm the proposed pathogenesis of mechanical shearing forces thought to be responsible for double capsule formation by analyzing histological specimens prospectively removed during revisional implant surgery. The hypothesis is that delamination of the capsule occurs due to micro-fractures occurring at multiple locations that merge over time to become a partial or complete double capsule.

METHODS

A prospective analysis was implemented on consecutive capsular specimens from breast implants requiring revision surgery form January 2015 to January 2017. Surgeries and specimen collection were performed by 2 surgeons from the United States and Canada. Both surgeons collected consecutive double capsule specimens encountered during revision procedures. Revision surgeries occurred in the context of capsular contracture of one or both breasts, size change requested by the patient, aging implant requiring replacement, late seroma formation, or suspected rupture of the device. The implant and its outer capsular layer wree either surgically dissected en-bloc, or the implant with its adherent double capsule was removed; the outer portion of the double capsule was removed via a complete capsulectomy (Figures 1 and 2). Specimens were placed in 10% neutral buffered formalin and shipped within 24 hours. All patients provided written consent for the donation of capsular tissue removed for diagnostic purposes. The study was performed under the guiding principles of the Helsinki declaration.

Implants included in this analysis were limited to Biocell macrotextured surfaces (Allergan, Irvine, CA) and included styles 153/110/115/ and 410 devices. Implants were removed 3 to 8 years after implantation.

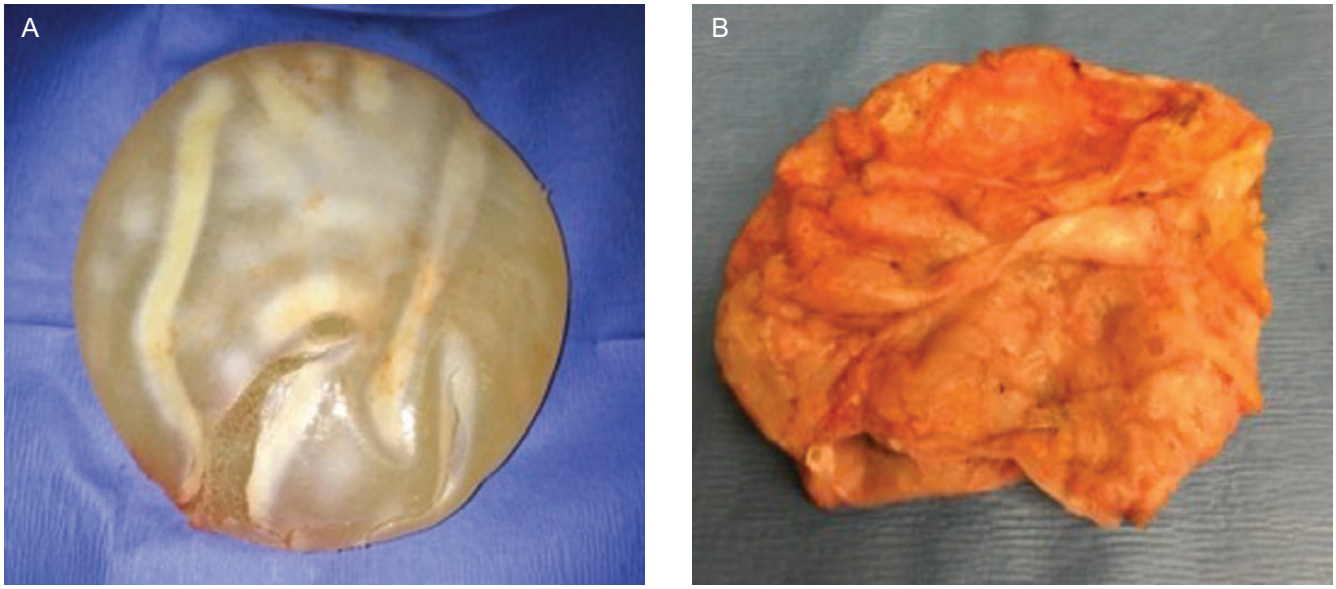

Figure 2. (A) Inner capsule adherent to a macrotextured device (patient #6, a 34-year-old woman). (B) Outer capsule removed during capsulectomy (patient #6).

Data collection at the time of surgery included the reason for surgical revision, the implant manufacturer with the style number, and the clinical capsular contracture grade according to the Baker score. The classification is defined as: grade I with a naturally appearing breast, grade II with minimal contracture wherein a person could tell a surgery was performed but without any associated symptoms, grade III with moderate contracture and firmness, and grade IV with severe contracture observed clinically and significant symptomatology.[9,10] Other clinical observation such as evidence of seromas, presence of unknown masses associated with the device/capsule, and evidence of rupture were also collected.

Collected specimens were sent for histological analysis to the Allergan Tissue Materials Science Group in Irvine, CA.[11] Histopathology was performed at 1 of 2 sites: Cancer Genetics, Inc. (Rutherford, NJ) or HistoTox Labs, Inc. (Boulder, CO). Following the collection of the capsule tissue samples, the samples were placed in 10% neutral buffered formalin fixative and sent directly to CGI or HistoTox where they were processed, sectioned, and stained. Sections of each tissue sample were stained with hematoxylin and eosin and alpha-smooth muscle actin (α-SMA) because cultured myofibroblasts are characterized by stress fibers, containing α-smooth muscle actin (α-SMA), and by supermature focal adhesions (FAs), which are larger than FAs of α-SMA–negative fibroblasts. The formation and stability of supermature FAs depends on a high α-SMA–mediated contractile activity of myofibroblast stress fibers.[11]

Slides were sent to the Tissue Materials laboratory for whole slide imaging using a NanoZoomer (Hamamatsu). Prior to sending the slides, a CGI or HistoTox pathologist reviewed the slides and provided a pathology report for each tissue sample that summarized the following: (1) a description of the basic capsule morphology; (2) a description of the inflammatory response, including a basic readout (mild, moderate, severe) and the type of cells present (giant cells, mast cells, plasma cells, etc.); and (3) a description of the α-SMA staining properties. Additional qualitative observations regarding capsule fiber alignment and presence of silicone within the capsule for each sample were made and reviewed.

RESULTS

Patients ranged in age from 32 to 70 years (mean, 41 years). A total of 8 double capsules were sent for histological evaluation (Table 1). All specimens demonstrated focal areas of granulation tissue with alpha-SMA + myofibroblasts due to repeated cycles of microtrauma (Figure 3). Furthermore, evidence of capsular folding with embedded implant silicone was found on all specimens (Figure 4). These were found in areas of subchronic healing process showing evidence of folding in chronic, healed, fibrosed capsules.

Interpretation of Histological Findings

Due to the granulomatous response to texture, a potential space or crack develops within the fibrosis, leading to a weak area characterized by layering and splitting (Figure 5). This delamination was observed at the crests

Table 1. Double Capsule Specimens Were Collected Over a Period of Two Years

Case no.	Surgeon	Texture	Implant style	Duration	Capsule grade	Indication for revision	Analysis
1	Glicksman	Biocell	410	6 years	I	Rotation	• H&E • Pathology
2	Glicksman	Biocell	410	5 years	II	Size change	• H&E • Alpha-smooth muscle actin
3	Khanna	Biocell	TSLP	N/A	III	Seroma	• H&E • Pathology • Alpha-smooth muscle actin • Gene expression
4	Glicksman	Biocell	115	8 years	III	Rupture capsular contracture	• H&E • Alpha-smooth muscle actin • Pathology • Gene expression
5	Khanna	Biocell	TSM	N/A	III	Capsular contracture	• H&E • Alpha-smooth muscle actin • Pathology
6	Glicksman	Biocell	153	7 years	II	R/O rupture	• H&E • Alpha-smooth muscle actin
7	Glicksman	Biocell	410	3 years	III	Capsular contracture	• H&E • Alpha-smooth muscle actin
8	Glicksman	Biocell	110	8 years	I	Size change	• H&E • Alpha-smooth muscle actin

H&E, hematoxylin and eosin; R/O, rule out; TSLP, textured shell low projection; TSM, textured shell moderate.
Indications for revisional surgery included capsular contracture, rotation, size change, ruptured implant, and seroma.

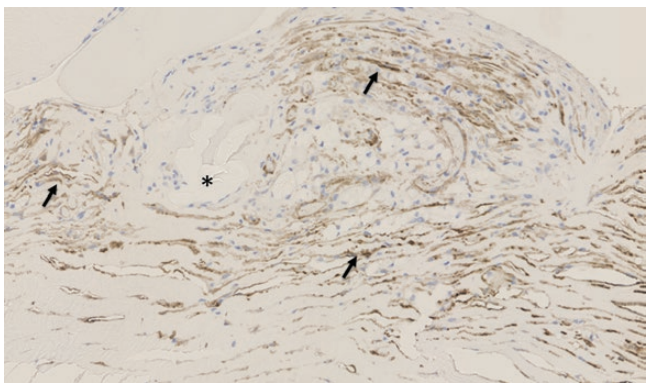

Figure 3. Inner capsule. Focal areas of active granulation tissue with alpha-SMA positive myofibroblasts (brown stain, black arrows). Note embedded silicone texture adjacent to granulation tissue (*).

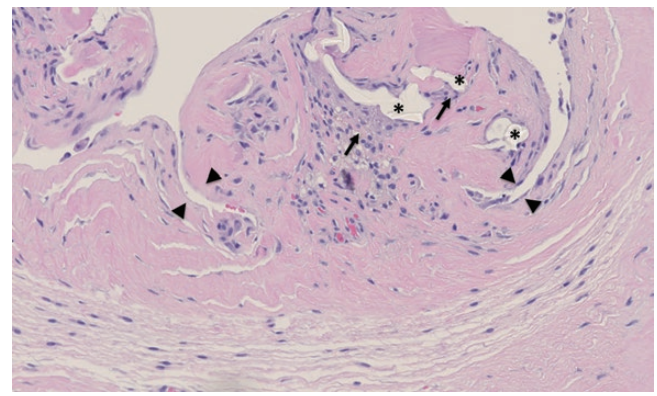

Figure 4. Outer capsule. Evidence of capsular folding with potential space (arrowheads) and embedded silicone texture (*) surrounded by granulation tissue (arrows).

of the texturization. The inner layers of the double capsule demonstrated folds with encompassed silicone texture such that the potential space created by it is prone to tears and delamination (Figure 6).

The occurrence of tears and folds with granulomatous reaction was also visible on the outer surface of the outer layer in all specimens, which was in contact with the patients' muscle and soft tissue. Histological slides demonstrated that silicone texture migrated through a significant layer of fibrosis because of folding of the capsule (Figure 7). There was also evidence of subchronic healing within the folding of the fibrosed outer capsule as the capsules "mature" over time and "healing" occurs. The occurrence of synovial metaplasia with an amyloid-like surface

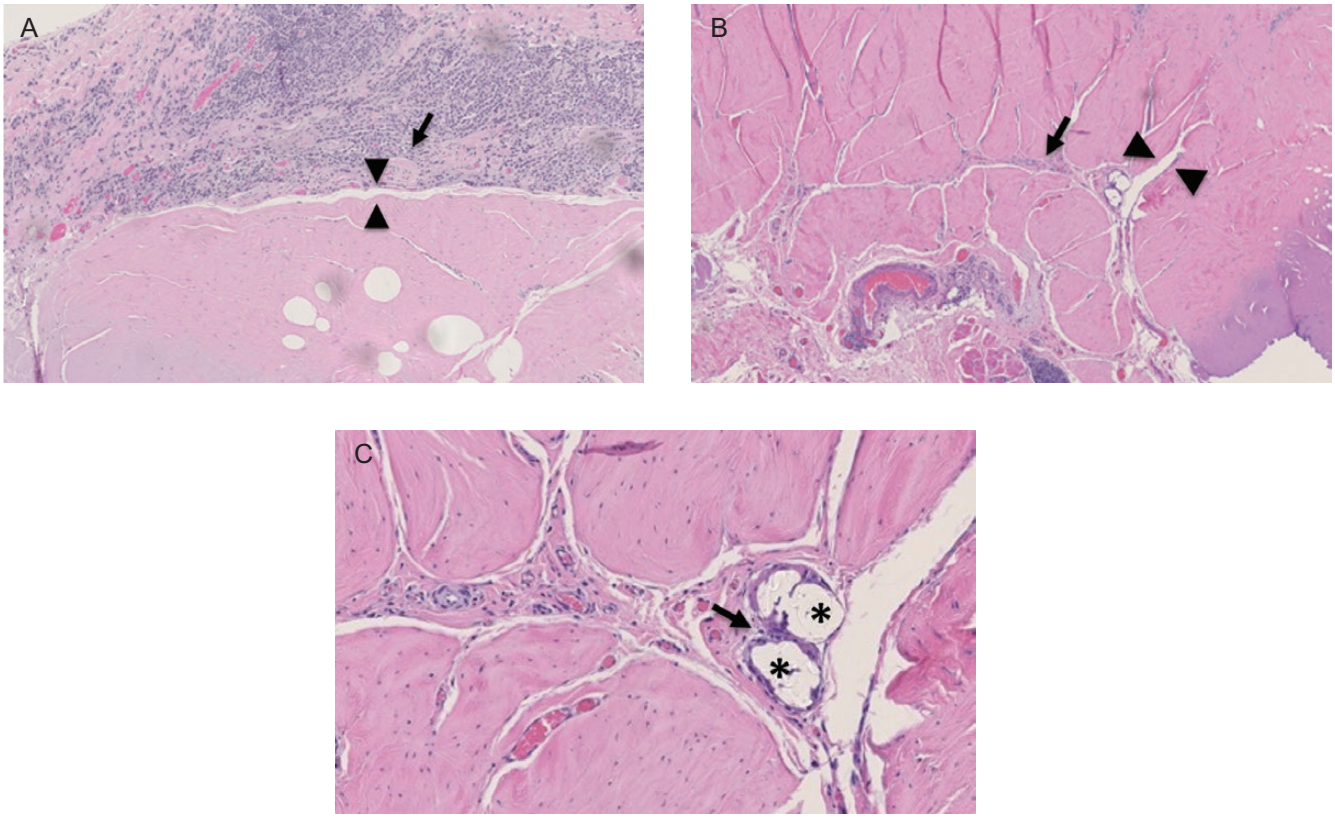

Figure 5. (A) Outer capsule (patient #3, a 39-year-old woman). (B) Outer capsule (patient #6, a 34-year-old woman). Potential spaces and cracks develop within the fibrosis leading to weak areas characterized by layering and splitting (arrow heads). (C) Outer capsule (patient #6). Granulomatous response (arrows) was characteristic of a foreign body response and surrounded silicone texture (*).

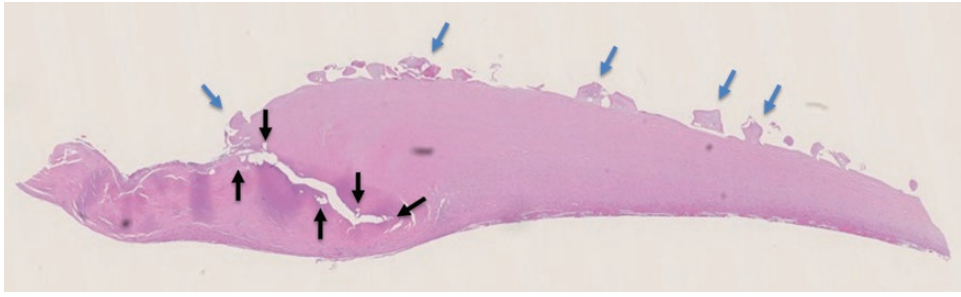

Figure 6. Inner capsule (patient #8, a 47-year-old woman). Fold with embedded texture at margins (black arrows) has created "potential space" (crack or fissure) within the fibrotic tissue composing the capsule. This crack creates a weak area in the capsule that is prone to tears and delamination, thus reinitiating the cycle of healing. Blue arrows point to texture on the surface that interfaces with the implant. The opposite "smooth" side is the interior between layers of the double capsule.

was present on the oldest, complete double capsules and interestingly mimics that found on joint surfaces.

DISCUSSION

Macrotexturing of breast implants serves the purpose of anchoring the device to the surrounding soft tissue and chest wall while minimizing movements that could displace the implant.[12] In this study, only one type of implant texturization was analyzed: Allergan's macrotextured Biocell implant.[3,13] These devices are created by a process described as the "lost salt technique." By pressing the implant's undried silicone sheet onto a layer of fine salt and removing it by rinsing the surface with water, an irregular open pore, textured surface is forged that has an average density of 3.1 pores/mm^2 and an average pore

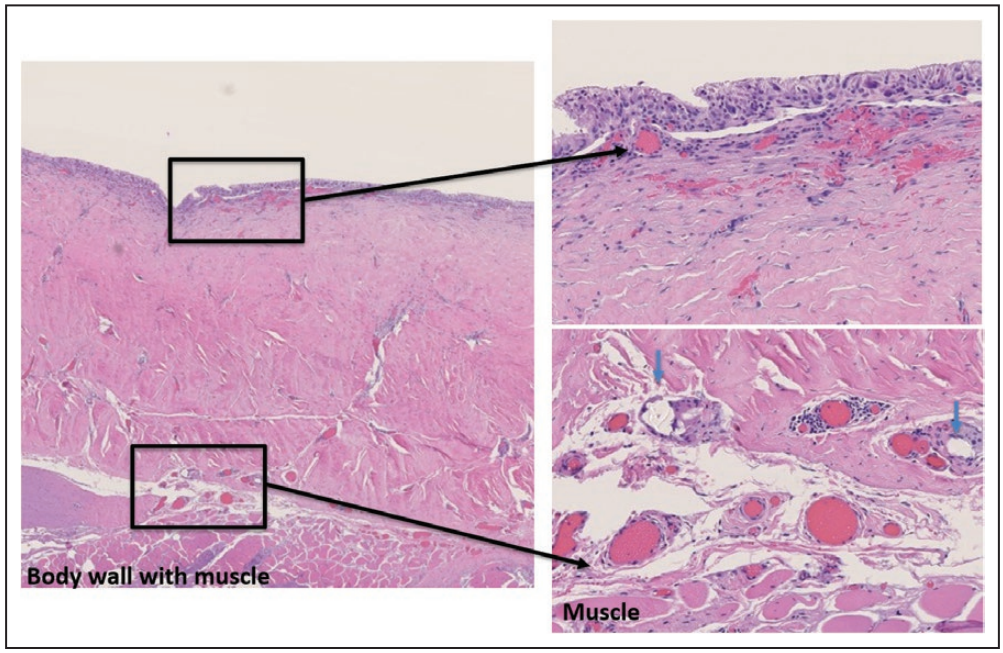

Figure 7. (Left) Outer capsule (patient #5, a 70-year-old woman). (Upper right) Intercapsular surface with synovial metaplasia, and evidence of recent hemorrhage. (Lower right) Granulomas surrounding silicone texture embedded within a deeper level in contact with the patient's body wall (muscle tissue from body wall).

size of 289 µm.[14-16] Fibroblasts from surrounding tissues (average size, 25 µm) have sufficient potential for cellular ingrowth into these pores, thereby creating the anchoring characteristic of macro-textured implants.

The occurrence of double capsules has been predominantly associated with textured implants such as Biocell. In 2011, Hall-Findley reported 14 cases of double capsules occurring exclusively in 105 macrotextured Biocell implants (13.3% incidence rate).[3] The author's hypothesis to explain this phenomenon seemed to be a mechanical one in which separation of the initial capsule from the implant's textured surface created shear forces between 2 rough forces. In this space, it would be theorized that a seroma could form containing cells that could seed onto another surface, thereby creating the double capsule.[3,17] Other theories for the etiology of double capsules have postulated that the inner surface of the initial capsule might undergo synovial metaplasia due to sliding forces of implant movement within the cavity.[18] This inner surface becomes prone to exudation, late seromas, and chronic infections, which in turn could be potentially responsible for the secondary formation of the inner layer of the double capsule.

If exudates and late seromas were responsible for the formation of the inner capsule, one would expect to see much higher numbers of reported double capsules. In addition, one would also expect to find traces of bacterial proliferation and biofilm in the intercapsular space to the same extent that can be found between the inner capsule and the prosthesis.[19] This study did not specifically look for bacteria within the capsule specimens. In a previous study, however, Giot et al refuted these theories when it was found that the intercapsular space did not contain the same bacterial load and biofilm as that seen at the prosthesis-inner capsule interface, which indicates that these potential spaces did not share the same initial fluid.[7] It was hypothesized at the time that mechanical delamination within the capsule was responsible for the formation of the double capsule phenomenon. This hypothesis was corroborated by Danino et al in a study where 20 specimens of double capsules demonstrated delamination of the inner capsule in proximity to peaks of macrotextured surfaces and significant levels of biofilm at the interface of prosthesis and inner capsules as seen under scanning electron microscopy.[20] This study expands on the histological analysis performed prior and supports the idea that focal areas of granulation can be found within every specimen of capsule analyzed and that evidence of folding in fibrosed, subchronically healed capsular tissue was found throughout the regions of double capsule formation.

In a recent paper by Efanov et al,[13] delamination of capsular tissue found in double capsules was reported in 10 patients with incidental finding of this phenomenon. These micro-fractures were present in most of the specimens studied on the lateral portion of the breast, whereas none were found in the upper dome of the breast pocket. Shear mechanical forces were thought to explain the delamination found in this portion of the breast pocket, an

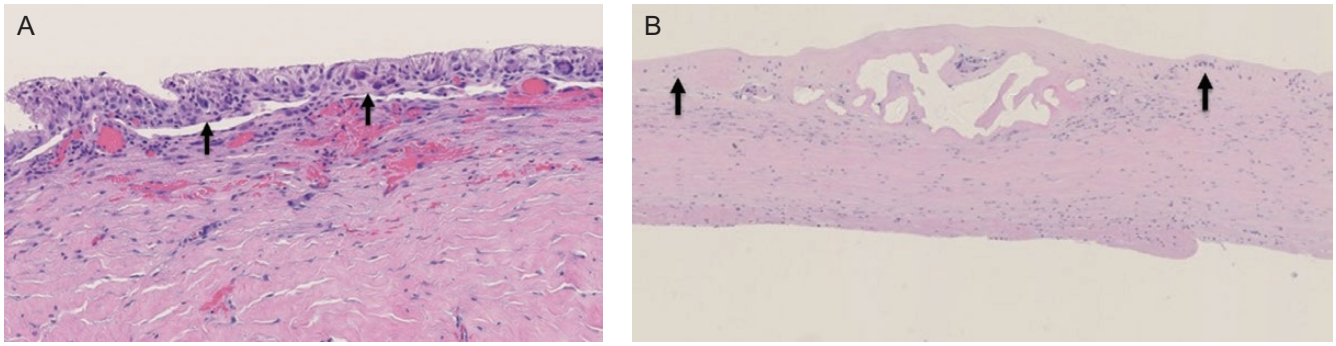

Figure 8. (A) Synovial metaplasia = synovial epithelium on interior surface between layers of double capsule with beginning accumulation of homogenous amyloid like acellular material within cells (black arrows) (G-outer). (B) Similar area where synovial membrane has become completely homogenized. Black arrows show areas where nuclei of synovial like cells are still recognizable (G-inner).

area that is firmly attached via the "Velcro effect" to the chest wall on one side and the soft tissues responding to gravity on the other side. Furthermore, delamination might be potentiated by biofilm formation around macrotextured implants. Although not measured with our methodological design, previous studies demonstrated higher bacteria load and biofilm formation at prosthetic interfaces rather than inter-capsular spaces.[20,21] It was hypothesized that an immune reaction to the bacterial expression might lead to weakening of capsule, which potentiates delamination and formation of double capsules. Whether weakening of the capsule secondary to bacterial proliferation is present or not, what is observable is a clear delamination process in all 8 specimens reported in this study, which supports the mechanical shearing hypothesis.

In our opinion, the repeated cycles of microtrauma from mechanical shear stress creates tears and folds within the capsular tissues, which in turn could explain the occurrence of silicone texture embedded within the connective tissue matrix of the capsule. There was evidence of silicone in most of the capsules, especially the inner capsule. It is important to note that it could not be determined whether they were silicone particles that broke off the implant during insertion, or silicone from the actual texture where the tissue was once integrated; when the capsule was dislodged from the implant surface, it took part of the texture with it. Around this detached texture, a process of healing and fibrosis is initiated along with a granulomatous response visible on histological slides presented in this study. This chain of events might explain why granulomas occurring in reaction to fragments of silicone encapsulation are found on the outer layer of the outer capsule of double capsules. This phenomenon of granulomatous reaction resembles what has been previously described in the literature with silicone injections.[22,23]

Furthermore, the granulomatous process creates a potential space with layering and splitting of the fibrosis within the connective tissue matrix of the capsule, which results in weak areas found throughout the specimens. These areas are subjected to instability and movement, which further potentiates the healing and fibrosis and eventually leads to areas of synovial metaplasia, as demonstrated by the extracellular material resembling an amyloid-like surface (Figure 8). The metaplasia could explain the production of fluid within the intercapsular space of double capsules, which in turn could result in additional tears and folds, thereby repeating the cycle of this proposed pathogenesis (Figure 9).

Some limitations of this study need to be addressed. First, the total number of cases with double capsules collected for analysis remains small. However, this remains a pilot study and despite a low prevalence of this phenomenon, reporting of double capsule formation has increased and it can be expected that further specimens will be collected for analysis. This study is a step forward toward an understanding of the possible pathogenesis of double capsules. Second, only Biocell macrotextured implants were included in this study design. An interesting addition to this study would be to design a prospective comparison of double capsules coming from different types of textured implants, such as Biocell compared with Siltex and Sientra textured devices. Third, the analysis was performed on cases of revision surgery for capsular contracture, aging implant, or implant rupture. The extent of impact that each of these processes can have on double capsule formation remains to be elucidated. Fourth, although delamination was found in the specimens analyzed in this study, it is impossible to prove that it will evolve into complete separation. It is nonetheless an association that is the best plausible explanation for the double capsule phenomenon. Finally, harvesting of the inner and outer capsules was sometimes performed separately rather than as a monobloc including both. Although not affecting the results found in this histological analysis, it would be interesting to investigate in the future whether the inner capsule reflects a similar delamination process as the outer capsule

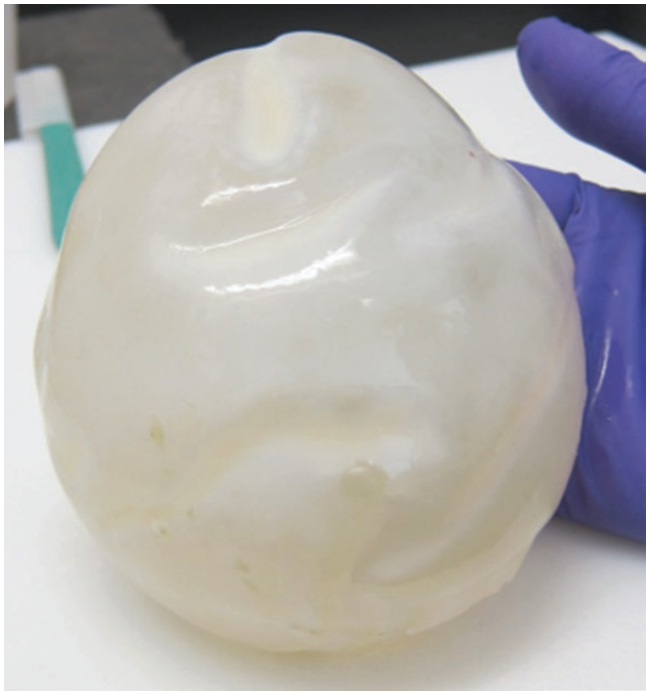

Figure 9. Implant removed at 5 years (patient #1, a 40-year-old woman). Mature, complete double capsule with amyloid appearance.

that is adjacent. We hypothesize that it would not be the case because the smooth surfaces of the intercapsular space prevent further shearing forces of the inner capsule.

CONCLUSIONS

In clinical practice, the significance of double capsules ranges from those that are barely detectable to both the surgeon and the patient, to more symptomatic, firm, mobile, and palpable double capsules. When clinically detectable, double capsules may alter the feel of a soft, textured gel implant to that of an overfilled smooth, saline device. This study corroborates the hypothesis that repeated shearing forces cause micro-trauma to the implant capsule interface surrounding a textured device. Further, this may not necessarily be a one-time event, and the development of a complete double capsule more likely occurs slowly over many years. The long-term histological evidence presented in this study also supports previously published concerns about the avoidance of shearing type activities in the early postoperative period for patients with macrotextured devices.[24] Continuous activities that produce shearing forces and micro-tears may lead to double capsule formation. Patient selection and education should include a discussion on the slight but possible potential for trauma-induced double capsules and should be part of the decision-making process when selecting smooth or textured devices.

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Disclosures

Dr Glicksman is an advisor and clinical investigator for Tepha (Galatea Surgical, Lexington, MA), an advisor for the Allergan Innovative Council (Allergan, Irvine, CA), and medical director for the Motiva US Clinical Trial (Establishment Labs, Alajuela, Costa Rica). Dr Danino is a consultant and speaker for Allergan and a consultant for Johnson & Johnson. The other authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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REFERENCES

1. Pandya AN, Dickson MG. Capsule within a capsule: an unusual entity. *Br J Plast Surg.* 2002;55(5):455-456.
2. Colville RJ, McLean NR, Cross PA. True double capsules in oil-based (Trilucent) breast implants. *Br J Plast Surg.* 2002;55(3):270-271.
3. Hall-Findlay EJ. Breast implant complication review: double capsules and late seromas. *Plast Reconstr Surg.* 2011;127(1):56-66.
4. Robinson HN. Breast implant complication review: double capsules and late seromas. *Plast Reconstr Surg.* 2011;128(3):818; author reply 818-818; author reply 819.
5. Maxwell GP, Brown MH, Oefelein MG, Kaplan HM, Hedén P. Clinical considerations regarding the risks and benefits of textured surface implants and double capsule. *Plast Reconstr Surg.* 2011;128(2):593-595.
6. Paek LS, Giot JP, Tétreault-Paquin JO, St-Jacques S, Nelea M, Danino MA. The impact of postoperative expansion initiation timing on breast expander capsular characteristics: a prospective combined clinical and scanning electron microscopy study. *Plast Reconstr Surg.* 2015;135(4):967-974.
7. Giot JP, Paek LS, Nizard N, et al. The double capsules in macro-textured breast implants. *Biomaterials.* 2015;67:65-72.
8. Danino A, Rocher F, Blanchet-Bardon C, Revol M, Servant JM. [A scanning electron microscopy study of the surface of porous-textured breast implants and their capsules. Description of the "velcro" effect of porous-textured breast prostheses]. *Ann Chir Plast Esthet.* 2001;46(1):23-30.

9. Spear SL, Baker JL Jr. Classification of capsular contracture after prosthetic breast reconstruction. *Plast Reconstr Surg.* 1995;96(5):1119-23; discussion 1124.
10. Headon H, Kasem A, Mokbel K. Capsular contracture after breast augmentation: an update for clinical practice. *Arch Plast Surg.* 2015;42(5):532-543.
11. Collis N, Coleman D, Foo IT, Sharpe DT. Ten-year review of a prospective randomized controlled trial of textured versus smooth subglandular silicone gel breast implants. *Plast Reconstr Surg.* 2000;106(4):786-791.
12. Hinz B, Dugina V, Ballestrem C, Wehrle-Haller B, Chaponnier C. Alpha-smooth muscle actin is crucial for focal adhesion maturation in myofibroblasts. *Mol Biol Cell.* 2003;14(6):2508-2519.
13. Efanov JI, Giot JP, Fernandez J, Danino MA. Breast-implant texturing associated with delamination of capsular layers: a histological analysis of the double capsule phenomenon. *Ann Chir Plast Esthet.* 2017;62(3):196-201.
14. Spear SL, Elmaraghy M, Hess C. Textured-surface saline-filled silicone breast implants for augmentation mammaplasty. *Plast Reconstr Surg*. 2000;105(4):1542-1552.
15. Barr S, Hill E, Bayat A. Current implant surface technology: an examination of their nanostructure and their influence on fibroblast alignment and biocompatibility. *Eplasty.* 2009;9:e22.
16. Mathur AB, ed. *Nanotechnology in Cancer*. Amsterdam, Netherlands: Elsevier; 2017.
17. Toscani M, Rizzo MI, Spinelli G, et al. Breast implant complication: calcifications in the double capsule. *Plast Reconstr Surg.* 2013;131(3):462e-464e.
18. Pinchuk V, Tymofii O. Seroma as a late complication after breast augmentation. *Aesthetic Plast Surg.* 2011;35(3):303-314.
19. Adams WP Jr, Culbertson EJ, Deva AK, et al. Macrotextured breast implants with defined steps to minimize bacterial contamination around the device: experience in 42,000 implants. *Plast Reconstr Surg.* 2017;140(3):427-431.
20. Danino AM, Giot JP, Nizard N, El-Diwany M, Paek LS, Nelea M. Delamination is a major etiologic factor of double capsules around textured implants. *Plast Reconstr Surg*. 2015;136(4S):84-85
21. Danino MA, Nizard N, Paek LS, Govshievich A, Giot JP. do bacteria and biofilm play a role in double-capsule formation around macrotextured implants? *Plast Reconstr Surg.* 2017;140(5):878-883.
22. Carpaneda CA. Inflammatory reaction and capsular contracture around smooth silicone implants. *Aesthetic Plast Surg.* 1997;21(2):110-114.
23. Ellis LZ, Cohen JL, High W. Granulomatous reaction to silicone injection. *J Clin Aesthet Dermatol.* 2012;5(7):44-47.
24. Maxwell GP, Scheflan M, Spear S, Nava MB, Hedén P. Benefits and limitations of macrotextured breast implants and consensus recommendations for optimizing their effectiveness. *Aesthet Surg J.* 2014;34(6):876-881.