SmoothSilk®/SilkSurface®
Recent Publications & Clinical Data

December 2018

Motiva® implants

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ISO 14607:2018

INTERNATIONAL STANDARD

ISO 14607

Third edition
2018-04

Non-active surgical implants — Mammary implants — Particular requirements

Implants chirurgicaux non actifs — Implants mammaires — Exigences particulières

H.6 Expression of results

The obtained data is meant to generate information to improve knowledge on the correlation of texture characteristics, performance and safety.

Based on the average roughness measurement on the finished device, the surface can be described by the following:

— smooth: less than 10 µm;

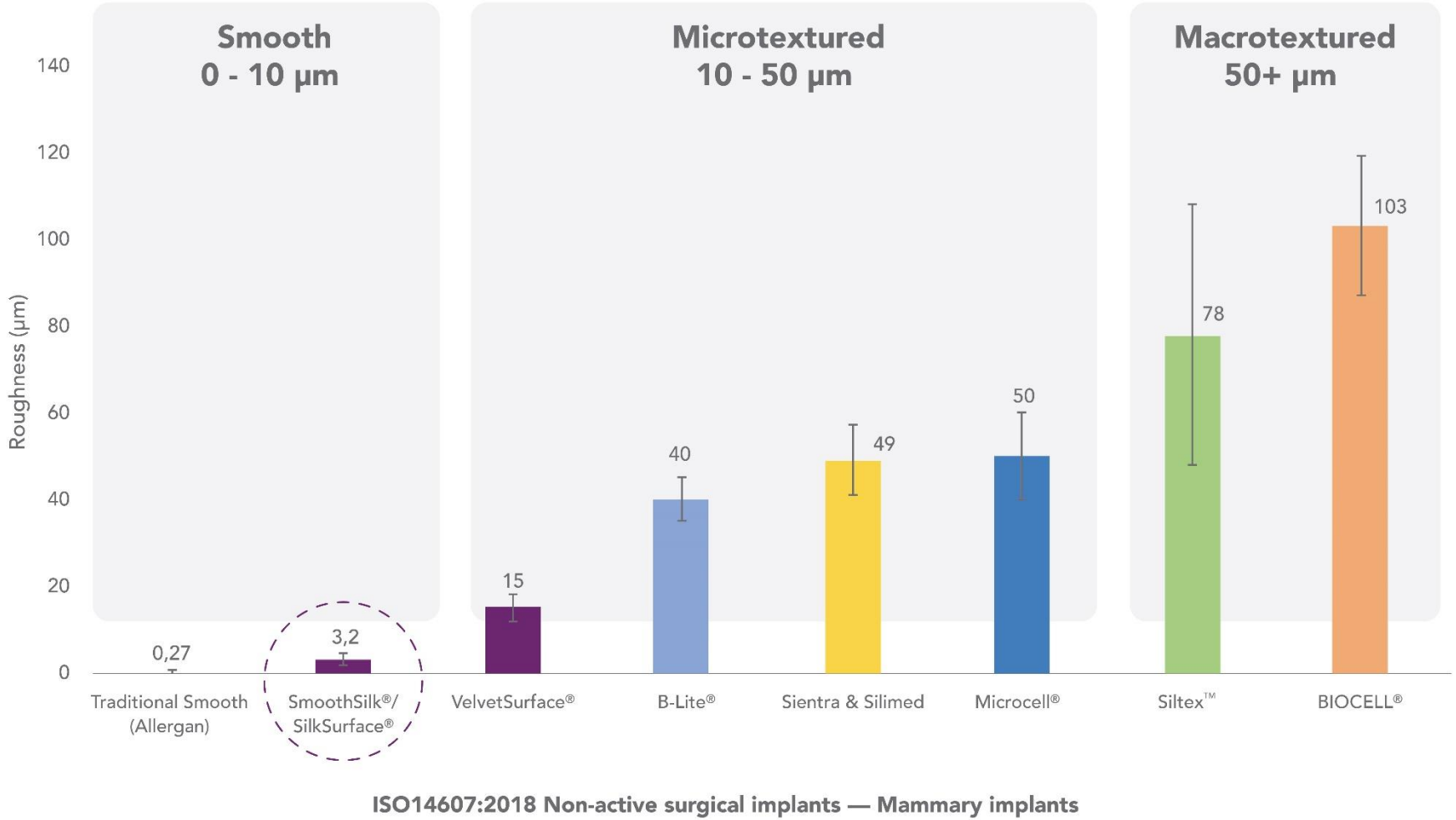
— microtextured: from 10 µm to 50 µm; and

— macrotextured: over 50 µm.

NOTE The data resulting from the test at this point in time cannot be related to the performance or safety of the device, but enough data points should be collected to have the ability to study such relation.

1. ISO 14607:2018. Non-active surgical implants – Mammary implants particular requirements. Geneva, Switzerland: International Organization for Standardization.

International Standards Organization Surface Categorization ISO 14607:2018



Note: TS-17-026.R; TS-17-029.R; Jones et al.(2018) Plast Reconstr Surg. 142:837-849; Atlan et al.(2018) Journal of the Mechanical Behavior of Biomedical Materials. 88:377-385; James et al. (2018) Aesth Plast Surg. Doi:10.1007/s00266-018-1234-7

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Kyle et al (Mentor publication) – optimal cell response

Biomaterials 52 (2015) 88–102

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Biomaterials

journal homepage: www.elsevier.com/locate/biomaterials

Development and functional evaluation of biomimetic silicone surfaces with hierarchical micro/nano-topographical features demonstrates favourable *in vitro* foreign body response of breast-derived fibroblasts

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Biomimetic topography
Micro and nano patterning
Cell-implant interface
Acellular dermal matrix (ADM)
Silicone breast implant
Capsular contracture

ABSTRACT

Reproducing extracellular matrix topographical cues, such as those present within acellular dermal matrix (ADM), in synthetic implant surfaces, may augment cellular responses, independent of surface chemistry. This could lead to enhanced implant integration and performance while reducing complications. In this work, the hierarchical micro and nanoscale features of ADM were accurately and reproducibly replicated in polydimethylsiloxane (PDMS), using an innovative maskless 3D grayscale fabrication process not previously reported. Human breast derived fibroblasts (n = 5) were cultured on PDMS surfaces and compared to commercially available smooth and textured silicone implant surfaces, for up to one week. Cell attachment, proliferation and cytotoxicity, in addition to immunofluorescence staining, SEM imaging, qRT-PCR and cytokine array were performed. ADM PDMS surfaces promoted cell adhesion, proliferation and survival ($p < 0.05$), in addition to increased focal contact formation and spread fibroblast morphology when compared to commercially available implant surfaces. PCNA, vinculin and collagen 1 were up-regulated in fibroblasts on biomimetic surfaces while IL8, TNFα, TGFβ1 and HSP60 were down-regulated ($p < 0.05$). A reduced inflammatory cytokine response was also observed ($p < 0.05$). This study represents a novel approach to the development of functionalised biomimetic prosthetic implant surfaces which were demonstrated to significantly attenuate the acute *in vitro* foreign body reaction to silicone.

1. Introduction

Surgical implants provide a diverse variety of site-specific tissue replacements for a number of functions, which are available to the practising surgeon. Common examples in use today include breast implants, dental implants, nerve conduits, vascular implants and orthopaedic implants [1]. The increasing demand for synthetically engineered body implants is a result of an ageing population and the associated tissue degeneration and malignancy [2]. This trend will continue until tissue regeneration techniques utilising autologous mesenchymal stem cells to engineer tissue-specific replacements becomes perfected and available to routine clinical practice. The biomaterials industry is expected to be worth $58.1 billion in 2014 [3] as medical devices such as breast implants are being increasingly required, with 385,813 breast augmentations/reconstructions (72% silicone implants) performed in the United States alone in 2013, up 2% from 2012 to 32% from 2000 [4].

However, current commercially available silicone mammary implants are not without their complications. For instance, silicone mammary implant surfaces suffer from significant limitation due to the formation of a constrictive fibrotic capsule post-implantation, known as capsular contracture, which results in firmness, deformity and pain in addition to device failure [5]. Capsular contracture formation remains the most common complication associated with silicone mammary implants, with rates ranging between 14.8 and 20.5% [6].

The exact pathoetiology of breast implant surface-related capsular contracture formation remains unclear, however, there

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Design:

- A 3D silicone matrix replicating the micro and nanoscale features of ADM was created.
- Human dermal fibroblasts were cultured on the surface and cellular responses were compared to smooth and textured implant surfaces

Results:

- The microenvironment of the silicone ADM replica promoted cell adhesion, proliferation and survival.
- A reduced inflammatory cytokine response was also observed.

Conclusion:

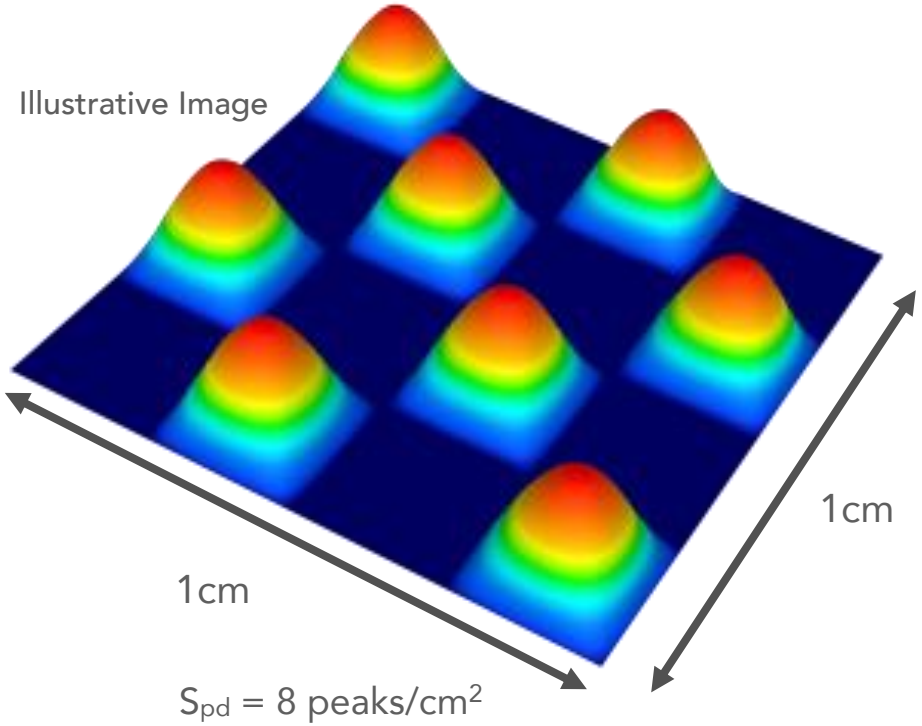
- The topography of a micro/nano surface (such as SmoothSilk®/SilkSurface®) possesses features "that a cell is able to sense, interact and respond to" which facilitates cell adaptation and may significantly reduce the acute foreign body reaction to silicone.

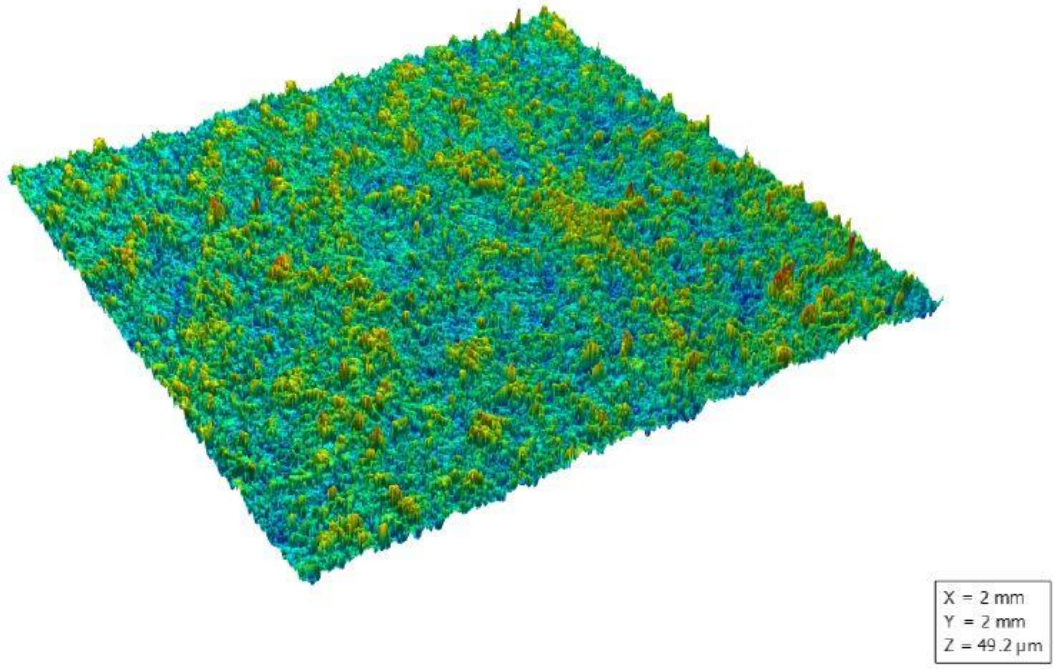
2. Kyle DJ, Oikonomou A, Bayat A. Development and functional evaluation of biomimetic silicone surfaces with hierarchical micro/nano-topographical features demonstrates favourable in vitro foreign body response of breast-derived fibroblasts. Biomaterials. June 2015;52:88-102. doi: 10.1016/j.biomaterials.2015.02.003

Smooth Surface but high density of peaks

Peaks that function as contact points for cells attachment during the immune response

SmoothSilk ® /SilkSurface®
Average Roughness: 3.2 µm ± 600 Nanometers
Density of Peaks: 25.820(S_{pd}) (Peaks/cm^2)

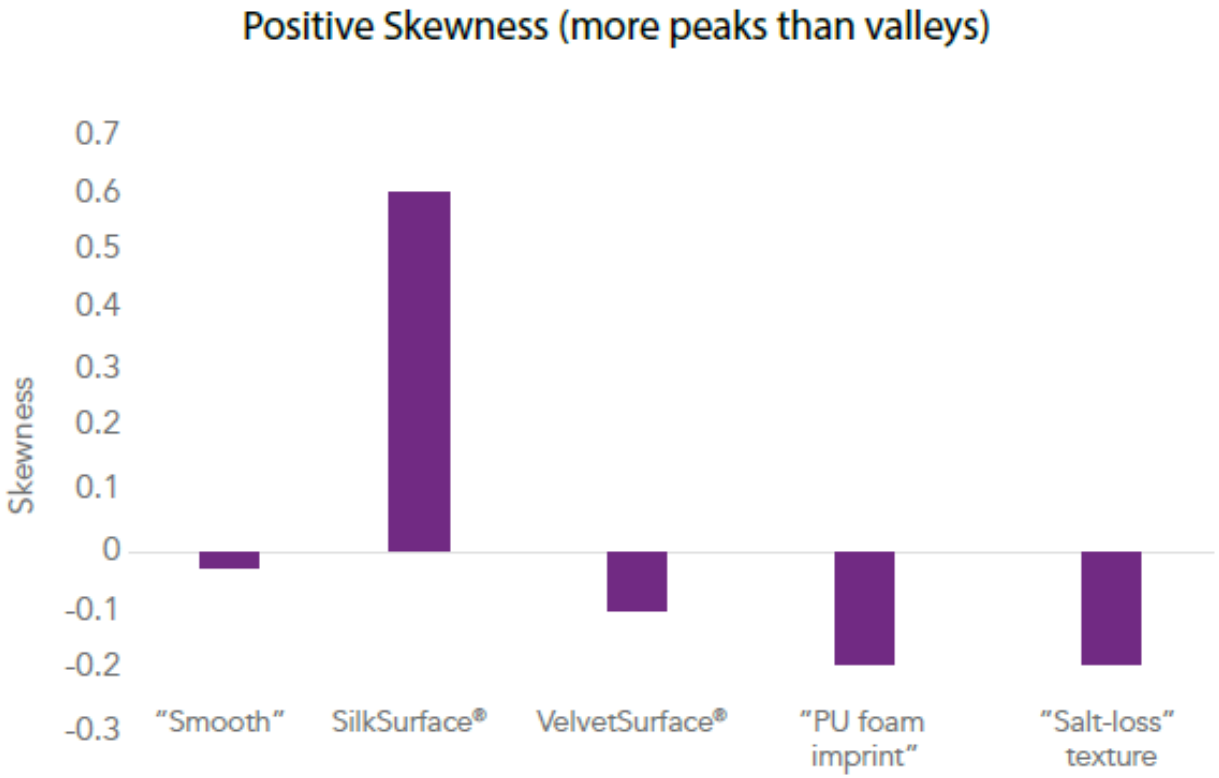


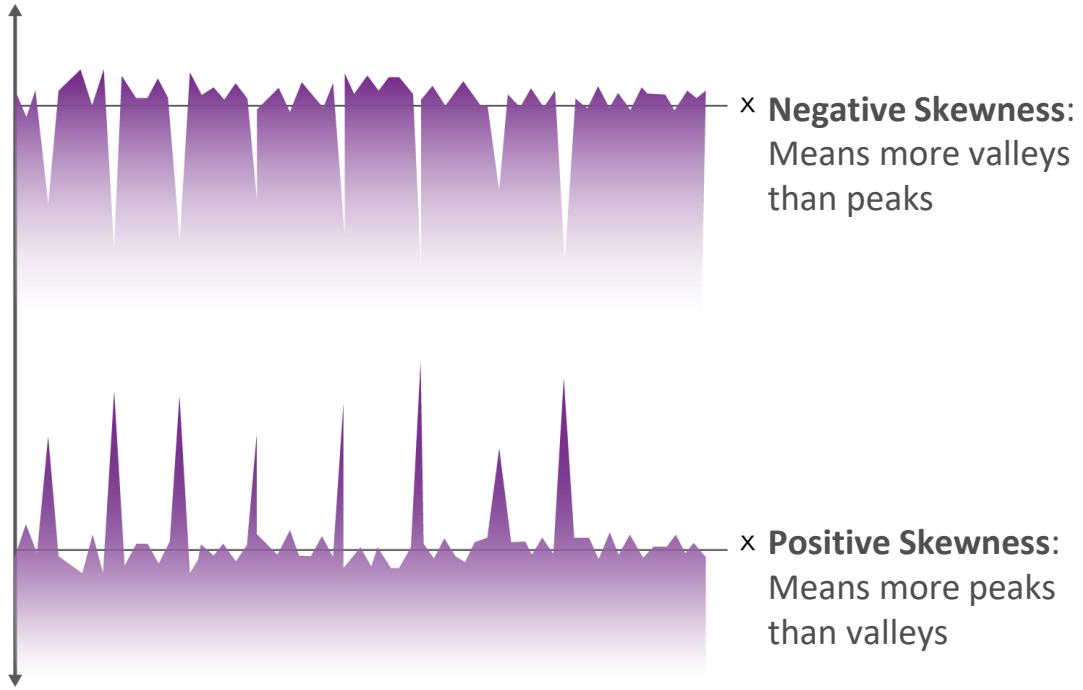


Establishment Labs. Data on File, TS-18-029 Motiva Implants Surface Characterization Oct 2018.

SmoothSilk®/SilkSurface® has more peaks than valleys

Peaks that function as contact points for cells attachment during the immune response





Skewness parameter comparison of different breast implants available in the market, measured with uSurf Mobile non-contact profilometer. Results Property of Establishment Labs (2017).

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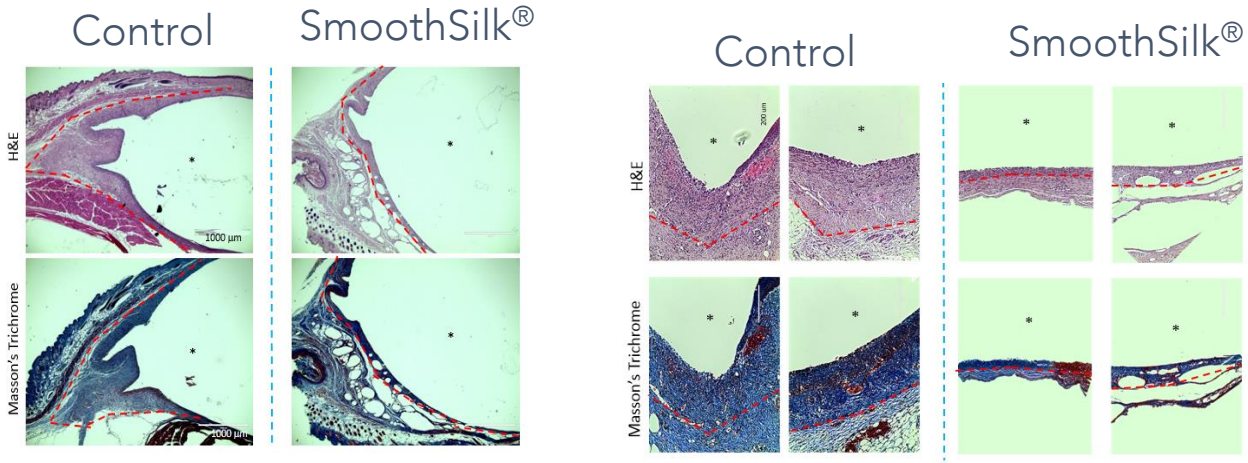
Research results presentation to Establishment Labs by Ph.D. Ardeshir Bayat Professor at the University of Manchester.

BL6 Mice Pilot at Langer Lab at MIT

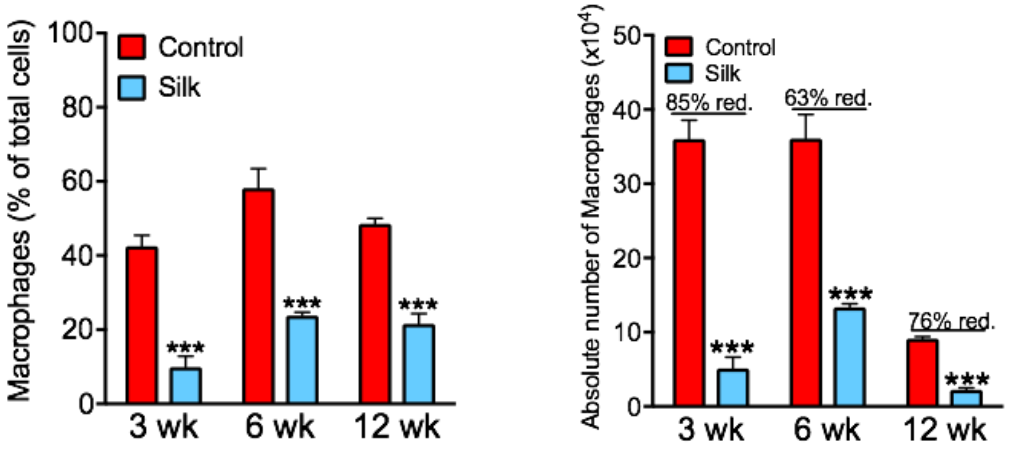
Low Inflammatory Response

SmoothSilk® /SilkSurface® ameliorates fibrosis in B6 mice



Histological analysis of the tissue capsule surrounding the SmoothSilk® /SilkSurface® and Smooth tiny implants with two different staining techniques.

Less Macrophages with SmoothSilk® /SilkSurface®



SmoothSilk® /SilkSurface® decreases fibrosis-dependent innate immune macrophages.

KOCH INSTITUTE for Integrative Cancer Research at MIT

Atlan et al (Allergan publication) – 12 implant surfaces evaluated

Journal of the Mechanical Behavior of Biomedical Materials 88 (2018) 377–385

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Journal of the Mechanical Behavior of Biomedical Materials

journal homepage: www.elsevier.com/locate/jmbbm

Breast implant surface texture impacts host tissue response

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ARTICLE INFO

Keywords:
Breast implants
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Scanning electron microscopy
Surface texture
Tissue adherence

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).

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

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

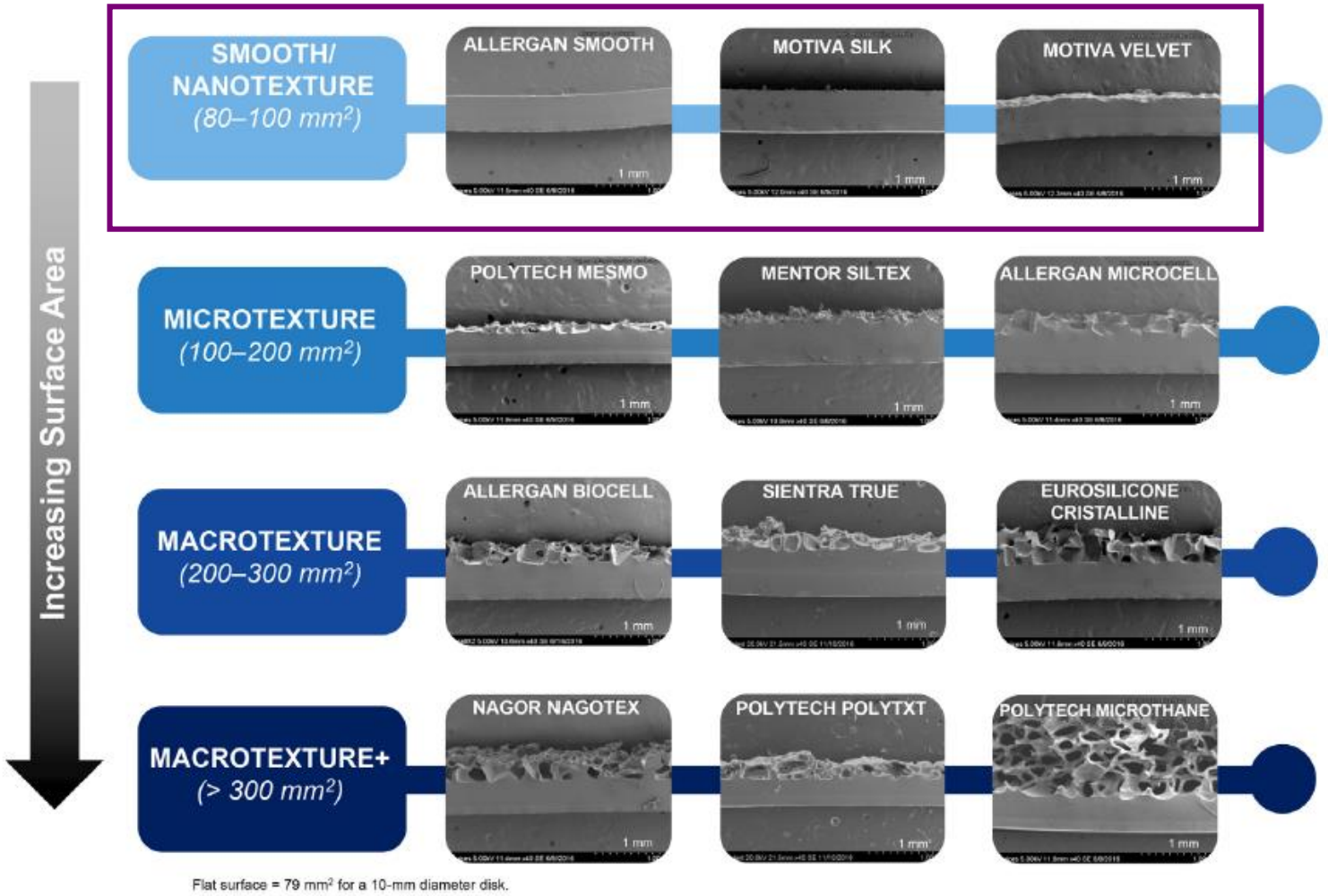
Implant texture	Mean (SD) texture surface area (mm^2)		Mean % greater texture surface area than flat surface[a]
	Anterior	Posterior	Anterior
Allergan Smooth[b]	85 (4)	85 (4)	9
Motiva SilkSurface	85 (1)	85 (2)	8
Motiva VelvetSurface	90 (2)	89 (2)	14
Polytech MESMOsensitive	115 (7)	119 (5)	47
Mentor Siltex	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.

4. Atlan et al. Breast implant surface texture impacts host tissue response. Journal of the Mechanical Behavior of Biomedical Materials. Dec 2018;88:377-385.doi:10.1016/j.jmbbm.2018.08.035

SilkSurface®/SmoothSilk® - same surface area as traditional smooth

Journal of the Mechanical Behavior of Biomedical Materials 88 (2018) 377–385



Flat surface = 79 mm² for a 10-mm diameter disk.

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.

4. Atlan et al. Breast implant surface texture impacts host tissue response. Journal of the Mechanical Behavior of Biomedical Materials. Dec 2018;88:377-385.doi:10.1016/j.jmbbm.2018.08.035

Atlan et al. – Tissue Adherence (peak force removal)

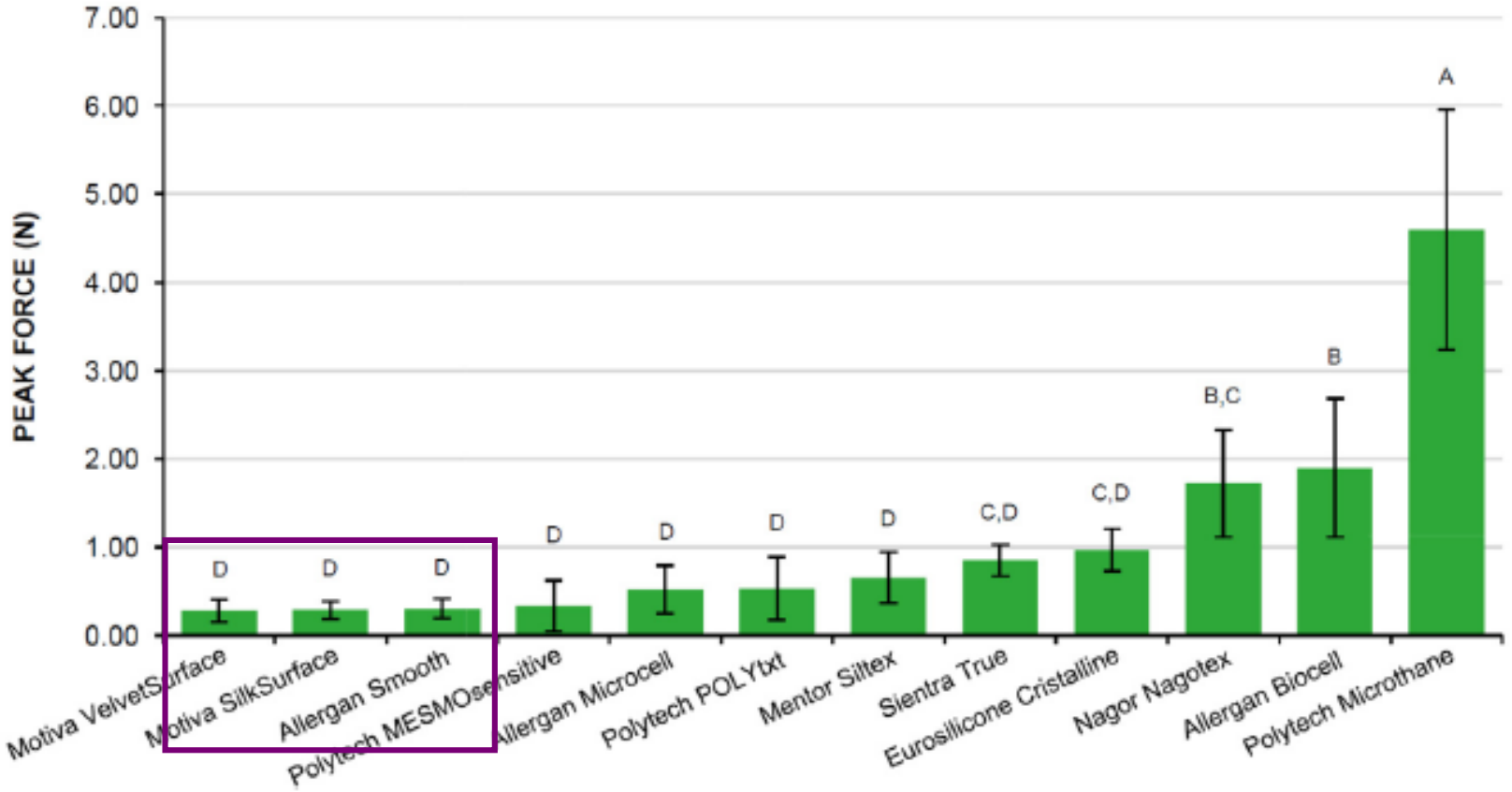
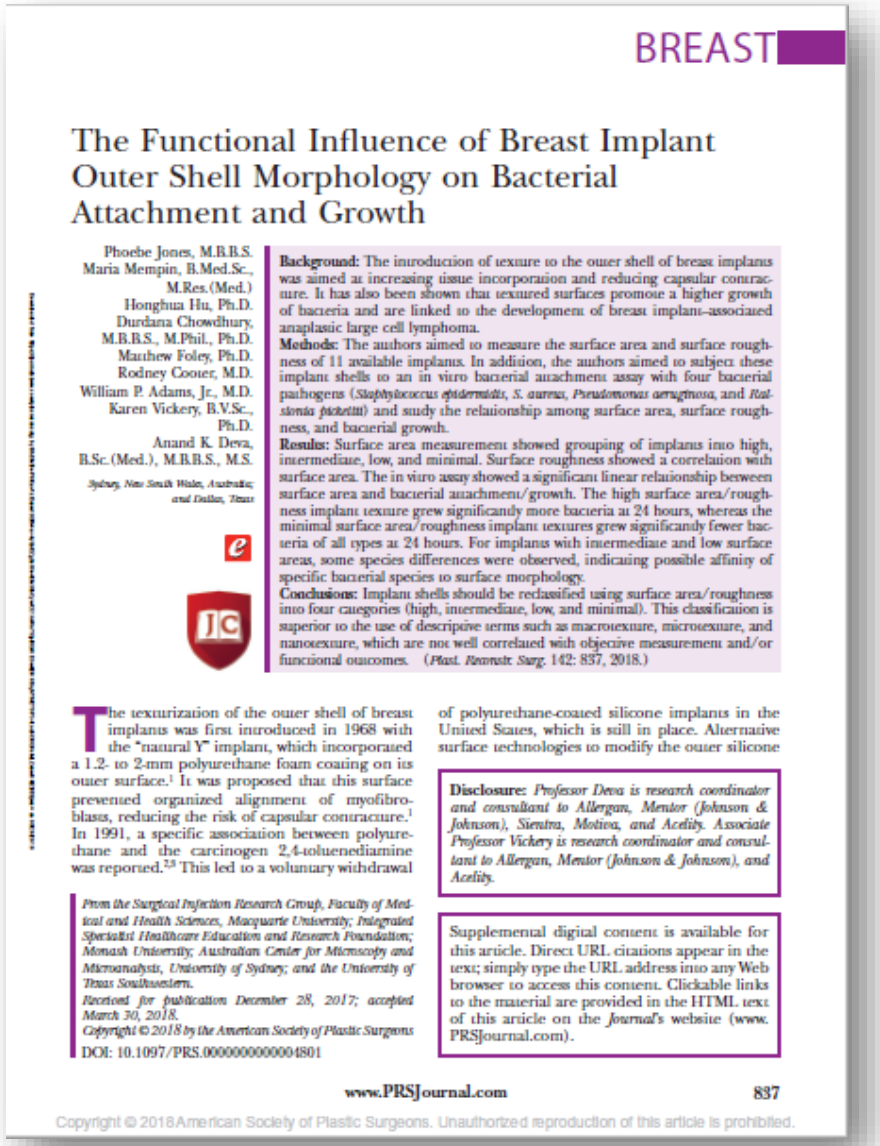


Fig. 6. Mean ± SD adherence force required to separate the tissue capsule from the implant surface assessed 6 weeks after implantation of the different surface textures in Sprague-Dawley rats. N = 8 for each texture. Means that do not share a letter are significantly different ($P \leq 0.05$).

4. Atlan et al. Breast implant surface texture impacts host tissue response. Journal of the Mechanical Behavior of Biomedical Materials. Dec 2018;88:377-385.doi:10.1016/j.jmbbm.2018.08.035

Jones et al – PRS Publication (Anand Deva)



BREAST

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

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Maria Mempin, B.Med.Sc., M.Res.(Med.)
Honghua Hu, Ph.D.
Durdana Chowdhury, M.B.B.S., M.Phil., Ph.D.
Matthew Foley, Ph.D.
Rodney Cooter, M.D.
William P. Adams, Jr., M.D.
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Anand K. Deva, B.Sc.(Med.), M.B.B.S., M.S.

Sydney, New South Wales, Australia; and Dallas, Texas

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

From the Surgical Infection Research Group, Faculty of Medical and Health Sciences, Macquarie University; Integrated Specialist Healthcare Education and Research Foundation; Monash University; Australian Center for Microscopy and Microanalysis, University of Sydney; and the University of Texas Southwestern.
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DOI: 10.1097/PRS.0000000000004801

Disclosure: *Professor Deva is research coordinator and consultant to Allergan, Mentor (Johnson & Johnson), Sientra, Motiva, and Acelity. Associate Professor Vickery is research coordinator and consultant to Allergan, Mentor (Johnson & Johnson), and Acelity.*

Supplemental digital content is available for this article. Direct URL citations appear in the text; simply type the URL address into any Web browser to access this content. Clickable links to the material are provided in the HTML text of this article on the Journal's website (www.PRSJournal.com).

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.

5. Jones et al. The functional influence of breast implant outer shell morphology on bacterial attachment and growth. Plast Reconstr Surg. 2018;142(4):837-849. doi: 10.1097/PRS.0000000000004801

SmoothSilk® & VelvetSurface® = Surface Type 1 (Minimal)

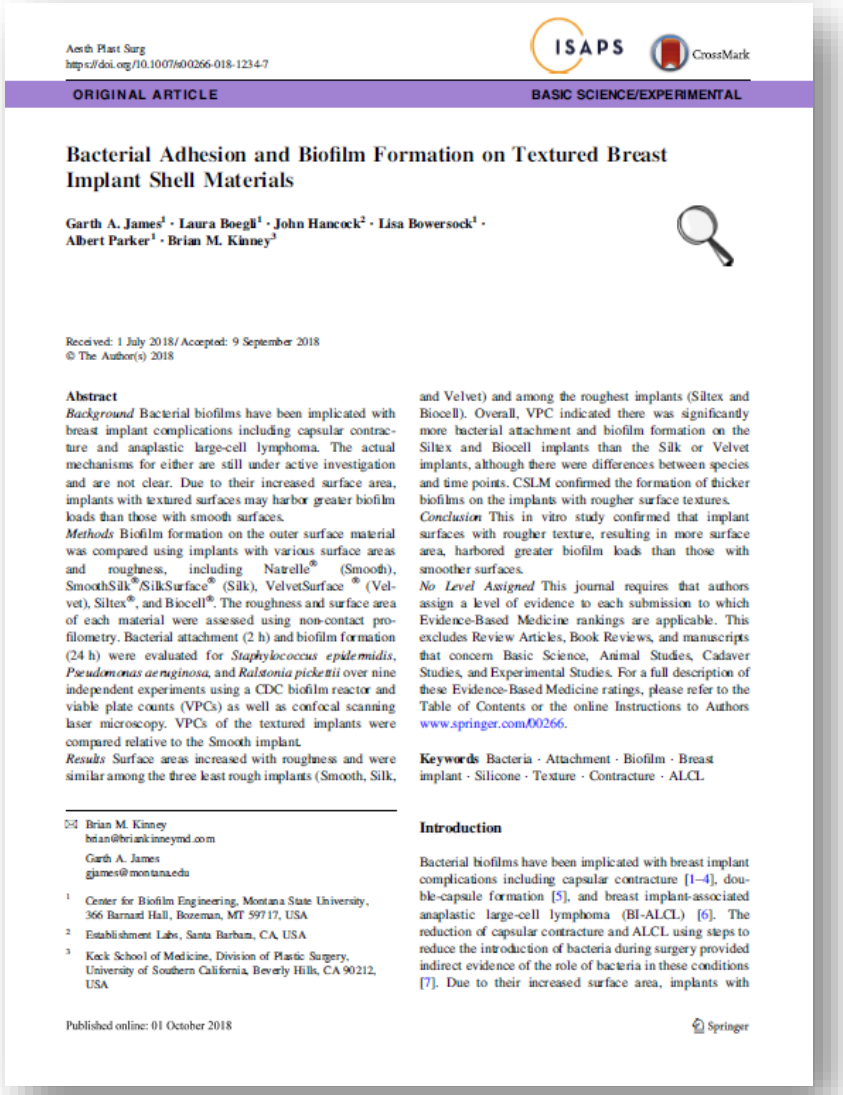
Process	Polyurethane foam	Salt Loss (Biocell/ Eurosilicone)	Vulcanisation	Salt Loss (Nagotex)	Imprinting	Smooth/Nano
Surface Area	High	Intermediate	Intermediate	Low	Low	Minimal
Roughness	High	Intermediate	Low	Low	Low	Minimal
SURFACE TYPE	4	3	3	2	2	1

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

Implant surfaces in the Type 1 (minimal) group classification (including SmoothSilk®/SilkSurface®) showed lower bacterial attachment and biofilm formation than implant surfaces in all other groups, due to the lower surface area / roughness.

5. Jones et al. The functional influence of breast implant outer shell morphology on bacterial attachment and growth. Plast Reconstr Surg. 2018;142(4):837-849. doi: 10.1097/PRS.0000000000004801

James et al. (ESTA Publication): Bacterial Adhesion & Biofilm Formation



Aesth Plast Surg
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ISAPS CrossMark

ORIGINAL ARTICLE BASIC SCIENCE/EXPERIMENTAL

Bacterial Adhesion and Biofilm Formation on Textured Breast Implant Shell Materials

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Received: 1 July 2018 / Accepted: 9 September 2018

Abstract

Background Bacterial biofilms have been implicated with breast implant complications including capsular contracture and anaplastic large-cell lymphoma. The actual mechanisms for either are still under active investigation and are not clear. Due to their increased surface area, implants with textured surfaces may harbor greater biofilm loads than those with smooth surfaces.

Methods Biofilm formation on the outer surface material was compared using implants with various surface areas and roughness, including Natrelle® (Smooth), SmoothSilk®/SilkSurface® (Silk), VelvetSurface ® (Velvet), Siltex®, and Biocell®. The roughness and surface area of each material were assessed using non-contact profilometry. Bacterial attachment (2 h) and biofilm formation (24 h) were evaluated for *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, and *Ralstonia pickettii* over nine independent experiments using a CDC biofilm reactor and viable plate counts (VPCs) as well as confocal scanning laser microscopy. VPCs of the textured implants were compared relative to the Smooth implant.

Results Surface areas increased with roughness and were similar among the three least rough implants (Smooth, Silk, and Velvet) and among the roughest implants (Siltex and Biocell). Overall, VPC indicated there was significantly more bacterial attachment and biofilm formation on the Siltex and Biocell implants than the Silk or Velvet implants, although there were differences between species and time points. CSLM confirmed the formation of thicker biofilms on the implants with rougher surface textures.

Conclusion This in vitro study confirmed that implant surfaces with rougher texture, resulting in more surface area, harbored greater biofilm loads than those with smoother surfaces.

No Level Assigned This journal requires that authors assign a level of evidence to each submission to which Evidence-Based Medicine rankings are applicable. This excludes Review Articles, Book Reviews, and manuscripts that concern Basic Science, Animal Studies, Cadaver Studies, and Experimental Studies. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Bacteria · Attachment · Biofilm · Breast implant · Silicone · Texture · Contracture · ALCL

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Introduction

Bacterial biofilms have been implicated with breast implant complications including capsular contracture [1–4], double-capsule formation [5], and breast implant-associated anaplastic large-cell lymphoma (BI-ALCL) [6]. The reduction of capsular contracture and ALCL using steps to reduce the introduction of bacteria during surgery provided indirect evidence of the role of bacteria in these conditions [7]. Due to their increased surface area, implants with

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Springer

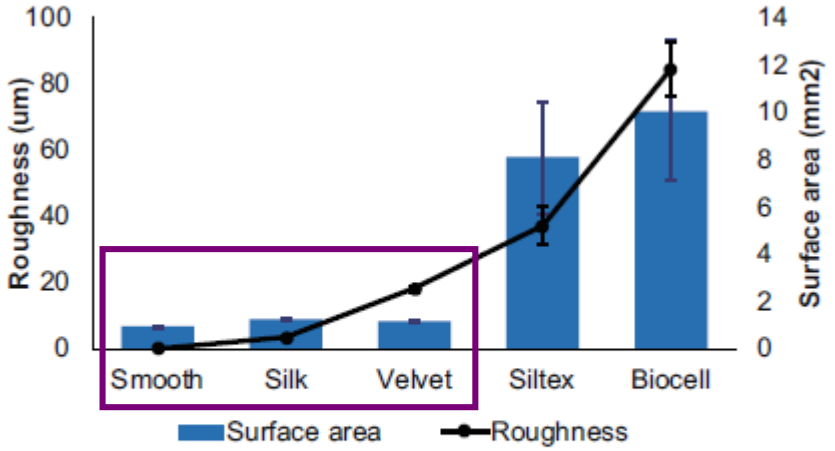


Fig. 1 Surface metrology results for the breast implant surfaces evaluated in this study. The two least rough surfaces (Silk and Velvet) had similar surface areas as did the two most rough surfaces (Siltex and Biocell)

5. James, G. et al. Bacterial adhesion and Biofilm formation on textured breast implant shell materials. Aesth Plast Surg. Oct 2018. doi:10.1007/s00266-018-1234-7

Negative values for SmoothSilk®/SilkSurface® indicate less attachment/biofilm formation than smooth

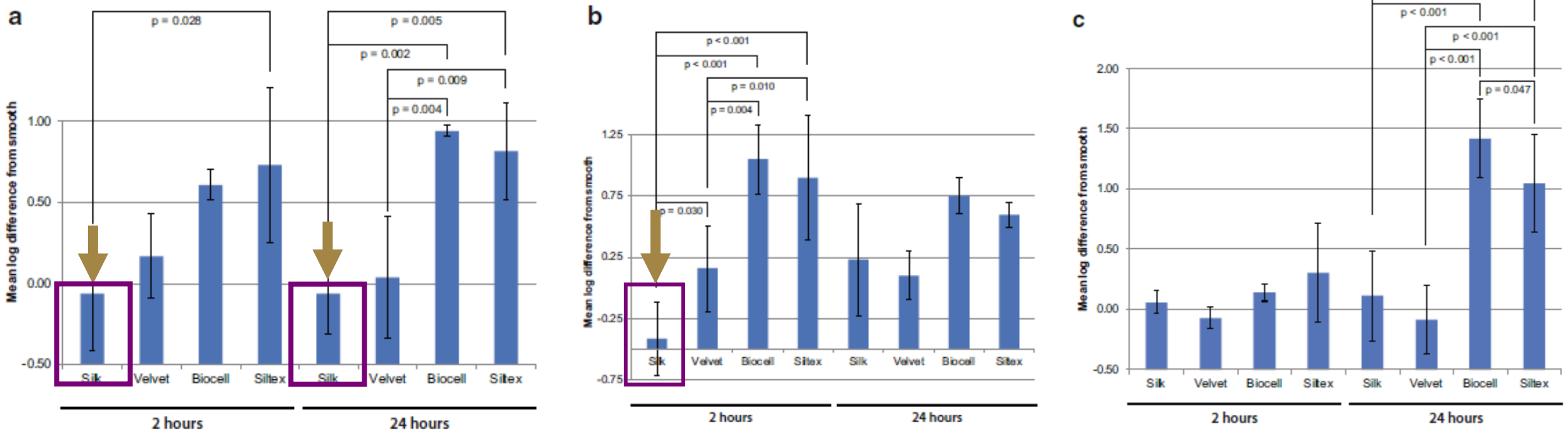


Fig. 2 Summary log difference from smooth data for *S. epidermidis* (a), *P. aeruginosa* (b), and *R. pickettii* (c). Error bars indicate ± standard deviation from the mean. Positive values indicate more attachment/biofilm formation than Smooth, while negative values indicate less attachment/biofilm formation than Smooth. Overall, the Biocell and Siltex textures had greater differences from Smooth [i.e., more attached bacteria (2 h) and biofilm formation (24 h)] than the Silk and Velvet textures

5. James, G. et al. Bacterial adhesion and Biofilm formation on textured breast implant shell materials. Aesth Plast Surg. Oct 2018. doi:10.1007/s00266-018-1234-7

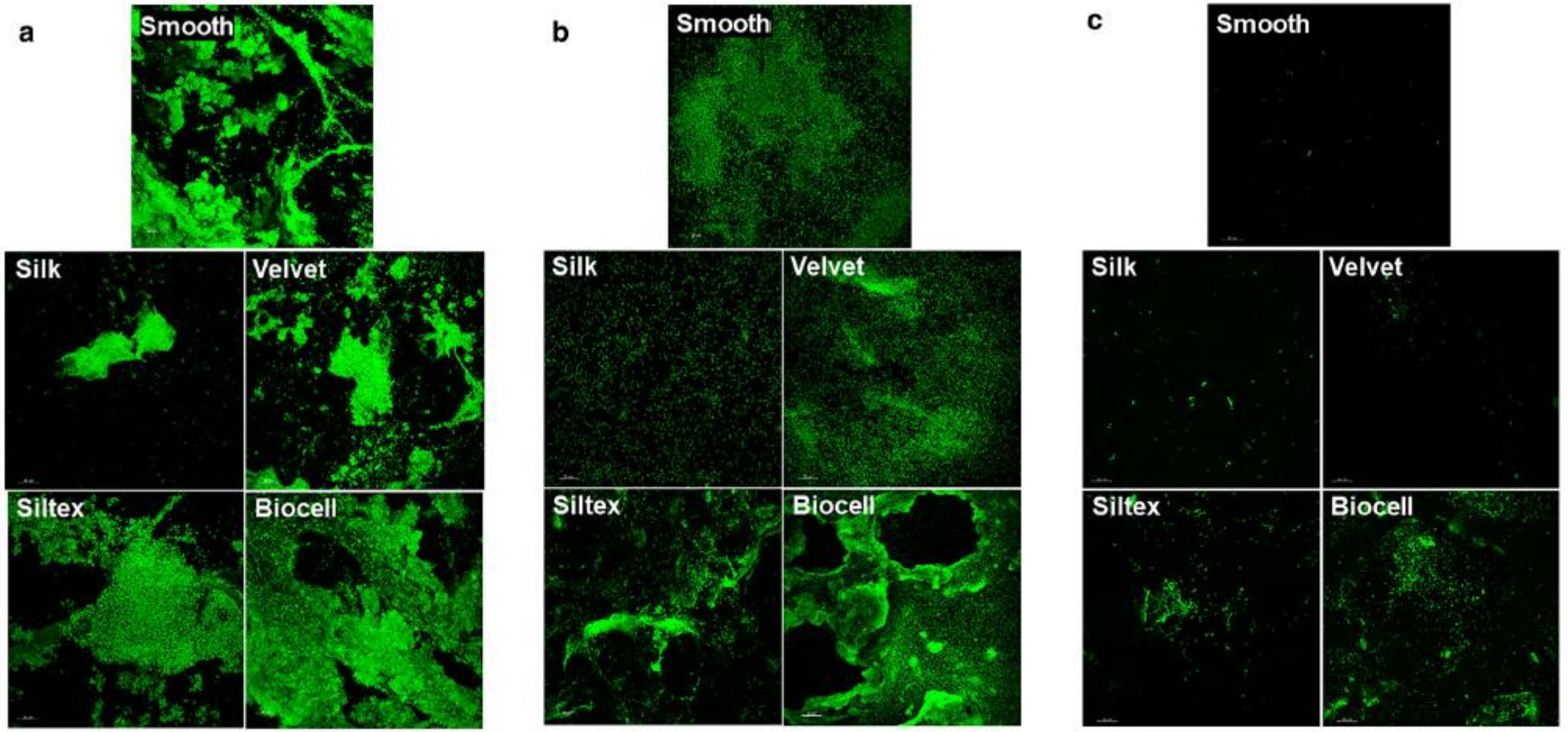
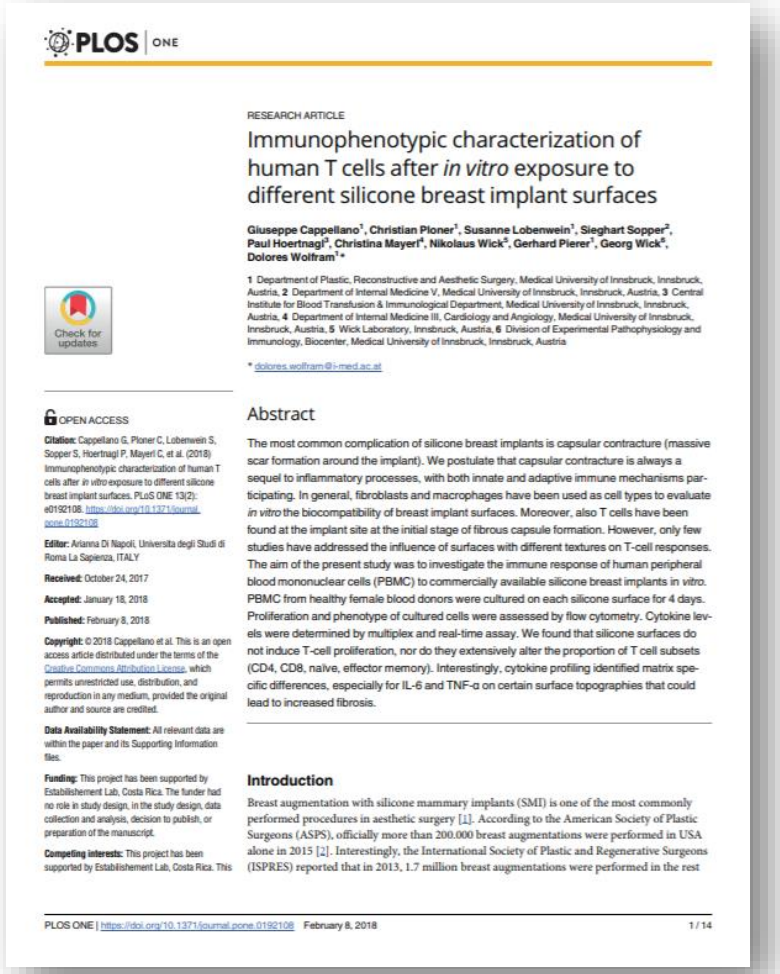


Fig. 3 CSLM images of *S. epidermidis* (**a**), *P. aeruginosa* (**b**), and *R. pickettii* (**c**) biofilms after 24 h of growth on breast implant surfaces. For all three species, more biofilm was observed on the Biocell and Siltex textures than the Silk and Velvet textures

5. James, G. et al. Bacterial adhesion and Biofilm formation on textured breast implant shell materials. Aesth Plast Surg. Oct 2018. doi:10.1007/s00266-018-1234-7

Cappellano et al (ESTA publication) – *in vitro* T cell response on 7 implant surfaces



PLOS ONE

RESEARCH ARTICLE

Immunophenotypic characterization of human T cells after *in vitro* exposure to different silicone breast implant surfaces

Giuseppe Cappellano[1], Christian Ploner[1], Susanne Lobenwein[1], Sieghart Sopper[2], Paul Hoertnagl[3], Christina Mayerl[4], Nikolaus Wick[5], Gerhard Pierer[1], Georg Wick[6], Dolores Wolfram[1]*

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Competing interests: This project has been supported by Establishement Lab, Costa Rica. This

Abstract

The most common complication of silicone breast implants is capsular contracture (massive scar formation around the implant). We postulate that capsular contracture is always a sequel to inflammatory processes, with both innate and adaptive immune mechanisms participating. In general, fibroblasts and macrophages have been used as cell types to evaluate *in vitro* the biocompatibility of breast implant surfaces. Moreover, also T cells have been found at the implant site at the initial stage of fibrous capsule formation. However, only few studies have addressed the influence of surfaces with different textures on T-cell responses. The aim of the present study was to investigate the immune response of human peripheral blood mononuclear cells (PBMC) to commercially available silicone breast implants in *vitro*. PBMC from healthy female blood donors were cultured on each silicone surface for 4 days. Proliferation and phenotype of cultured cells were assessed by flow cytometry. Cytokine levels were determined by multiplex and real-time assay. We found that silicone surfaces do not induce T-cell proliferation, nor do they extensively alter the proportion of T cell subsets (CD4, CD8, naïve, effector memory). Interestingly, cytokine profiling identified matrix specific differences, especially for IL-6 and TNF-α on certain surface topographies that could lead to increased fibrosis.

Introduction

Breast augmentation with silicone mammary implants (SMI) is one of the most commonly performed procedures in aesthetic surgery [1]. According to the American Society of Plastic Surgeons (ASPS), officially more than 200.000 breast augmentations were performed in USA alone in 2015 [2]. Interestingly, the International Society of Plastic and Regenerative Surgeons (ISPRES) reported that in 2013, 1.7 million breast augmentations were performed in the rest

Design:

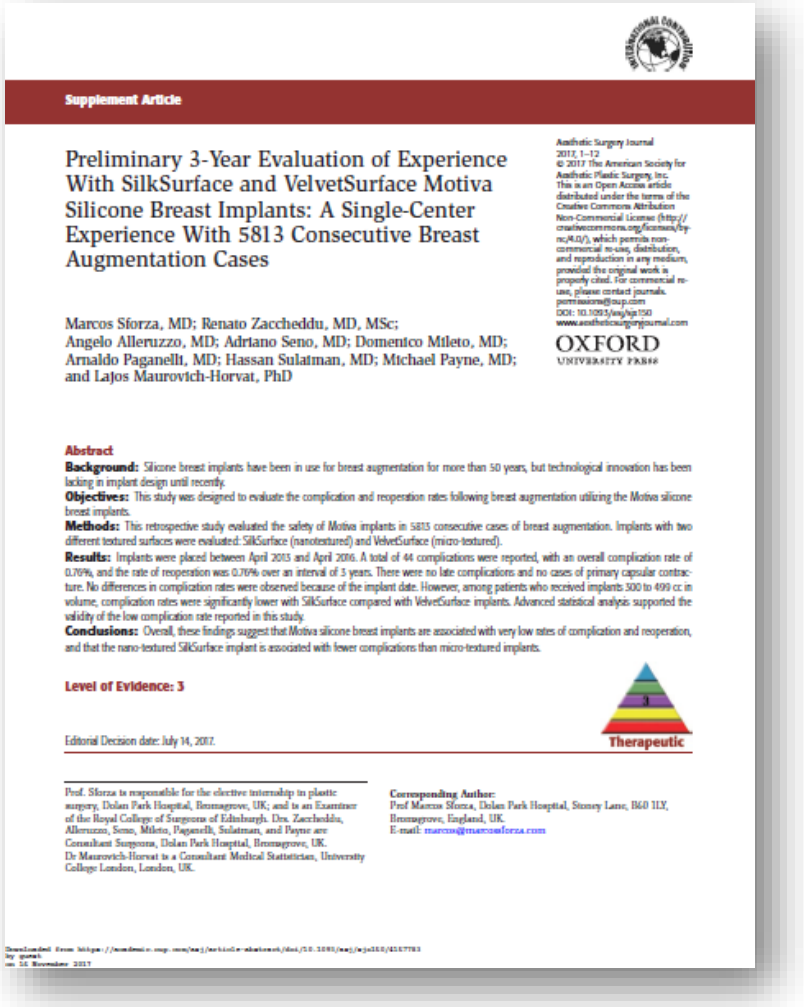
- Human PBMCs (lymphocytes, monocytes and dendritic cells) were cultured on different implant surfaces
- Certain surface textures are more prone to causing an inflammatory immune response.
- Looking at whether the different surfaces could stimulate lymphocytes and cause activation of the T-cells (because BIA-ALCL is a T-cell disorder)

Results:

- Found minimal changes in cytokine expression
- Compared to other surfaces, SmoothSilk®/SilkSurface®, VelvetSurface® and micropolyurethane foam surfaces showed lower degree of inflammation (downregulation of TNFα and IL-1β
- Only SmoothSilk®/SilkSurface®, reduced TGF-β1 levels (TGF-1β has anti inflammatory and profibrotic properties)
- Further work required to understand the clinical significance of these findings.

7. Cappellano G, Ploner C, Lobenwein S, Sopper S, Hoertnagl P, Mayerl C, et al. Immunophenotypic characterization of human T cells after in vitro exposure to different silicone breast implant surfaces. PLoS ONE. 2018;13(2): e0192108. doi: 10.1371/journal.pone.0192108

Sforza et al ASJ Publication: 5813 Cases 3 Years Retrospective



Supplement Article

Preliminary 3-Year Evaluation of Experience With SilkSurface and VelvetSurface Motiva Silicone Breast Implants: A Single-Center Experience With 5813 Consecutive Breast Augmentation Cases

Marcos Sforza, MD; Renato Zaccheddu, MD, MSc; Angelo Alleruzzo, MD; Adriano Seno, MD; Domenico Mileto, MD; Arnaldo Paganelli, MD; Hassan Sulaiman, MD; Michael Payne, MD; and Lajos Maurovich-Horvat, PhD

Aesthetic Surgery Journal 2017, 1–12

DOI: 10.1093/asj/sjx150
www.aestheticsurgeryjournal.com
OXFORD UNIVERSITY PRESS

Abstract

Background: Silicone breast implants have been in use for breast augmentation for more than 50 years, but technological innovation has been lacking in implant design until recently.

Objectives: This study was designed to evaluate the complication and reoperation rates following breast augmentation utilizing the Motiva silicone breast implants.

Methods: This retrospective study evaluated the safety of Motiva implants in 5813 consecutive cases of breast augmentation. Implants with two different textured surfaces were evaluated: SilkSurface (nanotextured) and VelvetSurface (micro-textured).

Results: Implants were placed between April 2013 and April 2016. A total of 44 complications were reported, with an overall complication rate of 0.76%, and the rate of reoperation was 0.76% over an interval of 3 years. There were no late complications and no cases of primary capsular contracture. No differences in complication rates were observed because of the implant date. However, among patients who received implants 300 to 499 cc in volume, complication rates were significantly lower with SilkSurface compared with VelvetSurface implants. Advanced statistical analysis supported the validity of the low complication rate reported in this study.

Conclusions: Overall, these findings suggest that Motiva silicone breast implants are associated with very low rates of complication and reoperation, and that the nano-textured SilkSurface implant is associated with fewer complications than micro-textured implants.

Level of Evidence: 3

Therapeutic

Editorial Decision date: July 14, 2017.

Prof. Sforza is responsible for the elective internship in plastic surgery, Dolan Park Hospital, Bromsgrove, UK; and is an Examiner of the Royal College of Surgeons of Edinburgh. Drs. Zaccheddu, Alleruzzo, Seno, Mileto, Paganelli, Sulaiman, and Payne are Consultant Surgeons, Dolan Park Hospital, Bromsgrove, UK. Dr Maurovich-Horvat is a Consultant Medical Statistician, University College London, London, UK.

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E-mail: marcos@marcossforza.com

MOTIVA IMPLANTS® 3 YEAR RETROSPECTIVE CLINICAL DATA[1]

Study published in Aesthetic Surgery Journal

5813 PATIENTS
2506 with Motiva Implants® SilkSurface® (Representing more than 5000 Implants)

100% OF ASSESSED PATIENTS
Mean of post-surgical follow-up interval: 23 months

KAPLAN-MEYER ANALYSIS

16 PLASTIC SURGEONS
One Study Site: Dolan Park Hospital in UK

SURGICAL TECHNIQUE

97% INFRAMAMMARY INCISION

79% DUAL PLANE

RESULTS

0.36% **OVERALL COMPLICATION RATE WITH MOTIVA IMPLANTS® SMOOTHSILK®**
Complications were: Early Seroma, Infection, Wound Dehiscence

1.06% **WITH MOTIVA IMPLANTS® VELVETSURFACE®**
Complications were: Early Seroma, Infection, Hematoma, Wound Dehiscence and Malposition

NO CASES OF:

0% CAPSULAR CONTRACTURE

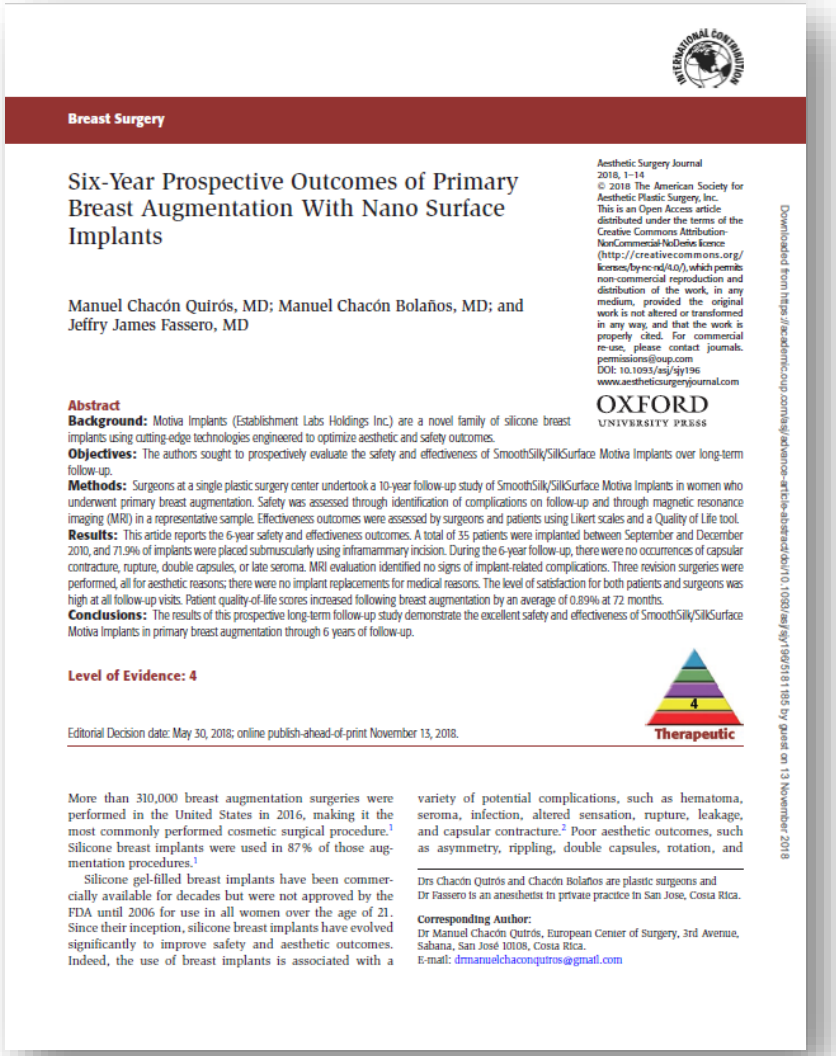
0% RUPTURE DUE TO DEVICE FAILURE

0% RIPPLING

0% LATE SEROMA

8. Sforza M, Zaccheddu R, Alleruzzo A, et al. Preliminary 3-year evaluation of experience with SilkSurface and VelvetSurface Motiva silicone breast implants: a single-center experience with 5813 consecutive breast augmentation cases. Aesthet Surg J. 2018;38(Suppl 2):S62-S73. doi: 10.1093/asj/sjx150

Chacon et al. ASJ Publication: 6 Year Prospective Safety Outcomes



Breast Surgery

Six-Year Prospective Outcomes of Primary Breast Augmentation With Nano Surface Implants

Manuel Chacón Quirós, MD; Manuel Chacón Bolaños, MD; and Jeffry James Fassero, MD

Aesthetic Surgery Journal
2018, 1–14

DOI: 10.1093/asj/sjy196
www.aestheticsurgeryjournal.com
OXFORD UNIVERSITY PRESS

Abstract

Background: Motiva Implants (Establishment Labs Holdings Inc.) are a novel family of silicone breast implants using cutting-edge technologies engineered to optimize aesthetic and safety outcomes.

Objectives: The authors sought to prospectively evaluate the safety and effectiveness of SmoothSilk/SilkSurface Motiva Implants over long-term follow-up.

Methods: Surgeons at a single plastic surgery center undertook a 10-year follow-up study of SmoothSilk/SilkSurface Motiva Implants in women who underwent primary breast augmentation. Safety was assessed through identification of complications on follow-up and through magnetic resonance imaging (MRI) in a representative sample. Effectiveness outcomes were assessed by surgeons and patients using Likert scales and a Quality of Life tool.

Results: This article reports the 6-year safety and effectiveness outcomes. A total of 35 patients were implanted between September and December 2010, and 71.9% of implants were placed submuscularly using inframammary incision. During the 6-year follow-up, there were no occurrences of capsular contracture, rupture, double capsules, or late seroma. MRI evaluation identified no signs of implant-related complications. Three revision surgeries were performed, all for aesthetic reasons; there were no implant replacements for medical reasons. The level of satisfaction for both patients and surgeons was high at all follow-up visits. Patient quality-of-life scores increased following breast augmentation by an average of 0.89% at 72 months.

Conclusions: The results of this prospective long-term follow-up study demonstrate the excellent safety and effectiveness of SmoothSilk/SilkSurface Motiva Implants in primary breast augmentation through 6 years of follow-up.

Level of Evidence: 4

4 Therapeutic

Editorial Decision date: May 30, 2018; online publish-ahead-of-print November 13, 2018.

More than 310,000 breast augmentation surgeries were performed in the United States in 2016, making it the most commonly performed cosmetic surgical procedure.[1] Silicone breast implants were used in 87% of those augmentation procedures.[1]

Silicone gel-filled breast implants have been commercially available for decades but were not approved by the FDA until 2006 for use in all women over the age of 21. Since their inception, silicone breast implants have evolved significantly to improve safety and aesthetic outcomes. Indeed, the use of breast implants is associated with a variety of potential complications, such as hematoma, seroma, infection, altered sensation, rupture, leakage, and capsular contracture.[2] Poor aesthetic outcomes, such as asymmetry, rippling, double capsules, rotation, and

Drs Chacón Quirós and Chacón Bolaños are plastic surgeons and Dr Fassero is an anesthetist in private practice in San Jose, Costa Rica.

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E-mail: drmanuelchaconquiros@gmail.com

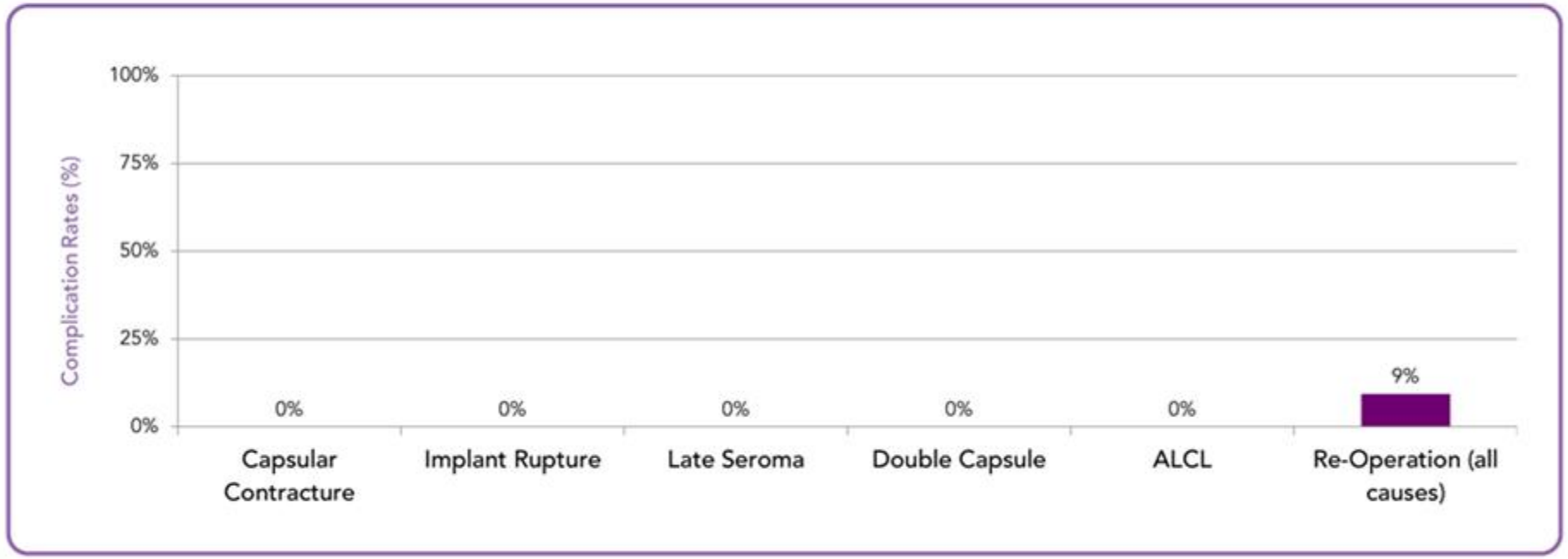
Table 3. Safety Outcomes

Duration of follow-up, years	6
Outcome (N = 32)[a]	**Value N (%)**
Changes in nipple sensitivity	3 (9.4%)
Implant rupture, capsular contracture, double capsules, late seroma, or ALCL	0 (0%)
Inadequate scarring	0 (0%)
Pain	2 (6.3%)
Pruritus	0 (0%)
Ptosis	17 (53.1%)
Reported loss of volume	0 (0%)
Symmastia	0 (0%)
Twinges	2 (6.3%)

ALCL, anaplastic large cell lymphoma. [a] .

9. Chacón M, Chacón M & Fassero J. Six-Year Prospective Outcomes of Primary Breast Augmentation with Nano-Surface Implants. Aesthet Surg J. Nov 2018; doi: 10.1093/asj/sjy196

Prospective Study: 10-year follow-up study of SmoothSilk®/SilkSurface® Motiva Implants® on 35 patients with MRI assessment (6-year report).



0% Safety Issues at 6-years

9. Chacón M, Chacón M & Fassero J. Six-Year Prospective Outcomes of Primary Breast Augmentation with Nano-Surface Implants. Aesthet Surg J. Nov 2018; doi: 10.1093/asj/sjy196

Establishment Labs 8 Year Post-Market Surveillance

Data collection to monitor the safety and effectiveness of Motiva Implants®.

Since the commercial launch of Sterile Silicone Breast Implants Motiva Implant Matrix® in October 2010, Establishment Labs® has placed a total of 578,613 breast implants in the market, including Latin America, Europe, Middle East, Africa, and Asia-Pacific regions.

477 (0.082%) complaints have been reported to Establishment Labs® up to the end of September 2018 and 179 events have been classified as clinically related.[1]

Motiva Implants® Clinical Complaints from October 2010 to September 2018

<1%

Complication	Number of reported cases	Risk rates %
Capsular contracture	122*	<1%
Rupture after implantation *(surgical damage)***	27	<1%
Infection	12	<1%
Early seroma (< 1 year)	6	<1%
Undetermined	6	<1%
Others	5	<1%
Hematoma	1	<1%
Late seroma (> 1 year)	0	0%
Double capsule	0	0%
Breast implant associated anaplastic large cell lymphoma (BIA-ALCL)	0	0%

** 75 confirmed cases (Baker Grade III/IV) and 47 unconfirmed cases | ** No reported cases of rupture due to device failure*

Ongoing post-market surveillance is important to us and we encourage reporting of all Motiva® product complaints:
https://motiva.health/support/

3. Establishment Labs Post-Market Surveillance Report Q3-2018

Time to onset for breast implant associated anaplastic large cell lymphoma (BIA-ALCL)

OPEN

BREAST

Risk Factor Analysis for Capsular Contracture, Malposition, and Late Seroma in Subjects Receiving Natrelle 410 Form-Stable Silicone Breast Implants

Patricia McGuire, M.D.
Neal R. Reisman, M.D., J.D.
Diane K. Murphy, M.B.A.

St. Louis, Mo.; Houston, Texas; and Irvine, Calif.

Background: Natrelle 410 silicone breast implants are approved in the United States for breast augmentation, reconstruction, and revision.
Methods: In two ongoing, prospective, multicenter 10-year studies, 17,656 subjects received Natrelle 410 implants for augmentation ($n = 5059$), revision-augmentation ($n = 2632$), reconstruction ($n = 7502$), or revision-reconstruction ($n = 2463$). Capsular contracture, implant malposition, and late seroma were documented. Cox proportional hazards regression analyses evaluated potential associations between subject-, implant-, and surgery-related factors and these complications.
Results: Median follow-up was 4.1, 2.6, 2.1, and 2.3 years in the augmentation, revision-augmentation, reconstruction, and revision-reconstruction cohorts, respectively. Incidence of capsular contracture across cohorts ranged from 2.3 to 4.1 percent; malposition, 1.5 to 2.7 percent; and late seroma, 0.1 to 0.2 percent. Significant risk factors for capsular contracture were subglandular implant placement, periareolar incision site, and older device age in the augmentation cohort ($p < 0.0001$), older subject age in the revision-augmentation cohort ($p < 0.0001$), and higher body mass index ($p = 0.0026$) and no povidone-iodine pocket irrigation ($p = 0.0006$) in the reconstruction cohort. Significant risk factors for malposition were longer incision size in the augmentation cohort ($p = 0.0003$), capsulectomy at the time of implantation in the reconstruction cohort ($p = 0.0028$), and implantations performed in physicians' offices versus hospitals or standalone surgical facilities in both revision cohorts ($p < 0.0001$). The incidence of late seroma was too low to perform risk factor analysis.
Conclusions: These data reaffirm the safety of Natrelle 410 implants. Knowledge of risk factors for capsular contracture and implant malposition offers guidance for reducing complications and optimizing outcomes. (*Plast. Reconstr. Surg.* 139: 1, 2017.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Risk, II.

RISK

Breast implants have been available for cosmetic augmentation and postmastectomy breast reconstruction for more than 50 years. During this period, advances in shape, surface features, and composition have led to improved safety and high levels of patient satisfaction. The Natrelle 410 breast implant (Allergan plc, Dublin, Ireland) is a teardrop-shaped, textured, highly cohesive silicone gel implant designed to mimic the natural slope of the breast.[1,2] It has a Biocell (Allergan) textured shell surface consisting of irregularly arranged depressions with a

From Parkcrest Plastic Surgery; Baylor College of Medicine; and Allergan, Inc.
Received for publication August 26, 2015; accepted August 4, 2016.

DOI: 10.1097/PRS.0000000000002837

Disclosure: *P. McGuire is a consultant and speaker for Allergan plc. N.R. Reisman has no conflicts of interest to report. D.K. Murphy is an employee and stockholder of Allergan plc, Irvine, Calif.*

Two ongoing, prospective, multicenter 10-year studies

The cases of late seroma were insufficient to perform a risk factor analysis. All cases occurred with submuscular device placement. No obvious trends toward the development of late seroma were observed in relation to subject age or body mass index, device size, style, or incision site. Four cases of breast implant–associated anaplastic large cell lymphoma were reported. One case each was reported in the augmentation, revision-augmentation, reconstruction, and revision-reconstruction cohorts. In these four subjects, breast implant–associated anaplastic large cell lymphoma was diagnosed from approximately 3.5 to 11.6 years after implantation.

Average of 7.6 years, as early as 3.5 years

n= 17,656 subjects
augmentation (n = 5059), revision-augmentation (n = 2632)
reconstruction (n = 7502), revision-reconstruction (n = 2463)

McGuire, P. et al. Plast Reconstr Surg. 2017 Jan; 139(1): 1–9. Published online 2016 Dec 28. doi: 10.1097/PRS.0000000000002837

In Summary

- Motiva SmoothSilk® / SilkSurface ® surface is categorized as smooth with no reported cases of BIA-ALCL to date
  - Supported by ISO 14607:2018 standards and numerous recent publications
  - There are different methodologies to measure surface area & roughness, all of them position SmoothSilk® / SilkSurface ® in the same category as traditional smooth
- This peculiar surface has demonstrated to be **less inflammatory** with low capsular contracture rates reported
- Establishment Labs' vision is to focus on patient safety by addressing both **high risk uncommon** entities like BIA-ALCL as well as **low risk common** clinical complications like capsular contracture