



Subclinical Infection of the Silicone Breast Implant Surface as a Possible Cause of Capsular Contracture: A Follow-Up

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Research on seemingly dormant microbes and biofilm at the surface of mammary implants was inspired by Dr. Burkhardt's original concepts on the role of subclinical infection and fibrous capsular contracture around breast implants [1]. Early on, the relevance of such a question as whether there is any local, cellular, genotypic or phenotypic predisposition necessary to “allow” contracture to develop was reaffirmed first by us and later on by the observations of others who noted that when implants were placed in a “sterile” tissue environment, capsular contracture was virtually unheard of [2, 3]. Questions began to focus on the clinical significance of the presence of bacteria and their by-products. These questions led to the investigation of whether bacteria and microbial by-products not only alter the healing and biological behavior of tissue in the immediate vicinity of the implant but also potentially exert systemic effects as well [4].

Although the hypothesis postulating whether microbes play a key role in the development of capsular contracture required (and still requires to this day) further investigation, practical suggestions emerged on how to prevent and/or treat presumed subclinical infections. Goals to eliminate bacteria from the surface of implants led the development of “therapeutic protocols” and, perhaps more importantly, precipitated research regarding the development of bacteria/biofilm-repellent surfaces [5, 6]. These attempts to prevent and to “treat” the presence of bacteria on the surface of implants led to inconsistent results [7]. Despite these inconsistencies, recognition of pathophysiological

details of the implant surface-breast tissue microenvironment and their interaction broadened plastic surgeons' perspectives on the issues of biofilms. Additionally, this helped guide plastic surgeons toward the understanding of the inconsistency and unpredictability of the effectiveness of local antimicrobials thus providing the impetus for some technical modifications of implant insertion (e.g., the Keller Funnel) [5, 8].

Skin and breast tissue (as specialized skin appendage) contain a robust environment of microbiota, and even with submuscular positioning of implants, some contact with breast tissue is unavoidable [6, 7, 9]. Interestingly, the isolates obtained from implants by the disruption of biofilm consist mostly of *Staphylococcus epidermidis*, which differs from the typical tissue microbiota isolated from breast tissue [1, 10]. This capability, phenotypic “effectiveness” and biologically rapid (in seconds) protective action make these bacteria themselves, which are quickly encased in biofilm, inaccessible to antibacterial agents. On the other hand, microbial species, less efficient in the formation of biofilm, may be successfully eradicated by antimicrobials [1, 7, 11–13]. In addition, the virulence of many of *Staphylococcal* biofilms, their resistance to the host's endogenous defenses and antibiotics, is related to their ability to form thicker and stronger biofilms with biofilm “protective” mechanisms in place compared to other species [13]. Currently, the importance of the development of a bacteria/biofilm-repellent medical device surfaces is recognized by many clinical specialties and goes well beyond the focus of mammary implants [13–15].

Both our study and the studies of others have evolved to focus on the further characterization of biofilm, its components and the potential significance it has on the development of systemic effects in some breast implant recipients. Polymerase chain reaction assay has allowed for

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the detection of heat shock proteins in tissue materials interacting with biofilms [4, 16–20]. In the context of the discussion of “Breast Implant Illness” (BII) and breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), it is worthy to mention that one of these proteins (heat shock protein-90) mediates self-nucleic acid recognition in systemic autoimmune diseases and has also become a known factor for promoting the development of anaplastic large cell lymphoma [16–21]. Therefore, although studies branching from the issues of “subclinical infection and capsular contracture” have generated more questions than answers, there should be no doubt that the interface between mammary implants and the host tissues may be the site of chronic inflammation and, in some molecular/genetic circumstances, may stimulate the immune system leading to secondary disorders and systemic illnesses [19]. Investigation of the role of toll-like receptors in peri-implant tissue is a very logical step forward in an attempt to establish the pathophysiology and molecular evidence behind BII. This study and others aimed to dissect molecular mechanisms behind the condition would perhaps allow us to determine whether indeed there are patients who should not be recipients of breast implants [20–23].

Considering the fact that immune alterations and chronic inflammatory profiles may have a similar pathophysiology regardless of whether reactions are considered “local”, and limited to the surrounding breast environment, or systemic; the hypothesis that capsular contracture and breast implant illness share the same initial pathogenesis and are on a continuum of the same chronic inflammatory spectrum is reasonable [22–26]. The combination of the presence of toxic or immunizing-capable detachment molecules from *Staphylococcus epidermidis* biofilms as well as some silicone gel adjuvant potency may lead to different reactions ranging from local—in some circumstances unilateral—fibrosis (capsular contracture) through systemic ones (fibromyalgia, BII) [10, 22–27]. Therefore, it should not be surprising that the outcomes from implant explanation or periprosthetic capsulectomy are inconsistent and often not permanent—once the systemic inflammatory cascade is activated, it tends to have its own dynamic course and the elimination of antigens and the site of local inflammation may not result in the resolution of the multitude of symptoms and problems that may be present [4, 17, 18, 22–26].

Reflecting back on the initial studies on “subclinical infection of mammary implants” and re-reading the last paragraph of the article from 1992, we are reaffirmed that although some issues and questions were raised rather intuitively, the research and concepts that originated at that time were “on the right track”. Additionally, in the particular context of BII, the recognition that the physical characteristics of the implant surface may modulate

microbial deposits and the nature of biofilms suggests that further investigations are warranted [28]. Large databases (e.g., the National Breast Implant Registry) should facilitate the accumulation of relevant information and the effective transition from data collection and analysis to scientific “synthesis” and clinical applications. We hope that further research in this field of investigation will bring us even closer to the concept of “precision” medicine and surgery, such that it may be possible to truly personalize breast implant surgery and increase the margin of implant safety.

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