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Functional biocompatibility testing of silicone breast implants and a novel classification system based on surface roughness

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ABSTRACT

Purpose: Increasing numbers of women undergo breast implantation for cosmetic and reconstructive purposes. Contracture of the fibrous capsule, which encases the implant leads to significant pain and reoperation. Texture, wettability and the cellular reaction to implant surfaces are poorly understood determinants of implant biocompatibility. The aim of this study was to evaluate the in-vitro characteristics of a range of commercial available implants using a macrophage based assay of implant biocompatibility and a quantitative assessment of wettability and texture.

Methods: Thirteen commercially available surfaces were subjected to wettability and texture characterisation using scanning and laser confocal microscopy. THP-1 macrophages were cultured on their surfaces and assessed using Integrin αV immunocytochemistry, SEM and RT-PCR for the expression of TNF-Alpha, IL-6, IL-10 and a cytokine array for the production of TNF-alpha, IL-10, IL-1RA and IL1β; important indicators of inflammation and macrophage polarization.

Results: Textured surfaces can be accurately sub-categorized dependent upon roughness and re-entrant features into four main types (macro, micro, meso and nano-textured surfaces). Significant ($P < 0.0001$) differences in implant hydrophobicity and texture exist. Certain surfaces promoted poor macrophage polarization and an innate potential to foster a proinflammatory response. A subgroup analysis showed that texture had a variable effect on markers of inflammation in these surfaces.

Conclusions: We propose a classification of implant surfaces based on roughness and present a macrophage based assay of breast implant biocompatibility with a quantitative assessment of implant wettability and texture. The breast implant surface-cell interaction is variable and sufficient to alter healing response and capsular contracture fate in-vivo.

1. Introduction

Implant texture has been shown by two meta-analyses and one systematic review to reduce capsular contracture (Barnsley et al., 2006; Wong et al., 2006; Liu et al., 2015). Capsular contracture, the tightening and hardening of the normal capsule that encases the breast implant causes pain, a poor aesthetic result, re-operation and ultimately patient dissatisfaction (Cash et al., 2002). Capsular contracture can occur in 17.5% of women who undergo breast augmentation whether for aesthetic or reconstructive purposes, a not insignificant number considering 10 million currently have breast implants in situ in the United States (Gabriel et al., 1997; Brody et al., 2015).

Three theories have been proposed to explain why implant texture is contracture protective, which include (i) the beneficial degradation of the contracted capsule by the presence of cells seen in the textured capsule/ implant interface. (ii) Ingrowth of breast tissue into the texture of the implant, thus increasing friction and reducing a synovial type metaplasia that has been seen in smooth, contracted capsules. (iii) The disruption of the planar arrangement of fibroblasts and the vectors of contraction seen on the surface of smooth implants (Taylor and Gibbons, 1983; Brohim et al., 1992;Hall-Findlay, 2011).

Currently available textured implants are manufactured using three main techniques: (i) the salt-loss technique, (ii) the formation of a texture from a textured, usually sandblasted mould or chuck, (iii) by imprinting polyurethane foam into the surface of the uncured implant (Barr and Bayat, 2009). These techniques have been inherited from the

Abbreviations: SEM, Scanning Electron Microscopy; PV, Peak to Valley; Sa, Roughness; PBS, Phosphate buffered saline; S.D., Standard deviation; ALCL, Anaplastic Large Cell Lymphoma

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historical necessity to produce texture on the surface of breast implants in the face of the changing breast implant market and in the belief that texture is beneficial. None of the current implant surfaces have a specific or inductive biological design or provenance to support their textures.

Since the inception of the first breast implant at least 240 styles and 8300 models have been reported and manufactured (Mentor, 2004). Direct comparisons between each implant manufacturer are difficult to make as no trial has sufficiently standardised the multiplicity of confounding variables that contribute to capsular contracture (Derby and Codner, 2015).

Biocompatibility is defined as: *"The ability of a material to perform with an appropriate host response in a specific application"* (Williams, 1999). The biocompatibility shortcomings of implants can disturb constructive wound healing and may provoke the fibrotic reactions seen in capsular contracture. Biocompatibility is in part dictated by the topography and hydrophobicity of the implant surface and the proteins that adsorb onto the surface of the implant (Fenoglio et al., 2011).

Implant capsules contain several cell types (Brazin et al., 2014). Traditionally the fibroblast has been the cell type used to evaluate the in vitro reaction to biomaterials, however, it has been increasingly apparent that macrophages have a powerful initial effect on the process of tissue repair, remodelling and biocompatibility (Martinez et al., 2008). Macrophages migrate into the wound from 24 to 48 h after injury in the inflammation stage of wound healing and are the predominant cell population before fibroblast migration (See Fig. 1) (Salthouse, 1984; Park and Barbul, 2004). Macrophages also influence the chemotaxis, proliferation and collagen synthesis of fibroblasts through their production of cytokines, with important downstream effects on wound healing (Wahl, 1985; Brodbeck et al., 2002; Brodbeck et al., 2003). Macrophages exist along a spectrum of M1 to M2 phenotype, where M1 macrophages are considered to be inflammatory and M2 macrophages are pro wound healing (Mantovani et al., 2004; Porcheray et al., 2005). Higher M2/M1 phenotype has been shown to reduce the fibrotic reaction to implants (See Fig. 1) (Madden et al., 2010).

Topography has been shown to have important effects on macrophages at both a micro and nano scale and demonstrable effects on wound healing, however, no previous study has assessed the in vitro effect of breast implants on this important cell type (Chen et al., 2010). Therefore, the aim of this study was to evaluate the in vitro characteristics of a range of commercial implants currently available to the patient undergoing breast augmentation using a macrophage based assay of breast implant biocompatibility with a quantitative assessment of implant wettability and texture.

2. Materials and methods

13 implant surfaces were included in this study. These surfaces were coded by texture type to group implant types with one another. "SL" corresponded to salt loss manufactured implants, "CM" to chuck moulded manufactured implants, "POLY" the polyurethane implant surface, "POLYM" the polyurethane moulded implant surface, "SM", the smooth surfaced implant and "AT" the alternatively textured implant surface.

SL1Biocell® (Allergan, Dublin, Ireland)
SL2Sebbin (Zurich, Switzerland)
SL3CUI (Allergan, Dublin, Ireland)
SL4Eurosilicone (Apt, France)
SL5Poly Implant Prothèse (PIP) (Paris, France)
CM1Cereplas Cereform™ (Sailly lez Cambrai, France)
CM2Silk Surface™ (Establishment Labs SA, Coyol de Alajuela, Costa Rica)
CM3Velvet Surface™ (Establishment Labs SA, Coyol de Alajuela, Costa Rica)
AT2Polytech (Polytxt®, Dieberg, Germany)
POLYMSiltex (Mentor, California, USA)
SMSmooth (Mentor, California, USA)
AT1TRUE Texture (Sientra, Rio de Janeiro, Brazil)
POLYPolytech Microthane surface

Further details of the methods used in this work can be found in the supplementary section.

2.1. Substrate characterisation

All surfaces included in this study were characterised using laser confocal imaging and Scanning Electron Microscopy (SEM) aside from the polyurethane surface due to the diffractive effect its fibres had on the confocal microscope. Height maps were exported to Gwyddion where data for maximum Peak to Valley (PV) height, roughness (Sa) and surface area were derived (Nečas and Klapetek, 2012).

2.2. Implant surface preparation

For the investigation of surface texture and wettability, a 6 mm disk was cut from the domed surface of each implant shell and mounted on a glass slide.

2.3. Wettability

Wettability assessment was performed on a Kruss Drop Shape Analyser DS100 (Hamburg, Germany).

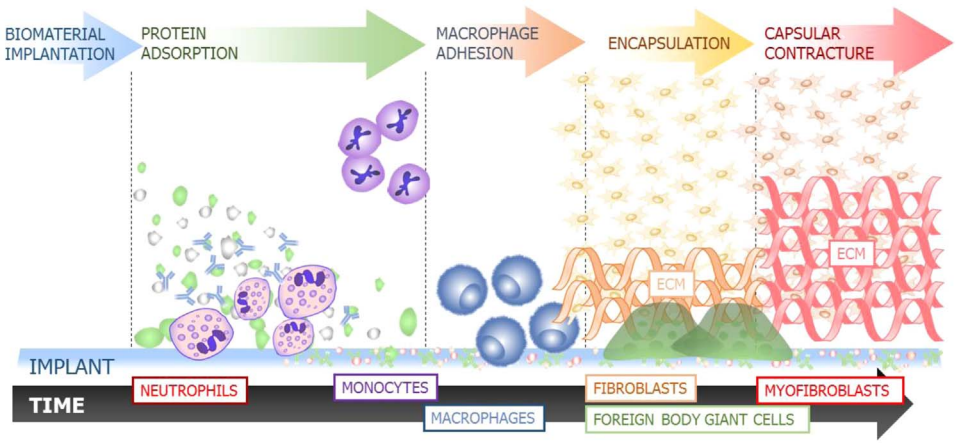

Fig. 1. The Phases of the Foreign Body Reaction. On implantation, the biomaterial is coated in a layer of protein from the surrounding wound fluid and neutrophils reach the wound site. Monocytes differentiate into macrophages which develop into foreign body giant cells and cause the recruitment of fibroblasts, which begin to wall the implant off from the surrounding tissue by depositing collagen and the fibrous capsule. It is this capsule which contracts and hardens in some women to cause the condition of capsular contracture.