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Research Paper

Physico-chemical characteristics of coated silicone textured versus smooth breast implants differentially influence breast-derived fibroblast morphology and behaviour

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ABSTRACT

Capsule formation is an inevitable consequence of silicone breast implantation. Clinically challenging dense fibrocollagenous capsular contractures occur at different rates between smooth compared to textured surfaces. Host response is influenced by several factors including implant surface texture, chemistry and interactions between cells and the extracellular matrix (ECM). Specific coatings can modify the physico-chemical properties of implant surfaces eliciting specific cellular reactions. Therefore, we evaluated the physico-chemical characteristics of coated smooth versus textured silicone breast implants on breast-derived fibroblast morphology and behaviour using (a) confocal laser microscopy, (b) Raman spectroscopy and (c) the effect of four unique protein and glycosaminoglycan (GAG) coatings (aggrecan, collagen I, fibronectin and hyaluronic acid) on breast-derived fibroblast attachment, proliferation, morphology, spreading, cytotoxicity and gene expression. Collagen I, fibronectin and hyaluronic acid coatings exhibited satisfactory fibroblast adhesion ($p<0.001$) in comparison to uncoated surfaces. Cell adhesion was less on smooth surfaces compared to textured surfaces ($p<0.001$). Fibroblasts cultured on collagen I, fibronectin and hyaluronic acid coated implants demonstrated improved cell proliferation than uncoated surfaces ($p<0.001$). LDH assay showed that coating surfaces with collagen I, fibronectin and hyaluronic acid did not induce cytotoxicity. Alpha-actinin expression and fibroblast adhesion to the substrate were upregulated ($p<0.001$), in textured versus smooth surfaces. FAK, vinculin and paxillin expression were upregulated ($p<0.001$), in all surfaces coated with fibronectin and collagen I. In conclusion, we present original data for expression of adhesion-related genes, cell

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morphology and proliferation in breast fibroblasts following the application of specific coatings on breast implant surfaces.

1. Introduction

Capsule formation is an inevitable consequence of implant insertion into a body cavity. Breast capsules are thus typically formed after silicone breast implant insertion into the breast cavity; however, some capsules can undergo contracture formation. A fibrous capsule usually forms around silicone breast implants. This is a relatively hypocellular membrane of rather uniform thickness which is rich in collagen. There may be a thin discontinuous layer of activated epithelioid myofibroblasts next to where the implant was situated and a thin acellular protein film between the implant and capsule. Both within and directly below this membrane, there are usually foam cells and lymphocytes, often in large numbers (Van Diest et al., 1998). However, whilst aetiology remains unknown, a variety of associations have been proposed that may predispose implants to capsular contracture formation including the filler material, implant placement technique, surface texture, presence of foreign bodies (such as glove talcum powder), subclinical infections near the area of implantation, hematoma and seroma (Berry et al., 2010). Breast capsular contracture is a clinical challenge for both the patient and the clinician in view of the degree of physical severity and availability of limited options for management. There are two types of surfaces for the most commonly used silicone breast implants today (Fig. 1). Silicone breast implant surface texture is considered to influence the rate of breast capsular contracture formation (Barr and Bayat, 2011). An implant surface is thought to interact directly with the breast tissue once inserted. A number of prospective studies have shown evidence of the benefit of textured compared to smooth implants in the first year post-implantation, although this benefit is maintained at 5 and 10 years (Poeppl et al., 2007, Barnsley et al., 2006, Hakelius and Ohlsen, 1997, Malata et al., 1997, Coleman et al., 1991, Ersek, 1991, Ma and Gao, 2008). Meta-analyses calculated the occurrence of breast capsular contracture on textured surfaces to be about fivefold less in comparison to smooth surfaces, which was maintained for 3 years (Wong et al., 2006, Barnsley et al., 2006). However, one previous study showed no statistically significant difference between saline-filled smooth and textured breast implants (Fagrell et al., 2001). Moreover, studies carried out in animal models are conflicting, as two studies found an increase in the rate of capsular contracture in smooth surface implants (Brohim et al., 1993, Clugston et al., 1994), while other studies found thicker and tighter capsules around textured surfaces (Barone et al., 1992, Bucky et al., 1994, Bern et al., 1992). Rationale behind the efficacy of reducing capsular contracture with textured breast implants is based on the fact that cells grow into and around the interstices of the surface resulting in an environment where contractile forces tend to cancel each other out, resulting in thinner capsule formation by contact inhibition (Harvey et al., 2013). Smooth surfaces elicit a fibrous reaction where collagen fibrils align cumulatively in a connective-tissue capsule adjacent to the implant.

Third-generation biomaterials are designed to stimulate cell behaviour in a specific manner at molecular level (Hench and Polak, 2002). Molecular modifications on the surface of the implants induce specific interactions with cell receptors such as integrins directing cell proliferation, differentiation and ECM production and organisation. Coating surfaces is an alternative route to influence the implant surface topography by creating cues for cellular adhesion and the subsequent induction of tissue integration (Harvey et al., 2013, Hauser et al., 2009). Different techniques of coating have been performed on breast implants with the aim of reducing the rate of capsular contracture. Polyurethane covered breast implants consists of silicone shell covered with fine-cell urethane and filled with silicone gel. The polyurethane coating is 1 mm thick and the septum is built into the prosthesis featuring a Y-shape thin-walled that allows the implant fixes within the chest wall (Ashley, 1970). This capsule surrounding the polyurethane consisted of five layers: a single layer of macrophages, foreign body giant cells, and epithelioid cells, a layer of subacute inflammatory tissue, a plasmacytic infiltrate, a thick layer of connective tissue and a layer of lax connective tissue along the breast parenchyma (Vazquez, 1999). The polyurethane coating induces a vascular foreign body reaction that prevents fibroblasts from producing collagen in a continuous plane so the contracture of the capsule is minimum and only 10% of patients have shown capsular contracture at 4 years; however, 25% of the patients showed capsular contracture at 10 years, and this may be due to the disintegration of the polyurethane coating (Berry and Davies, 2010). In the 1990s, polyurethane-covered Même breast implants were withdrawn from the market due to the risk of chemical breakdown of the polyurethane foam to carcinogen 2-toluene diamine (Collis et al., 2000). Currently, polyurethane is joined at the base to the implant, instead of being glued to the implant which was the case before it was withdrawn. Therefore, polyurethane does not become detached and a capsule is formed only around the polyurethane and not between the foam and the implant as it was previously (Vazquez, 1999, Vazquez and Pellon, 2007). Roca studied autologous fat grafting with textured silicone gel implants in porcine models showing softer capsules around the implants (Roca et al., 2014). Park covalently coated silicone implants with a biomembrane-mimicking polymer (PMPC) and showed a significant decrease in capsular thickness compared to non-coated implants in rat models (Park et al., 2014). Zeplin coated silicone implants with recombinant spider silk proteins and showed reduced post-operative inflammation and fibrosis in rat models only (Zeplin et al.,