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EDITORIAL BIOENGINEERING

Scaffold-guide breast tissue engineering: the future of breast implants

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Since the introduction of the Dow Corning silicone implant in 1963, the history of breast implants has been far from smooth sailing. Silicone leak, implant rupture, infection, malposition and capsular contracture led to the US Food and Drug Administration (FDA) in 1992 restricting the use of silicone implants due to a lack of safety and efficacy data.[1] Since the early 2000s, implants have steadily returned to the market but are no less controversial.

Implant-associated autoimmune diseases, psychiatric illness and chronic fatigue have been described,[2] a link between textured breast implants and anaplastic large cell lymphoma has been identified and,[3] more recently, cases of implant-associated squamous cell carcinoma have been reported.[4] Meanwhile, patients undergoing autologous breast reconstruction are significantly more satisfied than women who undergo alloplastic reconstruction.[5] Women undergoing autologous fat grafting for breast augmentation report satisfaction rates in excess of 90 per cent,[6] though this approach involves multiple procedures to achieve the desired volume. Scaffold-guided breast tissue engineering (SGBTE) proposes implantation of a scaffold to support the survival and regeneration of grafted fat. The key engineering considerations include materials, mechanical properties and porosity.

Medical grade polycaprolactone (mPCL) is a biodegradable polymer that is FDA and Conformite Europeenne (CE) approved for implantation.[7] It has a known degradation profile[8] with no toxicity.[9] Degradation of mPCL does not stimulate a foreign body reaction. This fact, along with the porosity of the implant, means a capsule does not form and related complications can therefore be avoided. It is important to ensure that the degradation profile of the scaffold matches the rate of tissue regeneration within it so that structural integrity is maintained.

The scaffold must have mechanical properties that match the native breast but be sufficiently rigid to support regenerating tissue. External shear forces inhibit fat graft survival[10,11] and scaffolds can protect against this.[12,13] Rehnke and colleagues created scaffolds by hand using absorbable mesh shaped with nylon sutures and coated with fat graft.[14] No long-term outcome data were reported and the technique has not been successfully reproduced by others.[15] Scaffolds manufactured with 3D printing are consistent and permit tuning

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of parameters. This means that the scaffold can be customised to balance competing demands of mechanical support and porosity.

Scaffold porosity is essential. Large pores allow a substantially reduced implant weight for a given volume when compared with other implantable materials. Large pores also allow tissue ingrowth. This includes neovascularisation, which supports the injected fat graft and promotes formation of regenerate fat, as well as connective tissue that prevents implant migration or rotation.

We have successfully applied SGBTE in a large animal model. Scaffolds of 100–150 mL were implanted in pigs and filled with autologous fat graft. Over the ensuing 12 months, all scaffolds became filled with soft tissue.[16] We have clinically translated SGBTE for camouflage of pectus excavatum in a Phase I clinical trial with encouraging results.[17] In parallel, we recently opened a Phase I clinical trial for patients in whom removal of breast implants is indicated. They are offered SGBTE to restore volume following explantation. This has been successfully performed in three patients and early results are encouraging. Future human trials will investigate SGBTE in mastectomy reconstruction or after breast-conserving surgery (BCS).

While a scaffold provides mechanical protection, the mechanism by which grafted and regenerate tissues survive within it is not clear but likely related to vascularity. We have been able to sustain volumes of regenerate tissue in scaffolds of up to 200 mL, but the upper limit using non-vascularised fat transfer is not known. Volumes conducive to breast reconstruction are much greater than this and, accordingly, an animal study using 400 mL scaffolds is underway.

These new materials and manufacturing techniques offer opportunities to introduce therapeutic capabilities to implants such as elution of antibiotic or chemotherapeutic agents. The ability of mPCL scaffold to tolerate adjuvant therapy, including radiation, is untested. However, scaffolds may be well suited to newer radiotherapy techniques such as intraoperative radiotherapy (IORT). Scaffolds could be implanted after the administration of radiotherapy and designed to fill a specific, predictable volume after BCS.

It seems that a fresh approach to breast implant manufacture and materials is warranted. Modern manufacturing offers the potential to reduce morbidity and expand therapeutic capabilities.

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