Chapter

Meshes in Implant-Based Breast Reconstruction: The Science and Technology

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Abstract

Breast reconstruction is a common choice post mastectomy or breast-conserving surgery for breast cancer. Reconstructive options currently include implant-based and autologous reconstruction, with adjunctive use of surgical meshes. Acellular dermal matrices (ADMs) of both human and animal origin, and synthetic meshes are well-established for use in implant reconstruction. With ADMs, there is reduced risk of capsular contracture, providing a strong scaffold for prosthetic-based immediate reconstruction. Reduced seroma formation and infection has been demonstrated with synthetic mesh, thus both techniques proving advantageous. Use of mesh in implant-based reconstruction is a quickly evolving field, with hybrid meshes, 3D printed meshes and antibiotic-loaded meshes being investigated within the current literature. Whilst these surgical techniques are relatively new, they provide a new approach to many of the ethical issues currently surrounding use of surgical mesh.

Keywords: breast cancer, breast reconstruction, implant reconstruction, acellular dermal matrices, synthetic mesh, meshed enhanced hammock

1. Introduction

Breast cancer is one of the most prevalent malignancies in the UK, with 55,000 women and 370 men diagnosed every year in the UK alone [1]. Lifetime risk for women in the UK is currently one in seven, with breast cancer accounting for approximately 50% of all cancer diagnoses in women between the ages of 45–54 years old [2].

Breast cancer involves the breast tissue and may be invasive or non-invasive, with ductal carcinoma in situ (DCIS) being the most common subtype [3]. Current management for breast cancer in the UK may involve breast-conserving surgery or mastectomy, dependent on subtype and whether invasive disease is present [4]. Mastectomy is removal of the breast tissue and may be superseded by adjunctive radiotherapy, which has been demonstrated across the literature to reduce recurrence and mortality in women with lymph node involvement [5]. Following mastectomy, women may opt for delayed or immediate reconstruction, with the current trend in

England towards immediate reconstruction, of which implant-based reconstruction accounts for 53% of cases in the UK [6]. Autologous reconstruction is another method, which may use the extended latissimus dorsi flap and provides good reconstruction for small to medium sized breasts [7]. Alternatively, the deep inferior epigastric perforator flap (DIEP) is another surgical technique deployed in breast reconstruction since 1994 [8] with added advantages of reduced ventral hernias and muscle weaknesses, previously seen with the free transverse rectus abdominus myocutaneous (TRAM) flap. In the TRAM flap, the TRAM muscle is removed from the abdomen and used to create the breast shape, whereas the DIEP flap creates the breast shape from tissue from the abdomen, sparing the abdominal muscle. The perforators of the deep inferior epigastric artery and vein are taken with the tissue and connected to the internal mammary artery and vein in the breast, advantageous due to increased sensory return of the breast compared to device-based reconstruction [9].

In early implant-based reconstruction, the implant was placed subcutaneously under the skin flaps and then the trend moved towards placing the implant in a pocket underneath the pectoralis major muscle [10]. However, there has been a change back to subcutaneous prepectoral implant insertions with the more widespread use of ADMs. There were initially increased complications pre-operatively [11]. Typically, tissue expanders are used first to expand the pocket under the pectoralis major muscle through a subcutaneous fluid injection, as this pocket is usually not large enough initially to house an implant [10]. Once the pocket has enlarged, the tissue expander is replaced in a further operation by a fixed volume implant. Newer combined expander implants can be used which is performed as one operation, reducing the number of operations required, and have good outcomes similar to other reconstructive methods [12] with low complication rates [13]. With an ADM more surgeons use a direct to implant approach, negating the use of a temporary expander in the prepectoral plane [14, 15].

Use of mesh as an adjunct in breast reconstructive surgery has been shown to have many advantages, providing a scaffold for host revascularisation and repopulation of cells, extending the pectoralis major muscle and space for the implant, thus forming a natural inframammary fold at the base of the implants [16]. Mesh reduces amount of tissue dissection required during surgery as well as the incidence of capsular contracture [17]. Despite this, they are also known to increase risk of seroma formation, skin necrosis, infection, and come at a high financial cost [18]. In a bid to reduce costs, use of absorbable vicryl mesh, alongside acellular dermal matrix (ADM), has been reported as safe and may provide a method to reduce material costs, without loss to the patient in terms of outcomes [19, 20].

2. History and development

Mesh, also referred to as 'matrices' is widely used across surgery in many different disciplines, including in abdominal and perineal wall closures, hernia repairs, colposuspension and rectoplexies. Prosthetic material was first suggested as a method to repair hernia defects in 1890 by Billroth [21] with original materials including silver metal braided as a weave, which led to problems surrounding toxicity due to silver sulphate formation on their surface [22].

Non-metallic materials were first considered for surgical use to repair defects by Koontz and Kimberly in 1959 [23]. However, the authors agreed that non-metallic

materials may better fit the contours needing repair, thus should be considered in some circumstances [23]. Non-metallic materials including Dacron, Nylon and Teflon prove troublesome with infection, loss of tensile strength and rigidity [24], however tantalum gauze, a metallic material which used to be widely used in hernia repairs, escapes this. Marlex mesh was developed later, which had large pores thus incorporated well into tissue, with increased fibroblast activity and scaffold strength [25]. First generation meshes were introduced in 1998 and are based upon polypropene systems with large pores and small surface areas and are categorised into microporous, macroporous, and macroporous meshes with multifilament or microporous components [26].

Second generation meshes have increased tensile strength compared to their first generation counterparts [26]. They are composed of polypropylene (PP), polyester (PL) or expanded polytetrafluoroethylene (e-PTFE) combined with other materials such as titanium, omega 3, polyvinylidene fluoride (PVDF) and poliglecaprone 25 (PGC-25), and reduce formation of adhesions as the visceral and non-visceral sides of the mesh are specific to its function. The visceral side prevents adhesion through its microporous surface whilst the non-visceral side enables growth of parietal tissue through its macropores. Second generation meshes can be either absorbable or permanent.

The most recent development of surgical mesh encompasses those made from biological donor sources such as human dermis, bovine or porcine and greatly improve on the issues with second generation meshes, such as adhesion formation [26]. Human ADM was the first biological mesh produced and grafted well with tissues, with reduced rates of infection [27]. However, there are some issues with homografts, including increased risk of eventration, whereby a hernia forms at the same time as scars post surgery, with amount of stretch in the material also increasing over time [27]. Recurrence of hernias and fluid collections are also commonly seen after ADM use in abdominal wall reconstruction [28]. It has been thought in the literature that biological meshes reduce risk of capsular contracture when used in breast surgery, however have been associated with increased incidence of breast implant losses [29].

Matrices were first reported in the literature as being used in aesthetic breast revisions in 2003 to reduce rippling commonly seen with implant use [30], and in 2005 for breast reconstructions to reduce requirement for tissue expansion [31]. Following concerns raised by silicone-gel filled implants manufactured by PIP in 2010 [32], the safety of silicone-gel filled implants has been heavily investigated throughout the literature and they have been deemed as safe [33] and at present are the most common form of implant used in the UK for aesthetic breast augmentation [34] and breast reconstruction [35]. Matrices can be differentiated into biological ADMs and meshes [17]. ADMs are usually human, bovine or porcine derived and are soft tissue grafts containing only extracellular matrix after original cells are removed. They have been used in breast surgery since 2001, originally used for soft tissue coverage and as a structural scaffold for prosthetic-based immediate reconstruction [36] and utilise the prepectoral technique, described above (**Figure 1**) [37]. The patient's own cells will then revascularize the matrix, creating an additional tissue layer [17]. Contrastingly, there are synthetic meshes, which have comparable aesthetic outcomes to ADMs and are lower in cost [16]. Synthetic mesh has been used in breast reconstruction since 2005 with non-absorbable Mersilene mesh being the first [38]. Synthetic mesh is usually available as a sheet of plastic-like material with different

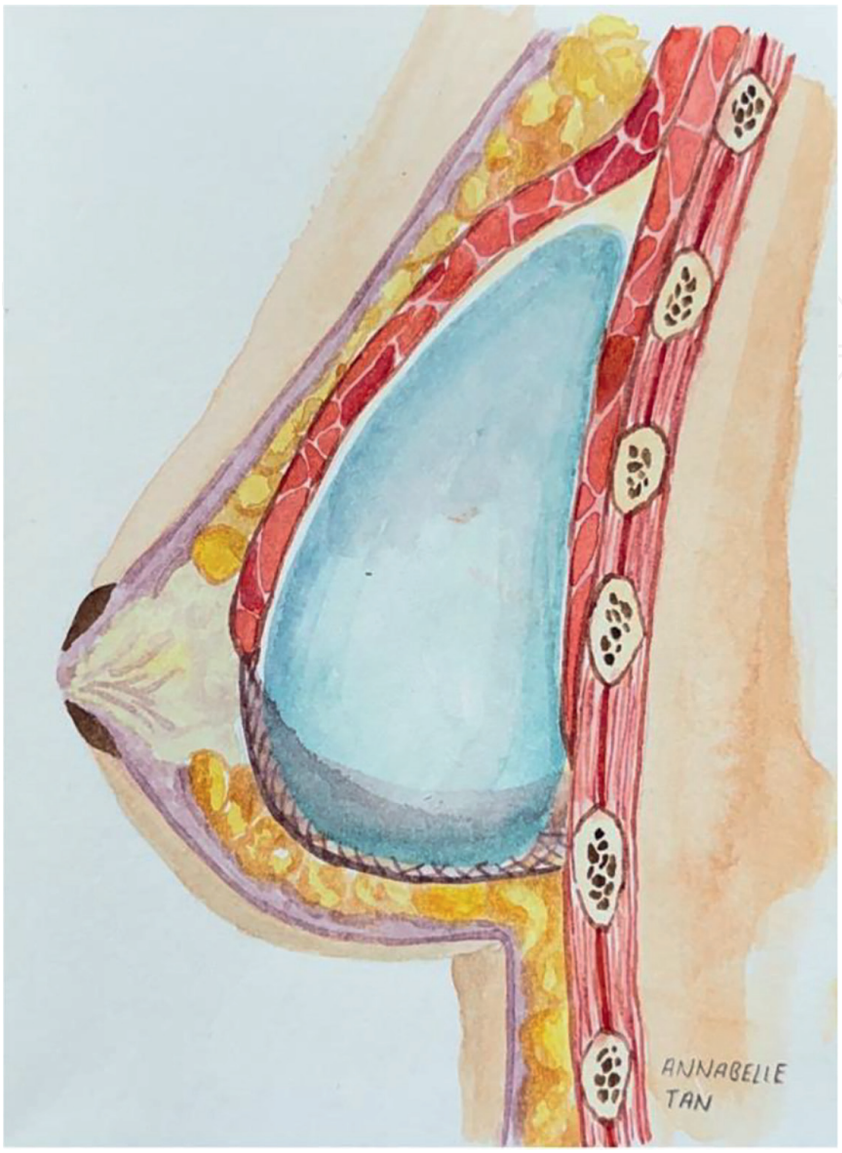
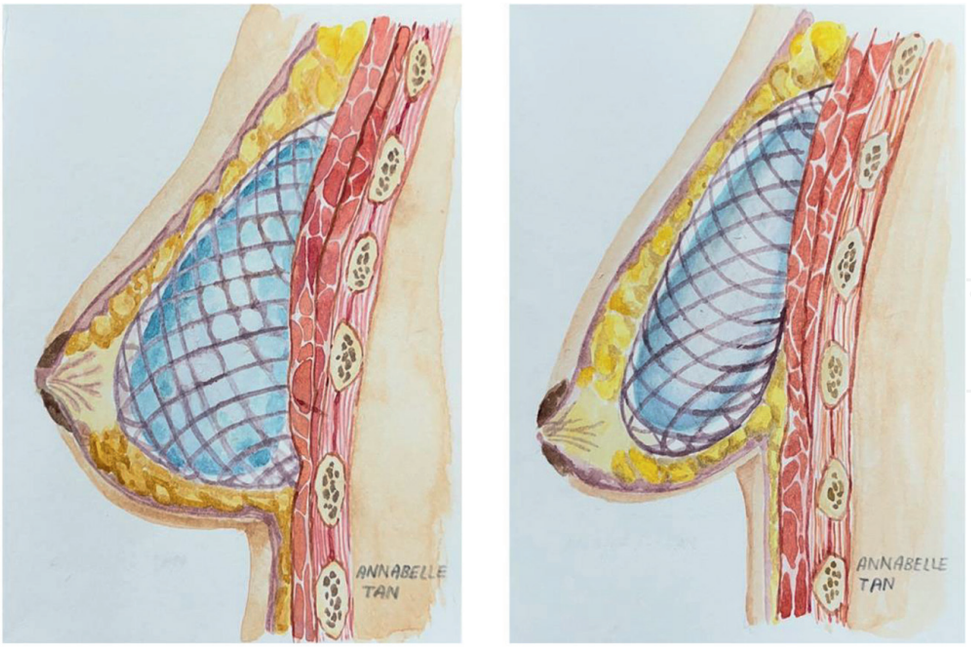


Figure 1.
Hand drawn image depicting subpectoral implant-based reconstruction [37].

sized pores dependent on mesh type, which affects how well the mesh is integrated into the breast tissue [39].

Within the prepectoral approach, ADMs can be used to recreate breasts when either a youthful appearance or ptotic breasts are desired, in a one-stage direct to fixed implant breast reconstruction [14]. The 'tent' technique, where the ADM is sutured to the pectoralis fascia can be utilised to create non-ptotic breasts; the 'enhanced hammock' technique allows for ptotic breast creation to recreate a similar breast where the alternate is already ptotic (**Figure 2**) [40], proving ADMs to be hugely versatile with regards to the final aesthetic appearance. The inferior free ADM edge is sutured a third up the implant edge on the pectoralis fascia, forming the 'hammock' [14]. Both of these techniques further promote a person-centred approach to implant-based reconstruction, with promising aesthetic results for patients due to superior breast symmetry.



A B

Figure 2.
Hand drawn image showing prepectoral 'tent' (A) and 'enhanced-hammock' techniques (B) [40].

3. Current types

3.1 ADMS

In the UK, single stage direct to implant using animal derived ADM products is the most common form of implant reconstruction [15]. ADMs may be human, bovine or porcine derived and are composed of original dermal collagen matrix, which functions as a scaffold for revascularisation by the host's tissues [41]. Common sources of tissue used in ADM products (**Figure 3**) [42] include skin, small intestinal submucosa, amniotic membrane and peritoneal membrane [42]. First used in burns patients in the 1990s, they are currently applied in plastic and burns reconstructive surgery, skin grafts, orthopaedic surgery and breast reconstruction [42]. Whilst costly initially, they have been shown to be a cost-effective surgical technique with lower cost at 2 years post surgery [43].

3.2 Synthetic

Synthetic meshes are also used in breast reconstruction and are produced from plastic-like material and may be absorbable, non-absorbable or a mixture of both. Generally, they are lower in cost to ADMs [20]. Some studies have reported reduced or no infection or seroma formation post surgery with synthetic mesh, with aesthetic outcomes and patient satisfaction comparable with both synthetic and biological mesh [16, 44]. Synthetic meshes have poor incorporation into host tissue, which is one drawback to this surgical technique; of all synthetic materials used in meshes, PL is reported as having better incorporation [16].

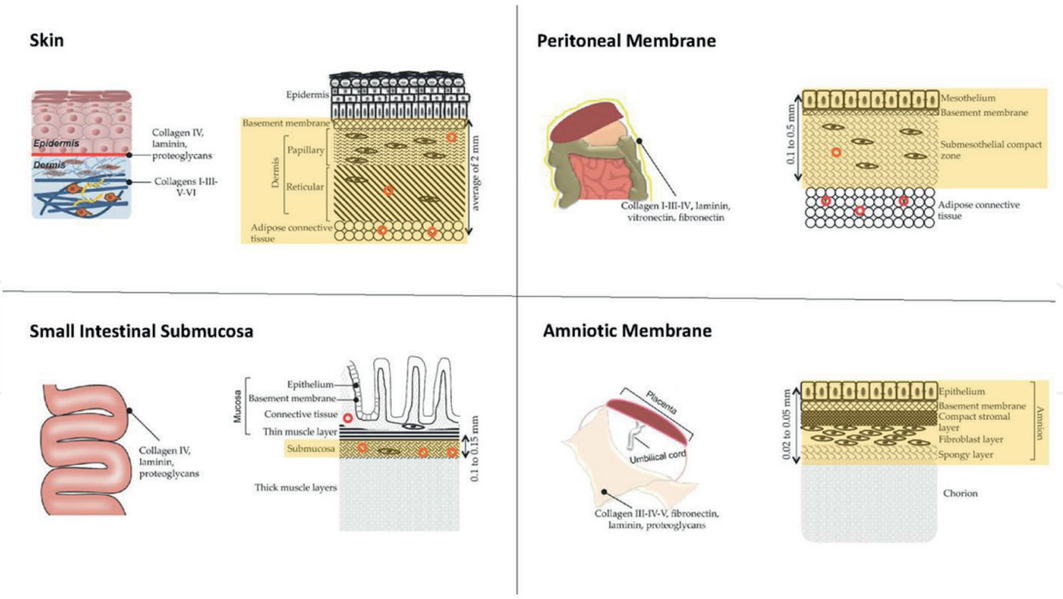


Figure 3.
Sources of ADM products [42].

3.3 Shapes

Meshes are available in different shapes, patches, plugs and sheets, all designed for various functions. Matrices may be knitted or woven; woven meshes have multiple parallel strands alternatively passed over and under another set of parallel strands, whilst knitted meshes are made using continuous loops of filaments [45]. Knitted meshes are the more traditional approach and are associated with increased post operative complications [46]. Patches and plugs are used in hernia repairs [26, 47], whilst flat sheet meshes are frequently used in implant-based breast reconstructions, notably sub-muscular and prepectoral reconstructions [48].

4. Indications

Popular indications for use of surgical mesh in breast surgeries are in implant-based total breast reconstructions post mastectomy, for patients with breast cancer or having risk reduction surgery, breast revision surgery, and surgery for congenital asymmetry or deformities. In the UK, biological and synthetic meshes have been used more frequently in ADM assisted procedures since 2013 [49]. Compared to traditional total submuscular techniques, mesh allows for better inframammary fold control and lower pole projection, with increased aesthetic results [50]. Synthetic meshes have been shown to be good substitutes for ADMs in aesthetic surgeries [51]. Lipomodelling is a more historical technique used to create symmetrical breasts in patients with congenital asymmetry [52]. Implants can be used in patients with amastia, uni-or bilateral absence of the breast and nipple-areola complex, Poland syndrome, where there is breast hypoplasia/aplasia and in tuberous breasts, where a fibrous ring blocks the radial development of the inferior mammary pole [53].

Risk reducing mastectomies may be chosen by women who are at higher genetic risk of developing breast cancer in their lifetime which may include those with the

BRCA1 or *BRCA2* genes or with a previous breast cancer diagnosis in the alternate breast [54] and is well reported as being the most effective way of reducing breast cancer risk in affected women [55]. *BRCA1* and *BRCA2* gene mutations increase a women's risk of breast cancer, with peak incidence at age 41–50 years in *BRCA1* carriers, and 51–60 years in *BRCA2* carriers [56]. For ovarian cancers, cumulative risk increases to 44% for *BRCA1* carriers and 17% for *BRCA2* carriers [56]. Risk reducing contralateral mastectomies have been illustrated as having a 48–63% survival advantage in patients with known *BRCA1* or *BRCA2* mutations [57, 58]. Implants may be placed prepectorally in these patients, and researchers argue that immediate reconstruction may be preferable to maintain self-esteem and aesthetic outcomes [55].

5. Complications

Common complications seen with surgical mesh use in breast reconstruction include infection, adhesion formation, capsular contracture and skin flap necrosis. Post operative adhesions can form after any type of surgery and carry increased risk of mortality and morbidity [59]. They increase operating time, as dissection can prove challenging, whilst can lead to patients requiring further surgeries to resolve [59]. There is currently poor understanding of the mechanism of adhesion formation with research suggesting the three main mechanisms include inhibition of extracellular and fibrinolytic degradation systems, an inflammatory response being induced by which cytokines and transforming growth factor-beta (TGF-beta) are produced, and tissue hypoxia, where vascular endothelial growth factor (VEGF) is expressed at increased levels [60]. Meticulous surgical technique is currently the gold standard prevention for adhesions, with liquid and solid anti-adhesive agents also able to be used, with limited evidence in laparoscopies [61].

Use of surgical mesh increases risk of site infection due to a prosthesis being introduced into the body, with risk post mastectomies being as high as 53% [62]. Notably, expander implants carried increased infection rates, compared to reconstructions using autologous tissues [63]. At present it is difficult to determine whether use of biological mesh in implant reconstruction leads to more complications [64], thus we must consider prevention of these complications. One trend to do this, is infection prophylaxis via antibiotics, alcohol-based skin preparation and pocket washout which feature in UK national guidance [15].

Capsular contracture commonly occurs post breast surgery due to an excessive fibrotic reaction to the foreign body known as the implant in the breast (**Figure 4**) [65], via an inflammatory response [66]. As a result, the collagen capsule that surrounds the implant contracts, distorting the breast tissue, and is categorised using the Baker classification system [67]. Class I describes a natural looking breast, II is a breast with minimal contracture, II, moderate contracture and IV, severe contracture [68] however recent literature reports poor reliability of this classification tool [69]. Capsular contracture can be caused by microbial biofilm formation [67], silicone or smooth implants, subglandular implant placement and prior radiotherapy to the breast [66]. At present, many techniques have been trialled to prevent and reduce risk of capsular contracture with breast implants post operatively, including use of biological and synthetic meshes adjunctively, anti-inflammatory and immune modulating drugs, anti-fibrotic drugs and antibiotics [65]. Physical modification of implants has been examined extensively and so research is now pointing towards pharmacological approaches in the hope that this will better reduce risk of capsular contracture.

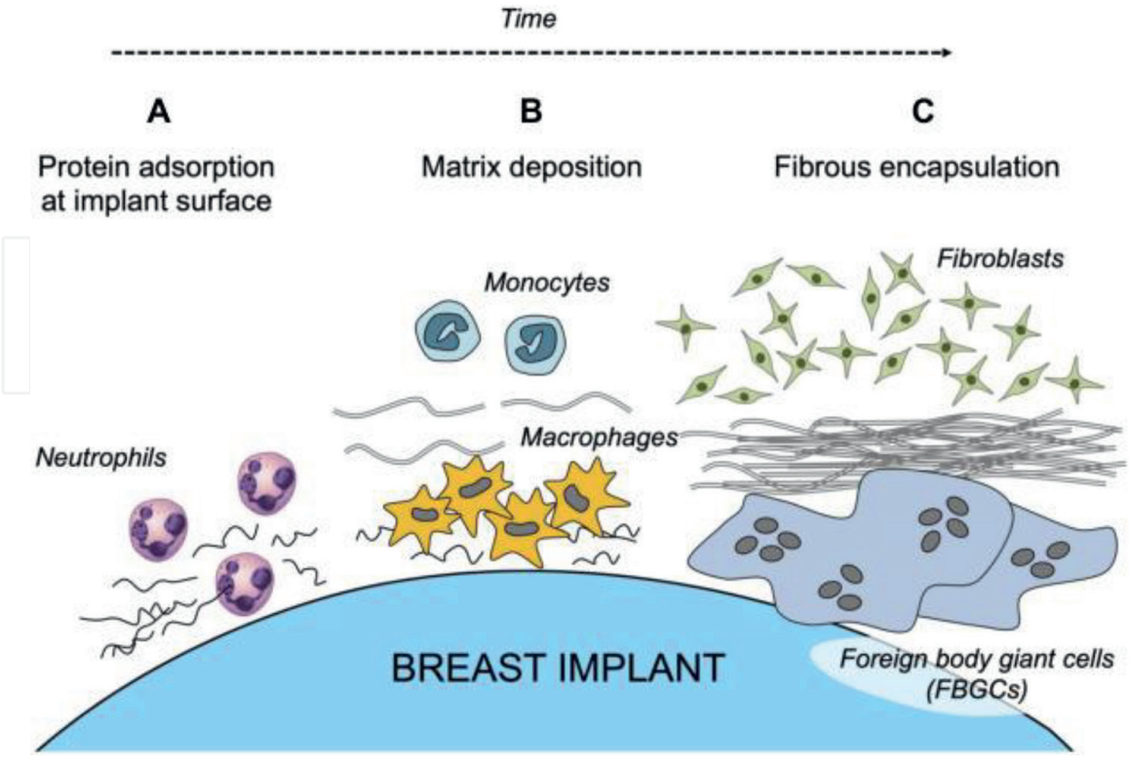


Figure 4.
Inflammatory response and foreign body reaction leading to capsular contracture [65].

Skin flap necrosis is another complication seen after implant reconstructions. Post mastectomy skin flap necrosis can lead to issues with wound management, infection of the implant and can look aesthetically displeasing [70]. The necrosis may be partial or full thickness and management can vary accordingly. Partial skin flap necrosis may require local wound care, whilst full thickness may need surgical debridement; it is known that adjunctive therapy such as chemotherapy or radiotherapy can be delayed if there is poor wound healing as a result of skin flap necrosis [70]. Risk factors for skin flap necrosis can include smoking, hypertension, increased breast volume [71–73]; modification of these pre-operatively may aid in reducing risk.

The long-term effects of the reconstructed breast, including breast symmetry, capsular contracture, infection rate, patient satisfaction, revisions and explantation rate are being evaluated in order to ascertain the long-term benefits and cost implications.

6. Future development

Surgical matrices are continually evolving, to suit the growing surgical requirements. Hybrid mesh, a mix of biological and synthetic materials are being explored further in the literature [27]. The combination is thought to combine the benefits of both materials, whilst reduce any complications they bring. Researchers believe that the biological part of the hybrid mesh, will protect the synthetic part from infection, and it is currently used in hernia repairs [27]. Hybrid meshes are seen as a cost-effective advancement in the field, with tensile strength of a synthetic mesh, but enabling for resorbable material to be used [74]. At time of writing, the literature presents us

with limited evidence of this mesh in clinical practice, however no differences have been found in complication and recurrence rates between patients where synthetic and hybrid meshes were used [75]. Further research is required to fully evaluate the long-term effects in patients.

Biological meshes, being animal derived, bring into question some ethical issues, notably surrounding religious beliefs [76]. Animal derived products have been used in surgery for many years and we know that as a society composed of multiple religions and faiths, that animal products may spark important conversations. Porcine is the most common form of animal derived mesh, with bovine being the most accepted by religious groups in England [76]. This study highlighted the importance of clinicians having knowledge of the origins of their surgical meshes used, and how their patients' religious beliefs, if any, may translate across.

3D printed meshes may aid in alleviating this issue surrounding religious beliefs for biological mesh. Synthetic materials which are both biodegradable and biocompatible may be used in future 3D printed meshes, and this method would allow for personalised meshes to be quickly created, specific to each patient [77]. 3D printed meshes have already been considered in vaginal surgery [78] and hernia repairs [79], and are now being considered for use in breast reconstruction [80]. They offer an innovative new technology for reconstructive scaffolds with personalised breast shapes and sizes able to be created at a low cost, with the pore structure of the mesh providing access for fat injection at the implant site postoperatively [81]. One paper has shown 3D printed scaffolds as able to regenerate breast glandular tissue [82], an exciting advancement for their use in breast reconstructive surgery; as such, 3D printed scaffolds could be used to facilitate flapless nipple reconstruction when seeded with autologous adipose tissue and implanted subdermally at the site of reconstruction [83].

Drug loaded meshes are another recent advancement in the surgical field. Multiple studies have explored local antibiotic loading into mesh for infiltration into the surgical repair site [84–86]. Antibiotic delivery directly into the surgical site, reduces and prevents related infection [84], with antibiotics loaded onto the mesh surface [87]. Rifampicin, vancomycin and ciprofloxacin are some of the many antimicrobials which have been trialled [85, 86, 88]. To date, antibiotic loaded mesh has been explored for use in hernia [89] and vaginal repairs [78]. Looking ahead, this may enable for further development of loaded meshes in surgery; notably, stromal cells have been loaded onto a breast scaffold in breast reconstructive surgeries which led to a longer lasting graft, with increased vascularisation [90]. Whilst antibiotics can be loaded onto meshes, meshes can also gain antimicrobial properties via newer, alternative methods such as metallic particles [77], which have shown promise in recent studies [91–93].

7. Summary points

- Matrices are used in abdominal and perineal wall closures, hernia repairs, colposuspension and rectoplexies and breast reconstructive surgeries
- They may be biological (human, bovine or porcine derived) or synthetic, and are available in many shapes and sizes
- Complications are low

- 3D printing may pave the way for alternative forms of surgical mesh in the future
- Research supports the use of matrices in implant-based breast reconstruction, with early data supporting low complication rates and better cosmesis. New studies currently are underway to evaluate prepectoral implant-based reconstruction with or without a matrix.

Conflict of interest

The authors declare no conflict of interest.

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