Chapter

Solutions in Breast Reconstruction

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Abstract

Breast reconstruction, after cancer surgery, is not only a reconstructive surgery but also an esthetic surgery. No woman should be expected to give up the breast tissue, which is the symbol of female identity, easily. The reconstruction stage after breast cancer is difficult enough in the early and late stages. It is generally not possible to cover the defect and to equalize the two breasts in a single step. General surgery and plastic surgery should work together. Recently, innovative solutions have been offered in breast reconstruction. Starting from skin grafts and local flaps, various flap options, dermal equivalents, fat transfer, and tissue expansion operations are among the options. Breast reconstruction is difficult enough in breasts that have undergone radiotherapy, and reconstruction with autologous tissue is preferred.

Keywords: breast reconstruction, breast surgery, oncoplastic surgery

1. Introduction

Breast reconstruction has become an important part of breast cancer treatment today. Its application with increasing frequency brings with it many innovations. Today, many techniques have been described in breast reconstruction. These techniques range from simple local flaps and implant reconstruction to free tissue transplants. The advantages and disadvantages of each technique bring many discussions on the subject. The timing of treatment is also an important issue of debate. In this study, we aim to present the current treatment options and the latest developments in breast reconstruction.

2. Autologous breast reconstruction

The main purpose of a reconstruction is to restore the damaged tissue as functionally and cosmetically as possible. Satisfactory results can be obtained by using autology tissues to attain this restoration. The main purpose is to restore the lost breast volume in patients who have undergone mastectomy, creating a new NAC if the NAC is not preserved, and creating a breast similar in shape to the other breast. Very satisfactory results can be obtained by using autologous tissues to provide it.

In general, breast-conserving surgery can be recommended for patients having tumors smaller than 3 cm. The treatment option is mastectomy in masses larger than 3 cm [1]. Removal of more than 10% of breast tissue has been determined to be associated with poor cosmetic results. In addition, masses in the central and lower quadrants have also been associated with poor cosmetic results [2]. Therefore, additional procedures may be required in cases in which more than 10–20% of breast tissue is removed.

We can consider our basic options in autologous breast reconstruction under the headings of local options, pedicle tissue transplantation, perforator flaps, and free tissue transplantation.

2.1 Local and pedicled flaps

Restoration by using existing breast tissues can be defined as local option. Breast tissue can be shaped or the missing breast volume can be completed, through local flaps or oncoplastic reduction [2]. Patient satisfaction can be increased by surgical procedures to be applied on the contralateral breast to ensure symmetry.

The first two flaps that come to mind are latissimus dorsi and TRAM flaps when it comes to pedicled flaps in breast reconstruction. The pedicled rectus abdominis muscle-skin flap in breast reconstruction was first described by Hartrampf et al. [3]. In this flap, the rectus abdominis muscle and the skin island on it are transferred to the defected area on the breast tissue over the superior epigastric artery. The biggest handicap of the flap is that the feeding of the superior epigastric artery is not occasionally sufficient [4]. Another handicap of the flap is weakness in the abdominal wall and long-term anterior wall hernias can be observed because the rectus abdominis muscle is used [5]. To overcome this situation, muscle-sparing TRAM flap, techniques in which anterior rectus sheath is preserved [6, 7] and DIEP [8] flaps are described. Studies have demonstrated that DIEP and muscle-sparing TRAM flaps have similar herniation rates [9]. However, there are also publications indicating that the DIEP flap has lower total-partial necrosis rates, and it is more reliable [10].

One of the biggest contraindications of the use of TRAM flap in breast reconstruction is that it got damaged to the internal mammary artery during mastectomy or it got injured previously. The superior epigastric artery is the continuation of this artery [11] and if it is damaged, the use of the superior pedicled rectus abdominis flap will not be possible. Likewise, if there are previous operations in the superior abdomen, it should be carefully investigated whether these arteries are damaged, and if there is damage, other alternatives should be considered.

TRAM flap continues to be a good pedicled tissue transplantation option, especially in patients for whom free tissue transplantation is not considered appropriate, since the tissue volume and skin island it provides are sufficient, it is a well-known and relatively safe flap, and it is simpler and more applicable than free tissue transplants.

Another frequently used option in pedicle tissue transplantation is the latissmus dorsi muscle flap. The flap, first discovered by Iginio Tansini in 1906, still maintains its popularity today [12]. This flap receives its blood supply from the thoracodorsal artery, which is the terminal branch of the subscapular artery [13]. This flap can only be used as a muscle flap or with the skin island on it as a muscle skin flap.

Unlike the TRAM flap in breast defects that require volume due to insufficient soft tissue volume, its use alone does not make it possible to achieve the desired results. That is why this flap is mostly used in combination with breast implants. However, it should not be overlooked that it can provide sufficient volume alone in cases such as small breast resections.

This flap with a pedicle of approximately 11 cm has a sufficient range of motion to close the breast tissues [14]. Another advantage of the flap is that it has a large surface area. The skin island can be designed in different sizes according to the needs [15]. It does not cause significant functional loss when the muscle is sacrificed [16]. It can be a good option for both simultaneous and late repairs.

Today, the frequency of use has decreased along with the development of microsurgery. However, it is still the most important option as a salvage flap in cases in which primary treatment fails. Therefore, it is important to preserve the thoracodorsal artery and the latissimus dorsi muscle as much as possible during breast reconstructions to have a safe second option in case of a possible complication. The fact that the learning curve is simple and it is an applicable flap easily is still a reason to be preferred by many surgeons.

2.2 Perforator flaps

Since it was defined by Koshima and Soeda [17] in 1989, perforator flaps have become one of the most popular topics in plastic surgery and their use is becoming more common day by day. Although its use in breast reconstruction is not as common as pedicled and free tissue transplants, its use in this field is also increasing. The biggest advantage of perforator flaps is that they do not require artery and vein anastomosis compared to free tissue transplants, so the application is easier and safer, and the donor site comorbidities are lower. However, the learning curve is longer than pedicled flaps and the surgical technique is more difficult. As they contain lower volume, they are generally more suitable for partial breast defects. Today, the most commonly used perforator flaps in breast reconstruction are the lateral intercostal artery perforator (LICAP) flap, thoracodorsal artery perforator flap (TDAP), anterior intercostal artery perforator flap (AICAP), and internal mammary artery perforator flap (IMAP) [18].

The LICAP flap is a good alternative, especially for use in lateral breast defects. Contrary to the TDAP flap, it is an important advantage to protect the pedicle of the latissimus dorsi while harvesting the flap. Some patients may have perforators arising from anastomoses between the intercostal artery and the serratus anterior muscle. If these serratus anterior perforators are used, a longer pedicle length can be achieved compared to LICAP [19]. The most dominant lateral intercostal artery perforators are usually observed in the 4–7 intercostal regions [20]. The flap skin island can be modified according to the existing defect, however, the borders of the 6 ribs and the inferior mammarian fold usually constitute the borders of this flap. The perforator is generally located at the level of the sixth rib and 2–3 cm posterior to the anterior axillary line [21]. In some patients, a vascular network consisting of intercostal artery perforators may appear in the dissection area. Pedicle dissection is typically more difficult in such patients [21]. The major disadvantage of the LICAP flap is that the donor site scar is visible in the lateral chest wall [21].

The TDAP flap is the most commonly used perforator flap in breast reconstruction [18]. It was first described in 1995 by Angrigiani et al. [22]. The TDAP flap has the same pedicle as the latissimus dorsi muscle flap. However, since the skin is only lifted over the perforator and the muscle is left intact, donor site complications are less [23]. It is a more difficult surgery compared to the latissimus dorsi flap, and its learning curve is longer than the latissimus dorsi flap. The borders of the latissimus dorsi muscle and the axillary artery are determined for the TDAP flap. Then, the perforators are marked with the help of a handheld doppler, and flaps are designed over the marked perforators. Skin island up to 15×25 cm can be included in the flap [24]. The thoracodorsal artery relatively always divides into two parts horizontal and lateral branches, approximately 4 cm distal to the inferior scapular border and 2.5 cm medial to the lateral border of the latissimus. The perforators leave these branches and reach the skin. Therefore, the design of the skin island on the lateral and upper border of the latissimus muscle facilitates the inclusion of perforators in the skin island while designing the flap [25].

The AICAP flap is harvested over the perforators of the anterior intercostal arteries. It is a relatively new flap. Its use in breast reconstruction was first described by Tenna et al. [26] in 2017. Intercostal artery perforators are commonly found in the thoracic region and supply the thoracic skin. There are more dominant perforators in the lateral thorax region. They were sparser and smaller caliber medially. Anterior intercostal perforators may be sufficient to feed a fasciocutaneous flap [27]. While designing the flap, the donor site scar can be designed to be hidden in the inframammarian fold [28]. In this way, a less visible donor site scar can be obtained. AICAP flap can be preferred especially in medial and inferior quadrant breast defects where LICAP flap is not preferred.

The IMAP flap is harvested over the perforator of the internal mammarian artery. The internal mammarian artery is mostly used as a recipient artery in breast reconstruction with free flaps. The IMAP flap can be lifted in dimensions up to 20 × 13 cm. The perforator emerging from the second intercostal space is usually the most dominant. If this perforator is small, usually one of the 1st and 3rd intercostal perforators is large enough to compensate for this [29]. There are few articles in the literature about IMAP flaps. In current articles, the use of this flap in thoracic wall reconstruction has been discussed [30, 31]. However, IMAP flap is an option that can be considered in medial quadrant defects.

2.3 Free tissue transplantation

With the development of microsurgical techniques and the increase in success rates, free tissue transplants are increasingly used in all areas of reconstruction. Today, one of the most preferred methods of breast reconstruction is free tissue transplantation. The most popular free tissue options for breast reconstruction are DIEP (deep inferior epigastric artery perforator) and TRAM (transverse rectus abdominis muscle) flaps. DIEP flap was described in 1989 by Koshima et al. [17]. Unlike the TRAM flap, its most important advantage is that it does not contain the rectus muscle. It is a less invasive technique because it does not involve the rectus muscle, and it is generally accepted among surgeons that it has lower donor site morbidity [32].

There are very detailed anatomical studies on DIEA perforators [33, 34]. According to these studies, DIEA perforators can be considered medial row and lateral row perforators. Medial row perforators are DIEA perforators that are close to the midline and have a wide perfusion field. These perforators are of a larger caliber than lateral perforators and can feed the contralateral medial half as well as the ipsilateral hemi-abdomen. Lateral row perforators typically lack anastomoses reaching the contralateral region and can feed the ipsilateral hemiabdomen. Therefore, larger DIEP flaps can be harvested by using medial row perforator [35]. Including more than one perforator in the flap may increase the success rate of the flap. It has been observed that fat necrosis is less common in DIEP flaps in which more than one perforator is included [36].

Flap size is another important parameter. As we mentioned earlier, different perforators have different perfusion patterns and are important in determining the boundaries of the flap to be removed. However, it is difficult to determine the exact borders of the flap due to the variations that can be seen in each patient. With the Indocyanine green angiography (SPY Elite System, Novadaq Technologies Inc., Toronto, Canada) method, the perfused parts of the lifted flap can be determined precisely and complications such as partial flap loss and fat necrosis can be prevented in the future [37]. With this method, Regardless of the perforasome concept, perfused flap tissues can be identified and modified as necessary before or after the flap is adapted to the recipient site.

Abdominal tissues are the gold standard in breast reconstruction with free tissue transplantation. However, in some cases, the use of abdominal tissues may not be possible. In such cases, we need to consider alternative flap options.

Superior and inferior gluteal artery perforator flap (SGAP-IGAP) is an important alternative in breast reconstruction. The SGAP flap is a flap that is harvested over the perforator of the superior gluteal artery, which is the terminal branch of the internal iliac artery [38]. These perforators are usually located on the imaginary line drawn from the posterior superior iliac crest to the greater trochanter. Perforators on this line can be found with the help of a handheld doppler and a flap can be designed to contain these perforators. Pedicle length can reach up to 12 cm [39].

The IGAP flap is also raised from the perforators of the inferior gluteal artery. The inferior gluteal artery, like the superior gluteal artery, is the terminal branch of the internal iliac artery. While the superior branch passes superiorly to the piriformis muscle, the inferior branch passes through the inferior border of this muscle [40]. While designing the IGAP flap, care is taken to conceal the donor site scar in the inferior gluteal fold. The perforators in this region are found and marked with the help of a handheld doppler. The flap is then designed so that the scar fits into the inferior gluteal fold and contains the perforators [39].

The most important advantages of these flaps are the absence of donor site scarring in visible areas and low donor site morbidity. Patients can be mobilized in the early period [39, 40]. They have sufficient pedicle length and volume. With all these advantages, the gluteal region is a good alternative to the abdominal region as a donor site.

Profunda femoris perforator flap (PAP) is another alternative for breast reconstruction. The profunda femoris artery passes between the adductor longus and pectineus muscles and reaches the posterior thigh, where it divides into two medial and lateral branches. The perforators of this artery are located on an imaginary line drawn from the ischium to the lateral femoral condyle [41]. While designing the flap, the superior border is drawn 1 cm below the inferior gluteal fold, and the inferior border is drawn approximately 7 cm below it. In this way, the donor site scar can be hidden in the inferior gluteal fold region [42]. The PAP flap is similar to the IGAP flap, but the longer pedicle and larger caliber make microsurgery easier [43].

Lumbar artery perforator (LAP) flap is another option. These perforators emerge between the erector spinal and quadratus lumborum muscles and feed the skin over them. This corresponds to approximately 5–9 cm lateral from the midline [44, 45]. Pedicle length may vary between 4.5 and 7 cm [46]. After deciding on the appropriate perforator, the axis extending from this perforator to the anterior iliac spine forms the axis of our flap, and a flap can be designed on this axis [47]. The pedicle of the flap is shorter than its alternatives, and its caliber is smaller than the internal mammarian artery, which is usually used as the recipient artery. Dissection is relatively challenging. However, donor site morbidity is low and can be removed as a sensate flap [46].

The Transverse Upper Gracilis (TUG) flap is a frequently used DIEP alternative flap. The pedicle of this flap is the gracilis branch, which leaves the profunda femoris artery. The anatomy of this branch is relatively stable and preoperative imaging is not recommended as standard. Dissection is easy. While designing the flap, the superior border of the flap is drawn 1–2 cm inferior to the inguinal crease to hide the donor site scar from the inguinal crease and inferior gluteal crease. Then, according to the pinch test, the inferior border is drawn to allow the primary closure of the donor site [48]. The most important disadvantage of this flap is that it has a higher donor site morbidity than perforator flaps [49].

3. Breast reconstruction with implant

Among the breast reconstruction options after mastectomy, the most commonly used method is implant-based reconstruction (alloplastic). In 2020, approximately 75% of reconstructive breast operations in the USA were performed through an implant [50]. Although the developing technology and surgical techniques have strengthened the surgeon's hand in reconstruction, these developments have also brought many questions to the agenda, such as stages of the operation (direct-two stages), implant type (silicone, saline, round, anatomical, polyurethane coated …), anatomical plan (total-partial submuscular, prepectoral), and use of ADM. To obtain superior esthetic results and successful surgical results in implant-based breast reconstruction, these questions should be evaluated and planned separately for each patient.

3.1 Direct-to-implant/2 stages

The traditional approach in implant-based breast reconstruction is the two-stage technique. In the first stage, controlled tissue expansion is completed after the placement of a temporary expander. Then, with the second operation, the expander is replaced with a permanent prosthesis. However, in recent years, the single-stage direct-to-implant method has come to the fore with surgical techniques, such as skin and nipple-sparing mastectomy, and especially with technological developments like the discovery of ADM [51]. The reason why this method is popular is the improvement of esthetic results with the use of ADM is the completion of the reconstruction process in one step with the direct placement of the permanent implant in the same session as the mastectomy. It is more cost-effective because it does not require additional surgical sessions [52].

Although the complication rates of the direct-to-implant method were previously thought to be higher, according to recent studies, no significant differences were observed in terms of complications when the two methods were compared [53, 54].

Candidates suitable for direct-to-implant reconstruction are patients with preoperative small-medium-sized symmetrical breasts and those who want the same breast size postoperatively. The most important criterion for a successful direct-to-implant repair is a good and robust blood supply of the skin flaps after mastectomy. If the skin flaps have insufficient blood supply or if a significant change in pre-postop breast size is planned, two-stage reconstruction should be considered [55].

3.2 Anatomical plan and soft tissue support

Preferable placements to place implants or expanders:

Prepectoral (subcutaneous).

Total submuscular.

Partial submuscular (dual plan).

The subpectoral placement was first preferred with the discovery of implants and their use in breast reconstruction [56], but over time due to the excess of major complications such as capsular contracture and implant loss, this was abandoned and the submuscular location was started to be used frequently [57]. In total submuscular placement, the pectoral muscle covers most of the implant, while the serratus muscle and/or fascia covers the lateral of the implant, and the rectus abdominis fascia covers the inferior depending on the need. The leading advantages of this technique include adequate soft tissue support and a well-blooded dressing, but animation deformity, muscle spasm, and associated chronic muscle pain are the negative aspects of total submuscular placement [58].

The discovery of supporting materials such as acellular dermal matrix and mashes made partial submuscular (dual plane) placement possible. After the pectoral muscle is dissected from its inferior and lateral borders and is elevated, the lower and lateral edges of the implant are covered with ADM. This method provides better esthetic results by providing adequate tissue support for the upper pole while allowing adequate expansion of the lower pole (**Figure 1**).

The prepectoral pocket has gained popularity again with the development of highly cohesive implants and ADM/meshes, by obtaining thicker skin flaps with better blood supply after changing mastectomy methods, and with improvements in autologous fat graft techniques [59]. The advantages of prepectoral placement include minimal animation deformity, less implant malposition, and less pain [58].

Although there are many studies on the advantages and disadvantages of pocket selection in the literature, a complete consensus has not been obtained. However,

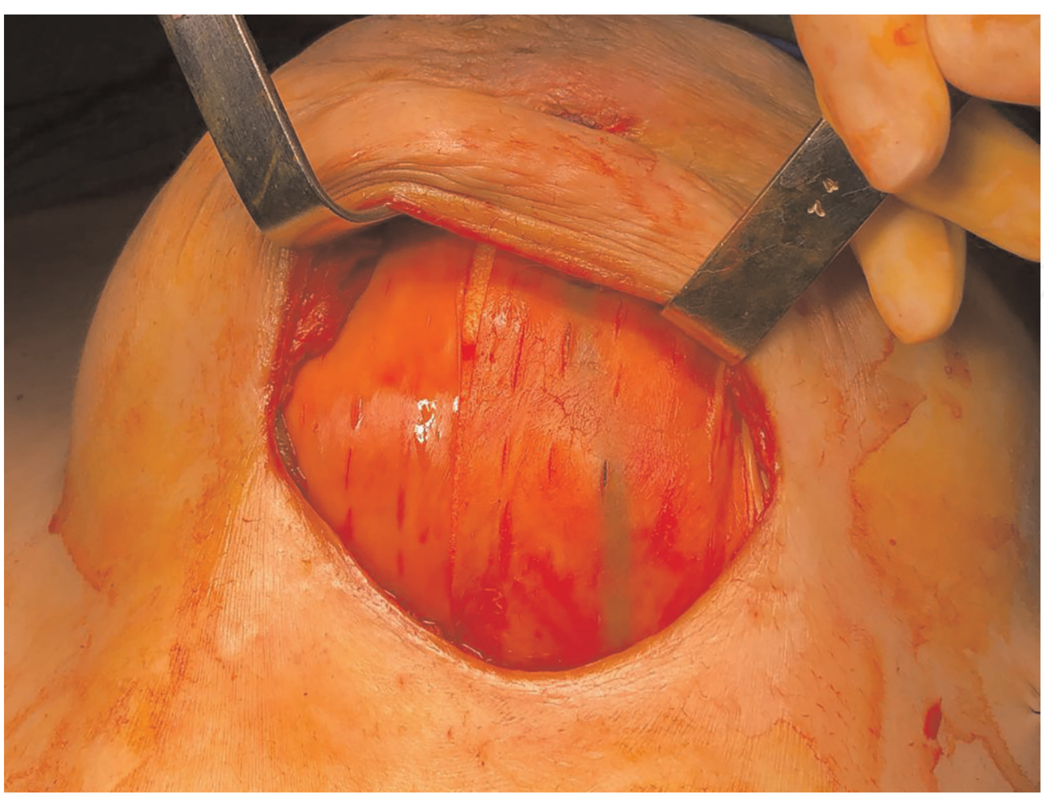

Figure 1.
Acelluler dermal matrix coverage on the inferior pole of the implant.

recent studies indicate that prepectoral pocket selection is similar to submuscular pocket selection in terms of complication rates. In a study by Ostapenko et al., prepectoral placement was demonstrated to be superior to subpectoral in complications such as capsule contracture, implant loss, and animation deformity, while complication rates such as infection, hematoma, and seroma were similar in prepectoral and subpectoral breast reconstructions [60]. According to another study by Bekisz et al., no significant difference was detected in the rates of complications such as skin flap necrosis, minor infection requiring antibiotics, hematoma, and the need for implant replacement in terms of prepectoral, dual plan, and total submuscular pocket choices [61]. According to a comprehensive meta-analysis study by Saldanha et al., the superiority of subpectoral-prepectoral and dual planes to each other in terms of complications could not be demonstrated in implant placement. There was only weak evidence that subpectoral and prepectoral location was associated with infection [62]. It is estimated that the breast reconstruction option with subpectoral implant placement will gradually increase in popularity due to the increase in studies that do not have a significant difference in terms of complications and shorter operation times.

3.3 Acellular dermal matrix

Implant-based breast reconstruction has gained a new concept with the use of biological and synthetic mashes. Acellular dermal matrix (ADM), a type of biological mash, was first used in direct-to-implant breast reconstruction in 2005 and has been increasingly preferred in breast reconstruction surgeries since then [63]. ADM can be used in direct-to-implant or two-stage expander/implant surgeries with submuscular or prepectoral placement. Many studies have indicated that the ADM is used as an inferolateral extension of the pectoralis muscle, by creating additional space and soft tissue support for the implant, filling the gap between the muscle and fascia, and creating a more natural IMF and a more esthetic lower pole [64]. In prepectoral repair, ADM is used to cover the anterior surface of the implant or to cover both the anterior and posterior surfaces of the implant to provide long-term soft tissue support [55].

In a 10-year prospective study by Ellsworth et al., breast reconstruction surgeries performed with ADM and without ADM were compared, and it has been observed that the use of ADM reduces capsular contracture, the amount of seroma is higher in patients who used ADM in the first year, and the rate of seroma between the two groups is similar on the 5th year. However, higher rates of infection were observed in repair with ADM [65]. According to another study, the use of ADM leads to an increase in complications such as infection, implant loss, reoperation, and re-admission to the hospital. Additionally, according to the same study, smoking, high BMI, operation time, and RT history are risk factors that increase complications in ADM use [66]. Another complication that should be known about ADM is Red Breast Syndrome. This syndrome is a clinical condition thought to arise from a hypersensitivity reaction characterized by non-infectious self-limiting erythema in patients undergoing breast reconstruction using ADM [67]. Although it usually resolves with time, it should be well differentiated from infection [67].

As a result, when we look at the literature, potential advantages include creating an additional implant cover, supporting the implant in the lower pole, providing faster expansion, emphasizing the breast contours and borders, and effects on capsule formation [68]. Although there are different findings, one of the most important factors for success in the use of ADM is the right patient selection.

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3.4 Implant selection

Breast prostheses are classified as saline/silicone gel according to their content, anatomical/round according to their shape, and smooth/rough/polyurethane-coated according to the sheath properties, and all of them can be used in breast reconstruction. Implant selection is made according to many factors such as desired breast size, pocket dissection, existing soft tissue support, and the dimensions of the contralateral breast if unilateral repair is to be made. Whether anatomical or round-shaped prosthesis will be chosen, the decision should be made by considering the width of the breast base, the shape of the chest wall, and the breast footprint on the chest wall when deciding on the size of the prosthesis, and the pocket dissection should be made to fit the selected implant exactly. This approach is essential for a successful reconstruction with a low complication rate.

Today, except for rare cases, silicon gel implants are generally used. Because anatomical highly cohesive gel implants have a higher ability to resist the forces exerted by the tissue, less rippling is observed [6]. These implants give better esthetic results, especially in prepectoral placement [55]. Many studies are comparing the advantages and disadvantages of anatomical-textured and round-smooth implants. In a prospective study conducted by Khavanin et al. [69], the use of anatomical and round implants in breast reconstruction was compared. According to this study, while the infection rates were found to be higher in patients who used anatomical implants, there was no significant difference between the two implant types in complications such as seroma, hematoma, capsule contracture, and explantation [69]. According to the same study, it has been shown that the use of round implants in unilateral repairs requires more operations to provide symmetry in the contralateral breast [69]. Anatomical implants provide better expansion and contour in the lower pole, better symmetry, and esthetics in the submammary fold, while round implants are better in providing upper pole fullness [70]. In terms of patient satisfaction, anatomical implants came to the fore with their more natural appearance and were evaluated negatively as being stiff and palpable, and round implants were found to be more satisfactory in terms of softness and volume [70]. Although it promises superior esthetic results, the biggest disadvantage of textured implants is the possibility of the development of implant-related anaplastic large cell (BIA-ALCL) lymphoma. This disease, a type of T-cell lymphoma, has been associated with implants with a textured surface [71]. In this disease, which presents symptoms such as late seroma, capsular contracture, pericapsular mass, and LAP, treatment consists of implant removal, mass eradication, capsulectomy, and chemotherapy in addition to surgery in some patients [72].

Another implant option in breast reconstruction is polyurethane-coated implants. The main advantage of polyurethane-coated implants is that the probability of developing capsular contracture is lower than with other implant coatings [73]. It is known that post-mastectomy radiotherapy is particularly associated with capsular contracture, and it has been shown that PU-coated prostheses have a low incidence of capsular contracture in patients receiving radiotherapy [73]. Another advantage of PU-coated prostheses is that they should adhere to the tissue. This is especially advantageous in breast reconstruction surgeries with prepectoral implants, in fixing the implant to the chest wall without the need for extra mechanical support [74]. As a result, although each implant type has advantages and disadvantages, the patient should be informed about the implant and the decision should be made by discussing it with each patient within the framework of expectations, possible adjuvant theory, and patient characteristics.

3.5 Tissue expanders

Reconstruction with the two-stage expander/implant method after mastectomy is the most commonly used breast reconstruction method [50]. In conventional tissue expanders, expansion is based on the inflation of the expander by serial percutaneous saline injections. This procedure, which can be performed in outpatient conditions, is uncomfortable for the patient, requires frequent hospital visits, and increases the susceptibility to infection. However, a new tissue expander system based on CO_2 has received FDA approval. In this system, the patient provides controlled inflation without the need for a needle by triggering the release of CO_2 from an internal reservoir with a wireless system with a remote control [75]. This new system has been shown to reduce the number of visits, the time required for full expansion, and the complication rates [75].

3.6 Conclusion

Implant-based breast reconstruction is still the most commonly used breast reconstruction method and will continue to be popular. It is possible to achieve all the aims of the reconstruction more esthetically, while changes are occurring in the surgical approaches established with the developing surgical techniques and medical devices.

3.7 Tissue engineering

Mastectomy and any surgical procedure that causes deformity in the breast leads to the idea that the woman is psychologically less sexual. The method of reducing this load is to provide reconstruction with a tissue close to the normal contour in form.

Tissue engineering and cell-based breast reconstruction options, when combined with surgery, are pleasing to the patient and physician.

It is especially enriched with stem cells and stromal vascular fraction (SVF), increasing the permanence of the fat, SVF; endothelial stem cells include pluripotent vascular progenitor cells, preadipocytes, and macrophages. Increasing skin quality with repeated applications is a desired result, especially in thinned skin after tissue expanders. It is a big problem that after the prosthesis, especially in breasts receiving radiotherapy, unwanted, third- and fourth-degree contractions around the prosthesis, impaired healing, lymphedema, and mastectomy flaps disrupt circulation and cause necrosis. For these reasons, cases of implant exposure are very common (**Figure 2**). In this way, it is possible to maintain the breast contour and keep the prosthesis in the proper position after the permanent implant is placed [76, 77].

As it is known, it is not always possible to replace a tissue loss with autologous tissue. The idea of reproducing that tissue using autologous cells was based on complications such as donor site problems and capsule contraction. In cases where reconstruction cannot be planned with sufficient and appropriate autologous tissue, products that resemble tissues and replace damaged tissue are used with innovative tissue engineering. The microenvironment and extracellular matrix (ECM) are important for stem cells [78]. In terms of ECM, platelet rich plasma (PRP) contains especially sufficient growth factors. In summary, with the signaling of growth factors, proliferation and differentiation between cells begin. Aside from the use of recombinant proteins as scaffolds in tissue engineering, it is only possible in cellular-based productions without a scaffold [79]. Cellular-only approaches without a biocompatible scaffold have a low chance of success [77]. Because, with the ideal scaffold

Figure 2.
Exposed implant on the left breast.

selection, natural tissues can be created that accurately mimic tissue in vivo, allow vascular ingrowth, and allow a porous and 3-dimensional microenvironment. In this way, biomaterials that remain intact until tissue is formed for a sufficient period but degrade at the appropriate time can be developed [77, 80]. Degradation must occur at the right time for tissue regeneration and the formation of new ECM [81].

Biomaterials can be obtained not only from humans but also from animal or natural sources. They are distinguished from synthetic materials in that they are incorporated into the host tissue during the natural degradation process. The main task of biomaterials is to act as a biophysical and chemical medium to enable cellular response. As biocompatibility increases, biointegration and vascularization increase. In the same environment, cells adhere, multiply, and differentiate appropriately. Anti-inflammatory cytokines are still released but result in a minimal foreign body reaction [82, 83]. Natural biomaterials used in adipose tissue engineering are primarily silk, alginate, collagen, and gelatin. Natural biomaterials can be combined with various biomaterials and their mechanical properties can be formed with different forms of cross-linking. Among the synthetic biomaterials, polyglycolic acid, polylactic acid, and polycaprolactone can be listed [83]. It is easy to add ECM and growth factors to synthetic components, so their use in tissue engineering is gaining momentum. Scaffolds in general; hydrogels, sponges, bioprinted or 3D structures, or electrospun scaffolds [83, 84]. The fact that the scaffold is hard is important in terms of providing structural integrity and imitating the natural tissue it has changed and being porous in terms of removing cellular wastes. The biggest problem in scaffolds consisting of synthetic components is the removal of harmful by-products formed after decomposition. Therefore, hybrid scaffold models containing both synthetic and natural components have been recently started to be studied to benefit from the strengths of both sides. Biological interactions are required to facilitate the natural secretion of proteases and cell migration [85]. Studies are showing that there may be a connection between these mechanical properties of scaffold and mesenchymal cell differentiation.

Nipple areolar complex (NAC), reconstruction; women's body image and patient satisfaction are more difficult, and the advantages of 3D-printed NAC have been emphasized recently [86]. In terms of adipose tissue regeneration, especially hydrogels are advantageous because their ability to mimic the extracellular matrix is very strong [80, 87].

3.8 Fat injection

As it is known, breast tissue is a common component of glandular tissue and adipose tissue. The most important problem encountered in replacing the formed defect with only fat is the inability to maintain resorption and adequate volume. Adipose-derived stem cell (ADSC) is widely used in breast reconstruction for both the awakening of autologous tissue sensation and contour correction after implant placement. When fat is enriched with ADSC, these cells can transform into new adipocytes, thus producing biocompatible, nonimmunological tissues. Likewise, studies are showing that the addition of SVF further increases angiogenesis in terms of interaction between endothelial precursor cells (**Figures 3**–**6**) [80, 88].

Studies continue to determine whether these cells increase the risk and recurrence of cancer with their secondary paracrine and autocrine effects after fat injection into the breast, which has become increasingly popular because it is more physiological [76, 78]. Insufficient follow-up time and the lack of clinical cases due to biases are among the study barriers.

Figure 3.
Fat ready for injection after centrifugation.

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Figure 4.
Fat injection into the breast.

Figure 5.
Fat enriched with the stromal vascular fraction.

Figure 6.
Cell counter device.

It is accepted that fat injection should be done in the form of repetitive injections, rather than a sufficient amount in a single session in breast reconstruction. It should be kept in mind that the formation of sebaceous cysts and microcalcifications after excessive injections may lead to misleading results in the follow-up of malignancy [76, 80, 89].

3.9 Acellular dermal matrix

The main use of ADM in breast reconstruction is to provide more support and to minimize ripling and implant exposure. Especially in post-tissue expander implant applications, wrapping the implant with ADM reduces the frequency of complications compared to the traditional technique.

The aim is to improve scaffold fabrication techniques, increase tissue similarity and compatibility, and find inexpensive means of obtaining and selling. In this way, the frequency of use can be increased.

Concurrent contralateral mastectomy rates have also increased with breast-conserving surgery. In general, the favorite approach is to place the implant in the pouch designed in the subpectoral plane, still in the reconstruction phase. In this way, while sufficient muscle tissue covers the upper pole of the implant, the implant contacts the skin at the inferior pole, and after a while, the expansion mechanism thins the skin and prepares the ground for exposure [90]. In addition to the development of implant technologies in recent years, the use of ADM has decreased the exposure rate by increasing the safety of the implanted pouch. At the same time, it supports single-session approaches by providing contour regularity [91]. Closing the subpectorally placed implants by suturing ADM to the inferior wall of the pectoral muscle provided more esthetically meaningful results. Another advantage of ADM in

Figure 7.
Prevention of expansion with polypropylene mesh.

Product	Material	Company	FDA
Alloderm	Human	Life Cell Corp.	Approved
Allomax	Human	CR Bard/Davol Inc.	Not approved
Dermacell	Human	LifeNet Health Inc.	Not approved
Flex HD	Human	Ethicon Inc	Approved
Permacol	Porcine	Medtronic	Approved
Strattice	Porcine	Allergan	Approved
Surgimend	Bovine	Integra Life Scienes	Approved
Veritas	Bovine	Synovis	Approved
Vicryl Mesh	Polyglactin	Ethicon Inc	Approved

Table 1.
ADM products in breast reconstruction.

breast reconstruction is improved tissue expansion and increased volume. In addition, ADM itself can produce a fibrotic reaction. Studies on the reasons for this focus on dead space between the flap and ADM, formation of seroma, placement in an infected area, or insufficient perfusion [84]. In titanium-coated polypropylene meshes, the chance of tissue expansion is lower due to the stretch of the polypropylene (**Figure 7**) (**Table 1**).

4. Conclusion

After breast cancer and nipple-sparing surgical approaches became active, cosmetic expectations have increased even more. The introduction of ADM, especially in the sense of emergency breast reconstruction, has been groundbreaking. Despite its complications such as infection and seroma, ADM is successful in its use with well-fed flaps that cover it. The main problem is economic, although it is human-induced, which is more flexible in the choice of ADM.

In terms of psychological recovery and patient satisfaction, the use of ADM and biomaterials among the reconstruction options close to breast normal tissue and appearance is becoming more common with contributions to the literature. It is possible to contribute to breast volume and increase skin quality in the early and late periods with fat injection into the breast. What is discussed at this stage is what can be done additionally for fat survival.

3D printer technology aims to produce serial and personalized bioprints at low cost and to make them widely used in clinics. With biomaterials produced in this way, it may be possible to minimize volume loss by increasing the vitality and vascularity of fat cells injected for breast reconstruction.

5. Reconstruction: when and how?

One of the most controversial issues in reconstructions after breast cancer diagnosis is the timing of surgery. In any case, the most important issue to be considered is that the patient can start oncological treatment as soon as possible if needed. It is recommended to start adjuvant radiotherapy within 8–12 weeks after the surgery. Late radiotherapy is determined to have a risk of recurrence [92].

This situation leads us to the following question: Would the reconstruction be performed together with tumor surgery or the reconstruction after the completion of oncological treatment (especially chemoradiotherapy) would be more appropriate?

The most important factor in choosing early or late treatment is whether the patient needs radiotherapy or not. Some of the publications in the literature state that the complication and success rates in patients who underwent simultaneous repair and received RT are close to or at an acceptable level when compared to late repair [93–96]. There are some publications stating that early repair has more successful results [97]. However, many publications show that simultaneous repair is associated with a higher risk of complications than late repair in patients who will receive radiotherapy [98–101].

When the advantages of early treatment are stated, one of these advantages is that it does not require additional surgery, and it is a relatively easy surgery because it is performed before the tissue damage is caused by radiotherapy. The most important disadvantages are that a possible complication may delay the patient's receiving radiotherapy and additional complications may occur with radiotherapy. The general belief is that although there may be a delay in initiating RT treatment due to complications from time to time, the simultaneous repair usually does not cause a delay in initiating RT [102]. Simultaneous repair may be a good alternative, especially when autologous reconstruction options are preferred [93, 96].

The biggest advantage of the delayed treatment is that RT treatment has been completed and the reconstruction can be spread throughout the process. The most important problem is that the tissues damaged after RT make surgery significantly more difficult, and patients who have had mastectonia spend a long time until they have definitive reconstructive surgery.

In the statement published by the Oncoplastic Breast Consortium [103], some current recommendations were included.

If late repair is performed, definitive surgery should be performed at least 6–12 months later.

Waiting 6–12 months for fat graft applications.

Concomitant repair may affect the onset of RT in some patients, however, it generally does not cause a delay in the onset of therapy.

RT is not an absolute contraindication for simultaneous implant repair, but it has a higher risk of complications.

The fact that the patient will receive chemotherapy is another factor affecting the chance of success. Different chemotherapeutic drugs have been demonstrated to have different complication rates [104].

If the patient has advanced breast cancer such as inflammatory breast cancer, it would be better for patient safety to wait at least 1 year from the completion of treatment and confirm that there is no recurrence [105].

Many surgeons also have reservations about fat graft applications. The idea that the adipose stem cells contained in the fat graft may stimulate the proliferation of cancer cells makes many surgeons hesitant in the application of fat grafts. However, studies indicate that fat graft applications do not increase recurrence and metastasis [106].

Another drawback of fat grafting is that it may complicate the radiological follow-up of the patient. However, in general, the abnormal radiological images encountered in these patients are observed far from areas containing fat grafts, and it is most likely due to changes that occur as a result of surgery rather than fat grafting [107].

Conflict of interest

The authors declare no conflict of interest.

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