Rezumat

Reconstrucția imediată versus reconstrucția întârziată a sânului pentru paciențele cu mastectomie. Controversie și soluții

Reconstrucția de sân implică două decizii majore: alegerea momentului optim și a tehnicii adecvate de reconstrucție pentru fiecare pacientă, luând în considerare complicațiile și riscurile care pot rezulta în urma acestor decizii. Prin selectarea atentă a pacientelor și individualizarea reconstrucției de sân, riscurile și complicațiile acestei proceduri pot fi minimitizate, cu rezultat estetic bun și satisfacție ridicată în rândul pacientelor. Reconstrucția de sân poate fi realizată prin 3 modalități distincte: reconstrucția imediată – la momentul mastectomiei, reconstrucția secundară – la finalizarea tratamentului adjuvant și reconstrucția imediat-întârziată care utilizează ambele metode precedente – include expansiunea tisulară la momentul mastectomiei și reconstrucția definitivă la finalizarea tratamentului adjuvant. Strategiile perfeccionate timp de decenii în chirurgia reconstructivă a sânului au făcut posibilă reconstrucția imediată a sânului oferind pacientelor șansa de a se recupera după o intervenție de mastectomie cu un nou sân reconstruit. Deși nu toate paciențele aleg reconstrucția sânului, procentele celor care optează pentru reconstrucție sunt în continuă creștere, iar tehnici noi și îmbunătățiri se dezvoltă rapid.

Cuvinte cheie: cancer de sân, mastectomie, reconstrucție de sân, conservarea țesutului cutanat, implant mamar
Abstract
When considering breast reconstruction, two main decisions have to be made: optimal timing and appropriate reconstruction technique, that would best suit each patient, while also taking into consideration the complications and risks that these decisions might lead to. By careful patient selection and individualized breast reconstruction approach, the risks and complications of the procedure can be minimized, while attaining successful aesthetic outcomes and high patient satisfaction. Breast reconstruction can be performed in three different settings: immediate reconstruction at the time of mastectomy; delayed reconstruction — after the completion of the adjuvant treatment and in a delayed-immediate setting that uses both previous methods — includes tissue expansion at the time of mastectomy and definitive reconstruction performed after completion of the adjuvant treatment. The strategies perfected for decades in breast reconstructive surgery have now made breast reconstruction more possible than ever, thus offering patients the chance to recover after a mastectomy procedure with a new reconstructed breast. Although, the choice of breast reconstruction is not addressed by all breast cancer patients, rates are gradually expanding while new and improved techniques are rapidly developing.

Key words: breast cancer, mastectomy, breast reconstruction, skin-sparing, breast implant

Introduction
Presently, breast reconstruction is considered an important step in the management of breast cancer as it not only brings shape to a new breast, but restores the patient's body image and quality of life, while reducing the psychological anxiety that a mastectomy procedure causes (1,2,3). Although the subject of delayed versus immediate breast reconstruction is still controversial, many studies have found that immediate breast reconstruction is oncologically safe for carefully selected patients (1,4,5,6).

Until 1980, breast reconstruction was considered oncologically safe only when 2 or more years had passed after the mastectomy (7,8). Presently, although notable advancements have been made in both immediate and implant-based breast reconstructions, the proportion of delayed reconstructions is still superior to the immediate procedures performed at the time of mastectomy. Moreover, there is a tendency for larger hospitals with high number of patients to perform more immediate reconstructions, as surgeons perform it on a regular basis (9). Accordingly, statistics prove that there is an annual 5% increase in the rate of immediate breast reconstructions, with 37.8% of reconstructions being reported in 2013 as immediate (10).

Currently, the management of breast cancer treatment and reconstruction includes new directions like bilateral and prophylactic mastectomy, as well as skin-sparing and nipple-sparing mastectomy which are frequently performed in an immediate reconstruction setting. At the same time, the indications for radiotherapy have been extended for some patients with early breast cancer (11), in the detriment of immediate breast reconstruction surgery, leading not only to better technique and planning for radiotherapy adjuvant treatment, but also to improved algorithms for implant-based and autologous breast reconstructions (12,13,14,15,16).

Pitfalls and Solutions for Choosing the Optimal Timing and Technique for the Breast Reconstruction Procedure
Patient selection is of great importance when deciding the optimal timing for the breast reconstruction. Whether a patient's breast reconstruction is delayed or immediate depends upon a multitude of variables that
have to be considered like: cancer stage, tumour size and location, status of the axillary sentinel lymph node, smoking habit, body constitution, history of previous surgeries and radiotherapy, planned radiotherapy or chemotherapy, existing comorbidities and the patient’s informed preference (11,17).

The main issue that interferes with immediate breast reconstruction is the uncertainty of post-mastectomy radiotherapy, which if required can lead to significant risks and complications. Generally, patients who are eligible for immediate breast reconstruction are diagnosed with stage I breast cancer, have a good cancer prognosis, a negative sentinel lymph node and no supposed requirement of axillary lymphadenectomy surgery or radiotherapy treatment (11). Some patients with stage II and most patients with stage III of breast cancer have a high risk for postmastectomy radiotherapy and current guidelines recommend breast reconstruction in a delayed or delayed-immediate setting for this category of patients (11).

Still, there are certain preoperative investigations that can better assess the radiotherapy requirement in some of the stage II patients, thus allowing them to benefit from an immediate breast reconstruction. The most accurate investigation that can predict radiotherapy, remains the lymphatic mapping with sentinel lymph node biopsy performed preoperatively which can guide the decision making process for immediate breast reconstruction (18,19,20). Also, a matter of debate is the radiotherapy indication depending on the number of positive lymph nodes (18,21,22,23). There is a generally accepted indication for radiotherapy when 4 or more lymph nodes are involved, but in 85% of patients a positive sentinel lymph node may be the only positive lymph node present.

Moreover, recent studies have proved that to better prevent locoregional recurrence and improve survival rates, radiotherapy should also be considered for patients with one or more positive lymph nodes (24,25,26,27,28). Generally, if a positive sentinel lymph node results at the preoperative investigations, then radiotherapy is predicted and it is recommended to avoid an implant-based or definitive autologous reconstruction and opt for the placement of a tissue expander at the time of mastectomy, in a delayed-immediate setting. In spite of these assessment methods, the absolute indication for radiotherapy is provided only after the definitive pathologic exam, as the tumor extension inside the breast parenchyma is another point to be considered when deciding the need for radiotherapeutic protocol (11).

Main Principles and Controversies for Breast Reconstruction Surgery Associated with Radiotherapy

In spite of the advancements made, outstanding results are difficult to achieve in immediate implant-based reconstructions followed by adjuvant radiotherapeutic treatment. The reconstruction challenges that arise after a radiotherapy treatment are determined by the various tissular transformations it causes as intense fibrosis and compromised vascular perfusion that eventually lead to a wide range of complications (29).

It is generally believed that patients who are considered for postmastectomy radiotherapy are better served by delayed reconstruction, as immediate reconstruction could influence not only the aesthetic outcome but also the delivery of radiotherapy (30). Firstly, the aesthetic complications that might arise after radiotherapy performed on a reconstructed breast include capsular contracture and fibrosis as reported by Javaid (31), but also implant loss, fat necrosis and architectural distortion as reported by Kronowitz (32). Nevertheless, in a study performed by Parsa who compared results for bilateral breast reconstruction patients who received radiotherapy unilaterally and implant-based breast reconstructions bilaterally, it was proven that in cases where the skin modifications caused by radiotherapy were low to moderate, final results of implant-based breast reconstructions were similar in the irradiated and the nonirradiated breast (33,34). Consequently, implant-based breast reconstruction is not a complete contraindication in patients receiving radiotherapy (35) and good results can be obtained with additional
fat grafting procedures, but it is usually recommended to opt for an autologous breast reconstruction for patients with moderate to severe skin flap changes following radiotherapy (34,36). Secondly, there is the issue of compromised delivery of radiotherapy, especially to the internal mammary lymph nodes and chest wall (37), caused by the interposition of a flap or implant as proved by Motvani in 52% of patients with immediate breast reconstruction and argued by Koutcher (38) who found a 97% control rate for a 30-months period. Although, traditionally believed that an immediate or delayed-immediate breast reconstruction with tissular expansion at the time of mastectomy can negatively influence the delivery and dosimetry of the radiotherapy treatment, numerous studies have currently demonstrated otherwise and this issue is no longer considered in the decision-making process (18,39,40,41,42).

We believe that although implant-based breast reconstruction is easier to achieve, in patients that receive radiotherapy treatment, autologous reconstruction should be considered as a first-line reconstructive option. This approach avoids the complications of immediate implant-based reconstructions like capsular contracture, implant infection and extrusion and grants for a more natural and aesthetic outcome of the reconstructed breast. Nevertheless, this option should be assessed in the light of the patient's informed wish as well as taking into account any additional comorbidities and risk factors that could limit a patient's ability to undergo complex breast reconstruction procedures (1).

**Immediate Breast Reconstruction**

Immediate breast reconstruction has been reported by numerous studies as a safe and viable procedure for patients that are not considered for adjuvant radiotherapeutic treatment. The main advantages include the aesthetic outcome determined by a well-preserved skin envelope which grants a more natural shape and contour to the reconstructed breast (43) and the psychosocial well-being that an immediate breast reconstruction can bring to a patient in the postmastectomy stage (Table 1).

Implant-based breast reconstruction, although a controversial field, is the most frequently performed breast reconstruction, with 75% of all breast reconstructions performed in the USA being implant-based (44).

This high demand is caused by a multitude of factors like the increase in number of both curative and prophylactic mastectomies in the context of surgical technique refinements like nipple-sparing or skin-sparing mastectomy (45), improvements in bioprosthetic technology and new tissue substitutes with predictable and better aesthetic outcomes (Fig. 1).

Implant-based breast reconstruction can be performed in an immediate one-stage setting with a direct to implant technique or a delayed setting for which a tissue expander is placed in a subpectoral pocket and once adequate expansion has been achieved can be replaced with a definitive implant.

Most frequently, implant-based breast reconstruction is an appropriate option for

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<th>Table 1. Advantages of immediate implant-based breast reconstruction (1)</th>
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<td>1. No donor site morbidity or additional scars</td>
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<td>2. A single-stage surgery at lower overall costs</td>
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<td>3. Short surgical time and recovery</td>
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<td>4. Psychosocial benefit and faster social reintegration</td>
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<td>5. Similar color, texture and sensation of the skin flaps</td>
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Figure 1. Skin-sparing bilateral mastectomy with immediate bilateral implant-based breast reconstruction
patients with small to moderate sized breasts and low degree of ptosis. Also, additionally to the implant a tissular substitute like a biological matrice or synthetic mesh can be used for support (17). Further, when deciding upon a breast reconstruction technique, it is always important to establish preoperatively the patient’s expectations of contour, sensation, firmness and consistency of the new-breast as these factors can sometimes lead to reduced patient satisfaction in an implant-based breast reconstruction (47).

Although implant-based breast reconstruction is the most widely used reconstructive procedure, studies worldwide have proved that this approach presents with higher complication rates than autologous reconstructions (48) (Table 2). Implant-based breast reconstruction complications can be the result of variable local risk factors like very large breasts (> 750 g), increased length from sternal notch to nipple (> 26 cm)(49), high implant volume (> 400 ml) (50), along with systemic factors like type 2 diabetes, obesity (51), hypertension, smoking status and an age greater than 65 years (52). Besides, Tamoxifen as an antagonist for estrogen receptors is associated with high risk of reconstructive failure in implant-based breast reconstruction (53). In fact, revision surgeries after immediate breast reconstruction are more common than after delayed breast reconstruction (57% for IBR vs. 27% for DBR), with a risk as high as 40.4% for developing capsular contracture after an immediate reconstruction and less than 17% after a delayed breast reconstruction (54).

Firstly, early complications with a reported incidence of 5.8% (52) include hematoma (1-2%), seroma, infection (1-24%) (56) and skin flap necrosis (2%), but also delayed healing, failed expansion, displacement or implant explantation (57). Likewise, late complications may include periprosthetic capsular contracture grade III-IV Baker, infection, implant exposure or extrusion and more frequently encountered implant rippling (6.6%) (1).

**Delayed Breast Reconstruction**

Delayed breast reconstruction is considered a good option for patients who have increased oncologic risk or present with indication for radiotherapy. Namely, delayed breast reconstruction is required when there is reduced skin flap perfusion caused by either the mastectomy procedure (58) or associated comorbidities like cardiopulmonary disease, diabetes, obesity or smoking (1). In fact, autologous breast reconstruction is the most frequently considered technique in a delayed setting, once clean margins have been established and adjuvant treatment completed (1, 59).

Autologous breast reconstruction includes a wide range of flaps, from the latissimus dorsi flap, the transverse rectus abdominis flap, the deep inferior epigastric perforator flap to the less elected flaps like the gluteal artery perforator flap or the upper gracillis flap (60).

The latissimus flap, usually combined with a definitive implant for breast reconstruction, is the most adequate flap for patients with diabetes or for smokers (61), as it is associated with very few complications (62). Moreover, it is a suitable flap for thin patients, who have a history of abdominal surgeries or intend to carry a future pregnancy (61). (Figs. 2, 3)

For patients with large breasts, evident ptosis and sufficient abdominal tissue, good options to consider would be the transverse rectus abdominis flap (as a pedicled or free myocutaneous flap) or the deep inferior epigastric perforator flap (based entirely on the

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<th>Table 2. Contraindications of immediate implant-based breast reconstruction (1)</th>
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<td>1. Tumor infiltration to the skin flap or chest wall muscles</td>
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<td>2. Risk of complication that would delay the adjuvant treatment scheme (especially in young patients with aggressive tumors or/and positive sentinel lymph node biopsy)</td>
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<td>3. Psychological issues or unreasonable expectations for the breast reconstruction</td>
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<td>4. Previous irradiation to the chest wall (in case of recurrence)</td>
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<td>5. Smoking status (higher risk of skin flap necrosis and infection)</td>
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<td>6. Severe breast hypertrophy or morbid obesity (poor aesthetic outcome)</td>
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<td>7. High levels of fibrinogen, prothrombin and factors VII, VIII, IX and X</td>
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<td>8. High risk of infection or implant extrusion/exposure</td>
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perforators of the deep inferior epigastric artery) (63,64), as with these flaps the reconstructed breast can resemble closely the native breast. However, this is not a good option for obese patients that present with high risk of fat necrosis and impaired wound-healing (11,65) or for patients with significant comorbidities that could increase the risk of complications. For smoking patients it is advisable that they cease smoking at least 3 months prior to the breast reconstruction procedure (66).

Delayed-immediate Breast Reconstruction

A solution to the controversial issues of breast reconstruction in association with radiotherapy was advocated by MD Anderson Cancer Center who in 2004 reported a different protocol named „delayed-immediate reconstruction“, destined for patients who might be considered for radiotherapy treatment once the final pathologic result is obtained (67). Usually, these patients have stage II breast cancer with one or more positive lymph-nodes at biopsy, evident microcalcifications on the mammography and/or apparent multicentric condition on the ultrasonography (11).

Delayed-immediate approach involves a skin-sparing mastectomy which is followed by the placement of an expander in the subpectoral pocket. This expander will be deflated during the radiotherapy treatment and inflated again once the radiotherapy is completed. After the tissue expansion is finished, there is a waiting period of 4-6 months that is followed by a breast reconstruction with an autologous flap and rarely if local conditions are favourable with a definitive implant (Fig. 4).

This algorithm permits the preservation of the skin envelope while reducing complication rates from 38 % which constitutes the rate for traditional delayed flap reconstruction to a 26 % rate for delayed-immediate reconstruction.
with autologous flap (68). Moreover, if the final pathologic exam contradicts the need for radiotherapy, then tissue expansion can be followed after the first 2 weeks by the placement of a definitive breast implant in the context of a well preserved skin envelope (11).

Conclusion

The management of breast cancer treatment and reconstruction must address both the long-term oncological safety and the final aesthetic outcome. These can only be achieved if the patient's assessment and treatment options are analyzed within a multidisciplinary team composed of the oncologist, the general surgeon, the radiotherapy specialist, the pathologist, the plastic surgeon and the patient herself who must be sufficiently well-informed to be able to participate in the decision-making step concerning the course of her treatment and reconstruction process.

Conflict of Interest

The authors have no conflict of interest to declare.

Authors’ Contribution

All authors have contributed equally in all stages of this article’s development.

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