# Update on the surgical management of breast cancer

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*Breast-conserving surgery has been introduced also in the treatment of patients with locally advanced tumors after tumor downsizing with preoperative chemotherapy, with acceptable rates of ipsilateral breast tumor recurrence.*
*When performing breast-conserving surgery all efforts should be made to ensure negative surgical margins in order minimize the risk of ipsilateral breast tumor recurrence as they are associated with worse distant-disease-free and breast cancer-specific survival rates. The recent introduction of "oncoplastic techniques", that may allow more extensive excisions of the breast without compromising the cosmetic results, has furtherly increased the use of breast-conserving procedures.*
*Mastectomy remains a valid surgical alternative in selected cases and is usually associated with immediate reconstructive procedures. Staging of the axilla has also gradually evolved toward less aggressive approaches with the adoption of sentinel node biopsy, but several controversies still remain about completion of axillary lymph node dissection in patients with a pathologic positivity in sentinel lymph node biopsy.*
*The present work will highlight the benefits and unresolved issues of the different surgical treatment options in breast cancer and axillary treatment.*

KEY WORDS: Axillary treatment, Breast Cancer, Conservative surgery, Mastectomy, Sentinel node

## Introduction

Breast cancer is acknowledged as an international priority in health care. It is currently the most common cancer in women worldwide, with demographic trends indicating a continuous increase in incidence. Only in the European Union, it is estimated that by 2020 there will be approximately 394,000 new cases of breast cancer per year and 100,000 deaths [1]. The surgical treatment of breast cancer has undergone continuous and profound changes over the last three decades. For patients with early stage breast cancer, breast-conserving surgery followed by radiation therapy has been definitively validated as a safe alternative to radical mastectomy, with similar survival rates, better cosmetic outcomes and acceptable rates of local recurrence. Thanks to the improvements in diagnostic work-up, as well as the wider dif-

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fusion of screening programs and efforts in patient and physician education, tumors are more often detected at an early stage, furtherly facilitating the widespread use of breast conserving techniques.
Breast-conserving surgery has been introduced also in the treatment of patients with locally advanced tumors after tumor downsizing with preoperative chemotherapy, with acceptable rates of ipsilateral breast tumor recurrence.
When performing breast-conserving surgery all efforts should be made to ensure negative surgical margins in order minimize the risk of ipsilateral breast tumor recurrence as they are associated with worse distant-disease-free and breast cancer-specific survival rates. The recent introduction of "onco-plastic techniques", that may allow more extensive excisions of the breast without compromising the cosmetic results, has furtherly increased the use of breast-conserving procedures.
Mastectomy remains a valid surgical alternative in selected cases and is usually associated with immediate reconstructive procedures. Staging of the axilla has also gradually evolved toward less aggressive approaches with the adoption of sentinel node biopsy.
The present work will highlight the benefits and unresolved issues of the different surgical treatment options in breast cancer.

## Breast conservation therapy

Breast-conserving surgery (BCS) implies complete removal of the breast tumor with appropiate margins of surrounding healthy tissue performed in a cosmetically acceptable manner. BCS with adjuvant radiotherapy is considered today the gold standard approach for patients with early stage breast cancer. Six prospective trials have shown no significant differences in overall survival rates when comparing BCS plus breast irradiation with mastectomy for early stage breast cancers [2-4].
The choice of BCS versus mastectomy is made taking into account tumor characteristics such as extensive mammographic calcifications, multicentricity, ability to obtain clear surgical margins, tumor size with respect to breast size, as well as for radiotherapy. Patient preferences are also a critical determinant of surgical choice.
For patients who are interested in breast conservation but have a large tumor to breast size ratio, preoperative chemotherapy can be considered to achieve preoperative tumor downsizing. Many trials have shown that patients with locally advanced tumors may become eligible for breast-conserving surgery after tumor downsizing with preoperative chemotherapy, with acceptable rates of ipsilateral breast tumor recurrence.
The long-term success of BCS can be measured by two end points: the rate of local control and the cosmetic appearance of the preserved breast. When performing BCS, it may occasionally be difficult for the surgeon to adequately meet both of these end points, particularly when attempting to remove larger lesions or in case of small breasts.
In order to optimize local control, it is mandatory to ensure negative surgical margins. The surgical margin status is considered the strongest predictor for local failure with an increased local recurrence rate in cases with positive margins (defined as tumor cells at the cut edge of the surgical specimen). Positive surgical margins are usually considered an indication for re-excision while the impact of 'close' margins (tumor at less than 2 mm from the surgical margin) remains controversial. It is generally agreed that best efforts should be made to achieve widely negative margins at the time of initial surgery and that the magnitudine of parenchymal excision should be adeguate to limit the need of re-excision for close or positive margins [5].
The Society of Surgical Oncology (SSO) and the American Society for Radiation Oncology (ASTRO) published evidence-based clinical practice guidelines on surgical margins for breast-conserving surgery with whole-breast irradiation in stage I and II invasive breast cancer in 2014. According to this guideline, the use of no ink on tumor (ie, no cancer cells adjacent to any inked edge/surface of specimen) as the standard for an adequate margin in invasive cancer in the era of multidisciplinary therapy is associated with low rates of ipsilateral breast tumor recurrence and has the potential to decrease re-excision rates, improve cosmetic outcomes, and decrease health care costs [6].
Cosmetic outcome is also directly correlated to the magnitude of parenchymal excision. When larger volumes of tissue are removed, the risk of an unpleasant cosmetic result increases, particularly for cancers located in the central, medial or lower pole of the breast.
In an attempt to optimize the balance between the risk of local recurrence and the cosmetic outcome in BCS, new surgical procedures that combine the principles of surgical oncology and plastic surgery have been introduced in recent years. These new techniques, called "oncoplastic" techniques, may allow removal of larger amounts of breast tissue with safer margins while limiting the risk of a poor cosmetic outcome [7-13]. Oncoplastic procedures are less technically demanding and time consuming than major reconstructive operations and surgeons experienced in routine breast surgery can easily incorporate them in their practice with a relatively short learning curve. These procedures are usually performed in a single surgical access, and the patient leaves the operating room without major residual asymmetry or deformity.
The oncoplastic surgery may be classified in two fundamentally different approaches according to the reconstruction techniques following BCS that have been established [10,11,13]:
– volume displacement techniques, when the resection defect is reconstructed using one of a range of local glandular or dermoglandular flaps within the breast, which are mobilised and advanced into the defect;

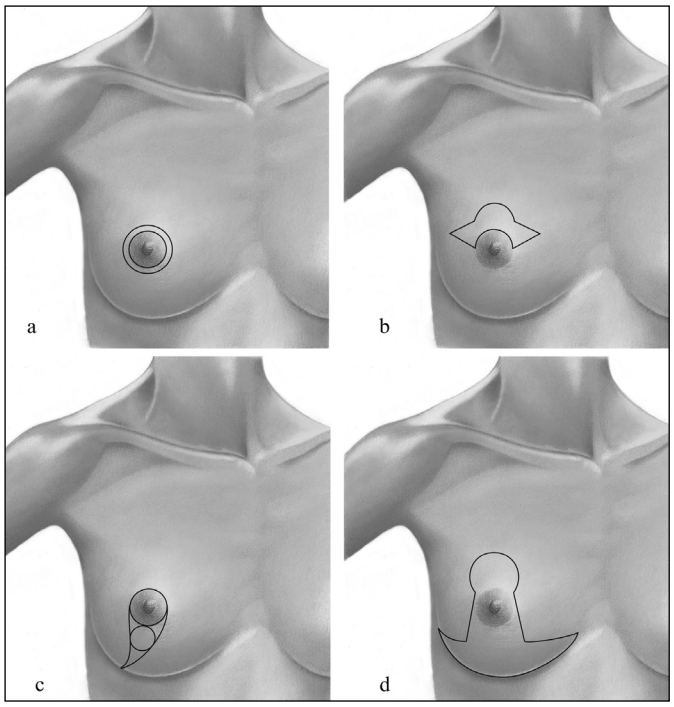


Fig. 1: Skin incisions in conservative oncoplastic surgery:
A) In the donut mastopexy, two concentric circles of different diameter are designed around the nipple;
B) In the batwing mastopexy, two half-circle are designed and connected with angled wings on each side of the areola;
C) In the Grisotti procedure, two circles are drawn, one along the borders of the areola, the other below the areola and lines from the medial and lateral sides of the areolar circle are connected down and laterally on the inframammary fold;
D) In the reduction mammaplasty, a key-hole pattern incision may be used.

– volume replacement techniques, when the resection defect is reconstrued by replacing the volume of tissue removed with a similar volume of autologous tissue from an extramammary site - usually latissimus dorsi.

Planning of an oncoplastic procedure requires the following steps:
– selection of the most appropriate skin incisions and parenchymal excisions;
– adequate reshaping of the gland after parenchymal excision;
– repositioning of the nipple-areola complex (NAC) to the center of the breast mound, if needed;
– correction of the contralateral breast for better symmetry, if needed.

Different oncoplastic techniques can be used for tumors located in the various quadrants of the breast:
A "**Donut mastopexy**" approach is indicated for periareolar lesions in breasts with moderate ptosis. Two concentric circles of different diameter are designed around the nipple and the donut of skin between the two circles is excised (Fig. 1a). Quadrant resection of the breast parenchyma can then be performed through a wide incision, allowing for better control of the tumor removal than when the resection is performed through conventional skin incisions. Reshaping of the breast is achieved separating the residual portions of gland off the pectoralis fascia with the electrocautery. Attention should be used to limit the number of major perforating vessels that are sectioned, in order not to threaten the blood supply to the residual glandular tissue. If needed, a purse-string suture is used to reduce the diameter of the larger circle and is then sutured to the new border of the areola, leaving only a periareolar scar at the end of the procedure.
A "**batwing mastopexy**" pattern is ideal for cancers located in the upper periareolar region.It allows for ample removal of the skin overlying the lesion, and therefore is particularly indicated when the lesions are in proximity of the skin. Two half-circle are designed, one on the border of the areola and one 20-25 mm above it, and connected with angled wings on each side of the areola (Fig. 1b). Designing of the skin incisions should be made with the patient sitting erect. Full-thickness lumpectomy is performed and the residual gland is partially lifted off over the pectoralis fascia in order to allow adequate advancement of tissue and to remodel the defect.
A "**central quadrantectomy**" with *the Grisotti technique* can be used for tumors located in the retroareolar region or for Paget disease. It include a complete excision of the tumor with the entire NAC and the correspondent underlying cylinder of parenchyma down to the pectoralis fascia, restoring the central defect with a skin-parenchymal flap. A circle is drawn along the borders of the areola; another circle is drawn below the areola and lines from the medial and lateral sides of the upper circle are connected laterally on the inframammary fold (Fig. 1c). Incisions are made along the drawings and the skin below the areola is excised, with exception of the skin included in the lower circle. After the tumor is completely excised, the skin-glandular flap is mobilized from the inferior lateral pole of the residual gland to create the new areola. Care should be taken to avoid excessive devascularization of the skin-glandular flap, to minimize the risk of ischemic injury to the neo-areola. At the end of the procedure, the breast may result slightly smaller than the controlateral, but with a pleasant shape. If desired by the patient, reconstruction of the nipple can be performed immediately or at a later stage, with tattoing of the areola.
A "**Reduction mammaplasty**" pattern may allow resection of large amounts of breast tissue with excellent cosmetic outcomes and wide surgical margins, even in small breasts. It results particularly convenient in women with very large and pendolous breasts, as it not only improves the cosmetic appearance of the breast but also can facil-

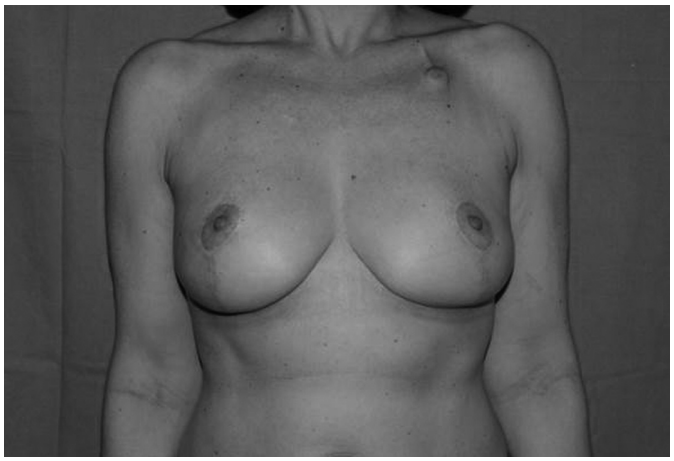

Fig. 2: Oncoplastic technique of reduction mammaplasty: postoperative view at 7 months

itate the delivery of postoperative radiotherapy. Due to the size of the breast, consistent positioning for radiotherapic treatment may be quite difficult in these patients, resulting in dosing inhomogeneity, a higher percentage of unacceptable late radiation reactions, and overall inadequate local treatment. By reducing the size of the breast with a mastoplasty approach, these risks may be avoided, without any significant interference with clinical or radiologic follow-up. A vertical pattern, a L-shaped pattern or a key-hole pattern incision may be used (Fig. 1d, Fig. 2).
The use of oxidized regenerated cellulose in oncoplastic breast surgery has been recently proposed as a simple technique that could improve cosmetic outcomes [13,14].

## Total mastectomy

When a breast conserving approach cannot guarantee adequate local control and good cosmetic results, total mastectomy should be selected. Common indications to mastectomy include extensive or multicentric disease, inability to obtain clear surgical margins with BCS, large tumor size with respect to the breast size, as well as cases with contraindications for radiotherapy as well as patient preference [15-31]. Recent progress in understanding the genetic basis of breast cancer has increased interest in prophylactic mastectomy as a method of preventing hereditary breast cancer.
Various surgical techniques can be adopted when planning a total mastectomy:
a) **Modified radical mastectomy***:* this technique involves complete removal of the breast with skin and nipple-areola complex, preserving the pectoralis major and minor muscles (Fig. 3a). It is indicated when the tumor involves the skin or is very close to it and in cases for which prosthetic breast reconstruction is not considered.

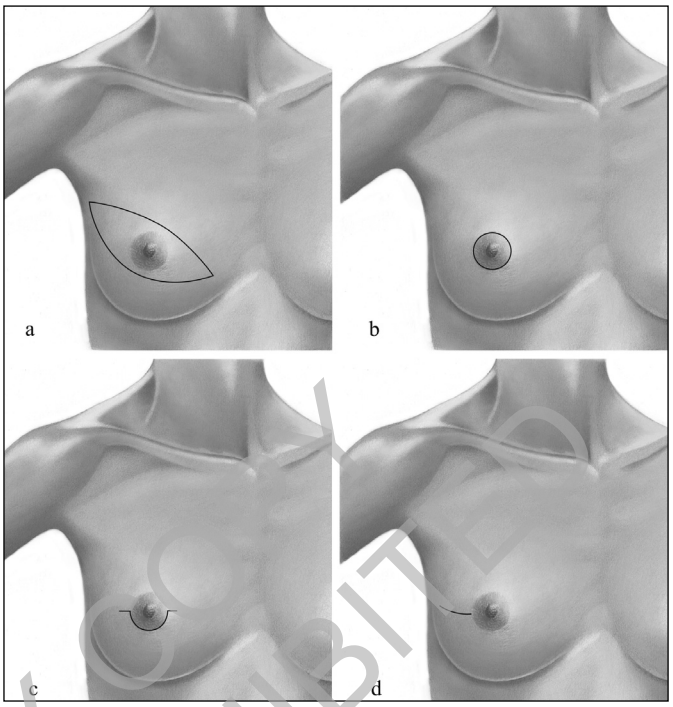


Fig. 3: Skin incisions in common types of mastectomy:
A) Modified radical mastectomy;
B) Skin sparing mastectomy;
C) Nipple-areola-sparing mastectomy (omega-type incision);
D) Nipple-areola-sparing mastectomy (lateral incision).

b) **Skin-sparing mastectomy***:* this technique preserves the natural skin envelope of the breast while removing the entire glandular tissue and nipple-areola complex (NAC) (Fig. 3b). Studies have shown that LR rates for skin-sparing mastectomies are comparable to those of non–skin-sparing mastectomies in patients with non invasive and early stage breast cancer. This technique is also well-suited for those patients at high risk for developing breast cancer who opt for a prophylactic mastectomy. Smoking, previous radiation, diabetes, and obesity can increase the risk of necrosis and infection of the skin. Skin-sparing mastectomy combined with immediate reconstruction can provide excellent cosmetic results [15-17].
c) **Nipple–sparing mastectomy***:* this technique involves removal of breast tissue with preservation of the nipple-areola complex (Fig. 3c-3d). It is not indicated in cases with large cancers or with tumors close to the nipple or centrally located, or those with clinical evidence of NAC involvement. Women with severe ptosis are poor candidates because nipple displacement is a problem. It is indicated in patients undergoing prophylactic surgery. Frozen sections on the retroareolar tissue need to be performed intraoperatively to rule out evidence of tumor cells. If cancer cells are detected, the NAC will have to be removed. Possible sequelae of the procedure may be partial or total necrosis of the NAC and loss of nipple

sensation. More extensive studies with long-term follow-up are necessary to fully evaluate the optimal technique and its long-term effects [18-21].

## Breast reconstruction after mastectomy

The option of breast reconstruction should be offered to any patient undergoing mastectomy, as it can improve the quality of life and does not interfere with further treatments.
Selecting the correct timing and method of breast reconstruction is a highly individualized process. The final choice must take into account the patient's body characteristics, size and shape of the contralateral breast, overall health, breast cancer treatment plan, personal habits and patient preferences. Women should be informed that while breast reconstruction can improve the quality of life and provide a good volume replacement, the cosmetic result will never duplicate the one of her natural breast.
Reconstruction may be performed at the time of mastectomy or at a later date. Immediate reconstruction provide psychological and clinical benefits by saving the patient from a temporary impairment of her body's image and reducing the numbers of operations. Nevertheless, delayed reconstruction may be appropriate for patients diagnosed with advanced disease that may need rapid completion of adjuvant therapies.
In general, options for reconstruction include either the use of breast implants (prosthetic reconstruction) or the patient's own tissue (autologous tissue recontruction)[22-26].

### Prosthetic Reconstruction

Breast reconstruction using implants is the simplest and most common method used today. In this technique, an implant is placed through the mastectomy incision in a pocket created beneath the pectoralis muscle [9,10,14,22].
If a pocket of appropriate dimensions can be created at the time of mastectomy, a definitive anatomical silicone-filled textured prosthesis can be positioned in a one-stage surgical approach (Fig. 4-5).
If the pocket is tight, the skin and muscle must be stretched gradually by means of a tissue expander placed under the pectoralis muscle, which is progressively inflated at weekly intervals, in an outpatient clinic, by percutaneous injection of saline solution. Once the expander is filled to the desired volume and the overlying tissues has been expanded sufficiently, a second procedure is performed to remove the expander and place a permanent implant.
Advantages of implant reconstruction include less time in the operating room, a technically easier surgical procedure and a shorter recovery compared with autologous reconstruction. The main disadvantages are that the implant tends to feel firm and round, and in case of variations of the body weight it does not modify its volume, with subsequent unpleasant asymmetry compared with the opposite breast. Women with large and/or ptotic breasts, who undergo implant reconstruction, will often require a breast reduction or mastopexy on the contralateral side to achieve symmetry.

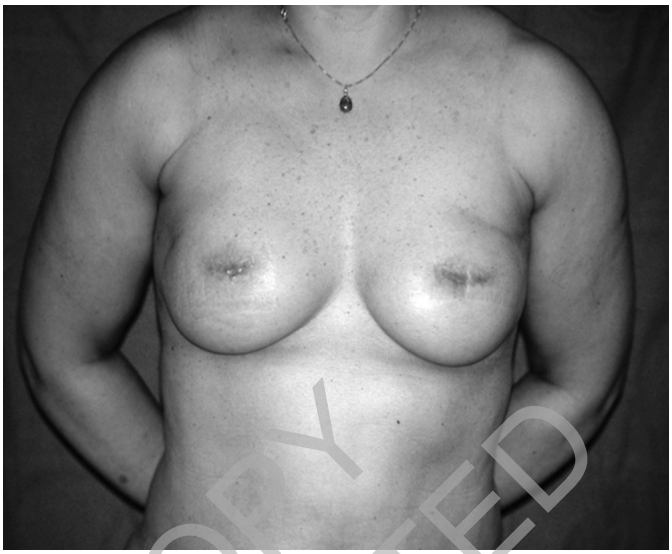

Fig. 4: A bilateral skin sparing mastectomy and immediate reconstruction with a definitive anatomical prosthesis.

Fig. 5: A bilateral nipple sparing mastectomy and immediate reconstruction with a definitive anatomical prosthesis.

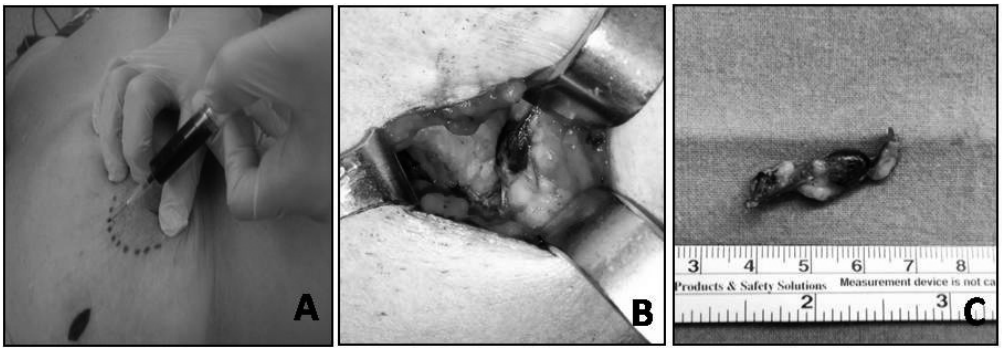


Fig. 6: Sentinel lymph node biopsy with blue dye identification technique:
A) Periareolar intraglandular injection of 50% solution of blue dye;
B) Identification of the sentinel lymph node;
C) Macroscopic exam of the excised lymph node.

Poor candidates for breast implants include patients who have severe connective tissue disease or previous radiation to the breast.
The most common complications of breast implants are capsular contracture, foreign body reaction, and rupture or leakage due to trauma or normal consumption of the surface of the implant over time. In this latter case surgical replacement of the implant is the indicated treatment.

## Autologous Reconstruction

Autologous breast reconstruction uses the patient's own skin, fat, and muscle as either a pedicled flap that is rotated to the mastectomy site (with its attached blood supply) or as a free flap which is completely separated from the body and transplanted at the mastectomy site (using microvascular surgery to reconnect the vessels). As the skin and fat from the donor sites are similar in consistency to breast tissue, the results of autologous reconstruction more closely resemble a real breast as compared with implant reconstruction. Moreover, there are no risks of a foreign body reaction or capsular contraction.
Disadvantages include the complexity of the procedures, longer time in the operating room, prolonged recovery and and a higher risk of minor and major complications (bleeding, infection, necrosis, complete flap loss).
The most commonly used autologous flaps are the latissimus dorsi flap and the transverse rectus abdominis myocutaneous flap or TRAM flap [14,23-26].
**Latissimus dorsi flap**. The latissimus dorsi muscle or myocutaneous (muscle and skin) flap implies the rotation of this muscle (with an ellipse of skin) from the patient's back to the mastectomy site. The dominant blood supply to this flap is the thoracodorsal artery with segmental blood supply from the posterior intercostals and lumbar vessels. Indications for this flap include previous implant or TRAM flap failure, need to reconstruct a partial mastectomy or quadrantectomy defect, abdominal obesity or extreme thinness resulting un inadeguate infraumbilical soft tissue. Controindications to this technique include prior surgery that may have interrupted the blood supply (eg, posterior thoracotomy). Because this flap is usually not bulky enough to provide an adequate breast mound, an implant is often also required [14,23].
**Transverse rectus abdominis myocutaneous pedicled flap (TRAM).** The TRAM flap is the most commonly performed tissue transfer procedure. In a pedicled TRAM, the rectus muscle along with skin, fat, and blood supply, is raised in the lower abdomen and tunneled under the skin of the upper abdomen to the mastectomy site to form a breast mound. In a pedicled TRAM flap the inferior epigastric artery is severed, and the rectus muscle and overlyng skin and subcutaneous tissue are rotated into the mastectomy defect based on the superior epigastric artery and the periumbilical perforators. Indications for the TRAM flap include patients who have mastectomy defects requiring a large amount of tissue for reconstruction or who have a history of chest wall irradiation. TRAM reconstruction are also useful in women who have a ptotic controlateral breast that will be hard to match using an implant. For TRAM reconstructions women must have adeguate soft tissue in the lower abdomen. Contraindications to the pedicled TRAM procedure include previous abdominal surgery such as abdominoplasty, liposuction, open cholecystectomy, or other major abdominal operations that would compromise circulation to the skin and tissue over the flap. Other controindications include obesity and severe comorbidities (e.g. vascular disease). Acute complications include infection, hematoma or seroma of the breast or abdomen, umbilical necrosis and partial or total flap loss. In the long term, potential complications include abdominal wall laxity or hernia [23-26].
**Free or microsurgical transverse rectus myocutaneous flap.** Another option with the TRAM flap is to perform a microsurgical or "free" transfer of the abdominal tissue to the mastectomy defect. In this procedure, a portion of the rectus muscle, fat and skin are completely detached from the abdominal donor site and its native blood supply. The blood supply is the deep inferior epigastric artery and its venae comitantes which are severed at the their origin. These vessels are anastomosed microsurgically to the thoracodorsal or internal mammary vessels. Relative indications for this procedure are similar to

those for the pedicled TRAM. Unlike the pedicled TRAM flap, however, this technique can be used when the superior epigastric artery has been divided (eg, in a patient who has had a previous open cholecystectomy). Disadvantages of this procedure include a potentially longer operating time and the need of microsurgical expertise [23-26].

**Deep inferior epigastric perforator flap (DIEP).** This technique, more widely used in recent years, is similar to the free TRAM flap, but the blood supply to this flap is based on only one or two of the perforator arteries off of the deep inferior epigastric artery. Using microvascular surgery, this procedure involves meticulous dissection of the vessels within the rectus abdominis muscle from their distal perforation through the rectus fascia all the way down to their proximal pedicle off of the external iliac artery and vein. Once these vessels are identified and isolated, they are transected and reanastomosed to the internal mammary or thoracodorsal vessels of the chest.

This procedure does not require harvest of rectus abdominis muscle, resulting in less abdominal wall morbidity. Specifically, the incidence of abdominal wall laxity or hernia is less than with techniques that remove abdominal fascia with rectus muscle. Disadvantages of this procedure include a longer operating time, the need of significant microsurgical expertise and an higher incidence of partial or total flap loss than with traditional TRAM procedures. The choice between the free TRAM and the DIEP flap should be base on the patient's weight, the required breast volume, the amount of abdominal fat available, and on the number, calibre and location of the perforating vessels [10,14,23-26]

**Gluteal Artery Perforator Flaps (GAP).** The SGAP and IGAP flaps are based on perforators from the superior and inferior gluteal arteries and veins, respectively. The skin incision are typically located at the upper buttock just lateral to the midline gluteal crease for the SGAP and along the inferior gluteal crease for IGAP. GAP flaps must be considered as a second-line donor site for patients with inadeguate abdominal soft tissue volume or with prior abdominal surgeries that have eliminated perforating vessels. Absolute contraindications specific to GAP flap breast reconstruction include history of previous liposuction at the donor site or active smoking.[14,26]

## Axillary treatment

Axillary lymph node status still represents a critical point when planning adjuvant treatments, as well as a strong predictor of local disease free and overall survival. Unfortunately, there is still no preoperative diagnostic tool that can reliably assess whether cancer cells have spread to the axillary lymphatic basins, so that this remains a great unanswered question until after the surgical procedure is completed.

Axillary lymph node dissection (ALND) has traditionally been a routine component of the management of early breast cancer. The benefits of ALND include its impact on disease control, its prognostic value, and its role in treatment selection. However, the anatomic disruption caused by ALND may result in lymphedema, nerve injury, and shoulder dysfunction, which compromise functionality and quality of life.

As a result, sentinel lymph node biopsy (SLNB), a minimally invasive technique, was developed to avoid ALND in patients who have a low probability of axillary metastasis [32-36] (Fig. 6).

The sentinel node (SLN) is the first lymph node which receives lymph from the anatomic site of the primary breast tumour. The rationale for the adoption of SLNB is that, due to the linear involvement of axillary nodes by tumour cells, the histological characteristics of this first lymph node would be representative of all the other axillary nodes. With this procedure, an ALND is performed only in case of pathologic evidence of metastatic disease in the SLN, thus avoiding unnecessary and potentially harmful surgical procedures.

After injection of vital blue dye and/or radiolabeled colloid around the area of the tumor, the identification of a SLN is consistently identified in approximately 96 percent of cases, and predicts the status of the remaining axillary LNs in ≥95 percent of cases in most series [36-37]. The false negative rate (FNR) of SLN was originally reported as 5 to 10 percent (sensitivity 90 to 95 percent), but lower rates are attainable by experienced surgeons [36-38].

In case of positivity of the SLNB, the classic treatment consisted in completion ALND that must be extended posteriorly in the axillar space until the axillary vein is visualized, with care not to open the axillary sheath and strip or skeletonize the vein unless there is extensive nodal disease, because this increases the risk of injury to the vessels and lymphatics, which can increase the risk of lymphedema [39]. During the lateral dissection, sensory intercostobrachial nerves are encountered along the latissimus dorsi. If the intercostobrachial nerve branches cannot be spared, ligation should be performed sharply to avoid electrocautery conduction injury. As well as preservation of sensory branches, it is very important to identify and preserve motor nerves: the long thoracic nerve is identified by blunt dissection just below the medial aspect of the axillary vein and just lateral to the chest wall. Once the nerve is identified, the plane is extended inferiorly for the length of the axillary field. The thoracodorsal neurovascular bundle can be identified by dissecting in the mid-axilla just inferior to the axillary vein. There is often a large superficial venous tributary arising from the axillary vein, called the thoracoepigastric vein, which is often just anterior to the position of the thoracodorsal neurovascular bundle. This superficial vein should not be transected until the neurovascular bundle is confirmed [40].

The extent of dissection is a tradeoff between the greater morbidity of a more extensive ALND and the possibility of leaving residual untreated axillary disease. In general, a level I and II anatomic ALND is the preferred procedure for axillary assessment that should yield ≥10 axillary lymph nodes, although the range is highly variable [38].
Routine removal of level III nodes is unnecessary for staging but should be carried out to maximize local control if grossly positive axillary lymph nodes are identified intraoperatively. Level III lymph node dissection significantly increases the morbidity of the ALND.
For patients with clinically node-negative early breast cancers, SLNB is confirmed as the gold standard for axillar staging in guidelines from the American Society of Clinical Oncology (ASCO) [39], the International Expert Consensus Panel on the Primary Therapy of Early Breast Cancer [41], and others [42-43]. These observations reduced ALND indications only to women who have positive nodes confirmed preoperatively by methods such as ultrasound guided fine needle aspiration or after SLNB.
One of the greatest concerns with SLNB is the potential of a false negative result, which could increase the potential for axillary recurrence. However, despite the approximately 5 to 10 percent false negative rate with SLNB found in studies in which completion ALND has been done, several series suggest that axillary recurrence rates are low after a negative SLNB alone in early stage breast cancer (range 0 to 4.5 percent) [38, 44-47].

## Indications For Sentinel Lymph Node Biopsy

SLNB should be performed in most women with clinically node negative (clinical stage I or stage II) invasive or microinvasive breast cancer [43].
This procedure has to be provided even in women with extensive ductal carcinoma in situ (DCIS), who are undergoing mastectomy, indeed, a SLNB will not be possible after mastectomy if invasive disease is found on final pathology, necessitating an axillary dissection for staging purposes.
When a SLNB is not successful or when clinically suspicious nodes are encountered in the axilla the surgeon should perform an axillary dissection for staging purposes and to ensure locoregional control [39].
SLNB can be omitted if the nodal information will not affect adjuvant treatment decisions. As an example, women ≥70 years of age who have a small (<2 cm) estrogen receptor-positive tumor and a clinically uninvolved axilla may be treated without a SLNB.

## Management of Sentinel Lymph Node Metastases And Current Controversies

SLN metastases are categorized as isolated tumor cells, micrometastases, or macrometastases, depending upon the size of the largest tumor deposit in the sentinel node and leading to different approaches in axillar treatment. Management of positivity to isolated tumor cells (small clusters of cells not greater than 0.2 mm, or nonconfluent or nearly confluent clusters of cells not exceeding 200 cells in a single histologic lymph node cross section) are considered prognostically similar to node negative. As a matter of fact, they are designated as pN0 (i+) and do not constitute an indication for further axillary treatment (even surgery, radiation treatment, or adjuvant systemic therapy).
Nevertheless, SLNB positivity to micrometastases (tumor foci >0.2 mm and no greater than 2.0 mm) and macrometastases (tumor foci >2 mm) represented a matter of debate and deep controversies in recent versions of evidence based guidelines.
The SLN is the sole tumor-bearing node in up to 60 percent of cases overall, and in almost 90 percent of patients who harbor only micrometastatic disease. These observations have led to speculation that completion ALND may not be necessary in selected patients with a positive SLNB in less than three nodes because the need for systemic therapy is established [48-53] and the risk of an axillary recurrence appears to be low [54-57].
The International Breast Cancer Study Group trial 23-01 (IBCSG 23-01) randomized patients with SLN micrometastases (<2 mm) and primary tumors <5 cm in size to either completion ALND or no additional axillary surgery [58] evidencing no significant difference in disease-free survival (DFS) and overall survival (OS) at a median follow-up of 49 months.
In breast cancer patients with T1 e T2 tumours, no palpable adenopathy and 1/2 sentinel lymph nodes containing macro- or micrometastases, the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial compared observation only to complete axillary lymph node dissection following sentinel node biopsy [59]. No significant differences in recurrence rates, DFS and OS were noted between the two groups at a median follow-up of 6.3 years.
Based upon the apparent lack of regional benefit and low risk of events in these trial, completion ALND may not be necessary for all women with T1-2 tumors that are clinically node negative, with less than three positive SLNs, who will be treated with whole breast radiation and systemic therapy, particularly in women with estrogen receptor positive tumors.
Importantly however, several criticism on major study bias on these two trials may configure that they are not sufficient to provide strong recommendations that could uniformly change the actual management of axillary nodes.
The effect of controversial interpretation of these studies, is that there is a lack of uniformity in axillar behavior in presence of SLNB positivity.
The 2014 American Society of Clinical Oncology (ASCO) guidelines reflect the most conservative treat-

ment, recommending completion ALND only for patients with more than 2 positive lymph nodes [39], whereas 2014 National Comprehensive Cancer Network (NCCN) guidelines, accepting these previously mentioned criticisms seem to be more prudent; NCCN still recommend completion ALND for patients with SLNB positivity and consider no further axillary surgery only in strictly selected patients (after complete information of risks and benefits), who meet precise criteria (T1-2 tumor, 1-2 positive lymph-nodes, absence of previous neoadjuvant therapy and for which is planned breast conserving surgery and whole breast irradiation) [43].
The future behaviour on axillary treatment seems to aim to consider SLNB as the only surgical manoeuvre for axillary staging in patients undergoing conservative breast surgery for early stage neoplasms for which is planned adjuvant therapy, but presently, further evidence and longer follow-up results must be provided in order to clearly delineate an uniformity in different treatment guidelines.

## Riassunto

Il trattamento chirurgico dei tumori della mammella ha subito continui e profondi cambiamenti negli ultimi 30 anni. La chirurgia conservativa ha progressivamente e definitivamente sostituito la mastectomia nel trattamento dei tumori in stadio iniziale; associata alla radioterapia, essa è in grado di garantire alle pazienti le stesse percentuali di sopravvivenza globale e migliori risultati estetici con un accettabile rischio di recidiva locale.
Grazie alla diffusione dei programmi di screening ed al perfezionamento delle indagini diagnostiche si è assistito ad un progressivo incremento della diagnosi dei tumori infraclinici ed all'elaborazione di sempre più accurate tecniche di localizzazione e trattamento mini-invasivo dei tumori non palpabili.
Nell'ambito della chirurgia conservativa, l'introduzione della chirurgia oncoplastica, coniugando tecniche di chirurgia generale con quelle proprie della chirurgia plastica, ha consentito di superare il conflitto tra estensione della resezione chirurgica e risultato estetico finale, contribuendo in maniera importante a migliorare la qualità di vita delle pazienti.
La mastectomia resta una valida alternativa chirurgica in casi selezionati ed è associata preferibilmente a procedure ricostruttive immediate che minimizzano l'impatto psicologico negativo dell'atto demolitivo.
La tecnica del linfonodo sentinella per i tumori in stadio iniziale ha permesso di evitare in casi selezionati la dissezione ascellare di principio senza rinunciare alle importanti informazioni prognostiche dei linfonodi locoregionali.
L'obiettivo di questo lavoro è di riassumere le recenti evoluzioni nella terapia chirurgica dei tumori della mammella e di mettere in evidenza i vantaggi e le questioni irrisolte delle diverse opzioni chirurgiche di trattamento.

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