



UNIVERSITÀ DI PISA

Department of Translational Research and of New  
Surgical  
and Medical Technologies

---

Degree Course in Medicine and Surgery

DEGREE THESIS

ONCOLOGICAL AND AESTHETIC-FUNCTIONAL  
EVALUATIONS OF  
ALMOST 200 PATIENTS WHO UNDERWENT IN 2014 TO  
BREAST CANCER SURGERY

Mentor: Doctor Manuela Roncella Candidate: KatrenaAssaf

Academic year: 2014-2015

# INDEX

CHAPTER 1: INTRODUCTION .....	3
1.1 Epidemiology of Breast Cancer: .....	3
1.2 Historical development of BC treatment.....	4
1.3 DESCRIPTION OF THE MODERN SURGICAL TREATMENT FOR BC AND RECONSTRUCTION TREATMENT.....	9
CHAPTER 2: BREAST CANCER CLINICAL PATHWAY, LEGISLATIONAL REQUIREMENTS AND QUALITY CARE INDICATORS IN THE BREAST UNITS .....	27
2.1 Breast cancer clinical pathway in the Breast Unit.....	27
2.2 Legislative requirements of the Breast Unit.....	34
2.3 Quality care indicators in the Breast Units.....	38
CHAPTER 3: MATERIALS AND METHODS .....	51
3.1 Aim of the study.....	51
3.2 Patients and Methods .....	51
3.3 Results .....	60
CHAPTER 4: DISCUSSION .....	63
CHAPTER 5: CONCLUSIONS .....	69
BIBLIOGRAPHY .....	71

# **CHAPTER 1: INTRODUCTION**

## **1.1 EPIDEMIOLOGY OF BREAST CANCER:**

Breast cancer, the most frequently occurring cancer in women, is a major public health problem, with 1,384,155 estimated new cases worldwide with nearly 459,000 related deaths.

Breast cancer incidence has been increasing throughout the world (according to 2012 GLOBOCAN statistics, nearly 1.7 million women were diagnosed with breast cancer worldwide with 522,000 related deaths - an increase in breast cancer incidence and related mortality by nearly 18 % since 2008). There are significant inequalities between rich and poor countries, with the incidence rates remaining highest in more developed regions, while mortality rates are much higher in less developed countries (the mortality is nearly 17% higher in the less developed countries).

Breast cancer incidence rates are expected to increase in many less developed countries because of longer life expectancy coupled with the adoption of a more “westernized” lifestyle such as delays in childbearing and less physical activity.

## 1.2 HISTORICAL DEVELOPMENT OF BC TREATMENT

The surgical management of breast cancer has significantly evolved over the years, trending away from radical procedures, and moving towards procedures with complete tumor resection while preserving normal parenchyma tissue thereby decreasing patient morbidity.

For most of the twentieth century, *Halsted radical mastectomy* (or radical mastectomy, RM) was the established and standardized operation for cancer of the breast in all stages, early and late stage<sup>1</sup>. Halsted radical mastectomy, introduced by William Halsted in 1882 at the Roosevelt Hospital in New York City, implies the excision of the breast glandular tissue, the associated skin and subcutaneous tissue, pectoral muscles (major and minor pectoral muscles) and axillary lymph nodes. When mastectomy is coupled with en-bloc resection (removal as a whole) of internal mammary nodes, it is often termed an *extended radical mastectomy*.

In 1948, two reports appeared that were destined to change the management of breast cancer. Indeed, they were accepted in 1989 as general principles in the management of breast cancer (as a localized disease)<sup>2</sup>. The first report on modified radical mastectomy (MRM) was introduced by D. Patey and W. Dyson from Middlesex Hospital in London. Modified radical mastectomy involves the removal of the entire breast, together with the nipple and the pectoralis major fascia, and axillary node dissection is done through the same incision. The second report was on Simple Mastectomy and radiotherapy which was introduced by R. McWhirter, a radiotherapist of the University of Edinburgh (Scotland). Simple Mastectomy consists of the excision of the entire

breast, axillary node dissection (usually through a separate incision), and 5 to 6 weeks of radiation therapy

Halsted mastectomy was performed *largely to prevent local or regional recurrence*. Halsted and many other surgeons believed that all tumors spread by direct extension (the theorem of “centrifugal spread”) <sup>3</sup>, for example, breast cancer can spread to the liver and lungs *directly* through the layers of the body into these organs. The cure of breast cancer was totally in the hands of the surgeon; if the tumor could be surrounded and removed, the patient could be cured and no recurrence was observed. On the one hand, Halsted mastectomy was associated with an important reduction in local and regional recurrence rates (Halsted study in 1892 reported 6% (from the prevailing 51-82% at that time) and 22% recurrence rates respectively) <sup>2</sup>, and on the other hand, despite the use of radical mastectomy and consequent loco-regional disease control, there was still a high mortality rate.

In the first decades of the 20<sup>th</sup> century, few doctors questioned the doctrine of radical surgery, nevertheless, no one dared to confront Halsted mastectomy until more than a generation after his death (in 1922). Slowly arguments against centrifugal theory began to surface and the theorem subsequently failed (in 1920).

N.E McKinnon (professor of epidemiology at the University of Toronto) said that “In most, if not all, lethal breast cancers, the eventual cause of death is *remote metastasis*, and remote metastasis is spread from the primary lesion via the blood stream” <sup>4</sup>. In essence, given what he believed about the natural history of breast cancer, if the disease had spread, it would have done so long before the surgeon’s knife touched the patient, and if this was true, radical mastectomy simply made no sense. Also Bernard Fisher (an American scientist and a pioneer

in the biology and treatment of BC) believed that, in early stage breast cancer, radical treatment would not affect patient survival, and systemic disease or micrometastasis determines the outcome of the patient. This theory led to a change in local treatment, from Halsted mastectomy to breast conservative surgery (BCS) together with adjuvant Radiation Therapy (RT).

Radiation therapy was introduced by Maria and Pierre Curie in the treatment of cancer in 1898 and became widely accepted by 1920. It was introduced first to treat inoperable breast cancers, and then as a postoperative supplement to mastectomy (and sometimes preoperative to reduce the bulk of large cancers). Radiotherapy was later approved for BCS. In 1922, an English surgeon, Geoffrey Keynes, began using *Local Excision and Radiotherapy* to treat STAGE I breast cancer. Over seventy percent of his patients had a 5 year survival rate and 8% developed local recurrence (this percentage was actually no higher than that following radical surgery) <sup>5</sup>. The benefit of ionizing irradiation after breast surgery (Adjuvant RT) is that it destroys occult cancer cells which can be left behind, thus reducing local recurrence rates.

Nowadays, RT is almost always indicated after Breast Conservation Surgery, and may be recommended after Mastectomy (PMRT, Post Mastectomy Radiotherapy). Adjuvant RT, in patients who undergo a Mastectomy, is indicated for: T4 tumor or T3 tumor and evidence of node involvement at pathologic review, evidence of positive margins showing invasive disease at pathologic review, and in the case of  $\geq 4$  pathologically involved nodes. The potential benefits of PMRT in patients with  $< 4$  positive axillary nodes remain controversial.

In 1973, Umberto Veronesi (Milan, Italy) began a scientific study comparing surgical techniques <sup>5</sup>. One technique implied the removal almost one-fourth of the breast plus RT. The second technique was Radical Mastectomy. He called the first technique, **Quadrantectomy**. Years later (In 1980), Veronesi statistically showed that survival and local recurrence results were equal for both forms of treatment. Randomized clinical trials established then the role of Breast Conservation Surgery, and concluded that there is no difference in survival of patients with early breast cancer whether treated with Halsted's Mastectomy or Quadrantectomy and radiation.

By 1991, a National Institutes of Health consensus statement recommended Conserving Surgery plus RT as an appropriate alternative primary therapy to mastectomy for early stage breast cancer <sup>6</sup>.

The major advantages of Breast Conservation Surgery compared with Mastectomy are: superior cosmetic results and reduced psychological and emotional trauma resulting from the procedure.

Nowadays, breast conservative surgery includes also more conservative techniques than ever, which implies only the resection of the tumor with a limited excision of the surrounding tissue. This technique, like almost all conservative breast surgery, involves the use of adjuvant RT. However, this technique has limits, such as, involved surgical margins (reported in 10-40% of cases) with an increase in re-excision surgical rates (reported in 20-30% of cases).

In some patients, mastectomy is still carried out due to: tumor size (relative to breast size), tumor multicentricity, inability to achieve negative surgical margins

after multiple resections, prior radiation to the chest wall/breast or other contraindications to RT, or patient choice.

Until recently, surgical management of Breast Cancer (BC) focused on two main choices: tumor resection using breast conservation therapy (BCT) and mastectomy with optional volume displacement by breast reconstruction. Since 2003, Oncoplastic Breast Surgery (OBS or OPS) has been introduced. This technique combines the skill of resection and reconstruction in one procedure <sup>7</sup>. This can be considered a third option of surgical treatment for breast cancer. It has been demonstrated that it is associated with less involved surgical margins and re-excision surgical rates and better cosmetic outcomes.

Moreover, since the last decade of the 20<sup>th</sup> century, new mastectomy techniques have been developed. These techniques are advocated in patients who have to undergo complete breast glandular removal, but at the same time the overlying skin and the nipple can be conserved. These new techniques of conservative mastectomy are the **Skin-Sparing Mastectomy** and the **Nipple-Sparing Mastectomy**. These two techniques imply, after the entire removal of the gland, an immediate reconstruction of the breast. So these approaches offer a one- or two-stage procedure for either oncologic and reconstruction surgery, and lead to a more natural aesthetic outcome.



### **1.3 DESCRIPTION OF THE MODERN SURGICAL TREATMENT FOR BC AND RECONSTRUCTION TREATMENT**

- **SKIN/NIPPLE-SPARING MASTECTOMY**

***A- SKIN SPARING MASTECTOMY:***

Skin sparing mastectomy (SSM), a new surgical technique that has advocated in the last years of the 20<sup>th</sup> century is an oncological safe approach for the management of patient with breast cancer that minimizes breast deformity and improves cosmesis by the preservation of the skin envelope of the breast <sup>8</sup>.

Skin-sparing mastectomy consists in the en-bloc removal of the glandular tissue, according to a simple or modified mastectomy, of the Nipple-areola complex, in some cases also the adjacent biopsy scars and skin overlying superficial tumors with immediate breast reconstruction. The overlying subcutaneous fat and dermis are separated from the glandular tissue and the breast skin envelope and infra-mammary fold are preserved. Care must be taken to avoid thin skin flaps which could lead to an increase of skin necrosis.

The preservation of the natural skin envelope during SSM lead to a more natural aesthetic outcome. Furthermore, SSM approaches reduce the need for contralateral breast adjustment in order to achieve symmetry. This approach offer a single-stage procedure to either oncologic and reconstruction surgery.

Skin-sparing mastectomy can be performed in the case of:

- Ductal carcinoma *in situ* (DCIS) spread to more than 3cm
- Multicentric T1 / T2 breast tumors
- Prophylactic mastectomy
- In much selected cases in stage III of BC
- Unfavorable ratio between diameters of tumors and breast

Skin-sparing mastectomy is contraindicated in:

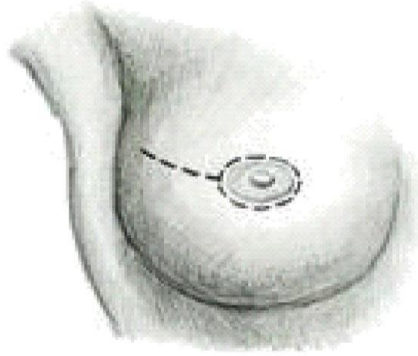
- Inflammatory carcinoma
- Locally advanced cancer
- Intensive smoking (relative contraindication).

Below 4 types of SSM are indicated. SSM types had been classified according to the type of incision used and the amount of skin removed. Factors like tumor location and depth and a previous biopsy scars influence the choice of the surgical incision <sup>9</sup>.

TYPE I SSM, PERIAREOLAR INCISION. It is commonly used in prophylactic cases and for non-palpable cancers diagnosed by needle biopsy. In patients with small diameter areola, a lateral extension or “tennis racquet incision” is sometimes necessary to improve exposure to the axillary tail, or to provide access for breast reconstruction. An “elliptical incision” can be fulfill if expander/implant reconstruction is performed. The incision should be obliquely

oriented toward the axilla to reduce flattening of the central breast mound. A periareolar incisions should have a significantly lower rates of complications compared to tennis racquet incisions <sup>9</sup> .

Type I

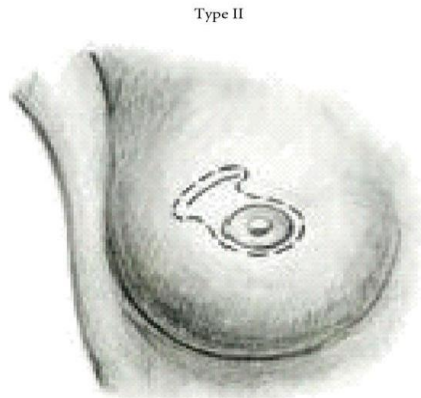


Tennis racquet incision

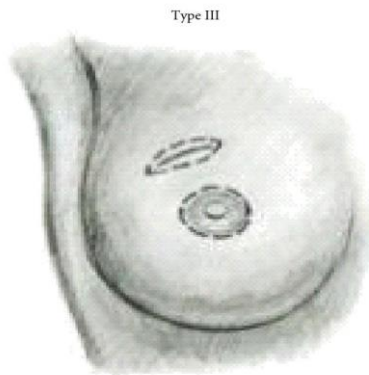


Peri-areolar incision

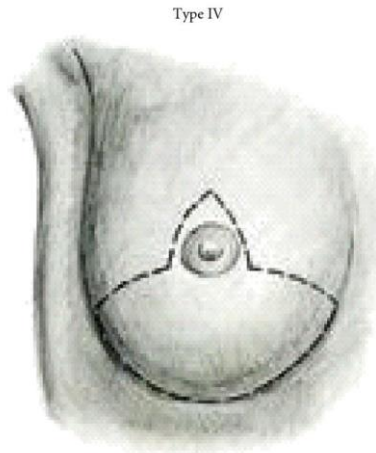
TYPE II SSM. It is used when a superficial tumor or previous biopsy is in proximity to the areola. In autologous reconstruction, the flap skin can be used to fill the defect. In implant-based reconstruction, the skin is closed to facilitate breast shape <sup>9</sup>.



TYPE III SSM. It is used when the superficial tumor or previous incision was remote from the areola, usually in the upper quadrants of the breast. Care must be taken to ensure the viability of the intervening skin <sup>9</sup>.



TYPE IV SSM . It is used in large, ptotic breasts when a reduction is planned on the opposite breast <sup>9</sup>.



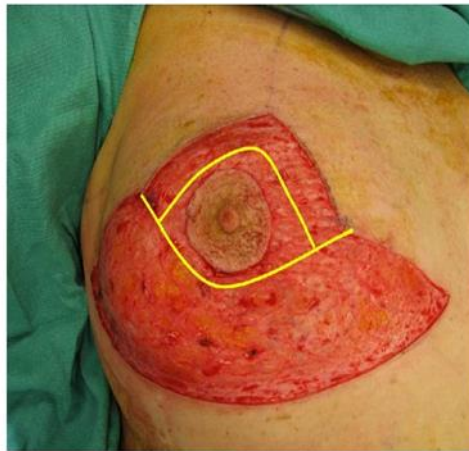
Wise pattern incision

*A common problem* with this technique is the occurrence of native skin flap necrosis of the most distal portions of the flap, particularly at the “T” junction. To avoid this complication, it was described a modification of the Wise pattern. The area between the vertical limbs of the T and an additional 2cm outside the horizontal limbs are deepithelialized but no resected.

Intraoperative photographs showing Wise pattern incisions with de-epithelialization of the skin :

- The area in yellow will be resected as part of the Type IV SSM. This excision leaves a rim of dermis along the vertical limbs of the skin excision.
- The inferior skin flap is elevated down to the inframammary fold.

- The deepithelialized inferior skin flap is draped over the tissue expander and sutured to the released inferior border of the pectoralis major muscle. Back cuts are made to allow inset of the dermal flap.
- The skin flaps just prior to closure. The deepithelialized vertical limbs serve as a buttress.



Wise pattern incisions

Skin-sparing mastectomy approach could be associated with complications, and the most frequent one, is the:

## **Necrosis of the Native Skin Flap**

The incidence of native skin flap necrosis after SSM, when followed by immediate breast reconstruction, was reported to be in 10% to 22% of cases <sup>9</sup>. It can vary in severity from superficial epidermolysis to full thickness skin loss. Complications predisposing factors include, age, breast size, type III and IV incisions, preoperative radiation, tobacco smoking, and obesity.

### ***B-NIPPLE- SPARING MASTECTOMY:***

Nipple-sparing mastectomy (NSM), another technique of breast conserving surgery advocated in women with early-stage cancer. The goal of the nipple-sparing mastectomy procedure is to remove all glandular breast tissue in order to maximize oncologic therapy, while leaving most of the skin and the nipple-areola complex (NAC) in place. The surgeon, in this manner, create a natural skin envelope, or pocket, that is filled with breast implant.

Nipple-sparing mastectomy spares the nipple-areolar complex, mandating removal of nipple-areola (NA) ducts, and leaving only the epidermis and dermis at the NA behind. The recommend thickness of skin flap is between 3-5 mm in order to preserve the sub-dermal vessels. When the dissection approaches to NAC area, 5 mm thickness is recommended to avoid necrotic complication of NAC. Similar to SSM, preservation of the NAC and skin envelope then mandates immediate reconstruction.

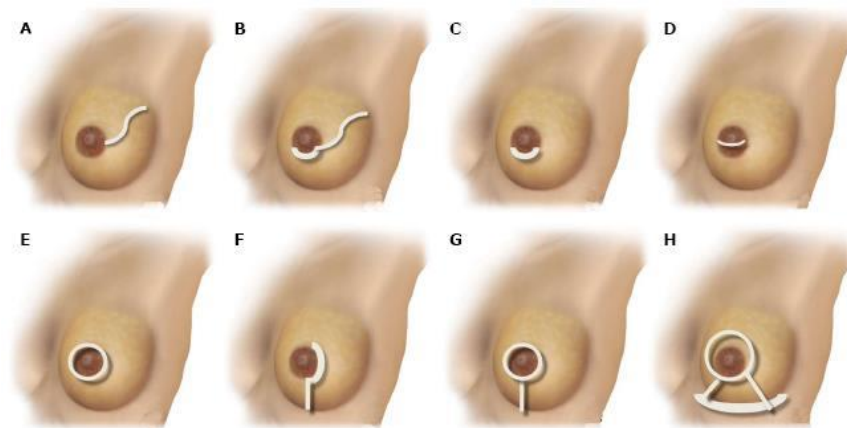
## **NSM INDICATIONS:**

- Extensive or Multicentric Ductal Carcinoma *in situ* (DCIS) and Lobular Carcinoma *in situ* (LCIS),
- Multifocal/Multicentric Invasive Ductal or Lobular Carcinomas >1-2cm distance from the nipple (without skin involvement and/or pathologic discharge from the nipple),
- Prophylactic Mastectomy in patient with BRCA1/2 mutation.

It is generally agreed that involvement of the skin/NAC, inflammatory tumors and Paget's disease represent **CONTRINDICATIONS FOR NSM**.

An increase risk of NAC involvement is correlated with: tumor location, number of positive lymph nodes, lymphovascular invasion, tumor size and distance from the NAC (as measured by magnetic resonance imaging).

Various **designs of skin incisions** for **NSM** can be drawn:



Various designs of skin incisions for NSM

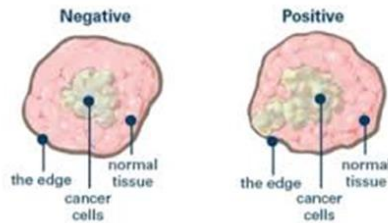


- A) Radial lateral incision.
- B) Peri-areolar with lateral extension.
- C) Hemi-periareolar.
- D) Transareolar.
- E) Circumareolar (periareolar total).
- F) Periareolar with vertical extension.
- G) Circumareolar with vertical extension.
- H) Wise-pattern mastectomy.

- **Breast conservation therapy:**

The attempt to preserve the breast without compromising survival in patients with early-breast cancer brought up the use of Breast Conserving Therapy (BCT). This includes breast conservation surgery (BCS) and breast adjuvant radiotherapy. Breast conservation surgery involves (beyond the **quadrantectomy approach**) the complete resection of the tumor with limited excision of surrounding breast tissue. The current standard is to accept a rim of normal breast tissue (of almost 2mm) all of the way around the tumor as evidence of complete excision.

Surgical margin is subjected to intraoperative pathologic assessment. If final pathologic results for resected tissue show that margins are involved (presence of tumor cells), patients undergo additional surgery to avoid local recurrence (because the risk of cancer recurrence is increased).



## Surgical margin

Tumor features can be associated with high risk of positive surgical margins such as:

- Presence of microcalcifications,
- Mammographic density,
- Lobular histology,
- Presence of extensive DCIS component on the core biopsy

Recent improvement in screening approaches (which allow to find most likely a smaller mass and still confined cancer to the breast), and neoadjuvant chemotherapy, BCS has become a common option and an established alternative to mastectomy.

Compared with mastectomy, breast conservation therapy allows greater preservation of the native breast and aesthetic outcomes with equivalent survival rates as has demonstrated by multiple randomized clinical trials.

Patients with no metastasis (M0), and for whom a primary surgical approach is technically not feasible and in patients with operable breast cancer who desire breast conservation, could undergo Neoadjuvant therapy. Neoadjuvant therapy

primary objectives here, is to get tumor down-staging and to improve surgical outcomes.

**BCS found indication in:**

*early-stage breast cancer; (TNM staging: T1-T2, N0-N1, M0, or group staging: STAGE I, STAGE IIA and IIB).*

**Traditional contraindication to perform BCT includes:**

- Large tumor size (>5 cm; although considered *relative contraindication*)
- Tumor-breast ratio (in case of high ratio)
- Skin or chest wall involvement
- Multicentric tumors
- Anticipated poor cosmetic outcome
- Contraindications to RT

Radiation therapy is almost always advocated after breast conservation surgery to eradicate any microscopic residual disease. However, it may not be indicated when a patient's prognosis is favorable or when it is not considered effective.

In adjuvant radiotherapy (RT) the entire breast and the contralateral breast get radiation, and an extra boost of radiation can be given to the area where the cancer was removed, where the risk to relapse is higher than the rest of the gland. Adjuvant radiation therapy and boost RT were become a safe option for the primary surgical treatment of early breast cancer. Especially boost RT is a widely accepted practice in patients at a higher risk of local recurrence,

particularly younger patients, and those with close surgical margins<sup>10</sup>. A number of different fractionation schedules for breast irradiation have been used. Although the most common fractionation schedule has been 50 Gy in 25 fractions (Traditional schedule).

The omission of Adjuvant Radiotherapy is known to reduce local recurrence risk and mortality rates after breast conservation surgery, also the success of BCT is contingent upon moderate-dose RT in eliminating subclinical foci of disease in the homolateral breast, when they exist. Nevertheless, radiotherapy is not devoid of side effects. Side effects after RT, include:

- Increasing breast parenchymal density.
- Skin thickness and tightening.
- Breast distortion.
- Pigmentation changes.
- Fibrosis.
- Reduction in breast volume in 10-20% of cases.

In case of pathological node negative or N1 status, there is no consensus amongst European and North-American guidelines for indications of adjuvant radiation therapy of the chest wall and axilla in breast conservation therapy. In case of N+, all patients should receive Adjuvant Chemotherapy. It should be indicated even in patients without N+, but in patients with poor prognostic factors based on primary tumor characteristics, such as grading (G; high nuclear or histological grade), diameter (cancers > 1cm and cancers <0.5cm with high G)

and negative hormone receptors. Nowadays, chemotherapy schedules containing *TAXANES* are standard of care

- **ONCOPLASTIC BREAST SURGERY (OPS or OBS):**

A novel surgical approach to the treatment of breast cancer, was developed in 1990 by German surgeon, Werner Audretsch.

Oncoplastic breast surgery has emerged as a new approach for extend breast conserving surgery possibilities.

Breast anatomic characteristics such as breast size, tumor size, tumor location, and tumor-breast ratio, could be limits for the indication of BCS. Besides this, the application of BCS is especially limited where a large resection would lead to major and definitive deformity of the breast (aesthetic sequel) and free margins can not be obtained, provided that aesthetic outcomes remain preserved.

One way of resolving this conflict is to use combined approach, which allow *wide excision of tumor and immediate reconstruction of the resection defects by volume displacement using adjacent tissue*. Wide excision of tumor helps to obtain higher rates of clear surgical margins and lower re-excision rates. Immediate reconstruction advocated in OPS is associated with improvement in the final appearance of breast by immediately reconstructive surgery without compromising cancer care. Furthermore, immediate reconstruction leads to greater increase in self-esteem, patient satisfaction and overall survival with, on the other hand, decrease in anxiety and depression rates.

In addition, after OPS, patients could undergo to a symmetrizing surgery for the contralateral breast to improve symmetry, especially in patients with high grade of ptosis or with macromastia. Furthermore, because surgery is completed prior to radiation (which is almost always indicated), wound-healing problems that occur with significant frequency with post-radiation surgery are minimized.

When compared with BCS, OPS allows much wider excision and positive margins seemed to be much lower in OPS than with BCS. In fact, positive margins rates in OPS are ranging from 5% to 18%, comparing with 10%-40% in BCS. Instead, when compared with MAS and *post-mastectomy reconstruction*, OPS reduces the burden and morbidity associated with multiple procedures.

Close collaboration between the breast surgeon and the plastic surgeon is essential in order to obtain the total removal of the tumor and good aesthetic results. Plastic surgeon as member of the breast care team, gradually assumes more responsibility for reconstruction of any result defect in the breast. Plastic surgeon has a crucial role to improve the breast appearance, which is associated with better psychosocial well-being, especially in immediate reconstruction.

Oncoplastic breast surgery can be indicated in extensive DCIS, invasive lobular carcinoma (ILC), multifocal disease, high tumor-breast ratio or in cases of partial or poor response to neoadjuvant treatment. Although, it can be indicated in cases where BCS would lead to a high risk of re-excision due to margin involvement or could cause major esthetic sequel. It also can be implemented within a second procedure when positive margins are found after BCS.

## **Surgical methods in case of small or large resection planned:**

1) When small resection is planned:

- In small breast with/without minimal ptosis **BCT.**
- In Large breast with moderate/sever ptosis **OPS.**

2) When large resection is planned:

- In large breast with moderate/sever ptosis **OPS.**
- In small breast **MAS.**

### **• RECONSTRUCTION SURGERIES:**

After a mastectomy the patient can undergo a breast reconstruction surgery. Breast reconstruction is achieved through several plastic surgery techniques that attempt to restore a breast to near normal shape, appearance and size following mastectomy. In addition, a breast lift, breast reduction or breast augmentation may be recommended for the opposite breast to improve symmetry of the size and position of both breasts.

Breast reconstruction, after Mastectomy, is an option which may improve psychosocial functioning. However, prospective studies show that in the long-

term breast cancer survivorship period (after mastectomy), improvement of the psychosocial functioning may be related to the effect of time post-treatment, rather than an effect of choice for or against breast reconstruction. Although, another prospective study who examined patients one year after their breast reconstruction, has indicate that breast reconstruction is not a universal panacea for the psychological consequences of mastectomy <sup>11</sup>.

Below are indicated several types of the breast reconstruction operations:

- Breast reconstruction can be made in at the same time as Mastectomy is done. This approach is called One-stage immediate breast reconstruction. This implies the placement of Silicon gel-filled implants into a newly formed pocket, surrounded by the minor pectoral muscle on the deeper side, and by the major pectoral muscle, together with the muscle's fascia, the epidermis and dermis on the other side. Complete muscle coverage is necessary in order to protect the implant from exposure. A special type of absorbable mesh can be used to hold the implant in place. This operation can be preferred in women with *medium-small* breast.

The immediate implant placement reduce the need for multiple surgical procedures. Anyway, it is not appropriate for all women and it should be use in appropriately selected patient. This operation can be preferred, for example, in women with *medium-small* breast.

Several difficulties and problems had to be faced in performing breast-reconstruction after Skin-Sparing Mastectomy. SSM enabled the *Pectoralis Major Muscle* to be detached inferiorly where the lower skin flap affords coverage to the implant. While expansion is facilitated with the release of the muscle inferiorly, pectoral muscle retraction and bottoming out of the implant



became problems. A solution might be the suture of the muscle to the fascia, but it is not the ideal resolution as frequently it needs more support for the muscle to hold in position, and furthermore, the tension might result in disruption while the suture cuts through the tissues.

A better resolution to these problems is offered by ADM – Acellular Dermal Matrices. The ADM reinforces the muscle and provides supplemental tissue between it and the infra-mammary fold. It allows the pectoralis muscle to be released, expands the space, allows fixation of the infra-mammary fold, and fills in the tissue void between the inferior edge of the pectoralis muscle and the infra-mammary fold. However, the use of ADM has reported problems such as: seroma, infections, slow vascularisation, disruption, reconstructive failure, patient concerns, and costs. But an alternative was found, a long-term resorbable synthetic mesh. There were several attempts before finding the right solution. Firstly, permanent synthetic mesh, which turned out to be too rigid. Secondly, Vicryl, which absorbed too rapidly, and finally, the Matrix Surgical Mesh, which offers greater tissue fixation and also functions as a scaffold and facilitates the native tissue in-grow.

- When the skin flap is not sufficiently stretched to support a full-sized implant right away and when adjuvant radiation therapy is indicated, breast reconstruction is made by two stages. Two-stages reconstruction implies the insertion of an *Expander* (balloon-like sac) into the newly formed pocket (similarly to the previous one) and it gradually filled with physiological saline through a tiny valve under the skin in order to stretch the muscle fibre and extend the skin above. After approximately six months, the expander, which meanwhile

sufficiently straightened the edges of the pocket, is replaced with a permanent implant in a second surgery.

- Breast reconstruction with autologous tissues: it is a technique based on the removing of autologous tissue flaps from the patient's:

- *Lower Abdomen area,*
- *Or Upper Back,*
- *Or Gluteus,*
- *Or Inner Thigh.*

This operation leave 2 surgical sites and scars. The most common types of *tissue flap reconstruction* are from the lower abdomen (called: *TRAM (transverse rectus abdominis muscle flap* or *DIEP (deep inferior epigastric perforator flap)*), and from the upper back (called: *latissimus dorsi flap*). Tissue flaps consist in skin, fat, blood vessels, and at least one muscle. Some women, have enough tissue in this area to shape the breast, so an implant may not be needed.

Often, this kind of operations don't include the remodelling of the other breast (to obtain bilateral symmetry) like usually happens during the operations previously described. In some cases, implants and autologous tissues may be used together for the same reconstruction.

- Breast reconstruction with fat (*lipofilling*): it consists in the removal of adipose tissue from the patient's own donor area, and its transplant in the mammary area. This technique especially helps to effectively correct the volume defect after wide excision, for example, after *Quadrantectomy*.

# **CHAPTER 2: BREAST CANCER CLINICAL PATHWAY, LEGISLATIONAL REQUIREMENTS AND QUALITY CARE INDICATORS IN THE BREAST UNITS**

## **2.1 BREAST CANCER CLINICAL PATHWAY IN THE BREAST UNIT**

Over the years, the incidence of breast cancer has gradually grown. This increase was associated, especially in the last three decades, with a progressive reduction in BC relative mortality (by almost one-third). This is due in part to increased screening programs and in part to the improved treatments for breast cancer. Screening programs are meant to detect cancers at an early stage when the chances of successful treatment are higher. They include bilateral mammography exam every 2 years in women aged from 50 to 69 years, and in women with familial breast cancer with or without proven BRCA mutations, an annual screening with magnetic resonance Imaging (MRI) of the breast, in combination with mammography.

The Pre-operative diagnosis of BC is based on clinical examination and imaging exams. Clinical examination includes Bimanual palpation of the breast and loco-regional lymph nodes (Axillary and Supraclavicular). Imaging exams include bilateral mammography and ultrasound of the breast, which allow to

identify size, site and possible multifocal and/or multicentric disease, and ultrasound of the regional lymph nodes. An MRI of the breast, is not routinely recommended, apart in cases of:

- Women with familial BC
- Breast implants
- Lobular cancers
- Suspicion of multifocality/multicentricity (particularly in lobular breast cancer)
- Large discrepancies between conventional imaging and clinical examination
- Before neoadjuvant Chemotherapy
- When Conventional imaging findings are inconclusive (such as CUP Syndrome).

Other clinical assessments include:

- Complete personal medical history, family history relating to breast/ovarian and other cancers
- Physical examination
- A full blood count
- Liver and renal function tests
- Alkaline phosphatase and calcium levels
- Menopausal status of the patient

- Cardiac function especially in patient who should undergo with *Anthracyclines* and/or *Trastuzumab* (neo)adjuvant therapy.

The clinical diagnosis should be confirmed by pathological assessment, which includes histological examination of the primary tumor (by needle biopsy), and cytology examination of the axillary nodes, whether lymph node(s) involvement is suspected. The core needle biopsy, must be obtained before any type of treatment is initiated. Needle biopsy is mandatory to ensure the clinical diagnosis of BC and to assess: Histological type, Grade, Hormonal receptors expression (ER & PgR) and Human Epidermal Growth Factor Receptor 2 (HER-2 or c-erbB2) expression by Immunohistochemical (IHC) evaluation.

Once the diagnosis of cancer is made, treatment should be carried out in Breast Units and provided by a multidisciplinary team. The Breast Unit (or Center) is defined as a specialized department (or departments) where all women have access to breast specialists/professionals from a range of disciplines with different but complementary skills, knowledge and experience. They work together to facilitate treatment planning, to provide the best possible outcome for the physical care and psychosocial needs of a patient and to carry out long-term follow-up programs.

It is demonstrated that a multidisciplinary approach increases the chances of survival and quality of life of the patient.

The multidisciplinary team includes:

- ❖ Oncological surgeons
- ❖ Plastic and reconstructive surgeons
- ❖ Radiotherapists
- ❖ Medical oncologists
- ❖ Radiologists
- ❖ Pathologists
- ❖ Breast care nurses: In a Breast Center, in addition to the nursing staff needed for the management of nursing care in the various services, there should be at least two breast care nurses with specific skills in counseling and communication and research.
- ❖ Psycho-oncologists: they should allow adequate psychological support
- ❖ Fertility specialists: All women diagnosed with breast malignant tumor under the age of 38, must be submitted, at the time of diagnosis, to counseling at a specialized center for fertility which cooperates with the BU.
- ❖ Geneticists: The Breast Unit must have a dedicated medical geneticist with experience in the field of hereditary-familial cancers of the breast / ovary who accomplish the genetic test during the genetic counseling in women with high risk.
- ❖ Physiotherapists: they should be available to evaluate the patient in pre-operative and in the immediate post-operative period. They evaluate

the occurrence of structural and functional alterations of the homolateral arm and shoulder in case of ALND.

Afterwards, they should ensure an adequate care of the woman with rehabilitative needs for complications and late outcomes.

- ❖ Palliative cares: patients with advanced disease should have a specialized service available for palliative care, coordinated with the multidisciplinary team to ensure continuity of care.

- ❖ Research services: the Breast Unit must provide training opportunities for students and specialists who want to devote themselves to breast cancer treatment and organize continuous training courses at regional, national and international levels.

- ❖ Voluntary associations: they give information on how to access the therapeutic process and the management of side effects. They help the patients during treatment, for example, with the services for wigs or, in some cases, organizing the transport to the radiotherapy centers or the Breast Unit. They create a listening area and organize programs for physical and psychological recovery during and after illness. Furthermore, they interact with the institutions to ensure the right to quality of care, giving patients the opportunity to improve the quality of services and to make their voices heard.

As patient needs may change with time, the composition of the team may also change to meet these needs.

The steps that characterize the path of the patients with breast cancer within the Breast Unit are:

- ►Step 1: Access / CORD. CORD, is run by trained nursing staff and it is accessed in person, by phone or by email. One of the main tasks is to perform a kind of triage in order to direct the patient to the next step.
  
- ►Step 2: More in depth diagnosis through imaging examinations and interventional radiology and histopathological diagnosis integrated, if necessary, by the biological studies.
  
- ►Step 3: The first multidisciplinary meeting (MDM). The surgeon or the radiologist along with the breast care nurse inform the patient of the diagnosis and discuss the treatment plan with her. During the interview, the patient receives an indication of the therapeutic strategy as set by the MDM.
  
- ►Step 4: According to the clinical stage, the path may continue with surgery or with medical treatments (in cases in where a neo-adjuvant chemotherapy is indicated or in metastatic disease).
  
- ►Step 5: The definitive histopathologic diagnosis and the second multidisciplinary meeting. The patient is informed of the definitive diagnosis and on how to continue her path (which in most cases includes drug therapy and radiation therapy).
  
- ►Step 6: The physical and the psychological rehabilitation phase. It starts



before the surgical treatment, and can continue during the hospitalization period and/or subsequently to it.

- ►Step 7: Follow-up program. Patients who have completed the initial treatment, undergo visits and periodic checks to verify an eventual recurrence of the disease and eventual treatment's side effects.

For women with breast cancer, having access to Breast Unit means having advanced level structures over all of the:

1- Italian

2- And European.

The performance of the BU must be evaluated regularly. It also should be a continuous upgrading of both staff and equipment.

The Breast Units are structured in a network. In order to enhance the performance and the resources, networking to smaller hospitals, territorial structures, (including hospices) and home care, is required.

This Network should be organized according to the Hub and Spoke model: the hub ("centre") is the breast centre that offers all the essential requirements to treat breast disease; the spokes ("radius") are the second-level centres connected to the hub. This system ensures greater presence in the regions, but also an equity of treatment for diverse complexity levels.

## **2.2 LEGISLATIVE REQUIREMENTS OF THE BREAST UNIT**

Breast Units were set up for the first time at the beginning of the 21th century after the publication of the “Requirements of a Specialist Breast Unit” in 2000 by the European Society of Breast Cancer Specialists (Eusoma).

These same guidelines were published (in the fourth edition of the European Guidelines for Quality Assurance in breast cancer screening and diagnosis drafted by Eusoma) and adopted by the European Parliament as a basis on which to rest the legal regulations (Resolution on Breast Cancer in the European Union INI 2002/2279 of 06.05.2003). Recently, the European Parliament has written a declaration (No 17/2015 under Rule 136 of Parliament's Rules of Procedure on the fight against breast cancer) on the fight against breast cancer in which states the importance to implement *nationwide mammography screening and multidisciplinary specialist breast units by 2016*. It was done as called for in the European Parliament resolutions of 2003 and 2006 and as required by the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis to reduce the mortality rates for patients with breast cancer (91495 women in the EU died from breast cancer in 2012). The commission has also recommended that breast cancer patients should have access and be treated according to their needs in the Breast Unites.

Following the European indications, every nation should ensure the presence of a Breast Unit per 250 thousand inhabitants, and the different states must ensure a national treatment discipline in accordance with the EUSOMA indications.

Furthermore, according to national and international standards, a Breast Unit should follow a set of basic and very precise requirements. It must treat more than 150 new cases of breast cancer each year, adopt guidelines for the diagnosis

and treatment of cancer in all stages and the psychological and physical rehabilitation of the patient. Furthermore, it must provide multidisciplinary meetings (MMD) with the participation of all members to discuss the treatment planning. This includes the assessment of the preoperative diagnosis, the stage, the formulation of the therapeutic strategy, the definitive postoperative diagnosis and follow-up. The treatment planning, must respect specific indications for: surgical, medical, radiation and rehabilitation therapy. The various proposals have to be shared with the patient taking in consideration patient's age, clinical features and preferences.

Is paramount importance to ensure the observance of the waiting time set in the National Plan of Government Lists Hold and the Diagnostic Therapeutic Paths for BC.

In the last 20 years the probability of healing all patients suffering from breast cancer has significantly increased. This is associated with greater survival, which implies higher rates of follow-up programs.

There is an important debate in the medical community regard the intensity of follow-up programs: minimalist or high intensity. It should be known that, it has not been shown an impact on better survival when *high intensity* follow-ups programs were advocated.

Patients, who have completed primary treatment, should have regular follow-up programs. Regular visits are recommended every 3–4 months in the first 2 years, every 6 months from years 3–5 and annually thereafter.

The frequency of visits can be adjusted according to the individual patient's needs, Patients should be encouraged to report new persistent symptoms promptly without waiting for the next scheduled appointment.

It was recommended that the responsibility for follow-up be formally allocated to a single physician and that the patient be fully informed of the arrangements for follow-up. The follow-up visits represent a good time to share the anxieties and fears and to put any question to the professionals.

The components of the follow-up program and the evidences supporting the goals of follow-up have been up-dated in 2005.

The goals of follow-up are :

- To detect early local recurrences or contralateral breast cancer.
- To evaluate and treat therapy-related complications (such as menopausal symptoms, osteoporosis and second cancers).
- To motivate patients continuing ET (endocrine therapy).
- To provide psychological support and information in order to enable a return to normal life after breast cancer.

*Summary of recommendations and indications :*

- Every visit should include a thorough history, eliciting of symptoms and a physical examination
- Annual ipsilateral (after BCT) and/or a contralateral mammography with ultrasound are recommended
- An MRI of the breast may be indicated for young patients, especially in cases of dense breast tissue and genetic or familial predispositions

- Ultrasound can be considered in the follow-up of Lobular Invasive Carcinomas
- Routine blood tests are usually indicated to follow-up patients on ET due to the potential side-effects of these drugs, namely in the lipid profile. Lipid-metabolism disorders can be the cause of a wide range of conditions, with cardiovascular disease being the most significant. Because of the high levels of estrogen deprivation caused by aromatase inhibitors, the effect of such inhibition on lipid profiles and thus cardiovascular disease (is the leading cause of death in postmenopausal women in the developed world) become less relevant. It is also important to evaluate the tumor markers, such as CEA & CA 15-3
- For patient on Tamoxifen therapy an annual gynaecological examination, possibly with a transvaginal ultrasound, by an experienced gynaecologist is recommended. Tamoxifen use (as adjuvant therapy) is associated with an increase risk of endometrial cancer. This risk is considered to be a consequence of tamoxifen partial estrogen-agonistic effect.
- Regular bone density evaluation is recommended for patients on aromatase inhibitors therapy. Women with a history of breast cancer may be at increased risk of osteoporosis because of loss of bone mineral density owing to premature ovarian failure from chemotherapy or to aromatase inhibitors used as adjuvant therapy. For these reasons, the steering committee recommends that osteoporosis be monitored in postmenopausal women with breast cancer by a bone mineral density test.

- Changes in lifestyle are also recommended such as: regular exercise to all suitable patients after treatment of breast cancer and nutritional counselling as part of the survivor care for all obese patients.

## 2.3 QUALITY CARE INDICATORS IN THE BREAST UNITS

In accordance with the EU resolution, a review of literature has been performed by an international steering committee in order to identify and define a set of indicators for breast cancer healthcare quality assurance. They took into consideration national and international guidelines and experts. They focused on four key properties of a quality measure. They were:

- ✓ Reliability, which means that the observation is highly consistent whenever measured.
- ✓ Validity, which means that the indicator is really measuring what it is intended to do.
- ✓ Usability, which means the observations have to be easily interpreted.
- ✓ Feasibility, which requires easy data collections during routine clinical activities with limited costs.

These indicators (see **Table-1**), defined by EUSOMA <sup>12</sup>, should be routinely measured and evaluated in order to confirm that the clinical outcome reaches the requested standards.

In according to this, the Breast unit of Pisa, one of the three independent Teaching Hospitals in Tuscany, is introducing an evaluation system of the

performance and quality care to check if it respects the indicators and respond to its mission. This is called QT-BREAST. The QT BREAST is the web software used for monitoring the quality of diagnosis, treatment and follow-up of BC. It is updated with modern practices, and it enables interactive data analysis and automatic calculation (evaluation) of the indicators defined by SENONETWORK and EUSOMA.

At a regional level, it is important to ensure parity between different BU(s). The use of QT Breast could lead to its common use on the entire regional system next.

There are two groups of indicators:

- The PROCESS / PATH indicators: they aim in monitoring these indicators is to assess the enter path of career and to identify any "weak" steps.
- The AESTHETIC AND FUNCTIONAL OUTCOME indicators: they aim to assess the treatment outcome in terms of aesthetic and functional results.

Both of these groups should be able to measure any "weakness" in the choice of the surgical techniques, such as incorrect incision lines, conservative interventions without use of Oncoplastic (in cases where these techniques may be necessary), removal of excessive tissue to obtain free margins (a phenomenon which is observed most frequently at centers with less experience), an excessive skin removal or a high-dose of RT even when not necessary on the basis of the margins and the type of lesion.

Table- 1: Process-path indicators

	Indicator	Level of evidence	Mandatory/ Recommended	Minimum standard	Target
<b>Diagnosis</b>					
1.	Completeness of clinical and imaging diagnostic work-up (Proportion of women with breast cancer who pre-operatively underwent mammography, ultrasound and physical examination)	III	M	90%	95%
2.	Specificity of diagnostic procedures (B/M ratio)	III	M	1:2	1:4
3.	Proportion of women with breast cancer (invasive or in situ) who had a pre-operative definitive diagnosis (B5 or CS)	III	M	80%	90%
<b>4. Completeness of prognostic/predictive characterization</b>					
4a	Proportion of invasive cancer cases for which the following prognostic/predictive parameters have been recorded: histological type, grading, ER&PgR, HER 2	II	M	90%	95%
4b	Proportion of invasive cancer cases with primary surgery, for which the following prognostic/predictive parameters have been recorded: histological type, grading, ER & PR, HER 2, pathological stage (T and N), size in mm for the invasive component, peritumoral vascular invasion, distance to nearest radial margin	II	M	95%	98%
4c	Proportion of non-invasive cancer cases for which the following prognostic/predictive parameters have been recorded: Dominant histologic pattern, Size in mm (best pathology or radiology estimate if 2 stage pathology), Grading, distance to nearest radial margin	II	M	95%	98%
5.	Waiting time (Time between the date of first diagnostic examination within the unit and the date of surgery or start of treatment within 6 weeks)	IV	R	75%	90%
6.	MRI availability (at least 5% of cancers preoperatively examined)	IV	R	5%	NA
7.	Genetic counselling availability (proportion of cancer cases referred)	IV	R	5%	NA
<b>Surgery and loco-regional treatment</b>					
8.	Multidisciplinary discussion (proportion of cancer patients to be discussed)	IV	M	90%	99%
<b>9. Appropriate surgical approach</b>					
9. a	Proportion of patients (invasive cancers) who received a single (breast) operation for the primary tumour (excluding reconstruction)	III	M	80%	90%
9. b	Proportion of patients (DCIS only) who received just one operation	II	M	70%	90%
9. c	Proportion of patients (invasive cancers) and a clinically negative axilla (+US aFNA/CNB) who had sentinel lymph-node biopsy	II	M	90%	95%
9d	Proportion of patients with invasive cancer and axillary clearance performed with at least 10 lymph nodes examined	III	M	95%	98%
<b>10. Appropriate post-operative RT</b>					
10. a	Proportion of patients (invasive cancer M0) who received postoperative radiotherapy after surgical resection of the primary tumour and appropriate axillary staging/ surgery in the framework of BCT.	I	M	90%	95%
10b	Proportion of patients with involvement of axillary lymph nodes (> pN2a) who received post-mastectomy radiotherapy	I	M	90%	95%
<b>11. Avoidance of overtreatment</b>					
11a	Proportion of patients with invasive breast cancer not greater than 3 cm (total size, including DCIS component) who underwent BCT.	I	M	70%	80%
11b	Proportion of patients with non-invasive breast cancer not greater than 2 cm who underwent BCT	II	M	70%	80%
11c	Proportion of patients with DCIS who do not undergo axillary clearance	IV	M	95%	98%
11d	Proportion of invasive breast cancer patients with pN0 who do not undergo axillary clearance	II	M	80%	90%
<b>Systemic treatment</b>					
<b>12. Appropriate hormonotherapy</b>					
12a	Proportion of patients with endocrine sensitive invasive carcinoma who received hormonotherapy, out of the total number of patients with this diagnosis	I	M	80%	90%
12b	Proportion of patients with ER- and PgR- carcinoma who did not receive adjuvant hormonotherapy out of the total number of patients with the same diagnosis	I	M	98%	100%

(continued on next page)



13. Appropriate chemotherapy and other medical therapy					
13a	Proportion of patients with ER- (T >1 cm or Node+) invasive carcinoma who received adjuvant chemotherapy, out of the total number of patients with the same diagnosis	I	M	80%	90%
13b	Proportion of patients with N+ or N- T >1 cm HER2+ (IHC 3+ or in situ hybridisation positive FISH +) invasive carcinoma treated with chemotherapy and who had adjuvant trastuzumab, out of the total number of patients with the same diagnosis.	I	M	80%	90%
13c	Proportion of patients with HER2 negative invasive carcinoma who did not have adjuvant trastuzumab, out of the total number of patients with the same diagnosis.	II	M	98%	100%
13d	Proportion of patients with HER2+ invasive carcinoma who had adjuvant chemotherapy, out of the total number of patients with the same diagnosis who had adjuvant trastuzumab	IV	M	95%	100%
13e	Proportion of patients with inflammatory breast cancer (IBC) or locally advanced non-respectable ER carcinoma who had neoadjuvant chemotherapy over the total of patients with the same diagnosis	II	M	90%	95%
Staging, counselling, follow-up and rehabilitation					
14. Appropriate staging procedure					
14a	Proportion of women with stage I breast cancer who do not undergo baseline staging tests (US of liver, chest X-ray and bone scan).	III	M	95%	99%
14b	Proportion of women with stage III breast cancer who undergo baseline staging tests (US of liver, chest X-ray and bone scan)	III	M	95%	99%
15	Perform appropriate follow up				
15.	Proportion of asymptomatic patients who undergo routine annual mammographic screening and clinical evaluation every 6 months in the first 5 years after the operation.	I	M	95%	99%
16. Avoid inappropriately intensive follow up					
16.	Proportion of asymptomatic patients who do not undergo a follow up protocol more intensive than routine annual mammographic screening and clinical evaluation every 6 months in the first 5 years after the operation.	I	R	95%	99%
17. Availability of nurse counselling					
17a	Proportion of patient referred for nurse counselling at the time of primary treatment	IV	R	85%	95%
17b	All women with a diagnosis of breast cancer should have direct access to a breast care nurse specialist for information and support with treatment related symptoms and toxicity during follow up and rehabilitation after initial treatment	IV	R	95%	99%

Below are mentioned some quality indicators.

**A) Quality indicators on diagnosis:**

1. Completeness of clinical and imaging diagnostic work-up before the operation.
2. Specificity of diagnostic procedures in order to minimize unnecessary operations.
3. Pre-operative diagnosis - the proportion of women with breast cancer (invasive or in situ) who had a preoperative definitive diagnosis. This

definitive diagnosis should overcome 80% (as a minimum standard), with the target of 90%.

4. Completeness of prognostic/predictive characterization. This include:

- Histological type
- Grading (according to EU guidelines)
- ER and PgR
- HER-2 (or c-erbB2, Human Epidermal Receptor protein-2)
- Pathological stage (T & N)
- Size in mm for the invasive component
- Peritumoral vascular invasion
- Distance to nearest radial margin

Estrogen and progesterone receptors (ER and PgR) are prognostic markers of outcome, and strong predictive markers of response to endocrine therapy and chemotherapy. ER status is strongly influenced by tumor grade and histology, for example, all Grade I tumors (well-differentiated tumor cells) are more likely ER positive. The presence of hormone receptors (ER and PgR) can be tested on the needle core biopsy as well as on the resection specimens. ER testing is recommended as a mandatory item. The determination of PgR expression is reported along with the ER one. PR status, according to what has been demonstrated, is independently associated with disease-free and overall survival. In fact, it seems that the presence of the Progesterone receptor, without the Estrogen receptor, is

associated with worse prognosis, and conversely, the presence of both PgR and ER is associated with better prognosis.

Human Epidermal Growth Factor Receptor 2, is a protein, which is expressed at low levels in a variety of normal epithelial cells. Amplification of HER-2 gene and concomitant protein overexpression were demonstrate in almost 10-20% of primary breast cancers. Determination of HER2 status in breast cancer is important, as it has been demonstrated that it is a prognostic as well as a predictive marker. In fact the presence of HER-2 is associated with a worse prognosis.

Breast cancers with HER2 alterations are targets for treatment with Trastuzumab, a humanized monoclonal antibody. Trastuzumab has shown to improve the response and survival rates when added to chemotherapy or used as a monotherapy.

5. Waiting time – The time between the date of the first diagnostic examination within the breast unit and the date of surgery/other medical treatments should be within *6 weeks*.
6. Use of MRI - The proportion of cancer cases examined pre-operatively by MRI.
7. Genetic counselling availability.

B) **Quality indicators on surgery and loco regional treatments:**

8. Multidisciplinary discussion - The proportion of cases to be discussed by a multidisciplinary team.
9. Appropriate surgical approach in patient with *invasive breast cancer*:

- a) The proportion of patients who received a *single* operation for the primary tumor should be higher than 80% (as a minimum standard). This means that the proportion of patients who undergo to surgical re-excision should be lower than 20%.
- b) The proportion of patients with DCIS who received one operation (and do not undergo to re-excision surgery secondary to the surgical margins involvement) should be higher than 70%.
- c) The proportion of patients with a clinically negative axilla who underwent sentinel lymph node biopsy should be higher than 90%.
- d) The proportion of patients who had no involvement of level I axillary lymph nodes (after the examination of 10 lymph nodes), should overcome 95%.

10. Post-operative RT

- a) The proportion of patients with invasive breast cancer and no metastasis (M0) who received post-operative radiotherapy after surgical resection of the primary tumor and appropriate axillary staging/surgery in the framework of BCT, should be more than 90%.
- b) The proportion of patients with involvement of axillary lymph nodes ( pN2a) who received post-mastectomy RT, should be higher than 90%

11. Avoidance of overtreatment

- a) The proportion of patients with invasive breast cancer not greater than 3 cm (includes also DCIS with T < 3cm) who underwent BCT should be higher than 70%.

b) The proportion of patients with non-invasive BC with  $T < 2\text{cm}$  who underwent BCT should be higher than 70%.

c) The proportion of patients with DCIS who do not undergo axillary clearance should be higher than 95%. \*( axillary involvement in DCIS occurs in 1-2% of cases, and it depends on grade and diameter of the cancer).

d) The proportion of patients with invasive BC and pN0 who do not undergo axillary clearance should be higher than 80%.

C) **Quality indicators on systemic treatment :**

12. Appropriate Hormonotherapy:

a) the proportion of patients with endocrine sensitive invasive carcinoma who received hormonotherapy, should be higher than 80%.

b) the proportion of patients with ER - and PgR - carcinoma who did not receive adjuvant hormonotherapy, should be more than 98%.

13. Appropriate chemotherapy and other medical therapy-

a) The proportion of patients with ER- invasive carcinoma (or  $T > 1\text{cm}$  or Node+) who received adjuvant chemotherapy, should be higher than 80%

b) The proportion of patients with invasive breast cancer and :  $T > 1\text{cm}$ , N positive/negative and positive HER2, treated with chemotherapy and who had adjuvant therapy with Trastuzumab, should overcome 80%.

- c) The proportion of patients with HER2- breast invasive carcinoma who did not received adjuvant therapy with Trastuzumab, should be higher than 80%.
- d) The proportion of patients with HER2+ invasive carcinoma who received adjuvant chemotherapy should be higher than 90%.
- e) The proportion of patients with Inflammatory Breast Cancer or with ER+ Locally advanced cancer who received neo-adjuvant chemotherapy should overcome 90%.

D) **Quality indicators on staging, counselling, follow-up and rehabilitation.**

14. The proportion of women with:

- a) Stage I BC who do not undergo baseline-staging tests (Ultrasound of liver, Chest X-ray and bone scan) should be more than 95%. It is shown that the percentage of patients with asymptomatic metastases detected with these tests is irrelevant.
- b) Stage III BC who undergo baseline-staging tests (Ultrasound of liver, Chest X-ray and bone scan) should be more than 95%

15. Perform appropriate follow-up – the proportion of asymptomatic patients who undergo routine annual mammographic screening and clinical evaluation every 6 months in the first 5 years after breast operations should be higher than 95%.

16. Avoid inappropriately intensive follow-up : The proportion of asymptomatic patients who do not undergo a follow-up protocol that is more intensive than local examination (Mammography, Ultrasound and clinical

evaluation every 3-4 months in the first 2 years, every 6 months from years 3-5 and annually thereafter) should be higher than 95%.

Recently, other quality indicators which concern the Aesthetic and Functional outcome after reconstructive surgery have been introduced. These indicators evaluate the adequacy of reconstructive surgery (after the oncological surgery) on the aesthetic and functional outcomes.

### **Indicators of functional outcomes :**

The aesthetic outcome must be evaluated in the second year follow-up.

The indicators include:

1. Proportion of patients who do not have diastasis or retracted scar after BCS and Mastectomy should be more than 80%.
2. Proportion of patients who do not have skin-discoloration after Mastectomy and BCS should be higher than 80% - skin discoloration could be evaluated by the definition of its presence or its absence. When it is present, it could be darker or lighter than normal skin color.
3. Proportion of patients who underwent Mastectomy with Immediate reconstruction should be higher than 60% - immediate reconstruction should be made especially in cases where RT is not indicated and according to the patient's desire.
4. Proportion of patients who underwent Skin-Sparing Mastectomy and/or Nipple-Sparing Mastectomy should be more than 50% - preservation of the skin envelope and the infra mammary fold improves breast cosmetics.

5. Proportion of patients who underwent Nipple-Sparing Mastectomy should be higher than 10% - Nipple Areola complex preservation considerably improves breast cosmetic outcome and psychological compliance. It is estimated that one-fourth of patients with BC could undergo NSM.
6. Proportion of patients with permanent implant in immediate reconstruction which does not come into direct contact with the subcutaneous mastectomy flap should be higher than 95% - direct contact can lead to Exposure, Extortion, Dislocation, or Contracture of the implant.
7. Proportion of patients who underwent reconstruction post mastectomy with Human Acellular Dermal Matrix or Synthetic Matrix should be higher than 95% - these “ devices” provide a scaffold on the implant.
8. Proportion of patients who underwent Oncoplastic Breast Surgery should be higher than 90%.
9. Proportion of patients with breast cancer surgery who underwent pre- and post-operation photography should be more than 90%.
10. Proportion of patients who had implant reconstruction failure within 6 months should be less than 9%.

**Indicators of functional outcomes :**

These indicators detect axillar overtreatment.

1. Proportion of patients who present Lymphedema of the arm after ALND should be less than 20% - Lymphedema occurs when protein-rich lymph fluid accumulates in the interstitial tissue. Lymphedema leads to arm volume



increase and it usually develops gradually over time. Lymphedema is an important consideration for clinicians and surgeons because it causes:

- Increased pain due to the compression of nerves
- Loss of Function due to swelling and limb changes
- Depression - Psychological coping as a result of the disfigurement and debilitating effect of lymphedema
- Lymphedema can occur more frequently in the following cases:
  - Level III Axillary Lymph Node Dissection
  - After radiation to the lymph node areas after lymph node surgery
  - Extensive cancer in lymph node
  - Mastectomy rather than BCS

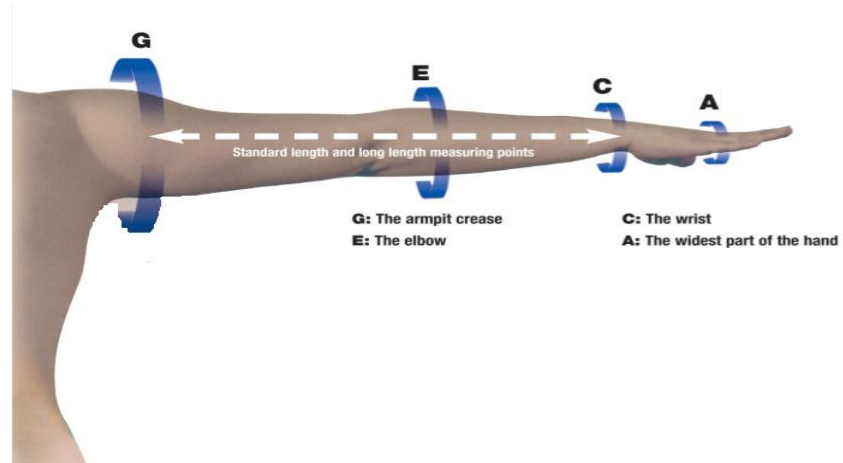
Patients with Lymphedema should undergo arm circumference measurement in specific points; these points are:

A-The widest part of the *hand*

C-The wrist

E-The elbow

G-The armpit crease



2. Proportion of patients who had Lymphedema after Sentinel Lymph Node Biopsy should be less than 5%.

3. Proportion of patients with 10% lower shoulder function in one or more postures (such as Flexure, Extension, Abduction, and Adduction) than the other shoulder, should be less than 10% :

Limited shoulder function is a good indicator because he can reveal post-operative complications such as:

1. Retracted scars.
2. Unnatural posture
3. Reduced strength
4. Radiotherapy.

# **CHAPTER 3: MATERIALS AND METHODS**

## **3.1 AIM OF THE STUDY**

The aim of my thesis is to demonstrate the importance of the follow-ups and of quality indicators monitoring in order to improve the quality of the breast cancer pathway.

## **3.2 PATIENTS AND METHODS**

During 2014, Pisa's Breast Unit performed 1100 breast operations, 649 of them for malignant tumor. Approximately 18 months after the surgery (a range of 12 to 20 months), all the patients were invited to undergo the follow-up program. The data emerging from the follow-up have been included in a specific software that can perform real-time monitoring of those indicators.

I personally took part in the examination of 200 patients

In most of the cases the patients were easily reachable and collaborative. 5% of them preferred to postpone the appointment, and 10% refused the follow-up for fear of potential negative results. It would be interesting to delve deeper the emergency of a similar data in the Psycho-oncological field.

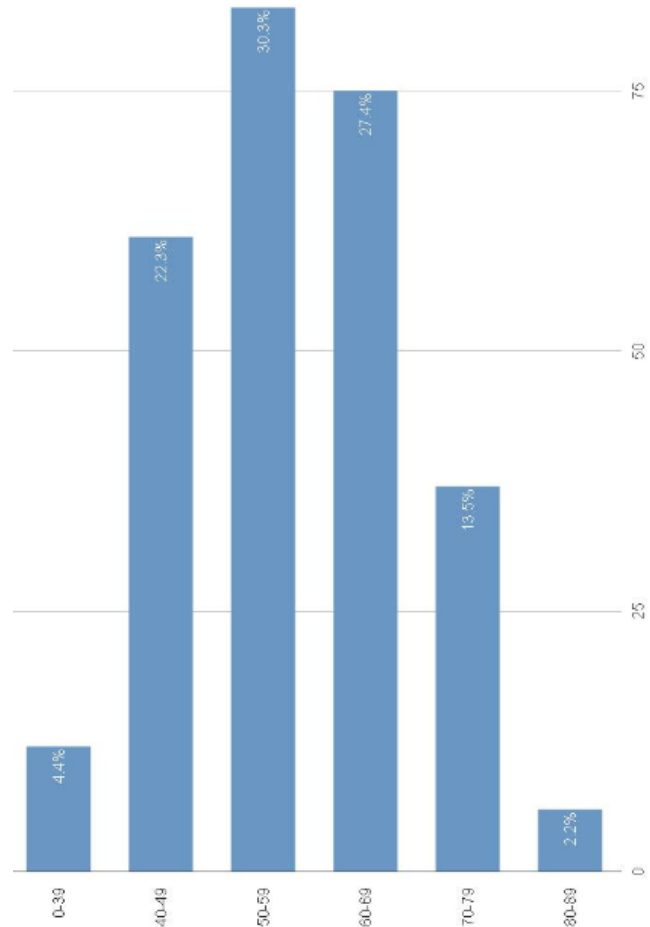
- **A DESCRIPTION OF THE SAMPLE:**

First of all, 63% of the cases were discussed throughout multidisciplinary meetings in the preoperative phase, and all of them during postoperative phase.

Analysing such data we obtain that:

4,3% are under 39 years old.  
22,3% are between the ages of 40 and 49.  
30,3% between the ages of 50 and 59.  
27,4% between the ages of 60 and 69.  
13,5% between the ages of 70 and 79.  
And 2,2% between the ages of 80 and 89.

Therefore, we can observe that more than half of the patients (57,7%) operated on for malignant tumor at Pisa's Breast Unit, during 2014, were between the ages of 50 and 69.



The familiar anamnesis revealed that 29% of the patients had at least one first-degree relative positive to breast cancer. 19 patients accomplished the Genetic Counselling path in order to verify possible gene mutations. One of them proved to be positive to BRCA1, and no one proved to be positive to BRCA2.

In the Personal Medical History, the 48,5% of patients has reported presence of mass with the *Breast self-examination* (BSE), and it had been unveiled by the clinical examination in the 68,2% (of all patients). Furthermore, 9% of them had a previous Breast Lesion.

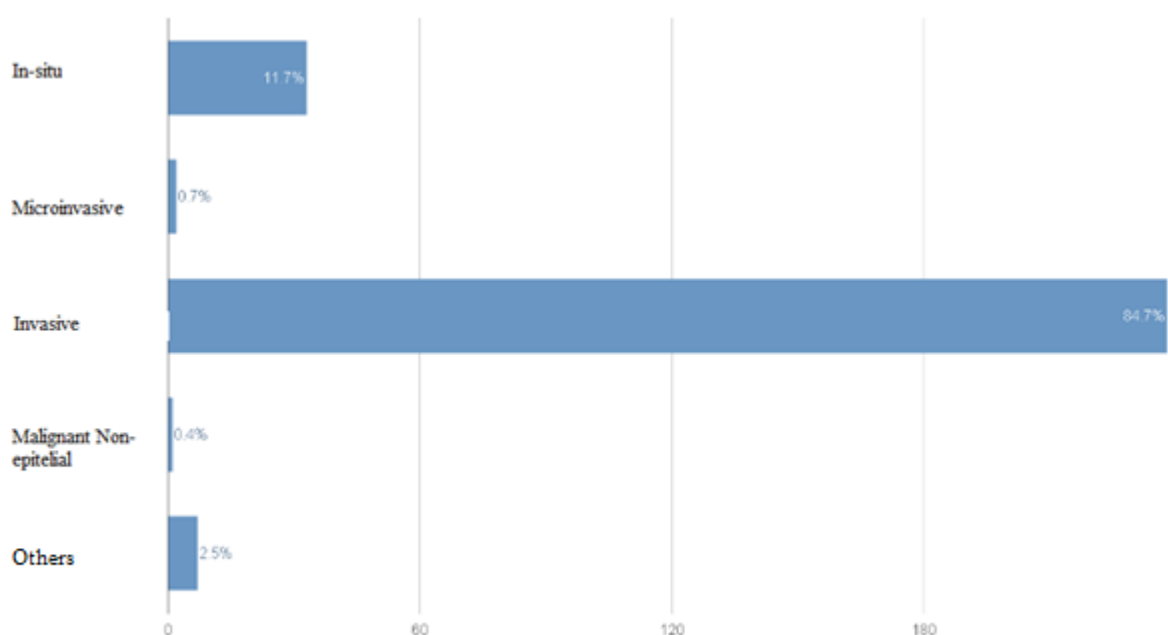
49,3% of the patients had the tumor on the right breast, and the 50,7% on the left one.

The tumour mass where located as shown below:

	<i>left breast</i>	<i>right breast</i>	<i>Total</i>
<i>Upper-outer</i>	16,2%	22,3%	38,5%
<i>Outer-central</i>	3,7%	2,7%	6,4%
<i>Lower-outer</i>	4%	3,7%	7,7%
<i>Lower-central</i>	2%	1,7%	3,7%
<i>Lower-inner</i>	4,4%	2,7%	7,1%
<i>Deep Central portion</i>	1%	1,7%	2,7%
<i>Upper-inner</i>	4,4%	4,4%	8,8%
<i>Upper-central</i>	9,5%	6,8%	16,3%
<i>Areolar region</i>	3,7%	2,7%	6,4%
<i>Diffuse</i>	1,7%	0,7%	2,4%
<i>Total</i>	50,7%	49,3%	100%

The pre-operative Histopathology examination made on the needle biopsy of the tumour mass, pointed out a definitive diagnosis of malignant breast tumor in almost 90% (C5/B5).

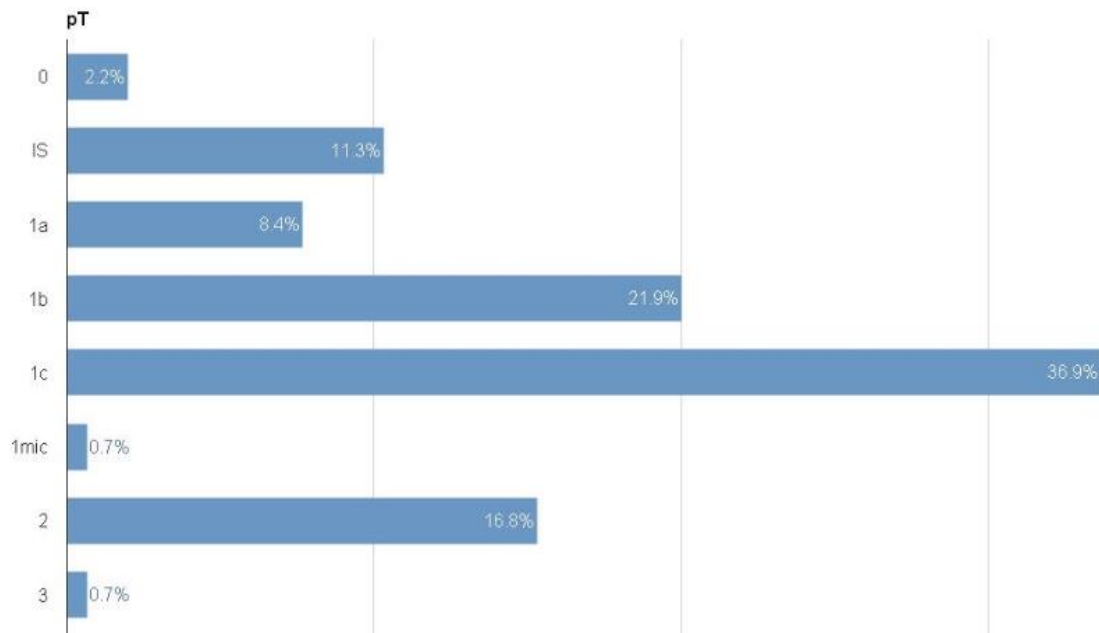
The post-operative diagnosis has reported in the 86,1% of the cases, Invasive Breast Cancer (84% of them was Ductal Carcinoma (or NOS)) , 0,7% was Microinvasive Breast Carcinoma, and 0,4% Non-epithelial malignant breast tumor. And in the 11,7% was Carcinoma In situ.



The percentage which concerns the Pathological T stage for the Invasive Breast Cancer is reported as below:

- 2,2% the tumor couldn't be assessed;
- 11,3% was carcinoma *in situ*,(Tis);
- 8,4% was less than 0,5cm (T1a);
- 21,9% was more than 0,5cm and less than 1cm (T1b);
- 36,9% was more than 2cm and less than 3cm (T1c);

- 16,8% was more than 2cm and less than 5cm (T2);
- 0,7% was more than 5cm (T3);
- And almost 1% has T4.



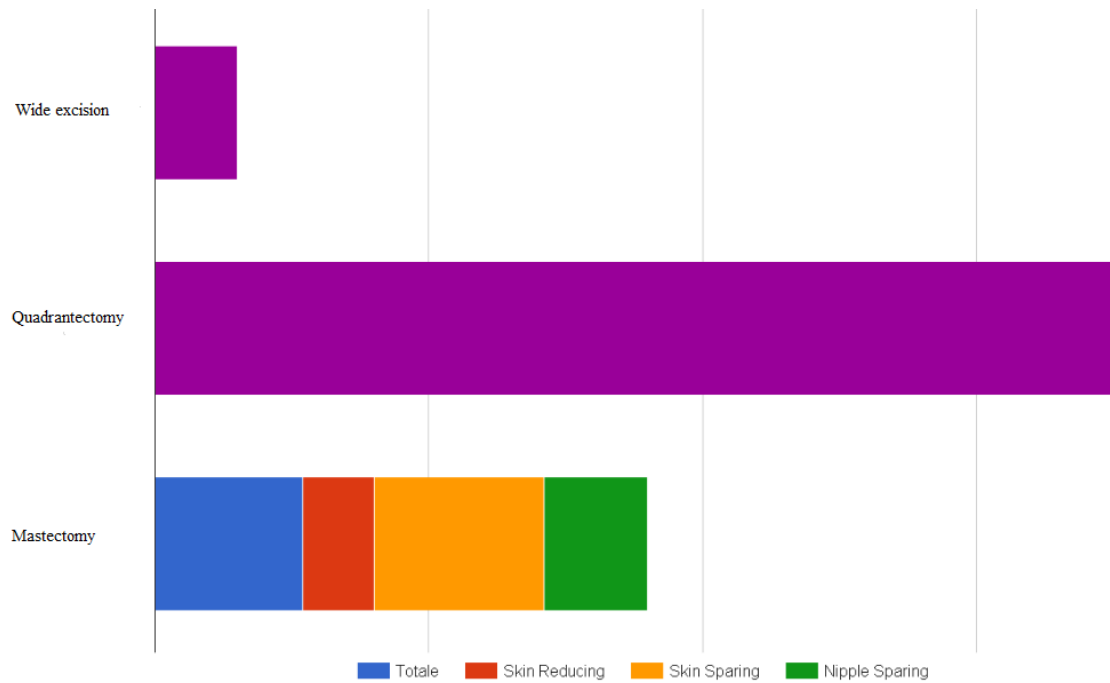
Cancer has spread to 1 to 3 axillary lymph node in the 19,7% of cases, and in the 59,5% of cases no Lymph Node(s) were involved.

The 81% underwent Sentinel Lymph Node Biopsy (SLNB), and the 31,4% underwent Axillary Lymph Node Dissection (ALND). 12% of them were positive for the SLN and consequently underwent ALND.

The surgical operations that were applied to the patients, with the related percentage are shown below:

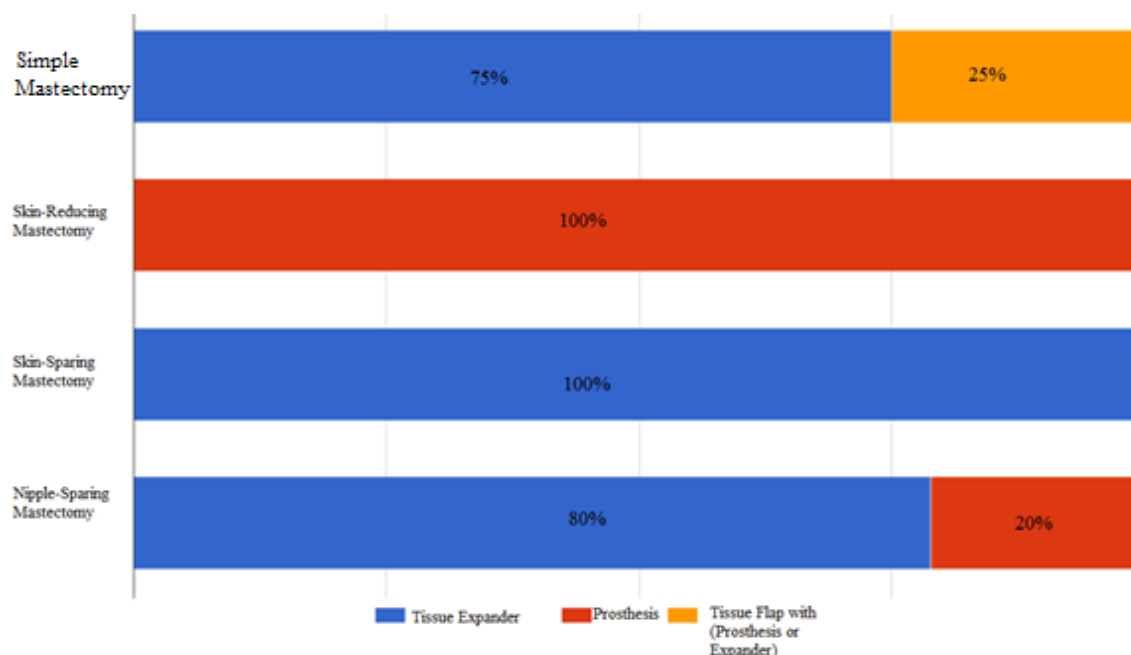
- 5.3 % underwent Wide Excision (OPS),
- 62,7% underwent Quadrantectomy (BCS),

- 32% underwent Mastectomy, of them: 30% underwent Simple Mastectomy, 14,4% to Skin-Reducing Mastectomy, 34,4% to Skin-Sparing Mastectomy, 21,1% to Nipple-Sparing Mastectomy.





The reconstruction surgeries that were applied and the related percentage are shown below:



Metastasis was reported in 2% of cases in the follow-up program after the surgical treatment. 50% of them were symptomatic for metastasis. One of them was positive to *central nervous system metastasis*. One had a positive *pulmonary metastasis*. And all of them were positive to *skeletal metastasis*.

Neoadjuvant Chemotherapy was taken in the 9,7%. And the 90,3% underwent at first hand to the surgery treatment.

10,9% of the patients underwent a second surgery; 63,6% of them underwent Mastectomy, and the 36,4 underwent Wide excision.

## **- The follow-up program:**

The day of the follow-up visit, it was used a tracking card with a characteristic flower icon for the recall. The patients were called for the medical examination in order of the booking date.

The follow-up visit for this group consisted in two parts:

- The first part of the assessment, made by the oncologist Surgeon, consisted of:
  1. Evaluation of the latest staging tests (blood chemistries test, Tumor Markers, Abdominal Ultrasound, and other eventual tests)
  2. Evaluation of the most recent Breast Imaging Exams (Mammography, Breast Ultrasound and other eventual tests)
  3. Clinical breast examination with:
    - Evaluation of oncological signs such as skin retraction, contour distortion and nodular density (particularly close to the surgical scars), which is perceived through palpation
    - Palpation of the axillary and supraclavicular lymph nodes
  
- The second part of the assessment (assessment of functional and aesthetic aspects) was implemented by the plastic surgeon as shown below:
  1. Evaluation of the final cosmetic result through inspection
  2. Measurement of the distance between:
    - The Jugular notch and the Nipple (in both left and right sides).

- The Nipple and the inter-mammary point.
- The difference, if any existed, in height between the 2 NAC on the inter-mammary line.

3. Evaluation of possible movement limitation of the homolateral shoulder, as a post-operative complications, by testing several postures (flexure, extension, abduction, and adduction), and revealing eventual differences of the movements within the homolateral and the contralateral shoulder.

4. Arm circumference measurement was taken in specific points: the widest part of the hand, the wrist, the elbow and the armpit crease, to evaluate the presence of lymphedema

5. Global functional-aesthetic evaluation by means of photographs in five projections (frontal, three-quarters (per 2) and profile (per 2)).

### 3.3 RESULTS

As regards process/path indicators it was highlighted that :

Definitive pre-operative diagnosis (proportion of C5/B5).	<b>90.5%</b> (standard 90%)
Proportion of pre-operative histopathology report with type, grading, ER and PgR status, stage and tumor size for invasive tumor.	<b>99%</b> (standard 90%)
Proportion of pre-operative histopathology report with type and grading for non-invasive tumor.	<b>98%</b> (standard 90%)
MRI use for invasive tumor.	<b>58.1%</b> (standard 5%)
Intraoperative Rx of surgical specimen in case of microcalcification treated with BCS.	<b>92.2%</b> (standard 90%)
Treatment within 30 days from the indication for treatment.	<b>80.6%</b> (standard 90%) <i>Indicator not reached</i>
Treatment within 42 days from the in-depth diagnostic analysis.	<b>30%</b> (standard 90%) <i>Indicator not reached</i>
Treatment within 60 days from the screening mammogram.	<b>30%</b> (standard 90%) <i>Indicator not reached</i>
A single surgery performing for the treatment of invasive carcinoma.	<b>97.5%</b> (standard 90%)
A single surgery performing for the treatment of non-invasive carcinoma.	<b>88.3%</b> (standard 90%) <i>Indicator almost reached</i>
At least 10 lymph nodes removed in the ALND (excluding sampling).	<b>98.2%</b> (standard 90%)
The only sentinel lymph node examination in case of pN0	<b>96.5%</b> (standard 90%)
No ALND (of any level, including sampling) in non-invasive carcinoma.	<b>98%</b> (standard 90%)

Removal of maximum 3 lymph nodes in the examination of the axilla with sentinel node biopsy.	<b>95.4%</b> (standard 90%)
BCS performing for invasive tumor $\leq$ 3cm (including the non-invasive component).	<b>77.8%</b> (standard 90%) <i>Indicator not reached</i>
BCS performing for non-invasive tumor $\leq$ 2cm.	<b>85.9%</b> (standard 90%) <i>Indicator not reached</i>
RT after the conservative surgery.	<b>96.2%</b> (standard 90%)
RT within 12 weeks after surgery in cases where adjuvant CT was not performed.	<b>40%</b> (standard 90%) <i>Indicator not reached</i>
Adjuvant endocrine therapy for endocrine-sensitive invasive cancer.	<b>96.6%</b> (standard 90%)
Adjuvant chemotherapy in ER-invasive tumor (T>1 cm o N+).	<b>91%</b> (standard 90%)
Adjuvant therapy with Trastuzumab in N+ or N- T>1cm HER2+ invasive tumor.	<b>100%</b> (standard 90%)
Neoadjuvant chemotherapy in cases of inflammatory carcinoma	<b>98%</b> (standard 90%)

As regards the aesthetic and functional indicators , it is highlighted that:

Proportion of BCS which does not report scar's retraction and diastases	<b>85%</b> (standard 80%)
Proportion of Mastectomy which does not report scar's retraction and diastases.	<b>88.2%</b> (standard 80%)
Proportion of BCS which does not report skin discolorations.	<b>83.3%</b> (standard 80%)
Proportion of Mastectomy which does	<b>85.8%</b> (standard 80%)

not report skin discolorations.	
Proportion of immediate reconstruction after Mastectomy	<b>73.5%</b> (standard 60%)
Proportion of SSM and NSM among all the Mastectomies.	<b>67.4%</b> (standard 50%)
Proportion of NSM among mastectomies with an immediate reconstruction.	<b>28.2%</b> (standard 10%)
Proportion of mastectomies with an immediate reconstruction with implants not in contact with the dermis.	<b>100%</b> (standard 95%)
Proportion of lesions discussed in the MMD (benign excluded ).	<b>98%</b> (standard 90%)
Proportion of prosthetic implants not removed on mastectomies with immediate reconstruction.	<b>96.3%</b> (standard 91%)
Absence of lymphedema of the ipsilateral arm after ALND.	<b>90%</b> (standard 80%)
Absence of lymphedema of the ipsilateral arm after SLNB.	<b>96.9%</b> (standard 95%)
Absence of shoulder movement limitations.	<b>97%</b> (standard 90%)
Absence of dystopia of the NAC.	<b>70.5%</b> (standard 80%) <i>Indicator not reached</i>

## **CHAPTER 4: DISCUSSION**

Breast cancer is an important cause of morbidity and mortality among women and, in recent years, incidence of this disease has increased progressively worldwide

The incidence and mortality rates increase along with age, with a peak incidence around 60 years old. By the end of the eighties, there was a moderate but continuous reducing in mortality rates. This, due to therapeutic advances and greater diagnosis in the early stage of BC, due to .in large part, the increasing use of screening programs.

The increase in incidence and simultaneous reduction in mortality is associated with an increase in the prevalence (women living after diagnosis of BC). The wide population of patients treated for BC, requires an extended monitoring over time.

Therefore, apart from the obvious need to set an adequate and correct oncological treatment, it is of absolute importance to create for the patients an organized and systematic program of follow-up.

Numerous findings from the international literature have in fact demonstrated that the prognosis of patients suffering from breast cancer is affected significantly by the possibility to contact and rely on a specialized center for the treatment of this disease, in order to have a multidisciplinary team that can individualize the treatments. An essential element in managing these patients is the presence of all the professionals needed to offer the best opportunities for care and the proper attention to the psychological and social needs with a

multidisciplinary approach, through which, every expert, help to accompany the patient in this difficult path.

In order to facilitate a uniform collection among the various Breast Units and for allowing their systematic processing, a specific software known as QT BREAST has been developed.

The QT BREAST, updated with respect to the most recent guidelines, enables interactive data analysis and automatic calculation of the indicators. It is an instrument that controls adhesion to EUSOMA indicators by the various breast centers and a system that monitors the quality of the interventions. It also enables each center to be able to act quickly on any identified 'weaknesses' in order to guarantee a standard quality of care.

Finally, it also represents an important upgrade tool for the recommendations and a significant starting point for research projects in the field of breast cancer treatment.

In fact, concerning those indicators for which the breast center does not reach the minimum required standards, the multidisciplinary team should agree on appropriate corrective actions.

The Breast Care Unit of the University Hospital of Pisa adopted the use of QT BREAST in July 2015 by introducing data on patients operated in the previous year into its software

Analyzing the findings from the evaluation of the path / process indicators at the Breast Unit of Pisa I observed:

- A correct and thorough pre-operative cytological and histological definitive diagnosis for malignant tumor (C5/B5) with more than 90% of cases (90,5).



- An accurate and complete pre-operative histopathology report with **type, grading, ER and PgR status, stage and tumor size** registered in 99% of the cases.

- A wide pre-operative Magnetic Resonance Imaging (MRI) use (58,1%, instead of 5%). It should be remembered that the Radiology School in Pisa was one of the first to introduce the use of MRI in the diagnostic clinical approach for breast disease.

Nowadays, there is no parity on MRI use in the different breast centers. Pisa Breast Unit falls within the group that most frequently adopts this imaging test with the following indications:

- In the preoperative study of dense breasts, when they are difficult to evaluate with a mammography and ultrasound in order to exclude multicentric forms, and a MRI is associated with increased diagnostic accuracy.
- To evaluate the response to primary systemic therapy.
- To search for *occult carcinoma* (CUP Syndrome).
- In familial breast cancer with or without *BRCA* mutations.
- Clinical-instrumental discrepancy (*palpable coarse lesions* against minimum mammographic findings).

- Proper use of Rx of the surgical specimen in non-palpable lesions (92,2%).

- Time between the date of initial breast cancer diagnosis and the date of surgery in the Breast Unit of Pisa is almost 35-40 days, while EUSOMA and Regional Resolutions and Recommendations provide for a maximum of 30 days. This moderate delay is caused, despite the best efforts of the medical and nursing

staff, by the fact that Pisa's Breast Unit is one of the most important centers in Italy for breast care so there is an influx and a high volume of patients also from other Regions.

- In relation to proper pre-operative planning by a multidisciplinary team, single surgery was advocated in the 97,5% for invasive cancer, and above the threshold for non-invasive cancer (88,3%).
- Absolute appropriateness for axillary treatment (SLN Biopsy and/or ALND where indicated).
- More Mastectomies were done than Conservative Surgeries (especially Quadrantectomies).

This datum is affected by:

1. An excessive rigidity of the indicators. Indeed, it must be taken into consideration that: the tumor/breast ratio, the multicentricity of the disease, local relapse after (previous) surgical treatments, and the preferences of the patients are conditions that require mastectomies.
  2. The specific features of the Center. (the increased use of mastectomy in this Center is associated also to the high volume of young patients as well as to the increased use of the genetic testing with, consequently, prophylactic mastectomies ).
- The use of Radiation therapy (RT) after BCS: The indications for RT are followed (96,2%) with the exception that the BU starts treatment after 16 weeks instead of 12.
  - Chemotherapy follows the best standards for: (T >1cm or N+) ER- Invasive tumor and for inflammatory breast cancer (91% and 98% respectively).

It should be emphasized that the previous indicators (Indicators of process/path) have had a broad consensus in the literature.

The detection of the aesthetic/functional outcomes is a recent approach, and still being debated and considered experimental. The aesthetic and functional outcome is related to surgical expertise, correctness and completeness of treatment planning and it is also related to the response of the tissue, which is unpredictable.

From the examination of the aesthetic / functional outcome indicators emerges:

- An acceptable percentage of scar retraction and diastases after conservative surgery (15%) and mastectomy (11.8%).
- Skin discolorations rates were higher in BCS (16,7%) than Mastectomy (14,2%). This because Adjuvant RT is almost always performed after BCS, while is not always indicated in mastectomies. Discoloration of the surgical scars reported a very lower incidence where adjuvant radiotherapy was not performed.
- An elevated use of immediate reconstruction after mastectomy (73.5%).

I would like to emphasize that I have personally witnessed that the general rule after mastectomy in Pisa BU is to propose breast reconstruction. This requires more time spent between the surgeons (oncological and plastic surgeons) and the patients to decide the best type of reconstruction. Breast reconstruction may be performed immediately after Mastectomy, or in two separate interventions. In fact, BU of Pisa do not resort to reconstruction in only two cases:

1. In case of locally advanced and/or inflamed breast cancer where RT post-operative is indicated.

2. In the case of elderly patients and/or patients with comorbidity that contraindicates a reconstruction and/or patients who choose not to have reconstruction.
- In regard to the proportion of cases discussed by multidisciplinary team, I have personally found that, in post-operations, all the cases of Malignant Breast Tumor are discussed by a multidisciplinary team (MDT). This also occurs with a large proportion of preoperative cases (recommended by the international guidelines).
  - The need to remove the prosthetic implant (due to infectious complications or to necrosis of the flap) is considered a sporadic event (3.7%).
  - The arm's lymphedema rates after each of, ALND and SLNB are absolutely acceptable as are the shoulder articular limitation rates.
  - Dislocation of the Nipple-Areola Complex (NAC) represents a frequent complication, and it relies on the increased use of Nipple Sparing Mastectomy in the BU of Pisa. During my internship, I spoke with surgeons and plastic surgeons, and I came to realize that, while preserving the NAC in order to optimize aesthetic shape of the breast is preferable, it is technically difficult to maintain the nipple centered and at the same level of the contralateral breast. Developments in surgical techniques may lead to an improvement in this area. In any case, the dislocation rates recorded in The BU of Pisa (29.5%) are absolutely in line with the data in the literature.

## CHAPTER 5: CONCLUSIONS

It is of fundamental importance to monitor the quality of care in multidisciplinary oncological pathways. Breast cancer care, patient's quality of life and survival can be maximized with a multidisciplinary team of specialists which include oncological surgeons, plastic and reconstructive surgeons, radiotherapists, medical oncologists, pathologists, radiologists and breast care nurses.

It is extremely important to monitor the outcomes in yearly follow-ups because breast cancer has a high incidence and, fortunately, a low mortality rate, meaning a high prevalence rate. This implies that follow-up programs must be carried out to evaluate treatment side effects such as scar's retractions and diastases, skin discolorations, dystopia of the NAC, inadequacy of the breast volume and shape, lymphedema, altered arm sensitivity, limited shoulder movements and to evaluate local recurrence or metastasis.

There is a relevant need for quality indicators and monitoring systems for the quality of diagnosis, therapy, reconstruction and rehabilitation. The measurement of these indicators is effective under many aspects; Reliability (which means that the observation is highly consistent whenever measured), Validity (which means that the indicator is really measuring what it is intended to do), Usability (which means the observations have to be easily interpreted), Feasibility (which requires easy data collections during routine clinical activities with limited costs), and Challenge (which means increasing the average quality of Breast Units).

As of today, both quality indicators as well as monitoring processes are still in an experimental phase. However, they are potential means to improve the quality of care in all breast units.

## BIBLIOGRAPHY

1-Indian J Cancer. 2012 Jul-Sep;49(3):277-82. doi: 10.4103/0019-509X.104486.

Breast cancer management: past, present and evolving.

Akram M1, Siddiqui SA.

2-Bland KI, Copeland EM. The Breast: Comprehensive Management of Benign and Malignant Diseases: Elsevier Health Sciences; 2009. Page 12, 779.

3-Kaluzny AD, Warnecke RB. Managing a Health Care Alliance: Improving Community Cancer Care: BeardBooks; 2000. Page 10.

4-Taghian AG, Halyard MY. Breast Cancer: Springer Publishing Company; 2012. Page 10.

5-Evans RA. Making the Right Choice: Treatment Options in Cancer Surgery: Avery Publishing Group; 1995. Page 20 , 27.

6-Onitilo AA, Engel JM, Stankowski RV, Doi SA. Survival Comparisons for Breast Conserving Surgery and Mastectomy Revisited: Community Experience and the Role of Radiation Therapy. Clin Med Res. 2015; **13**(2): 65-73.

7-Kaviani A, Sodagari N, Sheikhabaei S, Eslami V, Hafezi-Nejad N, Safavi A, et al. From radical mastectomy to breast-conserving therapy and oncoplastic breast surgery: a narrative review comparing oncological result, cosmetic outcome, quality of life, and health economy. ISRN Oncol. 2013; **2013**: 742462.

8-Salhab M, Al Sarakbi W, Joseph A, Sheards S, Travers J, Mokbel K. Skin-sparing mastectomy and immediate breast reconstruction: patient satisfaction and clinical outcome. *Int J Clin Oncol*. 2006; **11**(1): 51-4.

9-Carlson GW. Technical advances in skin sparing mastectomy. *Int J Surg Oncol*. 2011; 2011: 396901.

10-Amr Abd El-Aziz Ghannam, Rasha Abd El-Ghany Khedr. An accelerated hypofractionated schedule with a daily concomitant boost after breast conservation surgery: the feasibility and toxicity. *Journal of the Egyptian National Cancer Institute*. Volume 28, Issue 1, March 2016, Pages 39–44

11-Harcourt DM, Rumsey NJ, Ambler NR, Cawthorn SJ, Reid CD, Maddox PR, et al. The psychological effect of mastectomy with or without breast reconstruction: a prospective, multicenter study. *Plast Reconstr Surg*. 2003; **111**(3): 1060-8.

12-Del Turco MR, Ponti A, Bick U, Biganzoli L, Cserni G, Cutuli B, et al. Quality indicators in breast cancer care. *Eur J Cancer*. 2010; **46**(13): 2344-56.