

# Surgical approach of breast cancer: advances and limitations

A. Liberis, Z. Fasoulakis, N. Psarros, P. Kadari, E. Kontomanolis

*Department of Obstetrics & Gynaecology, Democritus University of Thrace, Dragana, Alexandroupolis (Greece)*

## Summary

New approaches in surgical methods and systematic therapy have led to a better prognosis for women including a better quality of life. Modified radical mastectomy, the treatment of choice in breast cancer, tends to be replaced by breast-conservation surgical procedures. Furthermore, the value of axillary lymph node dissection has been questioned. Sentinel lymph node biopsy has contributed in staging of the axilla in order to avoid extensive operations.

*Key words:* Surgery; Breast cancer; Mastectomy; Classification; Lymphadenectomy.

## Introduction

Breast cancer accounts for approximately 1.38 million new cases in 2008 and despite the spectacular steps that have occurred in terms of treating the disease, it is still considered the world's most frequent cause of mortality with 458,000 deaths each year [1]. The main predisposing factors include age, early menarche, late menopause, obesity in postmenopausal women, high concentration of endogenous estrogen, and heredity.

Factors contributing to an outbreak include oral contraceptives, hormone replacement therapy (HRT), and excessive alcohol consumption. Furthermore, an important role is heredity due to the fact that specific genes and mutants have been detected and are considered to be involved in the pathophysiological mechanism and course of the disease. Childbearing breastfeeding and intense physical activity are a protective shield against the disease [2]. In the last 50 years, after the introduction of the modified radical mastectomy by Patey, various techniques have been developed, and as a result, it is essential by scientists to define a classification system [3] (Figure 1). This article refers to the main surgical techniques and issues in the field of treatment of breast cancer (Figure 2).

## Radical and modified radical mastectomy

The real revolution in the surgical treatment of the breast was introduced by Halsted in 1891 with the appliance of a radical mastectomy. This included an en bloc removal of the mammary gland with the overlying skin, the pectoralis major muscle, and lymph excision of the same anatomical axillary [4, 5]. Radical mastectomy, compared to other al-

ternative therapies, does not appear to confer any advantage in the early stages of the disease compared to non-mutilating methods [6].

Postoperative complications such as morbidity, lymphedema, and deformation-end dyskinesia, are important. The modified radical mastectomy, meaning the removal of the mammary gland with the overlying skin and the lymph nodes of the ipsilateral axilla, is the next stage of radical mastectomy. The surgery is optional in locally advanced breast cancer or to patients who are not interested in maintaining the breast [7].

It is applied in the following cases: 1) invasive multifocal cancer, 2) cancer stages T1, T2, and T3 (with invasion of the pectoralis major that requires removal of the suspicious area without total muscle removal), 3) cancer stages T1 and T2, provided that the breast gland is very small with an acceptable aesthetic result or safe local control of the disease, and 4) breast cancer in elderly patients where there is no interest in maintaining the breast. In this method as far as complications are concerned, we should be aware of the following: lymphedema, infection, and necrosis of the abutment. Surgery is optional in locally advanced breast cancer or in patients who are not interested in maintaining the breast [7]. It is applied in the following cases: 1) invasive multifocal cancer, 2) cancer stages T1, T2, and T3 (with invasion of the pectoralis major that requires removal of the suspicious area without total muscle removal), 3) cancer stages T1 and T2, when the breast is very small with an acceptable aesthetic result or safe local control of the disease, and 4) breast cancer on elderly patients where there is no interest in maintaining the breast. In this method as far as complications are concerned, we should be aware of the

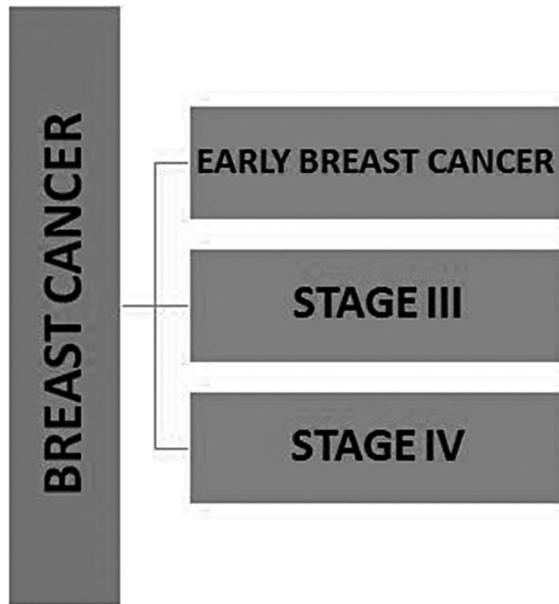


Figure 1. — The stages of breast cancer.

following: lymphedema, infection, and necrosis of the abutment [7, 8].

#### Skin-sparing mastectomy

In rare cases, filtered supernatant skin in breast cancer is detected, which is not considered necessary to remove during surgery. Skin filtration risk is associated with the tumor's location, stage of the disease, the presence of shrinkage of the skin or the presence of small embolus of lymph vessels. In this particular technique, there is an attempt that the skin portion that remains does not exceed a thickness of 5 centimeters to annihilate the probability of relapse.

This technique involves total removal of the mammary gland, while maintaining the overlying skin. It is recommended in cases where we cannot proceed with any breast-conserving surgery, i.e. women with multiple tumors, with extensive in situ carcinoma, with large tumors or in case of relapse. In addition, it is used when there is suspicion of unacceptable aesthetic results. On skin sparing mastectomy, where the overlying skin is maintained, the aesthetic result is much better, especially when this is combined with immediate breast reconstruction. The results are satisfactory and similar to those of mastectomy as far as local filtration and overall survival are concerned. Complications include coloboma necrosis and graft rejection [9].

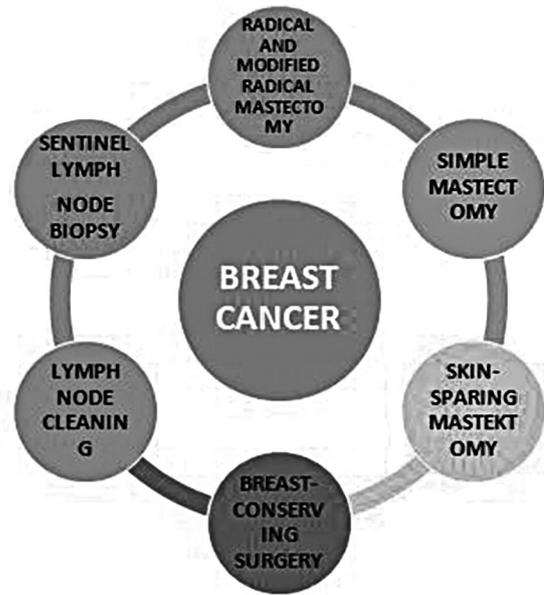


Figure 2. — Surgical treatment options for breast cancer.

#### Simple mastectomy

Since new techniques with aesthetically better results and increased survival rates have been developed, total mastectomy is no longer indicated and is rarely used. The operation involves removal of the breast with the overlying skin and fascia of the pectoralis major muscle. Total mastectomy can be applied: 1) When the patient has non-invasive carcinoma (ductal or invasive) with multifocal development; an alternative solution is sample removing axillary lymph nodes, where the normal biopsy reveals invasive outbreak and rapid biopsy is negative, 2) to elderly people or people with a burdened state of health, 3) to patients with locally advanced breast cancer, at the same time with systemic therapy in which a patient is subjected, 4) in cases tagged as precancerous, 5) in case of surgical removal with unhealthy resection limits during a breast conservation procedure, and 6) in case of local recurrence [10, 11].

#### Breast-conserving-surgery

Breast conserving surgeries are extremely important. It is a combination of quadrantectomy or lumpectomy or lumpectomy with wide limits, lymph node cleaning, and radiotherapy. Quadrantectomy is recommended in excision of the tumor in healthy range 2-3 cm and in the removal of the overlying skin and the underlying fascia, while with lumpectomy removal, the mass with only small excision limits is required. It is clinically approved that both procedures – quadrantectomy and lumpectomy – are not statistically significant different with regards to survival [12]. First

and second lymph cleaning level is applied to < 2 cm tumors with negative lymph nodes; for larger tumors, total lymph cleaning is preferred [13].

Based on the results of six major studies comparing breast-conserving surgery with radical treatments, the National Cancer Institute of the United States proposes breast-conserving surgery in patients with early breast cancer (T1 and T2). In these studies it became apparent that there is no difference in survival between the two techniques, although the former has higher rates of local recurrence (but within acceptable limits) [12, 14-17]. It is known, however, that breast cancer is not a simple disease, since there is a risk of relapse even after 20 to 30 years after initial treatment. It is therefore important to test the efficacy of these techniques over time. Jatoi and Proschan published in 2008 a meta-analysis that compared the long-term effects of these six large randomized studies. The results of the meta-analysis showed no statistically significant difference in survival, but breast-conserving surgeries had a higher local recurrence rate than radical treatment. In meta-analysis, the average patient follow-up was 14.7 years [18]. Contraindications of the aforementioned surgery are divided into absolute and relative. Absolute: 1) poorly circumscribed breast tumor (malignant multiple microcalcifications), 2) multiple primary tumors, 3) pregnancy, and 4) collagen diseases. Related: 1) large primary tumors in the breast, 2) prior radiation to the thorax, and 3) infiltration of the nipple. A significant drawback of this technique is the possibility of local relapse. Factors associated with an increased chance of local recurrence are: 1) size of the tumor, 2) multiple primary centres, 3) surgical margins, 4) lymph node metastases, 5) extensive intraductal component (extensive intraductal component), and 6) postoperative chemo-radiotherapy [13].

Studies which have been conducted since 1994 to date have local relapse rates of the disease (0-5%) in patients with multiple centres in which preservation breast operation was applied [19]. Perez in one of his publications in 2010, reported that patients younger than 40-years-old, especially those with pathologic features that do not give good prognosis (low differentiated tumors with negative hormone receptors, overexpression HER-2 / neu and lymphangitic filtration) have a higher rate of recurrence risk and therefore are not suitable to be treated with preservation of the breast. Their own series of patients confirm this correlation with age [20-23].

### Lymph node cleaning

Lymph node cleaning of axillary accompany all surgical techniques for treatment of breast cancer. This means surgical removal of axillary lymph nodes that is arranged in three levels. The first level includes the anatomical region of lymph nodes located outside of the pectoralis minor and latissimus dorsi muscle, namely the lymphs below and the

sides of the lower edge of the pectoralis minor muscle (pectoral lymph nodes). The second level includes the nodes behind and beneath the pectoralis minor muscle (central group). The third level includes lymph nodes that are found at the upper edge of the pectoralis minor muscle at the top of the armpit (lymph nodes are a part of group of subclavian lymph nodes). The filtration or not of the lymph nodes is considered the most important predictor of survival factor and contributes to the staging and limit to local disease. It has been estimated that approximately 80% of patients with a tumor size < 1 cm, -50% with purification, patients appear to have no positive impact on survival, but on the contrary, they have an increased rate of morbidity [24-26].

### Sentinel lymph node biopsy

The sentinel node biopsy is a novelty in the modern treatment of breast cancer. Giuliano *et al.* first described the method in 1994, which was based on the concept that lymphatic metastases progress towards a specific direction according to the flow of lymphatic fluid [26]. In anatomical mapping of the lymphatic system, several pigments have been used operatively. The Patent Blue-V and isosulfan blue which are being currently used, allow to clearly display the lymphatics and the lymph nodes. The infusion of the contrast material to palpable tumors is done with 22G needle injecting directly into the tumor an amount of 5-10 cc; the time required to search for the first node is five minutes. The circular massage in the breast region helps to better promote the radiopaque material to the anatomical region of the lymphatic node. In non-palpable tumors the pigment is injected in the region where the volume is detected by imaging method unless a marker wire is fitted. The finding of the first node is achieved by a transverse incision in the lower limit of hairy armpit, between the edge of the pectoralis major and latissimus dorsi to the anterior axillary line. The objective is to identify the stained lymph (afferent on the side of the tumor) and follow it up to the first node (sentinel node). In case of failure of the initial target, the removal of all labeled lymph nodes is required speculating that the sentinel lymph node will be within them [27, 28].

The use of radioactive substance and intraoperative probe in identifies the sentinel node; the success rate reaches 90% with a high negative predictive value (> 90%) [29, 30]. In this method, timing is not a problem in applying the technique, giving more comfort to the planning and preparation of the patient. Sampling sentinel node may reach a period of 15 minutes [31-33]. Obviously in hospitals where there is no nuclear medicine department, the choice is quite limited, so that the dye method is applied [27]. It is very likely to discover the existence of metastases in negative sentinel lymph node. The lymph node biopsy is an alternative to universal lymph node cleaning. Metastases are considered largely responsible for false negative results

of different studies, a percentage which appears to be estimated at 8.4% with a range of 0-29% [29, 31]. Researchers attempting to reduce the number of false negative sentinel node biopsies suggests the exclusion of patients with multifocal malignancies, with clinically palpable lymph nodes, with large palpable tumors and poor lymphatic drainage [32-35].

### Management of the axillary-making decisions

The complete dissection is an integral part of surgical treatment in breast tumor because of its accuracy in staging the disease, but also because at the same time it reduces local recurrence. The randomized National Surgical Adjuvant Breast and Bowel Project (NSABP) B04, in patients with negative clinical lymph nodes who received radical mastectomy with lymph node cleaning or simple mastectomy with axillary radiation or simple mastectomy, showed that dissection helps to control local relapse and prognosis but does not offer significant statistic difference on the issue of survival. Moreover, it appears that approximately 80% of patients with a tumor size of <1 cm, 50% with a tumor of up to 5 cm, and 30% with a tumor > 5 cm will not develop metastases in the lymph nodes [27].

Studies performed in patients with negative sentinel lymph node and in patients without lymph node cleaning for a second time show that there is no difference in local recurrence of the disease. Furthermore, it has been shown that the sentinel node biopsy alone is sufficient for satisfactory staging of disease in most women with clinically negative lymph nodes. With these data the American Society of Clinical Oncology (ASCO) estimates that extensive dissection in patients with negative sentinel lymph node can be omitted [29].

In patients with a positive sentinel lymph node, the prevalent perception is that general dissection should be applied. It has been observed in patients with positive sentinel lymph node and having not undergone axillary cleaning, that the local recurrence rates reached 3.4%, while the rates with applying cleaning of the axillary decreased to 0.25%; based on the literature; dissection offers better control of possible local recurrence of the disease [27].

In 60% of patients with a positive sentinel lymph node, this is also the only one who has been infected by the disease, for reassessment of the sentinel lymph node is required. Researchers at Memorial Sloan-Kettering Cancer Center were the first to propose a formula which calculates the possibility of extending to other lymph nodes beyond the sentinel node, taking into account numerous factors involving both the tumor and the sentinel lymph node.

It is easily accessible via the internet (<http://www.mskcc.org/mskcc/html/15938.Cfm>). The validity has been confirmed by many studies with a degree of accuracy. Various programs have been created with a reference to it. A meta analysis of 3,000 patients indicates that

the benefit in overall survival rate stands at 5.4% [35, 36]; the results of ASCOG 2011 come to overturn this view.

In this study patients with cancer staging T1-T2 without clinically palpable lymph nodes and positive sentinel lymph nodes underwent breast-conserving surgery with or without lymph node purification. The five-year survival and disease free interval were similar in both parts of the research [37]. The same study documents that the statistical difference in local recurrence is low among patients with a positive sentinel lymph node, with or without axillary lymph node purification [38].

ASCO lately suggests full lymph node cleaning in patients with positive sentinel lymph node. Considering the above scientific data, and awaiting the results of large randomized studies, questions are created for both the prognostic value of micrometastases and the efficiency of the complete lymph cleaning in all patients with positive lymph node. Patients with ductal carcinoma in situ (DCIS) or small tumors that exhibit minimal but significant percentage of metastatic disease in axillary lymph nodes will benefit from the identification and removal of sentinel lymph nodes [39, 40]. Identifying the sentinel lymph node accompanied by biopsy of the lymph node group to the internal mammary intended only for the staging of the disease does not offer anything more to survival unless it is accompanied by the coadministration of additional chemotherapy [29, 32].

### Early breast cancer

In early breast cancer procedures which preserve the breast are often preferred, for they provide the same survival rate compared to radical surgery and also offer the advantage of retaining the breast. In this patient group the necessity of cleaning the lymph nodes is questioned while contraindicated in those with a negative sentinel lymph node. Moreover recent studies have shown that no benefits are achieved in terms of survival in patients with positive sentinel lymph node biopsy [41].

Since 1975 Rosen *et al.* have diagnosed residual cancer in the breast or lymph nodes where the cancer was < 2 cm. in 26% and 6%, respectively, and 36% and 29% when the tumor was > 2 cm [42]. Complementary therapies such as radiotherapy, chemotherapy, and hormonal therapy appears to help control local recurrence and residual disease. The grant is dependent on pathological features of the disease.

### Advanced stages of breast cancer (Stage III)

Stage III refers to patients with tumors > 5 cm (Tables 1 and 2) or axillary lymph nodes coalesced together or riveted to the surrounding tissues (Stage IIIa). Here the combination of surgical treatment consists of radiotherapy and systemic therapy. The surgical treatment of choice is a modified radical mastectomy. If preoperative chemotherapy is administered and achieves inhibition of tumor

Table 1. — *TNM staging system for breast cancer.*

<b>Primary tumor (T)</b>	
<b>T<math>\chi</math></b>	Primary tumor cannot be assessed
<b>T0</b>	No evidence of primary tumor
<b>Tis</b>	Carcinoma in situ: ductal, lobular or Paget disease of the nipple without tumor
<b>T1</b>	Tumor 2 cm or less in greatest dimension
<b>T1a</b>	Tumor 0.5 cm or less in greatest dimension
<b>T1b</b>	Tumor more than 0.5 cm but not more than 1 cm in greatest dimension
<b>T1c</b>	Tumor more than 1 cm but not more than 2 cm in greatest dimension
<b>T2</b>	Tumor more than 2 cm but not more than 5 cm in greatest dimension
<b>T3</b>	Tumor more than 5 cm in greatest dimension
<b>T4</b>	Tumor of any size with direct extension to chest wall or skin
<b>T4a</b>	Extension to chest wall
<b>T4b</b>	Edema (included in peau d'orange) and/or ulceration of the skin and/or ipsilateral satellite nodules on the same breast
<b>T4c</b>	Both T4a and T4b
<b>T4d</b>	Inflammatory carcinoma
<b>Lymph nodes (n)</b>	
<b>N<math>\chi</math></b>	Regional lymph nodes cannot be assessed (e.g. previously removed)
<b>N0</b>	No regional lymph node metastasis
<b>N1</b>	Metastasis to movable ipsilateral lymph nodes
<b>N2</b>	Metastasis in ipsilateral axillary lymph node(s) fixed or matted 1 <sup>st</sup> or 2 <sup>nd</sup> level or in clinically apparent ipsilateral internal mammary node in the absence of clinically evident axillary lymph node metastasis
<b>N2a</b>	Metastasis in ipsilateral axillary lymph nodes fixed to one another (matted) or to other structures, 1 <sup>st</sup> or 2 <sup>nd</sup> level
<b>N2b</b>	Metastasis only in clinical apparent ipsilateral internal mammary node(s) and in the absence of clinically evident axillary lymph node metastasis 1 <sup>st</sup> or 2 <sup>nd</sup> level
<b>N3</b>	Metastasis in ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement of 1 <sup>st</sup> or 2 <sup>nd</sup> level, or in clinically apparent ipsilateral internal mammary lymph node(s) and in the presence of clinically evident axillary lymph node(s) of 1 <sup>st</sup> or 2 <sup>nd</sup> level
<b>N3a</b>	Metastasis in ipsilateral infraclavicular lymph node(s)
<b>N3b</b>	Metastasis in ipsilateral infraclavicular lymph node(s) and axillary lymph node(s)
<b>N3c</b>	Metastasis in ipsilateral supraclavicular lymph node(s)
<b>Distant metastases (M)</b>	
<b>M0</b>	No clinical or radiographic evidence of distant metastases
<b>cM0(i+)</b>	No clinical or radiographic evidence of distant metastases, but deposits of molecularly or microscopically detected tumor cells in circulating blood, bone marrow, or other non-regional nodal tissue
<b>M1</b>	Distant metastases (including metastasis on ipsilateral infraclavicular lymph node(s))

growth, conservative surgery in the mammary gland can be applied. Postoperative chemotherapy should include anthracycline. Tamoxifen can be administered in pre- and postmenopausal women for five years, although administration of anastrozole (aromatase inhibitor) in post-

Table 2. — *AJCC staging system*

STAGE	TUMOR	NODES	METASTASIS
<b>STAGE 0</b>	<b>Tis</b>	<b>N0</b>	<b>M0</b>
<b>STAGE I</b>	<b>T1</b>	<b>N0</b>	<b>M0</b>
<b>STAGE IIA</b>	<b>T0</b>	<b>N1</b>	<b>M0</b>
	<b>T1</b>	<b>N1</b>	<b>M0</b>
	<b>T2</b>	<b>N0</b>	<b>M0</b>
<b>STAGE IIB</b>	<b>T2</b>	<b>N1</b>	<b>M0</b>
	<b>T3</b>	<b>N0</b>	<b>M0</b>
<b>STAGE IIIA</b>	<b>T0</b>	<b>N2</b>	<b>M0</b>
	<b>T1</b>	<b>N2</b>	<b>M0</b>
	<b>T2</b>	<b>N2</b>	<b>M0</b>
	<b>T3</b>	<b>N1</b>	<b>M0</b>
<b>STAGE IIIB</b>	<b>T3</b>	<b>N2</b>	<b>M0</b>
	<b>T4</b>	<b>N0</b>	<b>M0</b>
	<b>T4</b>	<b>N1</b>	<b>M0</b>
<b>STAGE IIIC</b>	<b>T4</b>	<b>N2</b>	<b>M0</b>
	<b>Any T</b>	<b>N3</b>	<b>M0</b>
<b>STAGE IV</b>	<b>Any T</b>	<b>Any N</b>	<b>M1</b>

menopausal women provides longer disease-free survival with fewer side effects. Finally, radiation to the chest wall and axillary is indicated; The five-year survival can reach 50%.

Stage IIIb with skin ulceration, tumor fixation to the rib cage, satellite nodules, infiltrated lymph nodes above the clavicle or the internal mammary artery is classified as inoperable. Patients who respond to chemotherapy should be treated by surgery in order to limit local disease. Even those who do not respond to preoperative chemotherapy, efforts should be made to control the disease with surgery and radiotherapy. In Stage IIIc qualms are expressed about the benefits of surgery in patients who are likely to respond to additional chemotherapy or radiotherapy [42, 43].

#### Stage IV

At this stage distant metastases are found, thus the local treatment is intended to relieve the patient. Biopsy or removal of existing small tumors is essential for diagnosis and a check should be carried out for hormone receptors. Simple mastectomy is indicated, when the removal of a large tumor is intended to facilitate the chemo-radiotherapy when the ulcerating tumor bleeds, for total organic patient comfort, and cellular depletion without concomitant lymph node cleaning. It has been observed that even Stage IV patients who respond to chemotherapy, benefit in overall survival after total removal of primary site [35, 44, 45]. In Stage IIIb or IV the inflammatory breast carcinoma (5.1% forms of breast cancer in the US) is classified, which is characterized pathologically by dispersion and filtration of cutaneous lymphatic vessels. The inflammatory breast carcinoma is treated with systemic therapy, chemotherapy, and hormonal therapy in combination with local radiotherapy. In certain cases mastectomy may be added for the pa-

tient to get rid of the tumor. Three cycles of chemotherapy are followed by radiotherapy sessions, on condition that we have a good response of the tumor to chemotherapy when we perform a mastectomy. In younger patients (< 50 years), the prognosis is worse than older patients. Patients responding to chemotherapy have a better course compared to patients who did not respond; the survival rate of these patients is 30% [46-49] (Tables 1 and 2).

## Conclusion

Choosing an effective surgical treatment for breast cancer is based on achieving an impeccable oncological surgery, eliminating the amputation effect, offering a chance of survival in the patient and their quality of life. The invention of new techniques and the present knowledge on the biology of the disease, provides higher quality healthcare services to patients, having increased life expectancy especially in patients with early breast cancer. The success in the treatment in breast cancer is based on a disease-free survival and the quality of life and mental health of the patient. In breast reconstruction, it is a priority to create an aesthetically satisfactory breast symmetry between the two anatomical sides. The interval between cure of the breast and recurrence is the main comparison indicator regarding the survival of the patient.

## References

- [1] Ferlay J., Shin H.R., Bray F., Forman D., Mathers C., Parkin D.M.: "Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008". *Int. J. Cancer*, 2010, 127, 2893.
- [2] Key T., Verkasalo P., Banks E.: "Epidemiology of breast cancer". *Lancet Oncol.*, 2001, 2, 133.
- [3] Hoffmann J., Wallwiener D.: "Classifying breast cancer surgery: a novel, complexity-based system for oncological, oncoplastic and reconstructive procedures, and proof of principle by analysis of 1225 operations in 1166 patients". *BMC Cancer*, 2009, 9, 108.
- [4] Sakorafas G., Siafoleas M.: "Breast cancer surgery: an historical narrative. Part I. From prehistoric times to Renaissance". *Eur. J. Cancer Care*, 2009, 18, 530.
- [5] Sakorafas G., Siafoleas M.: "Breast cancer surgery: an historical narrative. Part II. 18th and 19th centuries". *Eur. J. Cancer Care*, 2010, 19, 6.
- [6] Ekmektzoglou K., Xanthos T., German V., Zografos G.: "Breast cancer: from the earliest times through to the end of the 20th century". *Eur. J. Obstet. Gynecol. Reprod. Biol.*, 2009, 145, 3.
- [7] Sainsbury J., Anderson T.J., Morgan D.: "ABC of breast diseases: breast cancer". *BMJ*, 1994, 309, 1150.
- [8] Bostwick J.: "Breast reconstruction following mastectomy". *CA Cancer J. Clin.*, 1995, 45, 289.
- [9] Mascaro A., Farina M., Gigli R., Vitelli C., Fortunato L.: "Recent advances in the surgical care of breast cancer patients". *World J. Surg. Oncol.*, 2010, 8, 5.
- [10] Babiera G., Simmons R.: "Nipple-areolar complex-sparing mastectomy: feasibility, patient selection, and technique". *Ann. Surg. Oncol.*, 2010, 17, 245.
- [11] Wéber B., Demange L., Rigaud C., Fernandes-Valoni A.: "Que reste-t-il des indications de mastectomie totale pour cancer?" *Bull Cancer*, 1998, 85, 755.
- [12] Veronesi U., Cascinelli N., Mariani L., Greco M., Saccozzi R., Luini A., et al.: "Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer". *N. Engl. J. Med.*, 2002, 347, 1227.
- [13] Moore M., Kinne D.: "The surgical management of primary invasive breast cancer". *CA Cancer J. Clin.*, 1995, 45, 279.
- [14] Bland K.I., Menck H.R., Scott-Conner C. E., Morrow M., Winchester D.J., Winchester D. P.: "The National Cancer Data Base 10 year survey of breast carcinoma treatment at hospitals in the United States". *Cancer*, 1998, 83, 1262.
- [15] Poggi M.M., Danforth D.N., Sciuto L.C., Smith S.L., Steinberg S.M., Liewehr D.J., Altemus R.M.: "Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy". *Cancer*, 2003, 98, 697.
- [16] Lazovich, D., Solomon C.C., Thomas D.B., Moe R.E., White E.: "Breast conservation therapy in the United States following the 1990 National Institutes of Health Consensus Development Conference on the treatment of patients with early stage invasive breast carcinoma". *Cancer*, 1999, 86, 628.
- [17] Mook S, Knauer M, Bueno-de-Mesquita J.M., Retel V.P., Wesseling J., Linn S.C., et al.: "Metastatic potential of T1 breast cancer can be predicted by the 70-gene MammaPrint signature". *Ann. Surg. Oncol.*, 2010, 17, 1406.
- [18] Jatoi I., Proschan M.: "Randomized trials of breast-conserving therapy versus mastectomy for primary breast cancer: a pooled analysis of updated results". *Am. J. Clin. Oncol.*, 2005, 28, 289.
- [19] Bauman L., Barth R., Rosenkranz K.: "Breast conservation in women with multifocal-multicentric breast cancer: is it feasible?" *Ann. Surg. Oncol.*, 2010, 17, 325.
- [20] Rosen P.P., Groshen S., Kinne D.W., Norton L.: "Factors influencing prognosis in node-negative breast carcinoma: analysis of 767 T1N0M0/T2N0M0 patients with long-term follow-up". *J. Clin. Oncol.*, 1993, 11, 2090.
- [21] Perez C.: "Breast conservation therapy in patients with Stage T1-T2 breast cancer: current challenges and opportunities". *Am. J. Clin. Oncol.*, 2010, 33, 500.
- [22] De Lorenzi F.: "Oncoplastic surgery: the evolution of breast cancer treatment". *Breast J.*, 2010, 16, S20.
- [23] Silverstein M.: "How I do it: oncoplastic breast-conservation surgery". *Ann Surg. Oncol.*, 2010, 17, 242.
- [24] Iwuchukwu O., Harvey J., Dordea M., Critchley A., Drew P.: "The role of oncoplastic therapeutic mammoplasty in breast cancer surgery - a review". *Surg Oncol.*, 2012, 21, 133.
- [25] Pinsolle V., Grinfeder C., Mathoulin-Pelissier S., Faucher A.: "Complications analysis of 266 immediate breast reconstructions". *J. Plast. Reconstr. Aesthet. Surg.*, 2006, 59, 1017.
- [26] Sclafani L., Baron R.: "Sentinel lymph node biopsy and axillary dissection: added morbidity of the arm, shoulder and chest wall after mastectomy and reconstruction". *Cancer J.*, 2008, 14, 216.
- [27] Samphao S., Eremin J., El-Sheemy M., Eremin O.: "Management of the axilla in women with breast cancer". *Lancet Oncol.*, 2007, 8, 331.
- [28] Giuliano A., Kirgan D., Guenther M., Morton D.: "Lymphatic mapping and sentinel lymphadenectomy for breast cancer". *Ann. Surg.*, 1994, 220, 391.
- [29] Lyman G., Giuliano A., Somerfield M., Benson A.I.B., Bodurka D., Burstein H., et al.: "American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer". *J. Clin. Oncol.*, 2005, 23, 7703.
- [30] Del Valle V., Bermejo Alvarez M., Maraui P., Femenandez R.: "Pneumothorax secondary to axillary sentinel lymph node biopsy". *Rev. Esp. Anesthesiol. Reanim.*, 2008, 55, 185.
- [31] Benson J., Querci della Rovere G.: "Management of the axilla in women with breast cancer". *Lancet Oncol.*, 2007, 8, 331.
- [32] Patani N., Dwek M., Douek M.: "Predictors of axillary lymph node metastasis in breast cancer: a systematic review". *EJSO*, 2007, 33, 409.
- [33] Collins C.: "The sentinel node in breast cancer". *Cancer Imaging*, 2008, 8, S10.
- [34] Roumen R., Geuskens L., Valkenburg J.: "In search of the true sen-

- tinel node by different injection techniques in breast cancer patients. *EJSO*, 1999, 25, 347.
- [35] Unal B., Gur A., Kayiran O., Johnson R., Ahrendt G., Bonaventura M., *et al.*: "Models for predicting non sentinel lymph node positivity in sentinel node positive breast cancer: the importance of scoring system". *Int. J. Clin. Pract.*, 2008, 62, 1785.
- [36] Orr R.: "The impact of prophylactic axillary node dissection on breast cancer survival—a Bayesian meta-analysis". *Ann. Surg. Oncol.*, 1999, 6, 109.
- [37] Giuliano A., Hunt K., Ballman K., Beitsch P., Whitworth P., Blumencranz P., *et al.*: "Axillary dissection vs no axillary dissection in women with invasive breast cancer and sentinel node metastasis: a randomized clinical trial". *JAMA*, 2011, 305, 569.
- [38] Giuliano A., McCall L., Beitsch P., Whitworth P., Blumencranz P., Leitch A., *et al.*: "Locoregional recurrence after sentinel lymph node dissection with or without axillary dissection in patients with sentinel lymph node metastases: the American College of Surgeons Oncology Group Z0011 randomized trial". *Ann. Surg.*, 2010, 252, 426.
- [39] Klauber-De More N., Tan L., Liberman L., Kaptain S., Fey J., Borgen P., *et al.*: "Sentinel lymph node biopsy: is it indicated in patients with high-risk ductal carcinoma-in-situ and ductal carcinoma-in-situ with microinvasion?" *Ann. Surg. Oncol.*, 2000, 7, 636.
- [40] Edge S., Byrd D., Compton C., Fritz, A.G., Greene, F.L., Trotti, A. (eds). *AJCC Cancer Staging Handbook*. 7<sup>th</sup> ed, New York, NY: Springer-Verlag, 2010.
- [41] Stebbing J., Delaney G., Thompson A.: "Breast cancer (non-metastatic)". *BMJ Clin. Evid.*, 2007, 2007, pii: 0102.
- [42] Rosen P.P., Fracchia A.A., Urban J.A., Schotenfeld D., Robbins G.F.: "Residual" mammary carcinoma following simulated partial mastectomy". *Cancer*, 1975, 35, 739.
- [43] Shenkier T., Weir L., Levine M., Olivotto I., Whelan T., Renyo L., *et al.*: "Clinical practice guidelines for the care and treatment of breast cancer: 15. Treatment for women with stage III or locally advanced breast cancer". *CMAJ*, 2004, 170, 983.
- [44] Cady B., Nathan N., Michaelson J., Golshan M., Smith B.: "Matched pair analyses of stage IV breast cancer with or without resection of primary breast site". *Ann. Surg. Oncol.*, 2008, 15, 3384.
- [45] Pagani O., Senkus E., Wood W., Colleoni M., Cufer T., Kyriakides S., *et al.*: "International guidelines for management of metastatic breast cancer: can metastatic breast cancer be cured?" *J. Natl. Cancer Inst.*, 2010, 102, 456.
- [46] Gonzalez-Angulo A., Hennessy B., Broglio K., Meric-Bernstam F., Cristofanilli M., Giordano S., *et al.*: "Trends for inflammatory breast cancer: is survival improving?" *Oncologist*, 2007, 12, 904.
- [47] Woodward W., Cristofanilli M.: "Inflammatory breast cancer". *Semin. Radiat. Oncol.*, 2009, 19, 256.
- [48] Robertson F., Bondy M., Yang Y., Yamauchi H., Wiggins S., Kamrudin S., *et al.*: "Inflammatory breast cancer: the disease, the biology, the treatment". *CA Cancer J. Clin.*, 2010, 60, 351.
- [49] Kumar S., Sacchini V.: "The surgical management of ductal carcinoma in situ". *Breast J.*, 2010, 16, S49.

Corresponding Author:  
Z.N. FASOULAKIS, M.D.  
Milon 102,  
104 41 Athens (Greece)  
e-mail: hzaxos@gmail.com