

ORIGINAL PAPER

NEW FRONTIERS FOR BREAST CANCER SURGERY IN ALBANIA

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ABSTRACT

Introduction. Cancers are becoming a priority for Albanian health care system. Breast Cancer (BC) is the first leading cause of malignant diseases among women and the second leading cause of malignant diseases in the general population of Albania.

The objective of the study was to provide an overview of latest breast cancer surgical techniques being provided to Albanian patients.

Materials and methods. Institute of Statistics data, and information from main national surveys in Albania were consulted to provide an overview of demographic transition and breast cancer epidemiology in Albania. Our experience in providing various type of surgical procedures to manage breast cancer cases, through the years, was described, focusing on novel techniques.

Results. Main reasons for increasing breast cancer incidence in Albania include demographic transition and lifestyle changes. There has been an evolution in breast surgery techniques offering to patients the ultimate technique at the Public Oncological Hospital, in the premises of University Hospital Center “Mother Theresa” in Tirana, with excellent results.

RÉSUMÉ

Nouvelles frontières pour la chirurgie du cancer du sein en Albanie

Introduction. Les cancers deviennent une priorité pour le système de santé albanais. Le cancer du sein (BC) est la première cause de maladies malignes chez les femmes et la deuxième cause de maladies malignes dans la population générale d’Albanie.

L’objectif de l’étude était de donner un aperçu des dernières techniques chirurgicales du cancer du sein fournies aux patientes albanaises.

Matériels et méthodes. Les données de l’Institut des statistiques et les informations des principales enquêtes nationales en Albanie ont été consultées pour fournir un aperçu de la transition démographique et de l’épidémiologie du cancer du sein en Albanie. Notre expérience dans la fourniture de divers types d’interventions chirurgicales pour gérer les cas de cancer du sein, au fil des ans, a été décrite, en nous concentrant sur de nouvelles techniques.

Résultats. Les principales raisons de l’augmentation de l’incidence du cancer du sein en Albanie sont la

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Conclusions. For a developing country we think that the use of ultimate type of breast cancer surgery: demolition and immediate reconstruction using prosthesis and biological mesh, represents new frontiers in breast surgical oncology and it is our aim to offer it properly to all patients, especially to young patients.

Keywords: Albania, breast cancer, surgery.

INTRODUCTION

Breast cancer in Albania is the main malignant disease affecting women. All the oncology specialist doctors are facing an increasing number of patients diagnosed with breast cancer at young age.

Albania is a developing country undertaking substantial reforms in the healthcare system, including oncology services, because oncology doctors often operate under limited resources including medications, drugs, devices, etc.

Every woman diagnosed with breast cancer has the right to have access and to be offered the highest standard of care, and the most appropriate treatment scheme. This is true especially regarding the surgical treatment, that should not exclusively offer the demolition surgery but also it has to provide the patient with reconstruction surgery options as well, as this is a very important and critical issue especially for young women, for both oncological and psychologically reasons, psychological health and well-being.

THE OBJECTIVE OF OUR STUDY was to provide a general overview of the breast cancer epidemiology and situation in Albania, as well as the new techniques that oncologists are providing to affected women, thus highlighting new possibilities and frontiers for breast cancer surgery that could have a significant positive impact on the survival and quality of life of these patients.

MATERIALS AND METHODS

This descriptive study was based on reviewing the most recent data on breast cancer incidence and other morbidity and mortality indicators related to breast cancer, published by the Institute of Statistics

transition démographique et les changements de mode de vie. Il y a eu une évolution dans les techniques de chirurgie mammaire offrant aux patientes la technique ultime à l'hôpital public d'oncologie, dans les locaux du centre hospitalier universitaire "Mère Theresa" à Tirana, avec d'excellents résultats.

Conclusions. Pour un pays en développement, nous pensons que l'utilisation du type ultime de chirurgie du cancer du sein : la démolition et la reconstruction immédiate à l'aide de prothèses et de treillis biologiques, représente de nouvelles frontières dans la chirurgie oncologique du sein et notre objectif est de l'offrir correctement à tous les patients, en particulier aux jeunes les patients.

Mots-clés: Albanie, cancer du sein, chirurgie.

of Albania. In addition, data about the activity of the Oncology Service in the University Hospital Center "Mother Theresa" in Tirana were used as well, to have a complete picture. Regarding the risk factors for breast cancer, various national surveys were consulted, including the Albanian Demographic and Health Survey 2008-2009, the Albanian Demographic and Health Survey 2017-2018, and the Albanian Reproductive Health Survey 2002. International sources of literature were consulted, as well. To bring the findings in the context, we have analyzed the demographic transition and lifestyle changes of the Albanian female population after the 90', that influence the risk of developing breast cancer.

In order to provide information on latest surgical techniques that are being employed by oncologist doctors in a tertiary university hospital in Albania, we have described our experience and the techniques we are currently employing in the Oncology Service of the University Hospital Center "Mother Theresa", providing the reader with a brief history of evolution of surgical oncology techniques to manage breast cancer case and the main contributing professionals to this field. This study has analyzed, for the first time in Albania, the evolution of surgical techniques used to treat patients with breast cancer, ranging from modified radical mastectomy to ultimate techniques of immediate reconstruction using prosthesis and biological meshes, in line with latest international guidelines.

To illustrate these new techniques and new frontiers of breast surgery in Albania, we have provided the reader with real cases of patients being treated in our Oncology Service. These were patients showing up at the premises of Surgical Unit of Oncological Hospital, University Hospital Center "Mother Theresa", with the diagnosis of breast cancer. All the

patients have had the first visit to a breast surgeon and for each of them, a clinical record was filled in, at the time of their presentation. The clinical record includes information on personal details, history, symptoms, clinical, imaging, histological, and laboratory examinations, surgical techniques, complications and final TNM classification.

RESULTS

Cancers are becoming a priority for Albanian health care system and health policy. The two main reasons are: 1) increased mortality and morbidity rates for several cancers, because of demographic transition and lifestyle changes; 2) late diagnoses, as most of breast cancer patients are diagnosed in advanced stages.

Breast cancer is the first leading cause of malignant diseases affecting women in Albania and is the second leading cause of malignant diseases affecting the general population. BC accounts for about 25% of all malignant tumours affecting women; annually, there are around 700 new cases of breast cancer and each year around 230 women die from breast cancer in Albania. Breast cancer is responsible for about 17% of all deaths caused by malignant tumours among Albanian women¹. About 65% of breast cancers patients presented at Oncology Hospital are diagnosed in stage T2, over 20% of cancers are diagnosed in stage T3 or T4 and about 75% of cases are stage N1, N2, and N3 at the moment of diagnosis, according to data from our hospital second their appearance in the Oncology Hospital.

The information system on cancer is based on:
 1. National Cancer Registry (new cases – incidence);
 2. Family physicians Registry – primary health care

centers (prevalent cases); 3. Mortality data collected by the Institute of Statistics. However, the best source of information is still GLOBOCAN, an online database, which provides global cancers statistics (estimates of incidence and mortality in 185 countries for 36 types of cancer, considering the quality of defective and gaps in national statistics).

In recent years it was observed an increase of the incidence of new breast cancer cases, based on 1) Breast cancer registry (Figure 1) of Oncological Hospital of University Hospital “Mother Theresa”, the only public tertiary university hospital structure that treats cancer by multidisciplinary staffs; 2) National Cancer Registry (Figure 2) based on the Institute of Public Health data.

The increase of the number of new breast cancer cases is thought to be the consequence of a change of lifestyle in Albania, that has affected the factors that influence breast cancer, such as the decrease of fertility among Albanian females (Figure 3)¹; overweight slightly decreased among Albanian men and women from 2008 to 2018, meanwhile obesity increased by 69% among women and 58% among men from 2008 to 2018^{2,3}; reduction of physical activity: 81.6% of women 15-49 years old do not practice aerobic exercises³; smoking among women in Albania has increased by 67% from 2002 to 2018, meanwhile smoking among men has decreased by 22% for the same period of time^{2,4}.

The Oncology Hospital is part of the University Hospital Centre “Mother Theresa” and the only specialized tertiary public institution, which makes it unique from a functional point of view in Albania. It was established in November 1969 as an Oncology Clinic, with the structure of a comprehensive centre for the fight against cancer. It currently operates with

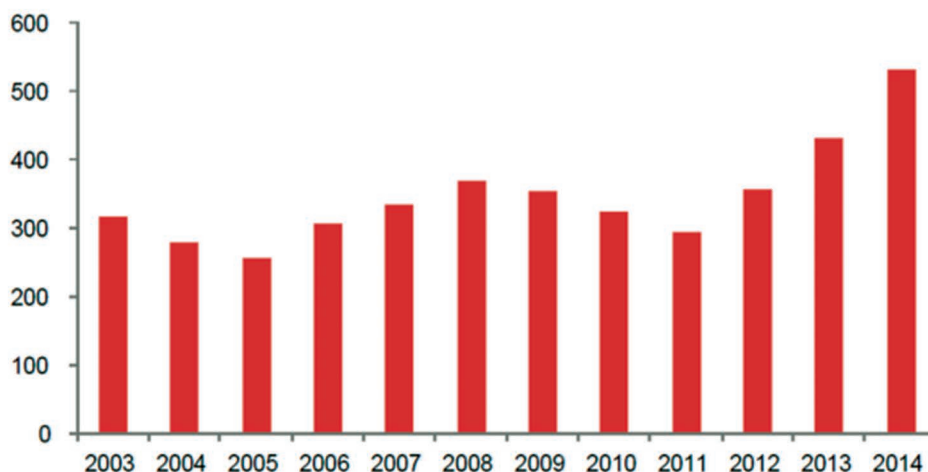


Figure 1. Breast cancer incident cases during 2003-2014 (Oncology Service)

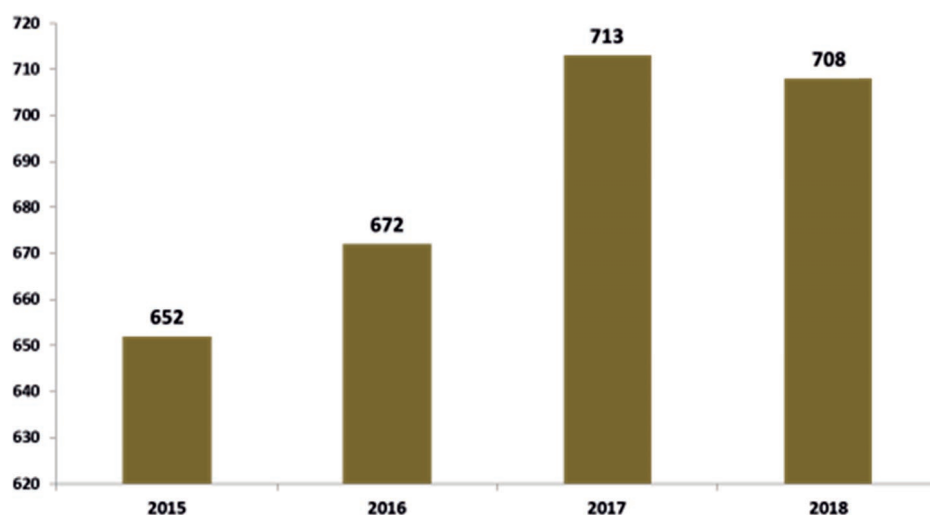


Figure 2. Breast cancer incident cases during 2015-2018 (Institute of Public Health)

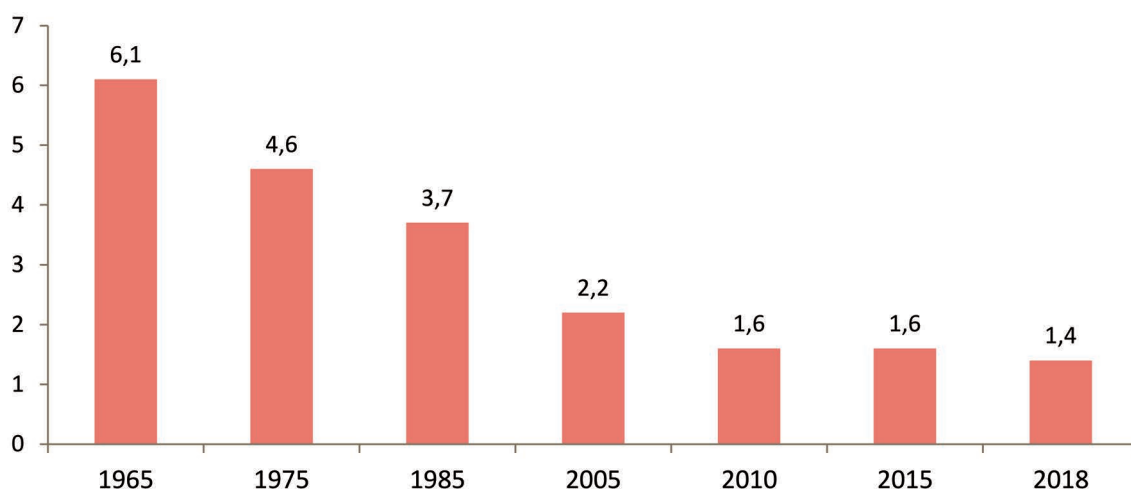


Figure 3. Fertility rate in Albania (INSTAT)¹

a multi-disciplinary team, which deals with diagnoses, treatments, education, tests, research, reporting, etc., about malignant pathologies.

The Surgical Unit of this hospital performs approximately 1750 surgical interventions per year. The main malignant disease treated is breast cancer, which had a significant evolution during the years. For operable tumours, initial mastectomy followed by adjuvant chemotherapy has been the only treatment for a long time. For locally advanced breast cancer after neoadjuvant treatment, the surgery performed is radical mastectomy, approximately in 90% of cases and breast-conserving surgery in about 10% of cases. Radical modified mastectomy is still the main surgical procedure in our Oncology Service, used in approximately 75% of cases. This is due to patients' mentality, distance and transport issues, lack of availability of certain services from time to

time, such as frozen section biopsy, immediate reconstruction, support by the insurance for prosthesis and mesh, etc.

In the early times (1974), the breast surgery has started with radical modified mastectomy and radical axillary dissection. In 2007, breast conserving surgery (BCS) was widely used for the treatment of early breast cancer and sentinel node biopsy (SNB) has emerged as a method to avoid radical axillary clearance for clinical negative axillary node. LNSB was offered using blue diet.

In 2012, due to several training programs abroad attended by some surgeons of our staff, we started to use oncoplastic breast surgery techniques like Madeleine Lejoure (Figure 4), Benelli, Latisimus flap (Figure 5), etc.

From 2010, private hospitals have started to use widely breast surgery and related techniques.



Figure 4. Madeleine Lejoure technique

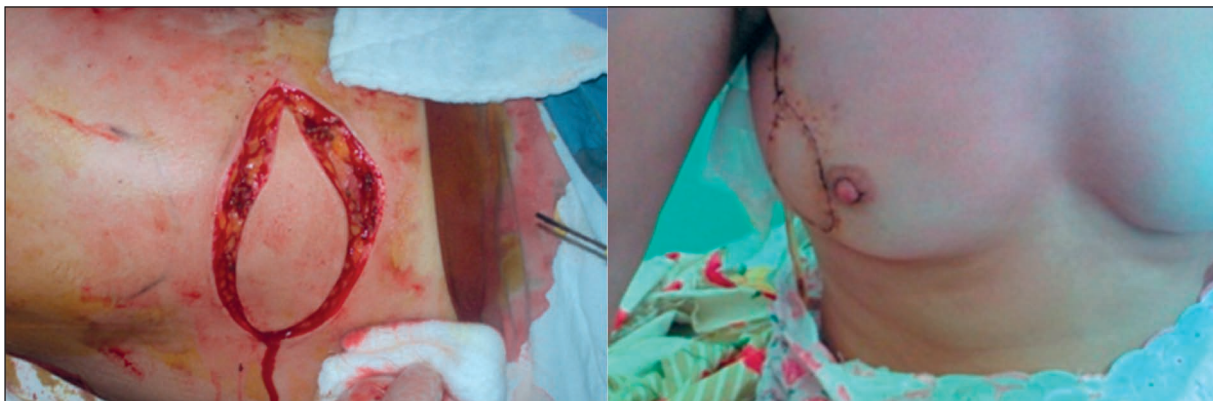


Figure 5. Latisimus Flap technique



Figure 6. The patient with bilateral skin sparing mastectomy. Left – before surgery. Right – one year after surgery.

In October 2019, the ultimate type of surgery was performed for the first time in Albania: bilateral skin sparing mastectomy et left lymph node sentinel biopsy of axilla using isotope mapping with technetium and immediate bilateral reconstruction with prosthesis and biological mesh pre-pectoral muscle, for a 45-year-old patient diagnosed with left breast

cancer (lobular type). The histopathological examination revealed a left breast multifocal lobular carcinoma middle grade; left retroareolar tissue negative for presence of malignant disease; negative metastases in 3 lymph nodes of lymph node sentinel biopsy (LNSB). Immunohistochemistry showed receptor positive and Her2: 3+ (mT2N0M0); right breast – some focus of

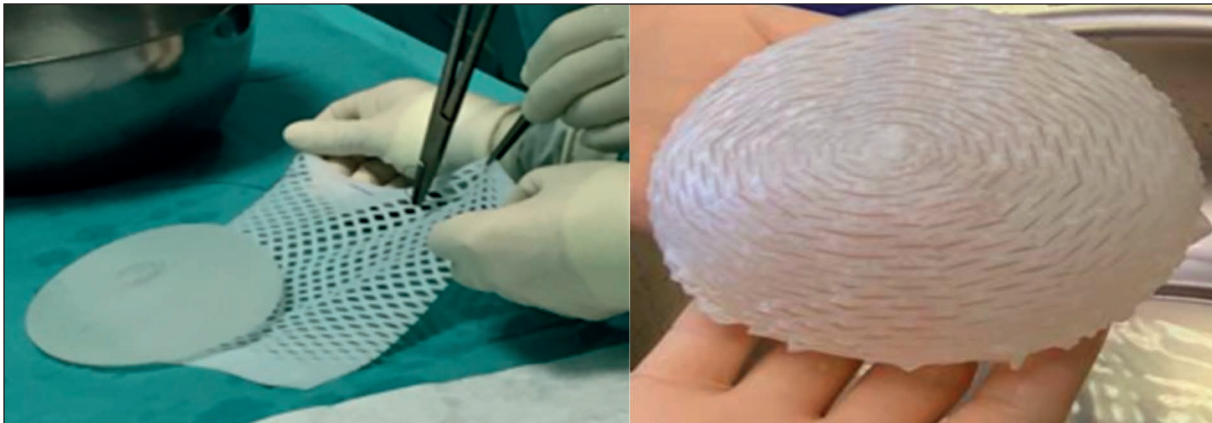


Figure 7. Photo of mesh cover

fibrocystic mastopathy. After re-consultation by the multi-disciplinary team, it was decided to start the chemotherapy regimen: Paclitaxel 140 mg i/v every week for 12 weeks and Herceptin s/c every 3 weeks for 18 weeks. The patient was in a good condition and very satisfied with the result of surgery and in good physical-emotional condition (Figures 6, 7).

DISCUSSION

After the 90', during the transition to a market economy system, Albania clearly faced demographic transition and lifestyle changes, and accompanying epidemiological transition as well. These dynamics (rapid ageing of the population mainly due to radical reduction of fertility rates and mass migration of young people) resulted in malignant diseases becoming a priority for the health system about four decades later¹.

Changes in the lifestyle of the Albanian population have also influenced the risk factors for breast cancer. For example, female sex and ageing are the main risk factors for breast cancer. Females are much more likely than males to develop breast cancer⁵. The risk for breast cancer increases with age. As people age, the risk of genetic mutations increases. Most breast cancers are diagnosed after the age of 50 years, and about 85% of cases occur in women aged over 50 years^{5,6}. Genetic mutations: about 5% to 10% of breast cancers are thought to be hereditary (genetic mutations). The most well-known gene mutations are BRCA1 and BRCA2. These genes can greatly increase a woman's risk of breast and ovarian cancer. On average, a woman with a BRCA1 or BRCA2 gene mutation has up to 7 in 10 risk of getting breast cancer by the age of 80 years^{5,7}. Women who started menstruating before the age of 12 years and those who go through menopause after the age of 55 years have a higher risk of breast cancer later in life. Women who

give birth to their first child after the age of 30 years and those who have never been pregnant have a greater risk of breast cancer than women who have had one or more pregnancies. Breastfeeding lowers the risk of breast cancer, particularly if a woman has children at younger age. The longer the woman breastfeeds, the more the risk is reduced⁵. Family history of breast cancer is known to increase an individual's risk of disease. The risk for breast cancer increases if a woman's mother, sister, daughter or close relatives were diagnosed with breast cancer, particularly at a young age. Having a first-degree male relative with breast cancer also raises a woman's risk^{5,8}. Personal history of breast cancer and other breast conditions is a risk factor, as well: women diagnosed with breast cancer have a higher risk of getting a new breast cancer than women who've never had breast cancer. If a woman had breast cancer in one breast, she has an increased risk of developing cancer in the other breast. Some non-cancerous breast diseases are associated with a higher risk of breast cancer⁵. Exposure to ionizing radiation has been established as one of the risk factors for development of breast cancer. A woman who had chest radiation therapy before the age of 30 years has a higher risk of getting breast cancer later in life^{5,9}. Women with dense breasts have a higher risk of breast cancer than women with fatty breasts, and the risk increases with breast density^{5,10,11}. Overweight or obese women after menopause have an increased risk of breast cancer than those with a normal weight. Many studies have shown that, in postmenopausal women, a higher body mass index is associated with a modest increase in the risk of breast cancer^{5,12}. Alcohol consumption increases the risk of breast cancer. The dose-effect relationship between alcohol and cancer is clear: the higher the alcohol consumption, the higher the risk of cancer^{5,13-14}. There is growing evidence that smoking may increase the risk of breast cancer, especially in women who started smoking

during adolescence or who have a family history of the disease^{6,15}. Women who are not physically active have a higher risk of breast cancer. Physical activity has been associated with a reduction in the risk of breast cancer among both premenopausal and postmenopausal women^{5,16}. Exposure to hormone replacement therapy (HRT) is associated with an increased risk of breast cancer. Estrogen-only therapy seems to lower breast cancer risk, while combinations of hormone replacement therapy increase the risk¹⁷.

In the Oncological Hospital of the University Hospital Centre “Mother Theresa” Tirana, breast surgery in breast cancer have consisted for a long time in modified radical mastectomy and axillary dissection. This is due to several factors: lack of doctors’ training until the 2000s, lack of frozen biopsy, patients living far from Tirana, where the only centres for radiotherapy are located, mentality of patients that radical surgery of breast is the best treatment, etc. Breast conserving surgery started after 2007 in our Oncology Service and the use of oncoplastic technique for breast surgery started to be widely used after 2010. These improvements in breast cancer surgery techniques were due to the abroad training of surgeons, implementation of frozen biopsy, availability of new acceleratory radiotherapy machine, etc. The possibility to offer techniques of reconstruction with prosthesis and biological mesh is a new frontier in the breast surgery in Albania.

The nipple sparing mastectomy is a conservative mastectomy, involving the removal of the all-mammary gland, excepting the cutaneous envelope. During this surgery the nipple areolar complex is conserved, after an intraoperative histological exam of the retroareolar tissue. For this type of surgery, different skin incisions are used, like upper periareolar, upper periareolar with lateral extension, transareolar or transnipple, inframammary /inferior lateral, upper-outer radial, omega (mastopexy). The preferred incision is the upper-outer radial incision, due to its various advantages: excellent scar outcome, easier access to the axilla, nipple and complete glandular demolition, the highest possibility of conserving the areolar vascularization, and the best reconstruction time, both in small and large breasts. During dissection, it is necessary to palpate the skin flap to have a uniform and adequate thickness, not too thin and devascularized (necrosis), and not too thick, as there would be a risk of glandular residue (local recurrence)¹⁸⁻²⁰. To assess the vitality of the flaps and nipple areola complex, some studies have evaluated the perfusion with fluorescence emitted after an infusion with indocyanine green dye²¹. The key to this surgery is the conservation of the nipple areola complex; for this reason, it is necessary to perform an intraoperative

histological exam of the subareolar tissue. During the glandular dissection, the surgeon should proceed with meticulous care while isolating the areolar conus, a process which is followed and sectioned until removal from within the nipple. The retroareolar tissue excise is sent to frozen biopsy and when positive, it specifies the presence of infiltrating or in situ tumour, extension, and distance from the edge of nipple. For this result the possibilities are to conserve the nipple, removal of the nipple areola complex or, given the rarity of areolar accessory ducts, removal of the nipple alone; this is a latter variant of the technique (areola-sparing mastectomy). The possibility of false negatives from the intraoperative histological exam is approximately 4.6%²²⁻²⁴. Nipple sparing mastectomy is the most advanced surgical technique of conservative mastectomies, even from the oncologic point of view and outcomes, that are reassuring. The outcome of the reconstruction is the conservation of nipple areola complex. The local recurrence is same as those of radical mastectomy or skin sparing mastectomy. It is necessary a good selection of cases to be treated and careful planning of the procedure²⁵.

After the demolition surgery for breast cancer, it is necessary to perform breast reconstruction to give patients’ satisfaction and quality of life. The delayed breast reconstruction using tissue expanders has demonstrated to cause dissatisfaction towards body image and emotional and social distress²⁶.

Nowadays, due to the use of medical devices like synthetic and biological meshes, acellular dermal matrices, providing complete covering of implants²⁷, surgical techniques such as skin-sparing and nipple-sparing mastectomies, surgeons must perform immediate breast reconstruction, avoiding the use of tissue-expanders²⁸.

Meshes used in immediate breast reconstruction can be classified in synthetic and biological, which can be further classified in human-derived acellular dermal matrices and xenografts, made from fetal bovine, porcine dermis, and bovine pericardium. Tissue processing removes the cellular antigens responsible for immunological response, while preserving the structural matrix that stimulates angiogenesis and tissue regeneration. Those meshes create a scaffold that the host cells can colonize, thus allowing prosthetic integration and encapsulation and promoting at the same time new vascularization^{29,30}.

CONCLUSIONS

In our experience of surgical breast cancer treatment at the Oncological Hospital, University Hospital Center “Mother Theresa” in Tirana, for the first time it has been possible to perform the sentinel

lymph node biopsy using isotope mapping and immediate reconstruction of the breast with prosthesis and biological mesh, avoiding that women experience unnecessary axillary dissection and disfigurement of body image, all being solved in a single surgical procedure. For Albania, this type of surgery represents a new frontier in breast surgical oncology and it is our aim to offer it properly to all women suffering from breast cancer, especially to young patients.

Author Contributions:

Primary oncological surgeon, H.N.; Plastic surgery consultant and clinical application of the surgical technique, G.Xh.; Clinical application of the surgical technique, G.P.; Writing-reviewer editor, N.A.; imaging investigations and invasive biopsy procedure, R.H.; Psychosocial assessment of the cases, K.M.; Writing original draft, G.E.; Assistant surgeon and oncoplastic consultant, D.V.; conceptualization, visualization and supervision, H.N. All the authors have read and agreed with the final version of article.

Compliance with Ethics Requirements:

"The authors declare no conflict of interest regarding this article"

"The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study"

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