# EVALUATION OF ADVANCED CLINICOPATHOLOGICAL AND STRUCTURAL ASPECTS OF MODERN ONCOPLASTIC BREAST CANCER SURGERY

## Ph.D. Thesis

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# Ph.D. Thesis

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**LIST OF FULL PAPERS THAT SERVED AS THE BASIS OF THE PH.D. THESIS**

**I. Dorogi B**, Bukovszky B, Mátrai T, Sávolt Á, Polgár Cs, Kelemen P, Kovács T, Rényi-Vámos F, Ivády G, Kovács E, Téglás T, Kásler M, Mátrai Z.

Mapping of the functional anatomy of lymphatic drainage to the axilla in early breast cancer: A cohort study of 933 cases.
*Eur J Surg Oncol. 2019 Feb; 45(2):103-109. doi: 10.1016/j.ejso.2018.08.030. Epub 2018 Oct 7.*
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**II. Dorogi B**, Újhelyi M, Kenessey I, Ivády G, Mátrai Z.

Clinicopathological correlations of areola-sparing mastectomies versus nipple-sparing mastectomies: Analysis of the oncological and cosmetic importance of the components of the nipple-areola complex
*Breast J. 2020 Oct; 26(10):2081-2086. doi: 10.1111/tbj.13957. Epub 2020 Jul 1.*
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**III. Dorogi B**, Mátrai T, Újhelyi M, Kenessey I, Kelemen P, Sávolt Á, Huszár O, Ping O, Pukancsik D, Mátrai Z.

Assessing the needs of Hungarian breast cancer patients for modern oncoplastic breast surgical treatment – questionnaire study of 500 patients.
*Orv Hetil. 2020 Jul;161(29):1221-1228. doi: 10.1556/650.2020.31768.*
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**OTHER PUBLICATIONS RELATED TO THE THEME OF THE THESIS**

**I. Dorogi B**, Gulyás G, Kunos Cs, Udvarhelyi N, Mátrai Z.

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*Eur J Plast Surg. 2014 Jun; 37:505–508. doi: 10.1007/s00238-014-0970-4.*
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*Orv Hetil. 2011 Apr;152(17):678-88. doi: 10.1556/OH.2011.29077.*
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**III. Dorogi B**, Pálházi P.

Az emlő és a regionális nyirokelvezetés anatómiája
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*Medicina, Budapest, 2015; 39-47.*
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**∑ 0.000**

**CONTENTS**

**LIST OF ABBREVIATIONS**

ACOSOG - American College of Surgeons Oncology Group
ALND – axillary lymph node dissection
AMAROS – After Mapping of the Axilla: Radiotherapy Or Surgery
ARM - axillary reverse mapping
ASM - areola-sparing mastectomy
BCS – breast-conserving surgery
BRESO - An European international educational and accreditation project
BU – breast unit
CEEBCSC - Central-Eastern European Breast Cancer Surgical Consortium
DFS – disease-free survival
EBCC - European Breast Cancer Conference
EUBRAST - European Breast Cancer Research Association of Surgical Trialists
ECIBC - European Commission Initiative on Breast Cancer
EORTC - European Organization for Research and Treatment of Cancer
ESMO - European Society of Medical Oncology
ESO - European School of Oncology
ESSO - European Society of Surgical Oncology
ESTRO - European Society for Radiotherapy and Oncology
EBSQ - European Board of Surgery Qualification
EUSOMA - European Society of Mastology
G.Re.T.A. - Group for Reconstructive and Therapeutic Advancements
HTgF - high tangential field
NAC - nipple-areola complex
NACT - neoadjuvant chemotherapy
NEAK - National Health Insurance Fund of Hungary, Nemzeti Egészségbiztosítási Alapkezelő
NIO - National Institute of Oncology, Országos Onkológiai Intézet
NSM - nipple-sparing mastectomy
OS - overall survival
OTOASOR - Optimal Treatment Of the Axilla – Surgery or Radiotherapy
PMRT - postmastectomy radiotherapy
PROM - patient-reported outcome measure
QoL - quality of life
RT - radiotherapy
RTOG - Radiation Therapy Oncology Group
SD - standard deviation
SLN - sentinel lymph node
SLNB - sentinel lymph node biopsy
SSM - skin-sparing mastectomy
STgF - standard tangential field
TDLU - terminal ductal lobular unit
UEMS - European Union of Medical Specialists
WBI - whole breast irradiation

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## 1. Introduction

Breast cancer is the most common malignancy in women with more, than 8.400 newly diagnosed cases and nearly 2.200 deaths in 2017, according to the Hungarian National Cancer Registry [1]. Breast cancer treatment has gone through a long evolutional process from Halsted's procedure to the nowadays practised complex multidisciplinary approach and oncoplastic surgical procedures appeared in the last decades [2-4]. The introduction of population-based breast screening programmes, supported by the development of molecular biology, histopathology, radio-, and oncotherapy resulted in a significant increase in five-year survival rate (from 52% to 85.1%) [5-7].

With the scientific endorsement of oncoplastic breast surgery, the main focus of breast cancer surgery shifted to treatment optimization by applying tailored de-escalation or escalation of the current protocols [8]: active surveillance or surgery for low-risk DCIS, the indication of nipple-sparing mastectomy (NSM) in appropriate cases, how to justify surgical margins, the implementation of sentinel lymph node biopsy (SLNB) after neoadjuvant chemotherapy (NACT), omitting axillary lymph node dissection (ALND) or targeted axillary surgery in certain cases [9-13].

Our aim in this dissertation was to evaluate yet not sufficiently studied issues related to modern breast surgery: 1. the associations between the lymphatic drainage pattern of the breast tumour with its clinicopathological features, which may provide further basic information for the interpretation of the American College of Surgeons Oncology Group (ACOSOG) Z0011, Optimal Treatment Of the Axilla – Surgery or Radiotherapy (OTOASOR) and After Mapping of the Axilla: Radiotherapy Or Surgery (AMAROS) trials; 2. the cosmetic role and oncologic importance of the nipple-areola complex (NAC) and its components in the context of the preservation of the complex anatomical unit of the nipple by NSMs or preserving only the pigmented skin of the areola by areola-sparing mastectomies (ASM) and 3. today's yet understudied questions, the needs and requirements of the Hungarian health care system to meet the rapidly expanding need for oncoplastic breast surgery.

### 1.1. Anatomy of the subregions of the axilla and its importance in breast cancer treatment

Anatomically, the axillary region is divided into five subregions: anterior, posterior, lateral, central and apical zones [14] (Figure 1).

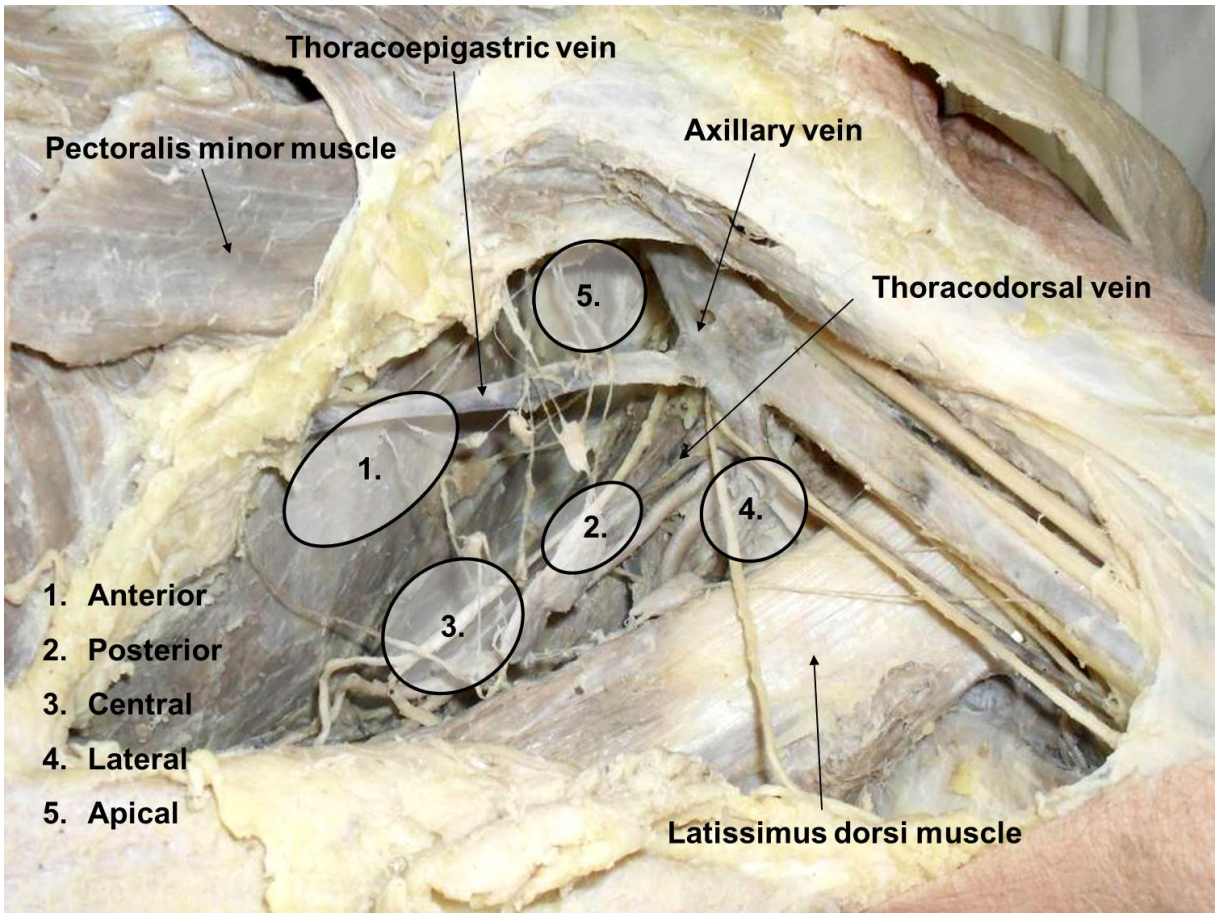



***Figure 1.*** *Anatomical subregions of the axilla (left side, human cadaveric dissection performed by the author)*

The anterior subregion is located under the lateral edge of the pectoralis minor muscle along the lateral thoracic vein. The posterior zone is found adjacent to the posterior wall of the axilla along the thoracodorsal nerve and vessels. The lateral subregion is located close to the lateral wall of the axilla, in relation to the proximal part of the axillary vein. The lymph nodes in this zone receive the vast majority of the efferent lymph vessels of the upper limb. The central zone is in the middle of the pyramid-shaped space of the armpit, close to the base of the axilla. The apical subregion is found in the apex medially to the distal part of the axillary vein.

These subregions correspond to the axillary node levels previously described by Berg [15]. The anterior, posterior and lateral subregions constitute Level I, the central zone forms Level II and the apical zone constitutes Level III [14]. Actually, traditionally these axillary node levels constitute the basis for driving both surgical care and radiation therapy.

Clear relationship between the anatomic location and metastatic status of the sentinel lymph node (SLN) have been revealed [16, 17]. Histologically positive SLN was detected in Level I in 96% of cases and in Level II in 4% of cases by SPECT/CT [17].

Regional lymph node status is one of the most important prognostic factors for disease-free (DFS) and overall survival (OS) in breast cancer [18-22]. Today, the gold-standard method for staging patients with early-stage breast cancer with clinically negative axillary lymph nodes is the SLNB [21, 22].

To optimise the effectiveness of SLNB, the precise pre- and intraoperative mapping of lymphatic drainage is mandatory [21-23].

A better understanding of the relationship between the subregional drainage pattern of the SLN, the subregional localisation of the SLN and the association between these features and the pathological characteristics of the primary breast tumour could have particular importance in determining whether ALND can be safely omitted.

The ACOSOG Z0011 trial did not perform ALND for early-stage breast cancer patients with 1-2 metastatic SLNs (cT1-2, pN1) in the SLNB-alone group, and in the majority of the patients, the axilla was treated only with tangential field irradiation following breast-conserving surgery (BCS). After a median follow-up of 9.3 years, the data compared to the traditional ALND group showed no differences in local recurrence-free survival [24, 25]. In the ACOSOG Z0011 trial, dose distribution in the axillary volumes was not reported in the initial publication. Later on, nevertheless, Jagsi et al. [26] analysed the radiotherapy (RT) coverage of the axillary lymph nodes in that trial. Most patients treated in the Z0011 trial received tangential RT alone, and some received no RT at all. Some patients received axillary nodal irradiation via a third field. They concluded that further research is necessary to determine the optimal RT approach in patients with low-volume axillary disease treated with SLNB alone.

A recent surgical technique that is less radical and therefore decreases the risk of morbidity of the SLNB and ALND procedures, especially that of lymphedema, is axillary reverse mapping (ARM) [27-29]. When applying this method, the lymphatic drainage of the upper limb that runs through the axilla - most often the lateral subregional lymphatic structures - is identified by injecting radioisotope or blue dye to the ipsilateral limb subcutaneously. Labelling helps to spare these nodes during the operation, removing only the lymph nodes that drain the lymph of the breast. The technique was proven to be more or less feasible but the question of oncological radicality still arises due to the uncertainty of the metastatic status of the ARM lymph nodes that are not removed [30].

### 1.2. Anatomy of the nipple-areola complex and its importance in breast cancer treatment

In recent decades, several types of mastectomy have been developed to enhance the cosmetic outcome of immediate breast reconstruction and hence patient satisfaction; these techniques include skin-sparing mastectomy (SSM), ASM and NSM. As a consequence, concerns of oncological safety have arisen in regard to not compromising cancer treatment by preserving the skin, especially the nipple [31, 32].

The main question behind the possible uncertainty of NSM is the anatomy of the NAC and the chance of cancer development in the remaining tissue after mastectomy. The nipple contains the ducts draining the mammary gland, and terminal ductal lobular units (TDLUs) - from where ductal and lobular breast cancer arise – can also be found in the NAC [33-37]. A recent anatomical study by Rusby et al. showed that the ducts form a central bundle in the nipple that narrows just under the skin before spreading to the breast parenchyma [38]. The central bundle is covered by a duct-free rim of tissue containing 50% of the vasculature of the nipple, allowing a complete ductal resection leaving a 2-mm peripheral rim behind without damaging the blood supply in 96% of the cases [39]. TDLUs can be present behind the areola in up to 25-26% of cases [34, 36] located at the base of the nipple [37]. By understanding these sophisticated anatomical details, the duct core and the possible TDLUs can be excised by applying a careful dissection at the level of the dermis below the NAC, resulting in an oncologically safe and cosmetically superior nipple-sparing procedure [36, 40-42].

Until the dispelling of oncological concerns regarding the preservation of the nipple, SSM was the preferred procedure for delayed-immediate breast reconstruction for suitable patients. Since the acceptance of NSM at the 13th St. Gallen International Breast Cancer Conference [43] and strengthening of its role and the broadening of its indications in the surgical treatment of breast cancer at the Oncoplastic Breast Consortium Consensus Conference on NSM in Basel [13], the importance of SSM has largely been reduced.

The anatomical and aesthetical complexity of the substructure of the NAC is an essential issue in oncoplastic breast surgery, and is coming more and more into the highlight. In all cases when the nipple has to be removed for oncological reasons, the oncological and cosmetic importance of the nipple and separately the pigmented skin of the areola should be considered on an individual basis if modern breast oncoplastic surgery is practised.

### 1.3. The Hungarian system of oncoplastic breast cancer care: present situation, strengths and weaknesses

Due to inequalities in special needs oncology care, the first European Breast Cancer Conference (EBCC) in Florence in 1998 called for multidisciplinary breast therapy units and the conditional and quality assurance requirements for so-called "breast units" (BU) have been defined [44]. A working group of the European Organization for the Research and Treatment of Cancer (EORTC) and the European Society of Mastology (EUSOMA) has defined the basic requirements among others regarding the participation of various breast cancer specialists in these BUs, which made the quality control of specialist care possible [45]. The European Union of Medical Specialists (UEMS) and the European Society of Surgical Oncology (ESSO) established the European Training Curriculum and European Board of Surgery Qualifications license exam in 2010, in which also the National Institute of Oncology (NIO), Budapest has been actively involved for years. At the second EBCC, the "Brussels Statement" established a set of accreditation criteria [46]. In 2019, ESSO, UEMS, the European Breast Cancer Coalition (Europa Donna), the European School of Oncology (ESO), the European Breast Cancer Research Association of Surgical Trialists (EUBREAST), the European Commission Initiative on Breast Cancer (ECIBC), the Hungary-initiated Central-Eastern European Breast Cancer Surgical Consortium (CEEBCSC) and the Group for Reconstructive and Therapeutic Advancements (G.Re.T.A.) launched the Breast Surgical Oncology (BRESO) project [47]. The

BRESO project has developed a continent-wide standardized breast surgery curriculum and quality assurance system and its accreditation requirements. As a result of these statements, the European Parliament issued a resolution in 2003 clearly supporting the extension of the institutional system of qualified BUs in Europe, and in 2013 a summary of the minimum requirements for Breast Centres was published [48].

The requirements for the accreditation of a BU is that in the given centre at least 150 newly diagnosed breast cancer patients receive complex oncological treatment per year based on the decision of the multidisciplinary breast therapy committee, according to continuously updated professional protocols. An essential part of the accreditation is the development and maintenance of a standardized database, the provision of population mammography screening programmes and the provision of educational and other scientific research activities [48-50]. The domestic situation and results of the BU system in Hungary was reported by our working group in the Orvosi Hetilap in 2016 [51].

As a consequence of the rapid spread of modern oncoplastic breast surgery in the recent decades, not only the removal of the breast tumour, but also the aesthetically complete preservation or post-mastectomy reconstruction of the breasts is now an essential part of the surgical care [52-54]. In the absence of contraindications, any woman with breast cancer undergoing mastectomy should be offered and provided with the possibility of breast reconstruction [55]. The resulting demand for breast reconstruction not only poses a challenge for breast and plastic surgeons, but also raises a number of system-related issues in all European countries.

Beside the basic reconstructive surgical procedures, however, additional indications and breast surgeries arising from the oncoplastic activity are awaiting clarification and regulation. The evaluation and controlled implementation of these extra procedures also contain a number of unknown factors even for the currently developed breast surgical care systems.

The primary system-level breast reconstruction on wide population significantly expands the secondary tasks. As a result, new issues arise, which mean further load for the health care system: aesthetic changes of the reconstructed or contralateral symmetrized breast due to weight gain known to occur as a result of long term (5-10 year long) endocrine treatment

[56-58], “aging” secondary to the excellent survival [59-61] or fibrosis after the oncological treatments (e.g. RT) [62].

Beyond the above mentioned expectations, to determine the optimal volume of human resources and surgical capacity of the health care system, complications due to technical problems (e.g. implant rupture) or conditions (e.g. capsular contracture) of implants and the increased need of further possible surgical corrections resulting from changes in contralateral breast symmetry should also be taken into account.

Taking into consideration all the professional aspects, the optimal aesthetic result and the maximum number of reconstructive surgeries that can be performed within the framework of the oncology care system has to be determined. However, oncoplastic surgery care has special features, including subjective elements, long-term difficulties such as the need of possible corrections of continuous cosmetic changes that go beyond primary breast cancer surgery and reconstructive surgery.

Understanding, scientifically based identification and realistic assessment of new breast surgery needs form an essential basis for evolving the necessary set of conditions. At present, the National Health Insurance Fund of Hungary (Nemzeti Egészségbiztosítási Alapkezelő, NEAK) finances postmastectomy breast reconstruction for all Hungarian patients who possess valid health insurance coverage, however, these complex new indications are currently not recognized at the system-level and hence cannot be managed accordingly. Breast reconstruction is a significant achievement for Hungarian breast cancer patients, but with the increase in its need and an expansion of the range of indications, an avalanche-like, unregulated situation may develop, the prevention of which requires professional knowledge and planning.

## 2. AIMS OF THE THESIS

1. Studying the location of the SLNs according to the axillary anatomical subregions and assessing the relationship between that and the clinicopathological characteristics, molecular subtype and location of the primary tumour by breast quadrants in order to characterize their functional and morphologic lymphatic drainage pattern

2. Assessing the coverage of the axillary nodal subvolumes by standard and high tangential fields (STgF and HTgF) during whole breast irradiation (WBI)

3. Based on our SLN mapping findings, comparing the SLN positivity rate in the studied anatomical subregions with the respective data from the literature gained by the ARM technique

4. Comparison of the oncological and cosmetic outcome after ASM and NSM

5. Collecting the opinion and expectations of Hungarian women with breast cancer regarding modern oncoplastic health care system

# 3. PATIENTS AND METHODS

## 3.1. Mapping the sentinel lymph nodes in the anatomical axillary subregions: a retrospective cohort study

This study - registered on Clinicaltrials.gov (identifier: NCT01804309) and approved by the Institutional Ethics Committee Board - was performed between March 2013 and February 2015 at the NIO, Hungary. Female patients older than 18 years were eligible with primary unilateral invasive or microinvasive, clinically lymph node-negative early-stage breast cancer (cT0-2N0M0) needing SLNB. Exclusion criteria included previous ALND, cN1-2, pregnancy, lactation and necessity of neoadjuvant treatment for breast cancer [63, 64].

### *SLNB technique*

The complex oncological therapy was performed according to the actual international guidelines [63-65] adopted by the NIO and was not different from those who were not included in the trial. Radiopharmaceutical (80 Mbq 99m Tc-labelled nanocolloid, particle size: 50-800 nm) was injected into the tumour if it was not palpable or periareolar tissue in case the tumour was palpable on the day before surgery. If the lymphoscintigraphy was unsuccessful, 2-3 ml of periareolar Patent blue 25 mg/ml® dye injection was applied 10 minutes before the operation.

Patients then underwent wide excision or mastectomy and axillary SLNB followed by ALND instantly if the SLN was positive by intraoperative imprint cytology or as a second operation if the SLN was positive only by histological examination. If only isolated tumour cells or micrometastases were found in the SLN, ALND was omitted.

### *Localisation of the SN into the anatomical axillary subregions*

SLNB was performed either from the incision used for the breast surgery or from a separate axillary incision. The dissection in the axillary adipose tissue was guided by gamma probe or in case the lymphoscintigraphy was unsuccessful, the blue-stained afferent lymph vessels were carefully followed to the stained lymph node(s). The subregion the SLN(s) belonged to was identified by the operating surgeons based on the previously described anatomical landmarks. All SLNs were removed separately and labelled with their subregional localisation for pathological processing. The subregional localisation was recorded immediately after biopsy in the operating theatre by putting the number of the removed SLNs

from each subregion to the corresponding field on a standardised data sheet (Figure 1). Imprint cytology was performed intraoperatively, and if the result was positive, the operation was completed with ALND. Postoperatively, all the removed lymph nodes were meticulously examined by the pathologists according to the guidelines [66, 67].

The axillary subregions where the SLNs were situated were analysed in relation with the tumour features such as the quadrant of the breast where the primary tumour was detected, and the molecular subtype according to the St. Gallen consensus [6].

***Lymph node coverage during postoperative RT***

Following BCS, all patients had 3D-conformal RT. Patients were placed supine with both arms up and both hands holding on to a support during CT simulation. CT scan images with 5-mm sections were obtained. The breast was irradiated with two opposing tangential fields with 6 MV photons. STgFs were planned based on the palpation and marking was placed to indicate the margin of the breast parenchyma with the addition of a 1-2-cm margin in all directions. The superior border of the fields was determined so that only the breast was intended to be irradiated, without regard to nodal coverage. In node-positive patients, an additional field was also used to deliver an effective dose to the axillary apex and supraclavicular fossa. The total dose to the whole breast and supraclavicular fossa was 50 Gy (25x2 Gy). Breast irradiation was given via STgFs. The STgF upper margin was generally the base (± 1 cm) of the clavicle. Retrospectively, for the purpose of this study in 61 randomly selected node-positive patients treated with breast-conserving therapy in whom the SLNs were found in the anterior or posterior axillary subregions (Level I), HTgFs were simulated using the same CT data. HTgF consisted of a superior border placed at the inferior edge (or below maximum 2 cm) of the humeral head. Before RT planning, axillary volumes (Levels I, II and III) were contoured using the Radiation Therapy Oncology Group (RTOG) contouring atlas [68]. Coverage of the axillary volumes by tangential fields was classified according to the tangential field target volumes (Levels I, II and III) overlap: 100% overlap (complete coverage), <100% overlap (partial coverage), and 0% overlap (lack of coverage: out of field).

***Analysis of the ARM nodes***

Multiple studies were conducted to analyse the feasibility and oncological safety of the ARM technique, however only a few authors focused on the detailed anatomical localisation of the ARM nodes. A review of the literature was performed and two studies were selected in which the precise anatomical description allowed the localisation of the ARM lymph nodes in the axillary subregions [69, 70]. The subregional distribution and metastatic rate of the ARM nodes reported in the selected studies of Ikeda et al. [69] and Bedrosian et al. [70] were retrieved and compared with the subregional distribution and positivity rate of the SLNs in the present study.

Ikeda et al. enrolled 60 patients who underwent breast surgery with ALND together with the application of ARM technique [69]. The study population was divided into two groups: twenty-five patients were clinically node-positive and underwent ALND without SLNB ("without SLNB group"), while thirty-five patients were clinically node-negative but lymph node-positive at SLNB ("with SLNB group"). Indocyanine green was applied for the ARM technique. The stained ARM nodes were removed from the ALND specimen after localisation and sent for histology. Patients with SLNB had clinical stage I (45.7%; n=16) and IIA (51.4%; n=18) breast cancer, whereas the clinical stages of the patients without SLNB were IIA (32.0%; n=8), IIB (44.0%; n=11), IIIA (8.0%; n=2), IIIB (4.0%; 1), and IIIC (12.0%; n=3). All patients (n=35) and 92.0% (n=23) of the patients had invasive ductal carcinoma in the SLNB and without SLNB groups, respectively.

Bedrosian et el. enrolled patients with invasive breast cancer and biopsy-proven axillary lymph node metastasis or patients with clinically negative but SLNB-proven positive lymph node status requiring completion ALND [70]. Blue dye was applied for the ARM technique. During the ALND procedure blue stained lymph nodes were identified, their location was noted and they were dissected from the remainder of the surgical specimen and sent for separate pathologic evaluation. The study enrolled a total of 30 patients with clinical stages I (10.0%, n=3), IIA (6.7%; n=2), IIB (30.0%, n=9), IIIA (26.7%; n=8), IIIB (3.3%; n=1), IIIC (23.3%; n=7). The vast majority of the patients (93.3%; n=28) had invasive ductal carcinoma. The ARM technique was successful in 50% (n=15) of the cases – the results of these cases were retrieved and further analysed.

The two studies did not use the same anatomical subregional classification of lymph node localisation in the axilla, but their precise description relative to surgical landmarks enabled us to localise their ARM nodes and match their “fields” in the axilla to the corresponding anatomical subregions of our terminology.

### 3.2. Comparison of oncological and cosmetic outcome after areola-sparing mastectomy versus nipple-sparing mastectomy: analysis of a prospectively collected database

This single-centre retrospective comparative study was performed between April 2013 and December 2018 at the NIO, based on the prospectively completed institutional database. The study was approved by the Institutional Ethics Committee Board. All female patients for whom the multidisciplinary team decided mastectomy with delayed-immediate implant-based breast reconstruction were eligible. Exclusion criteria included nipple involvement, inflammatory breast cancer, previous breast surgery, pregnancy and lactation.

The diagnosis of breast cancer, additional staging examinations, adjuvant treatments, and follow-ups were performed according to an institutional protocol based on the European Society of Medical Oncology (ESMO) and on the European Society for Radiotherapy and Oncology (ESTRO) guidelines [64, 71, 72].

The indication for mastectomy was either therapeutic for breast cancer or prophylactic for patients with inherited BRCA mutation. Both ASM and NSM operations were performed with exactly the same indications: based on the actual guidelines, ASM was the technique first applied at our department between April 2013 and April 2017, while it was subsequently replaced in our daily practice from May 2017 by NSM after its international acceptance [41, 43]. The operation time, postoperative complications, oncological and histopathologic parameters, aesthetic results as well as patient reported outcomes of both groups were recorded and analysed.

#### *Oncoplastic breast surgical techniques*

The procedures in both groups were performed by the same qualified breast surgeons (having European Board of Surgery Qualification (EBSQ) license), based on the decision of the breast multidisciplinary team with the same delayed-immediate implant-based breast reconstruction techniques [73].

In the case of ASM, the whole mammary gland was dissected in a standardized way with an electrosurgical device using an infero-lateral incision. After the complete mobilization of the glandular tissue from the chest wall muscles and the subcutaneous tissue along the superficial fascia, a circumferential incision was made around the nipple base allowing the complete excision of the mammary gland with the nipple attached to the breast tissue. The major pectoral and serratus anterior muscles were dissected and elevated from the chest wall, and a Mentor Smooth Round Tissue Expander with a remote injection valve (size 400 – 550 – 700 ml) was placed and inflated (to an average of 40 ml) in the previously prepared sub-muscular pocket. After the closure of the submuscular pocket by stitching to the lateral edge of the major pectoral and serratus anterior muscles, the subcutaneous and skin layers were closed with continuous subcutaneous and intradermal sutures. The expander implant was gradually inflated during the routine follow-up visits. The expander implant replacement with permanent implants and the contralateral symmetrisation was performed 3-14 months later depending on the completion time of the adjuvant treatments. The nipple was reconstructed using local flaps as an outpatient procedure after an additional 3-9 months.

For NSM, the same infero-lateral incision and standardized dissection technique was applied. To assess the surgical margins below the NAC, after the excision of the mammary gland, a biopsy (“coring”) was taken from the posterior aspect of the nipple and was sent as a separate specimen for postoperative histological analysis. If the pathological examination of that intramamillary tissue sample or the removed mammary gland, in the case of ASM, was positive for cancer cells, the NAC was excised, and the patient was excluded from the study. If the surgical margin was clear, the nipple was spared followed by breast reconstruction with a submuscular expander implant and the implant was replaced and symmetrisation was performed later as described above.

***Treatment of the axilla with surgery and/or RT***

In cases of clinically negative preoperative axillary lymph node status, SLNB was performed for axillary staging. If the SLN was positive, based on the decision of the multidisciplinary team either ALND was done as a second operation or in selected cases (when postmastectomy radiotherapy (PMRT) was indicated for T3-T4 tumours) axillary and supraclavicular radiation fields were applied to treat the axilla [74-76].

PMRT in node-positive patients was always recommended for high-risk patients with one to three positive axillary lymph nodes, or involved resection margins, four or more involved axillary lymph nodes and T3–T4 tumours independent of the nodal status. Internal mammary RT was indicated for patients with four or more positive axillary lymph nodes or involved parasternal lymph nodes [64, 72, 77]. Doses used for local and/or regional adjuvant irradiation were 50 Gy in 25 fractions of 2.0 Gy.

***Assessment of complications, aesthetic outcome and quality of life***

Postoperative complications were assessed by applying the Clavien-Dindo classification system [78, 79]. Minor, asymptomatic complications (e.g., infections, haematomas or suffusions, seromas, partial skin/NAC necrosis, rippling, wound dehiscence and lymphedema (redness of the skin)) without need for medical therapy or surgical intervention were considered Grade I, while the same complications treated with antibiotics or minor interventions (e.g., suture of wound dehiscence, chronic seroma puncture) were considered Grade II complications. Any complications (e.g., haematoma, chronic infections, full thickness skin/NAC necrosis, implant loss and wound dehiscence) requiring invasive surgical procedures were classified as Grade III. Life-threatening complications or patient death were categorized as Grade IV and V complications, respectively.

For the assessment of the aesthetic outcome, a 5-point Likert scale (statement: “This patient has an excellent aesthetic outcome.”; score: 1, strongly disagree; 2, disagree; 3, undecided; 4, agree; 5, strongly agree) was applied [80]. The evaluation was performed by a committee of 3 breast surgeons (who were not involved in the surgical procedure) by reviewing the whole series of photo documentation and individually scoring each patient six months after the operation.

The BREAST-Q validated patient-reported outcome measure (PROM) reconstruction module version 2.0 postoperative questionnaire was applied to measure quality of life (QoL) of the patients [81]. Selected scales were used to measure satisfaction with the breast and psychosocial, physical and sexual well-being. The BREAST-Q questionnaire was administered to the patients 6 months after surgery. The patients’ responses to each item on the scale were transformed using a scoring conversation table. The results ranged from 0-100, with higher scores reflecting higher satisfaction or better QoL.

### 3.3. A survey on the needs of Hungarian breast cancer patients regarding modern oncoplastic breast surgery

This study was conducted enrolling 500 patients who underwent mastectomy and the breast reconstruction was either done at the same time as the removal of the primary tumour (immediate) or was started (e.g. by implantation of a tissue expander) and completed in a second session (delayed-immediate breast reconstruction) between January 2015 and December 2017 at the NIO. The study and the questionnaire was approved by the Institutional Ethical Committee Board and did not infringe the requirements of the Declaration of Helsinki and Tokyo [82].

The diagnosis of breast cancer, additional staging examinations, adjuvant treatments and follow-ups were performed according to the current international guidelines applied at the NIO [72, 76, 83]. The operations were performed by experienced and internationally qualified breast surgeons (having the EBSQ license) and plastic surgeons based on the decisions of the institutional multidisciplinary team.

Questionnaires were distributed to patients the day before breast surgery and were completed voluntarily and anonymously prior to the intervention.

Following questions on age, highest level of education, and marital status, the questionnaire contained eleven structured questions to measure the emotional and mental condition and attitude related to the loss and reconstruction of breast, the expectation of cosmetic outcome, the qualification of the operating surgeon and the patient's demand for the health care system and funding (Table 1).

***Table 1.*** *A structured questionnaire of the survey on oncoplastic surgery care*

| | | | |
|---|---|---|---|
| **1. How much are you disturbed by breast loss and its aesthetic deformity on a scale of 1-10?** | | | |
| 1-no disturbance - 10-terrible disturbance | | | |
| **2. When do you undergo breast reconstruction?** | | | |
| Months or years after tumour removal | | Simultaneously with tumour removal | |
| **3. What you realistically expect from breast reconstruction?** | | | |
| "some kind" of breast | a pretty décolletage in brassiere | more beautiful breast, than before | perfect breasts |
| **4. To what extent can you realistically accept symmetry at the end of breast reconstruction?** | | | |
| My natural breasts were not symmetrical either, so it does not matter if my reconstructed breasts are not the same | Let my reconstructed breasts be roughly the same in a dress or brassiere | Let my reconstructed breasts be pretty much the same naked | Only perfect symmetry is acceptable for me |
| **5. How many surgeries under general anaesthesia would you take maximally to have your breast reconstructed?** | | | |
| Maximum two | Maximum 3 to 4 | Maximum 5 to 6 | Any |
| **6. In your opinion, how many "state-funded" reconstructive procedure is appropriate for an insured patient, known that sources are not endless?** | | | |
| Maximum two | Maximum 3 to 4 | Any | |
| **7. What is your opinion regarding the change of your reconstructed breast over time (by aging)?** | | | |
| Does not need further surgery, because it is a natural process | It is a natural process, that will be an individual aesthetic issue | Even decades later, I consider it reconstructive surgery and not aesthetic surgery | |
| **8. Would you agree to have your breast reconstruction performed by a general surgeon instead of a plastic surgeon?** | | | |
| Yes | | No | |
| **9. In your opinion, who should perform the modern surgical procedures of breast cancer treatment (oncoplastic surgery, breast reconstruction) in Hungary?** | | | |
| General surgeon, as usually in our country | Gynaecologist, as sometimes in our country | Plastic surgeon | Specially trained breast surgeon with the involvement plastic surgeon, if needed |
| **10. In your opinion, how acceptable is it that in Hungary, in the 21st century, only one or two hospitals have specially prepared, modern breast surgical centres / units?** | | | |
| As good as it is now | It's unfortunate, but that's it | It is very unfortunate, but who wants better goes to private care | Unacceptable, modern specialized breast surgery should be provided |
| **11. Do you think that being operated by a breast surgeon has a significant effect on your recovery?** | | | |
| Does not affect | Affects | Strongly affects | One of the most important |

### 3.4. Statistical analysis

For the study of mapping the sentinel lymph nodes in the anatomical subregions of the axilla, our database included all the histopathological characteristics of the primary breast tumours and the types of surgery gained from patients' records, as well as the subregional localisation and metastatic status of the removed SLNs of every patient. STgF and HTgF coverage fields were assessed for 61 node positive patients. The relationships between SLN localisation, breast tumour localisation, histopathological characteristics and radiopharmaceutical injection sites as well as the comparison of the RT coverage fields were statistically analysed using the Fisher's exact and Pearson's chi-square tests.

For the retrospective comparative study of ASM and NSM, the database included the patients' age, BMI, bra cup size, the indication for surgery and operative time. The database also included the pathological TNM stage, grade and hormone receptor status, histological type of the breast tumour and nipple-tumour distance. The type and initiation time of the adjuvant treatments, postoperative complications, follow-up times, oncologic status of the patients, aesthetic results (a 5-point Likert scale) and postoperative patient satisfaction (BREAST-Q) were all assessed. The Mann–Whitney U test was applied for BMI analyses, while all other categorical data were compared using the Fisher's exact and Pearson's chi-square tests. Survival was analysed using the Kaplan-Meier method.

For the survey on the needs of Hungarian breast cancer patients, the database included the answers to the questionnaire and the patients' age, highest level of education and marital status. All the answers were statistically analysed in the context of marital status and educational level applying the Fisher's exact and Pearson's chi-square tests.

P-values less than 0.05 were considered statistically significant. Statistical analysis was performed using the Statistica 12.0 software (StatSoft, Tulsa, OK) or PAST version 1.86b [84].

# 4. RESULTS

## 4.1. Mapping the sentinel lymph nodes in the anatomical axillary subregions: a retrospective cohort study

A total of 933 women were included in the study. The mean age of the patients was 64.1 years (range 19 to 91 years, median: 64 years). Three cases were excluded because the breast tumour was larger than 5 cm according to the postoperative pathologic examination. Another two patients were ruled out due to newly discovered lympho-proliferative disorder affecting the axillary lymph nodes. Another 58 patients were excluded because of an uninterpretable sentinel data sheet or incomplete clinical-histological data. As a result, a total of 870 patients' data was analysed.

The types of surgery and detailed pathologic characteristics of the primary breast tumours are summarised in Table 2 and Table 3.

***Table 2.*** *Types of surgery in the patient population of the SLN subregion mapping analysis*

| **Type of breast surgery** | | |
|---|---|---|
| Mastectomy | 352 | 40.5 |
| Breast conserving surgery | 518 | 59.5 |
| **SLNB** | | |
| SLN-negative patients | 694 | 79.8 |
| SLN-positive patients | 176 | 20.2 |
| Total number of SLNB | 870 | - |
| Total number of removed SLNs | 1397 | - |
| SLNs removed per operation | mean ± SD: 1.6 ± 0.9 | median (range): 1 (1-8) |
| **ALND** | | |
| Total number of ALND | 156 | 17.9 |
| Total number of removed lymph nodes | 2109 | - |
| Lymph nodes removed per ALND | mean ± SD: 14.4 ± 6.3 | median (range): 14 (4-39) |

***Table 3.*** *Tumour-related features in the patient population of the SLN subregion mapping analysis*

| **pT** | **n** | **%** |
|---|---|---|
| pTis | 104 | 11.9 |
| pT1mi | 3 | 0.3 |
| pT1a | 30 | 3.5 |
| PT1b | 92 | 10.6 |
| pT1c | 314 | 36.1 |
| pT2 | 297 | 34.1 |
| pT3 | 30 | 3.5 |
| **Grade (invasive tumours)** | | |
| I | 179 | 23.4 |
| II | 368 | 48.0 |
| III | 219 | 28.6 |
| **Grade (in situ carcinomas)** | | |
| Low | 28 | 26.9 |
| Medium | 50 | 47.8 |
| High | 26 | 25.3 |
| **Receptor status** | | |
| ER + | 755 | 86.8 |
| ER - | 115 | 13.2 |
| PR + | 646 | 74.3 |
| PR - | 224 | 25.7 |
| Her2 – or + | 761 | 87.5 |
| Her2 ++ | 36 | 4.1 |
| Her2 +++ | 73 | 8.4 |
| **Molecular subtype – according to the St.Gallen Consensus [6]** | | |
| Luminal A | 435 | 56.8 |
| Luminal B | 171 | 22.3 |
| Luminal B-Her2+ | 41 | 5.4 |
| Triple negative | 73 | 9.5 |
| Non-luminal-Her2+ | 14 | 1.8 |
| missing data | 32 | 4.2 |
| **Lymphovascular invasion** | | |
| Present | 324 | 42.3 |
| Not present | 442 | 57.7 |
| **Histological type** | | |
| Invasive ductal carcinoma | 634 | 72.9 |
| Invasive lobular carcinoma | 98 | 11.3 |
| Other invasive | 34 | 3.9 |
| DCIS | 75 | 8.6 |
| LCIS | 16 | 1.8 |
| Other in situ | 13 | 1.5 |
| **Palpability** | | |
| Palpable | 487 | 56.0 |
| Not palpable | 383 | 44.0 |
| **Mitotic activity** | | |
| <11 | 516 | 67.4 |
| 11-20 | 149 | 19.4 |
| 20< | 101 | 13.2 |

Regarding the location of the breast cancer, 46.9% (n=408) were in the upper-outer, 15.2% (n=132) in the upper-inner, 10.5% (n=91) in the lower-outer, 7.1% (n=62) in the lower-inner quadrant, and 3.1% (n=27) in the axillary process (tail of Spence); 13.4% (n=117) were central tumours and 3.8% (n=33) were multiplex.

The relationship between the molecular subtype and the location of the breast tumour was also analysed (Table 4). Non-luminal-Her2+ tumours were mainly localised in the upper quadrants (84.6% n=11). Similarly, the triple negative subtype was also likely to appear in the upper-outer quadrant (57.1%; n=40). However, cancers in the lower-inner quadrant were mostly Her2-enriched (17.1%; n=7). A statistically significant heterogeneity was found regarding the location of the tumour and its molecular subtype (p=0.035).

***Table 4.*** *Analysis of the relationship between the molecular subtype and the location of the primary breast tumour*

| Molecular subtype / Breast quadrant | **Luminal A** | | **Luminal B** | | **LumB – Her2+** | | **Non-luminal-Her2+** | | **Triple negative** | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | n | % |
| **Upper outer** | 210 | 48.3 | 73 | 42.7 | 18 | 43.9 | 7 | 50.0 | 40 | 54.8 |
| **Upper inner** | 65 | 14.9 | 39 | 22.8 | 5 | 12.2 | 4 | 28.6 | 9 | 12.3 |
| **Lower outer** | 47 | 10.8 | 20 | 11.7 | 4 | 9.7 | 0 | 0.0 | 9 | 12.3 |
| **Lower inner** | 36 | 8.3 | 13 | 7.6 | 7 | 17.1 | 0 | 0.0 | 1 | 1.4 |
| **Central** | 62 | 14.2 | 17 | 9.9 | 7 | 17.1 | 2 | 14.3 | 6 | 8.2 |
| **Axillary process** | 6 | 1.4 | 4 | 2.4 | 0 | 0.0 | 0 | 0.0 | 5 | 6.9 |
| **Multicentric** | 9 | 2.1 | 5 | 2.9 | 0 | 0.0 | 1 | 7.1 | 3 | 4.1 |

The average number of removed SLNs per operation was 1.6 ± 0.9 and the median was 1 (range 1-8). The SLN positivity rate was 20.2% (n=176).

We also analysed the distribution pattern and metastatic status of the SLN in the subregions of the axilla (Table 5). The most common site of the SLN was the anterior subregion (39.8%; n=346), while the least common was the apical subregion (3.4%; n=30). In contrast, the positivity rate was higher in the apical subregion (30.0%; n=9) than in the anterior subregion (21.1%; n=73). The SLN was present in the lateral subregion in 5.6% (n=48) of the cases. Of these 48 lymph nodes, 11 SLNs were positive (22.9%). In the central and posterior subregions, 53 and 43 SLNs, respectively, were found to be positive out of the 244 (21.7%) and 202 (21.3%) removed lymph nodes, respectively.

In 96.6% (n=840) of the cases, the SLN appeared in the anterior, posterior, lateral or central subregions, corresponding to the Level I and II zones (Table 5).

***Table 5***. *Distribution pattern and metastatic status of the SLN in the anatomical subregions of the axilla*

| Subregion | Site of SLN | Number of positive cases | Positivity rate |
|---|---|---|---|
| **anterior** | 346 (39.8%) | 73 | 21.1% |
| **central** | 244 (28.0%) | 53 | 21.7% |
| **posterior** | 202 (23.2%) | 43 | 21.3% |
| **lateral** | 48 (5.6%) | 11 | 22.9% |
| **apical** | 30 (3.4%) | 9 | 30.0% |

None of the examined characteristics of the primary breast cancer (molecular subtype p=0.360) had significant relationship with the subregional localisation of the SLN.

The tracer for lymphoscintigraphy was injected intratumourally and periareolarly in 40.3% (n=351) and 59.7% (n=519) of the cases, respectively. We used only radiopharmaceutical (80 Mbq 99m Tc labelled nanocolloid) in 90.5% (n=811), Patent blue dye in 4.6% (n=40) and both in 4.9% (n=43) of the cases.

We divided our study population into two groups based on the injection site and analysed the relationship between the location of the SLN and location of the primary breast tumour in each group separately. In case of intratumoural application, we found significant relationship between the situation of the breast cancer and the subregional location of the SLN (p=0.016); the results are summarized in Table 6.

According to our data, tumours in the upper-outer quadrant were most frequently drained to the anterior subregion (34.2%). The posterior subregion received lymph mainly from the upper-outer quadrant (31.6%) and the axillary process (36.3%), whereas the inner and central quadrants had very similar drainage patterns with a tendency to give efferent lymphatics more often to the anterior (53.9%, 69.6% and 54.5%) and central (28.8%, 26.1% and 22.7%)

lymph nodes. The central lymph nodes received lymphatic drainage equally from the different quadrants of the breast. (Table 6.)

***Table 6.*** *Analysis of the relationship between the situation of the primary breast tumour and the anatomical subregional localisation of the SLN if intratumoural injections were used (an overall heterogeneity between the groups was found, p=0.016)*

| Quadrant<br>Subregion | **Upper outer** | **Lower outer** | **Upper inner** | **Lower inner** | **Central** | **Axillary process** | **Multicentric** |
|---|---|---|---|---|---|---|---|
| **anterior** | 65 (34.2%) | 13 (41.9%) | 28 (53.9%) | 16 (69.6%) | 12 (54.5%) | 5 (45.5%) | 6 (50.0%) |
| **central** | 55 (28.9%) | 8 (25.8%) | 15 (28.8%) | 6 (26.1%) | 5 (22.7%) | 1 (9.1%) | 1 (8.3%) |
| **posterior** | 60 (31.6%) | 7 (22.6%) | 6 (11.5%) | 1 (4.3%) | 2 (9.1%) | 4 (36.3%) | 4 (33.4%) |
| **lateral** | 6 (3.2%) | 3 (9.7%) | 3 (5.8%) | 0 (0.0%) | 1 (4.6%) | 1 (9.1%) | 1 (8.3%) |
| **apical** | 4 (2.1%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (9.1%) | 0 (0.0%) | 0 (0.0%) |

In 548 (63.0%) patients, the SLN was located within the anterior or posterior subregions (Level I). 116 of them (21.2%) had axillary lymph node metastasis, out of whom 83 (15.1%) were treated with RT in our Institute. The planning CT series of 61 cases were subjected to additional HTgF simulation in the RT planning system. The coverage of axillary volumes by both kinds of tangential fields is given in Table 7. There was a significant difference between the two plans regarding the coverage of the Level I axillary region. HTgF increased the rate of cases with level I axillary region complete coverage from 0% to 65.6% (40 of 61; $p<0.0001$). Concerning the Level II volume, the rate of complete coverage with STgF or HTgF was 0% and 6.6% (4 of 61), respectively (p=0.1198). The rate of "out of field" cases was very high with STgF, 72.1% (44 of 61), but "out of field" cases were not observed with HTgF irradiation ($p<0.0001$). The coverage of the Level III volume was very poor (rate of "out of field" with STgF or HTgF: 91.8% and 9.8%, $p<0.0001$). The illustration how the coverage was evaluated in all the cases is given in Figure 2.

***Table 7.*** *Coverage of the axillary volumes by standard vs. high tangential fields (n=61)*

| % (No.) | | STgF | HTgF | p-value |
|---|---|---|---|---|
| **Level I** | Complete | 0 (0) | 65.6 (40) | < 0.0001 |
| | Partial | 100.0 (61) | 34.4 (21) | - |
| | Out of field | 0 (0) | 0 (0) | - |
| **Level II** | Complete | 0 (0) | 6.6 (4) | 0.1198 |
| | Partial | 27.9 (17) | 93.4 (57) | - |
| | Out of field | 72.1 (44) | 0 (0) | < 0.0001 |
| **Level III** | Complete | 0 (0) | 0 (0) | - |
| | Partial | 8.2 (5) | 90.2 (55) | - |
| | Out of field | 91.8 (56) | 9.8 (6) | < 0.0001 |

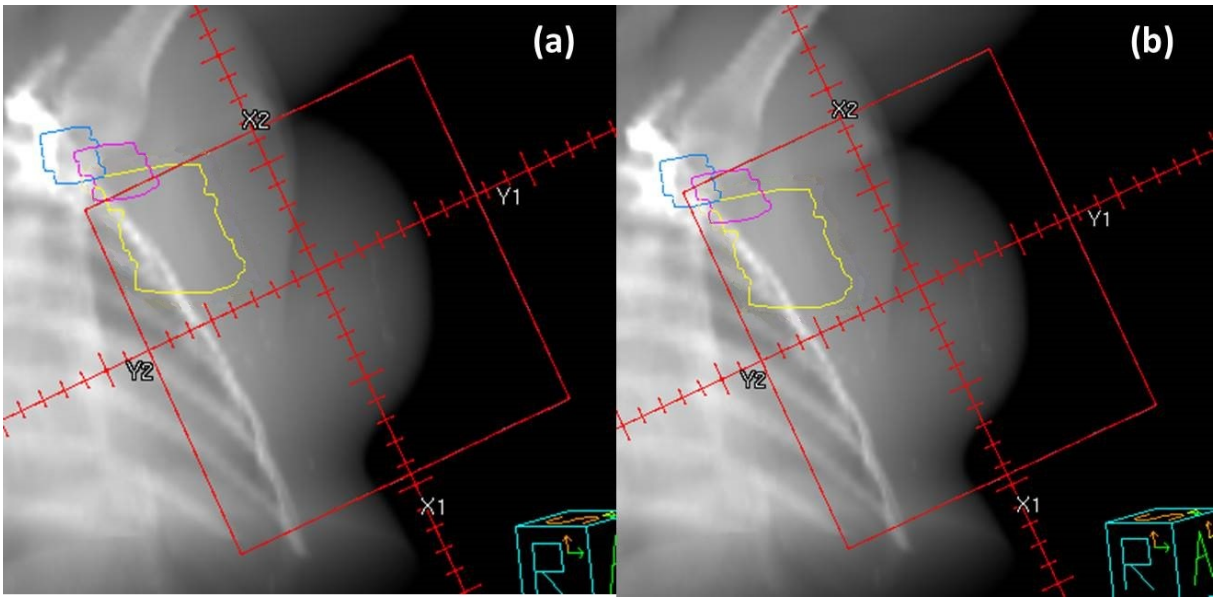



***Figure 2. Beam's eye views using standard (a) and high tangential fields (b)***

*(a) Standard tangential field (red square) and axillary nodal levels. Yellow line = Level I clinical target volume; note the partial coverage. Purple line = Level II clinical target volume; note that coverage is minimal. Blue line = Level III clinical target volume; no coverage, out of field*

*(b) High tangential field (red square) and axillary nodal subvolumes. Yellow line = Level I clinical target volume; complete coverage. Purple line = Level II clinical target volume; partial coverage. Blue line = Level III clinical target volume; minimal coverage*

We also analysed and compared the subregional localisation and positivity rate of SLNs of our study with the subregional localisation and positivity rates of ARM lymph nodes described in the studies of Ikeda et al. and Bedrosian et al. [69, 70] (Table 8). According to Ikeda et al., the most common site of the ARM lymph nodes was the lateral subregion in both the groups with and without SLNB (59.5%; n=25 – with SLNB group; 62.9%; n=22 – without SLNB group). Bedrosian et al. found the ARM nodes in the vast majority of the cases (86.6%; n=13) in the lateral and apical subregions. Both studies found positive lymph nodes only in these mostly favoured lateral and apical subregions: Ikeda et al. reported one lymph node each in the above mentioned subregions and six metastatic lymph nodes in the lateral subregion in the with and without SLNB groups, respectively, while Bedrosian et al. found an overall metastatic rate of 15.4% (n=2) in these subregions.

Summarizing the results in the three studies including ours, the least common SLN subregions (i.e. the lateral and apical subregions) seem the most common sites for the ARM lymph nodes. Regarding positivity, both studies selected from the literature found metastatic lymph nodes exclusively in the lateral and apical subregions, where we detected the highest positivity rates (22.9% and 30.0%, respectively).

**Table 8.** *Comparison of the subregional distribution and positivity rate of removed SLNs (data from the present study) with the subregional distribution and positivity rate in two studies that applied the ARM technique (data from Ikeda et al. and Bedrosian et al. [69, 70])*

| **Study** \ **Axillary subregion** | | | **anterior** | **central** | **posterior** | **lateral** | **apical** |
|---|---|---|---|---|---|---|---|
| **Present study** | Removed SLN n (number of cases) | *870* | 346 | 244 | 202 | 48 | 30 |
| | % | | 39.8% | 28.0% | 23.2% | 5.6% | 3.4% |
| | Positive SLN n (number of cases) | *189* | 73 | 53 | 43 | 11 | 9 |
| | Positivity rate | | 21.1% | 21.7% | 21.3% | 22.9% | 30.0% |
| | | | | | | | |
| **Ikeda et al. [69]** | | | | | | | |
| ***without SLNB group*** | Removed ARM nodes n (number of lymph nodes) | *35* | 2 | 0 | 9 | 22 | 2 |
| | % | | 5.7% | 0.0% | 25.7% | 62.9% | 5.7% |
| | Positive ARM nodes n (number of lymph nodes) | *7* | 0 | 0 | 1 | 6 | 0 |
| | | | | | | | |
| | | | | | | | |
| ***with SLNB group*** | Removed ARM nodes n (number of lymph nodes) | *42* | 1 | 1 | 8 | 25 | 7 |
| | % | | 2.4% | 2.4% | 19.0% | 59.5% | 16.7% |
| | Positive ARM nodes n (number of lymph nodes) | *2* | 0 | 0 | 0 | 1 | 1 |
| | | | | | | | |
| **Bedrosian et al. [70]** | Removed ARM nodes n (number of cases) | *15* | 0 | 1 | 1 | 13 | |
| | % | | 0.0% | 6.7% | 6.7% | 86.6% | |
| | Positive ARM nodes n (number of lymph nodes) | *2* | 0 | 0 | 0 | 2 | |
| | Positivity rate | | 0.0% | 0.0% | 0.0% | 15.4% | |

## 4.2. Comparison of the oncological and cosmetic outcome after areola-sparing mastectomy versus nipple-sparing mastectomy: analysis of a prospectively collected database

Out of the 251 selected cases (ASM: n=147; NSM: n=104), eight patients (ASM: n=5; NSM: n=3) were excluded from the study due to loss of follow-up or incomplete clinicopathological data; eleven women (ASM: n=6; NSM: n=5) from both groups were excluded because of previous breast surgery, and five patients (ASM: n=2; NSM: n=3) were omitted from further evaluation because of positive nipple-areola margins requiring NAC resection. As a result, a total of 134 and 93 patients were included having had ASM and NSM, respectively.

Detailed patient and tumour characteristics are summarized in Table 9 and Table 10, respectively.

***Table 9**. Patient characteristics of the ASM and NSM groups.*

| | ASM | NSM | p |
|---|---|---|---|
| **Number of patients** | **134** | **93** | |
| **Age (years)** | | | |
| median (min. – max.) | 41 (26 – 64) | 40 (26 – 70) | 0.365 |
| **BMI (kg/m$^2$)** | | | |
| mean ± SD | 21.6 ± 3.1 | 21.2 ± 3.4 | 0.285 |
| **Cup size** | **n (%)** | **n (%)** | |
| A | 23 (17.2) | 7 (7.5) | 0.003 |
| B | 75 (55.9) | 62 (66.7) | |
| C | 25 (18.7) | 24 (25.8) | |
| D | 11 (8.2) | 0 (0.0) | |
| **Indication** | **n (%)** | **n (%)** | |
| therapeutic | 89 (66.4) | 85 (91.4) | $1.2 \times 10^{-5}$ |
| prophylactic | 45 (33.6) | 8 (8.6) | |
| **Operative duration (minutes)** | | | |
| median (min. – max.) | 80 (50 – 150) | 76 (43 – 120) | 0.431 |
| **Neoadjuvant** | **n (%)** | **n (%)** | |
| chemotherapy | 20 (22.5) | 9 (10.6) | 0.244 |
| **Initiation of adjuvant therapy (weeks)** | | | |
| median (min. – max.) | 7.4 (4.6 – 11.9) | 8.1 (4.1 – 12.0) | 0.124 |
| **Adjuvant** | **n (%)** | **n (%)** | |
| Chemotherapy/Biological therapy<br>yes<br>no<br>not reported | <br>34 (25.4)<br>59 (44.0)<br>41 (30.6) | <br>19 (20.4)<br>61 (65.6)<br>13 (14.0) | 0.068 |
| Radiotherapy<br>yes<br>no<br>not reported | <br>32 (23.9)<br>63 (47.0)<br>39 (29.1) | <br>27 (29.0)<br>53 (57.0)<br>13 (14.0) | 0.993 |
| Endocrine therapy<br>yes<br>no<br>not reported | <br>46 (34.3)<br>45 (33.6)<br>43 (32.1) | <br>61 (65.6)<br>21 (22.6)<br>11 (11.8) | 0.001 |

There was no significant difference in duration of the surgical procedures between the two groups (p=0.431). The median time of ASM was 80 minutes (range: 50-150 minutes), while the NSM operations lasted for 76 minutes (range: 43-120 minutes) on average (Table 9).

***Table 10.*** *Characteristics of the primary breast tumours and regional lymph nodes in the ASM and NSM groups*

| | **ASM** | **NSM** | **p** |
|---|---|---|---|
| **Pathological TNM** | **n= 89 (therapeutic)** | **n=85 (therapeutic)** | |
| **pT** | **n (%)** | **n (%)** | 0.026 |
| pTis | 5 (5.6) | 6 (7.1) | |
| pT1 | 37 (41.6) | 33 (38.8) | |
| pT2 | 23 (25.8) | 19 (22.3) | |
| pT3 | 4 (4.5) | 18 (21.1) | |
| **pN** | **n (%)** | **n (%)** | 0.900 |
| pN0 | 47 (52.8) | 53 (62.3) | |
| pN1 | 18 (20.2) | 19 (22.3) | |
| pN2 | 3 (3.4) | 2 (2.4) | |
| pN3 | 1 (1.1) | 2 (2.4) | |
| **ypT** | **n (%)** | **n (%)** | |
| ypT0 | 5 (5.6) | 4 (4.7) | |
| ypT1 | 9 (10.2) | 2 (2.4) | |
| ypN2 | 4 (4.5) | 2 (2.4) | |
| ypN3 | 2 (2.2) | 1 (1.2) | |
| **ypN** | **n (%)** | **n (%)** | |
| ypN0 | 11 (12.4) | 6 (7.0) | |
| ypN1 | 7 (7.9) | 2 (2.4) | |
| ypN2 | 1 (1.1) | 0 (0) | |
| ypN3 | 1 (1.1) | 1 (1.2) | |

| | | | |
|---|---|---|---|
| **Grade (invasive breast cancer)** | | | 0.435 |
| I | 16 (18.0) | 11 (12.9) | |
| II | 34 (38.2) | 40 (47.1) | |
| III | 39 (43.8) | 34 (40.0) | |
| **Receptor status** | | | |
| ER<br>positive<br>negative | <br>60 (67.4)<br>29 (32.6) | <br>59 (69.4)<br>26 (30.6) | 0.004 |
| PR<br>positive<br>negative | <br>56 (62.9)<br>33 (37.1) | <br>56 (65.9)<br>29 (34.1) | 0.008 |
| Her2<br>positive<br>negative | <br>20 (22.5)<br>69 (77.5) | <br>15 (17.6)<br>70 (82.4) | 0.951 |
| **Histological type** | | | |
| Invasive ductal carcinoma | 74 (83.2) | 60 (70.6) | 0.349 |
| Invasive lobular carcinoma | 5 (5.6) | 11 (12.9) | |
| Other invasive | 4 (4.5) | 6 (7.1) | |
| DCIS | 5 (5.6) | 6 (7.1) | |
| LCIS | 1 (1.1) | 2 (2.3) | |
| **Nipple – tumour distance (cm)** | | | |
| median (min. – max.) | 2.7 (0.6 – 7.0) | 3.1 (0.7 – 7.0) | 0.497 |
| **Follow-up: 45 months (range: 20.1-82.7)** | | | |
| local recurrence | 3 (3.4) | 2 (2.4) | |
| distant metastatic disease | 5 (5.6) | 1 (1.2) | |
| distant metastases-related death | 2 (2.2) | 1 (1.2) | |
| **Axillary surgery** | | | 0.656 |
| Sentinel lymph node biopsy | 64 (71.9) | 62 (72.9) | |
| Axillary lymph node dissection | 23 (25.9) | 19 (22.4) | |
| No axillary surgery | 2 (2.2) | 0 | |
| Not reported | 0 | 4 (4.7) | |

The recorded early postoperative complications in the two groups are summarized in Table 11. In total, the overall complication rate was 13.4% (n=18) for ASM and 12.9% (n=12) for NSM. The majority of complications were Grade I, including partial skin/NAC necrosis, seroma, infection or wound dehiscence, which healed spontaneously in both groups.

***Table 11.*** *Early postoperative complications based on the Clavien-Dindo classification in the ASM and NSM groups*

| | **ASM** | **NSM** | **p** |
|---|---|---|---|
| | **134 n (%)** | **93 n (%)** | |
| **Grade I** | **12 (9.0)** | **9 (9.7)** | |
| infection | 4 (3.0) | 3 (3.2) | |
| seroma | 2 (1.5) | 2 (2.1) | |
| partial skin / NAC necrosis | 3 (2.2) | 2 (2.1) | |
| rippling | 2 (1.5) | 1 (1.1) | |
| wound dehiscence | 1 (0.7) | 1 (1.1) | |
| **Grade II** | **3 (2.2)** | **1 (1.1)** | |
| infection | 2 (1.5) | 0 (0.0) | |
| chronic seroma | 1 (0.7) | 1 (1.1) | |
| **Grade III** | **3 (2.2)** | **2 (2.1)** | |
| haematoma | 2 (1.5) | 1 (1.1) | |
| implant loss | 1 (0.7) | 1 (1.1) | |
| **Overall** | **18 (13.4)** | **12 (12.9)** | **0.908** |

The median follow-up period was 45.0 months (range: 20.1-82.7). During the follow-up period three distant metastases-related deaths were recorded (ASM:2.2%, n=2; NSM:1.2%, n=1), five local recurrences were observed in preserved areola or the nipple (ASM:3.4%, n=3; NSM:2.4%, n=2), while overall six distant metastatic diseases were recorded (ASM:5.6%, n=5; NSM:1.2%, n=1). There was no significant difference in DFS (p=0.762) and OS (p=0.601) between the two groups (Figures 3 and 4).

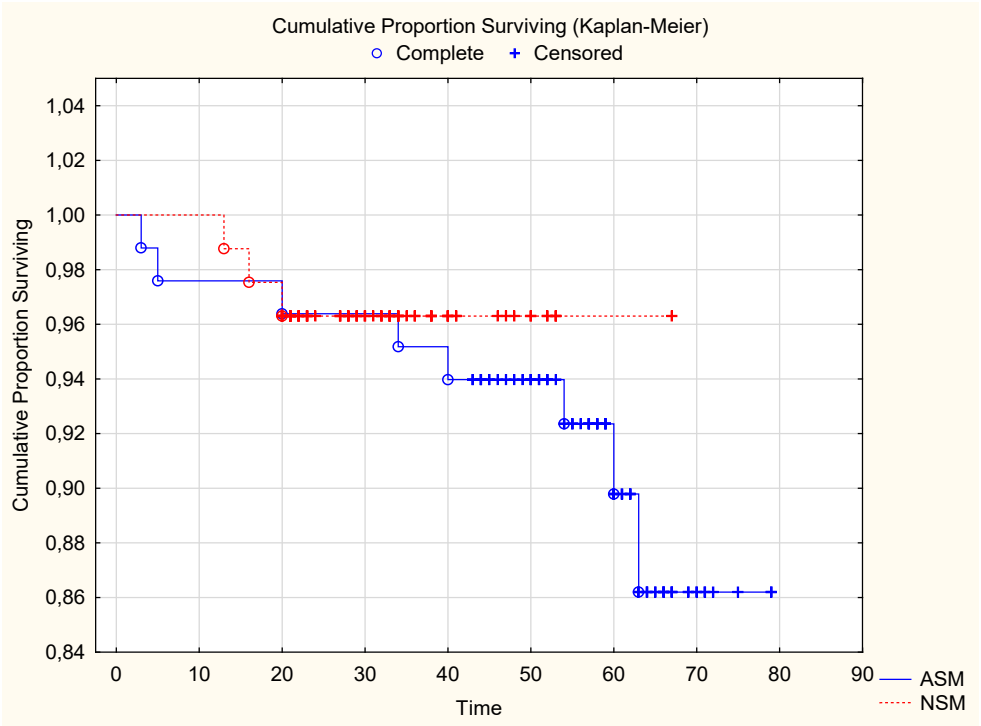



***Figure 3.*** *Kaplan-Meier curve showing the disease-free survival (DFS) of the patients in the ASM and NSM groups*

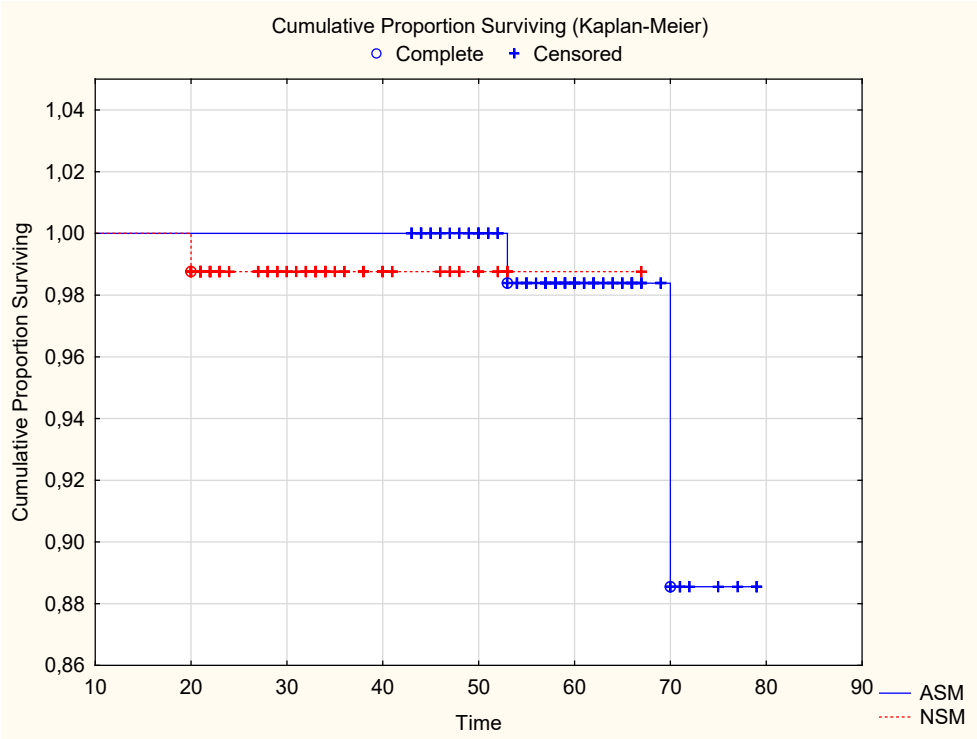



***Figure 4.*** *Kaplan-Meier curve* showing the overall survival (OS) of the patients in the ASM and NSM *groups*

The median time until adjuvant treatment initiation was 7.4 weeks (range: 4.6 – 11.9) for ASM and 8.1 weeks (range: 4.1 – 12.0) for the NSM group.

Both groups had the same objective aesthetic outcome as measured by a 5-point Likert scale system. The majority of breast surgeons agreed with the statement that "This patient had an excellent aesthetic outcome", with a median score of 4.1 (range: 2-5) in the ASM group and 4.3 (range: 2-5) in the NSM group.

The results of the corresponding BREAST-Q domains showed no significant difference between ASM and NSM patients (Table 12). The highest mean scores were observed for "physical well-being", while the median "satisfaction with breasts" and "psychosocial well-being" scores were slightly lower. The lowest mean scores were detected for "sexual well-being".

***Table 12.*** *Results of the BREAST-Q postoperative questionnaire*

| | **ASM** mean ± SD | **NSM** mean ± SD | **p** |
|---|---|---|---|
| **BREAST-Q postop. 1 -** Satisfaction with the breasts | 64.9 ± 21.2 | 67.8 ± 17.2 | 0.691 |
| **BREAST-Q postop. 2 -** Psychosocial well-being | 68.4 ± 18.4 | 72.4 ± 17.5 | 0.123 |
| **BREAST-Q postop. 3 -** Physical well-being | 80.0 ± 14.0 | 76.5 ± 15.5 | 0.232 |
| **BREAST-Q postop. 4 -** Sexual well-being | 59.1 ± 18.3 | 54.0 ± 20.9 | 0.252 |

### 4.3. A survey on the needs of Hungarian breast cancer patients regarding modern oncoplastic breast surgery

The median age of the women was 47 years (min.-max.: 26-73). Out of the 500 patients enrolled, 52% (n = 260) of had a higher education degree and the majority (59%; n = 294) were married. Characteristics of the study population are summarized in Table 13 and the answers received for the questionnaire are shown in Table 14.

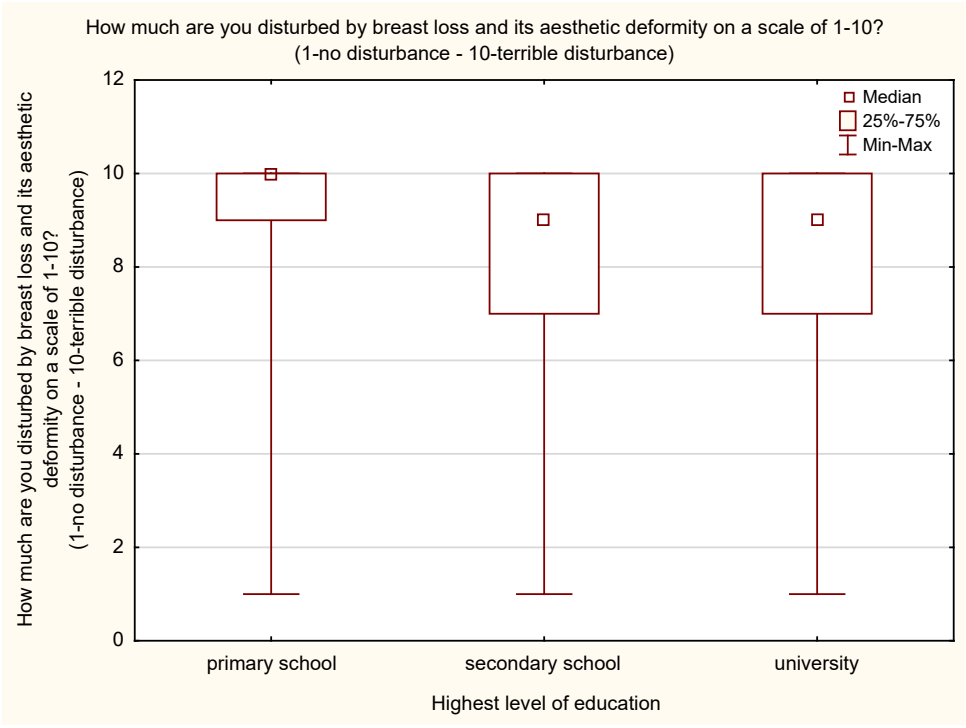
***Table 13.*** *Characteristics of the surveyed population*

| **Age** | | | | |
|---|---|---|---|---|
| n | mean | median | minimum | maximum |
| 485 | 48 | 47 | 26 | 73 |
| missing data = 15 (3%) | | | | |
| **Highest level of education** | | | | |
| primary school | | secondary school | | university |
| 7 (1%) | | 218 (44%) | | 260 (52%) |
| missing data = 15 (3%) | | | | |
| **Marital status** | | | | |
| single | | married | divorced | widow |
| 52 (10%) | | 294 (59%) | 119 (24%) | 20 (4%) |
| missing data = 15 (3%) | | | | |

Understandably, breast loss significantly embarrassed the respondents, with answers averaging 8 ± 3 (mean ± SD) on a scale of 1 to 10; and there was no difference between the responses in terms of education or marital status (Figure 5).

Immediate breast reconstruction was performed in almost two-thirds of cases (61%; n = 307), while in 167 patients (33%), breast reconstruction was delayed-immediate; in the latter case the survey was done months or years after the tumour removal, before the final session of the breast reconstruction.

Based on the answers, 39% (n = 194) of the interviewed women would have been satisfied with breasts resulting in a pretty décolletage in brassiere, however, 28% (n = 140) would have liked to have more beautiful breasts than the original ones were, and 20% (n = 99) wanted perfect breasts at the end of the reconstruction process. In terms of expectations, there was a significant relationship with education: higher education was associated with higher expectations ($p < 0.05$). Patients had a firm opinion regarding symmetry, there was no difference in either marital status or education: 70% (n = 348) of women would have liked to have roughly identical breasts naked at the end of the reconstruction process.



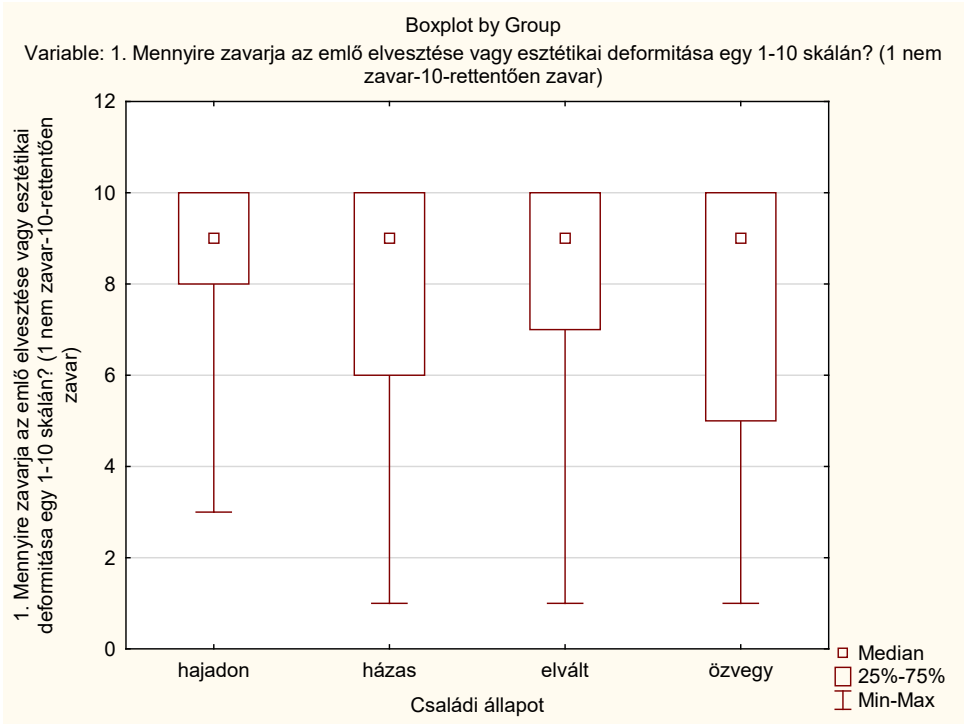




***Figure 5.*** *Analysis of the answers to the question "How much are you disturbed by breast loss and its aesthetic deformity on a scale of 1-10?" by education and marital status (boxplot)*

For an optimal aesthetic outcome, 43% (n = 217) of the survey participants would have undertaken a maximum of two and 37% (n = 184) up to three or four operations.

The opinions varied on how funding should be provided: according to 44% (n = 220) of the patients, the health insurance company should cover a maximum of three to four operations, 21% (n = 107) thought that a maximum of two surgeries should be funded, while almost a third of the study population (31%; n = 157) had the opinion that no matter how many interventions were needed, all should be paid by the NEAK. Women with a high school education were less likely to justify more surgeries by state funding, while those with a university degree favoured that ($p < 0.05$).

Fifty-five percent of the patients (n = 275) believed that age-related changes in the reconstructed breasts are just aesthetic plastic surgery issues, however, 28% (n = 139) shared the opinion that in the future, even after decades from the primary operation, the management of such problems will belong to the oncologic reconstructive surgery, and would not be an independent aesthetic surgical procedure only.

Patients had a clear view on the surgeon performing the procedure: 90% of them (n = 448) would have entrusted the reconstruction to a plastic surgeon, moreover, 86% (n = 430) said that modern surgical care for breasts cancer should be performed by specially trained breast surgeons, instead of general surgeons, as currently happens.

The vast majority of respondents (79%; n = 394) did not consider it acceptable that there are currently only one or two certified breast surgical centres in Hungary, whilst 10% (n = 51) accepted the current situation and a further 9% (n = 46) believed that it is necessary to turn to private care for better care.

Almost all of the surveyed women (96%; n = 481) believed that the recovery is significantly influenced by whether a breast surgeon performs the operation or not. Furthermore, 63% (n = 316) thought that this is one of the most important factors in regaining their health.

***Table 14.*** *The questionnaire of the survey on oncoplastic surgery care and the answers received*

| **1. How much are you disturbed by breast loss and its aesthetic deformity on a scale of 1-10? (1-no disturbance - 10-terrible disturbance)** | | | |
|---|---|---|---|
| n | mean | median | standard deviation (SD) |
| 495 | 8 | 9 | 3 |
| missing data = 5 (1%) | | | |
| **2. When do you undergo breast reconstruction?** | | | |
| Months or years after tumour removal | | Simultaneously with tumour removal | |
| 167 (33%) | | 307 (61%) | |
| missing data = 26 (5%) | | | |
| **3. What you realistically expect from breast reconstruction?** | | | |
| "some kind" of breast | a pretty décolletage in brassiere | more beautiful breast, than before | perfect breasts |
| 46 (9%) | 194 (39%) | 140 (28%) | 99 (20%) |
| missing data = 21 (4%) | | | |
| **4. To what extent can you realistically accept symmetry at the end of breast reconstruction?** | | | |
| My natural breasts were not symmetrical either, so it does not matter if my reconstructed breasts are not the same | Let my reconstructed breasts be roughly the same in a dress or brassiere | Let my reconstructed breasts be pretty much the same naked | Only perfect symmetry is acceptable for me |
| 12 (2%) | 105 (21%) | 348 (70%) | 32 (6%) |
| missing data = 3 (1%) | | | |
| **5. How many surgeries under general anaesthesia would you take maximally to have your breast reconstructed?** | | | |
| Maximum two | Maximum 3 to 4 | Maximum 5 to 6 | Any |
| 217 (43%) | 184 (37%) | 25 (5%) | 67 (13%) |
| missing data = 7 (1%) | | | |
| **6. In your opinion, how many "state-funded" reconstructive procedure is appropriate for an insured patient, known that sources are not endless?** | | | |
| Maximum two | Maximum 3 to 4 | Any | |
| 107 (21%) | 220 (44%) | 157 (31%) | |
| missing data = 16 (3%) | | | |

| **7. What is your opinion regarding the change of your reconstructed breast over time (by aging)?** | | |
|---|---|---|
| Does not need further surgery, because it is a natural process | It is a natural process, that will be an individual aesthetic issue | Even decades later, I consider it reconstructive surgery and not aesthetic surgery |
| 71 (14%) | 275 (55%) | 139 (28%) |
| missing data = 15 (3%) | | |

| **8. Would you agree to have your breast reconstruction performed by a general surgeon instead of a plastic surgeon?** | |
|---|---|
| Yes | No |
| 40 (8%) | 448 (90%) |
| missing data = 12 (2%) | |

| **9. In your opinion, who should perform the modern surgical procedures of breast cancer treatment (oncoplastic surgery, breast reconstruction) in Hungary?** | | | |
|---|---|---|---|
| General surgeon, as usually in our country | Gynaecologist, as sometimes in our country | Plastic surgeon | Specially trained breast surgeon with the involvement plastic surgeon, if needed |
| 5 (1%) | 3 (1%) | 54 (11%) | 430 (86%) |
| missing data = 8 (2%) | | | |

| **10. In your opinion, how acceptable is it that in Hungary, in the 21st century, only one or two hospitals have specially prepared, modern breast surgical centres / units?** | | | |
|---|---|---|---|
| As good as it is now | It's unfortunate, but that's it | It is very unfortunate, but who wants better goes to private care | Unacceptable, modern specialized breast surgery should be provided |
| 2 (1%) | 51 (10%) | 46 (9%) | 394 (79%) |
| missing data = 7 (1%) | | | |

| **11. Do you think that being operated by a breast surgeon has a significant effect on your recovery?** | | | |
|---|---|---|---|
| Does not affect | Affects | Strongly affects | One of the most important |
| 14 (3%) | 54 (11%) | 111 (22%) | 316 (63%) |
| missing data = 5 (1%) | | | |

## 5. DISCUSSION

In this thesis, we investigated a few currently interesting issues related to modern oncoplastic breast cancer surgery, namely: 1. the location of the sentinel lymph nodes in the anatomical subregions of the axilla and its significance relating recently emerging treatment options, 2. the experiences with ASM and NSM at the NIO 3. the needs and attitude of Hungarian breast cancer patients towards oncoplastic surgical care based on a representative cohort analysis.

### 5.1. The location of the SLNs in the anatomical axillary subregions: the importance of the careful implementation of the RT or ARM techniques

Nowadays, due to the early detection, the number of early-stage breast cancer requiring treatment is increasing. Around three-quarters of these patients have clinically negative axilla (cN0), in which cases SLNB is performed instead of ALND [85]. SLN has a metastatic involvement in 20-30% [86, 87]. Our SLN positivity rate was 20.2% (n=176). In most of these cases ALND is omitted and axillary RT is applied. In case of SLN positivity (pN1(sn)), the 4$^{th}$ Hungarian Breast Cancer Consensus Conference recommends the irradiation of all four axillary levels in most cases if the ACOSOG Z0011 criteria are fulfilled and ALND is omitted; Level I-II irradiation is sufficient in low-risk patients (favourable histology, pT1, unifocal tumour, only one of several sentinel lymph nodes affected, macrometastasis size <7 mm, effective systemic therapy, the patient is not young) [88]. Our results show that the coverage of the axillary subvolumes with conventional WBI or thoracic RT fields is not sufficient. Moreover, in some cases due to the rare location of the SLN, even the axillary subregion of SLN was not or wouldn't have been covered by the conventional tangential fields.

There are several studies concerning the coverage of axillary lymph nodes during whole breast tangential field irradiation. Reed et al. [89] reported that using STgFs, no patient received complete coverage of the axillary Level I–II lymph node volumes. They concluded that definitive irradiation of the Level I and II axillary lymph node regions required significant modification of the STgFs. Krasin et al. [90] showed that the use of STgFs does not therapeutically treat the regional lymph nodes. In their series, only 1 out of 25 patients had adequate coverage of the Level I region, and no patient had adequate coverage of Level II.

Reznik et al. [91] observed that adequate coverage of Level I, defined as 95% of the volume received 95% of the dose, was not achieved in any of the patients using usual tangent fields nor in 6 patients (6 of 35) using high tangents. In a study by Orecchia et al. [92], the Level I nodes were included partially only in the STgFs, and the mean dose was only 48.7% of the prescribed dose. Our study was performed to address the issue of axillary volume coverage according to tangential field size. We showed that no patient had complete coverage of the Level I or Level II region with STgFs, and in 72.1% of the patients, the Level II region was completely out of field. Using HTgFs, 65.6% of the patients had complete coverage of the Level I regions and the complete coverage rate was only 6.6% for the Level II region. The coverage of the Level III region was very poor both with STgFs (rate of out of field: 91.8%) and HTgFs (rate of out of field: 9.8%).

Our results are consistent with the earlier studies that showed that STgFs do not adequately cover the axillary volumes. With modern techniques, the adequate coverage of the axillary volumes depends on the cranial field edge. Ohashi et al. [93] used 3D-CRT with a field-in-field technique, nevertheless, about half of the humeral head was inside the volume. With this technique, even the dose to the Level III region was appropriate (V90 was 82.8%). In a study by Nagar et al. [94], when the tangential fields were modified to include the Level I and II volumes, the mean doses (STgF vs. modified HTgF) increased from 35 Gy to 51 Gy and 11 Gy to 50 Gy, respectively. In patients studied by Belkacemi et al. [95], STgFs were defined as the cranial border being set at 2 cm below the humeral head, while the HTgFs as a superior border being placed at the inferior edge of the humeral head. The mean doses delivered to Level I with STgFs versus HTgFs were 20 Gy and 33 Gy, respectively ($p<0.0001$). We analysed the implementation of classical HTgFs by collecting the beams' eye views; the coverage of the Level I region was limited (complete coverage rate 65.6%). Simply extending the fields, a significant increase of the lung doses occurred. Alco et al. [96] suggested shaping the tangential fields with multi-leaf collimators according to the axillary level volumes to ensure complete coverage, but the inclusion of the axillary regions in the target volume increased the irradiated lung volume. So, the mean lung doses using simple HTgFs or fields shaped with multi-leaf collimators were 6.5 and 9.6 Gy, respectively ($p=0.0001$). In summary, adequate coverage of the axilla including the Levels I, II and III should be defined (delineated) based on anatomical structures as all the guidelines suggest; STgFs provide limited coverage of the axilla, and

although HTgFs may provide complete coverage of Level I volume in some patients, this is not a rule.

The importance of the irradiation of the SNLB area is yet unknown, however, it seems rational to include that in continuum with the axillary nodal regions in SLN positive cases. This is the explanation why some groups and the Hungarian guidelines suggest the clip-marking of the SNLB region [88, 97]. In our study, in 9 (1.0%) of the positive SLN cases the affected nodes were related to the apical and 11 (1.3%) of the metastatic lymph node cases were related to the lateral subregions. In total, in 20 patients with positive lymph nodes (2.3% of all cases), the SLNB region would have been left untreated if STgFs were applied to treat the axilla.

In our view, for the proper treatment of the axilla, an additional axillary and supraclavicular RT field is needed. Actually this solution was applied in the Hungarian OTOASOR prospective randomised clinical trial with axillary and supraclavicular field irradiation in the case of a metastatic SLN without ALND [98].

Another yet in routine practice unaccepted technique is the ARM method invented with the aim of reducing the risk of lymphoedema by preserving the lymph nodes draining the ipsilateral upper extremity. Applying this intervention blue dye (isosulfan blue, patent blue or methylene blue), 99m Tc-labelled nanocolloid or indocyanine green is injected subcutaneously in the inner upper part of the ipsilateral arm. During the operation (SLNB or ALND) the stained lymphatic vessels and lymph nodes are identified with naked eye, a gamma probe or a near-infrared fluorescence imaging system and are preserved to prevent postoperative lymphedema [99]. The subregional localisation of the ARM nodes has not yet been deeply investigated or clearly identified, but it seems obvious that majority of the lymphatics draining the upper limb traverses deep in the axilla [30]. This was also confirmed by Ikeda et al. [69] and Bedrosian et al. [70], who found the ARM nodes in zones that correspond the most to the lateral, apical and posterior axillary subregions. Moreover, both studies reported positive ARM nodes only in the lateral and apical subregions, where our results showed the highest SLN positivity rates (22.9% and 30.0%, respectively).

In our study, 280 (32.2%) SLNs were found within one of these subregions, and 22.5% (n=63) of them were positive. This means that 7.2% of all our cases had at least one positive lymph node in the expected ARM lymph node regions. However, we are aware of the fact that

based on the comparison of the studies with our results, considering the relatively small number of cases and the heterogeneity between the study populations and methods, no firm conclusion can be drawn,

In fact, the ARM technique has been invented for the purposes of ALND exclusively. Nevertheless, our results should raise attention that by omitting the SLNB but applying the ARM technique critical risks of leaving behind metastatic lymph nodes and understaging and undertreating the case may manifest due to the high rate of posterior subregional SLN drainage (23.2% n=202) and SLN positivity (21.3%). Our results support the scepticism about the oncological safety of the ARM technique; we believe that proper indications, improved patient selection criteria and further investigations are needed for the safe application of the ARM technique [99].

### 5.2. Oncological and cosmetic outcome after areola-sparing mastectomy and nipple-sparing mastectomy

In recent years, in oncoplastic surgery centres NSM has become the primary mastectomy technique for prophylactic and therapeutic breast cancer surgical treatment [13]. Several reviews have been published regarding its indications, oncological safety and aesthetic outcomes [40-42]. Tuosimis et al. summarizing the results of three studies with a total of 838 patients, described the ideal candidate for NSM as a patient with breast sizes of cup A or cup B, the absence of ptosis and a BMI < 30 kg/m$^2$. Regarding their conclusions, the only absolute contraindications were nipple involvement and inflammatory breast cancer [42]. Mallon et al. focused on oncological safety and reported an overall nipple recurrence rate of 0.9% and an overall skin flap recurrence rate of 4.2% [41]. They also examined the complication of nipple necrosis. According to their data, full-thickness necrosis was 2.9%, while partial-thickness nipple necrosis was present in 6.3% of the cases [41]. Headon et al. also assessed the complications by a pooled analysis of 12.358 patients from studies published between 1970 and 2015. They found that the overall complication rate was 22.3% and the nipple necrosis rate was 5.9%. Reviewing 73 studies, Headon et al. reported a pooled locoregional recurrence rate of 2.39% [100]. Regarding aesthetic results, Didier et al.'s questionnaire study found that NSM was significantly better than SSM for body image, satisfaction with nipple appearance and sensitivity and feeling of being mutilated [101].

After the international acceptance of NSM in the field of breast cancer surgery, the implementation of SSM has declined significantly. Several papers analyse the oncological safety, feasibility and possible indications of SSM in breast cancer surgery [40, 102], but significantly less similar studies are available for ASM in the international literature. However as reported by Simmons et al., ASM seems to have similar oncological safety, based on the examined 217 mastectomy specimens. The authors reported areola involvement in only 0.9% (n=2) of the cases [103]. Banerjee et al. obtained exactly the same results and found 2 cases of areola involvement out of 219 mastectomy specimens [104].

The present study did not find significant differences in oncological safety between ASM and NSM. The local recurrence rates were 3.4% (n=3) and 2.4% (n=2) in the ASM and NSM groups, respectively. Significant difference was not proven in DFS (p=0.762) or OS (p=0.601) between the two groups.

Other studies by Simmons et al. examining 17 patients with ASM and immediate breast reconstruction reported one postoperative complication (localised wound infection) and no locoregional recurrence in the 2-year long follow-up period with excellent aesthetic outcomes superior to that after SSM [102, 105, 106]. The operation times in our study were almost equal (80 and 76 minutes) for both procedures. Moreover, the majority of the complications were minor (Grade I) for both ASM (n=12; 9.0%) and NSM (n=9; 9.7%), while the reoperation rates (Grade III complications) were only 2.2% (n=3) and 2.1% (n=2) for ASM and NSM, respectively. Areola necrosis was present in 2.2% (n=3) of the ASM cases, while NAC necrosis was detected in 2.1% (n=2) of the NSM cases. Regarding the initiation of adjuvant treatment after surgery, Harmeling et al. by reviewing fourteen studies of 5,270 patients found that the mean time from mastectomy with immediate breast reconstruction to adjuvant therapy varied between 29 and 61 days [107]. Albright et al. retrospectively analysed 129,951 cases comparing NSM to SSM and reported that NSM was not associated with a delay in delivery of adjuvant chemotherapy or hormonal therapy compared to SSM [108]. In our study, no delay was detected regarding the adjuvant treatment, it was initiated within 12 weeks after surgery in all cases (ASM: median 7.4 weeks (range: 4.6 – 11.9); NSM: median 8.1 weeks (range: 4.1 – 12.0)).

Weber et al. reported the recommendations of the Oncoplastic Breast Consortium consensus conference on NSM, which currently provides the highest level of evidence of NSM

application [13]. The expert panel of 44 breast surgeons from 14 countries of four continents agreed that NSM is comparable to conventional mastectomy without reconstruction, BCS or SSM if cases are selected appropriately. Regarding their recommendation for indications, NSM can be performed in cases with any tumour size without skin or NAC involvement independent of axillary status and for DCIS; NSM is also applicable in the risk-reducing settings. There was a strong consensus that nipple involvement and R1 resection at the nipple margin are contraindications for nipple preservation. However, the panel was divided in regard to the question of nipple excision with areola preservation if the retroareolar margins were positive. They also noted a 0.81% nipple recurrence rate after NSM after a follow-up period of 32 months in a large cohort. The consensus conference concluded that further randomized trials and longer follow-up periods are needed to provide missing evidence and to clarify indications to guide treatment.

The indications for both ASM and NSM in our study were primarily based on theoretical considerations strictly according to the actual international guidelines, not purely on the nipple-tumour distance [13, 41]. Hence ASM operations were replaced by NSM when it was internationally accepted for both the prophylactic and therapeutic indications [41]. This resulted in two homogenous study groups, enabling the comparison of the two surgical techniques.

### 5.3. The needs and attitude of Hungarian breast cancer patients towards modern breast reconstruction

The spread of the modern oncoplastic approach has resulted in a paradigm shift in breast cancer treatment [109-111]. Surgical treatment has shifted from breast tumour excision to a complex surgical process including complete breast reconstruction, even sometimes with bilateral interventions or a series of operations. This poses a number of system-level tasks, such as the need for lifelong plastic surgery follow-up of the reconstructed breasts and many times repeated cosmetic corrections in parallel with the oncological control check-ups. These needs and indications are new in breast cancer care, the precise definition of which, the clarification of the scope of care and the requirements of material and human resources are essential for the development and high-level long-term operation of a modern patient-centred care system. The basis of all is formed by the recognition and analysis of the needs and expectations of the patients.

The present study assessed the systemic needs and expectations of female patients who underwent mastectomy and breast reconstruction. It is clear from the results that breast loss significantly disturbs female patients regardless of education and marital status (Figure 5). These findings correspond to the results of a questionnaire survey of 500 female patients between 2010 and 2011 published by our working group in 2014 [110]. According to that study, 30% (n = 148) of patients were moderately and 40% (n = 198) were very much afraid of breast loss, nearly half of them (46%; n = 224) wanted reconstruction, but they knew almost nothing (32%; n = 158) or very little (56%; n = 279) about it [110]. Interestingly, according to the repetition of the same questionnaire survey in 2017-2018, women were still equally found afraid of breast loss then, but in contrast to the previous data (when only 10%, altogether 48 cases), 30% of the 152 respondents were already aware of the possibilities of breast reconstruction, which information was collected either from the surgeon (52%; n = 258) or the internet (27%; n = 135). Based on these, it can be generally stated that breast loss places a significant psychological burden on breast cancer patients regardless of social status or education, therefore, the extension of the oncoplastic care system is needed and necessary in Hungary. In the last 6-8 years, the oncoplastic approach has become widespread and well-known among Hungarian women. In parallel, the population's demand for this special health service is also growing, which the health care system must be able to provide in the near future.

Patients had high expectations for the aesthetic outcome of the operations; in total, almost half of the women (48%; n = 239) expected improvement, some of them wished more beautiful (28%; n = 140) while others perfect (20%; n = 99) breasts at the end of the reconstruction process. Informing patients preoperatively about the realistic outcome is one of the top priorities, because oncoplastic procedures are not aesthetic operations, and albeit due to the technique they are often capable of providing the same high level of result as aesthetic surgeries do, but are completely subordinated to oncological priorities and principles (e.g. resection site, extent, RT, etc.), thus, their effectiveness is influenced by a number of other factors beyond those of plastic surgery [112].

The majority of the surveyed female patients (70%; n = 348) would have liked to have roughly identical breasts naked at the end of the reconstruction surgery as before, regardless of the marital status or education. Given that the structure of the two breasts differs during the most frequently applied implant-based post-mastectomy reconstructions, breast asymmetry

increases over time, since the lifted own healthy breast will behave differently due to its biological properties than an implant-only breast. Based on this, later on patients have secondary surgical demands due to the changes in symmetry over time.

According to the surveyed women, the desired high cosmetic result was wanted to be achieved by two, or not more, than three or four operations at maximum, which, in their view, should be covered by the NEAK. On one hand, it is necessary to avoid oncology-funded aesthetic surgeries in the future, which is a tricky issue that also raises ethical and professional issues that are difficult to resolve. On the other hand, however, treatment consisting of a series of operations is a huge load on the health care system - especially if the increasing annual number of cases and resulting surgeries for breast cancer is considered. At present, the system is able to provide oncoplastic surgery capacity to an artificially limited number of cases and probably only with a limited number of elements of the field. It is a question, how could a full oncoplastic breast surgery capacity be ensured to all; for this aim the joint work of the patients, professionals and health care policy makers is essential and needed.

Patients would entrust specially trained breast surgeons practising in oncoplastic breast surgery centres with their surgical treatment, because, in their opinion, this would have a significant impact on their recovery. In the treatment of breast cancer, the breast surgeon is an independent prognostic factor [113], together with the availability and quality assurance of BUs in Hungary (possibly with BRESO accreditation) by which the survival as well as the QoL of patients can be further improved in the 21$^{st}$ century [47].

The need for oncoplastic breast reconstruction following mastectomy in Hungary is in line with the international trends: according to a British study, 50% of female patients are awaiting for breast removal [114], while according to a French study by Ananian et al., 81% of such patients would like to have breast reconstruction [115]. Similarly to the international situation, according to our survey, the main source of information for the Hungarian patients is also the surgeon and the internet [116, 117]. Understanding the needs of the affected women, providing adequate information and adequate access to surgical care, organizing patient routes and properly structuring the health care system is essential for the expansion of oncoplastic breast cancer care [118, 119].

## 6. CONCLUSIONS

**6.1. No significant relationship exists between the location or histopathological parameters of the primary breast tumour and the subregional localisation of the SLN; the majority of SLNs are located in the anterior and central anatomical subregions of the axilla**

**6.2. In the era of conformal radiotherapy, instead of schematic solutions, individualised radiotherapy planning according to the risk status is needed to ensure the adequate coverage of axillary nodal volumes**

**6.3. Further investigations and caution are needed for the use of the ARM technique during ALND; our results should draw attention to that the practice of the ALND plus ARM technique involves the risk of leaving behind metastatic lymph nodes in the apical, lateral or posterior axillary subregions in a significant proportion of cases resulting in understaging and undertreatment. The application of SLNB during the intervention of ARM + ALND in a selected group of cases should be investigated.**

**6.4. ASM and NSM are equivalent alternatives providing similar complication rates, oncological safety aesthetic outcome and patient satisfaction in adequately selected cases; our results indicate that preserving the natural pigmented skin envelope of the areola has the same importance as the conservation of the complex NAC itself. ASM could be a suitable treatment option if NSM is not oncologically feasible.**

**6.5. State-of-the-art surgeries performed by qualified breast surgeons in dedicated centres providing physical and psychological recovery is needed and required by a significant proportion of Hungarian breast cancer patients.**

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## 9. APPENDIX

**I.**

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# Mapping of the functional anatomy of lymphatic drainage to the axilla in early breast cancer: A cohort study of 933 cases

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BCS
Breast-conserving surgery
HTgF
High tangential fieldRT
Radiotherapy
SLN
Sentinel lymph node
SLNB

## ABSTRACT

*Introduction:* The aims of this study were to investigate the correlation between lymphatic drainage and the sentinel lymph node (SLN) status of the subregions in the context of the clinic-pathological parameters of the tumour and the coverage of the axillary volumes by standard and high tangential fields (STgF and HTgF) for whole breast radiotherapy and axillary reverse mapping (ARM).
*Patients and methods:* 933 women with early breast cancer and clinically negative axillary status underwent breast surgery and SLN biopsy followed by axillary lymph node dissection in SLN-positive cases. The subregional localisation of the SLN(s) was registered and statistically analysed with the clinic-pathological characteristics of the breast tumour. In node-positive patients treated with breast-conserving therapy in whom the SLNs were found in the anterior or posterior axillary subregions, the axillary volumes were contoured using the Radiation Therapy Oncology Group contouring atlas (n = 61).
*Results:* In 91.1% (n = 797) of the cases, the SLN appeared in the anterior, posterior or central subregions. Using HTgF, Level I or II were completely covered in 65.6% (40/61) and 6.6% (4/61) of the cases, respectively. With STgF, the complete coverage was 0% for both levels.
6.8% (n = 63) of all cases had one positive lymph node in the expected ARM lymph node regions.
*Discussion:* A SLN is more than likely to be present in the anterior, posterior and central axillary subregions. Tangential fields allow only limited coverage of the axillary volumes. Preserving the lateral subregion during ARM may increase the possibility of understaging.


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Sentinel lymph node biopsy
STgF
Standard tangential field
WBI
Whole breast irradiation
na
Not applicable

## Introduction

Regional lymph node status is one of the most important prognostic factors for disease-free and overall survival in breast cancer [1–5]. Today, the gold-standard method for staging patients with early-stage breast cancer with clinically negative axillary lymph nodes is the sentinel lymph node biopsy (SLNB) [4,5].

To optimise the effectiveness of SLNB, the precise pre- and intraoperative mapping of lymphatic drainage is mandatory [4–6].

Anatomically, the axillary region is divided into five subregions: anterior, posterior, lateral, central and apical zones [7] (Fig. 1).

The anterior subregion is located under the lateral edge of the pectoralis minor muscle along the lateral thoracic vein. The posterior zone is found adjacent to the posterior wall of the axilla along the thoracodorsal nerve and vessels. The lateral subregion is located close to the lateral wall of the axilla, in relation to the proximal part of the axillary vein. The lymph nodes in this zone receive the vast majority of the efferent lymph vessels of the upper limb. The central zone is in the middle of the pyramid-shaped space of the armpit, close to the base of the axilla. The apical subregion is found in the apex medially to the distal part of the axillary vein.

These subregions correspond to the axillary node levels previously described by Berg [8]. The anterior, posterior and lateral subregions constitute Level I, the central zone forms Level II and the apical zone constitutes Level III [7].

Clear relationships between the anatomic location and metastatic status of the SLN have been revealed [9,10]. Histologically positive SLN was detected in Level I in 96% of cases and in Level II in 4% of cases by SPECT/CT [10].

A better understanding of the relationships between the subregional drainage pattern of SLN, the subregional localisation of SLN and the correlation to location and pathological characteristics of the primary breast tumour could have particular importance in determining whether ALND can be safely omitted.

The ACOSOG Z0011 trial did not perform ALND for early-stage breast cancer patients with 1–2 metastatic SLNs (cT1-2, pN1), and in the majority of the patients, the axilla was treated only with tangential field irradiation following breast-conserving surgery (BCS). After a median follow-up of 9.3 years, the data compared to the traditional ALND group showed no differences in local recurrence-free survival [11,12]. However, in the ACOSOG Z0011 trial, dose distribution in the axillary volumes was not reported in the initial publication. Jagsi et al. [13] recently analysed the radiotherapy (RT) coverage of the axillary lymph nodes of that trial. Most patients treated in the Z0011 trial received tangential RT alone, and some received no RT at all. Some patients received directed nodal irradiation via a third field. They concluded that further research is necessary to determine the optimal RT approach in patients with low-volume axillary disease treated with SLNB alone.

A recent surgical technique that is less radical and therefore decreases the morbidity of SLNB and ALND, especially lymphedema, is ARM [14–16]. The lymphatic drainage of the upper limb that runs through the axilla - most often the lateral subregional lymphatic structures - is identified by injecting radioisotope or blue dye to the ipsilateral limb subcutaneously, and these nodes are spared during the operation, removing only the lymph nodes that drain the lymph of the breast. The technique was proven to be feasible with a low level of evidence; however, the question of oncological radicality still arises due to the uncertainty of the metastatic status of the ARM lymph nodes that are not removed [17].

We sought to determine whether there is a correlation between the lymphatic drainage and the SLN status of the subregions. Our main objectives were as follows:

- To examine the location of the SLN in the axillary subregions in a representative cohort of patients with early-stage breast cancer.
- To assess statistical correlations between the clinicopathological characteristics of the primary breast tumour and the subregion of the SLN.
- To analyse the subregional localisation of metastatic SLNs.
- To assess the statistical correlation between axillary subregions outside the tangential and extended tangential RT coverage field applied in the ACOSOG Z0011 trial and the SLN positivity within these subregions after BCS.
- To study the axillary coverage with STgF or HTgF irradiation in node-positive patients.
- To assess the SLN positivity rate in the lateral, unremoved subregion when the ARM technique is applied.

### *Patients and methods*

A retrospective cohort study was performed between March 2013 and February 2015. 933 female patients older than 18 years were enrolled with primary unilateral invasive or microinvasive, clinically lymph node-negative early-stage breast cancer (clinically $T \leq 5$ cm, N0M0). Exclusion criteria included previous ALND, cN1-2, pregnancy, lactation and necessity of neoadjuvant treatment for breast cancer [18,19].

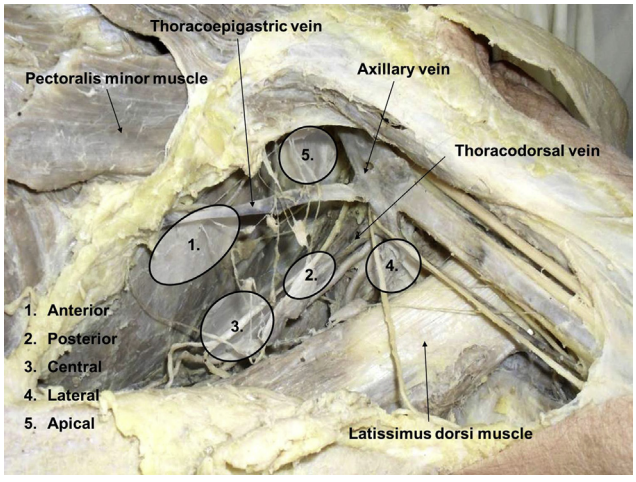


**Fig. 1.** Subregions of the axilla (left side, human cadaveric dissection).

The complex oncological therapy was performed according to the actual international guidelines [18–20] adopted by the National Institute of Oncology and was not different from those who were not included in the trial. Radiopharmaceutical (80 Mbq $^{99m}$ Tc labelled nanocolloid, particle size: 50–800 nm) was injected to the intratumoural area or periareolar tissue on the day before surgery. If the lymphoscintigraphy was unsuccessful, 2–3 ml of periareolar Patent blue 25 mg/ml® dye injection was applied 10 min before the operation.

Patients then underwent a wide excision or mastectomy and axillary SLNB followed by ALND instantly if the SLN was positive by intraoperative imprint cytology or as a second operation if the SLN was positive only by histological examination. If isolated tumour cells or micrometastases were found in the SLN (n = 33), ALND was omitted.

The subregional localisation of the SLN(s) was identified and recorded on a standardised data sheet by the operating surgeons immediately after biopsy in the operating theatre (Fig. 1). The harvested SLNs were separated and labelled with their localisation for pathological processing. Imprint cytology was performed intraoperatively, and if the result was positive, the operation was completed with ALND. Postoperatively, all the removed lymph nodes were meticulously examined by the pathologists according to the guidelines [21,22]. In cases of false negative SLNB, the subregional localisation and the number of metastatic lymph nodes left behind in the axilla could not be identified by our applied methods.

Following BCS, all patients had 3D-conformal RT. Patients were placed supine with both arms up and both hands holding on to a support during CT simulation. CT scan images with 5-mm sections were obtained. The breast was irradiated with two opposing tangential fields with 6 MV photons. STgF margins were determined by palpation of the breast parenchyma with the addition of a 1–2-cm margin in all directions. The superior borders of these fields intended to treat the breast only, without regard to nodal coverage. Approximately 2 cm (max. 3 cm) of the lung was included in the posterior aspect of the field. In node-positive patients, an additional field was also used to deliver an effective dose to the axillary apex and clavicular fossa. The total dose of the whole breast and supraclavicular fossa was 50 Gy (25 × 2 Gy). Breast irradiation was given via STgFs. The STgF upper margin was generally the base (±1 cm) of the clavicle. Retrospectively, for the purpose of this study in 61 randomly selected node-positive patients treated with breast-conserving therapy in whom the SLNs were found in the anterior or posterior axillary subregions (Level I), HTgFs were simulated using the same CT data. HTgF consisted of a superior border placed at the inferior edge (or below maximum 2 cm) of the humeral head. Before RT planning, axillary volumes (Levels I, II and III) were contoured using the RTOG (Radiation Therapy Oncology Group) contouring atlas [23]. Coverage of the axillary volumes by tangential fields was classified according to the tangential field-planning target volumes (Levels I, II and III) overlap: 100% overlap (complete coverage), <100% overlap (partial coverage), and 0% overlap (lack of coverage: out of field). Examples of coverages are given in Fig. 2.

The study was approved by the institutional ethical committee board and was registered on Clinicaltrials.gov (identifier: NCT01804309).

The clinical trial did not alter the lege artis oncological treatment and SLN intervention in any way.

All the collected data were registered in the institutional database and statistically analysed using Fisher's exact test. P-values less than 0.05 were considered statistically significant. Statistical analysis was performed using Statistica 12.0 software (StatSoft, Tulsa, OK) or PAST version 1.86b [24].

## Results

A total of 933 women were enrolled in the study. The mean age of the patients was 64.1 years (range 19–91 years, median: 64 years). Three women were excluded because the breast tumour was larger than 5 cm according to the postoperative pathologic examination. Another two patients were ruled out due to newly discovered lympho-proliferative disorders affecting the axillary lymph nodes. Another 58 patients were discarded because of an uninterpretable sentinel data sheet or incomplete clinical-histological data.

The detailed pathologic characteristics of the primary breast tumours are summarised in Table 1.

Regarding the location of the breast cancer, 44.7% (n = 417) were in the upper-outer, 14.7% (n = 137) in the upper-inner, 9.9% (n = 93) in the lower-outer, 6.7% (n = 63) in the lower-inner quadrant, and 2.8% (n = 27) in the axillary process (tail of Spence); 12.8% (n = 119) were central tumours and 3.5% (n = 33) were multiplex.

There was a significant correlation between the location and the molecular subtype of the tumour (p = 0.022). Non-luminal tumours were mainly localised in the upper quadrants (84.6% n = 11).

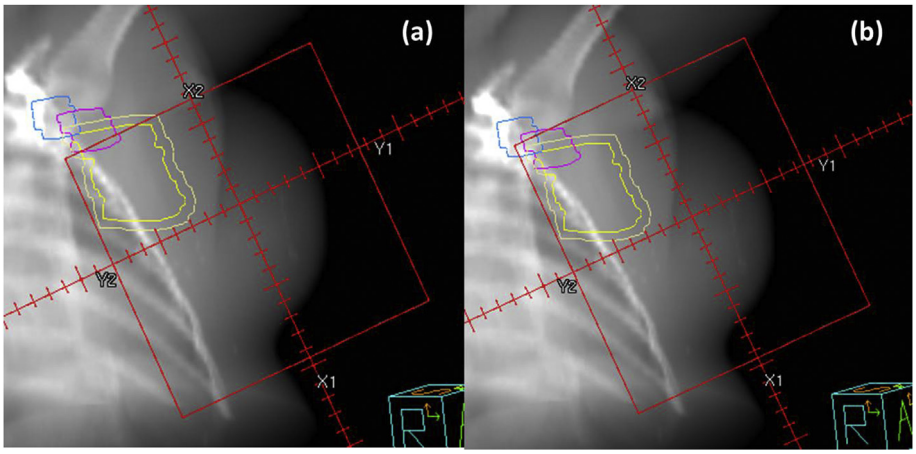


**Fig. 2.** (a) Coverage with standard tangential field (red square). Yellow lines = Level I volumes: inner line - clinical target volume; outer line - planning target volume; partial coverage. Purple line = Level II clinical target volume; partial coverage. Blue line = Level III clinical target volume; no coverage, out of field. (b) Coverage with high tangential field (red square). Yellow lines = Level I volumes: inner line - clinical target volume; outer line - planning target volume; complete coverage. Purple line = Level II clinical target volume; partial coverage. Blue line = Level III clinical target volume; partial coverage.

Similarly, the triple negative subtype was also likely to appear in the upper-outer quadrant (57.1%; n = 40). However, cancers in the lower-inner quadrant were mostly Her2-enriched (17.1%; n = 7). [Table 2.].

The tracer for lympho-scintigraphy was injected intratumorally and periareolarly in 38.8% (n = 362) and 57.6% (n = 537) of the cases, respectively. We used only radiopharmaceutical (80 Mbq $^{99m}$Tc labelled nanocolloid) in 86.9% (n = 811), Patent blue dye in 4.4% (n = 41) and both in 4.8% (n = 45) of the cases.

None of the examined characteristics of the primary breast cancer (molecular subtype p = 0.360) had significant correlation with the subregional localisation of the SLN.

We divided our study population into two groups based on the injection site and analysed the relationships between the location of the SLN and location of the primary breast tumour. In case of intratumoural application, we found significant correlation between the location of the breast cancer and the subregional location of the SLN (p = 0.016). However, examining only the histologically positive SLNs, the relationship between their location and the primary tumour location was not statistically significant (p = 0.674).

If periareolar injections were used, the location of the SLN was not dependent on the location of the primary breast tumour (p = 0.398), whilst the correlation between the location of the positive SLN and the location of the breast cancer was statistically significant (p = 0.039). [Table 3.].

According to our data, tumours in the upper-outer quadrant are least frequently drained to the anterior subregion (34.2%). Posterior subregion receives lymph mainly from the upper-outer quadrant (31.6%) and the axillary process (36.3%), whereas the inner and central quadrants have very similar drainage patterns with a tendency to give efferent lymphatics more often to the anterior (53.9%, 69.6% and 54.5%) and central (28.8%, 26.1% and 22.7%) lymph nodes. The central lymph nodes receive lymphatic drainage equally from the different quadrants of the breast [Table 3.].

An average of 1.6 (range: 1–8, median: 1) SLNs were harvested per operation, and the SLN positivity rate was 20.3% (n = 189).

We also analysed the distribution pattern and metastatic status of the SLN in the subregions of the axilla [Table 3.]. The most common site of the SLN was the anterior subregion (39.9%; n = 349), while the least common was the apical subregion (3.4%; n = 30). In contrast, the positivity rate was higher in the apical subregion (30.0%; n = 9) than in the anterior subregion (20.9%; n = 73). The SLN was present in the lateral subregion in 5.5% (n = 48) of the cases. Of these 48 lymph nodes, 11 SLNs - 1.3% of the total cases - were positive. In the central and posterior subregions, 53 (6.1%) and 43 (4.9%) SLNs, respectively, were found to be positive out of the 245 (28.0%) and 203 (23.2%) removed lymph nodes, respectively.

In 91.1% (n = 797) of the cases, the SLN appeared in the anterior, posterior or central subregions, corresponding to Level I and II zones [Table 3].

In 503 patients, the SLN was located within the anterior or posterior subregion (Level I). 111 of them (22.1%) had axillary lymph node metastasis, and 83 (16.5%) of them were treated with RT in our Institute. Sixty-one women were subjected to WBI. The coverage of axillary volumes by tangential fields is given in Table 4. There was a significant difference between the two plans regarding the coverage of the Level I axillary volume. HTgF increased the rate of complete coverage from 0% to 65.6% (40 of 61; p < 0.0001). Concerning the Level II volume, the rate of complete coverage with STgF or HTgF was 0% and 6.6% (4 of 61), respectively (p = 0.1198). The rate of "out of field" cases was very high with STgF, 72.1% (44 of 61), but "out of field" cases were not observed with HTgF irradiation (p < 0.0001). The coverage of the Level III volume was very poor

**Table 1**
Pathological characteristics of the primary breast tumour.

| pT | n | % |
|---|---|---|
| pTis | 104 | 11.8 |
| pT1mi | 3 | 0.3 |
| pT1a | 31 | 3.5 |
| PT1b | 95 | 10.8 |
| pT1c | 316 | 36.0 |
| pT2 | 300 | 34.1 |
| pT3 | 30 | 3.4 |
| **Grade (invasive tumours)** | | |
| I | 180 | 23.4 |
| II | 370 | 48.1 |
| III | 219 | 28.5 |
| **Grade (in situ carcinomas)** | | |
| Low | 28 | 26.9 |
| Medium | 50 | 47.8 |
| High | 26 | 25.3 |
| **Receptor status** | | |
| ER | 751 | 80.5 |
| PR | 641 | 68.7 |
| Her2 | 72 | 7.7 |
| **Molecular subtype** | | |
| Luminal A | 438 | 59.4 |
| Luminal B | 171 | 23.2 |
| Luminal B-Her2+ | 41 | 5.6 |
| Non-luminal | 73 | 9.9 |
| Triple negative | 14 | 1.9 |
| **Lymphovascular invasion** | | |
| Present | 322 | 39.3 |
| Not present | 497 | 60.7 |
| **Histological type** | | |
| Invasive ductal carcinoma | 643 | 73.1 |
| Invasive lobular carcinoma | 99 | 11.3 |
| Other invasive | 34 | 3.9 |
| DCIS | 75 | 8.5 |
| LCIS | 16 | 1.8 |
| Other in situ | 13 | 1.5 |
| **Palpability** | | |
| Palpable | 499 | 55.9 |
| Not palpable | 393 | 44.1 |
| **Mitotic activity** | | |
| <11 | 539 | 67.0 |
| 11–20 | 157 | 19.5 |
| 20< | 109 | 13.5 |
| **Type of breast surgery** | | |
| Mastectomy | 371 | 39.8 |
| Breast conserving surgery | 562 | 60.2 |
| **SLN positivity** | | |
| SLN-negative patients | 744 | 79.7 |
| SLN-positive patients | 189 | 20.3 |
| Total removed SLNs | 1538 | na |
| SLNs removed per operation | 1.6 | na |
| **ALND** | | |
| Total number of ALND | 156 | 16.7 |
| Total number of removed lymph nodes | 2109 | na |
| Lymph nodes removed per ALND | 13.5 | na |
| Positive lymph nodes per ALND | 406 | 19.3 |

**Table 2**
Correlation between molecular subtype (column) and the location (row) of the primary breast tumour (p = 0.022).

| | Luminal A | | Luminal B | | LumB – Her2 | | Non-luminal | | Triple negative | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | n | % |
| Upper-outer | 210 | 49.3 | 73 | 44.0 | 18 | 43.9 | 7 | 53.9 | 40 | 57.1 |
| Upper-inner | 65 | 15.3 | 39 | 23.5 | 5 | 12.2 | 4 | 30.8 | 9 | 12.9 |
| Lower-outer | 47 | 11.0 | 20 | 12.1 | 4 | 9.8 | 0 | 0 | 9 | 12.9 |
| Lower-inner | 36 | 8.5 | 13 | 7.8 | 7 | 17.1 | 0 | 0 | 1 | 1.4 |
| Central | 62 | 14.6 | 17 | 10.2 | 7 | 17.1 | 2 | 15.4 | 6 | 8.6 |
| Axillary process | 6 | 1.4 | 4 | 2.4 | 0 | 0 | 0 | 0 | 5 | 7.1 |

**Table 3**
Correlation between the location of the primary breast tumour (column) and the subregional location of the SLN (row) if intratumoural injections were used (p = 0.016) and distribution pattern and metastatic status of the SLN in the subregions of the axilla.

| | Upper outer | Lower outer | Upper inner | Lower inner | Central | Axillary process | Stained & removed SLN | Positive SLN | Positivity rate |
|---|---|---|---|---|---|---|---|---|---|
| anterior | 65 (34.2%) | 13 (41.9%) | 28 (53.9%) | 16 (69.6%) | 12 (54.5%) | 5 (45.5%) | 349 (39.9%) | 73 | 20.9% |
| central | 55 (28.9%) | 8 (25.8%) | 15 (28.8%) | 6 (26.1%) | 5 (22.7%) | 1 (9.1%) | 245 (28.0%) | 53 | 21.6% |
| posterior | 60 (31.6%) | 7 (22.6%) | 6 (11.5%) | 1 (4.3%) | 2 (9.1%) | 4 (36.3%) | 203 (23.2%) | 43 | 21.2% |
| lateral | 6 (3.2%) | 3 (9.7%) | 3 (5.8%) | 0 (0.0%) | 1 (4.6%) | 1 (9.1%) | 48 (5.5%) | 11 | 22.9% |
| apical | 4 (2.1%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 2 (9.1%) | 0 (0.0%) | 30 (3.4%) | 9 | 30.0% |

**Table 4**
Coverage of axillary volumes by tangential fields (n = 61).

| % (No.) | | STgF | HTgF | p-value |
|---|---|---|---|---|
| Level I | Complete | 0 (0) | 65.6 (40) | <0.0001 |
| | Partial | 100.0 (61) | 34.4 (21) | – |
| | Out of field | 0 (0) | 0 (0) | – |
| Level II | Complete | 0 (0) | 6.6 (4) | 0.1198 |
| | Partial | 27.9 (17) | 93.4 (57) | – |
| | Out of field | 72.1 (44) | 0 (0) | <0.0001 |
| Level III | Complete | 0 (0) | 0 (0) | – |
| | Partial | 8.2 (5) | 90.2 (55) | – |
| | Out of field | 91.8 (56) | 9.8 (6) | <0.0001 |

STgF, standard tangential field; HTgF, high tangential field.

(rate of "out of field" with STgF or HTgF: 91.8% and 9.8%, p < 0.0001).

## Discussion

The main objective of the study was to examine the presumable relationship between the quadrants of the breast and the subregions of the axilla and thus to describe a functional and morphologic lymphatic drainage pattern. Furthermore, the coverage of axillary volumes with tangential fields for WBI was also studied.

In summary, we did not find a significant correlation between the histopathological parameters of the primary breast cancer and the subregional location of the SLN. However, it is obvious from the data that the SLN is more than likely to be present in the anterior, posterior and central axillary subregions. Moreover, the SLN positivity rate in the lateral subregion (22.9%; n = 11) was not negligible. It is also clear from the data that upper-outer quadrant tumours spread least frequently to the anterior lymph nodes, while inner and central quadrant tumours have similar drainage patterns mainly to the anterior and central subregions.

There are several studies concerning the coverage of axillary lymph nodes from whole breast tangential field irradiation. Reed et al. [25] reported that using STgFs, no patient received complete coverage of the axillary Level I–II lymph node volume. They concluded that definitive irradiation of the Level I and II axillary lymph node regions required significant modification of the STgFs. Krasin et al. [26] showed that the use of STgFs does not therapeutically treat the regional lymph nodes. In their series, only 1 out of 25 patients had adequate coverage of the Level I region, and no patient had adequate coverage of Level II. Reznik et al. [27] observed that adequate coverage of Level I, defined when 95% of the volume received 95% of the dose, was achieved in none of the patients with normal tangents and in 6 patients (6 of 35) with high tangents. In a study by Orecchia et al. [28], the Level I nodes were only partially in the STgF, and the mean dose was only 48.7% of the prescribed dose. Our study was performed to address the issue of axillary volume coverage according to tangential field size. We showed that no patient had complete coverage of the Level I or Level II region with STgFs, and in 72.1% of the patients, the Level II volume was completely out of field. Using HTgF, 65.6% of the patients had complete coverage of Level I regions and the complete coverage rate was only 6.6% for Level II volume. The coverage of Level III region was very poor either with STgF (rate of out of field: 91.8%) or HTgF (rate of out of field: 9.8%).

Our results are consistent with the earlier studies that showed that STgF does not adequately cover the axillary volumes. With modern techniques, adequate coverage of the axillary volumes depends on the cranial field edge. Ohashi et al. [29] used 3D-CRT with a field-in-field technique, and half of the humeral head was inside the field. With this technique, even the dose to the Level III region was appropriate (V90 was 82.8%). In a study by Nagar et al. [30], when the tangential fields were modified to include Level I and II volumes, the mean dose (STgF vs. modified HTgF) increased from 35 Gy to 51 Gy and 11 Gy to 50 Gy, respectively. In patients studied by Belkacemi et al. [31], the STgF was defined with the cranial border set at 2 cm below the humeral head, while the HTgF consisted of a superior border placed at the inferior edge of the humeral head. The mean dose delivered to Level I with STgF or HTgF was 20 Gy and 33 Gy, respectively (p < 0.0001). We also used classical HTgF such as Belkacemi et al. [31], and the coverage of the Level I region was limited (complete coverage rate 65.6%). Attempts to increase the volume of complete coverage could induce a significant increase in lung dose. Alco et al. [32] suggested shaping the tangential field with multi-leaf collimators according to axillary level volumes to ensure complete coverage, but the inclusion of the axillary region in the target volume increased the irradiated lung volume. Mean lung dose was with the HTgF or multi-leaf collimators HTgF 6.5 and 9.6 Gy, respectively (p = 0.0001). To study the adequate coverage of the axilla, Levels I, II and III should be defined (delineated) by anatomical structures. STgFs provide limited coverage of the axilla, but HTgFs may provide complete coverage of Level I volume in some patients.

In our study, 9 (1.0%) positive SLNs were in the apical and 11 (1.3%) metastatic lymph nodes were in the lateral subregions. In total, 20 patients with positive lymph nodes (2.3% of our cases) would be left untreated if we applied tangential WBI to treat the axilla.

In our view, for the proper treatment of the axilla, an additional axillary and supraclavicular RT field is needed. This correlates with the findings of the Hungarian OTOASOR prospective randomised

clinical trial with axillary and supraclavicular field irradiation in the case of a metastatic SLN without ALND [33].

Applying the ARM technique, the lymph nodes stained with blue dye or radioisotope are preserved to prevent postoperative lymphedema. The subregional localisation of the ARM nodes has not yet been clearly identified, but it seems obvious that majority of the lymphatics draining the upper limb traverses deep in the axilla [17]. This was also confirmed by Ikeda et al. [34], who found ARM nodes in zones that correspond to mainly the lateral, apical and posterior axillary subregions.

In our study, 281 (32.1%) SLNs were found within one of these subregions, and 22.4% (n = 63) of them were positive. This means that 7.2% of all our cases had one positive lymph node in the expected ARM lymph node regions.

According to these results, due to the high rate of posterior subregional SLN drainage (21.8% n = 203) and SLN positivity (21.2%), not only the ALND but also the SLNB carry a high risk of a preserved positive lymph node and have a negative effect on the patient's successful treatment. This corresponds to the results that showed that the oncological safety of the ARM technique in patients with axillary lymph node metastasis from breast cancer is questionable [35,36], and proper indications, patient selection and further investigations are needed for the safe application of ARM [37].

## Conclusion

Our findings suggest that there is no significant correlation between the histopathological parameters of the primary breast tumour and the subregional localisation of the SLN. The majority of SLNs are located in the anterior and central subregions.

When primary RT is used to treat the axilla, the contouring of the axillary lymph node levels is necessary for the proper design of the tangential field borders. Our analysis leads to the conclusion that STgF did not provide complete coverage of level I-II axillary lymph nodes. The use of high tangential fields is one means of improving axillary coverage with whole breast irradiation.

Tangential field WBI provides limited coverage of the axilla. Only 65.6% of our patients had complete Level I coverage with high tangential fields.

Moreover, using the ARM technique and leaving lymph nodes behind in the apical, lateral or posterior axillary subregions may leave behind up to 7.2% of metastatic lymph nodes, which may elevate the risk of possible understaging or undertreatment. In these cases, clipping the preserved lymph nodes is mandatory for adjuvant axillary RT.

## Conflict of interest statement

All authors certify that there is no actual or potential conflict of interest in relation to this article.

## Role of funding source statement

All authors certify that there were no funding sources; therefore, they did not play any role in data collection, analysis, interpretation, trial design, patient recruitment or any aspect pertinent to the study.

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COMMENTARY

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# Clinicopathological correlations of areola-sparing mastectomies versus nipple-sparing mastectomies: Analysis of the oncological and cosmetic importance of the components of the nipple-areola complex

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**Keywords:** areola-sparing mastectomy, breast cancer, nipple-sparing mastectomy

In recent years, nipple-sparing mastectomy (NSM) has become the primary mastectomy technique.[1] The oncological and cosmetic importance of the nipple and separately the pigmented areola should be better understood by the modern breast oncoplastic surgery.

The aim of this study was to perform a long-term comparison of the oncological safety and cosmetic outcomes of areola-sparing mastectomy (ASM) with those of NSM.

This single-center retrospective comparative study was performed between April 2013 and December 2018 at the National Institute of Oncology, Hungary, based on the prospectively led institutional database.

The diagnosis of breast cancer, staging examinations, oncological treatments, and follow-up was performed according to the institutional protocol based on the actual ESMO guideline.

The indication for mastectomy was either therapeutic for breast cancer or prophylactic for patients with BRCA mutation. ASM was the technique first applied, while it was subsequently replaced by NSM after its international acceptance.

All procedures in both groups were performed with the same technique, applying the same type of submusculary placed tissue expander with delayed-immediate implant-based breast reconstruction.

For the axillary staging, sentinel lymph node biopsy was performed according to the criteria of the ACOSOG Z0011 trial.

Postoperative complications were assessed by applying the Clavien-Dindo Classification system.

For the assessment of the esthetic outcomes, a 5-point Likert scale was applied.

The BREAST-Q reconstruction module version 2.0 postoperative questionnaire was applied at 6 months after surgery.

All the collected data were statistically analyzed using Statistica 12.0 software (StatSoft, Tulsa, OK) or PAST version 1.86b.

After the exclusion of 24 patients, a total of 134 and 93 patients were enrolled in the study.

Detailed patient and tumor characteristics are summarized in Table 1.

The recorded early postoperative complications in the two groups are summarized in Table 2.

At the mean follow-up of 45 months, there was no significant difference in the disease-free survival (DSF) ($P$ = .762) and overall survival (OS) ($P$ = .601) between the two groups [Figure 1].

Both groups had the same objective esthetic outcomes by the 5-point Likert scale system [Table 3].

The results of the corresponding BREAST-Q domains showed no significant difference between ASM and NSM patients [Table 3].

This study revealed that preservation of the nipple does not make oncological difference, while preserving breast projection and pigmented areola seems to have the same importance than the

  

**TABLE 1** (A) Patient characteristics (B) Characteristics of the primary breast tumor

| (A) | | | |
|---|---|---|---|
| | **ASM** | **NSM** | ***P*** |
| Number of patients | 134 | 93 | |
| Age (y) | | | |
| Median (min.–max.) | 41 (26-64) | 40 (26-70) | .365 |
| BMI ($kg/m^2$) | | | |
| Mean ± SD | 21.6 ± 3.1 | 21.2 ± 3.4 | .285 |
| Cup size | n (%) | n (%) | |
| A | 23 (17.2) | 7 (7.5) | .003 |
| B | 75 (55.9) | 62 (66.7) | |
| C | 25 (18.7) | 24 (25.8) | |
| D | 11 (8.2) | 0 (0.0) | |
| Indication | n (%) | n (%) | |
| Therapeutic | 89 (66.4) | 85 (91.4) | $1.2 \times 10^{-5}$ |
| Prophylactic | 45 (33.6) | 8 (8.6) | |
| Operative duration (minutes) | | | |
| Median (min.–max.) | 80 (50-150) | 76 (43-120) | .431 |
| Neoadjuvant | n (%) | n (%) | |
| Chemotherapy | 20 (22.5) | 9 (10.6) | .244 |
| Initiation of adjuvant therapy (weeks) | | | |
| Median (min.–max.) | 7.4 (4.6-11.9) | 8.1 (4.1-12.0) | .124 |
| Adjuvant | n (%) | n (%) | |
| Chemotherapy/Biological therapy | | | .068 |
| Yes | 34 (25.4) | 19 (20.4) | |
| No | 59 (44.0) | 61 (65.6) | |
| Not reported | 41 (30.6) | 13 (14.0) | |
| Radiotherapy | | | |
| Yes | 32 (23.9) | 27 (29.0) | .993 |
| No | 63 (47.0) | 53 (57.0) | |
| Not reported | 39 (29.1) | 13 (14.0) | |
| Endocrine therapy | | | |
| Yes | 46 (34.3) | 61 (65.6) | .001 |
| No | 45 (33.6) | 21 (22.6) | |
| Not reported | 43 (32.1) | 11 (11.8) | |

| (B) | | | |
|---|---|---|---|
| | **ASM** | **NSM** | |
| **Pathological TNM** | **n = 89 (therapeutic)** | **n = 85 (therapeutic)** | ***P*** |
| pT | n (%) | n (%) | .026 |
| pTis | 5 (5.6) | 6 (7.1) | |
| pT1 | 37 (41.6) | 33 (38.8) | |
| pT2 | 23 (25.8) | 19 (22.3) | |
| pT3 | 4 (4.5) | 18 (21.1) | |
| pN | n (%) | n (%) | .900 |
| pN0 | 47 (52.8) | 53 (62.3) | |

(Continues)

**TABLE 1** (Continued)

| (B) | | | |
|---|---|---|---|
| | ASM | NSM | |
| Pathological TNM | n = 89 (therapeutic) | n = 85 (therapeutic) | *P* |
| pN1 | 18 (20.2) | 19 (22.3) | |
| pN2 | 3 (3.4) | 2 (2.4) | |
| pN3 | 1 (1.1) | 2 (2.4) | |
| ypT | n (%) | n (%) | |
| ypT0 | 5 (5.6) | 4 (4.7) | |
| ypT1 | 9 (10.2) | 2 (2.4) | |
| ypN2 | 4 (4.5) | 2 (2.4) | |
| ypN3 | 2 (2.2) | 1 (1.2) | |
| ypN | n (%) | n (%) | |
| ypN0 | 11 (12.4) | 6 (7.0) | |
| ypN1 | 7 (7.9) | 2 (2.4) | |
| ypN2 | 1 (1.1) | 0 (0) | |
| ypN3 | 1 (1.1) | 1 (1.2) | |
| Grade (invasive breast cancer) | | | |
| I | 16 (18.0) | 11 (12.9) | .435 |
| II | 34 (38.2) | 40 (47.1) | |
| III | 39 (43.8) | 34 (40.0) | |
| Receptor status | | | |
| ER | | | .004 |
| Positive | 60 (44.8) | 59 (63.4) | |
| Negative | 32 (23.9) | 10 (10.8) | |
| Not reported | 42 (31.3) | 24 (25.8) | |
| PR | | | .008 |
| Positive | 56 (41.8) | 56 (60.2) | |
| Negative | 35 (26.1) | 13 (14.0) | |
| Not reported | 43 (32.1) | 24 (25.8) | |
| Her2 | | | .951 |
| Positive | 20 (14.9) | 15 (16.1) | |
| Negative | 71 (53.0) | 52 (55.9) | |
| Not reported | 43 (32.1) | 26 (28.0) | |
| Histological type | | | |
| Invasive ductal carcinoma | 74 (83.2) | 60 (70.6) | .349 |
| Invasive lobular carcinoma | 5 (5.6) | 11 (12.9) | |
| Other invasive | 4 (4.5) | 6 (7.1) | |
| DCIS | 5 (5.6) | 6 (7.1) | |
| LCIS | 1 (1.1) | 2 (2.3) | |
| Nipple—tumor distance (cm) | | | |
| Median (min.–max.) | 2.7 (0.6-7.0) | 3.1 (0.7-7.0) | .497 |
| Follow-up 45 mo (range: 20.1-82.7) | | | |
| Local recurrence | 3 (3.4) | 2 (2.4) | |
| Distant metastatic disease | 5 (5.6) | 1 (1.2) | |

(Continues)

**TABLE 1** (Continued)

| (B) | | | |
|---|---|---|---|
| | ASM | NSM | |
| **Pathological TNM** | **n = 89 (therapeutic)** | **n = 85 (therapeutic)** | ***P*** |
| Distant metastases-related death | 2 (2.2) | 1 (1.2) | |
| Axillary surgery | | | |
| Sentinel lymph node biopsy | 64 (71.9) | 62 (72.9) | .656 |
| Axillary lymph node dissection | 23 (25.9) | 19 (22.4) | |
| No axillary surgery | 2 (2.2) | 0 | |
| Not reported | 0 | 4 (4.7) | |

**TABLE 2** Early postoperative complications based on the Clavien-Dindo Classification

| | ASM | NSM | |
|---|---|---|---|
| | **134 n (%)** | **93 n (%)** | ***P*** |
| Grade I | 12 (9.0) | 9 (9.7) | |
| infection | 4 (3.0) | 3 (3.2) | |
| seroma | 2 (1.5) | 2 (2.1) | |
| partial skin/ NAC necrosis | 3 (2.2) | 2 (2.1) | |
| rippling | 2 (1.5) | 1 (1.1) | |
| wound dehiscence | 1 (0.7) | 1 (1.1) | |
| Grade II | 3 (2.2) | 1 (1.1) | |
| infection | 2 (1.5) | 0 (0.0) | |
| chronic seroma | 1 (0.7) | 1 (1.1) | |
| Grade III | 3 (2.2) | 2 (2.1) | |
| hematoma | 2 (1.5) | 1 (1.1) | |
| implant loss | 1 (0.7) | 1 (1.1) | |
| Overall | 18 (13.4) | 12 (12.9) | .908 |

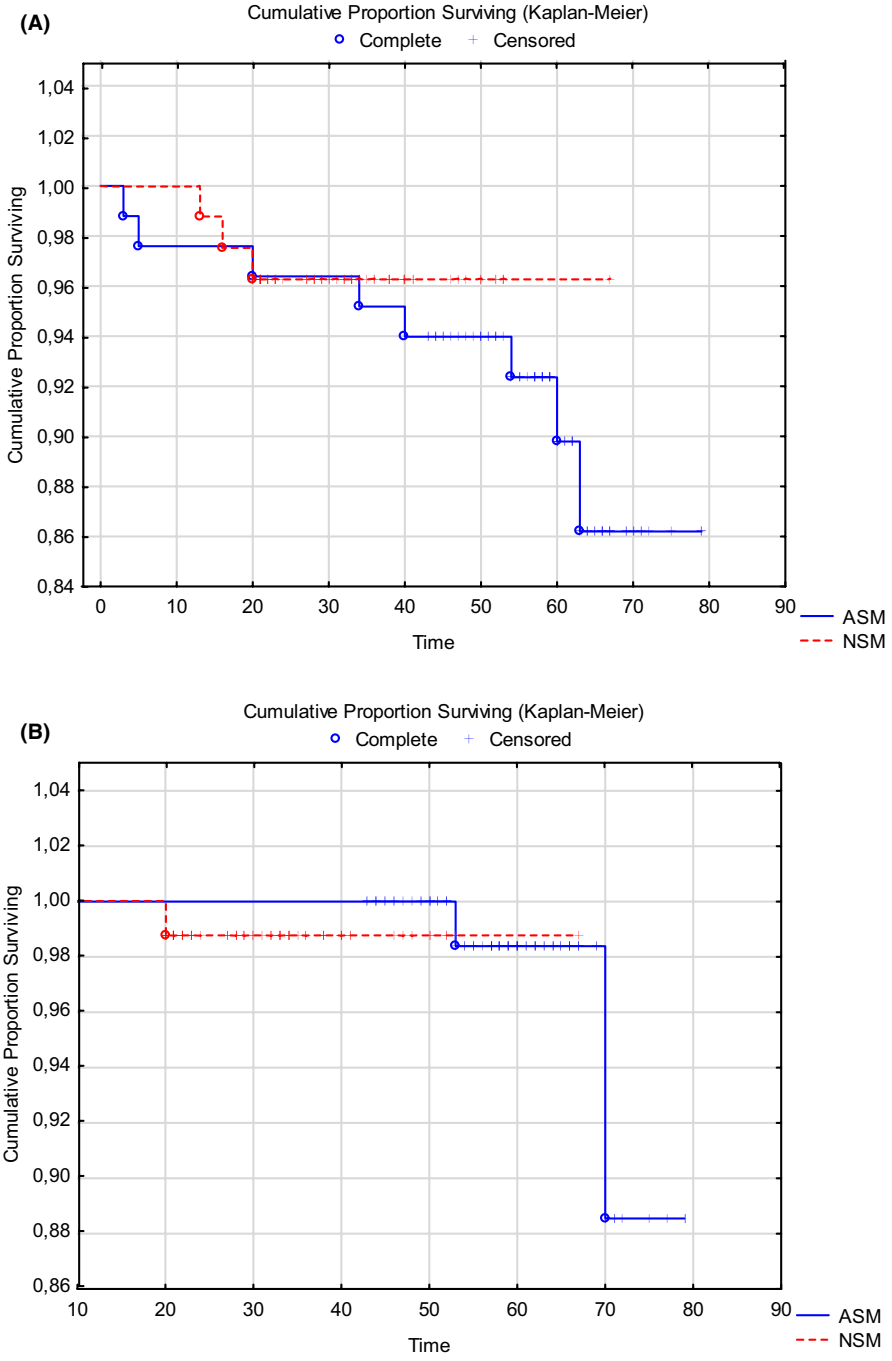


**FIGURE 1** Kaplan-Meier curve showing (A) DSF and (B) OS of the two groups

**TABLE 3** Results of the Likert scale system (A) and the BREAST-Q postoperative questionnaire (B)

| (A) | | |
|---|---|---|
| | ASM median (range) | NSM median (range) |
| Likert score | 4.1 (2-5) | 4.3 (2-5) |

| (B) | | | |
|---|---|---|---|
| | ASM mean ± SD | NSM mean ± SD | *P* |
| Satisfaction with breasts | 64.9 ± 21.2 | 67.8 ± 17.2 | .691 |
| Psychosocial well-being | 68.4 ± 18.4 | 72.4 ± 17.5 | .123 |
| Physical well-being | 80.0 ± 14.0 | 76.5 ± 15.5 | .232 |
| Sexual well-being | 59.1 ± 18.3 | 54.0 ± 20.9 | .252 |

complex NAC itself. Therefore, ASM could be a suitable treatment option, if NSM is not oncologically feasible.


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**III.**

# A magyar emlőrákos betegek igényei a korszerű onkoplasztikus emlősebészeti ellátásra

## *500 beteg kérdőíves vizsgálata*

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*Bevezetés:* A korszerű onkoplasztikus emlősebészet következményeként megjelenő jelentős emlőrekonstrukciós igény számos rendszerszintű kérdést vet fel. Vizsgálatra és szabályozásra várnak az onkoterápiák hatására és az idő múlásával bekövetkező esztétikai változások, illetve hosszú távú szövődmények miatti korrekciós műtétek indikációi; meghatározandó a helyreállító beavatkozások optimális és maximális száma, az elérni kívánt esztétikai végcél és az ezekhez szükséges emlősebészeti kapacitások, valamint finanszírozás.
*Célkitűzés:* A jelen vizsgálat célja, hogy kérdőíves vizsgálattal felmérje a magyar emlőrákos populáció korszerű emlőrekonstrukciós igényeit és véleményét.
*Anyag és módszer:* A vizsgálatba 500, mastectomián és azonnali vagy halasztott-azonnali emlőrekonstrukción átesett nőbeteg került bevonásra. Tizenegy kérdésből álló kérdőív segítségével történt az emlő rekonstrukciójához való ismereteknek és személyes viszonyulásnak, az esztétikai végeredménnyel és az ellátás szakmai színvonalával kapcsolatos elvárásoknak, továbbá az ellátórendszerrel és a finanszírozással kapcsolatos igényeknek a felmérése, majd elvégeztük az eredmények biostatisztikai elemzését.
*Eredmények:* A betegek medián életkora 47 év (min.–max.: 26–73) volt, döntő részük (59%; n = 294) házas volt, és 52% (n = 260) rendelkezett egyetemi végzettséggel. A betegek 70%-a (n = 348) az emlő-helyreállítás eredményeként mezítelenül is nagyjából egyforma emlőket szeretett volna. Ehhez 43%-uk (n = 217) maximum kettő, 37%-uk (n = 184) maximum három-négy műtétet vállalna. A felmérésben részt vettek 44%-a (n = 220) szerint az egészségbiztosítónak három-négy rekonstrukciós beavatkozást kellene támogatnia. A betegek 86%-a (n = 430) a daganatos emlő korszerű sebészi kezelését speciálisan képzett emlősebészre bízná.
*Következtetés:* Az emlőrák modern onkoplasztikus sebészi ellátása összetett, rendszerszintű kérdéseket vet fel. Az emlőrákos betegek jól képzett emlősebészeket szeretnének, akik az emlőrák korszerű sebészi kezelésén túl mastectomia esetén az egészségbiztosító által támogatott formában, maximum két műtéttel képesek magas esztétikai eredménnyel az emlők helyreállítására.
Orv Hetil. 2020; 161(29): 1221–1228.

**Kulcsszavak:** onkoplasztikus emlőrekonstrukció, emlőrák, mastectomia, finanszírozás, kérdőíves vizsgálat

## Assessing the needs of Hungarian breast cancer patients for modern oncoplastic breast surgical treatment

### *Questionnaire study of 500 patients*

*Introduction:* The significant need for breast reconstruction resulting from the spread of oncoplastic breast surgery raises a number of systemic issues. Clarification and regulation of the indications are needed for aesthetic changes of the reconstructed breast due to oncotherapy treatments, ageing and technical problems of implants; a number of operations, targeted aesthetic goals as well as surgical capacities and financial background should also be determined.

*Aim:* Our aim was to conduct a survey on the opinions and needs of the Hungarian breast cancer population about a modern breast reconstruction system.
*Patient and method:* A study was conducted enrolling 500 patients who underwent mastectomy with immediate or delayed reconstruction. A structured questionnaire containing eleven questions was used to measure the attitude for loss and reconstruction of breast, the expectation of cosmetic outcome and qualification of the operating surgeon and the needs relating to the health system and funding.
*Results:* The median age was 47 years (min.–max.: 26–73), 59% (n = 294) was married and 52% (n = 260) had graduated in university. The majority of women (70%; n = 348) would like to have nakedly also similar breasts after the reconstruction process. To achieve this, 43% (n = 217) and 37% (n = 184) would undergo maximum two or four procedures, respectively, supported by the national health insurance company. 86% (n = 430) would like to choose qualified breast surgeon for her treatment.
*Conclusion:* The modern oncoplastic treatment raises complex, systemic issues. Women with breast cancer would like to have qualified breast surgeons restoring their breasts by two operations, all funded by the national health insurance company.

**Keywords:** oncoplastic breast reconstruction, breast cancer, mastectomy, questionnaire study, financing

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**Rövidítések**

BRESO = (Breast Surgical Oncology) mellsebészeti onkológia projekt; BU = (breast unit) emlőterápiás szervezeti egység; CEEBCSC = (Central-Eastern European Breast Cancer Surgical Consortium) Kelet-közép-európai Emlőráksebészeti Konzorcium; EBCC = (European Breast Cancer Conference) Európai Emlőrák Konferencia; ECIBC = (European Commission Initiative on Breast Cancer) „Európai összefogás a mellrák ellen!"; EORTC = (European Organization for the Research and Treatment of Cancer) Európai Rákkutató és Terápiás Szervezet; ESO = (European School of Oncology) Európai Onkológiai Iskola; ESSO = (European Society of Surgical Oncology) Európai Sebészeti Onkológiai Társaság; EUBREAST = European Breast Cancer Research Association of Surgical Trialists; EUSOMA = European Society of Mastology; G.Re.T.A. = Group for Reconstructive and Therapeutic Advancements; NEAK = Nemzeti Egészségbiztosítási Alapkezelő; OOI = Országos Onkológiai Intézet; SD = standard deviáció; UEMS = (European Union of Medical Specialists) Európai Szakorvosi Szövetség

A Nemzeti Rákregiszter adatai alapján hazánkban évente 8300–8500 új emlőrákos megbetegedést diagnosztizálnak, és évente sajnálatosan mintegy 2200 nő hal bele a betegségbe [1]. Az emlőrák incidenciája Európában lassan, de emelkedik. Kontinensünkön még a hasonló gazdasági helyzetű országok esetében is észlelhető érdemi különbség az emlőrákellátási rendszerekben [2, 3]. A speciális igényű onkológiai ellátás egyenlőtlenségei miatt 1998-ban Firenzében az első Európai Emlőrák Konferencián (EBCC) a multidiszciplináris emlőterápiás szervezeti egységek, az ún. „breast unitok" (BU-ok) feltétel- és minőségbiztosítási elvárásai kerültek meghatározásra [4]. A European Organization for the Research and Treatment of Cancer (EORTC) és a European Society of Mastology (EUSOMA) munkacsoportja megalkotta az emlőrák gyógyításával foglalkozó szakorvosokkal szemben támasztott alapkövetelményeket, melyek lehetővé tették a szakellátás minőségbiztosítási kontrollját [5]. A European Union of Medical Specialists (UEMS) és a European Society of Surgical Oncology (ESSO) 2010-ben emlősebészeti licencvizsgát hozott létre, amelynek vizsgáztatási folyamatában az Országos Onkológiai Intézet (OOI) és a szerzők évek óta aktív szerepet vállalnak. A második Európai Emlőrák Konferencián a „Brüsszeli Nyilatkozatban" (The Brussels Statement) az akkreditációs feltételrendszer került létrehozásra [6]. 2019-ben az emlősebészeti szakismeretek intézeti, osztályos vagy egyéni szintű egységes európai akkreditációjára az ESSO, a UEMS, a European Breast Cancer Coalition (Europa Donna), a European School of Oncology (ESO), a European Breast Cancer Research Association of Surgical Trialists (EUBREAST), a European Commission Initiative on Breast Cancer (ECIBC), a magyar kezdeményezésre létrejött Central-Eastern European Breast Cancer Surgical Consortium (CEEBCSC) és a Group for Reconstructive and Therapeutic Advancements (G.Re.T.A.) életre hívta a Breast Surgical Oncology (BRESO-) projektet [7]. A BRESO-projekt megalkotta a teljes kontinensre kiterjedő, standardizált emlősebészeti curriculumot és minőségbiztosítási rendszert, valamint annak akkreditációs feltételeit. A felsorolt nyilatkozatok hatására az Európai Parlament 2003-ban állásfoglalást adott ki, amely egyértelműen támogatta a minősített BU-ok intézményrendszerének európai elterjesztését, illetve 2013-ban megjelent a komplexebb ellátásra alkalmas emlőközpontok (breast centres) minimálfeltételeinek összefoglalója [8].

Az akkreditált BU-minősítés követelménye, hogy az adott centrumban a multidiszciplináris emlőterápiás bizottsági döntést követően évente legalább 150, újonnan diagnosztizált emlőrákos beteg komplex onkológiai kezelése történjen, folyamatosan frissített szakmai protokollok alapján. Az akkreditáció elengedhetetlen része a standardizált adatbázis kialakítása és vezetése, a lakossági mammográfiás szűrés biztosítása, valamint oktatási és egyéb tudományos kutatási tevékenységek ellátása is [8–10]. A BU-rendszer hazai helyzetéről és eredményeiről munkacsoportunk 2016-ban számolt be az *Orvosi Hetilap*ban [11].

A korszerű onkoplasztikus emlősebészet elmúlt évtizedekben történő gyors elterjedése következtében napjainkban nemcsak az emlőtumor eltávolítása, hanem a nőiesség szimbólumának számító emlők esztétikailag teljes megőrzése vagy postmastectomiás helyreállítása is a sebészeti szakellátás alapvető része [12–14]. Minden olyan emlődaganatos nő számára, akinél sajnálatosan mastectomia szükséges, ellenjavallatok hiányában fel kell ajánlani és biztosítani kell tudni az emlő rekonstrukciójának lehetőségét [15]. A fentiek miatt megjelenő emlőrekonstrukciós igény már önmagában nemcsak az emlő- és plasztikai sebészeket állítja kihívás elé, hanem rendszerszintű feladatokat ró minden európai országra.

Az alap helyreállító sebészeti feladatokon túl azonban szakmailag tisztázásra várnak az onkoplasztikus működésből eredő további emlősebészeti feladatok és indikációk, amelyek értékelése és szabályozott ellátása még a jelenleg már fejlett emlősebészeti ellátórendszereknek is számos ismeretlen faktort tartalmaz. A primer, rendszerszinten tömegeken végzett emlő-helyreállítás másodlagos feladatköre jelentősen kibővül. Új ellátási feladatok jelennek meg, melyek szintén az onkológiai ellátórendszert terhelik, mint – a hosszan (akár 5–10 évig) tartó endokrin kezelések következtében ismerten fellépő testsúlygyarapodásból [16–18] vagy a kiváló túlélési eredmények alapján az életkor előrehaladásával („aging") [19–21], illetve az onkoterápiás beavatkozások (például radioterápia) következtében [22] – a rekonstruált emlőn vagy a szimmetrizált ellenoldali emlőn jelentkező esztétikai változások és az ezekből eredő további lehetséges műtéti indikációk. A fenti új szakmai elvárásokon túl a szükséges emlősebészeti ellátórendszer humánerőforrás- és műtéti kapacitásainak meghatározásához számba kell venni az onkológiai emlőrekonstrukció során beültetett implantátumok hosszú távú technikai problémáiból eredő szövődmények (például implantátumruptura), illetve állapotok (például kapszuláris kontraktúra) szakellátásának igényét is, valamint az ellenoldali emlő szimmetrizációjának megváltozásából eredő további lehetséges műtéti korrekciók tömeges jelentkezésének kérdéskörét is. Mindezen szakmai tények figyelembevételével szükséges meghatározni az onkoplasztikus rekonstrukciós beavatkozásokkal elérni kívánt, reális esztétikai végcélt, illetve az ehhez szükséges, az onkológiai ellátórendszer keretein belül elvégezhető helyreállító műtétek optimális, illetve maximális számát. Az onkoplasztikus ellátás mint standard emlőráksebészeti ellátás tehát a primer onkológiai és helyreállító sebészeten túlmutató, sokszor szakmailag nehezen meghatározható szubjektív indikációkat vagy élethosszig tartó kozmetikai változások lehetséges korrekcióit is magában foglalja.

Az új emlősebészeti igények megismerése, tudományos alapú meghatározása és reális értékelése nélkülözhetetlen alap a szükséges feltételrendszer kialakításához. Jelenleg hazánkban a Nemzeti Egészségbiztosítási Alapkezelő (NEAK) az eltávolított daganatos emlő helyreállítását minden magyar biztosított számára finanszírozza, ugyanakkor ezen összetett új indikációkat jelenleg rendszerszinten nem ismeri fel, és ennek megfelelően szakmailag nem is kezeli. Az emlő-helyreállítás jelentős vívmány az emlőrákban szenvedő magyarok számára, de a rekonstrukciós igény emelkedése és az indikációs kör kibővülése esetén e népbetegség magas esetszámánál a közeljövőben lavinaszerű, szabályozatlan helyzet alakulhat ki, amelynek megelőzése szakmai ismereteket és tervezést igényel.

A fentiek alapján a jelen kérdőíves prospektív vizsgálat célja a korszerű onkoplasztikus ellátással kapcsolatban a betegek igényeinek és elvárásainak megismerése és tudományos igényű elemzése.

## Módszer

A vizsgálatba az OOI Emlő-Lágyrész Daganatsebészeti Osztályán 2015. január és 2017. december között 500, emlőrák miatt mastectomiára szoruló nőbeteg került bevonásra, akiknél vagy a daganatos emlő eltávolításával egy időben (azonnali) vagy egy időben megkezdett (például szövettágító expander beültetésével) és második lépésben befejezett (halasztott-azonnali emlő-helyreállítás) emlőrekonstrukció történt. A vizsgálatot és a kérdőívet az intézet Etikai Bizottsága jóváhagyta. A közlemény nem sérti a helsinki, illetve a tokiói deklaráció követelményeit [23].

A betegek kivizsgálása és kezelése minden esetben az OOI által alkalmazott aktuális nemzetközi és hazai irányelvek szerint történt [24–26]; a műtéteket az intézeti Emlőrák Terápiás Bizottság döntését követően tapasztalt és nemzetközi szakvizsgával minősített emlősebészek és plasztikai sebészek végezték.

A kérdőívek az emlőműtétet megelőző napon kerültek kiosztásra a betegeknek, kitöltésük a beavatkozás előtt történt önkéntesen és anonim módon.

Az életkorra, a legmagasabb iskolai végzettségre és a családi állapotra irányuló kérdéseket követően a kérdőív további tizenegy, strukturált kérdést tartalmazott. A kérdések a betegeknek az emlő elvesztésével kapcsolatos érzelmi és pszichés állapotára és viszonyulására, illetve az emlő helyreállításával kapcsolatos ismereteikre és akaratukra, valamint a rekonstruált emlők esztétikai végeredményével és az operáló orvos szakképzettségével kapcsolatos elvárásaikra, továbbá az emlősebészeti ellátással

**1. táblázat** | Az onkoplasztikus ellátás felmérését vizsgáló strukturált kérdőív és a kapott válaszok

| 1. Mennyire zavarja az emlő elvesztése vagy esztétikai deformitása egy 1-től 10-ig terjedő skálán? (1: nem zavar – 10: rettentően zavar) | | | |
|---|---|---|---|
| n | Átlag | Medián | Standard deviáció |
| 495 | 8 | 9 | 3 |
| Hiányzó adat = 5 (1%) | | | |
| 2. Mikor történik Önnél az emlő rekonstrukciója? | | | |
| A daganat eltávolítása után hónapokkal, évekkel. | | A daganat eltávolításával egy időben. | |
| 167 (33%) | | 307 (61%) | |
| Hiányzó adat = 26 (5%) | | | |
| 3. Ön reálisan mit vár az emlő helyreállításától? | | | |
| Legyen „valamiféle” emlőm. | Legyen melltartóban szép dekoltázsom. | Legyen szebb emlőm, mint a betegség előtt. | Legyenek tökéletes emlőim. |
| 46 (9%) | 194 (39%) | 140 (28%) | 99 (20%) |
| Hiányzó adat = 21 (4%) | | | |
| 4. Önnek reálisan milyen mértékű szimmetria fogadható el az emlő-helyreállítás végén? | | | |
| A természetes emlőim sem voltak szimmetrikusak, ezért nem fontos, ha nem egyformák a rekonstruált emlőim. | Legyenek ruhában vagy melltartóban nagyjából egyformák a rekonstruált emlőim. | Legyenek mezítelenül is nagyjából egyformák a rekonstruált emlőim. | Csak a teljes szimmetria az elfogadható számomra. |
| 12 (2%) | 105 (21%) | 348 (70%) | 32 (6%) |
| Hiányzó adat = 3 (1%) | | | |
| 5. Maximum hány műtétet vállalna altatásban az emlők helyreállításához? | | | |
| Maximum kettőt. | Maximum 3-4-et. | Maximum 5-6-ot. | Akármennyit. |
| 217 (43%) | 184 (37%) | 25 (5%) | 67 (13%) |
| Hiányzó adat = 7 (1%) | | | |
| 6. Ön szerint hány rekonstrukciós műtét „állami” finanszírozása jogos egy általános biztosítottnak, ha ismert, hogy a lehetőségek nem végtelenek? | | | |
| Maximum kettőnek. | Maximum 3-4-nek. | Akármennyinek. | |
| 107 (21%) | 220 (44%) | 157 (31%) | |
| Hiányzó adat = 16 (3%) | | | |
| 7. Ön szerint a most helyreállítandó/helyreállított emlők, ha idővel például az öregedéssel megváltoznak, akkor az: | | | |
| nem indokol további helyreállítást, mert természetes folyamat. | természetes folyamat, amely a jövőben egyéni esztétikai sebészeti kérdés. | évtizedek múlva is rekonstrukciós sebészetnek és nem esztétikai műtétnek számít. | |
| 71 (14%) | 275 (55%) | 139 (28%) | |
| Hiányzó adat = 15 (3%) | | | |
| 8. Beleegyezne-e abba, hogy az Ön emlő-helyreállítását ne plasztikai sebész szakorvos, hanem általános sebész szakorvos végezze? | | | |
| Igen. | | Nem. | |
| 40 (8%) | | 448 (90%) | |
| Hiányzó adat = 12 (2%) | | | |
| 9. Ön szerint a daganatos emlők korszerű sebészeti ellátását (onkoplasztika, emlő-helyreállítás stb.) ki végezze hazánkban? | | | |
| Általános sebész, mint hazánkban ma a legtöbbször. | Nőgyógyász, mint hazánkban ma néhány helyen. | Plasztikai sebész. | Speciálisan felkészült emlősebész, ha kell, plasztikai sebészt is bevonva. |
| 5 (1%) | 3 (1%) | 54 (11%) | 430 (86%) |
| Hiányzó adat = 8 (2%) | | | |
| 10. Ön szerint mennyire fogadható el, hogy hazánkban a XXI. században csak egy-két kórházban van speciálisan felkészült, korszerű emlősebészet? | | | |
| Így jó, ahogy van. | Sajnálatos, de ez van. | Nagyon sajnálatos, aki jobbat akar, az elmegy magánellátásba. | Elfogadhatatlan, biztosítani kell a korszerű, specializált emlő-sebészetet. |
| 2 (1%) | 51 (10%) | 46 (9%) | 394 (79%) |
| Hiányzó adat = 7 (1%) | | | |
| 11. Ön szerint gyógyulását érdemben befolyásolja-e, hogy emlősebész specialista operálja? | | | |
| Nem befolyásolja. | Befolyásolja. | Nagyon befolyásolja. | Az egyik legfontosabb. |
| 14 (3%) | 54 (11%) | 111 (22%) | 316 (63%) |
| Hiányzó adat = 5 (1%) | | | |

szemben rendszerszinten támasztott igényekre és azok feltételrendszerére (például finanszírozás) vonatkoztak *(1. táblázat)*.

A kapott válaszok adatai, valamint azok szociális összefüggései Fisher-egzakt teszt és khi-négyzet-próba alkalmazásával kerültek biostatisztikai elemzésre. A 0,05 alatti p-érték számított szignifikánsnak.

A statisztikai analízis Statistica 12.0 (StatSoft, Tulsa, OK, Amerikai Egyesült Államok) és PAST version 1.86b szoftverek segítségével történt [27].

## Eredmények

A nőbetegek medián életkora 47 év (min.–max.: 26–73) volt. A felmérésben részt vettek 52%-a (n = 260) rendelkezett felsőfokú végzettséggel, és nagyobb részük (59%; n = 294) házasságban élt. A vizsgált populáció adatait a *2. táblázat* foglalja össze.

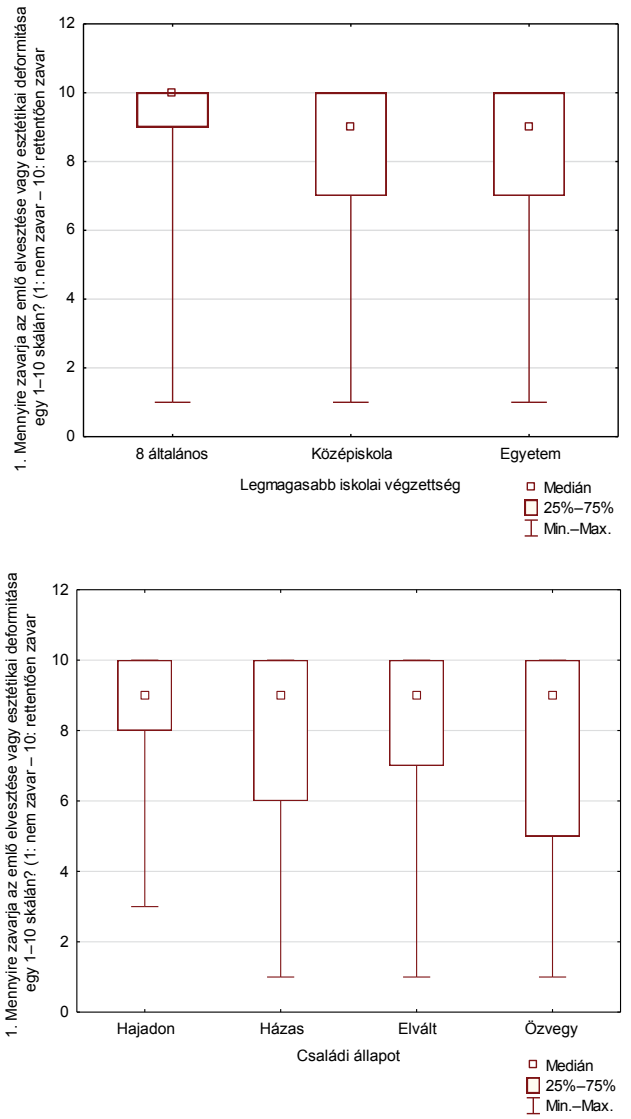
Érthetően az emlő elvesztése jelentősen zavarta a megkérdezetteket, az 1-től 10-ig terjedő skálán átlag 8 ± 3 (átlag ± standard deviáció [SD]) értéket adtak az erre a kérdésre vonatkozó válaszok; illetve a válaszok között sem az iskolai végzettség, sem a családi állapot tekintetében nem volt különbség *(1. ábra)*.

Az esetek közel kétharmadában (61%; n = 307) történt azonnali rekonstrukció, míg 167 beteg (33%) esetén az emlő-helyreállítás halasztott-azonnali módon történt, és a válaszadás a daganat eltávolítását követően hónapokkal vagy évekkel később, a rekonstrukció befejező lépésekor történt meg.

A válaszok alapján a megkérdezett nők 39%-a (n = 194) megelégedne a melltartóban szép dekoltázst eredményező emlőkkel, azonban 28%-uk (n = 140) az eredetinél szebb, 20%-uk (n = 99) pedig egyenesen tökéletes emlőket szeretne a rekonstrukciós folyamat végén. Az elvárások tekintetében szignifikáns összefüggés mutatkozott az iskolai végzettséggel: a magasabb iskolai végzettség magasabb elvárásokkal társult (p<0,05). A szimmetria tekintetében határozott véleményt képviseltek a

**2. táblázat** | A vizsgálatban részt vett betegek általános tulajdonságai

| Életkor | | | | |
|---|---|---|---|---|
| n | Átlag | Medián | Minimum | Maximum |
| 485 | 48 | 47 | 26 | 73 |
| Hiányzó adat = 15 (3%) | | | | |
| A legmagasabb iskolai végzettség | | | | |
| 8 általános | | Középiskola | | Egyetem |
| 7 (1%) | | 218 (44%) | | 260 (52%) |
| Hiányzó adat = 15 (3%) | | | | |
| Családi állapot | | | | |
| Hajadon | | Házas | Elvált | Özvegy |
| 52 (10%) | | 294 (59%) | 119 (24%) | 20 (4%) |
| Hiányzó adat = 15 (3%) | | | | |




**1. ábra** | Az emlő elvesztésének értékelése iskolai végzettség és családi állapot szerint (boxplot)

betegek, nem volt különbség sem a családi állapot, sem az iskolázottság tekintetében: a nők 70%-a (n = 348) kívánna a rekonstrukciós folyamat végén mezítelenül is nagyjából egyforma emlőket.

Az emlők optimális esztétikai végeredményéhez a felmérésben részt vevők 43%-a (n = 217) maximum kettő, 37%-a (n = 184) akár három vagy négy műtétet is vállalna.

A beavatkozások finanszírozásának kérdésében megoszlottak a vélemények: 44% (n = 220) szerint maximum három-négy, 21% (n = 107) szerint legfeljebb csak két műtétet kellene térítenie az egészségbiztosítónak, míg a betegek közel harmada (31%; n = 157) van azon az állásponton, hogy akármennyi beavatkozásra van is szükség, mindegyiket fizetnie kellene az állami biztosítónak. A középiskolai végzettségűek kevésbé tartják jogosnak állami finanszírozásból a több műtétet, az egyetemi végzettségűek inkább (p<0,05).

A betegek 55%-a (n = 275) gondolja úgy, hogy a helyreállított emlőknek az életkor miatt bekövetkező változása egyéni esztétikai, plasztikai sebészeti kérdést jelent, azonban 28% (n = 139) szerint ez akár évtizedek múlva is a rekonstrukciós műtétsorozat, tehát az onkológiai helyreállító sebészet és nem az esztétikai sebészet megoldandó feladatát képezi.

Egyértelmű állaspontot képviselnek a betegek a beavatkozást végző orvossal kapcsolatban: 90%-uk (n = 448) plasztikai sebészre bízná a rekonstrukciót, továbbá 86%-uk (n = 430) szerint a daganatos emlők korszerű ellátását speciálisan felkészült emlősebészeknek kellene végezniük a jelenlegi általános sebészeti ellátással szemben.

A válaszadók döntő többsége (79%; n = 394) nem tartja elfogadhatónak, hogy jelenleg Magyarországon csak egy-két, speciálisan felkészült emlősebészeti központ működik, míg 10% (n = 51) beletörődik a jelenlegi helyzetbe, és további 9% (n = 46) úgy vélekedik, hogy a jobb ellátás érdekében a magánellátás felé szükséges fordulni.

A betegek 96%-a (n = 481) szerint a gyógyulást érdemben befolyásolja, hogy emlősebész végzi-e a műtétet, 63% (n = 316) pedig egyenesen úgy gondolja, hogy ez az egyik legfontosabb tényező egészsége visszanyerése érdekében.

## Megbeszélés

A modern onkoplasztikus szemlélet elterjedése paradigmaváltást eredményezett az emlőrák ellátásában [28–30]. A sebészi kezelés az emlődaganat eltávolítását jelentő műtéttől az emlők teljes helyreállítását is magában foglaló komplex, akár kétoldali műtétek vagy műtéti sorozatok felé mozdult el. Ez számos rendszerszintű feladatot vet fel, például azt, hogy az onkológiai kontrollokkal párhuzamosan folytatandó a rekonstruált emlők élethosszig tartó plasztikai sebészeti utánkövetése és szükséges kozmetikai korrekciói. A fenti igények, indikációk az emlő onkológiai ellátásában újszerűek, melyek pontos meghatározása, az ellátás feladatkörének és tárgyi, valamint humánerőforrás-kívánalmainak tisztázása a korszerű, betegközpontú ellátórendszer kialakítása és magas szintű, hosszú távú üzemeltetése céljából elengedhetetlen. Mindezek alapját képezi a betegek igényeinek és elvárásainak megismerése és elemzése.

A jelen tanulmány az emlő elvesztésén és rekonstrukciós folyamaton átesett nőbetegeknek a rendszerrel kapcsolatos igényeit és elvárásait mérte fel. Az eredményekből látható, hogy az emlő elvesztése iskolai végzettségtől és családi állapottól függetlenül jelentősen zavarja a nőbetegeket *(1. ábra)*. Ezek az adatok megfelelnek azoknak az eredményeknek, amelyeket munkacsoportunk 2014-ben közölt, 500 nőbeteg 2010 és 2011 közötti kérdőíves vizsgálata alapján [28]. A felmérés szerint a betegek 30%-a (n = 148) közepesen, 40%-a (n = 198) nagyon félt az emlő elvesztésétől, közel 50%-uk (46%; n = 224) szeretett volna rekonstrukciót, de erről szinte semmit (32%; n = 158) vagy nagyon keveset (56%; n = 279) tudtak [28]. Az intézetben folyó onkoplasztikus emlősebészeti tevékenység alapján, a 2017–2018-ban elvégzett ugyanazon kérdőíves felmérés megismétlése szerint a nők továbbra is ugyanúgy félnek az emlő elvesztésétől, de a korábbi adatokkal (10%; n = 48) szemben a megkérdezetteknek már a 30%-a (n = 152) ismerte az emlőrekonstrukciós lehetőségeket, mely információkat főleg a sebésztől (52%; n = 258) vagy az internetről (27%; n = 135) gyűjtötték be. Ezek alapján kimondható, hogy az emlő elvesztése jelentős mértékben terheli pszichésen az emlőrákos betegeket szociális helyzettől és iskolai végzettségtől függetlenül, tehát az onkoplasztikus ellátórendszer kiterjesztése hazánkban indokolt és szükséges. Az elmúlt 6–8 évben az onkoplasztikus szemlélet a magyar nők között elterjedt és ismertté vált, amivel párhuzamosan nő a lakosság igénye is erre a speciális egészségügyi szolgáltatásra, melyet az ellátórendszernek ki kell tudnia elégítenie.

A páciensek a műtétek esztétikai eredményét tekintve magas elvárással rendelkeznek, összesen a nők közel fele (48%; n = 239) szeretne az eredetinél is szebb (28%; n = 140) vagy tökéletes (20%; n = 99) emlőket a rekonstrukciós folyamat végén. A reális elvárásokkal kapcsolatban történő preoperatív betegfelvilágosítás kiemelt fontosságú, ugyanis az onkoplasztikus beavatkozások nem esztétikai műtétek, és bár technikájukból eredően gyakran az esztétikai műtétekkel megegyező, magas szintű eredményekre képesek, teljesen alárendeltek az onkológiai beavatkozásoknak (például a reszekció helye, mértéke, radioterápia stb.), így eredményességüket a plasztikai sebészeti beavatkozáson túl számos egyéb tényező is befolyásolja [31].

A felmérésben részt vett nőbetegek döntő része (70%; n = 348) családi állapottól és végzettségtől függetlenül kívánna a rekonstrukciós folyamat végén mezítelenül is nagyjából egyforma emlőket. Tekintettel arra, hogy a legtöbbször implantátumalapú postmastectomiás rekonstrukciók során a két emlő szerkezete különbözik, idővel az emlők aszimmetriája fokozódni fog, mivel a felvarrt saját egészséges emlő máshogy fog viselkedni biológiai tulajdonságai miatt, mint a csak implantátumból és bőrből álló emlő. Ez alapján a szimmetria időbeli változása miatti másodlagos műtéti igények jelennek meg a betegek részéről.

A kívánt magas kozmetikai eredményt a nők leginkább kettő, de maximum három-négy műtét segítségével szeretnék elérni, melyeket véleményük szerint az egészségbiztosítónak kellene térítenie. Egyészt a jövőben kerülni szükséges az onkológiai finanszírozású esztétikai műtéteket, aminek kérdésfelvetése is nehezen megoldandó etikai és szakmai problémát jelent, másrészt a műtéti so-

rozatból álló kezelés óriási megterhelést jelent az ellátórendszer számára, mintha több száz vagy ezer esettel nőne az emlőrák miatt operáltak éves száma. Jelenleg a rendszer ezt elemeiben képes, de összességében kérdéses-e, hogy képes lenne biztosítani, így ebben az irányban a betegek, a szakma és a szakmapolitika együttes munkájára van szükség.

A betegek sebészi kezelésüket specializált centrumokban, speciálisan képzett emlősebészekre bíznák, mert véleményük szerint gyógyulásukat ez érdemben befolyásolja. Az emlőrák kezelésében az emlősebész is önálló prognosztikai faktor [32], de a BU-ok hazai elterjesztése, minőségbiztosítása, valamint a BRESO-akkreditációval a betegek túlélése és életminősége is tovább javítható a XXI. században [7].

A hazánkban tapasztalt mastectomiát követő onkoplasztikus emlő-helyreállítás iránti igény megfelel a nemzetközi trendeknek: brit tanulmány szerint az emlőeltávolításra váró nőbetegek 50%-a [33], míg az *Ananian és mtsai* által végzett francia tanulmány szerint a megkérdezettek 81%-a szeretne rekonstrukciót [34]. A nemzetközi helyzethez hasonlóan vizsgálatunk alapján a magyar betegek fő információs forrása szintén a sebész, illetve az internet [35, 36]. Az érintett nők igényeinek megismerése, a megfelelő tájékoztatás, a hozzáférhetőség növelése, a betegutak megszervezése és az egészségügyi rendszer megfelelő strukturálása nélkülözhetetlen az onkoplasztikus emlőrákellátás magas szintű kiterjesztéséhez [37, 38].

## Következtetések

A korszerű onkoplasztikus ellátás új, összetett, rendszerszintű onkológiai és helyreállító sebészeti szakmai kérdéseket vet fel, amelyek a betegek informáltságával, a humánerőforrás szakképzésével, az ellátórendszer kapacitásaival és a finanszírozásával kapcsolatos új feladatokat eredményeznek. Az emlőrákban szenvedő betegek jól képzett emlősebészek által szakmai központokban végzett korszerű műtéteket szeretnének, amelyektől testi és lelki gyógyulásukat bizalommal remélhetik.

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*Anyagi támogatás:* A közlemény megírása, illetve a kutatómunka anyagi támogatásban nem részesült. A klinikai feldolgozás a 2019-es Témakiválósági Program (TUDFO/51757/2019-ITM) támogatásában részesült.

*Szerzői munkamegosztás:* A szerzők egyenlő mértékben vettek részt a kutatómunkában és a kézirat elkészítésében. A cikk végleges változatát valamennyi szerző elolvasta és jóváhagyta.

*Érdekeltségek:* A szerzőknek nincsenek érdekeltségeik.

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