

## **Breast cancer. Modern aspects of surgical treatment. (from data of the National Cancer Institute)**

I.Shchepotin<sup>1</sup>, I.Smolanka<sup>1</sup>, S.Skliar<sup>1</sup>, O.Sydorchuk<sup>2</sup>,  
I.Motuzyuk<sup>2</sup>, O.Ivankova<sup>1</sup>, A.Kostriba<sup>1</sup>

National cancer institute<sup>1</sup>

National medical university named after O.O. Bogomolets<sup>2</sup>

### **Summary.**

Morbidity and Mortality from Breast Cancer in Ukraine and remote results of treatment of 11272 patients of breast cancer, which passed treatment in the National cancer institute are analysed for 20 years. The evolution of surgical methods of treatment of patients with breast cancer has submitted and modern principles of complex treatment of patients with breast cancer are described. Actuality of breast-conserving cancer surgery, plastic and reconstructive breast surgery is described for women with breast cancer, in the conditions of modern society.

**Key words:** breast cancer, morbidity, surgical treatment, breast-conserving cancer, surgery efficiency of treatment, quality of life, results of treatment, fast track surgery, reconstructive breast surgery.

### INTRODUCTION

A considerable increase of breast cancer (BC) frequency is the one of the most characteristic features of distribution of malignant tumors among the women of the economically developed countries. BC occupies the first place in the structure of oncological pathology in the world. The level of BC morbidity in Ukraine for last 45 years (1965-2010) has grown from 17,6 to 69,7 on a 100 thousand woman population. The every year increase of this oncological pathology presents more than 2 percent. There were 128 thousand women with BC at the beginning of 2010 in Ukraine. According to Bulletin of National cancer registry of Ukraine in 2011 there were 16325 new cases of disease, 7643 women died due to BC [5]. Morbidity and mortality due to BC rates over the recent years in Ukraine are presented in the table 1.

The prevalence of BC in Ukraine has the expressed territorial character. Morbidity of population dominances at south-east region that has the greatest environmental pollution by carcinogenic substances due to the developed industry and agriculture.

It is determined that more then 37 % patients among diseased and more then 30 % among the deceased are working-age persons, that results to the considerable losses of vital woman population potential of Ukraine [5]. Increasing of efficiency of complex treatment and improving of quality of life radically operated patients is actual now considering the number of persons, diseased in reproductive (38,2 %) and working (39,4 %) age.

The surgical method is the most significant component of complex BC patients treatment. Gradually with the development of clinical oncology, surgical treatment at the initial stages of disease diminished from radical and modified mastectomies to organ preservative operations (quadrantectomy and tumorectomy). Until 80th the mastectomy by Halsted was standard operation for BC, including the small tumors. Halsted treatment approach allowed to cure the early stage disease. It stimulated early diagnostics progress. It was 50 % patients with advanced BC 10 years ago. For the last 5 years 1-2 stage is determined in 70 % patients. At present the majority of patients at diagnosis BC a primary tumor has small sizes or determined only radiographically (table 2).

The breast preserving is very actual at this category of patients, considering psychosocial factor in their complete rehabilitation. The questions of early rehabilitation and development of saving treatment methods that allow to reduce the duration of invalidity stay, to improve life quality of operated patients become actual in modern clinical oncology.

Identification of initial stages BC reduces the volume of surgical operations and increases the role of systemic treatment due to more clear understanding of the disease [1-4]. In the last decade the cardinal changes of tactics of conduct and treatment of BC patients. Firstly, at the initial stages of tumor process extended radical operative interventions changed on less destructive functionally-saving and organ preservative. Secondly, indications to the organ preservative and restorative operations in patients with the locally advanced BC due to wide introduction of neoadjuvant antitumoral therapy. The greater amount of patients, especially reproductive age renounces for mastectomy and insists to preserve the organ. Advantage of organ preservative operations before mastectomies is an important factor, that determines the complete social and labor rehabilitation of the operated women. The whole category of new operations was developed as alternative to the mastectomies with the simultaneous surgical rehabilitation of patients.

Recommendations of previous schools, that mark "rational radicalism" of surgical interferences and at treatment of BC nodular forms consider Patey`s or Madden`s mastectomies that remain widespread to this time. However, these operations are accompanied by complications that result in disability more, than 50 % of patients, conduce not only to the physical and moral damage but also to deep psychological disorders that brake the processes of adaptation, considerably reduce quality of life of the operated women [1-4].

The first positive results of realization of organ preservative operations (OPO) BC patients were published in 1960. By the 1990 appeared a number of scientific papers in which it was observed that the application is accompanied by a traumatic surgical complications (postmastectomy syndrome) and aesthetic disabilities assumed that lean OPO can provide the same survival rate, but excluding most of the complications. Next to the modified radical mastectomy organ preservative treatment became the standard of local BC treatment. There are problems with introduction of preservative treatment in practical oncology in Ukraine. On the one hand – it is conservatism that can not be explained (organ preservative and restoration operations are not executed at all); on the other hand – this is unwise application of method, without the observance of oncological principles, that is accompanied by the high percent of local recurrence.

## SUBJECTS AND METHODS

In the National Cancer Institute from 1990 to 2011 to examine the effectiveness of combined treatment with organ and restorative operations, conducted research, which included

11,272 BC patients. Analysis of the treatment based on the results of years of research conducted in the research department of breast cancer and her reconstructive surgery.

In recent years, increased number of patients with BC, with the I - IIA stage of disease (Table 3). This fact indicates the improvement of diagnostics BC in Ukraine (introduction of screening mammography can detect small tumors) and creates conditions for OPO. Perfection of protocols of chemotherapy and hormonotherapy promotes efficiency of treatment BC patients and improves their survival after OPO. This allows to pay special attention to OPO and restoration operations at surgical treatment of BC and widely implement them. Characteristics and evolution of surgical treatments, that were conducted to the patients in the National Cancer Institute for 20 last years are presented in a table 4.

It is noted that the percentage of radical mastectomy (RME) gradually decreased from 96.24% in 1990-1994 to 45.5% in 2011, the volume of the extended mastectomy (removal of both pectoral muscles) reduced to functional lean (with preservation of the pectoral muscles). Patients with BC I - II stages in the absence of contraindications, is performed mainly OPO, and widely implemented reconstructive and restorative surgery.

## RESULTS AND DISCUSSION

In the analysis of long-term results of treatment of patients with BC I-IIA stages, we found no statistically significant difference in efficacy during radical mastectomy and functional lean operations aimed at maintaining body functions and upper extremity (Table 5). This conclusion is not changed after 10 years of observation, long-term outcomes have improved, both found that the development of local recurrence after quadrantectomy followed by conservative or surgical treatment to the extent mastectomy does not affect the prognosis. Long-term results OPO during the initial stages of the disease were even better than during the classical radical mastectomy. Found that the size of the tumor to 2 cm and the absence of metastases in regional lymphatic nodes almost 100 % of patients after OPO live more than 5 years after mastectomy - 93.55%. When tumor sizes of 2 to 3 cm and the absence of regional metastases, 5-year survival in lean operations is reduced, but not statistically different from those in the group with conducting extended operations. But the size of tumors 4-5 cm and conducting the first phase of a comprehensive treatment operations (without neoadjuvant chemotherapy) - 5-year survival rates are greatly reduced and are in accordance with OPO - 63.4% after mastectomy - 70.2% .In the study of the direct and immediate treatment results revealed that as at OPO, and when mastectomy, the incidence of local regional recurrence in stage I and IIA were not statistically different. Relapses occur in 2.1% of BC patients with T1-2N0M0 - at OPO, and 1.7% - with mastectomy ( $P > 0.05$ ). When IIB and IIIA stages of the process, this difference is probably greater. In lean operations recurrences were detected in 4.3%, while mastectomy - in 1.8% of patients ( $P < 0.05$ ). The results of treatment showed that the risk of local recurrence increased in invasive ductal cancer in background pronounced breast dysplasia, with a high degree of malignancy of the tumor and in its hypervascularization, presence of cancer in situ in the tissue that surround tumor. The goal of OPO is to achieve efficient local control by excision of the tumor tissue adjacent to the tumor and the express histologic study of resection margin. Adjuvant radiotherapy is necessary in all cases of OPO in dose of 45-50 Gy for prophylactics of locoregional recurrence [2,6].

Short-term results analysis of OPO showed significant reduction of postoperative complications risk. At such operations the function of the upper extremity recovers in a 5-8 days (after mastectomies - only in 1-1,5 month, sometimes in a half-year, from what patients often are forced to pass to invalids). Postoperative wounds after OPO healed over much faster, almost never observed marginal necrosis, healing was by primary intention. One week after surgery the

patient is transferred to outpatient treatment. After mastectomy patients were hospitalized from 3 weeks to 1.5 months in 28% of patients were recorded marginal necrosis and partial secondary healing wounds.

OPO are deserved the treatments of early BC already accepted as a standard [14 - 16], but they may not always be effective, equal efficiency modified RME. The careful selection of patients, margin resection control, realization of postoperative RT are components that allow to conduct radical organ preservative treatment. We consider that realization of OPO with further RT is the major component of complex treatment at the early BC stages and also in case of complete or partial tumor response after neoadjuvant chemotherapy in patients with the locally advanced disease. The method of choice for young patients with IIB - IIIA stage at the central location of the tumor and defeat of nipple-areolar complex now count a nipple-sparing subcutaneous mastectomy with simultaneous implantation or reconstruction. In this case a neoadjuvant chemotherapy is conducted to decrease the sizes of tumor and perform the most preserving operation.

Complex therapy based on prognostic factors makes it possible to successfully use OPO in most patients. This also contributes to the control of radical surgery by examining the margins of resection on presence of tumor cells [10,11]. Found that careful assessment of the performance margins of resection OPO can help reduce the frequency of relapses. Analysis of disease-free survival advantage demonstrated long-term results of treatment for more than 8-12% in groups where during surgery evaluated the margins resection. We think that it is necessary to make a histological examination of the removed tissues and margins of resection. The margins of resection study for the presence of tumor cells allows to control the local disease, efficiently determine the extent of surgery, follow oncological principles and increase effectiveness of treatment [6, 9, 10, 11].

Expanding indications for the use of organ treatment can be justified only in the development of clear selection criteria tactics surgery. To determine the feasibility of neoadjuvant therapy and self-determination of prognostic criteria and considering the results of immunohistochemical studies is required before planning of operations.

Criteria for choosing operations tactics:

1. Considering the location of the tumor.
2. Considering the size of the tumor and correlation between the size of tumor and the size of breast.
3. Determination the possibility of distance from the primary tumor (>2 cm)
4. Considering the presence of pathognomonic for malignant lymph nodes (LN) features: according to a comprehensive ultrasound or CT scan - a conglomerate LN presence, absence of LN bias, rounded or indefinite form, the loss of characteristic acoustic structural organization, uncertain or vertical orientation, middle (II) and high (III) degrees of vascularization, vascular arrangement of color signals in the middle.
5. Defining features of block tumor removal with the lymph pathways and regional lymph nodes.
6. When you delete a sector or quadrant the margins of resection study for the presence of tumor cells is the mandatory condition for planning of operation volume.

The important aspect of modern researches at planning of rational volume of surgical interference at BC is individualization of operations on the lymph pathways and detection of sentinel node. It is known that radical I-II-III levels dissection complicates the postoperative period, contributes postmastectomy syndrome, reduces immunological protective response of patients. Recognition of the concept lymphogenic dissemination sequence was the basis for sentinel node biopsy during radical surgery for early stages BC. At present in Ukraine increased possibility of early BC diagnosis and number of patients with tumors of the small (often less than 1 cm) sizes (Table 2). It is also confirmed by the data of the National Cancer Institute (Table 3). Possible presence of metastases in the axillary LN in patients with initial stages does not exceed 3-6% [1, 4, 13, 14]. This means that perform axillary dissection more than 90% of women lead to the removal of intact LN, which affects the immune status of patients. In the National Cancer Institute during surgery in BC patients with T in situ and T1-2 (tumor size less than 3 cm) intraoperative detection is conducted and the signal node status is investigated for tumor staging in patients with clinically defined regional metastases, which allows plan required and reasonable amount of dissection.

Indications for intraoperative sentinel node biopsy is the presence of a malignant tumor in the breast, the size of which does not exceed 3 cm, and determine clinical and radiographic methods no damage spread to regional lymph collector. Sentinel lymph node (SLN) detection is performed by using chrome lymphography (dyes), or by using radiopharmaceuticals. It is currently optimal the combination of preoperative ultrasound studies and SLN detection using radioisotope methods and chrome lymphography that increase diagnostic accuracy. According to the literature it is known that the absence of metastases in the SLN at the initial BC stages may be evidence of lack of affection all regional LN [13]. So if morphological rapid methods proved negative SLN state in BC patients with T in situ and T1N0M0 it is only SLN resection recommended but not dissection. Adherence to these principles to avoid unnecessarily traumatic surgery and reduce postoperative complications that significantly enhance the quality of life of patients, reduce the term of their disability and the cost of hospital treatment.

Since the development of OPO methods, SLN detection in BC patients - is the second most significant advance in surgical treatment. At present, the statement to be executed complete regional dissection to radical surgical treatment is refuted in early BC when SLN does not contain metastases. Prevalent choice principle of tactics surgery selection at BC must be sick woman's health and quality of life. Quality of life of patients with intact or not removed regional lymph collector in combination with OPO surgery is much better and can be compared to the life of a healthy person.

On the 11-th and 12-th St. Gallen Breast Cancer Conferences (St. Gallen, 2009, 2011), it was decided that the failure to perform axillary dissection is advisable in BC patients with low risk of relapse, such as the early stages of disease in N0, G1, at max. 1 LN impressed among the 5 studies, with ER / PgR-positive and HER2-negative.

Today in conducting regional dissection the following recommendations are considered to be adopted:

- for patients with pN0 (sn) should give up axillary dissection, and enter it in the standards,
- for patients with pN0 (and +) (sn) should give up axillary dissection only in case of the favorable properties of the tumor (considered mandatory preliminary immunohistochemical study of the tumor using a trepan-biopsy),
- when deciding whether to dissection in patients with pN0 (and +) (sn) must consider tumor size, malignancy grade, receptor status.

Thus, by modern surgical interferences at treatment of patients with the initial BC forms or at the achievement of objective response after neoadjuvant chemotherapy there are the operations aimed at preserving or restoring the breast in the amount determined after the SLN detection and study of resection margin.

To improve the quality of life of patients receiving treatment for BC we referred to the existing multi-modal program «Fast track surgery» (FTS - fast recovery surgery) or «Enhanced Recovery After Surgery» (ERAS - speed up recovery after surgery), first developed by Henrik Kehlet [12]. The purpose of the program «Fast track surgery» - is a recovery as soon as possible by reducing injuries and struggle with postoperative pain, decreasing body's response to stress and the risk of thromboembolic complications (due to precise actions surgical and anesthetic teams), accelerating term recovery by early mobilization [7, 9, 12]. The importance of early activation is one of the priorities of the postoperative conduct of patients. Expediency of long-term postoperative wound drainage is discussed. Drainage tubes pose significant psychological and physical discomfort, support a patient in complex, detain social rehabilitation. In recent years numerous randomized studies show the link between an increase in the number of infectious complications and long-term routine postoperative wound drainage [7,12]. To date no evidence of long-term feasibility of drainage as a standard manipulation, often observed rejection of it.

We developed an algorithm of conducting BC patients, which is adapted from the principles of FTS [6,7,8,9]. It includes preoperative stage: a survey of patients according to the "Standards for the diagnosis and treatment of cancer patients" (Ministry of Health "On approval of the protocols of care in" Oncology "from 17.09.2007 № 554) and, if necessary, the study of comorbidity, psychological preparation of the patient, of conversations explaining the need to perform standard methods and anticancer treatment, need for compression underwear, etc.; operation planning based on the selection criteria for surgical intervention tactics and by the developed algorithm [6,8,9] (Table 6). When planning the breast reconstruction by autologous tissues doppler vascular ultrasound of graft should perform to assess its circulation and optimizing the selection of donor tissue [6].

Intraoperative phase includes: saving relation to gland tissue, if necessary, surgery is performed by two teams, the introduction of broad-spectrum antibiotics at the start of the operation, the use of infusion solutions with temperature 37°C, a thorough hemostasis during surgery, the use of cosmetic suture material, reducing compression of vascular pedicle during reconstructive operations and reduce tissue tension, if necessary, use biomaterials [7].

The postoperative stage includes: early activating of patient (3-4 hours after surgery), a non-narcotic analgesics anesthesia, minimizing of antibiotics setting, use of low vacuum drainage, if possible, quick removal drainage, using of compression underwear, warm up the transplant to 37°C after surgery and during the first 24 hours, from the next day after surgery use the topical heparin gel (hepatrombin, Lioton, etc.), if necessary, sonographic monitoring wounds, stimulation of peristalsis (after TRAM flap breast reconstruction).

To evaluate the use of FTS programs we analyzed the results of preserving and reconstructive plastic treatment 1199 BC patients with I-III A stages of disease (T1-4N0-2M0) aged 25 to 65 years. At the National Cancer Institute all patients received complex treatment according to national standards. Patients were divided according to the method of conduct (Table 7).

Postoperative complications after reconstructive intervention in one breast were observed in 4.2% of patients in group FTS and 4.9% in the standard conduct. For bilateral intervention (+ correction of the second breast), these figures were respectively 4.8% and 5.7%, indicating a preferred method FTS for large volumes of operations. A postoperative bed-day at one-sided

interference at FTS was marked within 10.8 days, with a standard conduction - 12.1. For bilateral intervention (+ correction of second cancer) method FTS showed a significant advantage: (10.9 days-at FTS, against 14.1 - the conduct of the standards).

At the analysis of intensity of postoperative pain syndrome we applied the digital rating scale of NRS (Numerical Rating Scale, NRS) - from 0 ("no pain") to 10 ("unbearable pain"). In 45% of patients with FTS for 3 days after surgery pain was absent in 45 % was marked as insignificant and in 10% of patients - as moderate. The standard method only in 20% of patients at 3 days after surgery pain was absent, in 25% - it was marked as insignificant, 45% - as moderate and in 10% of patients - as strong.

Thus, application of method of fast track surgery allows to decrease the postoperative complications rate, duration of patient's stay in hospitals and estimate of treatment, improves quality of life of patients that received treatment for BC.

## CONCLUSIONS

The principles of the modern approach to the BC treatment used in the National Cancer Institute are: 1. Early diagnosis of BC tumors, preferably at the stage of cancer in situ, T1, 2. Considering the molecular characteristics of BC tumors and prognostic factors for rational planning neoadjuvant and adjuvant chemotherapy, namely, individualized approach to the complex BC treatment. 3. The timely radical surgery with certain choice of surgical access and the amount of removed tissue considering oncological principles and the mandatory study of resection margin. 4. Estimation of necessity for neoadjuvant and the possibility of adequate adjuvant chemotherapy. 5. SLN detection at the initial stages of BC to intraoperative staging and choice of rational volume dissection. 6. Application of fast track surgery in reconstructive and plastic surgery in BC patients, that allows to decrease the amount of postoperative complications, duration of patient stay in a hospital and improves quality of life of patients.

The complex BC treatment considering discounted principles can expand the indications for the OPO, reconstructive and restorative operations, improve the quality of life of operated patients without reducing the effectiveness of anticancer therapy (Table 5).

Such approach, together with the use of FTS principles creates terms for the wide use of the operations sent to preserving and improving quality of life of BC patients without deterioration of survival rates.

**Table 1****Morbidity and mortality of BC  
in Ukraine (2004 - 2011 years)**

	<b>Core Performances by Year (absolute numbers)</b>							
	<b>2004</b>	<b>2005</b>	<b>2006</b>	<b>2007</b>	<b>2008</b>	<b>2009</b>	<b>2010</b>	<b>2011*</b>
Total number of cases of disease	15183	16346	16042	16195	16507	16384	17410	16325
The usual morbidity rate per 100 thousand female population	59,5	64,5	63,7	64,7	65,7	65,6	69,8	69,7
Total number of deaths	7565	7891	7826	7743	7902	7989	7969	7455
The usual mortality rate per 100 thousand female population	29,7	31,1	31,1	30,9	31,7	32,24	32,0	32,4

Note: \* - operative information.

**Table 2.**  
**Distribution of BC patients in stages with the first number  
III in Ukraine in 2004-2011 years (according to TNM)**

<b>BC stage</b>	<b>Years of research, %</b>							
	<b>2004</b>	<b>2005</b>	<b>2006</b>	<b>2007</b>	<b>2008</b>	<b>2009</b>	<b>2010</b>	<b>2011</b>
I-II	71,7	73,1	72,4	74,1	75,1	75,5	75,6	76,7
III	17,0	16,3	16,9	15,7	15,3	14,3	14,2	13,2
IV	8,2	8,2	7,9	7,7	7,6	7,5	7,5	7,6



**Table 3.**

**Distribution of BC patients in stages by year  
(according to the National Cancer Institute).**

BC stage	Number of patients (absolute numbers,%)		
	1990-1998*	1999-2009*	2010-2012*
I	129 (4,64)	346 (8,04)	461 (11,01)
IIA	578 (20,78)	1067 (24,79)	1290 (30,81)
IIB	680 (24,45)	1341 (31,16)	955 (22,81)
IIIA	902 (32,43)	1027 (23,86)	898 (21,45)
IIIB	492 (17,7)	523 (12,15)	583 (13,92%)
Total	2781 (100)	4304 (100)	4187 (100)

\* - Years of the diagnosis establishment

**Table 4.**

**Distribution of BC patients by type of surgery  
(according to the National Cancer Institute data).**

Operations	1990-1994	1995-1999	2000-2004	2005-2008	2009	2010	2011
	abs. (%)	abs. (%)	abs. (%)	abs. (%)	abs. (%)	abs. (%)	abs. (%)
Mastectomy	1255 (96,24)	1249 (92,18)	1173 (80,12)	1035 (68,27)	209 (57,73)	193 (37,26)	368 (42)
Quadrantectomy with axillary dissection	46 (3,53)	106 (7,82)	264 (18,03)	419 (27,64)	129 (35,64)	269 (51,93)	399 (45,5)
Reconstructive operations	3 (0,23)	-	27 (1,85)	62 (4,09)	24 (6,63)	56 (10,81)	111 (12,5)
Total	1304	1355	1464	1516	362	518	878

**Table 5**

**Results of complex breast cancer treatment according to the National  
Cancer Institute data**

BC stage	5-year survival (%)		
	1988 – 1998 yrs *	1999 – 2009 yrs *	2010 – 2012 yrs
II A	87,3 ± 1,4	93,3 ± 0,8	96,7 ± 0,9
II B	78,0 ± 1,7	84,34 ± 1,4	91,5 ± 1,6
III A	65,3 ± 1,9	77,5 ± 1,6	88,0 ± 2,2
III B	52,9 ± 3,5	64,7 ± 2,7	66,2 ± 3,1

\* - Years of the diagnosis establishment

**Table 6**

**Algorithm of radical surgery choice in BC patients**

Parity of removed tissue volumes to the size of breast	Operation	Correction of contralateral breast
Till 15%	Organ preservative operation	Not required
15-25%	Organ preservative operation	Most expedient
More than 25%, autotransplantation is possible	Mastectomy with simultaneous reconstruction breast autograft	Method for choice
More than 25%, autotransplantation is not possible	Subcutaneous mastectomy with simultaneous reconstruction breast implant	Method for choice

**Table 7**  
**Distribution of patients according to the method of BC treatment**

	Fast track surgery	Standard treatment
The operation on one breast	513 (58%)	192 (62%)
The operation on one breast + second breast correction	375 (42%)	119 (38%)
Total	888 (100%)	311 (100%)

## REFERENCES

1. Letyahin V.P. (2004) Breast cancer. Medicine, Moscow, 248 p.
2. Oncology (2006) Ed. I.B. Schepotin. Kniga plus, Kyiv, 496 p.
3. Portnoy S.M., Laktionov K.P. (2005) Treatment of primary operable breast cancer. Breast cancer. Moscow: 267-288.
4. Kharchenko V.P, Rozhkova N.I. (2009) Mammology. National guidelines. HEOTAR-Media, Moscow, 324 p.
5. Fedorenko Z.P, Haysenko A., Gulak L.O et al (2012) Edited by I.B Schepotin. Cancer in Ukraine, 2010-2011. Bulletin of the National Cancer Registry number 13. Kyiv: 116.
6. Schepotin I.B, Smolanka I.I, Motuzyuk I.M, Sydorhuk O.I (2010) Conception of surgical choice in breast cancer patients (results of treatment 1199 patients). Abstr. VI congress of oncologists and radiologists of CIS countries. Tajikistan, Dushanbe 01-04.10: 161.
7. Schepotin I.B. Smolanka I.I., Motuzyuk I.M. et al (2011) The use of a multi-modal program fast track surgery in breast cancer patients. Clinical Oncology. Proceedings of the XII Congress of the oncologists of Ukraine. - Sudak, Crimea. - 20-22.09.2-11. - Special Issue № II: 86-87.
8. Shchepotin I.B., Smolanka I.I., Motuzyuk I.M. et al (2010) Criteria volume and the possibility of reconstructive surgery for treatment of patients with breast cancer. Abstracts of IV int. scientific-practical. Conference "Problems of the situation in plastic and reconstructive surgery," Kyiv: 168.
9. Shchepotin I.B., Sydorhuk O., Motuzyuk I.M. (2010) Conception of choice the operation to breast cancer patients — Results of treatment 1199 patients. Eur. J. Cancer Supplements, 8(3): 137.
10. Aziz D., Rawlinson E., Narod S.A. et al. (2006) The role of reexcision for positive margins in optimizing local disease control after breast-conserving surgery for cancer. Breast J., 12(4): 331-337.
11. Balch G.C., Mithani S.K., Simpson J.F., Kel-ley M.C. (2005) Accuracy of intraoperative gross examination of surgical margin status in women undergoing partial mastectomy for breast malignancy. Am. Surg., 71(1): 27-28.
12. Wilmore D.W., Kehlet H. (2001) Management of patients in fast track surgery. BMJ., 3(22): 473-476.
13. Fisher B., Dignam J., Tan-Chiu E. et al. (2001) Prognosis and treatment of patients with breast tumors of one centimeter or less and negative axillary lymph nodes. J. Natl. Cancer Inst., 93(2): 112-20.
14. Fisher B., Anderson S., Bryant J. et al. (2002) Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N. Engl. J. Med., 347(16): 1233-41.
15. Veronesi U., Cascinelli N., Mariani L. et al. (2002) Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N. Engl. J. Med., 347(16): 1227-32.

16. Van der Hage J.A., Putter H., Bonnema J. et al. (2003) EORTC Breast Cancer Group. Impact of locore-gional treatment on the early-stage breast cancer patients: a retrospective analysis. *Eur. J. Cancer*, 39(15): 2192-9.