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# Влияние лучевой терапии на реконструкцию молочной железы у больных раком молочной железы

**Обоснование.** Хирургический этап остается базовым в комбинированном и комплексном лечении рака молочной железы. Радикальная мастэктомия и реконструктивно-пластическая хирургия являются основными вариантами хирургического лечения подавляющего большинства пациенток. Лучевая терапия может привести к развитию осложнений после реконструкции молочной железы, и, наоборот, реконструированная молочная железа может вызвать у врача-рентгенолога технические трудности с правильным планированием перед лучевой терапией. **Цель** — выбрать оптимальный метод реконструкции молочной железы с использованием различных имплантов для минимизации постлучевых осложнений и сохранения высокого уровня качества жизни пациенток после лечения рака молочной железы. **Методы.** Ретроспективное исследование проведено на базе отделения онкологии и реконструктивно-пластической хирургии молочной железы и кожи МНИОИ им. П.А. Герцена, где с июня 2013 по ноябрь 2017 г. выполнено 132 операции — подкожной мастэктомии с одномоментной реконструкцией эндопротезом. Распределение по стадиям: I — 57, IIA — 39, IIB — 17, IIIA — 13, IIIC — 4; 2 случая саркомы молочной железы. Профилактическая мастэктомия контралатеральной железы выполнена 22 пациенткам, мастопексия — 8, аументация — 20. Полиуретановые имплантаты были установлены препекторально в 82 (62%) случаях, остальным пациенткам установлены текстурированные эндопротезы субмускулярно. Лучевая терапия проведена 47 пациенткам в суммарной дозе 45 Гр. Двусторонняя реконструкция выполнена 22 пациенткам. **Результаты.** Средний период наблюдения составил 28,44 ± 14,66 мес (от 6 до 48 мес). Наиболее частым осложнением в послеоперационном периоде было развитие капсулярной контрактуры: серомы — 20 больных, гематомы — 2, краевого некроза — 6, протрузии — 6, инфекции — 2 больных. Наиболее часто встречалась капсулярная контрактура по Бейкеру III степени (n = 18). Средний срок развития капсулярной контрактуры составил 7,6 ± 11,65 мес. **Заключение.** Несмотря на большее количество осложнений при одномоментной реконструкции, при выборе метода лечения рака молочной железы имплантаты сохраняют преимущество как у пациентки, так и у хирурга.

**Ключевые слова:** рак молочной железы, одномоментная реконструкция молочной железы, ацеллюлярный дермальный матрикс, АДМ, сетчатый имплантат, мастэктомия, лучевая терапия, капсулярная контрактура, полиуретановый имплантат

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## Background

The surgical stage remains the main one in the combined and complex treatment of breast cancer, and radical mastectomy is still the main option for surgical treatment.

Modern methods of one-stage breast reconstruction in breast cancer can be divided into three groups: reconstruction using synthetic materials (expanders and implants), own tissues and their combinations. The issue of preventing the development of complications after surgical treatment remains unresolved.

**Aim** — improving the quality of life of patients with breast cancer while maintaining a high level of effectiveness of antitumor treatment by reducing the number of post-radiation complications.

## Methods

### Research design

The study included 132 patients with breast cancer receiving complex treatment. In 25 cases, due to the prevalence of the tumor process/unfavorable prognostic factors, neoadjuvant chemotherapy was performed. Further, all patients underwent surgical treatment according to the scheme below. In 47 cases,

radiation therapy was performed in accordance with the recommendations of the council, based on the data of postoperative histological material.

### Conformity criteria

Women with breast cancer after complex treatment with subcutaneous — skin-sparing mastectomy.

### Research facilities

132 operations were performed: 111 subcutaneous mastectomy with one-stage reconstruction with an endoprosthesis and 21 mastectomy with a one-stage reconstruction with an endoprosthesis. To strengthen the lower slope of the reconstructed gland (in 65 patients — mesh implant (22 with conservation of large pectoralis muscle (LPM); in 18 patients — acellular dermal matrix (ADM) of which 12 — perforated ADM; latissimus dorsi flap (LD) — 15, thoracic dorsi flap (TDL) — 8, without shelter — 26).

### Research duration

The research was conducted from June 2013 to November 2017 in the Department of oncology and reconstructive plastic surgery of the breast and skin of the Moscow Research Institute of Oncology named by P.A. Herzen.

### Medical procedure description

Patients with breast cancer were distributed in the stages as follows: I — 57, IIA — 39, IIB — 17, IIIA — 13, IIIC 4; 2 cases of breast sarcoma. According to the results of immunohistochemical study, the luminal type A — 40 patients, 25 — luminal type B, Her2/neu negative, 15 — luminal type B, Her2/neu positive, 21 — triple negative type and 10 Her2/neu — positive type. Neoadjuvant chemotherapy was performed in 25 patients, of which in 5 cases a complete response was achieved in the form of complete regression of the tumor node (CR) and in 20 cases partial regression of the tumor node (PR). Histology of grade differentiation: G1 — 4; G2 — 76; G3 — 50. Lympho-vascular invasion was detected in 34 cases, intravenous at 21. Implants of various firms were used: 38 Silimed, 49 Polytech, 5 Allergan, 38 Mentor, 1 Eurosilicon, 1 Natrelle. Polyurethane implants were applied in 82 (62%) cases. In 21 patients, a germline significant mutation of the BRCA1 gene was detected, in 1 case the mutation of the BRCA2 gene and in 3 cases mutation of the CHEK2 gene. Prophylactic mastectomy of the contralateral gland was performed in 22 patients, mastopexy in 8, augmentation in 20.

## Results

### Research findings

**The main research outcome.** The average age of the patients was  $43.72 \pm 8.59$  years. The mean follow-up period was  $28.44 \pm 14.66$  months (from 6 to 48 months). As an adjuvant treatment, 43 patients underwent chemotherapy, 64 had hormone therapy, 11 had targeted therapy, 22 had ovarian failure, and 47 had radiation therapy. Radiation therapy for the reconstructed mammary gland was performed by SOD 45 Gr. Bilateral reconstruction was performed in 22 cases and did not

pose any problems for planning the performance of radiation therapy (Fig. 1).

The most frequent complication in the postoperative period was the development of capsular contracture. There were following complications: seroma — 20; hematoma — 2; edge necrosis — 6; protrusion — 6; infection — 2. The degree of capsular contracture by Baker has not developed in 45 patients and was found in 46 patients (I stage — 16; II — 12; III — 18). The average period of development of capsular contracture was  $7.6 \pm 11.65$  months.

**Additional research outcomes.** Also, it was assessed an analysis of the patient quality of life depend on covering the endoprosthesis with additional shelter (ADM, TDL, mesh implant, de-localized flap) or without using the international questionnaire Breast-Q (module reconstruction) (Table 1).

Thus, with the additional shelter of the lower slope of the reconstructed gland by any of the methods under consideration, the patient's quality of life is higher than in the group without additional shelter of the endoprosthesis.

### Methods for registration of outcomes

All patients were examined by the operating surgeon 1, 3, 6, 12 months after the operation. Additionally, the quality of life was assessed using the Breast-Q international questionnaire (reconstruction module).

### Ethical review

This study took place in a research institute where the proposed therapies are used as standards for the treatment of patients with breast cancer.

### Statistical analysis

Statistical processing of the material and calculations of indicators were carried out using the statistical software

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## Effect of Radiation Therapy on Breast Reconstruction in Breast Cancer Patients

**Background.** The surgical stage remains the main one in the combined and complex treatment of breast cancer. Radical mastectomy and reconstructive plastic surgery are the main option for surgical treatment of vast majority patients. Radiation therapy can lead to the development of complications after breast reconstruction, and vice versa, the reconstructed mammary gland can cause technical difficulties for the radiologist to properly adjust the required dose of irradiation. **Aim** — to choose the optimal method of breast reconstruction using various implants, as well as endoprostheses to minimize post-radiation complications and maintain a high level of quality of life for patients after breast cancer treatment.

**Methods.** The retrospective study was conducted in the department of oncology and reconstructive plastic surgery of the breast and skin in the P.A. Herzen Moscow Research Oncology Institute from June 2013 to November 2017. There were performed 132 operations: 111 subcutaneous mastectomy with one-stage reconstruction with an endoprosthesis and 21 mastectomy with a one-stage reconstruction with an endoprosthesis. The distribution by stages: I — 57, IIA — 39, IIB — 17, IIIA — 13, IIIC 4; 2 cases of breast sarcoma. Prophylactic mastectomy of the contralateral gland was performed in 22 patients, mastopexy in 8, augmentation in 20. Polyurethane implants were applied in 82 cases (62%). Radiation therapy was performed in 47 patients with total dose 45 Gy. Bilateral reconstruction was performed in 22 patients. **Results.** The mean follow-up period was  $28.44 \pm 14.66$  months (from 6 to 48 months). The most frequent complication in the postoperative period was the development of capsular contracture: seroma — 20 patients, hematoma — 2, edge necrosis — 6, protrusion — 6, infection — 2 patients. The most common capsular contracture by Baker was III degree,  $n = 18$ . The average period of development of capsular contracture was  $7.6 \pm 11.65$  months. **Conclusion.** Despite the greater number of complications during the one-stage reconstruction, the implants remain in advantage in choosing a method of treating breast cancer by both the patient and the surgeon.

**Keywords:** breast cancer, one-stage breast reconstruction, acellular dermal matrix, ADM, mesh implant, mastectomy, radiation therapy, capsular contracture, polyurethane implant

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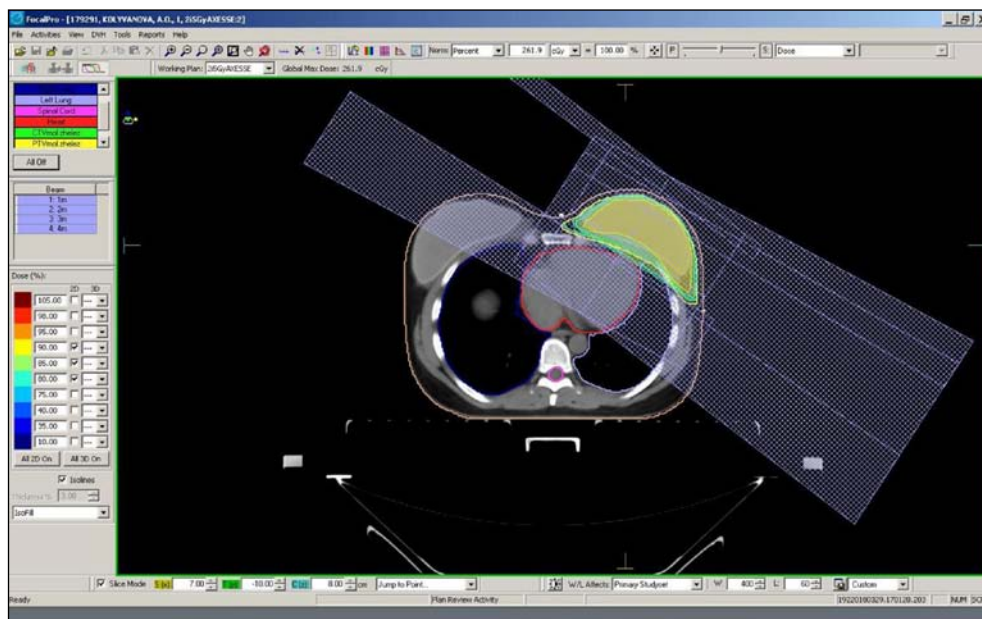


Fig. 1. Planning of radiation therapy for left breast cancer after bilateral reconstruction.

package Statistica for Windows v. 10 and SPSS v. 21. The degree of relationship between the parameters was assessed using the Spearman correlation analysis. Differences were considered significant at  $p < 0.05$  (acceptable level of  $\alpha$ -error 5%).

### Discussion

Nowadays, preference is given to a one-stage reconstruction of the breast, because it can significantly improve the quality of life of a woman by improving the physical condition and overall psychological well-being. In addition, according to numerous studies conducted by meta-analyzes [1–3], there was no difference in the incidence of local and loco-regional recurrence in the mastectomy group and in the group of one-stage breast reconstruction.

According to numerous randomized trials, patients receiving adjuvant radiation therapy have a lower risk of developing a loco-regional recurrence and a significant improvement in overall survival [4, 5]. However, despite the reduction in loco-regional relapses and the increase in relapse-free survival, radiation therapy after mastectomy can adversely affect the outcome of reconstruction.

Complications after radiation therapy (RT) can be early, from several days to several weeks, and late, arising from several months to several years after the completion of RT. Early complications are usually inflammatory processes that can lead to tissue necrosis and protrusion of the endoprosthesis.

Late are atrophy and fibrosis lead to the emergence of capsular contracture.

In a M. Barry study [5], it was found that patients who received RT after breast reconstruction using autologous tissues had fewer complications in comparison with reconstruction using endoprotheses. Another systematic review [6] showed that the use of an endoprosthesis increases the risk of re-operation compared to the use of autologous grafts. A large analysis conducted in the clinics of MSKCC [7] showed, that 20–30% of all patients after reconstruction using an endoprosthesis required a second operation. In the prospective cohort multicenter study MROC for the period from 2012 to 2015 years [8] complications after breast reconstruction group without carrying out radiation therapy ( $n = 1625$ ) and carrying out radiation therapy ( $n = 622$ ) were compared. The advantage of using autologous flaps (37.9 vs 25.0%;  $p < 0.001$ ) was given in the group with planning of carrying out RT in the postoperative period. Also, in a group with radiation therapy, a one-stage reconstruction was less common (83.0 vs 95.7%;  $p < 0.001$ ). At least one complication occurred after two years in 38.9% of irradiated patients with implant reconstruction, 25.6% with autologous grafts reconstruction, in 21.8% of unirradiated patients with implant reconstruction and 28.3% of unirradiated patients with autologous reconstruction. Among the irradiated patients, autologous reconstruction was associated with a lower risk of complications than implant reconstruction ([OR]  $\frac{1}{4}$  0.47; 95% confidence interval [CI] 0.27 to 0.82;  $P\frac{1}{4}$  0.007). There was no difference between patients without radiation therapy. The

Table 1. Assessment of the quality of life using the questionnaire Breast-Q

Breast reconstruction types	Satisfaction with mammary gland	Satisfaction with the result	Psycho-social well-being	Sexual well-being	Physical well-being
ADM	71.75 ± 19.02	91.66	64.17	59.18	78.92
TDL	57.44	69.44	67.66	61.17	75.11
Mesh implant	52.7	80	67.4	57.4	72.02
De-localized flap	65.9	74.6	59.5	60.11	75
Without covering the endoprosthesis	49.4	68.4	54.9	36.5	61

recent prospective study [9] showed the effect of radiotherapy in two different groups — a two-stage expander / implant reconstruction and one-stage reconstruction (Table 2). All patients were monitored for at least 2 years after the operation.

In a total proportion of 10.7% cases, there were unsuccessful breast reconstructions, without a significant difference between the two groups. Among all patients, more than a quarter of all patients (28.7%) had complications (Table 3). The most common complication was infection (22 patients, 14.7%).

The optimal plan for the implementation of RT includes target areas (reconstruction site, chest wall and regional lymph nodes) with the established dose of radiation, while minimizing

the dose of irradiation of the heart and lungs. There is a large number of studies on this topic, for example, a well-known study by MSKCC [10], comparing the carrying out of RT for the mammary gland with reconstruction and without it. According to the results, the biggest problem for radiologists is the planning of irradiation for internal mammary lymph nodes (internal mammary lymph nodes), which significantly increases the dose for the heart and lungs.

Radiation therapy significantly ( $p = 0.00001$ ) increased the risk of developing capsular contracture (Fig. 2). It was also found that the incidence of capsular contracture with polyurethane endoprotheses is lower than in the group using

Table 2. Patient characteristics,  $n$  (%)

Patients characteristics	$n = 150$	Tissue expander, 104 (69.3)	Implant, 46 (30.7)
One side	48 (32.0)	32 (30.8)	16 (34.8)
ADM	73 (48.7)	58 (55.8)	15 (32.6)
Chemotherapy:			
During/after reconstruction	98 (65.3)	58 (55.8)	40 (87.0)
Before reconstruction	52 (34.7)	46 (44.2)	6 (13.0)
Local RT to mammary gland	31 (20.7)	28 (26.9)	3 (6.5)
RT to regional zone	119 (79.3)	76 (73.1)	43 (93.5)
Subcutaneous mastectomy	12 (8)	8 (7.7)	4 (8.7)
Skin protective mastectomy	137 (91.3)	1 (1.0)	42 (91.3)

Table 3. Various complications after carrying out RT,  $n$  (%)

Complications	%	Tissue expander, 104 (69.3)	Implant, 46 (30.7)	$p$ -value
Seroma	10 (6.7)	8 (7.7)	2 (4.4)	0.456
Gematoma	5 (3.3)	4 (3.9)	1 (2.2)	0.632
Infection:	22 (14.7)			
Antibiotic therapy	10 (6.7)	7 (6.7)	3 (6.5)	0.962
Antibiotic therapy + implant removal	12 (8.0)	7 (6.7)	5 (10.9)	0.395
Seam divergence	5 (3.3)	5 (4.8)	0	0.324
Capsular contracture	4 (2.7)	3 (2.9)	1 (2.2)	0.804
Implant removal	3 (2.0)	3 (2.9)	0	0.553
Other complications	43 (28.7)	32 (30.8)	11 (23.9)	0.395
Unsuccessful reconstruction	16 (10.7)			

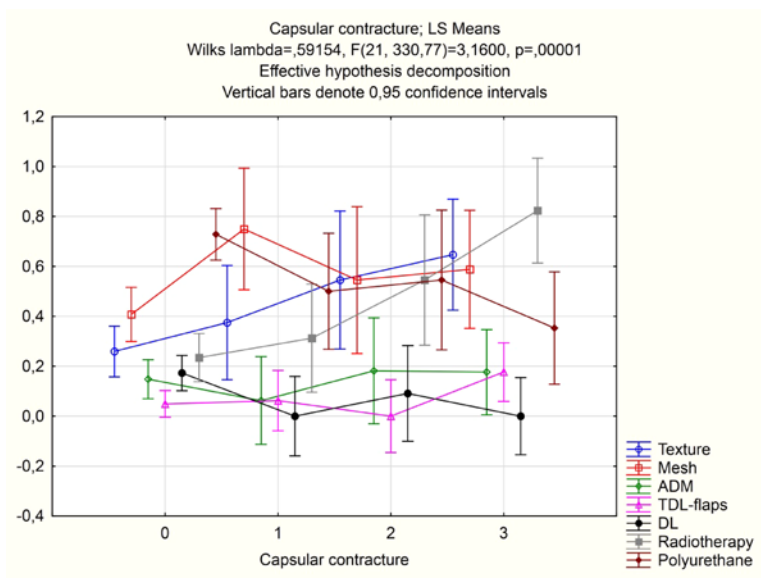


Fig. 2. The degree of development of capsular contracture in different observation groups



textured endoprotheses. When using textured endoprotheses, capsular contracture III, IV degree according to Baker developed more often. The use of an additional shelter for the lower slope of the reconstructed mammary gland (ADM, reticular implant, DL, TDL flap) does not have a significant effect on the development of capsular contracture.

## Conclusion

The use of additional implants to cover the lower slope of the reconstructed mammary gland can be used by oncologists as a prevention of the development of complications, especially after exposure to radiation therapy.

## Discussion of the primary research results

A typical approach to integrating radiotherapy with breast reconstruction raises a strong controversy in the treatment of breast cancer among radiologists. Despite the greater number of complications during the one-stage reconstruction, the implants remain in advantage in choosing a method of treating breast cancer by both the patient and the surgeon. Also, in many studies, it has been revealed that there is no advantage between RT, carried out on the expander and RT, conducted on the implant. Minimization of complications and maximum satisfaction of women receiving RT after mastectomy are our unifying common goal.

## Additional information

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**Author contributions.** I.M. Shirokikh — data processing article writing; Sh.G. Khakimova — data processing article writing; A.D. Zikiryahodzhaev — data processing article writing; G.G. Khakimova — statistical analysis, collecting data, translation.

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