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DIAGNOSTIC AND TREATMENT METHODS

DOI 10.25789/YMJ.2025.91.11

UDC 616-006.66

ZHARNIKOVA Tatyana Nikolaevna – PhD, Associate Professor of the Basic Department of Oncology, Medical Institute of M.K. Ammosov North-Eastern Federal University, Deputy Chief Physician for Clinical Expert Work, Surgeon, Mammologist, State Budgetary Institution of the Republic of Sakha YAROD, zharnikova_tn@mail.ru, <https://orcid.org/0000-0002-7967-3704>;

OKONESHNIKOVA Alena Konstantinovna – PhD, Associate Professor of the Department of Surgery and Dentistry, the Medical Institute of M.K. Ammosov North-Eastern Federal University, neurosurgeon, surgeon ORCHMDiL SBI RS (Y) YAROD, alena-okoneshnikova@mail.ru, <http://orcid.org/0000-0003-1556-3095>;

SOLOVYOVA Aitalina Eremeevna – surgeon, mammologist SBI RS (Y) YAROD, ayyta@yandex.ru, <https://orcid.org/0009-0005-5094-7918>;

NIKIFOROV Pyotr Vladimirovich – Director of the State Budgetary Institution of the Republic of Sakha (Yakutia) "YARMIAC", Associate Professor of the Basic Department of Oncology, the Medical Institute of M.K. Ammosov North-Eastern Federal University, niciforof@mail.ru, <https://orcid.org/0000-0002-2758-155X>;

NIKOLAEVA Tatyana Ivanovna – PhD, Associate Professor of the Basic Department of Oncology, Medical Institute of M.K. Ammosov North-Eastern Federal University, Head of the State Budgetary Institution of the Republic of Sakha (YAROD), NTI_Nika@mail.ru, <https://orcid.org/0000-0002-1099-573X>;

AFANASYEVA Lena Nikolaevna – MD, Associate Professor, Head of the Basic Department of Oncology, the Medical Institute of M.K. Ammosov North-Eastern Federal University, Minister of Health, the Republic of Sakha (Yakutia), lenanik2007@mail.ru, <https://orcid.org/0000-0003-2592-5125>;

IVANOVA Feodosia Gavrilievna – PhD, head of the department of drug treatment, SBI RS(Y) "YaROD", leading oncologist of the Ministry of Health of the Republic of Sakha (Yakutia), Associate Professor of the basic department "Oncology" of the Medical Institute of the FSAEI HE M.K. Ammosov North-Eastern Federal University, e-mail: feodossiaiv@inbox.ru, <https://orcid.org/0000-0001-7661-1279>

T.N. Zharnikova, A.E. Solovyova, A.K. Okoneshnikova, P.V. Nikiforov, T.I. Nikolaeva, L.N. Afanasyeva, F.G. Ivanova

EXPERIENCE OF USING SENTINEL LYMPH NODE BIOPSY IN BREAST CANCER USING ICG FLUORESCENCE IN THE REPUBLIC OF SAKHA (YAKUTIA)

Breast cancer is the leading cause of malignant neoplasms among women worldwide. Today, lymph node biopsy is one of the main diagnostic methods to assess the extent of the oncological process. The aim of the study has been to investigate the possibilities of conducting and evaluating the performance of diagnostic statistical methods of ICG fluorescence for sentinel lymph node biopsy in breast cancer in the Republic of Sakha (Yakutia). The study included 223 patients diagnosed with cT1-3N0M0, occurring in the period from 2022 to 2023. Surgical treatment for the mammary gland with sentinel lymph node biopsy using the ICG fluorescence method was performed in the Department of Breast Oncology and Skin Oncology of the State Autonomous Institution of the Republic of Sakha (Yakutia) in the OOMZhIOK (Department of Breast Oncology and Skin Oncology) of the Yakut Republican Oncology Dispensary. As a result of the study, metastases in the lymph nodes were detected in 44 (19.73%) cases out of 223. It has been established that the use of the method of sentinel lymph node biopsy in breast cancer using ICG fluorescence of the gland allows for large-scale surgical treatment of the initial form of mammary gland cancer.

Keywords: sentinel lymph node biopsy, fluorescence lymphography, breast cancer, lymph node dissection, indocyanine green.

For citation: Zharnikova T.N., Solovyova A.E., Okoneshnikova A.K., Nikiforov P.V., Nikolaeva T.I., Afanasyeva L.N., Ivanova F.G. Experience of using sentinel lymph node biopsy in breast cancer using ICG fluorescence in the Republic Of Sakha (Yakutia). Yakut Medical Journal, 2025; 91(3): 42-45. <https://doi.org/10.25789/YMJ.2025.91.11>

Introduction. Currently, one of the leading sites of cancer among oncological diseases in women is the mammary gland (BC). According to GLOBOCAN, in recent years, the propensity index for the incidence of BC cancer has increased; in 2020, 2.3 million cases of BC cancer were registered worldwide, which is 11.7% of all cancer cases [11]. In Russia, BC in the female population ranks 1st among all malignant neoplasms, and its incidence is 22.1% [3]. This problem is relevant in the oncology service in the Republic of Sakha (Yakutia). It was reg-

istered that in the period from 2013 to 2022, high rates of BC indicators were observed in the population of Yakutia at the early stages (I-II) of the disease in 72.7% of cases.

It has been proven that timely diagnosis of regional lymph node involvement is essential for determining the prognosis and selecting the optimal treatment strategy [1]. Today, the standard principle of surgical treatment of malignant neoplasms of various organs is the mandatory removal of all lymphatic collectors. Extended lymph node dissection in breast

cancer often leads to a decrease in the patient's quality of life up to disability. Some of the most common complications may be: prolonged lymphorrhea, lymphostasis of the upper limb, severe chronic pain syndrome with a neuropathic component due to plexitis, ligature fistulas, postoperative serums, and granulomas of the postoperative scar [4]. Today, one of the urgent tasks in oncology is the development of minimally invasive interventions in regional zones in patients with unaffected lymph nodes in the early stages of breast cancer [1,4,7].

In 1923, the British scientist L.R. Braithwaite first introduced the term "sentinel" lymph node (SLN), by which he meant the very first lymph node in the regional lymphatic basin from the transitional organ [1,6,10,15]. SLN biopsy determines the volume of lymph node dissection depending on the country or the state of metastases in it. According to many authors, the absence of metastases in the SLN in 95% of cases allows us to predict the presence of altered lymph nodes in the axillary and connective tissue. [6,8].

To date, two main methods of early detection of SLNs have been presented, using a radiopharmaceutical and a fluorescent dye with intraoperative histological examination of sentinel lymph nodes [6,9]. The first method is based on a solution of sodium pertechnetate, ^{99m}Tc from a technetium- 99m generator and lyophilisate. The result of this method is high radioactivity at the site of the first injection, which requires additional radiation protection measures [9,12,14].

The ICG fluorescence method is based on a fluorescent drug – indocyanine green (indocyanine green (ICG)). Indocyanine green (ICG) is a water-soluble green dye with fluorescent properties. This method is based on molecular fluorescence due to the binding of ICG to proteins of lymphovascular system cells. The absolute advantage of this method is the absence of radiation and simplification of the procedures [2,9,11].

The aim of the study: to study the possibilities of conducting and evaluating the diagnostic characteristics of the ICG fluorescence method for performing sentinel lymph node biopsy in breast cancer in the Republic of Sakha (Yakutia).

Materials and methods of the study: in the period from January 2022 to December 2023, 223 surgical interventions for late-stage breast cancer (Tis . T1-3) were performed in the departments of breast oncology and skin tumors (OOMZhIOK) of the State Budgetary Institution of the Republic of Sakha (Ya-

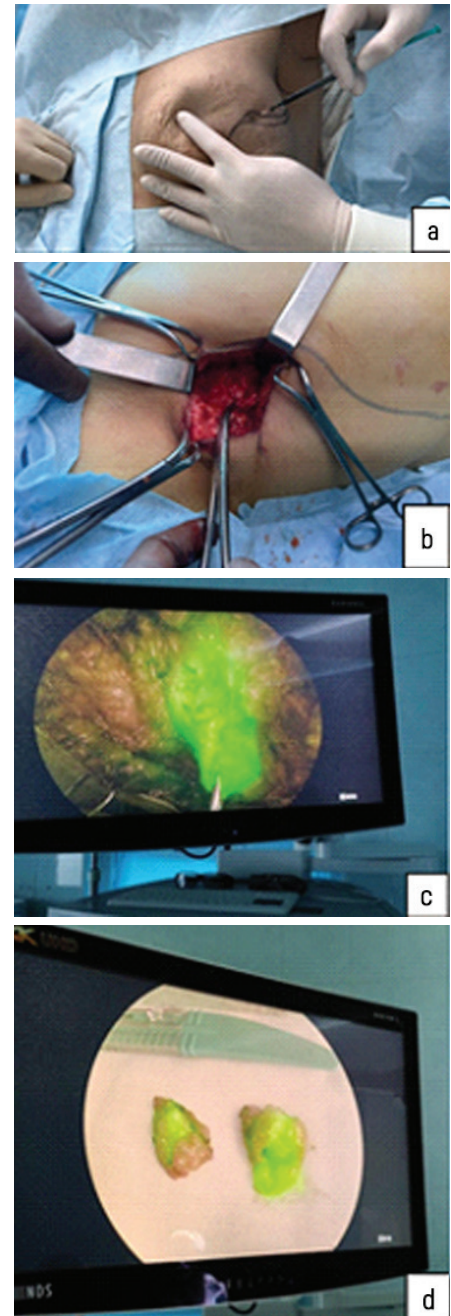
kutia) "Yakutsk Republican Oncology Dispensary". The average age of the patients was 61 years (from 32 to 86 years). At the examination stage, all patients undergo a study of regional lymph nodes and fine-needle aspiration biopsy of the axillary lymph nodes.

Surgical technique. Under the conditions of the procedure, the preparation of 5 mg indocyanine green (ICG) in a room of 1 ml was administered immediately before the operation using a disposable 1 ml syringe subcutaneously into the periareolar zone of the affected mammary gland in the projection of the tumor, followed by massage of the area, carried out for 3-5 minutes (Fig. a). Then, a 2-6 cm long incision was formed in the axillary region. After layer-by-layer excision of the skin and subcutaneous fat and installation of retractors, layer-by-layer excision of tissues in the axillary fossa was performed observing a bloodless surgical technique to prevent bleeding and damage to the lymphatic vessels, which could cause leakage of the preparation into a narrow strip axillary wound (Fig. b). The axillary stage of the operation consisted of a biopsy of the SLN using a fluorescence technique and lymphadenectomy of levels I-II-III, with verification of metastatic lesions of the lymph nodes. Mapping was performed using the Karl Endoscopic Fluorescence Imaging System. Storz SE & Co. KG. Dr /-Karl-Storz-Strasse-37 78532. Tittlingen (Germany) for visualization and image processing with a kitchen stove H3-Z FI TH102. SN ZQ019077-K and optics 26003 BRA Hopkings 30 NIR/ICG at first (Fig. c). Then, after visualization of the SLN with the help of holding instruments, the SLN was captured. The SLN wire was isolated in compliance with the atraumatic surgical technique in order to preserve the lymph node capsule (Fig. d). After removal of the SLN, control visualization of the removed specimen and revision in the axillary region were performed. Then the specimen was sent for histological analysis to the pathological clinic. The time of fixation and formation of fresh frozen sections is on average up to 20 minutes. Further, depending on the presence of metastases, the volume of surgical intervention is defined. In the event of data on metastatic damage, the cavity of the axillary wound was sutured layer by layer after revision and careful hemostasis.

Statistical processing of the research results was carried out using applied data processing programs based on Microsoft Excel and Statistics-8.

Results and discussion. The nature of the material is presented in Table

1. As a result of the study, it was found that the T1 tumor categories accounted for 25 (11.2%) patients, in most cases 111 (49.78%) patients were assigned the T1 category, in a third of patients 74 (33.18%) were assigned the T2 category, and in 13 (5.83%) patients the T3 category was assigned. Most often, in 115



Intraoperative photographs of sentinel lymph node biopsy using ICG fluorescence lymphography using the Karl Storz SE & Co endoscopic fluorescence imaging system. KG. Dr/-Karl-Storz-Strasse-37 78532: a – introduction of a fluorescent drug – indocyanine green, b – removal of the sentinel lymph node, c – visualization of the sentinel lymph node, d – macroscopic specimens with removed sentinel lymph node

(51.57%) patients, the tumor was located in the upper outer quadrant of the mammary gland.

In most cases, organ-preserving surgery was performed in 147 (65.92%) cases, and mastectomy was performed in 76 (34.08%) cases. According to the degree of tumor differentiation, moderately differentiated carcinoma was detected in the vast majority of patients (147 (65.92%)), highly differentiated carcinoma was detected in 56 (25.1%) patients, and poorly differentiated carcinoma was detected in 14 (4.04%) patients.

In the pathomorphological examination, in most cases ductal carcinoma was diagnosed in 116 (52.02%) patients, in a third of patients lobular carcinoma was detected, in isolated cases - 16 (7.17%) long duct carcinoma, carcinoma, 10 (4.48%) mucinous carcinoma, in 24 (10.76%) ductal carcinoma *in situ* (DCIS), in 1 (0.45%) lobular carcinoma *in place* (LCIS). During the immunohistochemical study, molecular biological subtypes of the tumor were established. In the overwhelming majority of cases, Luminal subtype A was detected in 122 (54.71%) cases.

Metastases in sentinel lymph nodes were detected in 44 patients (19.73%). The average number of lymph nodes removed during lymph node dissection was 10.25. According to the planned histological examination, the number of affected lymph nodes ranged from 1 to 5. A false-positive result in intraoperative histological examination was obtained in 1 patient (0.45%). During the study, we did not identify a single case of occurrence and systematic adverse effects with subcutaneous administration of indocyanine.

The effectiveness and safety of using the fluorescent dye indocyanine green to determine metastases in the SLN, according to specialized literature, varies from 80% to 98% [6, 9, 13, 14].

According to the results of a meta-analysis on the effectiveness of using fluorescent visualization of SLNs with indocyanine and methylene blue dyes, it was found out that the indocyanine group had a higher detection rate [OR = 8.64, 95% CI: 5.46–13.66, $p = 0.000$] and a lower rate of false negative results [OR = 0.10, 95% CI 0.02–0.43, $p = 0.002$] [13].

In addition, in a systematic review, the authors conducted a comparative analysis of the effectiveness of using indocyanine green fluorescence with a radioisotope for SLN biopsy in early stages of breast cancer. The analysis included 2301 patients from 19 studies. The authors did not find any indicators between traditional studies (OR = 0.90,

Material characteristics (n=223)

| | Sign | Number of patients | % |
|----------------------------|---|--------------------|-------|
| Tumor size | Tis | 25 | 11.21 |
| | T1 | 111 | 49.78 |
| | T2 | 74 | 33.18 |
| | T3 | 13 | 5.83 |
| Localization of the tumor | Upper lateral | 115 | 51.57 |
| | Upper medial | 45 | 20.18 |
| | Center. | 23 | 10.1 |
| | Lower lateral | 16 | 7.17 |
| | Lower medial | 15 | 6.73 |
| | Common | 9 | 4.9 |
| Degree of differentiation | G1 | 56 | 25.1 |
| | G2 | 147 | 65.92 |
| | G3 | 14 | 6.28 |
| | Unknown | 6 | 4.04 |
| Morphological variant | Flowing carcinoma | 116 | 52.02 |
| | Lobular carcinoma | 44 | 19.73 |
| | Lobular ductal carcinoma | 16 | 7.17 |
| | Mucous carcinoma | 10 | 4.48 |
| | Flowing carcinoma <i>in situ</i> (DCIS) | 24 | 10.76 |
| | Lobular carcinoma <i>in situ</i> (LCIS) | 1 | 0.45 |
| | Other | 8 | 3.59 |
| | Unknown | 4 | 1.79 |
| Molecular biology subtype | Luminal type A | 122 | 54.71 |
| | Luminal type B, Her2 negative | 22 | 9.87 |
| | Luminal type B, Her2 positive | 17 | 7.62 |
| | Her2/ neu 2 positive | 11 | 4.93 |
| | Triple type | 14 | 6.28 |
| | Unknown | 37 | 16.59 |
| Volume of operation | Sectoral resection | 147 | 65.92 |
| | Mastectomy | 76 | 34.08 |
| Sentinel lymph node status | Mts - | 179 | 80.27 |
| | Mts + | 44 | 19.73 |

95% CI 0.66-1.24) and sensitivity (OR = 1.23, 95% CI 0.73-2.05). With the combined use of indocyanine green fluorescence with a radioisotope, the sensitivity was significantly higher compared to single mapping using only the radioisotope method (OR = 3.69 95% CI 1.79-7.62) or indocyanine green fluorescence (OR = 3.32 95% CI 1.52-7.24) [6].

A study of the remote results of fluorescence- and blue-dye-guided SLN biopsy in 237 patients found that after 5 years of follow-up, 0.64% of patients with a negative SLN had ipsilateral regional recurrence [14]. A similar study conducted in 2021, where the authors reported that patients with a negative SLN biopsy result have a 0% five-year probability of regional recurrence [5]. Krivorotko et al. presented 3-year results of treatment of patients who underwent SLN biopsy. The authors reported that the 3-year over-

all survival of the structure was 99.3% (SE 0.4%), recurrence-free survival was 99.2% (SE 0.4%). The survival rate of patients with unaffected sentinel lymph nodes reached 100%, with affected ones – 97.4% (SE 1.8%) [2].

In our series (n = 223), it was found that the frequency of detection of SLNs in the group was 100%. In 80.27% of cases, patients did not require an extended stage of surgery with lymph node dissection, which resulted in metastases in the SLNs.

Conclusion. Biopsy of sentinel lymph nodes is the standard of medical care. Thus, the method allows us to determine the adequate radical volume of the operation and the lowest possible risk of the operation, duration and trauma of the operation.

The authors declare that there are no conflicts of interest.

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DOI 10.25789/YMJ.2025.91.12

UDC 616.31-08-039.71

USHNITSKY Innokenty Dmitrievich – MD, Professor, Head of the Department of Therapeutic, Surgical, Orthopedic and Pediatric Dentistry, MK Ammosov North-Eastern Federal University, e-mail: incadim@mail.ru, ORCID.org/0000-0002-4044-3004; **UNUSYAN Onik Sarkisovich** – Ph.D., Associate Professor, Department of Surgical Diseases and Dentistry, M.K. Ammosov North-Eastern Federal University, e-mail: onikunusyan@gmail.com, ORCID.org/0000-0002-8839-4205; **SEMENOV Alexander Dmitrievich** – PhD, Associate Professor of the Department of Therapeutic, Surgical, Orthopedic Dentistry and Pediatric Dentistry, M.K. Ammosov North-Eastern Federal University, e-mail: sadstom@mail.ru, ORCID ID: 0009-0008-2937-5232; **IVANOV Andrian Vladimirovich** – PhD, Associate Professor of the Department of Surgical Diseases and Dentistry, M.K. Ammosov North-Eastern Federal University, e-mail: andrian_ivanov@mail.ru, ORCID.org/0009-0003-9352-1111; **UNUSYAN Larisa Sarkisovna** – dentist, dental clinic of M.K. Ammosov North-Eastern Federal University, e-mail: lara.unusyan77@gmail.com, ORCID.org/0009-0002-6506-1077

I.D. Ushnitsky, O.S. Unusyan, A.D. Semenov, A.V. Ivanov, L.S. Unusyan

THE METHOD OF SPLINTING MOBILE TEETH IN COMPLEX TREATMENT OF CHRONIC PERIODONTITIS

Nowadays, the prevalence of inflammatory periodontal diseases in the population remains at a high level. Meanwhile, periodontal diseases are chronic foci of oral infection, which often cause the development of focal-related diseases. In addition, tooth loss due to complications of chronic periodontitis leads to dysfunction of the dental alveolar system and mandibular joint. In this regard, the study of these aspects is an urgent general medical problem, including clinical dentistry. Thus, a comprehensive study of chronic periodontitis was carried out in the population living in the North, and on the basis of the obtained results, a method for splinting teeth in periodontitis was developed. To carry out the developed method in periodontological practice, a double silicone cast of the upper and/or lower jaw is first taken with further personalized planning of the splinter apparatus on a plaster model of the jaws, further, a splinting structure for immobilisation of movable teeth is made from colourless plastic and titanium woven wire, and the ready combined splint is additionally fixed from lingual or palatal sides of teeth with light hardening composite material on upper and/or lower jaw; splinting is performed with duration from 1 to 3 months. Depending on the complexity of the clinical situation, patchwork operations are performed to reduce the size of the periodontal pockets and create conditions for the formation of a new tight attachment of the gum to the teeth, followed by orthopedic treatment. The results of clinical-functional analysis of developed method application in complex treatment of chronic periodontitis of moderate severity confirm its clinical efficiency, connected with fixation of vestibular, oral sides of movable teeth and additionally composite filling material, which contribute to improvement of biomechanics and functional properties of dental alveolar system, and also aesthetic qualities of