SECONDARY LYMPHEDEMA AS A COMPLICATION OF SURGICAL TREATMENT FOR BREAST CANCER: AUTOTRANSPLANTATION OF LYMPH NODES USING ICG LYMPHOGRAPHY

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Abstract

Secondary upper limb lymphedema remains one of the most significant complications of surgical and radiation treatment of breast cancer and is characterized by progressive impairment of lymphatic drainage, chronic inflammation, and soft tissue fibrosis. In cases of pronounced anatomical and functional damage to lymphatic collectors, the effectiveness of conservative therapy and lymphovenous anastomoses is limited, necessitating the use of physiological microsurgical reconstruction techniques. Vascularized lymph node transfer (VLNT) is considered a pathogenetically substantiated approach to restoring lymphatic drainage, combining the mechanical «lymphatic pump» effect with stimulation of lymphangiogenesis through growth factor secretion. Imaging modalities of the lymphatic system, including indocyanine green (ICG) lymphography and lymphoscintigraphy, play a crucial role in patient selection and in the assessment of surgical outcomes by enabling visualization of dermal backflow, collector obliteration, and the formation of new lymphatic pathways. The paper presents a clinical case of a patient with stage IIA lymphedema following comprehensive breast cancer treatment, in whom the absence of clinical improvement after lymphovenous bypass served as an indication for delayed breast reconstruction with a free DIEP flap combined with inguinal vascularized lymph node transfer. Postoperative follow-up demonstrated a reduction in limb volume, decreased dermal backflow, and the appearance of linear lymphatic flow patterns in the transplant area. These findings confirm the potential of vascularized lymph node transfer as a component of a comprehensive surgical strategy for the treatment of secondary lymphedema in patients after combined breast cancer therapy.

Key words: lymphedema, breast cancer, lymph node transfer, ICG lymphography, microsurgery

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For citations: Troshenkov E.A., Polyak M.A., Shakhbanova K.A., Kaprin A.D., Filonenko E.V., Kutsuradis A.F., Mantaridis D. Secondary lymphedema as a complication of surgical treatment for breast cancer: autotransplantation of lymph nodes using ICG lymphography, *Biomedical Photonics*, 2026, vol. 15, no. 1, pp. 30–36. doi: 10.24931/2413–9432–2026–15-1-30-36

ВТОРИЧНАЯ ЛИМФЕДЕМА КАК ОСЛОЖНЕНИЕ ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ: АУТОТРАНСПЛАНТАЦИИ ЛИМФАТИЧЕСКИХ УЗЛОВ С ИСПОЛЬЗОВАНИЕМ ICG-ЛИМФОГРАФИИ

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Резюме

Вторичная лимфедема верхней конечности остаётся одним из наиболее значимых осложнений хирургического и лучевого лечения рака молочной железы и характеризуется прогрессирующим нарушением лимфатического оттока, развитием хронического воспаления и фиброза мягких тканей. При выраженных анатомо-функциональных изменениях лимфатических коллекторов эффективность консервативной терапии и лимфовенозных анастомозов ограничена, что определяет необходимость применения физиологических микрохирургических методов реконструкции. Аутотрансплантация васкуляризованных лимфатических узлов рассматривается как патогенетически обоснованный способ восстановления лимфодренажа, сочетающий механический эффект «лимфатического насоса»

и стимуляцию лимфангиогенеза за счёт секреции факторов роста. Существенную роль в отборе пациенток и оценке эффективности вмешательства играют методы визуализации лимфатической системы, включая ICG-лимфографию и лимфосцинтиграфию, позволяющие выявлять дермальный рефлюкс, облитерацию коллекторов и формирование новых путей лимфатического транспорта. В работе представлено клиническое наблюдение пациентки с лимфедемой IIA стадии после комплексного лечения рака молочной железы, у которой отсутствие эффекта от лимфовенозного шунтирования послужило основанием для выполнения отсроченной реконструкции молочной железы свободным DIEP-лоскутом в сочетании с трансплантацией паховых лимфатических узлов. В послеоперационном периоде отмечено уменьшение объёма конечности, снижение выраженности дермального рефлюкса и появление линейных участков лимфатического транспорта в зоне трансплантата. Полученные данные подтверждают перспективность трансплантации васкуляризованных лимфатических узлов как компонента комплексной хирургической стратегии лечения вторичной лимфедемы у пациенток после комбинированного лечения рака молочной железы.

Ключевые слова: лимфедема, рак молочной железы, трансплантация лимфатических узлов, ICG-лимфография, микрохирургия.

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Для цитирования: Трошенков Е.А., Поляк М.А., Шахбанова К.А., Каприн А.Д., Филоненко Е.В., Куцурадис А.Ф., Мантаридис Д. Вторичная лимфедема как осложнение хирургического лечения рака молочной железы: аутотрансплантации лимфатических узлов с использованием ICG-лимфографии // Biomedical Photonics. – 2026. –Т. 15, № 1. – С. 30–36. doi: 10.24931/2413–9432–2026–15-1-30-36

Introduction

Lymphedema is a chronic disease caused by impaired lymphatic transport and characterized by the accumulation of protein-rich fluid in the interstitial space, followed by chronic inflammation, fibrosis, and structural remodeling of soft tissues [1]. According to the literature, lymphedema is considered a dynamic pathological process that includes not only mechanical obstruction of the lymphatic pathways but also complex immune-inflammatory changes leading to progressive tissue remodeling [2].

Upper extremity lymphedema following breast cancer surgery remains one of the most significant challenges in modern oncology and reconstructive surgery. Despite the introduction of sentinel lymph node biopsy and the de-escalation of axillary surgery, the incidence of lymphedema after axillary lymph node dissection remains high, reaching 40% [3]. Additional risk factors include radiation therapy, a high body mass index, infectious complications (recurrent episodes of erysipelas or cellulitis), and the extent of surgical intervention [2].

The development of lymphedema leads to a significant decrease in the patient's quality of life, limited upper limb function, chronic pain, and an increased risk of infectious complications, making this problem not only medically but also socially significant [4].

A modern approach to treating lymphedema involves a stepwise approach. In the early stages, the leading method remains comprehensive physical anti-edema therapy, including compression therapy, manual lymphatic drainage, exercise therapy, and meticulous skin care [5]. However, with the development of severe fibrotic changes and destruction of lymphatic collectors, the effectiveness of conservative therapy is significantly reduced, necessitating the use of surgical correction methods [6].

The development of microvascular surgery has led to the introduction of physiological methods for reconstructing lymphatic drainage—lymphatic venous anastomoses (LVA) and vascularized lymph node autotransplantation (VLNT). LVA is most effective in the early stages of the disease when lymphatic vessels are preserved, while VLNT is considered the preferred method for severe anatomical and functional changes and the development of fibrosis, providing both mechanical restoration of lymphatic drainage and the potential lymphangiogenic effect of transplanted nodes [7].

Thus, the search for optimal surgical tactics for the treatment of secondary lymphedema after breast cancer surgery remains a *relevant task* of modern oncomammology and reconstructive surgery. This article presents a clinical case of vascularized lymph node autotransplantation and reviews the current literature on this topic.

Technical Aspects and Mechanisms of Effectiveness of Vascularized Lymph Node Transplantation

Autotransplantation of vascularized lymph nodes is a physiological microsurgical method for reconstructing lymphatic drainage and is used in secondary lymphedema, primarily in cases of severe anatomical and functional changes in the lymphatic system. This technique involves isolating a block of lymph nodes with surrounding adipose tissue and feeding arterial and venous vessels, forming a vascular pedicle, followed by transferring the flap to the lymphedema area and performing microsurgical arterial and venous anastomoses [8].

The most commonly used donor sites are the inguinal region, as well as the axillary, omental, submental, lateral thoracic, supraclavicular, and cervical regions [9]. The choice of donor site is determined by anatomical

features, the required tissue volume, and the risk of developing donor lymphedema.

Considering that secondary lymphedema of the upper limb most often develops after axillary lymph node dissection combined with radiation therapy, a pronounced fibrous scarring process often develops in the recipient site. Preparation of the graft bed is a fundamentally important stage of the surgery and includes excision of fibrous tissue, decompression of vascular and nerve structures, and creation of conditions for neoangiogenesis and lymphangiogenesis. Removal of scar tissue reduces mechanical compression and eliminates the barrier to the formation of new lymphatic collaterals [10].

Transplantation is performed by placing the vascularized lymphatic complex into the prepared bed and fixing it with soft tissue. Vascular anastomoses of arteries and veins are performed microsurgically, ensuring the restoration of blood flow and integration of the graft into the lymphatic system of the limb [11].

The clinical effect of autotransplantation of vascularized lymph nodes is achieved through several complementary mechanisms.

The first theory, the so-called "lymphatic pump" or pressure gradient concept, suggests that the transplanted lymphatic complex functions as a zone of reduced interstitial pressure. Active blood flow within the graft creates conditions for passive lymphatic influx from surrounding tissues, which ensures early reduction of edema in the postoperative period [12].

The second theory involves the induction of lymphangiogenesis. Experimental and clinical studies have shown that transplanted lymph nodes are capable of secreting vascular endothelial growth factor-C (VEGF-C), which stimulates the proliferation of lymphatic endothelial cells and the formation of new lymphatic collectors. Thus, new lymphatic drainage pathways and lymphovenous connections are formed in the long-term period [13].

The functional activity of the graft is confirmed by instrumental methods. Lymphography using indocyanine green (ICG) and lymphoscintigraphy demonstrate a redistribution of lymphatic flow to the graft area already in the early postoperative period, followed by the formation of new lymphatic collaterals and improved drainage function of the limb [12].

Thus, vascularized lymph node transplantation represents a pathogenetically substantiated method for the surgical correction of secondary lymphedema, combining mechanical, angiogenic, and immunomodulatory effects.

Indications and Contraindications for Vascularized Lymph Node Transplantation

The choice of vascularized lymph node transplantation as a treatment for lymphedema is based on the stage of the disease, the severity of structural changes in the lymphatic system, and the results of previous conservative therapy. This method is primarily considered for patients with stage II-III lymphedema according to the International Society of Lymphology (ISL) classification, in whom conservative therapy has failed to achieve a stable functional result [14].

The key selection criterion is the presence of anatomical and functional failure of the lymphatic collectors, confirmed by instrumental methods (ICG lymphography, lymphoscintigraphy), with signs of severe dermal reflux, segmental vascular obliteration, or complete vascular destruction. In such cases, performing lymphovenous anastomoses is technically difficult or impractical, which justifies the choice of lymph node transplantation as a pathogenetically targeted reconstruction method.

The main indications for vascularized lymph node transplantation include:

- ISL stage II-III lymphedema with severe soft tissue fibrosis;
- lack of clinically significant effect from adequate conservative therapy;
- recurrent episodes of cellulitis (erysipelas);
- obliteration or a sharp decrease in the number of functioning lymphatic vessels;
- severe pain, decreased limb function, and a significant deterioration in quality of life.

An additional factor in favor of surgical treatment may be disease progression despite adherence to a compression regimen and rehabilitation measures.

Contraindications to vascularized lymph node transplantation can be divided into absolute and relative. This approach allows this intervention to be considered not as a universal method, but as a component of a personalized surgical strategy for the treatment of secondary lymphedema.

Absolute contraindications include:

- local recurrence of breast cancer or progression of the oncological disease;
- the presence of distant metastases.

Relative contraindications include:

- severe microcirculation disorders in the recipient site (post-radiation vasculitis, critically reduced perfusion);
- severe forms of neuropathy or neuritis of the brachial plexus, limiting the possibility of full postoperative rehabilitation;
- lack of suitable recipient vessels for the formation of microsurgical anastomoses;
- severe somatic diseases that increase the risk of microsurgical intervention.

Thus, indications for VLNT are determined based on a comprehensive assessment of the stage of lymphedema, instrumental imaging data, the effectiveness of

conservative treatment, and the patient's oncological status. Optimal patient selection is a key factor in achieving a sustainable clinical outcome [15, 16].

Clinical Observation

A 49-year-old female patient presented to the P.A. Herzen Moscow Oncology Research Institute – a branch of the National Medical Research Center of Radiology of the Ministry of Health of Russia with a diagnosis of stage IIIC right breast cancer, pT2N3aM0, luminal type A, status after combined treatment in 2023 (05.08.2023 – right radical mastectomy, 4 cycles of neoadjuvant chemotherapy according to the DC regimen from 28.08.2023 to 01.11.2023, external beam radiotherapy from 21.11.2023 to 26.12.2023, total focal dose 50 Gy).

From the medical history, it is known that after completion of the combined treatment for the primary disease, the patient began to notice increasing swelling of the right upper limb. The patient did not wear a compression sleeve, as a result of which the swelling became persistent.

At the A.F. Tsyb Medical Radiological Research Center – a branch of the National Medical Research Center of Radiology of the Ministry of Health of Russia, on 15.02.2024 and 02.05.2024, lymphovenous bypasses of the right upper limb were performed: at the level of the forearm and the hand, respectively.

Despite surgical interventions, conservative therapy, and wearing of compression garments, the desired effect on swelling was not achieved. Furthermore, the patient noted a significant decrease in quality of life due to the absence of a breast.

The patient was referred to the P.A. Herzen Moscow Oncology Research Institute for further evaluation and determination of treatment strategies for secondary

Рис. 1. Внешний вид правой верхней конечности до начала лечения. Лимфедема IIA стадии по классификации ISL.
Fig. 1. Clinical appearance of the right upper limb before treatment. Stage IIA lymphedema according to the ISL classification.

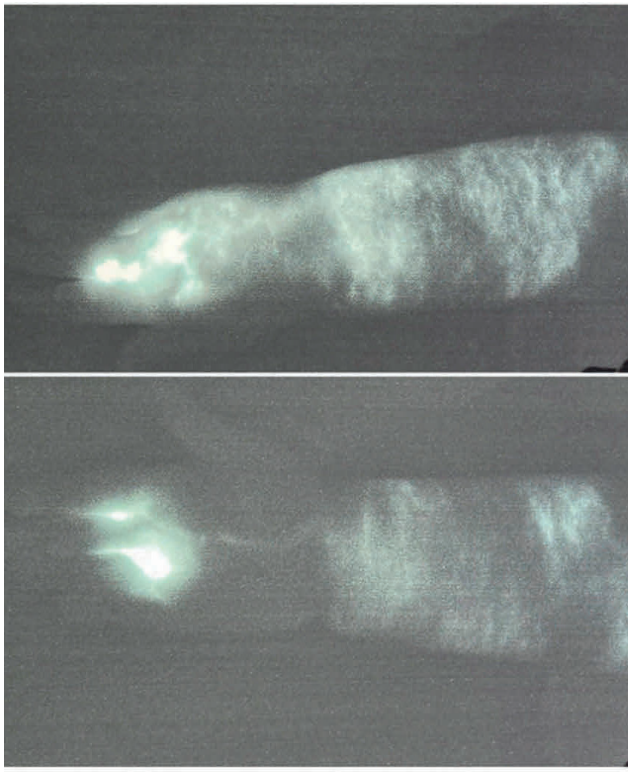

Рис. 2. ICG-лимфография правой верхней конечности до лечения: выраженный дермальный рефлюкс, отсутствие линейных лимфатических коллекторов в проксимальных отделах.
Fig. 2. ICG lymphography of the right upper limb before treatment: pronounced dermal backflow and absence of linear lymphatic collectors in the proximal segments.

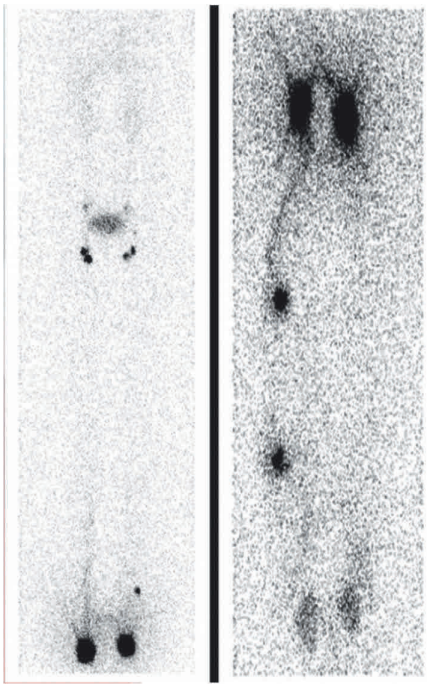

Рис. 3. Лимфосцинтиграфия правой верхней конечности: лимфатический транспорт замедлен, регионарные подмышечные узлы не визуализируются.
Fig. 3. Lymphoscintigraphy of the right upper limb: lymphatic flow is slowed, and regional axillary nodes are not visualized.

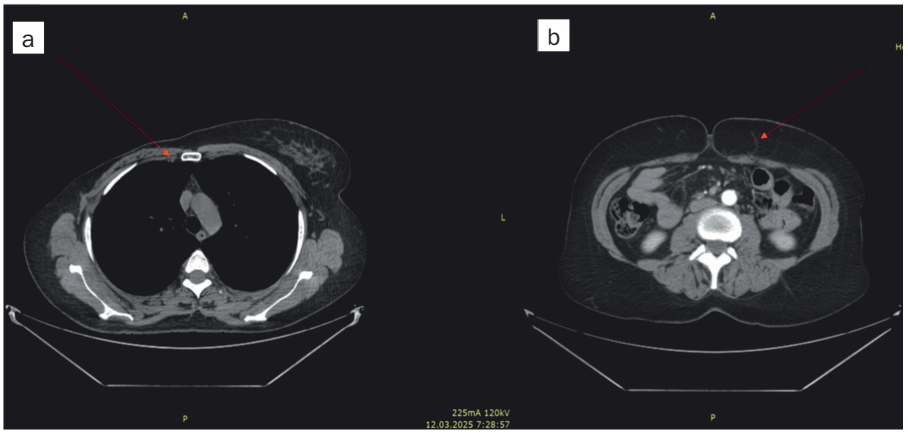

Рис. 4. КТ-ангиография для планирования микрохирургической реконструкции: a – передняя брюшная стенка: виден перфорант глубокой нижнеэпигастральной артерии для выделения сосудистой ножки; b – грудная клетка со стороны ранее выполненной мастэктомии: сохранные внутригрудные сосуды, пригодные для реконструкции.
Fig. 4. CT angiography for microsurgical reconstruction planning: a – anterior abdominal wall: perforator of the deep inferior epigastric artery visible for harvesting the vascular pedicle; b – chest on the side of prior mastectomy: preserved intrathoracic vessels suitable for reconstruction.

lymphedema and the possibility of right breast reconstruction.

On examination: the right upper extremity was enlarged, primarily in the forearm and shoulder area, with moderate fibrotic changes in the soft tissues and decreased skin elasticity. The lymphedema corresponded to stage IIA according to the ISL classification.

According to ICG lymphography data, pronounced dermal reflux, the absence of formed linear lymphatic collectors in the proximal parts of the limb and signs of failure of previously performed lymphovenous anastomoses were revealed.

Lymphoscintigraphy confirmed a significant slowdown in lymphatic transport and lack of visualization of regional axillary lymph nodes.

CT angiography visualized a perforator of the deep inferior epigastric artery on the anterior abdominal wall, necessary for isolating the vascular pedicle, as well as preserved intrathoracic vessels on the side of the previously performed mastectomy, which made it possible to plan microsurgical reconstruction.

Given the severe anatomical and functional impairment of lymphatic drainage, the lack of response to lymphovenous bypass, and the patient's desire to restore the lost breast, a decision was made to perform delayed reconstruction of the right breast using a free DIEP flap combined with vascularized inguinal lymph node transplantation.

During the surgery, after excision of scar-fibrous tissue in the axillary region, an adequate recipient bed

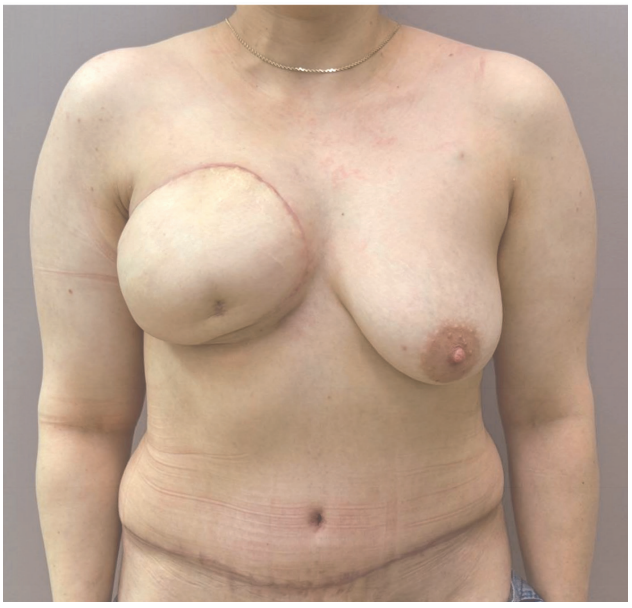

Рис. 5. Клинический осмотр через 6 мес после лечения: видна восстановленная молочная железа, уменьшение объема конечности и снижение симптомов лимфостаза.
Fig. 5. Clinical examination 6 months after treatment: reconstructed breast visible, limb volume reduced, and lymphedema symptoms improved.

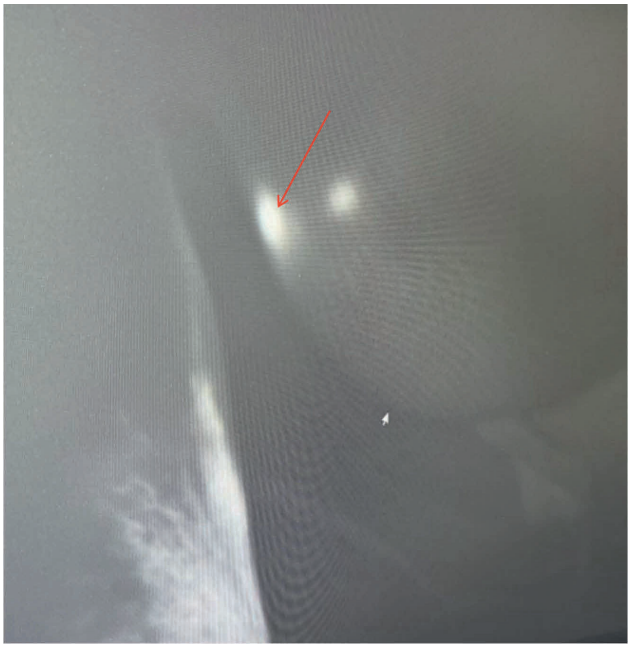

Рис. 6. ICG-лимфография после реконструкции: накопление контраста в зоне трансплантата.
Fig. 6. ICG lymphography after reconstruction: contrast accumulation in the transplant area.

was created. A DIEP flap was harvested, incorporating superficial inguinal lymph nodes on a vascular pedicle. End-to-end microvascular anastomoses were formed with the thoraco-dorsal vessels. The lymphatic component was placed orthotopically in the axillary area. No intraoperative or early postoperative complications were noted.

Six months after surgery, the patient noted a decrease in the feeling of heaviness and tension in the limb, decreased tissue density, and a reduced dependence on constant compression therapy. Follow-up ICG lymphography showed a reduction in the severity of dermal reflux and the appearance of linear areas of lymphatic transport with contrast accumulation in the transplant area. Clinically, a 2-3 cm reduction in limb circumference at the forearm level was recorded. No episodes of erysipelas were observed postoperatively.

Conclusion

Vascularized lymph node autotransplantation is a modern and highly effective microsurgical method for treating lymphedema, especially at stages characterized by destruction of lymphatic drainage and decreased effectiveness of conservative therapy. This method ensures sustainable limb volume reduction, restoration of lymphatic drainage, a reduction in the incidence of inflammatory complications, and a significant improvement in patients' quality of life. Optimization of donor site selection, the use of imaging techniques, and microsurgical techniques minimize risks and improve the effectiveness of the procedure. VLNT represents a promising tool for a comprehensive approach to lymphedema treatment, particularly in patients following comprehensive breast cancer treatment, where lymphatic system changes are most pronounced.

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