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Treatment of Breast Cancer-Related Lymphedema Using Combined Autologous Breast Reconstruction and Autologous Lymph Node Transplantation

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1. Introduction

Lymphedema can appear after lymphadenectomy and radiotherapy for cancer treatment of the breast. The reported incidence of lymphedema, which can occur many years after the initial treatment, varies due to different methods of long follow-up. Patients requiring more extensive breast cancer treatment with axillary lymph node dissection and radiation have the greatest risk for development of lymphedema.[3,4]

In a study of 20 years follow-up of breast cancer patients [3], 49% of patients reported having lymphedema and 13% (33 of 263 women) had augmented measurements of the affected arm. The incidence of lymphedema following breast cancer treatment ranges from 24% to 49% after mastectomy, and 4% to 28% after lumpectomy. [1]. It appears that removing lymph nodes around the axillary vein is responsible for the development of lymphedema. Lymphangitis is an inflammation of the lymphatic channels that occurs in response to a distal infection such as paronychia, an insect bite, or secondary infections in the inter-digital spaces. Erysipelas may require hospitalization in acute cases. Then, the skin becomes progressively more fibrotic and thick, and transformation in elephantiasis may be observed. Lymphangiosarcoma is a rare malignant tumor that occurs in long-standing cases of lymphedema. The sarcoma first appears as an ecchymotic mark, or a tender skin nodule in the extremity. Stewart-Treves syndrome (STS), defined as lymphangiosarcoma arising from post-mastectomy lymphedema, has an extremely poor prognosis, with an overall mortality rate of 70-90% even following limb amputation. This is why it is particularly important to treat the lymphedema. Physiotherapy is essential in managing the edema, but it will not be effective if there are no remaining lymphatic channels. The most effective

form of physiotherapy appears to be manual lymphatic drainage and multilayer bandages. Physiotherapy must be combined with the other techniques. The major drawbacks of conservative treatment are: significant time commitment, labor intensive, requirement for specialized therapists, and lifelong commitment by the patient.

This pathology destroys the quality of life of the patients both functionally (lost of work in 70% definitively) and psychologically and the cost to insurance companies are increasing (infections, physiotherapy for life, etc.)[2]

2. Surgical treatment in iatrogenic upper extremity lymphedema

The surgery is divided in 2 groups: debulking techniques and the reconstructive techniques.

1. Debulking techniques include lipoaspiration and excisions:

- excisions of fat and soft tissue were used in cases of severe elephantiasis, but rarely:
- lipoaspiration performed for fatty lymphedema often required continuous compression garments for life. This technique is used for fatty and soft tissue lymphedema and is mostly used in Sweden (cold climate).(Brorson)

2. reconstructive techniques are more sophisticated and attempt to reestablish the anatomy:

- The autologous lymph node transplantation (ALNT) may provide an effective solution by replacing the scarred tissue with new lymphatic pathways because the transplanted nodes contain lymphatic growth hormone.[7] The incidence of infections decreases because the nodes contain immune cells.
- The combination of this lymph node flap with the DIEP or SIEA (and even TRAM) provides simultaneous treatment for lymphedema and breast reconstruction. The lymph node flap can also be added as a second free flap with the other flaps for breast reconstruction such as the TDAP, SGAP, TUG, PAP and even with more traditional techniques such as the latissimus dorsi flap.
- The quality of lymphovenous anastomosis (supermicrosurgery) is improved thanks to the improved quality of microsurgical materials. However, the pressure within the lymphatic system must be maintained above the venous pressure (normally, the venous pressure is higher than lymphatic pressure) to avoid collapse of the tiny anastomosis. This is achieved by permanent external compression. This may explain the poor long-term results of this surgery, but this technique can be used as an adjunct to ALNT.
- lympho-lymphatic grafts are technically extremely difficult. This procedure results in large donor site scars in the lower extremities with inconsistent results. [8]

For each individual patient, combinations of these procedures may be indicated to achieve improved results.

3. Clinical evaluation and indications of surgery

Patients are evaluated by a multidisciplinary team (oncologist, physiotherapist, surgeon, pain management specialist, neurologist, radiologist) to understand the etiology of the lymphedema, and/or pain and paresthesias.

The patient must be oncologically cleared and free of cancer recurrence. Appropriate physiotherapy must be applied preoperatively. The clinical exam is essential: fibrotic areas, folds, compression, sequelae of radiotherapy, type of pain, evaluation for the neuroma, palsy or paresthesia, quality of the skin, and skin lesions are all components of the pathology that must be evaluated.

Radiologists are now performing lymphatic MRI which allows us to visualize a map of the lymphatic system of the arm and thorax. Specific pathology can be identified such as hypoplasia of the vessels due to chronic infection, lack of lymph nodes and/or vessels in the axilla following lymphadenectomy, radiotherapy and chronic infections, and collateralization of lymphatic vessels. If these pathways do exist [6], surgery should be delayed following satisfactory physiotherapy. In some cases, lymphangiography combined with the scan, provides more dynamic information, but is less useful.

EMG can be used to identify the site of nerve compression or degeneration along with the affected muscle (useful for tendon transfers in plexitis). The pain specialist can help diagnose the cause of pain, provide appropriate medical treatment if necessary and help determine if there is an indication for surgery.

In subclinical cases, if the patient desires breast reconstruction, the indication for an adjunct autologous lymph node flap will depend on establishing the presence of lymphatic pathology by using preoperative mri (or isotopic lymphoscintigraphy). If the lymphedema is present, the DIEP or SIEA will include the lymph node transplant.

4. Operative technique

4.1. Autologous lymph node transplantation for upper limb lymphedema

The dissection begins at the axillary region. The fibrosis is dissected and the thoracodorsal vessels are identified. This part of the operation can be extremely difficult, because normal anatomy may be severely distorted due to scar contracture from surgery and radiation. The location of the axillary artery, vein, and brachial plexus are often changed because of radiotherapy-related contracture. The plexus and axillary vein can be compressed by large fibrotic bands and the surgeon must be particularly cautious during dissection in these areas. Vascular branches with suitable sizes for microanastomosis are prepared. Neuromas may be encountered around these vessels which are treated when present. If paresthesia or palsy is present, external neurolysis is performed and the thoracobrachial space must be decompressed. The dimensions of the flap requirements will then be estimated as well as the need for fat and skin.

The superficial inguinal lymph node flap starts with an incision performed over a line located between the iliac crest and the pubis. The length of the incision depends on the flap size needed to fill the defect. The subcutaneous tissue is incised to the depth of the fascia cribiformis, where a superficial diagonal vein can be found. The fatty tissue located deeper to this superficial fascia and superficially to the muscular aponeurosis contains 4-5 lymph nodes that can be transferred based on the superficial circumflex iliac vessels. This pedicle is dissected and the flap is elevated around these isolated vessels. Inferiorly, the inguinal crest is a very important limit of the dissection, and preserving the deep lymph nodes is critical in preventing secondary lymphedema at the donor site.

The flap is then transferred to the axillary recipient site with microsurgical technique.

4.2. Extended abdominal flaps

The inguinal lymph nodes flap can be incorporated into the flap of the adjacent skin and fat in the lower abdomen, based on the superficial inferior epigastric vessels (SIEA) or the deep inferior epigastric vessels (free TRAM or DIEP). To harvest the nodes, the incisions of the abdominal flap must be lowered to the level of the iliac crest, including the inguinal lymph node flap previously described (subcutaneous tissue containing the nodes, vascularized by the circumflex iliac vessels). If the microsurgical anastomosis of the flap are made to the internal mammary vessels, the lymph node extension should be harvested at the opposite side of the pedicle. If the flap is reattached at the thoracodorsal system, the nodes can be harvested at the same side. The lymph node flap should be placed in the axillar region. It has to be inserted around the axillary vein, where the lymphatic tissue was first resected.

The need for a second set of anastomosis will be assessed during surgery. SPY imaging can be used intra-operatively to evaluate the perfusion of the transferred nodes and the flap

4.3. Lymphovenous anastomosis

LVA can be performed in the proximal and/or distal regions of the limb, depending on indication (elevated pressure in the lymphatic system). PDE is a mapping device of the superficial lymphatic pathways, useful to determine the locations of the LVAs. These are performed under big magnification, with 11-0 or 12-0 (where available) nylon sutures.

4.4. Selective external liposculpture

After 6 month min, the water disappears but the fat remains sometimes because the lipocytes were not circulated for many years. A special Mercedes canula is more convenient, the fibrosis can still be important. The liposuction is only performed on the external part of the arm and very softly on the forearm (post part also).

5. Complications and concerns

Lymphocele at the donor site can be avoided with the use of a drain on the initial post-operative period (48h) and local compression. If the deep lymph nodes beyond the inguinal ligament or in the axilla are not disturbed, no iatrogenic lymphedema of the donor limb should be noted. Local infections and delayed wound healing are rare, even in irradiated tissues. The autologous lymph node flap is a buried flap. Flap monitoring is difficult. Vascular thrombosis is believed to occur in 2% of the cases, in which no improvement is perceived. For enlarged flaps, thrombosis will lead to exploration of anastomoses, and eventually flap loss. When 2 sets of anastomoses are performed, the ALNT part of the flap can remain viable. Infection risks are present in chronic infected patients, but prophylactic antibiotic therapy limits their occurrence (no exceed 2%).

Scars can become enlarged, and even hypertrophic, but they are concealed under a the slip or bra.

6. Clinical outcomes

On a series of more than 2.500 patients operated in 20 years, with stage 1,2 and 3 lymphedemas (International Society of Lymphology), 98% of patients present some degree of improvement, and 40% of the stages 1 or 2 lymphedemas have complete remission and do not need additional physiotherapy treatment. Follow-up of at least 3 years are included. Elephantiasis is never completely healed and patients will still need physiotherapy. 95% state some kind of amelioration. Only 2% of patients keep having infection episodes. Results will depend on the longevity of the lymphedema and the presence of fibrotic tissue. Bilateral lymphedemas will have worse outcomes. Generally, the patients do loose 2 cm /months, and this during 2 years, progressively.[9-10]

The results are better for short duration and less severe lymphedemas. In moderate cases, MRL shows new lymphatic pathways, with effective lymph drainage. Even the long-standing lymphedema (over 15y) can show some improvement.

When neuromas of the intercostal nerves are encountered, neurolysis and removal of surgical clips is effective, achieving pain-relief in 98% of patients. For brachial plexus neuropathies, neurolysis of the nerves and coverage with a non-irradiated, well-vascularized tissue (ALNT or enlarged abdominal flap) will be effective. These patients experience less pain and palsy stabilization. Although sensation can be slightly recovered the 2 following years, motor recovery is rare, and can only be expected in young patients. Tendon transfers can be beneficial for some patients with partial palsies, once the lymphedema disappears. We do not advise the use of a tourniquet.

The lymphovenous anastomosis can destroy the remaining lymphatic channels if they became thrombosed. The addition seems not very helpful except in particular cases where the lymphatic vessels are well seen with the fluorescein.

The combination of the autologous lymphnodes transfer with addition of 1 lympholymphatic anastomosis is not necessary because the VGEFc are creating new pathways.

In conclusion, patients resistant to any kind of physiotherapy, showing no drainage of the upper limb, can benefit from the autologous lymph node transfer to restore the anatomy. The nodes containing VGEF3 induce new lymphatic vessels growth. After chronic infections, it is well known that the vessels becomes obstructed. The patients can expect good results in 98% and normalization in 40% after 2 years. The post operative lymphatic MRI does explain the indications of the surgery, and the results (new ways, transplanted nodes visible....). No morbidity of the donor site is observed if the dissection doesn't pass under the inguinal ligament.

The combination with different free flaps to restore the breast at the same time is ideal.

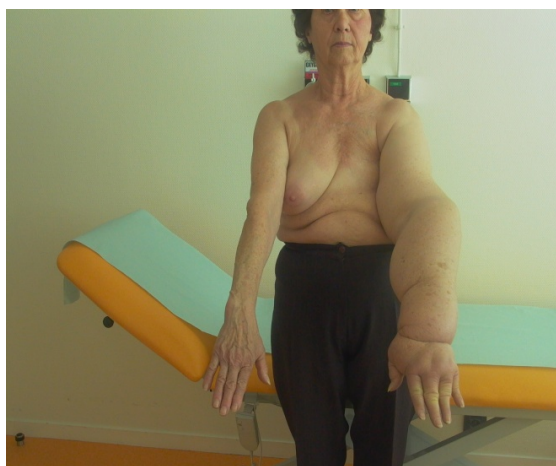


Figure 1. Typical case of lymphoedema



Figure 2. Lymphatic MRI showing lack of lymphnodes and lymphatic vessels after adenectomy and radiotherapy for breast tumor. Evidence of complete absence of drainage. Physiotherapy cannot treat such cases.

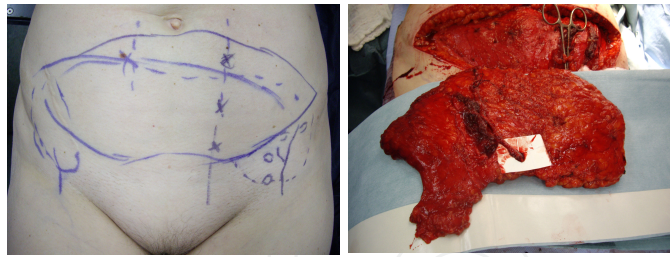


Figure 3. Design of the enlarged DIEP based on the deep epigastric vessels connected with the superficial circumflex iliac art.

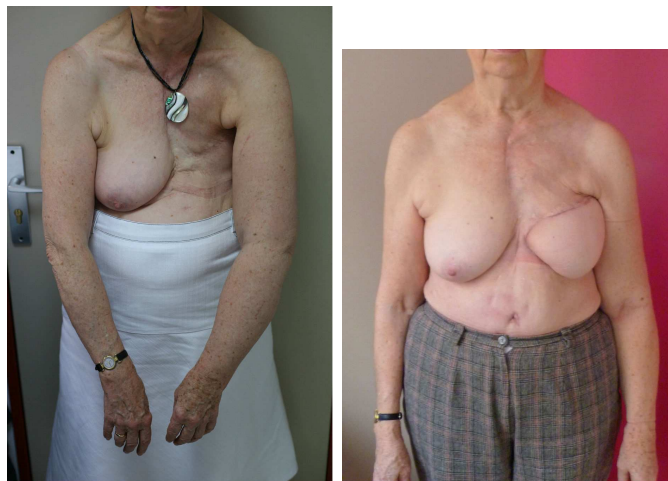


Figure 4. 76-year-old woman operated 25 years ago who underwent mastectomy, adenectomy and radiotherapy. Suffering from lymphoedema for the last 20 years. She was operated post radiotherapy from bypass for cardiac ischemia. Results 6 months later after breast reconstruction by DIEP combined with ALNT.

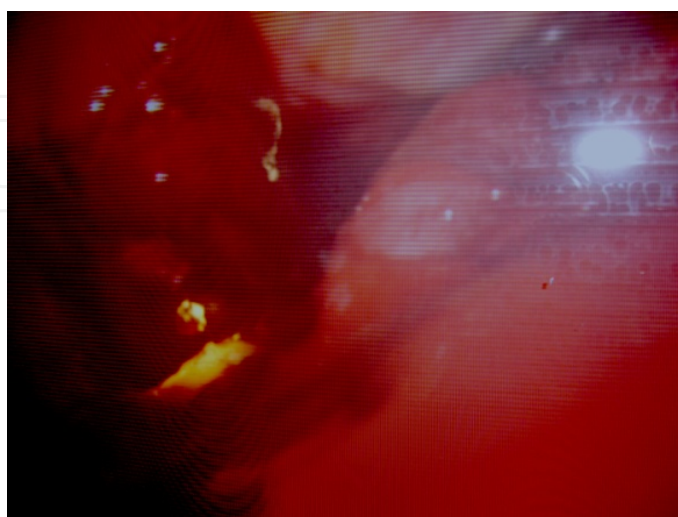


Figure 5. Living transplanted nodes observed by endoscopy



Figure 6. Spy of the flap



Figure 7. Post operative lymphatic MRI

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