Medical Coverage Policy

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Lymphedema and Lipedema Surgical Treatments

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Complex Lymphedema Therapy (Complete Decongestive Therapy)
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Overview

This Coverage Policy addresses surgical treatments for lymphedema and lipedema.

Coverage Policy

Lipedema

Liposuction, (i.e., water jet-assisted liposuction, micro-cannular) or lipectomy for the treatment of lipedema of the extremities is considered medically necessary when ALL of the following criteria are met:

- pain in the affected areas
- easy bruising
- nodularity of fat deposits in lipedema affected areas (dimpled or orange peel texture)
- tenderness
- physical function impairment (e.g., difficulty ambulating, performing activities of daily living)
- absence of pitting edema (no "pitting" when finger or thumb pressure is applied to the area of fat) unless the individual has coexisting lymphedema
- negative Stemmer sign, unless the individual has coexisting lymphedema (Stemmer sign is negative when a fold of skin can be pinched and lifted up at the base of the second toe or at the base of the middle finger)
- lack of improvement in lipedema-affected areas following weight loss if applicable
- lack of improvement in swelling with limb elevation
- lack of response to at least three consecutive months of medical management (e.g. conservative treatment with compression garments and manual lymph drainage)
- photographs confirm the presence of bilateral symmetric adiposity (fat accumulation) in the affected extremities

Lymphedema

An excisional procedure (e. g. debulking, liposuction) for the treatment of lymphedema is considered medically necessary when an individual meets ALL of the following criteria:

- physical function impairment (e.g., difficulty ambulating, performing activities of daily living)
- lack of response to at least three consecutive months of medical management (e.g., compression garments, manual lymphatic drainage)
- postoperatively will continue to wear compression garments as instructed to maintain the benefits of treatment

EITHER of the following procedures is considered medically necessary for the treatment of lymphedema:

- microsurgical treatment (e.g., microsurgical lymphatico-venous anastomosis, lymphatic-capsular-venous anastomosis, lymphovenous bypass)
- vascularized lymph node transfer

When an individual meets ALL of the following criteria:

- **ONE** of the following signs and symptoms:
  - physical function impairment (e.g., difficulty ambulating, performing activities of daily living)
  - history of chronic or recurrent skin conditions (e.g. cellulitis, ulcerations)
  - significant pain or weakness in the affected extremity
- **ONE** of the following quantitative measurements:
  - volumetry differential (circumferential measurements and/or perometry differential) >10% (if affected extremity dominant extremity) or >7% (affected extremity is non-dominant extremity)
  - lymphoscintigraphy results show delayed transit time to first-level lymph nodes or a dermal back flow pattern
- lack of response to at least three consecutive months of medical management (e.g., compression garments, manual lymphatic drainage)
- postoperatively will continue to wear compression garments as instructed to maintain the benefits of treatment

The following surgical procedures for the treatment or prevention of lymphedema are considered experimental, investigational or unproven:

- tissue transfer (e.g., omental or mesenteric flap)
- immediate lymphatic reconstruction (e.g., lymphatic microsurgical preventing healing approach [LYMPHA]) for prophylactic purposes)
- axillary reverse mapping (ARM)/reverse lymphatic mapping

General Background

Lipedema is characterized by the abnormal patterns of fat deposition with associated edema and usually have normal lymphatic function (Mehrara, 2023). Lymphedema is defined as the abnormal accumulation of interstitial fluid and fibroadipose tissues resulting from injury, infection, or congenital abnormalities of the lymphatic system (Mehrara, 2023).

Lipedema

Lipedema is a rare disorder of adipose tissue that primarily affects females and is often misdiagnosed as obesity or lymphedema. There are numerous synonyms to refer to this condition (e.g. adipositas dolorosa, lipomatosis dolorosa, painful lipohypertrophy). The disorder is well-known in Europe but is largely unrecognized and underdiagnosed in the United States. Lipedema is a distinct entity that must be differentiated from obesity and lymphedema, although it may progress to involve the venous and lymphatic systems, which increases the difficulty of its diagnosis. In contrast to primary lymphedema, the lymphatic system remains unimpaired in the initial stages of lipedema and can keep up with the increased amount of interstitial fluid. In the majority of the cases, lipedema is located in lower limbs with the trunk and feet unaffected (Herbst, 2021). There is usually minimal pitting edema. The typical presentation is of a woman with bilateral "stovepipe" enlargement of the legs and without involvement of the feet with a sharp demarcation between normal and abnormal tissue at the ankle, referred to as the "cuff sign." This is often combined with a symmetrical involvement of arms, particularly the upper arms, with sparing of hands. Lipedema may be isolated to the arms without involvement of the

legs, but this is extremely rare. The pathogenesis is unknown and no curative treatment is available. Patients may complain of tenderness and pain and sustain easy bruising. Elevating the limbs has no effect on the involved limbs. Advanced lipedema may progress into lymphedema. When lipedema remains untreated, increased lymphatic load continually exceeds lymphatic transport capacity resulting in the decompensation of the lymphatic system therefore, uni-, or much more typically, bilateral lymphedema can develop. The pressure of the fat tissue itself causes obstruction of the lymphatic vessels resulting in secondary lymphedema. Additionally, the deposition of protein-rich edema causes fibrosis of the tissue, further impairing lymphatic drainage. The combination of lymphatic insufficiency and lipedema is called lipolymphedema or lympho-lipedema. Concomitant severe venous insufficiency is rare; however, varicosity is often seen among lipedematous patients. Diagnosis of lipedema is generally made on the basis of clinical features (See Appendix A). Usually, the medical history and clinical examination are enough to suspect the diagnosis. The most common comorbidities associated with lipedema include: hypertension, obestity (BMI ≥ 35), hypothyreosis, atopic diseases, osteoporosis, lymphedema, varicose veins of leg, depression and anxiety (Mehrara, 2023; Sandhofer, et al., 2019; Shavit, et al., 2018; Canning, et al., 2018; Dadras, et al., 2017; Forner-Cordero, et al., 2012; Stutz, et al., 2009).

There are currently four reported stages of lipedema: Stage 1 involves an even skin surface with an enlarged hypodermis; Stage 2 involves an uneven skin pattern with the development of a nodular or mass-like appearance of subcutaneous fat, lipomas, and/or angiolipomas; Stage 3 involves large growths of nodular fat causing severe contour deformity of the thighs and around the knee; and Stage 4 involves the presence of lipolymphedema (Buck and Herbst, 2016).

The standard conservative therapy for lipedema significantly differs from that of lymphedema. Management of lipedema is complex and distinct from lymphedema. The proposed main conservative treatment is complete or complex decongestive therapy (CDT). (Please refer to Medical Coverage Policy Complex Lymphedema Therapy [Complete Decongestive Therapy]). CDT combines several approaches including manual lymph drainage (a massage technique), compression therapy, and physical mobilization. Manual lymphatic drainage, compression stockings, intermittent pneumatic compression, skin care and exercise are often used to control pain and symptoms. Diet is also used to prevent or treat obesity associated with lipedema. It is suggested that lipedema patients avoid weight gain. Obesity and "yo-yo" dieting have been shown to exacerbate lipedema. Even with conservative and supportive treatments, the disease may progress and further treatment may be necessary. For a defined subset of lipedema patients who are unresponsive to conservative treatment, a surgical option may be liposuction using specialized techniques (e.g., water jet-assisted liposuction). Often, multiple sessions of liposuction are necessary to adequately treat the extremities circumferentially and along their entire length. Liposuction can only reduce the amount of fatty tissue, but not completely remove it. Many patients often require ongoing conservative treatment postoperatively to maintain results. Additionally, the avoidance of postoperative weight gain is essential in order to maintain the results of surgery (Sandhofer, et al., 2019; Wollina, 2019; Dadras, et al., 2017; Warren and Kappos, 2016; Buck and Herbst, 2016).

Literature Review: Although the evidence in the published peer-reviewed literature evaluating the effectiveness of liposuction for the treatment of lipedema consists primarily of observational studies, case series and retrospective reviews, outcomes have have demonstrated positive results for reduction of limb size, pain, bruising, skin problems and improvement in the ability to move and has evolved into a standard of care (Ghods, et al., 2020; Witte, et al., 2020; Buso et al., 2019; Wollina, et al., 2019; Forner-Cordero 2012; Schmeller et al., 2006).

Professional Societies/Organizations
No evidence-based clinical practice guidelines were located for lipedema.

Use Outside of the US
The Austrian Academy of Cosmetic Surgery and Aesthetic Medicine and the International Society for Dermatologic Surgery held the First International Consensus Conference on lipedema with the purpose of reviewing current European guidelines and the literature regarding the long-term benefits that have been reported to occur after lymph-sparing liposuction for lipedema using tumescent local anesthesia. Lipedema is well-known in Europe but is largely unrecognized and underdiagnosed in the United States. The authors state that multiple studies from Germany have reported long-term benefits for as long as eight years after liposuction for lipedema using tumescent local anesthesia. The international experts concluded that lymph-sparing liposuction using tumescent local anesthesia is currently the only effective treatment for lipedema (Sandhofer, et al., 2020).

In June 2019, the Canadian Agency for Drug and Technologies in Health Canadian Agency for Drugs and Technologies in Health (CADTH) published a Rapid Response Report: Summary with Critical Appraisal on Liposuction for the Treatment of Lipedema-A Review of Clinical Effectiveness and Guidelines. The key research questions were: what is the clinical effectiveness of liposuction for the treatment of lipedema and what are the evidence-based guidelines regarding the use of liposuction for the treatment of lipedema? The authors' conclusions state that "information about the clinical effectiveness of liposuction for the treatment of lipedema was sourced from five uncontrolled before-and-after studies (Dadras, et al., 2017; Wollina, et al., 2019; Schmeller, et al., 2012, Rapprich, et al., 2011; Baumgartner, et al., 2016). Data from the studies indicated that in patients with lipedema, treatment with liposuction resulted in a significant improvement of pain, sensitivity to pressure, edema, bruising, feeling of tension, and quality of life. The patients also experienced significant reductions in size extremities and restriction of movement, and the need for conservative therapy for lipedema. The benefits of liposuction remained up to 88 months follow-up assessments. Liposuction was generally well tolerated; most adverse events occurred in <5% of patients. However, the quality of the evidence was limited, with sources of uncertainty such as systematic biases due to lack of randomization, and the use of instruments that have not been validated for the collection of data and assessment in lipedema-related complaints. Studies to validate tools to assess lipedema-related outcomes and define a minimally clinically important difference for the condition may also be necessary to put the benefit of liposuction for the treatment of lipedema in a clinical perspective".

Revised guidelines on lipedema were developed under the auspices of and funded by the German Society of Phlebology (DGP) (Reich-Schupke, et al., 2017). The recommendations are based on a systematic literature search and the consensus of eight medical societies and working groups. The guidelines stated that the diagnosis of lipedema is established on the basis of medical history and clinical findings and is characterized by localized, symmetrical increase in subcutaneous adipose tissue in arms and legs in marked disproportion to the trunk. In addition edema, easy bruising, and increased tenderness may be seen. Further diagnostic tests are typically reserved for special cases that require additional workup. Lipedema is a chronic, progressive disorder with individual variability and unpredictability of its clinical course. Treatment consists of four therapeutic mainstays that may be combined as necessary to address current clinical symptoms. These four treatments include: complex physical therapy (manual lymphatic drainage, compression therapy, exercise therapy, and skin care), liposuction and plastic surgery, diet, and physical activity, as well as psychotherapy if necessary. According to the Society, surgical procedures may be indicated if, despite thorough conservative treatment, symptoms persist, or if there is progression of clinical findings and/or symptoms.

Halk and Damastra (2017), in a systematic review of the literature to June 2013, reported on Dutch guidelines for lipedema. In 2011, the Dutch Society of Dermatology and Venereology organized a task force to create guidelines on lipedema, using the International Classification of

Functioning, Disability and Health of the World Health Organization. Clinical questions on significant issues in lipedema care were proposed, involving making the diagnosis of lipedema; clinimetric measurements for early detection and adequate follow-up; and treatment. The authors concluded that there is little consistent information about the diagnosis or therapy of lipedema in the literature and indicate lipedema is frequently misdiagnosed as only an aesthetic problem and therefore under- or mis-treated. Treatment is divided into conservative and surgical treatment. The guideline recommendations state "To ensure early detection and an individually outlined follow-up, the committee advises the use of a minimum data set of (repeated) measurements of waist circumference, circumference of involved limbs, body mass index and scoring of the level of daily practice and psychosocial distress. Promotion of a healthy lifestyle with individually adjusted weight control measures, graded activity training programs, edema reduction, and other supportive measures are pillars of conservative therapy. Tumescent liposuction is the treatment of choice for patients with a suitable health profile and/or inadequate response to conservative and supportive measures". The authors reported that consistent criteria to determine the ideal time or patient characteristics for liposuction are not available. The strength of the recommendations in this clinical guideline and the links to supporting evidence were not provided.

Lymphedema

Lymphedema is a chronic condition that develops over months to years due to an increasing lymphatic load that exceeds the lymphatic system's transport capacity. Impairment of lymphatic transport leads to interstitial accumulation of a protein-rich fluid that includes excess water, plasma proteins, extravascular blood cells, and cell products that are normally transported by the lymphatic system from the interstitium into the circulation. Symptoms of lymphedema include pain, swelling and tightness. As lymphedema progresses, increased volume and heaviness of the affected limb, dermal fibrosis, recurrent infections and episodes of cellulitis, skin changes and impaired range of motion occur. Lymphedema can affect any body part including trunk, limbs, head/neck, and genitals. Lymphedema is classified into primary and secondary forms. Primary lymphedema occurs when the lymphatic system does not mature properly during fetal development. It can be familial, genetic, or hereditary. Female individuals have a higher incidence of primary lymphedema, with a ratio of 3.5:1 to male individuals and incidence peaks during puberty (between ages 12 and 16 years) (Fort and Anilowski, 2024). Secondary lymphedema occurs secondary to a disruption or obstruction of the lymphatic system caused by: filariasis (primary cause worldwide), lymph node surgery/radiation due to cancer (primary cause in the United States) or by another cause such as chronic venous insufficiency (CVI), deep vein thrombosis (DVT), infection, surgery/trauma, lipedema, older age and obesity (Fort and Anilowski, 2024; Christensen, et al., 2023; Mehrara, 2023).

Components of the physical examination that can aid with the diagnosis of lymphedema are limb circumference and volume measurement. Limb volume can be estimated by taking several circumferential measurements at standard distances or measured by the water displacement method, optoelectronic volumetry, or by calculation using the truncated cone formula. A volume increase of ≥10% in the affected limb when compared to the unaffected limb is indicative of lymphedema (Christensen, et al., 2023; Tidhar et al., 2022). The International Society of Lymphology (ISL) (2020) notes that some clinicians use volume differences (VD) between the affected limb and the normal contralateral limb (equally applicable to upper and lower extremities) to define the severity of lymphedema as mild: VD >10 percent but less than <20 percent; moderate: VD 20 to 40 percent; and severe: VD >40 percent.

Lymphedema may be clinically apparent but imaging is required for confirmation and to rule out other conditions that may confound the clinical presentation. Imaging technologies to confirm lymphedema or plan surgery include duplex ultrasound, lymphoscintigraphy, or indocyanine green lymphangiography, possibly complemented by magnetic resonance imaging or computed

tomography (CT) (Christensen, et al., 2023; Mehara, 2023; International Society of Lymphology [ISL], 2020).

Lymphoscintigraphy is an imaging test that gives a global evaluation of the functionality of the lyphatic system (Masia et al., 2018). It is an objective and reliable imaging modality to diagnose lymphedema, categorize the severity, and guide appropriate treatment. The test is performed by injecting subcutaneous or intradermal radioactive tracers in the web space of the extremities, and imaging is performed 30 to 120 minutes after injection. The patient then performs a stress activity (such as walking, massage, or squeezing a ball for approximately 20 minutes), which is followed by repeat imaging. Criteria for impaired lymphatic function for qualitative lymphoscintigraphy include delayed, asymmetric, or absent visualization of the regional lymph nodes and dermal backflow (Mehara, 2023). A transport time of 60 minutes is considered delayed (Pappalardo and Cheng, 2022). The asymmetry or delayed appearance of radiocontrast material in the proximal nodal tissue can be used as a semiquantitative measure of the severity of lymphatic vascular insufficiency. When dermal backflow (accumulation of radiotracer in the subcutaneous tissue) occurs, there is a greater likelihood of a beneficial response to therapeutic intervention (Rockson, 2023).

Once diagnosed, lymphedema may be staged by severity. There are 2 main staging methods—the International Society of Lymphology (ISL) scale and the Campisi scale. The International Society of Lymphology (ISL) staging guidelines for lymphedema states (Christensen, et al., 2023; Mehrara, 2022; ISL, 2020):

- Stage 0: Latent or Subclinical
  - impaired lymphatic transport
  - no evident swelling/edema, subtle changes in tissue fluid/composition
  - changes in subjective symptoms
  - may last months or years before progression
- Stage I: Spontaneously Reversible
  - early accumulation of protein-rich fluid
  - pitting edema, no evidence of dermal fibrosis
  - subsides with elevation
- Stage II: Spontaneously Irreversible
  - accumulation of protein-rich fluid
  - pitting edema may progress to nonpitting as excess fat and fibrosis develop
  - does not resolve with elevation alone
- Stage III: Lymphostatic Elephantiasis
  - nonpitting
  - significant fibrosis
  - trophic skin changes such as fat deposits, acanthosis, and warty overgrowths

The Campisi staging system for lymphedema:

- Stage IA: Latent lymphedema without clinical evidence of edema, but with impaired lymph transport capacity (provable by lymphoscintigraphy) and with initial immune-histochemical alterations of lymph nodes, lymph vessels, and extracellular matrix.
- Stage IB: Initial lymphedema, totally or partially decreasing by rest and draining position, with worsening impairment of lymph transport capacity and of immune-histochemical alterations of lymph collectors, nodes, and extracellular matrix.

- Stage IIA: Increasing lymphedema, with vanishing lymph transport capacity, relapsing lymphangitic attacks, fibroindurative skin changes, and developing disability.
- Stage IIB: Column *shaped* limb fibrolymphedema, with lymphostatic skin changes, suppressed lymph transport capacity, and worsening disability.
- Stage IIIA: Properly called elephantitis, with scleroindurative pachydermatitis, papillomatous lymphostatic verrucosis, no lymph transport capacity, and life-threatening disability.
- Stage IIIB: Extreme elephantitis with total disability.

Nonsurgical or conservative treatment options for lymphedema are primarily physical and include elevation, exercise, skin care (to prevent drying, cracking, and infection), limb elevation, elastic stockings or other pressure garments or bandages, physical therapy, manual lymph drainage, massage therapy, and pneumatic compression devices. These are often used together in combination such as with complex decongestive therapy (CDT) or intermittent pneumatic compression therapy. CDT, also known as complex lymphedema therapy (CLT) or complete decongestive physiotherapy (CDP) is a noninvasive treatment that is considered a standard of care for lymphedema. The main goal of treatment of lymphedema is volume reduction of the affected limb, improvement in patient symptoms as well as a reduction of or elimination of any recurrent infections (Christensen, et al., 2023; Garza, et al., 2017; Macdonald, et al., 2003; Lasinski and Boris, 2002).

Nonsurgical treatments can be intensive and may require extensive, and time-consuming, ongoing intervention. For some individuals the nonsurgical treatments yield inadequate lymphedema control. Lymphedema surgery is used to reduce limb size and improve quality of life (QOL) and function when conservative nonsurgical management yields inadequate results. The goals of surgical management of lymphedema are to retain or restore function, alleviate pain and discomfort, reduce the risk of infection, prevent disease progression, improve cosmesis, and limit deformity. There is no consensus regarding the role of surgery, the optimal surgical approach, or the timing of an operative procedure for extremity lymphedema. Conservative or nonsurgical treatment options are often resumed after surgery to maintain surgical benefits (Christensen, et al., 2023; Mehrara, 2021; Garza, et al., 2017).

Operations for lymphedema are classified in two main categories: excisional operations and lymphatic reconstruction. Surgical management of lymphedema is categorized into two general approaches: physiologic techniques and reductive/ablative techniques. Physiologic procedures such as lymphaticovenular anastomosis (LVA) are indicated for individuals with early stage lymphedema prior to deposition of excess fat and extensive tissue fibrosis. Reductive/ablative techniques such as liposuction are indicated for individuals who present with more advanced lymphedema after fat deposition and tissue fibrosis has occurred. Liposuction aimed at adipose tissue removal can provide significant symptom relief for affected patients. Individuals with more advanced lymphedema have been treated with physiologic techniques, however, the results are variable, and only limited numbers of patients have been analyzed (Mehrara, 2021). Recently, combined surgical approaches including a reductive/ablative and a physiological procedure, have been investigated in order to address the different pathological components of lymphedema (Ciudad, et al., 2020). Uncontrolled comorbidities are a contraindication for surgical treatment and include: venous disease (deep vein thrombosus [DVT], superior vena cava syndrome); congestive heart failure (CHF); medication-induced swelling; liver disease, including but not limited to cirrhosis, hypoproteinemia; nephropathy including end-stage renal disease; peripheral arterial disease - clinically significant such as rest pain, claudication or ischemic ulcers; pregnancy; dye anaphylaxis; and active infection of the affected extremity (cellulitis/erysipelas) (Tidhar, et al., 2022; Kokosis, et al., 2020; Dayan, et al., 2017).

The issue in monitoring success of surgical interventions is that there is no set standard for measuring degree of lymphedema and no standardized conservative treatment protocol before or after surgery. Additionally, presently there is no uniformity in the literature with regards to a protocol for diagnosing and monitoring lymphedema. Providers who follow these patients have reported objective and subjective improvements in the majority of lymphedema patients who have undergone surgical intervention. Most studies that report on the surgical management of lymphedema monitor limb circumference, volume reduction, and incidence of cellulitis as their endpoints. Recently, patient self-reported quality of life outcome tools specific for lymphedema have been included as an additional end point. The most commonly performed surgical procedures for lymphedema are lymphaticovenular anastomosis and vascularized lymph node transfer (Garz, et al., 2017).

Multiple ongoing clinical trials for the surgical treatment of lymphedema can be found on the ClinicalTrials.gov database.

Lymphatic Microsurgical Preventing Healing Approach (LYMPHA) has been proposed as a surgical technique for the prevention of lymphedema. Lymphatic pathways in the arm are identified using axillary reverse mapping (ARM) and then lymphaticovenous anastomosis is performed. The evidence in the published peer reviewed literature is primarily in the form of small case series (n=3–74) with short-term follow-ups and retrospective reviews (n=59–194) (Ozmen, et al., 2022; Pierazzi, et al., 2022; Wagner, et al., 2022; Herremans, et al., 2021; Jørgensen, et al., 2018). There is insufficient evidence in the published, peer-reviewed scientific literature to support the safety and effectiveness of immediate lymphatic reconstruction for the prevention of lymphedema. Prospective comparative studies with large patient populations and long-term follow-ups are needed to support the prophylactic use of microsurgical procedures for the prevention of lymphedema.

Axillary reverse mapping (ARM), also known as reverse lymphatic mapping, has been proposed for the identification and visualization of arm lymphatic drainage and lymph nodes. The proposed purpose of ARM is to preserve the upper extremity lymphatics during axillary lymph node dissection (ALND) to reduce the risk of postoperative lymphedema. The procedure requires an injection of blue dye in the upper inner ipsilateral arm. The identified blue lymphatics and nodes are then avoided during ALND (Margenthaler, 2022). The evidence in the published peer reviewed literature is in the form of randomized controlled trials, systematic reviews, non-randomized prospective studies, and review articles. Although short term results show a reduction in lymphedema development, long-term results are lacking and there is the question of cancer being found in the remaining lymph nodes in the future and therefore is considered experimental and not standard of care.

Reductive/Ablative Techniques
Reductive techniques, also called ablative techniques, remove fibrofatty tissue that has formed from sustained lymphatic fluid stasis. Reductive techniques include direct excision and liposuction (Mehrara, 2021; Trinidad-Hernandez and Gloviczki, 2013):

- **Direct excision:** A variety of direct excision procedures have been described for the treatment of extremity and genital lymphedema. Excisional operations remove excess subcutaneous tissue to decrease the volume of the extremity. Lymphedematous tissues are excised together, including the skin and soft tissues. The resulting defects are covered either with tissue flaps (e.g., Sistrunk, Homans, Thompson procedures) or with skin grafts (e.g., Charles procedure). Prolonged hospitalization, poor wound healing, large surgical scars, sensory nerve damage, and residual edema of the foot and ankle are reported problems. These common complications limit such procedures to individuals with disabling, advanced or end-stage lymphedema that is not responding to maximal medical therapy.

- **Liposuction:** This ablative surgery removes fatty and fibrotic depositions through multiple small incisions of the affected limb in patients with more advanced lymphedema. It is sometimes called suction-assisted lipectomy. It is proposed for patients with stage II or III lymphedema. Postoperative placement of compression garments prevents swelling recurrence, must be refitted regularly, and may be required for life to maintain surgical benefits.

Physiologic Techniques
The surgical approaches include lymphatic bypass procedures, flap transposition procedures, and vascularized lymph node transfers. The lymphatic bypass procedures are the most commonly used of the physiological techniques. These procedures require a high level of technical skill, and it is recommended that performance of these procedures be reserved for those surgeons who have expertise in microvascular surgery (Mehrara, 2021).

Lymphatic bypass procedures: The lymphatic bypass procedures are categorized as lymphatic-lymphatic bypass and lymphovenous bypass procedures. Lymphaticovenular bypass procedures are a variation of the lymphovenous approach. Lymphatic bypass procedures have been used in the following settings: failure of nonoperative management; recurrent cellulitis or lymphangitis; dissatisfaction with compression garments or impaired quality of life. Contraindications to lymphatic bypass procedures include: extensive tissue fibrosis, late-stage lymphedema changes, venous hypertension, recurrent cancer in the ipsilateral extremity or metastatic disease, patient noncompliance with compression therapy or postoperative care plans. There are several methods used to perform a bypass procedure. There is no consensus for the specific type of lymphatic bypass procedure to be performed; these decisions are made based on surgeon preference and experience. To help identify the lymphatic vessels, prior to making an incision, isosulfan blue dye is injected into the subcutaneous tissue distal to the operative site. The most common approaches are described as follows (Mehrara, 2021; Schaverien, et al., 2019; Garza, et al., 2017):

- **Lymphatic-lymphatic bypass:** Lympholymphatic bypass transfers soft tissue resected from an unaffected site to a site that is proximal to that affected by lymphedema and followed by a direct anastomosis of the lymphatic vessels.
- **Lymphovenous bypass:** Lymphovenous bypass is an alternative to the lymphatic-lymphatic technique. A vein interposition graft is used to connect the distal lymphatic vessels with vessels proximal to the obstruction. Proximal vessels used in this technique include lymphatic vessels, adjacent veins, or deeper and larger veins. Multiple lymphatic vessels can be anastomosed to the vein graft.
- **Lymphaticovenular anastomosis (LVA):** This is a super microsurgical technique used to anastomose distal subdermal lymphatic vessels and adjacent venules less than 0.8 mm in diameter. Distal subdermal lymphatics are less affected by lymphedema and are more readily available for a bypass procedure than deeper lymphatic channels.
- **Vascularized lymph node transfer (VLNT):** This approach utilizes microsurgical techniques to transfer lymph nodes from an unaffected site to the affected limb with the intent of restoring lymphatic function and promoting lymph drainage. A limiting factor of this approach is that lymphedema can develop in the donor extremity.
- **Flap/tissue transfer:** To avoid risk of donor extremity lymphedema or visible donor-site scars, intraabdominal lymph node flap options are increasingly being performed, including the omental (gastroepiploic) flap, which may be harvested laparoscopically, and the jejunal mesenteric flap. Results from these approaches have yet to be fully validated.

U.S. Food and Drug Administration (FDA)
The FDA does not regulate surgical procedures. Any medical devices, drugs, biologics, or tests used as a part of this procedure may be subject to FDA regulation.

Literature Review

Reductive/Ablative Techniques: Although the evidence in the published peer-reviewed literature evaluating the effectiveness of liposuction for the treatment of lymphedema consists primarily of observational studies, case series and retrospective reviews, outcomes have demonstrated positive results for improvement in the ability to move, reduction of limb size, and reduction of skin infections and has evolved into a standard of care. It is noted that the use of compression garments both before and after lymphedema liposuction are essential for successful results.

In a prospective registry study, Hoffner et al. (2018) evaluated the five-year results after liposuction in combination with controlled compression therapy (CCT). Between 1993 and 2012, a total of 127 consecutive women were operated on. Twenty-two could not be followed for five years: 18 died before the last follow-up (10 because of breast cancer and eight of other causes), one had recurrence of breast cancer, one stopped using CCT, one moved abroad, and in one case, data from the therapist was missing. A total of 105 women with non-pitting lymphedema remained in the study. Inclusion criteria was: diagnosis of secondary arm lymphedema following breast cancer treatment; a significant excess volume, that is the volume of the affected arm was at least 10% larger than that of the unaffected arm and concomitant subjective discomfort; inability of previous conservative treatment to reduce the excess volume completely; no or minimal pitting (<5mm) as a sign of adipose tissue hypertrophy; and accustomed to the use of compression garments preoperatively. Exclusion criteria included active cancer, wounds, or infections and patients unwilling to undergo continuous postoperative CCT. Power-assisted liposuction was used during the period 1993–1997, the "dry technique". During the period 1997–2012, a tourniquet was utilized in combination with the tumescence technique to minimize blood loss. There was no comparator. The primary outcome was excess volume reduction. Standardized forms were used to collect pre-, peri-, and postoperative data. Patients were followed up regularly at 0.5, one, three, six, nine months and at one year after surgery, and then every year. If complete reduction was not reached at one year, three-month visits were scheduled. Patients with complete reduction at two years were followed up by their previous lymph therapist, who reported arm volumes yearly. Total aspirate mean volume was 1,831 ± 599 ml (range, 650–3,780) for all patients (n=105). Postoperative mean reduction five years postoperatively was 117% ± 26% as compared with the healthy arm. No adverse events were reported. The authors concluded that liposuction combined with CCT is an effective and safe method for treatment of chronic, nonpitting arm lymphedema resistant to conservative treatment. A mean reduction of 117% was achieved, and such normalization can be anticipated in patients with an excess volume of around 3,000 ml. This study is limited by small sample size and no comparator.

In a cohort study, Lamprou et al. (2017) reported the long-term results of circumferential suction-assisted lipectomy (CSAL) in end-stage primary and secondary lymphedema of the leg. Patients were treated with CSAL for unilateral chronic irreversible lymphedema of the leg (n=88). Compression therapy was resumed after surgery. Leg volumes were measured before surgery, and at one, six, 12 and 24 months after the procedure. A total of 47 patients with primary lymphedema had a median preoperative volume difference between affected and unaffected legs of 3686 (interquartile range [IQR]), 2851 to 5121) ml. Two years after surgery, this volume difference was reduced to 761 ml, a 79% reduction. In the 41 patients treated for secondary lymphedema, the median preoperative volume difference was 3320 (IQR 2533-4783) ml, decreasing after two years to -38 ml indicating a 100% reduction in excess volume on average. The preoperative volume difference and the sex of the patient significantly influenced the final outcome after two years. The outcome was not related to body mass index (BMI) or other patient characteristics. Subsequent continuous compression, weight control, physical exercise, and lifestyle alterations are still needed to achieve the maximum effect.

In a cohort study, Hoffner et al. (2017) assessed liposuction plus controlled compression therapy in patients with lymphedema of an arm secondary to breast cancer treatment. The aim of the study is to test the hypothesis that liposuction improves health-related quality of life (HRQoL). Sixty female patients with arm lymphedema were followed for a one-year period after surgery. The 36-item short-form health survey (SF-36) was used to assess HRQoL. Patients completed the SF-36 questionnaire before liposuction, and after one, three, six, and 12 months. They reported a mean difference between affected and unaffected limbs of 1365 mL (standard error of the mean [SEM] 73) at baseline, which declined to 75 mL (SEM 35) at one month, –26 mL (SEM 40) at three months, –133 mL (SEM 40) at six months, and –213 mL (SEM 35) at one year, indicating > 100% reduction in excess volume on average. They reported that 82% (49 of 60) patients had complete resolution of their lymphedema. The adipose tissue volume removed at surgery was 1373 – 56mL. One month after liposuction, better scores were found in mental health. After three months, an increase in physical functioning, bodily pain, and vitality was detected. After one year, an increase was also seen for social functioning. The physical component score was higher at three months and thereafter, while the mental component score was improved at three and 12 months. Limitation of this study include: a lack of control or comparator group; observational study; insufficient length of follow-up to determine long-term outcomes.

In a 2021 UptoDate topic on surgical treatment of primary and secondary lymphedema, the author states operative management of primary and secondary lymphedema is typically reserved for localized primary malformations, failed medical management, or recurrent cellulitis in affected extremities. Reductive procedures can be curative in patients with localized primary lymphatic malformations and palliative for patients with secondary lymphedema. Most of the outcome data for reductive/ablative techniques for the treatment of lymphedema are from retrospective reviews, small case series and case reports. At this time there are no randomized trials to determine the optimal reductive procedure to treat lymphedema (Mehrara, 2021).

Lymphatic bypass procedures: Garza et al. (2022) conducted a retrospective review to assess the outcomes of simultaneous vascularized lymph node transplant and lymphovenous bypass for treatment of both early and late stages of primary and secondary lymphedema. Two hundred twenty patients underwent simultaneous vascularized lymph node transplant and lymphovenous bypass. Thirty patients (13.6 percent) had primary lymphedema and 190 patients (86.4%) had secondary lymphedema. Ninety-two patients (41.8%) had lymphedema of the lower extremity, 121 (55%) had upper extremity involvement, and seven had lymphedema of upper and lower extremities (3.2%). Patients were excluded if they did not have a preoperative assessment by a lymphedema therapist or if they underwent a staged procedure. Average duration of lymphedema was 95.4 ± 103.6 months. Mean body mass index was 26.9 ± 4.7 kg/m^2. The median baseline preoperative volume difference between affected and unaffected limbs was 25.7 ± 21.9. Volume reduction was reduced an average of 21.4% at one year ($p < 0.0001$), 36.2% at two years ($p < 0.0001$), 25.5% at three years ($p = 0.1$), and 19.6% at four years. Median Lymphedema Life Impact Scale scores were 7.0 points lower ($p < 0.0001$) at three months and improved progressively over time to 27.5 points lower at three years postoperatively ($p < 0.005$). The complication rate was 12.7%, with 56 complications occurring in the 440 procedures performed. Complications included vascular compromise requiring operative intervention (n = 6, 1.4%) chyle leak (n=6), cellulitis (n=15), seroma (n=12), and incisional dehiscence (n=6). There was an overall flap survival rate of 99.6% with one flap loss. Author noted study limitations included non-randomization of patients due to treatment selection according to algorithm, patients lost to follow up, variation in measurements by different therapists, and patient compliance with postoperative nonoperative modalities to manage lymphedema. Overall, volume differential reduction of 20-36% was observed at four years postoperatively and the majority (88%) of patients reported subjective improvement in their lymphedema symptoms.

Rodriguez and Yamamoto (2022) conducted a retrospective review of 229 patients with symptomatic secondary extremity lymphedema who underwent lymphovenous anastomosis (LVA) at a single institution. Preoperative assessment included lymphoscintigraphy, indocyanine green lymphography, noncontrast magnetic resonance lymphography, and high-frequency ultrasonography. Median follow-up was 33 months (range, 13–51 months). A median of 3.1 (range, 1–7) LVA were performed on 2.7 (range, 1–6) incision sites per patient. For upper-extremity lymphedema (47 of 229; 20.6%), volume reduction was achieved in 100% (47 of 47) of the cases, with a median volume reduction rate of 67% (range, 7–93%). In lower-extremity lymphedema (182 of 229; 79.4%), volume reduction was achieved in 86.8% (158 of 182) of the cases, with a median volume reduction rate of 41% (range, 7–81%). Cellulitis episodes decreased from 2.1 to 0.2 episodes/year after LVA ($p<0.05$). Adverse events were not reported. Author noted limitations included lack of a control group and retrospective nature of the study. Lymphovenous anastomosis (LVA) resulted in successful volume reduction in patients with symptomatic secondary extremity lymphedema.

Gupta et al. (2021) conducted a systematic review analyzing outcomes and complication rates associated with lymphovenous anastomosis (LVA) for the treatment of primary or secondary lymphedema of the upper extremity (UE). A total of 16 studies met the inclusion criteria (n=349, range 2–100). Thirteen studies were prospective studies and three were retrospective. The average patient's age ranged from 38.4–64 years. The duration of lymphedema before LVA ranged from nine months to seven years. Patients included had varying severity of lymphedema, ranging from Campisi stage I to IV. The mean number of anastomoses ranged from 1.5–5.4. The mean length of follow-up ranged from six months to eight years. Objective measures of lymphedema included limb circumference measurements, volume measurements, and volume differential (the excess volume of the edematous limb compared to the unaffected limb). Eleven studies reported on subjective symptom relief and/or validated quality of life measures. Objective improvement in limb circumference or volume measurements following LVA were reported in 11 studies, ranged from 0% to 100%. Six studies reported ≥90% improvement and one study reported no significant improvement. Three studies reported a significant decrease in episodes of cellulitis following LVA. Fifty-three percent to 100% of patients across all studies reported an improvement in their quality of life. The two reported adverse events were one episode of skin irritation at the site of contrast injection and one episode of hypertrophic scarring. Author noted limitations included: differences in what the studies examined (type of extremity, surgical technique, or stage of lymphedema), short term follow-up, small patient populations, and lack of comparator to other procedures or techniques.

Fallahian et al. (2021) conducted a systematic review of the literature to evaluate the efficacy and safety of microsurgical techniques (vascularized lymph node transplant [VLNT] and lymphovenous bypass/anastomosis [LVB]) in the treatment of primary lymphedema. Ten studies (n=254) were included with 357 microsurgical operations performed: 314 LVBs (88% of operations) and 43 VLNT (12%). Only 202 patients had data regarding gender and 66.7% were female, average age of 47.3 years. For patients who underwent VLNT, the most common lymph node donor site was the submental region (82.6%), followed by the lateral thoracic region (8.7%) and omental region (8.7%). The most common recipient site was the ankle region at the anterior tibial artery (75%). Length of follow up ranged from 6–24 months with an average of 12.4 months. Postoperative outcome measures varied between the studies and included lower extremity lymphedema index (LEL), the circumference tap measurement volumetric method, leg circumference, and volumetric measures of edema. All of the studies that reported postoperative results showed an improvement in at least one type of measurement compared with preoperatively. The studies that reported on episodes of cellulitis reported a decrease in frequency postoperatively. Other adverse events were not reported. Author noted limitations included the variety of metrics used to report outcomes and the degree of improvement after surgery was not consistently reported in the studies included. Other limitations include inclusion of retrospective studies; limited number of studies,

heterogeneous and small patient populations, variations in surgical technique and short term follow ups. There is a need for a systematic objective quantitative universal classification system, imaging modalities, and outcome measures for lymphedema.

In a prospective cohort study, Salgarello et al. (2018) reported the outcomes of patients' health-related quality of life (HRQoL) after super microsurgical lymphaticovenular anastomosis (LVA) for lower and upper extremities lymphedema (ULL or LLL) (n=70). Forty-four patients (62.8%) were affected by ULL and 26 (37.1%) were affected by LLL. Five patients (7.1%) had a primary lymphedema, while 65 patients (92.9%) were affected by secondary lymphedema. The study included Caucasian patients with ULL and LLL. The intervention was super microsurgical lymphaticovenular anastomosis (LVA). There was no comparator. Quality of life (QoL) was assessed by lymphedema QoL questionnaire (LyMQoL), which is a validated disease-specific instrument to measure the impact of lymphedema on patient's lives, covering four domains: function, body image, symptoms, and mood. There was a mean follow-up of 8.5 months (range: 2–21 months). Additionally, the episodes of lymphangitis and the need for conservative therapy before and after surgery was evaluated. Among the sample, 61 patients (87.1%) underwent physical therapy or a rehabilitation program preoperatively. Postoperatively, the number of subjects who needed physical therapy, including manual compression, lymphatic massage, bandaging, or compression garments, remained stable, but 58.6% of the patients had a reduction in the number of sessions and/or compressive classes necessary to their well-being, difference in which was also significant ($p<0.01$). The average for overall QoL score before surgery was 5.5 for the upper limb group and 5.7 for the lower limb group. After a mean follow-up ranging from 8.5 months, there was an average increase for the global QoL score of 2.3 for upper limb and 2.6 for lower limb. The QoL average observed postoperatively was 7.9 for upper limb and 8.3 for lower limb ($p<0.001$). A statistically significant improvement in all four domains ($p<0.01$) was reported after surgery, being present from the first postoperative months for both upper and lower extremities. No adverse events were reported. The authors concluded that lymphaticovenular anastomosis improves HRQoL in patients affected by ULL and LLL. Additionally, both a reduction of episodes of lymphangitis and a decrease in the need of conservative therapy were observed in this cohort of patients. This study was limited by lack of a comparator group and short-term follow-up.

In a retrospective study, Engel et al. (2018) investigated the outcome of lymphedema microsurgery with or without microsurgical breast reconstruction for breast cancer-related lymphedema (BCRL) (n=124). Patients with BCRL who underwent three treatment modalities without or with microsurgical breast reconstruction were included in this study as groups I and II. (Cheng grading: grade I: n = 56; grade II: n = 45; grade III: n = 20; grade IV: n = 3). Patients were offered the lymphedema microsurgery depending on the availability of patent lymphatic ducts on indocyanine green lymphography if they failed to complete decongestive therapy. Patients who underwent simultaneous lymphovenous anastomosis and vascularized lymph node flap transfer were excluded from this study. Group I consisted of 87 patients who did not receive microsurgical breast reconstruction, and 30 (group Ia), 23 patients (group Ib), and 34 patients (group Ic) were treated with complete decongestive therapy, lymphovenous anastomosis, and vascularized lymph node flap transfer, respectively. Of the 37 patients in group II who underwent microsurgical breast reconstruction, 22 were treated with complete decongestive therapy (group IIa), 4 received a lymphovenous anastomosis (group IIb), and 11 were treated by vascularized lymph node flap transfer (group IIc). The circumferential difference, reduction rate, and episodes of cellulitis were used to evaluate the outcome of treatments. Mean follow-up period was 19.1 +/- 5.3 months (range 5.7-62.8 months). Improvements in the circumferential difference (12.8±4.2% vs 11.5±5.3%), the reduction rate (20.4±5.1% vs 14.7±6%), and episodes of cellulitis (1.7±1.1 vs 2.1±2.4times/yr) did not significantly differ between groups I and II ($p=0.06$, 0.07, and 0.06, respectively). In both groups, vascularized lymph node flap transfer was significantly superior to lymphovenous anastomosis or complete decongestive therapy in terms of improvements in the circumferential difference, reduction rate and episodes of cellulitis ($p=0.04$,

0.04, and 0.06, respectively). The re-exploration rate was 16.9% (n=21), and the overall complication rate was 8.1% (n=10). Flap losses did not occur. One (in group II) of 18 patients who underwent vascularized groin lymph node flap transfer developed right lower limb lymphedema, which was successfully treated with a lymphovenous anastomosis in the ankle one year after surgery. None of the 27 patients who received vascularized submental lymph node flaps developed face lymphedema. The authors concluded that microsurgical breast reconstruction did not improve the outcome of BCRL. Improvements in BCRL were better for lymphatic microsurgery than complete decongestive therapy. Vascularized lymph node flap transfer provided greater improvements in the BCRL than lymphovenous anastomosis.

In a prospective cohort study, Poumellec et al. (2017) analyzed the results of lymphaticovenous anastomoses (LVA) on 31 patients and reviewed the existing literature. This study comprised 31 female patients presenting lymphedema of the upper limb following treatment for breast cancer for which surgical treatment was given by microsurgery consisting of three stepped LVA performed in an outpatient setting. The post-LVA arm circumference was measured at three levels (wrist, forearm, and arm) in 31 female patients. Mean follow-up time was 12.8 months. Reduction in the circumference was 22.5, 21.32, and 30.2%, respectively, in the wrist, forearm, and arm. Functional improvement was observed in the majority (84%) of patients ranging from moderate to substantial. Only two patients had no result. The only patients to experience recurrence were those with a high level of lymphedema. The review of the current literature and the present study revealed modest results in terms of decreased excess volume, although a major improvement in function points to LVA as a useful technique in this indication. Progress in imaging techniques has enhanced the results achieved with this procedure, although further studies on recurrence rates are needed with a follow-up greater than one year.

In a prospective study, Cornelissen et al. (2017) analyzed the effect of lymphaticovenous anastomosis (LVA) on quality of life (n=20). Inclusion criteria consisted of an evidenced upper limb lymphedema secondary to breast cancer in stage 1 or 2A according to the International Society of Lymphology (ISL) classification, patent lymphatic ducts seen by indocyanine green (ICG) lymphangiography and an absence of skin infections and complex decongestive therapy for at least three months. Quality of life was considered as the primary outcome, measured by the Lymphedema international classification of functioning (Lymph-ICF) questionnaire. Secondary outcomes were the use of compressive stockings and arm volume changes according to the Upper Extremity Lymphedema index (UEL-index). Measurements were obtained preoperatively and at one, three, six and 12 months postoperatively. The mean follow-up was 7.8 ± 1.5 months. Statistically significant improvement in quality of life was achieved in the total score and for all the quality of life domains after one year of follow-up ($p<0.05$). The discontinuation rate in compressive stockings use was 85%. The mean relative volume difference in UEL between a healthy and lymphoedematous arm preoperatively was 14.92 ± 8.01 and postoperatively 12.99 ± 7.47. The difference did not reach statistical significance ($p=0.582$). This study is limited by small sample size, lack of a comparator and short-term follow-up.

Forte et al. (2020) conducted a systematic review to analyze the surgical outcomes of lymphaticovenous anastomosis (LVA) in the treatment of lower extremity lymphedema (LEL). A total of 58 studies met inclusion criteria for a total of 1363 patients with LEL who had undergone LVA. Follow-up was one to 87 months. The number of patients in each study ranged from one to 216 with a female predominance in all. The mean age at presentation ranged from six to 94 years. The mean duration of LEL ranged from 22 days to 585 months. The patients included in the studies more commonly had secondary lymphedema. The studies included in this review describe variations in surgical techniques, number of anastomoses, and supplementary interventions. All, except one study, reported positive outcomes based on limb circumference and volume changes or subjective clinical improvement. The largest reduction rates achieved after LVA for LEL ranged between 51.1 to 63.8%, with better results presented in early stages of lymphedema. Almost all

studies reported a decrease in episodes of infection. The reported limitations include the considerable heterogeneity among the reported outcomes in each study. Therefore there is a potential for bias in interpreting data, as it is possible that not all studies captured reliable comorbidity data or outcomes over a long-period of time.

Rosian et al. (2019) conducted a systematic review evaluated the clinical effectiveness and safety of lymphovenous anastomosis (LVA) in comparison to conservative or other surgical treatments for primary or secondary lymphoedema patients. A total of five studies (n=217) were assessed eligible for final inclusion (one non-randomized controlled trial and four prospective single-arm studies). A total of 204 patients were treated with LVA and 13 with vascularized supraclavicular lymph node transfer (VSLNT). The mean follow-up periods differed considerably between the studies with a range of 7.8 to 30.4 months. The patients suffered from primary or secondary lymphoedema, mostly due to breast cancer and its treatments (e.g., radiation or chemotherapy). All studies showed a moderate to high risk of bias. The strength of evidence for the effectiveness and safety of LVA is very low which means that the evidence either is unavailable or does not permit a conclusion. There were various methods of LVA performed in the studies. Data on upper extremity lymphoedema were reported more frequently. The estimation of ongoing post-interventional treatments (e.g., compression treatment) is scarce and varied.

Cornelissen et al. (2018) conducted a systematic review to assess the clinical effects (improvement in arm circumference and quality of life) of lymphaticovenous anastomosis (LVA) in treating breast cancer-related lymphedema (BCRL). A total of 15 studies, 11 prospective and four retrospective studies, were included. All studies reported on BCRL in terms of volume or circumference reduction. Study population consisted of 268 patients; 263 patients presented with BCRL, one patient with upper limb lymphedema after an elbow fracture, and four patients with primary upper limb lymphedema. A control group was provided in two articles. One study included a control group where the patients who only received continuous bandaging were compared with those who underwent the intervention and continuous bandaging. Another study included several groups to compare the effect of different interventions, including LVA and lymph node transfers in combination with or without microvascular breast reconstruction, to groups only receiving decongestive therapy. The average follow-up was 20 months, ranging from two months to eight years. Thirteen out of the included studies reported a positive surgical effect on reduction in volume or circumference. Twelve articles mentioned qualitative measures, being symptom improvement and improvement in quality of life. The number of patients who experienced symptoms relief ranged from 50%-100% in the studies. Adverse events were not reported. Many limitations were reported. The volume and level of evidence of the studies on the effects of LVA in this specific patient population were low. No randomized controlled trial could be included, which displays the lack of solid evidence on this topic. The follow-up time in some studies was too short, with follow-up ranging from two months to six years. It remains unknown whether this reduction was maintained over a period of time. A broad variety in the years from onset till the LVA contributed to the heterogeneity of our study population. The way the outcomes were described varied enormously between studies. Some reported in terms of absolute or relative volume reduction while others mentioned circumference reduction. The authors concluded that heterogeneous results of LVA in the volume/circumference reduction for the treatment of BCRL were reported among studies. Improvement of the subjective symptoms was presented in most of the studies. This review showed that LVA may be particularly useful to improve quality of life in breast cancer-related lymphedema, in particular, in early-stage lymphedema in the distal arm.

Basta et al. (2014) conducted a systematic review and meta-analysis to quantify the efficacy and safety of microsurgery for lymphedema. Studies meeting criteria for inclusion were rated on methodologic quality based on the American Society of Plastic Surgeons levels of evidence. Demographic information, cause of lymphedema, and surgical technique were recorded. Quantitative change in lymphedema and perioperative complications were noted. A total of 27

studies were included, with 24 level IV evidence and three level III evidence. Overall, the study population consisted of 1619 patients, with a female-to-male ratio of approximately 3:2. The vast majority of patients suffered from postsurgical lymphedema associated with oncologic conditions, including breast cancer and various gynecologic cancers. The staging system of lymphedema was inconsistent across studies. Lymphovenous shunt procedures were performed in 22 studies and lymph node transplantation was performed in five studies. Excess circumference was reduced by 48.8 ± 6.0%, and absolute circumference was reduced by 3.31 ± 0.73 cm. Studies reporting change in volume demonstrated reduction in excess volume by 56.6 ± 9.1%, and absolute volume was reduced by 23.6 ± 2.1%. The incidence of no improvement in lymphedema postoperatively was 11.8% and 91.2% of patients reported subjective improvement. Approximately 64.8% of patients discontinued compression garments at follow-up. Complications included operative-site infection (4.7%), lymphorrhea (7.7%), reexploration for flap congestion (2.7%), and additional procedures (22.6%). Limitations of this study are: heterogeneity of the patient population; assessment modalities; and inconsistent reporting of complications. The authors concluded that lymph node transplantation may provide better outcomes compared with lymphovenous shunt, but well-designed head-to-head comparisons are needed to evaluate this further.

Scaglioni et al. (2017) conducted a systematic review on the topic of lymphovenous anastomosis (LVA), assessing both objective and subjective improvements in lymphedema of extremities. The primary endpoint was the objective of a subjective postoperative lymphedema reduction. Ten of the observational cohort studies were retrospective and eight prospectively designed totally 939 patients. No randomized controlled trials were available for inclusion. The number of patients per study ranged from 5-154. The duration of lymphedema prior to surgery ranged from 22 days to 29 years, although not all studies revealed this data. The studies included in this review describe significant variations in surgical techniques, number of anastomoses and supplementary interventions. All studies reported objective reductions in circumference measurements. Subjective symptom relief was found in 50-100% of the patients as well as a reduction in the number of cellulitis episodes in all investigated cases. In 11 out of 18 studies, additional compressive therapy was reported. The studies included in this review showed great heterogeneity. The authors concluded that the time of follow-up in the vast majority of the included studies was too short to make a reliable statement about sustained benefits of LVA surgery. Additionally, the deficiency of comparative designed studies and uniform outcome measurements continues to prevent drawing evidence-based conclusions.

Guiotto et al. (2019) conducted a systematic review analyzing outcomes and complication rates from palliative procedures involving excision of the affected tissue and reconstruction by either local flaps or skin grafts, and reconstructive procedures to restore lymphatic flow through microsurgical lymphaticovenous anastomoses, (LVAs) for the treatment of genital lymphedema (GL). A total of 20 studies met the inclusion criteria (n=151). Eight were case reports, 11 retrospective studies, and one prospective study. Three main surgical treatments for GL were identified. Surgical resection and primary closure or skin graft was the most common procedure (46.4%) with a total complication rate of 10%. Surgical resection and flap reconstruction accounted for 39.1% of the procedures with an overall complication rate of 54.2%. Lymphovenous shunt (LVA) procedures (14.5%) had a total complication rate of 9%. The authors concluded that this review demonstrates a lack of consensus in both the preoperative assessment and surgical management of GL. Patients receiving excisional procedures tended to be later stage lymphedema. Patients in the excision and flap reconstruction group seemed had the highest complication rates. The authors concluded that microsurgical LVAs may represent an alternative approach to GL, either alone or in combination with traditional procedures.

In a 2021 UptoDate topic on surgical treatment of primary and secondary lymphedema, the author states that "outcome data for physiologic techniques are from retrospective reviews of mostly lymphatic bypass procedures. However, later important prospective studies have also been

reported. Lymphatic bypass procedures result in highly variable responses, ranging from a complete response to none. The variability of results among the different studies is likely due to a number of factors including differences in assessing volume or circumference, length of follow-up, variable use of postoperative compression garments and/or physical therapy, and the use of non-standardized or non-validated questionnaires for subjective analysis. There has been no standardization of assessing volume of lymphedematous limb, and numerous techniques are reported to approximate volume changes following an operative procedure. Few studies report the use of complimentary techniques (e.g., volume measurements and bioimpedance or lymphoscintigraphy) to corroborate measurements. However, these limitations have been addressed in later studies. Other caveats include mixed series of patients, either based upon etiology (e.g., primary congenital conditions, or secondary lymphedema following nodal resections, trauma, or filariasis); location of lymphedema (e.g., upper or lower extremity); and/or variable criteria for patient selection, selection of procedures, timing of intervention, and identification of suitable lymphatic vessels for bypass surgery. In spite of these limitations, most authors report modest improvements in limb volumes (30 to 50 percent decreased), although a few individual patients experienced marked reductions, particularly for the upper extremity" (Mehrara, 2021).

Vascularized Lymph Node Transfer (VLNT): Bolletta et al. (2022) conducted a prospective case series to evaluate the effectiveness of the combined approach of gastroepiploic vascularized lymph node transfer (VLNT) followed by suction-assisted lipectomy (SAL) for the treatment of lymphedema. Patients (n=94) with upper (n=11) or lower (n=83) limb stage IIb-III lymphedema who did not benefit from a minimum of six months conservative treatment met inclusion criteria and were followed for an average of three years. Preoperative evaluation included circumferential measurements taken at four levels both in the lower limb (midfoot, ankle, 10 cm below knee, 10 cm above knee), and in the upper limb (midhand, wrist, 10 cm below elbow, 10 cm above elbow). Additional evaluation included lymphoscintigraphy and ICG lymphography. Patients were 75.5% females and 24.5% males. The patient's mean age was 50 ± 17.9 years with a mean BMI of 26.2 ± 3.1 kg/m^2. Mean circumference reduction rates (CRR) in the lower limb lymphedema group were 60.4%, 56.9%, 29.6%, and 55.4% above and below the knee, above the ankle, and at the foot level, respectively. A statistically significant difference was noted at all the levels ($p<0.05$), but above the ankle ($p=0.059$). Upper limb lymphedema mean CRR were 80.7%, 60.7%, 65.0% and 49.6% above and below the elbow, at wrist and at mid-hand, respectively. CRR were reported at all the levels but no statistical difference was noted. There was a significant decrease in episodes of cellulitis ($p<0.05$). Adverse events included partial loss of the skin graft (n=12) requiring secondary procedure of debridement. No other adverse events occurred. No donor site related complications. Author noted limitations included low number of patients with ULL and lack of control group.

Jarvis et al. (2021) conducted a systematic review to evaluate the efficacy and associated complications of vascularized omental lymphatic transplant (VOLT) for the treatment of upper extremity lymphedema. Seven studies (n=91) were included (three prospective, four retrospective cohort). Age range was 27–72 years with all patients being female except one. All patients had secondary lymphedema with the majority from breast cancer. Variations of the surgery included single VOLT, double VOLT, and double VOLT with suction-assisted lipectomy (SAL). Follow up ranged from 0.5-4.0 years. Average limb circumference reduction ranged from 37.8%-74.5% with an average volume reduction ranged from 22.7%-39.5%. Three studies reported a significant reduction in cellulitis postoperatively. Complications included sensory abnormalities (5.5%), partial skin graft loss (4.4%), vascular compromise of flap (2.2%), ileus (2.2%), flap loss (1.1%), transient pancreatitis (1.1%), and infection (1.1%). No donor site lymphedema was reported. Author noted limitations included variation in surgical technique used, variable recipient site, limited number of studies, small patient populations, and heterogeneous methodology for objective limb measurements.

Li et al. (2021) conducted a systematic review and meta-analysis to evaluate outcomes of various intra-abdominal vascularized lymph node (VLN) flaps in vascularized lymph node transfer (VLNT) for treatment of lymphedema. Twenty-one studies met the inclusion criteria (n=594, range 5–177). There was one non-randomized controlled trial, three retrospective cohort studies, five prospective case series, and 12 retrospective case series. Donor-sites of flaps were omental (65 flaps)/gastroepiploic (362 flaps), double omental/gastroepiploic (126 flaps), jejunal (45 flaps), ileocecal (two flaps), and appendicular (one flap). Primary outcomes were circumference/volume reduction, cellulitis reduction and lymph flow assessment. Secondary outcomes were recorded as donor-site complication and recipient-site complication. The range of follow-up was from two weeks to 52 months. The mean reduction rate ranged from 0.38% to 70.8%. Ten studies reported a significant reduction in infectious episodes. Viable lymph flow assessment was reported in eight studies. The pooled donor-site complication rate was 1.4% with the most common donor-site complication being minor ileus requiring prolonged nasogastric tube replacement. No donor site lymph dysfunction occurred. The pooled recipient-site complication rate was 3.2%. Complications reported were partial skin graft loss (n=12), flap loss (n=9), venous congestion (n=3), lymphatic leakage (n=2), hematomas (n=3), seromas (n=3), delayed wound healing (n=2), paresthesia (n=3), and hyperesthesia (n=1). Author noted limitations included substantial heterogeneity between studies and incomplete data. Additional limitations included the small patient populations and short term follow up. Large, controlled studies performed prospectively are needed to validate the results as well as for ongoing investigation of VLNT effectiveness in lymphedema treatment.

In a prospective study, Chang et al. (2020) compared patients who underwent free flap breast reconstruction VLNT and anastomosis to a retrospective cohort of patients who underwent free flap breast reconstruction with VLNT alone for breast cancer–related lymphedema. A total of 33 patients underwent deep inferior epigastric perforator (DIEP) flap reconstruction with vascularized inguinal lymph node transfer and lymphovenous anastomosis, and 21 received a free flap with lymph node transfer alone. There were no significant differences in demographics, adjuvant chemotherapy, or radiation therapy. The average number of nodes removed was also equivalent (21.2 vs. 21.4 nodes). Two anastomoses per patient, on average, were performed (range, one to four) in the combined cohort, and all patients (100%) reported a subjective improvement in symptoms, compared with 81.0% of patients undergoing only lymph node transfer (p=0.019). Perometer measurements demonstrated a significant reduction between the groups at early time points [3 months, 40.7% vs. 20.0% (p=0.037); six months, 57.0% vs. 44.5% (p=0.043)]; however, the difference was not statistically significant at 12 months (60.4% vs. 57.8%; p= 0.43). The reported study limitations include small sample size and lack of randomization. The most significant limitation is the lack of a validated patient-reported outcomes and quality-of-life assessment.

In a retrospective study, Ciudad et al. (2020) noted that VLNT is an emerging surgical treatment for lymphedema. The authors compared the long-term clinical outcomes on upper limb lymphedema (ULL) and lower limb lymphedema (LLL) in patients treated with VLNT. The study included data from patients with International Society of Lymphology (ISL) stages II to III who underwent different VLNTs. Demographics pre-operatively, and clinical data (limb circumference, infectious episodes, lymphoscintigraphic studies) pre-operatively and post-operatively were recorded. Clinical outcomes by extremity were also analyzed. A total of 83 patients with lymphedema (ULL n=30, LLL n=53) were included. Mean follow-up time was 32.8 months (range of 24-49 months). Mean circumference reduction was higher in patients with ULL compared to with LLL (28.6 ± 8.6 versus 22.3 ± 10.1, p<0.001), and for patients with secondary lymphedema (24.8 ± 9.6, p<0.001) than for patients with primary lymphedema (18.9 ± 14, p>0.05). Infectious episodes per year pre-operative and post-operative showed that LLL patients had higher reduction on infection rate compared with ULL patients (2.4 ± 1.1 versus 1.9 ± 1.2, p<0.001). The authors concluded that VLNT is a promising surgical therapeutic option for patients with lymphedema. The

findings of this study suggested that VLNT may have a more beneficial outcome in patients with ULL and with secondary lymphedema. The reported limitations of this study are the retrospective design and small sample size. The type of each flap used on the upper versus lower lymphedematous extremity was considered as a single group rather than individually.

Fish et al. (2020) conducted a systematic review to analyze the published evidence on predicting long-term health-related quality of life (HRQoL) outcomes for vascularized lymph node transfer (VLNT) and complex decongestive therapy (CDT) used in the treatment of breast cancer-related lymphedema. Studies using validated measurement instruments to assess HRQoL in patients with breast cancer-related lymphedema relative to baseline were included. A total of 16 articles were included in this review. Evidence regarding VLNT was reviewed from two prospective cohort studies involving 65 patients, and HRQoL was evaluated using the Lymphoedema Quality of Life Study questionnaire. Data on VLNT indicated favorable HRQoL outcomes at 12-month postoperative follow-up. Evidence regarding CDT was reviewed from 14 prospective cohort and randomized controlled studies involving 569 patients, and HRQoL was evaluated using the 36-Item Short Form Health Survey, Functional Assessment of Cancer Therapy-Breast, European Organization for Research and Treatment of Cancer, and Functional Living Index-Cancer measures. Data on CDT demonstrated variable association with HRQoL, and a majority of articles reported improvement in at least one subscale. The use of diverse patient-reported outcome measures and variability in CDT protocol limited interpretation of results in this population and between treatment modalities. The authors reported that additional studies are needed to better understand the best lymphedema treatment options and direct evidence-based care.

Forte et al. (2020) states that surgical treatment of lymphedema can be conducted alone or in combination with microsurgical autologous breast reconstruction. The authors conducted a systematic review regarding autologous breast reconstruction for deep inferior epigastric perforators (DIEP) or muscle-sparing transverse rectus abdominis myocutaneous (ms-TRAM) and vascularized lymph node transfer (VLNT) in patients with lymphedema following breast cancer surgery. Eligibility criteria included investigations reporting data studies evaluating female patients with lymphedema in an upper extremity after breast cancer who underwent autologous breast reconstruction combined with VLNT. The search resulted in six studies (n=103). The follow-up period ranged from 3-64 months. The population included patients with initial lymphedema symptoms, for which the duration varied from 6-182 months before the surgical treatment. The studies described groin lymph node transfer as treatment for lymphedema. In most of the studies, all patients reported a reduction of arm circumference, volume, and symptoms of the upper extremity with lymphedema comparing the preoperative to the postoperative period. In three studies, six patients did not notice any arm circumference reduction during the follow-up period. Overall, patients experienced successful breast reconstruction. All authors reported reduction of the circumferential size of the affected upper limb, as well as a decrease in cellulitis, in addition to favorable breast reconstruction results. A reported limitation of the studies is that the authors could not quantitatively evaluate the circumference or volume reduction, as well as cellulitis rate reduction, since several authors did not quantify it in detail in the studies. The authors concluded that although breast reconstruction combined with VLNT is a promising treatment, it requires additional studies including prospective and randomized trials to validate its utility.

In a case series study, Ciudad et al. (2019) described the clinical and patient reported outcomes of combining a physiologic (dual gastroepiploic VLNTs) and an excisional procedure (the modified radical reduction with preservation of perforators [RRPP]) in sixteen patients with extremity lymphedema stage III, as defined by the International Society of Lymphology (ISL). Diagnosis was based on past medical history, clinical examination, and lymphoscintigraphy using technetium-99m. All patients had failed at least six months of conservative treatment. Patients with prior history of abdominal surgery were excluded. The intervention was double gastroepiploic VLNT with laparoscopic harvest in combination with RRPP. There was no comparator group.

Demographics, outcomes including circumference reduction rates, preoperative and postoperative lymphoscintigraphy, complications, and responses to the Lymphedema Quality of Life (LYMQOL) questionnaire were analyzed. The mean follow-up period was 14.2 months (range, 12-19). The mean circumference reduction rate was 74.5% ± 6.9% for the upper limb and 68.0% ± 4.2% for the lower limb. LYMQOL showed a 2.7-fold quality-of-life improvement ($p<0.01$). Postoperative lymphoscintigraphy showed improved lymphatic drainage in all cases. There were no major complications. Minor complications, including numbness and hyperesthesia, were treated conservatively. The study was limited by lack of a comparator and small sample size. The authors concluded that combination of VLNT with modified RRPP in a one stage procedure is safe and reliable and provides optimal outcomes for patients with advanced extremity lymphedema. Larger series using this technique are required to standardize the combined approach and offer better and more efficient outcomes.

Forte et al. (2019) conducted a systematic review of vascularized omentum lymph node transfer (VOLT) in patients with lymphedema. A total of six studies (n=137) fulfilled the study eligibility criteria. Three studies described single VOLT, two studies described double VOLT and one study described two cohort patients, one that was treated with single VOLT and another one that was treated with double VOLT. The population included 88 patients with upper extremity lymphedema, 78 of which had lymphedema after breast cancer treatment, 48 patients had lower extremity lymphedema, and two patients had breast lymphedema. Follow-up ranged from 0.5-48 months. Postoperative reduction of arm volume, circumference, and symptoms of the upper extremity were reported in all patients. In one study, seven patients did not notice any extremity circumference reduction during the follow-up period and four patients noticed an increase in arm volume. Flap loss was reported by two authors in a total of two patients. Overall, patients experienced successful lymphedema treatment with VOLT. All authors presented results with reduced circumferential size of the affected upper and lower limbs, as well as reduction of the infectious intercurrences, such as cellulitis, with a small incidence of associated complications. The reported limitations of this review included a small number of studies and, consequently, a small cohort. The lack of prospective randomized studies and the nonstandardization of the obtained results make it difficult to establish protocols. Finally, the absence of objective measurement of arm circumference and volume, as well as cellulitis rate reduction, impeded a quantitative evaluation of outcomes. In addition, the duration of follow-up in the studies is too short to evaluate the persistent benefit of these procedures.

In a retrospective observational study, Leppäpuska et al. (2019) reported results of chronic lymphedema patients (n=21) who have undergone lymph node transfer and liposuction simultaneously in one operation and compared the results with patients who have undergone lymph node transfer without liposuction. Lymphangiogenesis associated growth factor (VEGF-C, VEGF-D) concentrations in the wound fluids of these patients was analyzed. The study included post mastectomy patients and one Hodgkin's lymphoma patient. All patients had a long history (range between 12 and 185 months, average 52 months) of chronic lymphedema with nonpitting edema and deposition of fat and fibrotic tissue after axillary lymphadenectomy and radiation therapy. Indications for procedure included clinically diagnosed lymphedema with more than 500mL of nonpitting edema compared with contralateral arm and reduced lymphatic function in lymphoscintigraphy. A total of 11 patients underwent lymph node transfer combined with liposuction (LIPO) of the affected arm and 10 patients underwent simultaneous breast reconstruction and lymph node transfer combined with liposuction of the affected arm. Compression therapy was started immediately after the operation and the patients used compression 24 hours/day at least six months postoperatively. Changes in clinical parameters (number of erysipelas infections, pain), arm volume, transport indexes calculated form lymphoscintigraphy images, and daily usage of compression garments were compared preoperatively and postoperatively and between groups (combined technique vs lymph node transfer). Mean follow-up time was 48.9 ± 15.4 months. In the combined technique group, the

average arm volume excess decreased postoperatively 87.7%, and in 7 of 10 patients, the edema volume did not increase even without compression. Seventeen of 21 patients were able to reduce the use of compression garment. Lymphoscintigraphy results were improved in 12 of 15 patients and the improvement was significantly greater in the combined technique group than in the lymph node transfer group (p=0.01). The number of erysipelas infections was decreased in seven of 10 patients and the decrease was significantly greater in the combined technique group than in the lymph node transfer group (p=0.02). In the lymph node transfer group, the average excess volume decreased postoperatively 27.5%. Fourteen of 27 patients were able to reduce the use of compression garments. Lymphoscintigraphy results were improved in 8 of 19 patients, and the number of erysipelas infections was decreased in one of three patients. There were no complications of the liposuction arm. Nine of 21 patients had minor complications (postoperative numbness, wound infection, limited skin necrosis, seroma) of the flap donor or recipient area. One patient needed a reoperation because of a thrombosis of the arterial anastomosis on the first postoperative day (wet liposuction technique). The authors concluded that liposuction can safely be performed with lymph node transfer in one operation to achieve optimal results in patients with chronic lymphedema. The combined technique provides immediate volume reduction and further regenerative effects on the lymphatic circulation. The significantly greater reduction in lymphoscintigraphy values and erysipelas infections suggests that the combined technique might be better for late-stage lymphedema patients than lymph node transfer alone. Limitations of this study include the retrospective nature of the data gathering and the small number of patients. A randomized controlled trial for stage II lymphedema patients comparing lymph node transfer, liposuction with controlled compression therapy, and the combination of these two techniques in the future would be feasible to compare these techniques in the same patient material.

In a comparative study, Maruccia et al. (2019) retrospectively evaluated and compared surgical and patient-related outcomes in women affected by stage II and III post mastectomy upper limb lymphedema by two approaches: a combined physiological procedure of lymph node flap transfer and release of the axillary scar with fat graft versus only the lymph node transfer. Inclusion criteria was history of breast cancer treated with either mastectomy or breast-conserving therapy and axillary lymph node dissection; Stage II and III (International Society of Lymphology staging system) breast cancer-related upper limb lymphedema exclusively treated by combined lymph node transfer to distal site and axillary scar release with fat graft or just with lymph node transfer to the distal site. Patients were excluded if they underwent the ancillary excisional procedure to treat lymphedema. Group A was combined procedure (VLNT + fat graft) (n=18); Group B had VLNT only (n=21). The primary outcome measure was the reduction rate (RR) of upper limb circumference (above elbow and below elbow). The secondary outcome was incidence of cellulitis and the specific quality of life parameters. An average follow-up time to lymphodynamic evaluation was 29 months (range, 24–38 months) for Group A and 32 months (range 28–44) for Group B. Flap survival rate was 100%, with no donor site morbidity in all patients. A statistically significant difference between the circumference reduction rates (RR) at above elbow level was observed at 3 and 6 months of follow-up comparing the two groups (p< 0.00001), with higher values in Group A than in Group B. No significant difference was detected comparing RR values at above and below elbow at 12 and 24 months postoperatively. LYMQOL metrics showed significantly better scores (p<0.0001) in all domains at all follow-up appointments in Group A. No adverse events were reported. This study was limited by small sample size. The authors advocate further larger research to corroborate and expand the results of the study.

In a review of the literature, Pappalardo et al. (2019) concluded that vascularized lymph node (VLN) transfer has become a promising treatment for moderate and advanced stages of extremity lymphedema. Consensus among the experts regarding most of the current issues, including the mechanism of VLN transfer, staging system or donor and recipient sites, is needed to provide more predictable outcomes. Patient selection criteria, careful preoperative evaluation of donor site

and recipient site and mastering anatomy and surgical skills are key factors for successful treatment of lymphedema of the extremities.

In a case series study, Liu et al. (2018) evaluated the outcome of vascularized groin lymph node (VGLN) transfer using axilla as a recipient site in patients with breast cancer-related lymphedema (BCRL) and reported on radiological evidence of lymphangiogenesis in VLNT. A total of 30 patients with BCRL were included in this study with a mean age of 60. All 30 patients had axillary dissection. Twenty-seven patients received adjuvant radiotherapy. One patient had stage I lymphedema, 25 patients had stage II disease, and four patients had late stage II disease and 28 received chemotherapy. The mean duration of lymphedema was six years. All patients received preoperative decongestive physiotherapy. None of the patients had received prior surgery for lymphedema. Patients with active axillary disease (i.e., axillary lymph node metastasis or documented deep vein thrombosis of the axillary vessels), were excluded from this study. A skinless VGLN flap nourished by the superficial circumflex iliac vessels was transferred to the axillary region of the lymphedematous limb. Mean follow-up was 22.11 ± 7.83 months (range, 12-34 months). The outcomes were assessed clinically with limb circumference measurement and radiologically with lymphoscintigraphy. No patient developed increase in limb circumference, 9 (30%) patients had no limb circumference reduction, and 21 (70%) patients had limb circumference reduction. The mean circumference reduction rate of the lymphedematous limb was 47.06% ± 27.92% (range, 0% to 100%). Eleven (37%) patients showed radiological improvement in postoperative lymphoscintigraphy that included seven cases of faster contrast transport and four cases of visualization of transplanted lymph node. No adverse events were reported. The authors concluded that the effectiveness of VGLN flap transfer in the treatment of BRCL is supported by limb circumference reduction and improvements in lymphoscintigraphy parameters. This study was limited by small sample size and lack of a comparator.

In a review of the literature, Scaglioni et al. (2018) evaluated outcomes and complications of vascularized lymph node transfer (VLNT) for the treatment of lymphedema. A total 24 studies encompassing 271 vascularized lymph node transfers were included. There were 260 free vascularized lymph node transfers performed, and 11 pedicle lymph node flaps. Measurements reported were heterogeneous. The follow-up time ranged from 1 to 96 months. The inguinal nodes were the most commonly used donor site followed by the lateral thoracic lymph nodes. The lateral thoracic lymph nodes were the least effective and had the highest complication rates (27.5%) compared to other lymph node donor sites (inguinal: 10.3% and supraclavicular: 5.6%). Upper extremity lymphedema responded better compared to lower extremity (74.2 vs. 53.2%), but there was no difference in placing the lymph nodes more proximally versus distally on the extremity (proximal: 76.9% vs. distal: 80.4%). The number and degree of improvement following VNLT was not thoroughly or consistently documented in the majority of studies. Twenty-five patients underwent additional adjuvant debulking procedures secondary to the lymph node transfers. The authors reported that more structured, prospective research to document outcomes in a more objective fashion is needed to know which donor and recipient site is best. Many of the studies included in the current analysis did not specify these details. Standardization in the parameters used to measure lymphedema following surgical intervention is needed.

In a prospective study, Maldonado et al. (2017) evaluated the flap and the donor site morbidity of the supraclavicular (SC) VLNT. A review of a prospective database was performed for patients who had undergone SC VLNT to treat upper or lower extremity lymphedema. Flap and donor site complications were registered for each patient. One hundred consecutive patients with lower or upper extremity lymphedema underwent SC VLNT (84% from the right side) with a mean of 11-months follow-up (range 3-19 months). There were no flap loss but three flaps (3%) required re-exploration due to venous congestion of the skin paddle. Two patients had local infection and three patients developed chyle leak (3%) at the donor site but resolved spontaneously. No donor

site secondary lymphedema was noted. This study focused on donor site. No limb size reduction outcomes were reported.

In a prospective study, Gratzon et al. (2017) evaluated the clinical, psychosocial, and functional outcomes of patients who underwent VLNT to the axilla for the treatment of upper extremity lymphedema after breast cancer therapy (n=50). Patients were evaluated preoperatively and postoperatively at one-, three-, six-, nine-, and 12-month intervals by circumferential measurements, pain/heaviness scales, and lymphedema quality of life (LYMQOL) questionnaires. Preliminary results showed a decrease in arm volumes by 34.57 % at one month, 52.03 % at three months, 42.34 % at six months, 65.23 % at nine months, and 58.68 % at 12 months. Pain and heaviness consistently decreased over time at 12 months. Overall quality of life scores steadily improved at 12 months. There was a significant decrease in the number of infections of the affected arm postoperatively and a decreased need for physiotherapy. Complications occurred in 17 patients and consisted mainly of minor wound complications. The authors reported that a consensus of surgical and postoperative protocols for VLNT is needed among studies to assess adequately its utility in the treatment of lymphedema. Although preliminary results are promising, larger studies with longer follow-up are needed to evaluate the efficacy and safety of this procedure.

In a randomized prospective control study, Dionyssiou et al. (2016) evaluated the effectiveness of free vascularized lymph node transfer (LNT) in stage II breast cancer-related lymphedema patients in comparison with non-surgical management. A total of 36 cases were included in this study and randomly divided in two groups: group A patients (n=18) underwent microsurgical LNT; followed by six months of physiotherapy and compression, while group B patients (n=18) were managed by physiotherapy and compression alone for six months. Patients of both groups removed their elastic garments after six months and were re-examined one year later. Limb volume reduction was observed in both groups; mean reduction was greater in group A (57%) than in group B (18%). Infection episodes in group A were significantly reduced compared to those in group B patients. All group A patients reported painless and feeling of heaviness-free extremities with overall functional improvement, while the corresponding changes in group B patients were no more than marginal. This study is limited by small sample size and short-term follow-up.

Raju et al. (2014) completed a review of the literature for VLNT with updates and comparisons on current application, techniques, results, studies and possible future implications. The authors concluded that "Although the results with the use of VLNT for treatment of lymphedema have been largely positive, further exploration into standardized protocols for diagnosis, treatment optimization, and patient outcomes assessment is needed".

In a case series study, Saaristo et al. (2012) describe a modified breast reconstruction flap containing lymph nodes from the groin area to reconstruct both the missing breast and the lymphatic network anatomy in the operated axilla. Breast reconstruction was completed in 87 patients. For all patients with lymphedema symptoms (n=9), a modified lower abdominal reconstruction flap containing lymph nodes and lymphatic vessels surrounding the superficial circumflex vessel pedicle was performed. Operation time, donor site morbidity, and postoperative recovery between the two groups (lymphedema breast reconstruction and breast reconstruction) were compared. The effect on the postoperative lymphatic vessel function was examined. The average operation time was 426 minutes in the lymphedema breast reconstruction group and 391 minutes in the breast reconstruction group. The postoperative abdominal seroma formation was increased in patients with lymphedema. Postoperative lymphoscintigraphy demonstrated at least some improvement in lymphatic vessel function in five of six patients with lymphedema. The upper limb perimeter decreased in seven of nine patients. Physiotherapy and compression was no longer needed in three of nine patients. No edema problems were detected in the lymph node

donor area. None of the operated patients with lymphedema reported pain, hernias, or edema symptoms in the donor area (low abdominal wall or lower limb). A total of three of nine patients with lymphedema have discontinued the use of compression and physiotherapy eight months to two years after the breast reconstruction and lymph node transfer. The authors reported that the lymph node transfer is still considered an experimental surgery and this study is the third report on the efficacy of the lymph node transfer in the treatment of lymphedema.

In a case series study, Gharb et al. (2011) reported the outcome of vascularized lymph node transfer with hilar perforators compared with the conventional technique. A total of 21 patients affected by early stage II upper limb lymphedema were included in the study. A total of 11 patients received a free groin flap containing lymph nodes, and 10 patients received vascularized inguinal lymph nodes with hilar perforators. Mean follow-up was 46 and 40 months, respectively. Complications, secondary procedures, circumference of the limb, and subjective symptomatology were registered. There was no statistical difference in the limb circumference measurements between the two groups preoperatively. Differences between preoperative and postoperative measurements were statistically significant only in the perforator-based group at the levels below elbow, wrist, and midpalm ($p=0.004$, 0.002, 0.007, respectively). All the other differences were not statistically significant. The number of secondary procedures was significantly higher in the standard group ($p=0.03$). There were two cases of partial flap loss and donor site lymphorrhea in the standard group. In both the groups, visual analog scale scores improved after the operation.

In a case series study, Lin et al. (2009) evaluated the outcome of vascularized groin lymph node transfer using the wrist as a recipient site in patients with post-mastectomy upper extremity lymphedema. A total of 13 consecutive patients underwent vascularized groin lymph node transfer for post-mastectomy upper extremity lymphedema. A vascularized groin lymph node nourished by the superficial circumflex iliac vessels was harvested and transferred to the dorsal wrist of the lymphedematous limb. The superficial radial artery and the cephalic vein were used as the recipient vessels. Outcome was assessed by upper limb girth, incidence of cellulitis, and lymphoscintigraphy. All flaps survived, and one flap required re-exploration, with successful salvage. No donor-site morbidity was encountered. At a mean follow-up of 56.31 ± 27.12 months, the mean reduction rate (50.55±19.26%) of the lymphedematous limb was statistically significant between the preoperative and postoperative groups ($p<0.01$). The incidence of cellulitis was decreased in 11 patients. Postoperative lymphoscintigraphy indicated improved lymph drainage of the affected arm, revealing decreased lymph stasis and rapid lymphatic clearance.

In an initial report of this surgery which was performed in France, Becker et al. (2006) reported on retrospective data collected on 24 patients treated with inguinal lymph node transfers to the axillary region. Patients with lymphedema for more than five years underwent lymph node transplantation. In this case series, upper limb perimeter returned to normal in 10 cases, decreased in 12 cases, and remained unchanged in two cases. The 10 cases in which upper limb perimeter returned to normal were described as being "cured." The authors reported that "no current gold standard for evaluation of lymphedema exists; hence, evaluating results of treatments remains difficult and appears controversial". Long-term results were evaluated according to skin elasticity and existence of infectious disease, decrease or disappearance of the lymphedema assessed by measurements, effects observed on isotopic lymphangiography, and ability to stop or to discontinue physiotherapy after six months. Long-term results were also evaluated according to the duration of the lymphedema before surgery and occurrence of downstaging after surgery. Physiotherapy was discontinued after six months in 14 patients and after 12 months in one patient. In the nine other patients, physiotherapy remained necessary and was performed once weekly in seven patients. Physiotherapy was thus discontinued in 15 patients (62.5%). No results were reported after 12 months.

Flap/Tissue Transfer: In a prospective study, Nguyen et al. (2017) report the long-term outcomes of the minimally invasive free vascularized omental lymphatic flap for the treatment of lymphedema. All consecutive patients with advanced lymphedema undergoing minimally invasive free vascularized omental lymphatic flap transfer were included (n=42). Perioperative evaluation included qualitative assessments, lymphoscintigraphy, and volumetric measurements with a mean follow-up of 14 (3–32) months. Subjective improvements were noted in 83% of patients. Mean volumetric improvement was 22%. Complications occurred in 16% (n=7) of patients. There was one episode of pancreatitis and one flap loss. Postoperative imaging revealed viable lymphatic transfers. Cellulitis history was present in 74% (n=31) patients with post-operative cellulitis occurring in 5% (n=2) patients. The collection of quality of life outcomes measures was incomplete.

Axillary reverse mapping (ARM)/reverse lymphatic mapping: Co et al. (2023) conducted a systematic review of five randomized control trials (RCTs) (n=1696) that compared axillary reverse mapping (ARM) (n=802) with the standard axillary lymph node dissection (n=894) during breast cancer surgery. The RCTS were conducted in China, Egypt, and the Netherlands. The average age of patients at diagnosis was 51.9 years (ARM group) and 52.1 years (standard group). The majority of patients had T2 tumor staging (47.4% and 43.3%) and N1 nodal metastasis (37.9% and 54.5%). Tumor pathology revealed invasive ductal carcinoma in 67.5% and 70.6% of patients, respectively. Primary outcome was to compare post-operative rate of lymphedema development. Secondary outcome was the safety of ARM as evidenced by nodal metastasis and axillary recurrence rate in the ARM group. The length of follow up ranged from 6–37 months. Pooled ARM node detection rate was 85.2% (Range 79.2%–94.9%). The rate of lymphedema in the ARM group ranged from 3.3%–22.9%, with a pooled lymphedema incidence of 4.8% (37/766). The rate of lymphedema in the standard surgery group ranged from 15.3%–33.1%, with a pooled incidence of lymphedema of 18.8% (164/873). The pooled axillary recurrence rate was 1.03% in both groups. Three RCTs reported no recurrence in either group. Author noted limitations of the review included small patient populations in four of the five RCTs (n=48–265), several studies excluded patients who received neoadjuvant treatment or had recurrent disease, and one study was terminated early due to the publication of trial results of an alternative treatment with adjuvant radiotherapy for early-stage cancer patients. An additional limitation included the short-term follow-up. Long-term follow up of larger, randomized, multicenter studies are needed to validate the results found from this systematic review of the literature.

Systematic Reviews: Chang et al. (2021) conducted a systematic review and meta-analysis sponsored by the American Association of Plastic Surgeons to assess the safety and efficacy of surgical treatments including lymphovenous bypass, vascular lymph node transplantation, and liposuction for the treatment and prevention of lymphedema. Randomized controlled trials (n=2 studies), observational studies including prospective (n=7 studies) and retrospective cohort (n=14 studies), case-control studies and case series (n=43 studies) were included. Patient inclusion criteria were adult patients with secondary lymphedema (stages 1, 2, 3, 4). Excluded were abstracts, studies including pediatric patients or utilizing other surgical techniques (excisional or lymph vessel transplant). Eight studies reported on liposuction and compression therapy, 16 studies on lymphovenous bypass and compression therapy and 17 on vascular lymph node transplantation and compression therapy. Patient populations ranged from 4–124 with follow-ups from 6–48 months. Primary outcomes for treatment were reduction in limb volume and circumference. The primary outcome for surgical prevention was the proportion of patients who developed lymphedema within one year of surgery. Secondary outcomes included complications from surgery, discontinuance of compression therapy and quality of life outcomes. Studies reported different outcome measures. Reported outcomes were reported based on the type of procedure.
Results from studies using combined liposuction and controlled compression therapy included:

- Two comparative studies on patients with stage II lymphedema (n=48 patients) reported a pooled analysis average of 63.95% reduction in volume compared to controlled compression therapy (CCT) only (very low-quality evidence); a pooled analysis of the same two studies (n=69 patients) reported reduction in limb volume by 895 ml compared to CCT.
- Two case series on patients with stage II-III lymphedema (n=163) reported 26.59% reduction in excess limb volume (very low-quality evidence).
- Six case series on patients with stage I-III lymphedema (n=294) reported liposuction combined with compression therapy reduced excess limb volume by an average of 1,702 ml (very low-quality evidence).
- One case series on liposuction in lymphedema patients (n=10) reported preoperative cellulitis occurred in 7/10 patients and postoperatively occurred in 1/10 patients (very low-quality evidence).

Studies investigating lymphovenous bypass and compression therapy reported the following outcomes:

- Three retrospective cohort studies (n=102) compared lymphovenous bypass to pressure therapy in lymphedema patients with upper extremity lymphedema (UEL) or lower extremity lymphedema (LEL). Results showed a higher percentage of circumference reduction in the lymphovenous bypass (LVB) patients than in compression alone. One study (n=24) reported 4.7cm reduction in leg circumference in the lymphovenous bypass (LVB) group compared to 0.6cm reduction in the compression therapy (CT) group ($p<0.05$). The second study (n=25) reported a mean arm circumference reduction of 4.1cm with LVB and 0.8cm with compression therapy ($p<0.05$). The third study (n=124) reported a 17.4% reduction in arm circumference in LVB group and 9.8% in complex decongestive therapy group ($p<0.00001$).
- Ten studies (case series and retrospective reviews) (n=134) on the combination of lymphovenous bypass and compression garment therapy in patients with stage II-V lymphedema reported a combined average reduction in (upper or lower) limb circumference of 3.8 cm ($p<0.00001$) (very low quality evidence).
- One case series of five patients with lower extremity lymphedema who underwent lymphovenous bypass with compression garments reported no significant difference in postoperative excess circumference reduction (mean difference 3.5%, $p=0.51$).

Studies reporting volume reduction reported varying results:

- One case series of 20 patients with upper and lower extremity lymphedema reported a reduction in limb volume of 504 ml ($p<0.05$) after lymphovenous bypass combined with compression.
- One case series of seven patients with lower extremity edema reported 1,858.6 ml reduction ($p<0.00001$) after lymphovenous bypass combined with compression garment use.
- One case series of 29 patients with upper extremity lymphedema reported a reduction of 234 ml ($p=0.02$).

Cellulitis reduction:

- Three case series (n=14 LEL, n=23 UEL) reported reduced cellulitis infections after lymphovenous bypass surgery (mean difference 2.57).
- Three case series (n=141 upper or lower extremity lymphedema) reported pre-operative cellulitis in 67% of patients reduced to 21% after lymphovenous bypass and compression therapy.

Studies investigating vascularized lymph node transfer:

- Four studies (n=300) comparing vascularized lymph node transfer combined with physiotherapy to physiotherapy alone reported decreased excess arm volume and arm circumference in the combination group with no significant reduction in infections. The randomized control trial (n=20) reported a mean difference of -15.00 ml ($p<0.001$); the pooled analysis of two prospective cohort studies showed improvement of circumferential

differentiation (mean difference 3.99 cm, n=200); the pooled analysis of a retrospective and prospective cohort showed circumferential. reduction (mean difference 24.29%, n=84).
- A pooled analysis of two studies (n=56) showed a nonsignificant reduction of infections per year (mean difference -0.48, p=0.22); reduced pain (n=36) (mean difference -4.00, p<0.00001); heaviness (n=36) (mean difference -4.17, p<0.00001) and improved overall function (n=36) (mean difference -3.39, p<0.00001).
- Five studies (n=72) on vascularized lymph node transfer for reducing limb circumference in stage II UEL when combined with compression garments and complex decongestive therapy reported that arm circumference was reduced by an average of 1.64 cm (p<0.0001) (very low quality evidence).
- Two case series (n=28) reported a decrease in limb circumference with a mean difference of 1.15 cm (p=0.03).
- Two case series (n=101) reported a decrease in limb volume by 9.6% (p<0.00001).
- One case series (n=15) of patients with LEL reported a reduced leg volume of 900 ml (p=0.08).
- A retrospective cohort (n=27) of UEL reported an average arm volume reduction of 112.6 ml (p=0.26).
- Three studies (two case series and one prospective cohort) (n=175) reported 59% of patients required physiotherapy and complex decongestive therapy prior to vascularized lymph node transfer and 33% required it after surgery (p<0.00001).
- Eight case series (n=248) reported a reduction in cellulitis infections (mean difference 2.34, p<0.00001).
- Six case series (n=233) reported the incidence of cellulitis before surgery was 53% and 18% after surgery (p<0.0001).
- One case series (n=25) reported quality of life was improved after VLNT (mean difference -3.95, p<0.00001).

Lymphatic microsurgery for Preventive Healing:

- Three studies (n=154) reported on the development of lymphedema more than 15 months post lymphovenous bypass. Nine of 62 patients developed lymphedema compared to 52 of 92 patients in the control group (p<0.0001, very low-quality evidence).

Reported adverse events included hyperpigmentation, cellulitis, skin paddle congestion, venous thrombosis, partial skin ulceration, hypertrophic scar, seroma, hematoma, wound dehiscence, lymphatic leakage, numbness, hyperesthesia, pulmonary embolus, and skin necrosis. Author noted limitations included the lack of randomized control trials, and variation in outcome measurements. In conclusion, due to the poor quality of the studies and the small patient populations, well designed prospective randomized controlled trials with large patient populations and long term follow up are needed to determine efficacy and safety of microsurgical techniques for primary lymphedema.

Markkula et al. (2019) conducted a Cochrane systematic review to assess and compare the efficacy of surgical interventions for the prevention of the development of lymphedema (LE) in the arm after breast cancer treatment and to assess and compare the efficacy of surgical interventions for the treatment of established LE in the arm after breast cancer treatment. The authors considered any surgical intervention for the treatment or prevention of secondary LE of the arm after breast cancer treatment. Both reductive and reconstructive techniques were considered including, but not limited to: liposuction; lymphaticovenular anastomoses; lymphatico-lymphatic bypass; lymph node transfer. All randomized controlled trials (RCTs) that compared a surgical intervention for the treatment or prevention of LE in the arm after breast cancer treatment to either standard intervention (conservative measures such as compression garments, lymphatic massage, bandaging, and intermittent pneumatic compression), placebo intervention (surgery performed without the critical surgical step), or another surgical intervention were included in this review. Three studies (n=131) were included: two studies reported on the effectiveness of

lymphaticovenular anastomosis as part of preventive management protocols in the prevention of breast cancer-related lymphedema and one study reported on the effectiveness of vascularized lymph node transfer in the treatment of established breast cancer-related lymphedema. The author conclusions state that there is currently not enough evidence to support the widespread adoption of lymphaticovenular anastomosis or vascularized lymph node transfer techniques. This review has shown that when these techniques are applied by well-trained surgeons who are expert in its use, there is potential to make a real impact in outcomes for breast cancer patients but there is currently not enough evidence to support the widespread adoption of lymphaticovenular anastomosis or vascularized lymph node transfer techniques.

In a systematic review, Forte et al. (2019) investigated the efficacy of the combination of lipoaspiration and lymph node transfer reporting the outcomes in breast cancer-related lymphedema patients. From a total of 20 articles, five met inclusion criteria (n=1-48). All patients included in these studies had stage II or III lymphedema. Two studies considered lipoaspiration as the first step followed by lymph node transfer, two considered lymph node transfer as the first step followed by lipoaspiration, and one applied both procedures simultaneously. A meaningful volume reduction was achieved in all cases. Patients who underwent lymph node transfer first followed by lipoaspiration appeared to have the best outcomes. The authors concluded that this systematic review suggests that the combination of lymph node transfer and lipoaspiration is a potential surgical treatment that may improve outcomes achieved by one single procedure in patients with stage II to III breast cancer-related lymphedema. A limitation of this review is heterogeneity due to the nature of the studies, the presence of different protocols, and the follow-up of patients, which makes it difficult to compare results and perform statistical analysis.

In a systematic review (SR), Carl et al. (2017) reviewed the literature to develop a treatment algorithm based on highest-quality lymphedema research. The SR addressed lymphovenous anastomosis (LVAs), vascularized lymph node transfer (VLNT), liposuction, excision, and multiple/combination surgical approaches for the treatment of lymphedema. The inclusion criteria was surgical therapy of extremity lymphedema studies with ≥ eight patients. A total of 69 articles met inclusion criteria and were assigned Methodological Index for Nonrandomized Studies (MINORS) scores with a maximum score of 16 or 24 for noncomparative or comparative studies, respectively. The average MINORS scores using noncomparative criteria were 12.1 for excision, 13.2 for liposuction, 12.6 for LVA, 13.1 for VLNT, and 13.5 for combined/multiple approaches. Loss to follow-up was the most common cause of low scores. A total of 39/69 cohort studies rated as high quality by MINORS instrument were included in the review: LVA (12), VLNT (10), excision (5), liposuction (4), combined/multiple approaches (8). The sample size was 8-2600. Follow-up 6-120 months. In studies measuring excess volume reduction, the mean reduction was 96.6% for liposuction, 33.1% for LVA, and 26.4% for VLNT. Included excision articles did not report excess volume reduction. The authors stated that further studies with a particular focus on patient follow-up will improve the validity of lymphedema surgery research. The authors also noted that the biggest drawback of this study was the heterogeneity of the included studies in terms of lymphedema stage and etiology, method of assessing surgical outcomes, and inconsistent reporting of complications and quality of life outcomes. Additionally, to better delineate indications for LVA versus VLNT and validate their proposed algorithm, more head-to-head comparative studies that adopt an accepted staging system, such as the ISL system, are needed. Randomized controlled trials with homogeneous patient populations in term of etiology and stage that compare surgical treatments to conservative therapies would help further define the most appropriate interventions for patients according to their clinical stage.

In a systematic review, Cormier et al. (2012) evalutated the surgical treatment of lymphedema. A total of 20 retrospective and prospective studies met inclusion criteria; procedures were categorized as excisional procedures (e.g., debulking, amputation, and liposuction) (n=8), lymphatic reconstruction (n=8), and tissue transfer (e.g., lymph node transplantation, pedicled

omentum, bone marrow stromal cell transplantation). (n=4). The reported incidence of volume reduction of lymphedema in these studies varied from 118% reduction to a 13% increase over the follow-up intervals ranging from six months to 15 years. The largest reported reductions were noted after excisional procedures (91.1%), lymphatic reconstruction (54.9%), and tissue transfer procedures (47.6%). Procedure complications were rarely reported. The authors concluded that most of these reports are based on small numbers of patients, use non-standardized or inconsistent measurement techniques, and lack long-term follow-up. In addition, although these surgical techniques have shown promising results, nearly all note that the procedures do not obviate the need for continued use of conventional therapies, including compression, for long-term maintenance.

Sudduth et al. (2020) reported on a cohort of patients from their lymphedema program database who were referred to a lymphedema program. Seven hundred patients were referred with a diagnosis of "lymphedema"; 71% were female and 38% were children. Lymphedema was confirmed in 71% of the cohort: primary (62%), secondary (22%), and obesity-induced (16%). Twenty-nine percent of the individuals labeled with "lymphedema" had another condition. One-half of the patients had not received treatment, and 36% resided outside of the local referral area. One-third of the subjects with lymphedema had an infection and 30% had >1 visit to the center. Patients with confirmed lymphedema were managed with compression stockings (100%), pneumatic compression (69%), and/or an excisional procedure (6%). The authors concluded that patients with suspected lymphedema need to be referred to specialists focused on lymphedema. Since the condition is chronic, individuals need to return for longitudinal follow-up. Lymphsocintigraphy is the most accurate test to confirm or rule-out the disease. Maintaining a normal body mass index and avoiding infections are important variables influencing the severity of the disease. Most patients are able to be managed conservatively with compression strategies and, if not, liposuction is an effective procedure to reduce the size of the extremity and potentially improve lymphatic function.

Gallagher et al. (2019) conducted a review of surgical treatment options for lymphedema reduction. Water displacement remains the gold standard for measuring limb volume and classification of lymphedema; however, lymphoscintigraphy and ICG lymphography are two novel imaging techniques that are now utilized to characterize lymphedema and guide management. Complete decongestive therapy (CDT) remains the mainstay of treatment. Vascularized lymph node transfer (VLNT) and lymphovenous bypass have shown promising results, particularly in advanced lymphedema stages. Combination therapy, incorporating both surgical and non-surgical approaches to lymphedema, yields best patient outcomes. The authors concluded that "Further research must be conducted in order to establish the absolute best practices in lymphedema diagnosis and treatment. Standardization in lymphedema staging, key outcome indicators, and quantitative data will be critical to future research. This will enable high-quality, randomized control trials that are needed to clarify indications and refine techniques for optimal patient care".

Professional Societies/Organizations
National Cancer Institute (NCI): The NCI Health Professional Version [Physician Data Query (PDQ®)] on lymphedema states that "The surgical options for the treatment of lymphedema include lymphatico-venous anastomoses (LVA), vascularized lymph node transplantation (VLNT), and reduction of excess tissue volume by excision of liposuction. Several informative reviews describe the surgical decision making involved in selecting patients and the type of operation. There are limited data to guide the choice between liposuction and microsurgical techniques, and some investigators propose a combined approach. The choice of microsurgical techniques may be aided by imaging and clinical grading of lymphedema severity. One proposal suggests that patients are candidates for LVA if they have partial obstruction seen on lymphoscintigraphy and grade 1 or 2 lymphedema with patent lymphatic ducts observed on indocyanine green lymphography . On the other hand, VLNT may be better for patients exhibiting a total obstruction

seen on lymphoscintigraphy and grade 3 or 4 lymphedema without patent lymphatic ducts observed on indocyanine green lymphography (NCI, 2023).

National Comprehensive Cancer Network Guidelines™ (NCCN®): The National Comprehensive Cancer Network Guidelines™ (NCCN Guidelines™) on Breast Cancer (Version 4.2022) does not specifically mention surgical treatments for lymphedema. The guideline recommends educating patients on lymphedema, monitoring for lymphedema and referring for lymphedema management as needed (NCCN, 2023).

The NCCN Guideline on Survivorship (Version 1.2023) has a section on lymphedema. The guideline recommends referral to a lymphedema surgeon for select patients.

National Lymphedema Network (NLN): The NLN published a position paper on the diagnosis and treatment of lymphedema in 2011. Per the NLN website, this position paper has been retracted and is currently in the process of being updated.

American Society of Plastic Surgeons (ASPS): The ASPS does not have a guideline or position statement with evidence-based recommendations for the treatment of lymphedema. They do address surgical options for lymphedema on the ASPS website.

Use Outside of the US
National Institute for Health and Care Excellence (NICE): NICE issued an updated clinical guidance addressing the use of liposuction for chronic lymphedema in 2022 (NICE, 2022). The guidance reviewed the evidence and concluded that current evidence on the safety and efficacy of liposuction for chronic lymphedema is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit. Patient selection should only be done by a multidisciplinary team as part of a lymphedema service.

International Society of Lymphology (ISL): The updated 2020 consensus document regarding the diagnosis and treatment of peripheral lymphedema discusses operative treatments. The consensus statement notes that "liposuction (or suction-assisted lipectomy) using a variety of methods has been shown to completely reduce non-pitting, primarily non- fibrotic, extremity lymphedema due to excess fat deposition (which has not responded to non-operative therapy) in both primary and secondary lymphedema". Additionally, the statement notes that liposuction "does not alter the need for compression therapy beyond appropriate garment after surgery." The document states that "Operations designed to alleviate peripheral lymphedema by enhancing lymph return have gained increasing acceptance and application worldwide but in advanced stages usually require long-term combined physiotherapy and/or other compression after the procedure to maintain edema reduction and ensure vascular/shunt patency. In some specialized centers, operative treatment within specific guidelines is now a preferred approach depending on the treatment team's training and the availability of various treatments. As is the case with any category of surgery, differences in surgical treatment will exist among different centers and patients are strictly selected."

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD		No National Determination found	
LCD		No Local Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Appendix A

Differential diagnosis of lymphedema and lipedema (Shavit, et al., 2018)

Characterstics	Lipedema	Lymphedema
Pathophysiology	Genetic, primary	Defects in lymph vessels, primary or secondary
Disproportion	Yes	No
Age of onset	Puberty	Any age
Gender	Female	Both genders
Skin consistency	Firm	Soft
Skin color	Normal, sometimes ecchymosis	Brown, warty, sclerotic
Extent of involvement	Bilateral, mainly legs	Unilateral or bilateral most commonly on legs and arms
Symmetry	Symmetric	May be asymmetric
Clinical cues	"Cuff sign" ankle pad fatty retromalleolar sulcus or lack of Achilles tendon definition	Verruca papillomatosis, pebbly stone skin, positive stemmer sign*
Involvement of feet	No	Yes
Response to compression therapy	No	Yes
Common associations	Anxiety, depression, hypermobility	Venous disease, recurrent cellulitis
Easy bruising	Yes	No

* A positive Stemmer sign is the inability to pinch the fold of skin at the base of the second toe or finger, indicating the presence of lymphedema

Coding Information

Notes:

1. This list of codes may not be all-inclusive.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when used to report lipectomy or liposuction for the treatment of lipedema of the extremities when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
15832	Excision, excessive skin and subcutaneous tissue (includes lipectomy); thigh
15833	Excision, excessive skin and subcutaneous tissue (includes lipectomy); leg
15836	Excision, excessive skin and subcutaneous tissue (includes lipectomy); arm
15837	Excision, excessive skin and subcutaneous tissue (includes lipectomy); forearm or hand
15878	Suction assisted lipectomy; upper extremity
15879	Suction assisted lipectomy; lower extremity

Considered Medically Necessary when used to report the surgical treatment of lymphedema when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
15832	Excision, excessive skin and subcutaneous tissue (includes lipectomy); thigh
15833	Excision, excessive skin and subcutaneous tissue (includes lipectomy); leg
15836	Excision, excessive skin and subcutaneous tissue (includes lipectomy); arm
15837	Excision, excessive skin and subcutaneous tissue (includes lipectomy); forearm or hand
15839	Excision, excessive skin and subcutaneous tissue (includes lipectomy); other area
15878	Suction assisted lipectomy; upper extremity
15879	Suction assisted lipectomy; lower extremity

Considered Medically Necessary when used to report surgical treatment for lymphedema (e.g., microsurgical lymphatico-venous anastomosis, lymphatic- capsular-venous anastomosis, lymphovenous bypass, vascularized lymph node transfer) when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
38589	Unlisted laparoscopy procedure, lymphatic system
38999	Unlisted procedure, hemic or lymphatic system

Considered Experimental/Investigational/Unproven when used to report tissue transfer (e.g., omental or mesenteric flap), immediate lymphatic reconstruction (e.g., Lymphatic Microsurgical Preventing Healing Approach [LYMPHA]) for prophylactic purposes), or axillary reverse mapping (ARM)/reverse lymphatic mapping:

CPT®* Codes	Description
38589	Unlisted laparoscopy procedure, lymphatic system
38999	Unlisted procedure, hemic or lymphatic system

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Revision Details

Type of Revision	Summary of Changes	Date
Annual review	• Title changed • Updated to new template and formatting standards • Added not covered statement for the procedure Axillary Reverse Mapping/Reverse Lymphatic Mapping	10/15/2023