Anthem

Medical Policy

Subject: Bioimpedance Spectroscopy Devices for the Detection and Management of Lymphedema
Document #: MED.00105 **Publish Date:** 06/28/2023
Status: Reviewed **Last Review Date:** 05/11/2023

Description/Scope

This document addresses the use of bioimpedance spectroscopy, a device which uses impedance ratios to measure extracellular fluid volume differences between limbs to aid in the clinical assessment of lymphedema.

Note: Please see the following related document for additional information:

- CG-DME-06 Compression Devices for Lymphedema

Position Statement

Investigational and Not Medically Necessary:

The use of bioimpedance spectroscopy testing in the assessment, diagnosis, or management of individuals with known or suspected lymphedema is considered **investigational and not medically necessary.**

Rationale

Breast cancer survivors remain at risk for the development of secondary lymphedema (that is, excessive lymph fluid and protein accumulation in the extracellular space) despite advances in breast conserving surgical procedures and axillary dissection techniques of the affected limb. Studies suggest that 6-40% of breast cancer survivors will develop lymphedema at some point during their lifetime (Ridner, 2009). Serial measurements of limb circumference and limb volume (water displacement volumetry) are the conventional methods to diagnose and monitor lymphedema. Early treatment of lymphedema with compression sleeves may prevent the development of chronic breast cancer-related lymphedema.

Bioimpedance spectroscopy, the measurement of electrical impedance of tissue in response to an electric current, is proposed as a method to diagnose and quantify lymphedema. When an electrical current is applied, it is mainly distributed by intracellular and extracellular fluid and the cell membranes resist the electric current. The bioimpedance unit is calculated by the L-Dex score which quantifies lymphedema and represents the ratio of the impedance of extracellular fluid in the unaffected limb to that in the affected limb. As the volume of extracellular fluid increases, the L-Dex score also increases.

Czerniec and colleagues (2010) reported on individuals with lymphedema (n=33) and individuals without lymphedema (n=18) to examine the relationship between physical methods of measuring lymphedema and self-reported swelling. The purpose of the study was to compare the reliability of the most commonly used measures of lymphedema. Measurement techniques included self-report, bioimpedance spectroscopy, truncated cone (circumference) method and infrared perometry. The study concluded that the physical measurement tools studied were reliable with high concordance (0.89 to 0.99) while self-report correlated only moderately with physical measurements (0.65-0.71) and was therefore only moderately reliable. The authors concluded that while lymphedema assessment methods showed good concordance and reliability, they were not interchangeable.

Ridner (2009) reported a feasibility study of single-frequency bioelectrical impedance to detect upper limb lymphedema in non-laboratory settings. Impedance ratios among healthy normal women and breast cancer survivors, both with and without lymphedema were compared. Ratios of healthy normal controls and breast cancer survivors without clinical evidence of lymphedema were similar with nearly complete overlap in confidence intervals. However, those values were markedly different from the values measured in the breast cancer survivor group with lymphedema ($p<0.001$).

In a 2011 study by Czerniec, the authors sought to determine if bioimpedance spectroscopy could detect lymphedema of the arm and compare the measurements of bioimpedance spectroscopy to that of perometry. With a sample size of 29 women with known lymphedema and 11 women with no history of lymphedema, arm volume was measured by both perometry and bioimpedance spectroscopy. Both techniques were sensitive enough to detect localized lymphedema of the arm and there was a high degree of concordance between the bioimpedance spectroscopy ratio and that determined by perometry. However, bioimpedance was not shown to improve the net health outcome.

Fu and colleagues (2013) reported on a study which sought to examine the reliability, sensitivity and specificity of bioimpedance spectroscopy in the detection of lymphedema. Circumferential tape measurement was used to validate the presence of lymphedema in 250 women. Bioimpedance was used to measure lymph fluid changes. The 250 women in the study included healthy females, breast cancer survivors with lymphedema, and those who were at risk for developing lymphedema. Bioelectrical impedance analysis, as indicated by L-Dex ratio, for healthy women was highly reliable (intraclass correlation coefficients [ICC] =0.99) (95% confidence interval [CI], 0.99-0.99), for survivors at-risk for lymphedema (ICC=0.99; 95% CI, 0.99-0.99), and for all women (ICC=0.85; 95% CI, 0.81-0.87); reliability was acceptable for survivors with lymphedema (ICC=0.69; 95% CI 0.54 to 0.80). The bioimpedance ratio correlated with limb volume by sequential circumferential tape measurement. The L-Dex ratio had a diagnostic cutoff of > +7 which missed 20% of true lymphedema cases. The authors noted that “it is important for clinicians to integrate other assessment methods (such as self-report, clinical observation, or perometry) to ensure the accurate detection of lymphedema.”

In a prospective study by Barrio and colleagues (2015), diagnosis of breast cancer-related lymphedema using volume displacement was compared to bioimpedance in 186 participants. All participants received volume displacement and bioimpedance measurements at baseline. The follow-up was for 3 years and measurements were taken at 3- to 6-month intervals. A total of 21 participants had an abnormal bioimpedance measurement, but no lymphedema found by volume displacement, 4 participants had both an abnormal bioimpedance measurement and lymphedema found by volume displacement, and 9 participants developed lymphedema without a prior abnormal bioimpedance measurement. There was no correlation between changes in volume displacement and changes in bioimpedance measurement at 3 months ($r=0.31$) or 6 months ($r=0.21$). Of the participants with abnormal bioimpedance measurement, few progressed to lymphedema and those with lymphedema did not have prior abnormal bioimpedance measurements.

In 2019 Spitz and colleagues completed a retrospective review to evaluate the accuracy of bioimpedance spectroscopy measurements in the diagnosis of breast cancer-related lymphedema. In this single center study, participants had preoperative and postoperative evaluation for possible lymphedema by bioimpedance spectroscopy and limb circumference measurements. The authors used the device manufacturer's criteria to diagnose lymphedema (which lie outside the normal range of -10 to +10 or a 10-point increase from prior measurements). At each visit, participants received an examination which included checking for pitting edema, Stemmer's sign, range of motion, participant report of symptoms, and sensory and motor function. All participants also had bioimpedance measurements taken during the same visit. Diagnosis of lymphedema was determined by a lymphedema physical therapist. The mean follow-up period was 10.2 months. There were 134 participants with lymphedema and 261 participants without lymphedema based on physical exam and limb circumference measurements. The average postoperative bioimpedance spectroscopy score for all participants was 2.1 ± 6.4. For participants with lymphedema, the average absolute bioimpedance spectroscopy score was 2.2 ± 8.8; 10 participants demonstrated an absolute bioimpedance >10, 124 participants had an absolute bioimpedance <10, 33 participants had a relative change in bioimpedance >10, and 101 participants had a relative change in bioimpedance <10. For the participants without lymphedema, the average absolute bioimpedance score was 2.1 ± 4.6; 4 participants had an absolute bioimpedance >10, 258 had an absolute bioimpedance < 10; 21 had a relative change in bioimpedance > 10, and 241 had a relative change in bioimpedance < 10. When using the manufacturer's criteria of an absolute bioimpedance measurement of greater than 10 units to diagnose lymphedema compared to those with a clinical diagnosis by physical exam and tape measurements, the bioimpedance demonstrated a sensitivity of 7.5%, specificity of 98.5%, positive predictive value of 71.4%, and a negative predictive value of 67.5%. When using criteria of a relative change in bioimpedance of +10 between two separate measurements, the bioimpedance showed a sensitivity of 24.6%, specificity of 92.0%, positive predictive value of 61.1%, and negative predictive value of 70.5% when compared to diagnosis based on physical exam and tape measurements. This study has limitations which include a limited long-term follow-up, its retrospective and single center nature, no control for arm dominance, and lack of a gold standard for diagnosing lymphedema. Currently there are variables between studies to draw conclusions to the accuracy of bioimpedance spectroscopy in the diagnosis of lymphedema. Specific protocols should be in place before drawing firm conclusions.

A 2019 randomized trial by Ridner and colleagues reported interim analysis results in which they evaluated lymphedema by comparing the use of bioimpedance spectroscopy (n=263) to volume circumference measurement using a tape measure (n=245) in 508 newly diagnosed individuals with breast cancer. The primary goal was to determine if subclinical detection of extracellular fluid accumulation measured by bioimpedance spectroscopy and subsequent early intervention reduces the rate of progression to complex decongestive physiotherapy compared to the rates seen using standard tape measurements. The median follow-up was 17.8 months following surgery. Progression was defined as a tape measure volume change ≥ 10% above the presurgical baseline in the at-risk arm. The baseline median bioimpedance measurement was 0.0. The median arm volume in the at-risk arm was 1943.2 mL and 1949.6 mL in the arm not at risk. There were 6 participants in the tape measure group and 4 participants in the bioimpedance spectroscopy group who progressed at either their initial post-randomization visit or between other study visits before an intervention could be started. These 10 participants were excluded from the primary analysis. Of the remaining participants, fewer bioimpedance spectroscopy participants triggered an intervention (15%) compared to tape measure (28.5%). The time from randomization to trigger in the bioimpedance group was a median 9.5 months versus a median 2.8 months in the tape measure group. Not including those who progressed without intervention and did not meet inclusion criteria for the endpoint analysis, progression was observed in 12 individuals who triggered an intervention (n=2 in the bioimpedance group and n=10 in the tape measure group). The median time to progression was 6.0 months in the circumference group and 6.7 months in the bioimpedance spectroscopy group. With 109 participants who triggered early intervention and 12 who have progressed, the stopping criteria has not been met and follow-up will continue for the complete study period. Further data from a longer follow-up period is expected.

In a 2020 prospective cohort study Cavezzi and colleagues reported on 41 participants with unilateral lymphedema of the lower limb who received complex decongestive treatment daily for 6 days. The primary outcome was to assess immediate and early outcomes of complex decongestive treatment using circumference-based limb volumetry and bioimpedance spectroscopy. Secondary outcome was to assess correlation between the two methods during treatment. Each treatment session consisted of manual lymphatic drainage, electro-sound lymphatic drainage, compression bandage, low-carb nutrition, anti-edema/anti-inflammation dietary supplements, and anti-stasis exercising. Participants underwent volumetry by tape measurements and bioimpedance spectroscopy immediately before the start of complex decongestive treatment. Three days after treatment, resistance and reactance of the total limb were recorded. Following the last treatment, volumetry and measurements by bioimpedance spectroscopy of the treated limb were repeated. Before treatment, mean total limb volume was 11,072.9, mean resistance was 200.4, mean reactance was 12.3,and mean total limb lymphatic index was 18.9. At day 3, mean resistance and reactance was 225.7 and 15.0 respectively. Following 6 days of treatment, mean total limb volume was 10,493.1, mean resistance was 237.5, mean reactance was 16.6, and mean lymphatic index was 14.9. Leg mean volume before treatment was 3150.8 and 2980.3 after treatment. Mean leg resistance before treatment was 117.5 and 150.0 following treatment. Leg mean reactance before treatment was 7.7 before treatment and 11.5 following treatment. Leg mean lymphatic index before and after treatment was 24.7 and 14.8 respectively. Treatment was noted to be effective with reduction of limb volume seen in the leg and total limb. Resistance and reactance showed an increase with a decrease in lymphatic index. There is noted correlation between the two methods of lymphedema measurement, however the outcomes do not show superiority of bioimpedance spectroscopy to volumetry.

A 2020 prospective cohort study by Bundred and colleagues compared multi-frequency bioimpedance spectroscopy with arm volume measurement to detect breast cancer related lymphedema. Primary outcome measure was to ascertain if bioimpedance spectroscopy had equal sensitivity and specificity as perometry in the detection of lymphedema. Secondary outcomes included effect of lymphedema on quality of life, cancer survival, and risk factors for lymphedema. The study included 1100 individuals who underwent axillary clearance surgery. There were 309 individuals who either withdrew from the study, were lost to follow-up or died. For this study, relative arm volume increase was defined as greater than or equal to 10% increase from baseline. Self-reported symptoms were obtained by using the Lymphedema and Breast Cancer Questionnaire and the Functional Assessment of Cancer Therapy Breast+4 questionnaires. Participants who developed lymphedema were prescribed a compression-sleeve garment. By 24 months following surgery, the incidence of lymphedema was 22.4% by relative arm volume increase and 45.2% using bioimpedance spectroscopy. Compression-sleeve garments were required by 24.5%. Median time to lymphedema development was 11.3 months. At 6 months, sensitivity for bioimpedance spectroscopy greater than 10 was 69%, specificity was 82% and positive predictive value (PPV) was 28%. For bioimpedance greater than 7.5 sensitivity was 80%, specificity was 77% and PPV was 24%. Diagnostic accuracy was 89.3%. At 24 months, sensitivity and specificity for bioimpedance spectroscopy was unchanged, but PPV was improved at 31%. Diagnostic accuracy was 85.7%. Swelling and heaviness were associated with larger increases in the exact relative arm increase but not exact bioimpedance spectroscopy. Arm swelling was reported by 65.8% of participants. For the 221 participants who wore the compression-sleeve, sensitivity and specificity were compared between relative arm volume increase and bioimpedance spectroscopy. The authors noted bioimpedance spectroscopy identified high false positives in the diagnosis of lymphedema. Negative predictive value (NPV) was similar for both types of measurements. Quality of life scores increased for those wearing compression-sleeve garments. Relative arm volume increase changes were associated with increased reporting of symptoms. Swelling and heaviness in the ipsilateral limb before surgery was reported in up to 25% of participants. Changes in relative arm volume increase were associated with increased symptom reporting. The lack of standardized criteria for lymphedema makes it difficult to accurately diagnose the true incidence of lymphedema.

In a 2021 prospective study by Keeley and colleagues, the authors reported on whether bioimpedance spectroscopy is a better tool than limb volume measurement for early detection of breast cancer-related lymphedema. The authors also sought to determine if it's possible to create a risk assessment tool to distinguish those at high risk versus those at low or no risk. There were 1100 participants with breast cancer who had arm volumes measured by perometer and multifrequency bioimpedance spectroscopy preoperatively, then at 1, 3, 6, 9, and 12 months, then 6-monthly up to 5 years postoperatively. A relative arm volume increase of greater than 10% from baseline and a change of 10 or more L-dex units from baseline was used as the definition of lymphedema. For those who developed a relative arm volume increase of greater than 10%, and those who were determined to have clinical lymphedema (for example localized swelling) but relative arm volume increase less than 10%, a compression sleeve was provided. At 6 months, there was moderate correlation between relative arm volume increase and bioimpedance spectroscopy. By 24 months, lymphedema was diagnosed in 22% of participants by relative arm volume increase and 45% by bioimpedance spectroscopy and 24% of participants received a compression sleeve. At 24 months, use of a compression sleeve increased the incidence of breast cancer-related lymphedema measured by relative arm volume increase less than 10% from 22.8% to 24.5%. Conversely, bioimpedance measurement showing an incidence of breast cancer-related lymphedema of 45.6% suggests using bioimpedance alone may result in overtreatment, with the authors concluding limb volume measurement performing better than bioimpedance in the early detection of breast cancer-related lymphedema. Using logistic regression, there were eight risk factors thought to be predictors of lymphedema (relative arm volume increase at 1 month, feeling of swelling, age, preoperative body mass index, number of positive nodes, chemotherapy, radiotherapy, and stage of breast cancer). A scoring model was produced based on the regression coefficients of the multivariable logistic regression with accuracy assessed by the area under the receiver operating characteristic curve method. At 1 month, relative arm volume increase less than 1 predicted 12% of participants had risk of lymphedema at 36 months, relative arm volume increase of 2-3 predicted 32% of participants had risk of lymphedema at 36 months, and relative arm volume increase of 3.5-4.5 predicted 77% of participants with risk of lymphedema at 36 months. The authors noted "Changes in L-Dex were not found to be significant predictors by univariate or multivariable analysis." Other risk models are in development and additional validation is needed.

A 2020 systematic review by Forte and colleagues evaluated the literature regarding the use of bioimpedance spectroscopy in evaluating individuals with breast cancer-related lymphedema. There were 11 studies included; 4 were prospective, 4 were retrospective, and 3 were cross-sectional. Six of the studies evaluated the use of bioimpedance spectroscopy in assessing response to treatment for breast cancer-related lymphedema and all reported reduction in bioimpedance scores which correlated with improvement of lymphedema. One study evaluated the use of bioimpedance spectroscopy to assess L-Dex changes within 12 months after surgery. The authors reported that 17.1% of participants had a maximum L-Dex change of 7 units or more from baseline. The maximum change occurred at a median of 6 months after surgery. Another study assessed volume changes following breast cancer surgery. The authors reported that L-Dex scores changed according to lymph node action and those with four or more lymph nodes removed had higher L-Dex values. One study assessed changes in volume by using a special equation and reporting bioimpedance measurements into units of volume. The authors noted that the volumes measured with perometry strongly correlated with the fluid volumes predicted by bioimpedance spectroscopy however cautioned that further studies were necessary to determine accuracy of predicted fluid volumes. Another study correlated clinical staging with bioimpedance spectroscopy scores and reported that L-Dex ratios increased as the interlimb circumference differences increased. Another study compared two types of bioimpedance analysis: single-frequency bioimpedance analysis and multiple-frequency bioimpedance analysis. It was reported that both types of bioimpedance spectroscopy detected extracellular fluid in the affected lymphedematous limb. There was a lack of heterogeneity among the studies with different objectives, evaluations, and protocols. Further studies with similar purpose and evaluations are necessary.

Another systematic review by Forte and colleagues (2021) described and evaluated the efficacy of bioimpedance spectroscopy for surveillance and diagnosis of early breast cancer-related lymphedema. There were 22 studies included in the analysis, 12 prospective, 3 retrospective, and 7 cross-sectional. There were 13 studies (12 prospective and 1 retrospective) which used bioimpedance spectroscopy as a tool for surveillance and diagnosis of subclinical breast cancer-related lymphedema. The 8 studies which evaluated bioimpedance spectroscopy for diagnosis of breast cancer-related lymphedema were cross-sectional and retrospective. These studies compared bioimpedance ratios between healthy subjects and those with breast cancer-related lymphedema. Bioimpedance ratios were found to be different between the two cohorts and correlated positively with volume of lymphedema. Of the studies included in this systematic review which evaluated bioimpedance for breast cancer-related surveillance, an increase of 10 or greater from baseline L-Dex score was used as the threshold to initiate compression garment therapy. However, there is no standard, specific cutoff value considered to diagnose subclinical lymphedema and other published studies have reported using different cutoff values. Limitations including heterogeneity among the studies and differing protocols in each study makes it difficult to evaluate accuracy, sensitivity and specificity of bioimpedance spectroscopy. Varying study designs also make it difficult to perform statistical comparison of outcomes.

A 2021 meta-analysis by Shah and colleagues sought to determine the relative reduction in progression to chronic breast cancer-related lymphedema in subjects with breast cancer by comparing bioimpedance spectroscopy, tape measurement, and background. Primary outcome was the annual progression to chronic breast cancer-related lymphedema comparing background rate of progression (n=35 studies), monitoring with bioimpedance with early intervention (n=7 studies), and tape measurement of limb circumference with or without intervention (n=11 studies). There were 50 articles included in the analysis; 27 prospective surveillance studies, 14 retrospective chart reviews, and 9 randomized controlled trials. Mean or median length of follow-up ranged from 1 to 10 years across the studies. Pooled estimate for cumulative incidence of breast cancer-related lymphedema was 12.9% for background monitoring, 17.0% for tape measurements, and 3.1% for bioimpedance spectroscopy. Annualized incidence of breast cancer-related lymphedema was 4.9% for background monitoring, 7.7% for tape measurements, and 1.5% for bioimpedance spectroscopy. The reduction in progression to breast cancer-related lymphedema among those monitored with bioimpedance spectroscopy was observed in all studies regardless of study duration or study type, with the exception of comparison to circumference monitored individuals in the randomized controlled trial studies. Limitations are that there were only seven studies that used bioimpedance to monitor progression to chronic breast cancer-related lymphedema. Most of the studies included in this analysis were lacking information about body mass index, taxane-based chemotherapy, or regional nodal irradiation, which are also considered risk factors for breast cancer-related lymphedema. It is also noted that 28% of subjects monitored by bioimpedance had axillary-lymph node dissection versus 73% of the tape measurement cohort. This could be suggestive the tape measurement group was at a disproportionately higher risk of breast cancer-related lymphedema. Variations among study designs and objectives make it difficult for true comparisons.

A 2022 randomized trial by Ridner and colleagues reported on whether subclinical detection of increasing extracellular fluid found by bioimpedance spectroscopy and early intervention of a 4-week trial of a compression sleeve and gauntlet (worn for 12 hours per day) reduced the rate of progression to chronic breast cancer-related lymphedema. The study compared bioimpedance spectroscopy and tape measurements for surveillance of breast cancer-related lymphedema. Subjects were included if they had histologically confirmed new diagnosis of breast cancer (invasive carcinoma or ductal carcinoma in situ) with a planned surgical procedure. Since the study was designed to capture those with an elevated risk of subclinical breast cancer-related lymphedema, subjects were evaluated again 2 months following surgery to confirm eligibility. Baseline bioimpedance spectroscopy and tape measurements were obtained for all subjects. Once eligibility was confirmed following surgery, subjects were randomized with 1:1 allocation to continued measurement by

either bioimpedance or tape measurement. Measurements were taken at 3, 6, 12, 18, 24, and 36 months and after compression intervention. In this study, chronic breast cancer-related lymphedema was defined as greater than or equal to 10% change in arm volume from baseline. Final analysis was available on 879 subjects (bioimpedance = 442 subjects, tape measurement = 437 subjects). The subjects who were measured via bioimpedance had a 61% prevalence of Stage I disease compared to 52% in the tape measurement group. Also, for those in the bioimpedance group, 84% of the subjects had sentinel lymph node biopsy compared to 78% in the tape measurement group. Median follow-up was 32.9 months. In the bioimpedance group, 89/442 subjects triggered an intervention compared to 120/437 subjects in the tape measurement group. Median months from randomization to intervention triggering was 9.7 months in the bioimpedance group compared to 3.9 months in the tape measurement group. Of those who triggered an intervention, 30 subjects progressed after intervention. There was no difference between the measurement groups in the rates of intervention completion. After intervention, 7/89 (7.9%) participants in the bioimpedance group progressed to complex decongestive physiotherapy versus 23/120 (19.2%) in the tape measurement group. Median follow-up months between intervention trigger and progression for the bioimpedance group was 4.9 months compared to 10.7 months for tape measurement group. Overall there were three study-related adverse events (two complaints of Grade 1 skin itching/tingling/redness during intervention and one report of perceived swelling which was not confirmed on physical exam). While the study suggests those who receive bioimpedance spectroscopy may benefit from earlier intervention than tape measurement, there is no information about long-term outcomes and improvement of net health outcomes.

A study by Borman and colleagues in 2022 reported the results of a 6 month surveillance program to determine the comparative frequency of subclinical and clinical breast cancer-related lymphedema identified by bioimpedance spectroscopy and circumferential volume measurement in a cohort of individuals with breast cancer. There were 100 participants in the study with results available for 82 at the end of the study. Baseline measurements were taken, and then again at 3 and 6 months. Functional status was evaluated by quick Disability of Arm, Shoulder and Hand questionnaire (Q-DASH). Quality of Life (QoL) was assessed using the Lymphedema Quality of Life Questionnaire-Arm (LYMQOL-Arm). For the circumferential measurements, there were 12 (14.6%) and 10 (12.2%) participants diagnosed with subclinical lymphedema at the third and sixth month follow-ups respectively. There were 6 (7.3%) and 9 (10.9%) participants diagnosed with clinical lymphedema at the third and sixth month follow-ups respectively. In terms of bioimpedance spectroscopy, there were 51 participants (62%) who had an abnormal L-Dex score at some point during surveillance. There were 19 (23.1%) and 7 (8.53%) participants diagnosed with subclinical lymphedema at the three and sixth-month follow-ups respectively. Lymphedema was found in 11 (13.4%) and 14 (17.1%) participants at the three and sixth month follow-ups respectively. Mean Q-DASH scores increased during the follow-up, but did not reach significance at any time point. There was no significant change in the mean scores of LYMQoL subgroups. There was no correlation between volume measures by either by bioimpedance spectroscopy or circumferential measurement and functional and QoL scores at the sixth month follow-up. Limitations include loss of 18 participants in the final results and short-term follow-up period. The study remains ongoing.

Whitworth and colleagues (2022) reported on a systematic review of four randomized controlled trials and seven prospective studies which evaluated breast cancer-related lymphedema surveillance with early intervention. While the studies suggest bioimpedance spectroscopy can identify breast cancer-related lymphedema, variations among the studies including follow-up times, multiple diagnostic modalities studied, and lack of heterogeneity make it difficult for true comparison.

The National Comprehensive Cancer Network® NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) in their 2023 guideline for Breast Cancer recommends that individuals be educated about lymphedema, monitored for lymphedema and referred for management as necessary. The guidelines do not address the methods of measurement or monitoring. The 2023 NCCN guideline for Survivorship states:

> Early detection/diagnosis and early referral are key for optimal lymphedema management because stages 0 and 1 are reversible, whereas stages 2 and 3 are less responsive to treatment. Therefore, survivors at risk for lymphedema should be regularly screened for lymphedema by symptom assessment, clinical exam, and, if available, bioimpedance spectroscopy. Patients should be educated about early symptoms and signs of lymphedema including fullness, tightness, heaviness, and pain.

However, the Survivorship guideline does not cite studies that demonstrate the effectiveness of bioimpedance spectroscopy as a screening tool.

Data is limited from comparative clinical trials which demonstrate an impact on net health outcomes. Clinical definitions and measurements of lymphedema are inconsistent between studies. Further study of bioimpedance spectroscopy as a tool for the diagnosis and treatment of early, subclinical lymphedema continues, but based on current evidence, the use of bioimpedance spectroscopy testing in the diagnosis or management of individuals with known or suspected lymphedema is considered investigational.

Background/Overview

Lymphedema is swelling from fluid build-up caused by improper functioning of the lymphatic system. Symptoms of lymphedema include arm swelling, heaviness, chest/breast swelling, tightness, firmness, pain, numbness, stiffness or impaired limb mobility. There are two types of lymphedema: primary lymphedema which occurs in those who have a congenital abnormality or dysfunction of their lymphatic system, and secondary lymphedema which is an acquired condition caused by a disruption or obstruction of the normal lymphatic system. Individuals with breast cancer are at risk for the development of arm lymphedema. Axillary lymph node sampling compromises lymphatic drainage and lymphatic function can be further compromised by radiation delivered to the lymph node beds. Secondary lymphedema can develop days or years after treatment. Most lymphedema occurs within 3 years of surgery and is associated with discomfort, heaviness, functional limitations and risk of infection. Early lymphedema can be difficult to diagnose. Various methods can be used for evaluating limb volume including water displacement, circumferential measurement, infrared perometry and bioelectrical impedance.

Measurement of limb volume with water displacement requires the individual to submerge the affected limb into a cylinder filled with a known volume of water. The amount of water that is displaced can be weighed or the volume measured. Water displacement is a reliable method to measure limb volume, but it can be cumbersome and difficult to perform in the physician's office. It cannot be used for those individuals with open wounds or sores.

Circumferential measurement of limb volume involves the use of a measuring tape to measure limb circumference at various anatomical landmarks or marked distances from the fingertips or toes. A hindrance to circumferential measurement is that individuals must remove the clothing over the affected limb. There is also concern about the reliability of the measurements. Different individuals measuring the limbs may hold the tape measure tightly or loosely around the limb causing a variation in the measurements.

Infrared perometry uses infrared light to measure the limb volume. The affected limb is placed in a frame and the perometer scans the limb taking measurements at different segments. The limb volume is then calculated by a special computer program. Perometry is a quick method and it does not touch the skin so it can be used for individuals with sensitive or broken skin. Clinical application may be limited by the fact that the equipment is not portable and requires individuals to come into a clinic or facility for limb measurement.

Bioelectrical impedance involves the response of a living organism to a mild electrical current. Skin electrodes are used to pass a small alternating current through a limb and measure the opposition (impedance) to the flow of the current. The measure of the body's resistance to the current can be converted into measurements such as fluid levels. Bioimpedance spectroscopy is a direct measurement of extracellular fluid volume. The device is used to detect extracellular fluid in an individual's limb and is being studied as a tool to detect early signs of subclinical lymphedema.

Definitions

Lymphedema: A condition in which extra lymph fluid builds up in tissues and causes swelling. It may occur in an arm or leg if lymph vessels are blocked, damaged, or removed by surgery.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When services are Investigational and Not Medically Necessary:
When the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

CPT

93702	Bioimpedance spectroscopy (BIS), extracellular fluid analysis for lymphedema assessment(s)

ICD-10 Diagnosis

	All diagnoses

References

Peer Reviewed Publications:

1. Bar Ad V, Cheville A, Solin LJ, et al. Time course of mild arm lymphedema after breast conservation treatment for early-stage breast cancer. Int J Radiat Oncol Biol Phys. 2010; 76(1):85-90.
2. Barrio AV, Eaton A, Frazier TG. A prospective validation study of bioimpedance with volume displacement in early-stage breast cancer patients at risk for lymphedema. Ann Surg Oncol. 2015; 22 Suppl 3:370-375.
3. Borman P, Yaman A, Doğan L, et al. The comparative frequency of breast cancer-related lymphedema determined by bioimpedance spectroscopy and circumferential measurements. European journal of breast health. 2022; 18(2):148-154.
4. Bundred N, Foden P, Todd C, et al. Increases in arm volume predict lymphoedema and quality of life deficits after axillary surgery: a prospective cohort study. Br J Cancer. 2020; 123(1):17-25.
5. Cavezzi A, Urso SU, Paccasassi S, et al. Bioimpedance spectroscopy and volumetry in the immediate/short-term monitoring of intensive complex decongestive treatment of lymphedema. Phlebology. 2020; 35(9):715-723.
6. Coroneos CJ, Wong FC, DeSnyder SM, et al. Correlation of L-Dex bioimpedance spectroscopy with limb volume and lymphatic function in lymphedema. Lymphat Res Biol. 2019; 17(3):301-307.
7. Czerniec SA, Ward LC, Lee MJ, et al. Segmental measurement of breast cancer-related arm lymphoedema using perometry and bioimpedance spectroscopy. Support Care Cancer. 2011; 19(5):703-710.
8. Czerniec SA, Ward LC, Refshauge KM, et al. Assessment of breast cancer-related arm lymphedema--comparison of physical measurement methods and self-report. Cancer Invest. 2010; 28(1):54-62.
9. Erdogan Iyigun Z, Selamoglu D, Alco G, et al. Bioelectrical impedance for detecting and monitoring lymphedema in patients with breast cancer. Preliminary results of the Florence Nightingale breast study group. Lymphat Res Biol. 2015; 13(1):40-45.
10. Forte AJ, Huayllani MT, Boczar D, et al. Bioimpedance spectroscopy for assessment of breast cancer-related lymphedema: a systematic review. Plast Surg Nurs. 2020; 40(2):86-90.
11. Forte AJ, Huayllani MT, Boczar D, et al. Use of bioimpedance spectroscopy for prospective surveillance and early diagnosis of breast cancer-related lymphedema. Breast Dis. 2021; 40(2):85-93.
12. Fu MR, Cleland CM, Guth AA, et al. L-dex ratio in detecting breast cancer-related lymphedema: reliability, sensitivity, and specificity. Lymphology. 2013; 46(2):85-96.
13. Hayes S, Janda M, Cornish B, et al. Lymphedema secondary to breast cancer: how choice of measure influences diagnosis, prevalence, and identifiable risk factors. Lymphology. 2008; 41(1):18-28.
14. Jain MS, Danoff JV, Paul SM. Correlation between bioelectrical spectroscopy and perometry in assessment of upper extremity swelling. Lymphology. 2010; 43(2):85-94.
15. Keeley V. The early detection of breast cancer treatment-related lymphedema of the arm. Lymphat Res Biol. 2021; 19(1):51-55.
16. Ridner SH, Dietrich MS, Boyages J, et al. A comparison of bioimpedance spectroscopy or tape measure triggered compression intervention in chronic breast cancer lymphedema prevention. Lymphat Res Biol. 2022: 20(6):618-628.
17. Ridner SH, Dietrich MS, Cowher MS, et al. A randomized trial evaluating bioimpedance spectroscopy versus tape measurement for the prevention of lymphedema following treatment for breast cancer: Interim Analysis. Ann Surg Oncol. 2019; 26(10):3250-3259.
18. Ridner SH, Dietrich MS, Deng J, et al. Bioelectrical impedance for detecting upper limb lymphedema in nonlaboratory settings. Lymphat Res Biol. 2009; 7(1):11-15.
19. Shah C, Zambelli-Weiner A, Delgado N, et al. The impact of monitoring techniques on progression to chronic breast cancer-related lymphedema: a meta-analysis comparing bioimpedance spectroscopy versus circumferential measurements. Breast Cancer Res Treat. 2021; 185(3):709-740.
20. Spitz JA, Chao AH, Peterson DM, et al. Bioimpedance spectroscopy is not associated with a clinical diagnosis of breast cancer-related lymphedema. Lymphology. 2019; 52(3):134-142.
21. Stout Gergich NL, Pfalzer LA, McGarvey C, et al. Preoperative assessment enables the early diagnosis and successful treatment of lymphedema. Cancer. 2008; 112(12):2809-2819.
22. Whitworth P, Vicini F, Valente SA, et al. Reducing rates of chronic breast cancer-related lymphedema with screening and early intervention: an update of recent data. Journal of cancer survivorship : research and practice, 2022.

Government Agency, Medical Society, and Other Authoritative Publications:

1. NCCN Clinical Practice Guidelines in Oncology®. © 2023 National Comprehensive Cancer Network, Inc. For additional

information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on April 13, 2023.
- Breast Cancer (V.4.2023). Revised March 23, 2023.
- Survivorship (V1.2023). Revised March 24, 2023.

2. U.S. Food and Drug Administration 510(k) Premarket Notification Database. SOZO. No. K180126. Rockville, MD: FDA. April 16, 2018. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf18/K180126.pdf, Accessed on April 13, 2023.

Websites for Additional Information

1. National Cancer Institute (NCI). Available at: http://www.cancer.gov/. Accessed on April 13, 2023.

Index

Document History

Status	Date	Action
	07/20/2023	Updated Rationale and References sections.
Reviewed	05/11/2023	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Rationale and References sections.
Reviewed	05/12/2022	MPTAC review. Updated Rationale and References sections.
Reviewed	02/17/2022	MPTAC review. Updated Rationale, References, and Index sections.
Reviewed	02/11/2021	MPTAC review. Updated Rationale and References sections.
Reviewed	02/20/2020	MPTAC review. Updated Rationale, References, and Index sections.
Reviewed	03/21/2019	MPTAC review.
Reviewed	03/20/2019	Hematology/Oncology Subcommittee Review. Updated References section.
Reviewed	05/03/2018	MPTAC review.
Reviewed	05/02/2018	Hematology/Oncology Subcommittee Review. The document header wording updated from “Current Effective Date” to “Publish Date.” Updated Rationale and References sections.
Reviewed	05/04/2017	MPTAC review.
Reviewed	05/03/2017	Hematology/Oncology Subcommittee Review. Updated Rationale and References sections.
Reviewed	05/05/2016	MPTAC review.
Reviewed	05/04/2016	Hematology/Oncology Subcommittee Review. Updated Rationale and References sections. Removed ICD-9 codes from Coding section.
Reviewed	05/07/2015	MPTAC review.
Reviewed	05/06/2015	Hematology/Oncology Subcommittee Review. Updated Rationale and References.
	01/01/2015	Updated Coding section with 01/01/2015 CPT changes; removed code 0239T deleted 12/31/2014.
Reviewed	05/15/2014	MPTAC review.
Reviewed	05/14/2014	Hematology/Oncology Subcommittee Review. Updated Rationale and References.
Reviewed	05/09/2013	MPTAC review.
Reviewed	05/08/2013	Hematology/Oncology Subcommittee Review. No change to Position Statement.
Revised	05/10/2012	MPTAC review.
Revised	05/09/2012	Hematology/Oncology Subcommittee Review. Clarification to Position Statement. Updated Rationale, Background/Overview, and References.
Reviewed	08/18/2011	MPTAC review. Updated Rationale and References.
New	08/19/2010	MPTAC review. Initial document development. Coding section includes CPT changes effective 01/01/2011.

Applicable to Commercial HMO members in California: When a medical policy states a procedure or treatment is investigational, PMGs should not approve or deny the request. Instead, please fax the request to Anthem Blue Cross Grievance and Appeals at fax # 818-234-2767 or 818-234-3824. For questions, call G&A at 1-800-365-0609 and ask to speak with the Investigational Review Nurse.

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.